Thesis Presented for the Degree of

DOCTOR OF PHILOSOPHY

In the Faculty of Humanities

Euphoria in Multiple Sclerosis: An Investigation of Constructs and Symptoms

Amy Duncan

NRTAMY001

Department of Psychology

UNIVERSITY OF CAPE TOWN

May 2014

Declaration

I hereby declare that this submission is my own work, both in concept and execution, and that to the best of my knowledge and belief it contains no material written by another person nor material that has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledgement has been made in the text.

Amy Duncan Date _____

Style of dissertation

This dissertation has been written in accordance with the style and referencing guidelines of the American Psychological Association (APA), set out in the *APA Publication Manual* (6th ed.).

Acknowledgements

I would like to extend a very sincere thank you to my supervisors, Prof Mark Solms and Dr Susan Malcolm-Smith, for their invaluable input and support throughout this dissertation, but particularly in the final months and weeks.

To Non Smit, the chairperson of Multiple Sclerosis South Africa, I send my humble and most sincere thanks. Without her incredible support, I would not have managed to recruit more than approximately 25 multiple sclerosis participants. I am forever in her debt.

I'd like to thank the various neurologists, neurosurgeons, neuropsychologists, and other medical practitioners, and in particular Dr Ozayr Ameen, Dr Bridget Hodkinson, and Dr Sharon Truter, for their support in terms of the identification and recruitment of both multiple sclerosis and control group patients.

To Dr Pedro Wolf, I send a big thank you for his great knowledge and appreciation of all things statistical, and for his enthusiasm to assist in developing the most appropriate plan for analysis of the data of this study.

I'd like to thank each and every participant of this study, who gave of their time, their personal stories, and in particular their energy. Having learned a considerable amount about multiple sclerosis and the other conditions involved in this research, I have the utmost respect for those who persevered in the face of fatigue and who still had a smile at the end of their interview.

To my family, and in particular my mother, Rosemary, and my husband, Craig, I thank you for reading my endless drafts, and for putting up with and supporting me during long hours of writing up. I'd also like to thank my husband for helping me plan the most incredible wedding during the increasingly stressful final year of my dissertation.

Finally, I'd like to thank both the AW Mellon Foundation and the National Research Foundation for their generous support throughout the three years of this degree. Without their backing, this degree would not have been possible.

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List of Abbreviations

AI	Awareness Interview
AIDS	Acquired Immune Deficiency Syndrome
ANCOVA	Analysis of Covariance
APA	American Psychological Association
ApBat	Aprosodia Battery
BDI	Beck Depression Inventory
BDI-FS	Beck Depression Inventory-Fast Screen
BNT-SF	Boston Naming Test-Short Form
BVMT-R	Brief Visuospatial Memory Test-Revised
CA	Cube Analysis
CCST	California Card Sorting Test
CNS	Central nervous system
COWAT	Controlled Oral Word Association Test
CRJRF	Comparative Risk Judgement Rating Forms
CWIT	Colour Word Interference Test
CWQ	Cottrell and Wilson (1926) Questionnaire
D-KEFS	Delis-Kaplan Executive Function System
DST	D-KEFS Sorting Test
EDSS	Expanded Disability Status Scale
GSH	Groote Schuur Hospital
HC	Healthy control
HIV	Human Immunodeficiency Virus
ICC	Intraclass correlation coefficient
IQ	Intelligence quotient
ISS	Internal State Scale
JLO	Judgement of Line Orientation
LOT-R	Life Orientation Test-Revised
MACFIMS	Minimal Assessment of Cognitive Function In MS
MG	Myasthenia gravis
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MSSA	Multiple sclerosis South Africa
MVA	Motor vehicle accident

NPI	Neuropsychiatric Inventory
NP-SLE	Neuropsychiatric systemic lupus erythematosus
OPS	Optimism and Pessimism Scale
OPT	Optimistic
PAS	Physical Ability Scale
PANAS	Positive And Negative Affect Schedule
PASAT	Paced Auditory Serial Addition Task
PCRS	Patient Competency Rating Scale
POS	Positive
PPMS	Primary progressive multiple sclerosis
RAVLT	Rey Auditory Verbal Learning Test
RH	Right hemisphere/hemispheric
ROCF	Rey-Osterrieth Complex Figure
RPMS	Relapsing-progressive multiple sclerosis
RRMS	Relapsing-remitting multiple sclerosis
SA	South Africa(n)
SD	Standard deviation
SF-36	Medical Outcomes Study 36-Item Short-Form Health Survey
SLE	Systemic lupus erythematosus
SPMS	Secondary progressive multiple sclerosis
SPSS	Statistical Package for the Social Sciences
TBH	Tygerberg Hospital
TBI	Traumatic brain injury
UCT	University of Cape Town
WAB	Western Aphasia Battery
WC	Western Cape
WM	Working Memory

Abstract

In multiple sclerosis (MS), some patients are said to present with unawareness of deficit, and positive mood and optimism that is out of place or incongruous given the patient's circumstances. The history of these symptoms, collectively known as euphoria, however, is characterised by marked inconsistencies regarding a number of aspects of these symptoms. This research attempted to investigate both the constructs, and the symptoms themselves, with the aim of better defining and broadening our understanding of euphoria. Results revealed that a change in the definition of euphoria appears to have occurred since the concept was introduced by Cottrell and Wilson. Different operational definitions appear to be partly responsible for the very different incidence rates reported throughout the literature. Instead of the classical three types of euphoria identified by the classical authors, or the single type utilised in the contemporary literature, the current research revealed two types of euphoria in MS (viz. positivity and unawareness). Positivity appears to be a subjective mood/outlook experienced by the patient and not an outward façade projected by the euphoric individual, and was defined in fairly subtle terms. Unawareness appears to relate to a number of domains (including physical, cognitive and mood or behavioural deficits), and was measured via participant/informant discrepancies on self-report questionnaires. Both positivity and unawareness were represented on a continuum and appeared to have different demographic, disease and cognitive correlates. Positivity was significantly predicted by a medical history of conditions that can affect neuropsychological functioning. Unawareness of physical deficits was associated with a female gender, a younger age, a lower income, relapsing-remitting course, a current disease state of relapse or exacerbation, a shorter disease duration, but a greater disease severity in terms of physical disability. Severity of the disease and the cognitive composite representing cognitive functions sub-served by the orbitobasal frontal cortex were also significant individual predictors of unawareness of physical deficits. Visuospatial ability significantly predicted unawareness of cognitive deficits. No demographic, disease or cognitive correlates of unawareness of mood or behavioural deficits were identified. Finally, no indisputable single cause underlying the two types of euphoria in MS identified by this research was isolated by the exploratory investigations undertaken; however interesting preliminary findings that may tentatively implicate executive dysfunction as well as, possibly, immunological disease processes in the etiology of euphoria in MS were revealed. These results have broadened our understanding of euphoria in MS and may shape both the research and clinical work with euphoric patients going forward.

Introduction

Positive mood and optimism as to the future and recovery that is incongruous with a patient's circumstances, as well as unawareness of increasing difficulties or impairment are symptoms (collectively known as euphoria) that occur within a sub-group of individuals with multiple sclerosis (MS). A wealth of literature regarding the historical development of the constructs relating to these symptoms is available within this body of research (Finger, 1998), but this brings with it an extensive array of inconsistencies, regarding the definition of these symptoms, which types constitute euphoria, the incidence with which they occur, which MS patients might be expected to present with these symptoms, and the cause underlying the symptoms.

A re-investigation of each of the constructs that underpin these symptoms is, therefore, of value, as without clear and consistent definition of the constructs, it is not possible to generate reliable knowledge about these symptoms. Following on from this, an investigation of the symptoms themselves, improved by a better understanding of their underlying constructs, may enrich our understanding of euphoria and enable us to better predict at what stage, and with which disease and/or cognitive parameters, these symptoms are likely to present.

Although not the focus of this research, euphoric symptoms can also impact significantly on a patient's work and social life, as well as on their family and the social support they are able or willing to provide (Benedict et al., 2000; Clarke, Lovegrove, Williams, & Machperson, 2000; Minden, 2000). Conversely, the identification, and direct treatment and management of these symptoms, as well as of being cognisant of them when treating the patient's disease in general, can improve the quality of life both for these patients and their loved-ones, as well as the quality of care received by these patients (Minden, 2000; Rabins et al., 1986). Even if treatment is not pursued, family members can benefit greatly simply by understanding that such symptoms (i.e. euphoric mood, optimism regarding a recovery that will probably not take place, and unawareness of increasing impairment) are the result of an underlying disease process and not due to the patient being stubborn, unrealistic, or unhelpful, and this can vastly improve their quality of life and allow them to better provide and care for their loved-one (Rabins et al., 1986). Thus, a potential application of an investigation of euphoria (i.e. unawareness of deficit and positive mood and optimism that is out of place) may be that of being better able to identify and treat such patients.

Literature Review

In order to contextualise this research, a review of the relevant literature follows. This provides an overview of (a) the definitions of and theory in which the individual symptoms of positive mood, unawareness of deficit and optimism (collectively known within the MS literature as euphoria) are grounded; (b) the disease of MS; and (c) what is known about these symptoms within MS. A thorough understanding of the symptoms of positive mood, unawareness of deficit and optimism, as well as the historical development of the description of these euphoric symptoms within MS, allows for a specific examination of the constructs underpinning them, and a more in-depth exploration of ideas concerning their definition and number of types. It is, furthermore, important in the investigation and broadening of our knowledge of the euphoric symptoms themselves. Additionally, an understanding of the disease in which they commonly occur can assist us in better understanding their cause.

Euphoric symptoms: positive mood, unawareness of deficit and optimism

As noted above, the symptoms of positive mood, unawareness of deficit and optimism constituted the central focus of this research. A review of the literature most relevant to the definitions, descriptions and underlying mechanisms of each of these phenomena, in general, is presented below.

Positive mood. Even though definitions of euphoria in MS vary, what is clear is that euphoria is distinct from a number of other, similar appearing, symptoms of mood and affect. For example, euphoria (i.e. positive mood) should not be confused with hypomania or mania. According to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (American Psychiatric Association, 2013), a manic episode is characterised by elevated or irritable mood and increased energy or goal-directed activity, that persists for the period of at least one week, and is accompanied by three or more of the following symptoms: (a) exaggerated self-esteem or grandiosity, (b) less need for sleep, (c) racing thoughts, (d) a need to keep talking, (e) distractibility, (f) an increase in goal-directed activity or psychomotor agitation, and (g) an increased and extreme involvement in activities that may have harmful consequences. A hypomanic episode is defined by the same criteria as a manic episode, but lasts for a shorter period of time (it needs to have been present for at least four consecutive days; American Psychiatric Association, 2013). Euphoria is also different from pathological laughing, which is defined as brief, uncontrollable expressions of intense affect (i.e. laughing or crying) that may be congruent or incongruent with the underlying feelings of the patient as

well as the context that appeared to trigger them, and that do not produce a change in the mood of the patient, but are the result of neurological involvement (Wortzel, Oster, Anderson, & Arciniegas, 2008). Emotional lability and emotional incontinence are also different: The former refers to rapid mood swings, while the latter involves exaggerated expressions of emotion that are out of proportion to the situation (Harel, Barak, & Achiron, 2007). In contrast, euphoric mood, in terms of a lay understanding, is defined as "a feeling of excited happiness" by the South African Student's Dictionary (1999), "a feeling of intense happiness" by The Oxford Concise Dictionary (1999), and as "a feeling of extreme happiness and wellbeing" by the Chambers Concise Dictionary (2004). The definitions of euphoria in MS and the discrepancies between them will be addressed in much more depth later in this section.

An issue that has received greater attention, than that of a generally accepted definition of euphoria, is that of the neuroanatomical correlates of positive mood. While in MS, the cause of euphoric mood largely remains unknown, in terms of general mood, for many years, the right hemisphere (RH) has been considered to be responsible for the processing of emotion, while the left hemisphere was considered to be more analytical, being responsible for particular cognitive processes. Cortical processing of emotion was, thus, thought to be lateralised to the RH and this was known as the RH hypothesis (Borod, 1992; Borod, Bloom, Brickman, Nakhutina, & Curko, 2002; Tondowski, Kovacs, Morin, & Turnbull, 2007). Evidence for this hypothesis came from research which found that RH patients performed poorly with regard to facial affect recognition (Borod et al., 2002), and processing of the emotional prosody of speech (Borod et al., 2002; Kucharska-Pietura, Phillips, Gernand, & David, 2003; Ross & Monnot, 2008).

This hypothesis, however, does not present an explanation for an increase in positive or negative mood following unilateral brain damage, and, in 1912, Babinski noted that euphoria, as opposed to depressed mood change, could occur with damage to the RH (Starkstein & Robinson, 1989). This eventually led to the valence hypothesis which, in contrast to the RH hypothesis, stated that both hemispheres are responsible for emotional processing, but that they process it in different ways. While the dominant (left) hemisphere was specialised for the expression of positive emotion, the non-dominant (right) hemisphere was responsible for the expression of negative emotion (Borod, 1992; Borod et al., 2002; Silberman & Weingartner, 1986). Thus, damage to, or inactivation of, one side allowed the other to triumph and was said to result in "euphoric-maniacal" mood change with involvement of the RH and "depressive-catastrophic" reactions with involvement of the left (Gainotti, 1972, p. 41). These ideas persisted for many years. For example, Rowe (1937)

found that complete removal of the RH was linked to an increase in positive mood. Sackeim et al. (1982) reported on three studies that found right-sided damage to be associated with euphoric mood change. And, even as late as 1990, Starkstein and colleagues published a study on eight patients who all demonstrated euphoric and/or manic symptoms following right sided brain injury.

More recently, however, the valence hypotheses has been replaced by the approach-withdrawal hypothesis, and Davidson, Ekman, Saron, Senulis, and Friesen (1990) hypothesise that the left hemisphere activates an "approach" system, which can result in positive emotion, while the RH activates a "withdrawal" system, which can result in negative emotions. Therefore, rather than focusing on mood, they focus on systems of behaviour that may result in particular mood states. Furthermore, instead of the more general hypotheses of the past, they associate the approach-withdrawal systems with the anterior cortical regions of both the left and right hemispheres (Davidson et al., 1990). This may account for increases in positive mood which have been demonstrated in a number of other patient groups, including that of Alzheimer's disease and frontotemporal dementias (Bozeat, Gregory, Ralph, & Hodges, 2000; Cummings et al., 1994), neurosyphilis (Roberts & Emsley, 1992), frontal meningioma (Avery, 1971), and, perhaps, MS.

Determining the causes or underlying mechanisms of positive emotion is important in better understanding the symptom of euphoria in MS; and in addition to the neuroanatomical correlates, there may be relevant aspects related to immunological processes. We know that positive affect can improve our immune functioning and general health (Barak, 2006; Dockray & Steptoe, 2010; Stone, Cox, Valdimarsdottir, Jandorf, & Neale, 1987), while negative affect can have a detrimental effect (Kemeny et al., 1995; Stone et al., 1987). But, our immune systems can also influence our emotions, and this phenomenon has been particularly well researched within the depression literature (see, e.g., Capuron et al., 2001; Harrison et al., 2009; Pollak & Yirmiya, 2002). A dysregulation of fatty acids, an immune modulated process, has also been implicated in mania (Horrobin & Bennett, 1999). In addition, manic and euthymic bipolar patients have shown increased levels of proinflammatory cytokines (another immunological marker) compared with healthy controls (HC; Brietzke et al., 2009). Immunological correlates have been implicated in the study of positive mood in general, and may, thus, also be relevant in our understanding of euphoria in MS, particularly given that MS is an auto-immune disease.

Unawareness of deficit. Originally described in 1912 by Babinski to refer to a very specific unawareness of left sided paraplegia following a RH stroke (Amador, Strauss, Yale, & Gorman, 1991; Hartman-Maeir, Soroker, & Katz, 2001), the term anosognosia has been broadened and is now often used to denote other forms of unawareness (Jenkinson, Preston, & Ellis, 2011). It has, thus, been demonstrated in a variety of patient groups other than only patients with RH damage. These include Alzheimer's disease and other dementias such as Huntington's disease (Flashman, 2002; Seltzer, Vasterling, Yoder, & Thompson, 1997), cortical blindness as in the case of Anton's syndrome (Goldenberg, Müllbacher, & Nowak, 1995), schizophrenia (Amador et al., 1991), bipolar mood disorder, obsessive-compulsive disorder, traumatic brain injury (TBI; Flashman, 2002; Toglia & Kirk, 2000) and in patients with MS (Cottrell & Wilson, 1926; Finger, 1998). In Alzheimer's disease an unawareness of memory and other cognitive deficits is seen (Barrett, Eslinger, Ballentine, & Heilman, 2005; Seltzer et al., 1997; Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996). Barrett et al. (2005) refer to this as "cognitive anosognosia". Anosognosia in schizophrenia is more broad and refers to an unawareness of the illness and its symptoms (Amador et al., 1991), and anosognosia in Huntington's disease and TBI can often relate to an unawareness of physical, cognitive and emotional or behavioural deficits (Flashman, 2002; Toglia & Kirk, 2000). Therefore, anosognosia no longer refers purely to unawareness of a physical deficit, and there is a broad array of symptom domains about which various patient groups can be unaware. Defining the use of the term in research is therefore of particular importance as it may present differently, and be brought about by different underlying mechanisms (Amador et al., 1991; Jenkinson et al., 2011).

Unawareness in MS, however, has historically been circumscribed to the physical domain, and descriptions appear similar in nature to that of anosognosia for hemiplegia. For example, Surridge's (1969) description of the reduction in intensity of euphoric MS patients' self-reported positive mood upon confrontation with reality will be described in a later sub-section; but this appears similar to the distinction between explicit and implicit knowledge of deficit which can be revealed in an anosognosic (for hemiplegia) patient during confrontation with the reality of their deficits (Turnbull, Jones, & Reed-Screen, 2002). Furthermore, hemiplegic patients often reveal delusional ideas regarding their paralysed limb and may insist, for example, that it belongs to someone else (Amador et al., 1991), or that it is "just tired because I was playing tennis so much this morning" (Turnbull et al., 2002, p. 69). For these patients, the new reality that is created almost always appears more positive than the patients' actual reality at the time (Fotopoulou, Solms, & Turnbull, 2004). This may lead one to think that these patients are unduly happy, which may be similar to the presentation of the

MS patient. However, unawareness in MS may well be a different type of unawareness to that of anosognosia for hemiplegia, and not at all governed by damage to the RH, and although described using the same terminology may represent a very different construct.

Anosognosia for hemiplegia typically occurs following damage to the RH, and frontoparietal cortical regions, and basal ganglia and thalamic subcortical structures are often implicated (Jenkinson et al., 2011; Pia, Neppi-Modona, Ricci, & Berti, 2004). However, in terms of the other types of anosognosia discussed at the beginning of this sub-section, such as unawareness of cognitive or mood and behavioual changes, Flashman (2002), whose ideas were later supported by the findings of Sherman, Rapport and Ryan (2008), noted that there does not appear to be a single mechanism underlying all types of unawareness. Underlying mechanisms of unawareness may, therefore, be domain specific with the cause of unawareness of physical deficit being quite different from that of the cause underlying unawareness of cognitive deficits. However, Flashman (2002) did state that there is evidence, from neuropsychological testing, of frontal and parietal involvement in unawareness across a number of patient groups. In contrast to mood (addressed above) and optimism (to follow), no research could be found on any immunological correlates of unawareness. The information presented above, however, is important in terms of gaining a deeper understanding of unawareness in general, in order to be better able to understand unawareness in MS.

Optimism. Optimism that is out of place to the patient's circumstances is a symptom that has also been described in MS patients (Cottrell & Wilson, 1926; Finger, 1998). However, while unawareness, for example, has been researched in other patient groups, general research on optimism appears most often to be conducted in non-neurological populations (Goodin & Bulls, 2013). Thus, while dispositional optimism, including more transient state optimism influenced by environmental factors, or more stable trait optimism reflective of one's general outlook (Burke, Joyner, Czech, & Wilson, 2000) may be considered abnormal within MS patients, it is often only unrealistic optimism which is considered to be abnormal and harmful in the general literature. Unrealistic optimism, defined as an individual's tendency to underestimate his/her chances of experiencing negative events and to overestimate his/her chances of experiencing positive events in relation to other people in similar circumstances (Clarke et al., 2000; McKenna, 1993; Sparks, Shepherd, Wieringa, & Zimmermanns, 1995), can have a negative impact, particularly on one's health. For example, Clarke et al. (2000) found both men and women to have unrealistic optimism regarding their risk of developing cancer which impacted on cancer screening behaviour.

Sparks et al. (1995) found that people were unrealistically optimistic about the healthiness of their diets and of their risk for developing diseases related to poor diet. Thus, in these studies, unrealistic optimism resulted in harmful behaviours and ideas that prevented the participants from taking protective actions that would benefit their health. But, these were healthy individuals who were deemed relatively entitled to experience optimism. Thus, optimism at less extreme levels amongst MS patients may be considered to be just as abnormal with potentially detrimental effects as unrealistic optimism is amongst the healthy population.

In connecting this symptom with the others reviewed above, little could be found relating unrealistic optimism with euphoric mood, except for a possible case for mild hypoxia (see Gilbey et al., 2010). Unrealistic optimism does, however, appear to be linked somehow with anosognosia for hemiplegia, as anosognosic patients often over-emphasise their abilities, or are overly optimistic about their condition (Turnbull, Evans, & Owen, 2005). In addition, vestibular stimulation via left-ear caloric irrigation has been shown to reduce both anosognosia for hemiplegia in RH patients, as well as unrealistic optimism in healthy individuals, although this effect is transient (Cappa, Sterzi, Vallar, & Bisiach, 1987; Tamagni et al., 2010).

Studies of the actual neuroanatomical correlates of general optimism and/or unrealistic optimism are scarce though, and some are confounded by other factors. For example, Sharot, Riccardi, Raio, & Phelps (2007) found enhanced activation in the amygdala and anterior cingulate cortex during a functional magnetic resonance imaging (MRI) study of unrealistic optimism. But, they read their participants descriptions of events such as winning an award or the ending of a romantic relationship and then asked them to remember either the actual experience of this event in the past, or to imagine such an event in the future. Not only are these descriptions not obviously related to optimism or pessimism, but brain areas involved in memory, imagination, and emotion, among countless others, may also be activated in such a paradigm.

In contrast, immunological processes may be an area that could be of relevance in the etiology of optimism, as increased optimism has been related to higher numbers of helper T cells (Segerstrom, Taylor, Kemeny, & Fahey, 1998), which are central to the inflammatory immune response (Boyce, 1998). Thus, again since MS is an auto-immune disease, immunological correlates may be of relevance.

A general introduction to the constructs and symptoms of positive mood, unawareness of deficit and (unrealistic) optimism was presented above. Since a sub-group of patients with MS is known to demonstrate varying combinations of cheerful and positive mood, unawareness of or indifference to their condition, and an optimism regarding the future and

prospects for recovery that is disproportionate to their situation (Cottrell & Wilson, 1926; Finger, 1998), a review of the disease of MS is also important in order to contextualise the possible cause of these symptoms.

Multiple sclerosis

The inflammatory response is the body's natural protective reaction against invading pathogens such as viruses and bacteria (Jones, 2011). However, in autoimmune disease, an abnormal immune response occurs whereby the body's own tissues are mistaken for foreign infectious agents, and instead of attacking an invader, the immune system attacks itself and can result in the injury or destruction of multiple organ systems (Jones, 2011; Wraith, Goldman, & Lambert, 2003). A notable number of auto-immune disorders exist, including systemic lupus erythematosus (SLE), myasthenia gravis (MG) and MS.

MS is a chronic, inflammatory, degenerative disease of the central nervous system (CNS), of unknown etiology (DeSousa, Albert, & Kalman, 2002; Mohr et al., 1999; Savettieri et al., 2004). It results in demyelination and wide-spread lesions, or plaques, which affect the myelin sheath surrounding the axons, resulting in a disruption of nerve conduction (Chalk, 2007; Chiaravalloti & DeLuca, 2008; Mohr et al., 1999). The disease is one of the most common causes of neurological[1] disability in young and middle-aged adults (Chiaravalloti & DeLuca, 2003; Miller & Leary, 2007), usually being diagnosed between the ages of 20 and 40 (Mohr, Hart, & Goldberg, 2003). It affects women twice as often as men (Mohr et al., 1999) and has a prevalence rate of approximately 13 per 100,000 in South Africa (SA; Kurtzke, 2000; Rosati, 2001).

MS is a complicated disease to diagnose. However, a diagnosis of MS, as opposed to possible MS, according to the "McDonald criteria", requires (a) the exclusion of other diseases that may simulate MS, and (b) objective evidence of at least 2 lesions or physical events involving different parts of the CNS that are indicative of MS, which last at least 24 hours each and occur at least 30 days apart, or objective evidence, over the period of one year, of "insidious neurological progression suggestive of MS" (McDonald et al., 2001, p. 124; Polman et al., 2011).

[1] The term "neurological" is used in the MS literature to refer to both spinal, cranial and peripheral nerve involvement (e.g. optic neuritis) as well as brain involvement (e.g. white matter lesion load and/or atrophy). Therefore, in order to avoid confusion within this dissertation, the term "physical" will be used to describe the former and "cerebral" the latter.

Disease courses and/or sub-types. Once diagnosed, the clinical course of MS is variable and difficult to predict. Four clinical courses, or sub-types, are accepted today.

The most common form, relapsing-remitting MS (RRMS) is characterised by clearly defined acute attacks, or relapses, which involve either the appearance of a new symptom or lesion, or the reappearance of a previous symptom or evidence of re-involvement of a previously affected part of the CNS. These attacks may remit with either full recovery or with residual deficit upon recovery. There is a stable course, and a lack of disease progression, between attacks. Primary progressive MS (PPMS) does not present with relapses, and is rather characterised by a gradual, but continuous, progression of disease and disability from onset; either with or without occasional plateaus or remissions. Secondary progressive MS (SPMS) initially follows an RRMS course but is then characterised by progression, either with or without occasional relapses and remissions. Although approximately 85% of patients begin with an RRMS course, many eventually progress to the SPMS sub-type. Finally, relapsing-progressive MS (RPMS) is characterised by progression of disease and disability from onset, with clearly defined acute relapses, either with or without full recovery. Although similar to RRMS, in RPMS the periods between relapses are characterised by disease progression (Jones, 2011; Lublin & Reingold, 1996).

The pathology of multiple sclerosis. Demyelination (i.e. an inflammatory response whereby the body's own immune system attacks the myelin sheath surrounding the axons in the CNS), reactive gliosis (i.e. the formation of hard plaques or lesions at the site of inflammation), and atrophy (i.e. the loss of neurons and the connections between them) have traditionally been viewed as the main disease processes in MS (Jones, 2011; Rich et al., 2008; Schapira et al., 2007), and are routinely detected using conventional MRI techniques, such as T2 weighted images (Polman et al., 2011; Zivadinov & Bakshi, 2004a, 2004b). Demyelination and the destruction of oligodendrocytes (i.e. the brain cells responsible for the production and maintenance of the myelin sheath) result in a lack of neuronal insulation and a disruption of nerve conduction, causing a relapse or exacerbation of symptoms. This impairment in nerve conduction can be caused by either a thinning or complete loss of myelin, or the inflammatory processes associated with MS (Jones, 2011; Schapira et al., 2007). Remyelination, along with a remission of symptoms, occurs up to a point, but repeated attacks, or a progressive disease course, can eventually lead to a cessation of this process, plaques being built around the damaged axons, or the remyelinated areas being re-affected by demyelination (Jones, 2011; Patrikios et al., 2006; Prineas, Barnard, Kwon, Sharer, & Cho, 1993). As the disease advances, cutting, or transection, of axons also occurs, followed by

Wallerian degeneration (i.e. a process occurring after axonal transection resulting in axonal degeneration and loss) and this damage results in atrophy, mainly of the axonal regions (Rich et al., 2008; Schapira et al., 2007; Trapp et al., 1998). Thus, because all of the above disease processes primarily affect the axons, MS has traditionally been viewed as a subcortical, white matter disease (Ge, Law, & Grossman, 2005; Jones, 2011). However, developments in imaging techniques, which reveal more subtle abnormalities (Ge et al., 2005; Lazeron et al., 2000; Rovaris et al., 2005), have identified additional disease processes affecting more than just the axons or subcortical white matter. Processes, such as the cutting or severing of dendrites (i.e. dendritic transection) and apoptosis (i.e. a process of programmed cell death whereby cells either commit suicide upon receiving a signal, or simply do not receive the signal to remain alive) particularly in the cortex (Jones, 2011; Peterson, Bö, Mörk, Chang, & Trapp, 2001), as well as damage to cortical, juxtacortical and deep grey matter structures (Bakshi, Ariyaratana, Benedict, & Jacobs, 2001; De Stefano et al., 2003; Lazeron et al., 2000; Pirko, Lucchinetti, Sriram, & Bakshi, 2007) and subtle damage to normal appearing grey matter (Davies et al., 2004; Oreja-Guevara et al., 2005; Rovaris et al., 2005), have also been demonstrated and reveal a more widespread picture of cerebral involvement. Despite these findings, however, MS predominantly affects the white matter and appears to have a propensity for the spinal cord, brainstem, cerebellum, optic nerve, corpus callosum, periventricular regions, and the white matter of frontoparietal regions (Barnard & Triggs, 1974; Figved et al., 2005; Narayanan et al., 1997; Sperling et al., 2001).

A basic understanding of the immunological disease processes in MS is also important. White blood cells are central to the immune system and consist of B-cells and T-cells. There are various kinds of each, but the helper T-cells are responsible for recognising the foreign (or in the case of MS, mistaken) pathogens and for producing cytokines (Boyce, 1998), and are thus important in the inflammatory response. In MS, due to this response, there is an increase in cytokines, including interferons, tumour necrosis factor and interleukins; and tumour necrosis factor has, in particular, been related to the damage of oligodendrocytes and the myelin sheath, as well as disease exacerbation and progression (Horrobin & Bennett, 1999; Jones, 2011; Sharief & Hentges, 1991). A process affecting the fatty acids in MS patients appears to occur concurrently and the resulting abnormal levels affect not only the immune system, but the neurons directly (Horrobin & Bennett, 1999). Polyunsaturated acids appear to decrease and are replaced by saturated and nonessential fatty acids in the plasma, red blood cells and adipose tissues (Holman, Johnson, & Kokmen, 1989; Horrobin & Bennett, 1999; Nightingale et al., 1990). This leads to a dysregulation of phospholipid-based signal transduction, which results in a break-down of the transmission of

the molecular signals that trigger a particular cell response (Horrobin & Bennett, 1999). As immunological processes have such a fundamental involvement in this disease, it is important to be aware of them and their possible involvement in the symptoms of MS.

The sequelae of multiple sclerosis. Although MS appears to favour particular regions, it can affect any part of the CNS. Thus, it can produce a wide variety of symptoms relating to the domains of physical, cognitive, as well as those of mood, affect and behaviour (Finger, 1998; Jones, 2011). These will each be addressed individually below.

Physical sequelae. Physical impairment is common in MS and damage to the CNS areas involved can result in a wide range of symptoms. Table 1, below, provides a comprehensive list of the physical symptoms of MS.

Table 1

The Physical Sequelae of MS

Domain	Symptom
Visual	Optic neuritis, diplopia, nystagmus, blindness[a]
Auditory	Partial or transient loss of hearing, deafness[b]
Motor	Limb weakness, paraplegia, spasticity, spasms, cramps, facial palsy, loss of dexterity, hyperreflexia[c], seizures[b], dysphagia[b], dysarthria, inability to control breathing[a]
Sensory	Proprioceptive loss, paraesthesias (including pins and needles, buzzing or tingling, electric shock sensations, partial or complete loss of feeling in limbs and/or face)[a], dysthesias, hyperthesias[c], "useless hand syndrome"[b]
Balance and coordination	Ataxia, intention tremors, dysmetria, vertigo, loss of balance[a], telekinetic tremor, dysrhythmia[c]
Autonomic	Hypothermia, paroxysmal atrial fibrillation, orthostatic hypotension, exercise-induced tachycardia, breathlessness[a b]
Bowel, bladder and sexual symptoms	Urinary and faecal urgency, frequency and incontinence, constipation, erectile dysfunction[a]
Other	Fatigue[a], sleep disturbances, pain, headaches[b]

Note. [a] = Jones (2011).
[b] = Schapira et al. (2007).
[c] = Rich et al. (2008).

Cognitive sequelae. Cognitive impairment in MS has been well researched and is said to occur in approximately 45% to 65% of MS patients (Bobholz & Rao, 2003; Rao, 1995; Schulz, Kopp, Kunkel, & Faiss, 2006). It can occur early in the disease along with little or no physical disability (Rovaris et al., 2002; Schulz et al., 2006; Simioni, Ruffieux, Bruggimann, Annoni, & Schluep, 2007) but is more often present, or tends to worsen, with a progressive

course, longer disease duration, and increased physical impairment and cerebral involvement (Beatty, W., Goodkin, Monson, & Beatty, P., 1989; Heaton, Nelson, Thompson, Burks, & Franklin, 1985; Henry & Beatty, 2006). MS patients are also more likely to experience cognitive impairment than healthy controls (Amato, Ponziani, Siracusa, & Sorbi, 2001; Ruggieri et al., 2003), and patients with other non-CNS neurological diseases such as muscular dystrophy (Jambor, 1969; Surridge, 1969). Accordingly, cognitive dysfunction in MS is regarded as being a consequence of cerebral involvement, often of the white matter (Benedict, Carone, & Bakshi, 2004; Benedict, Weinstock-Guttman et al., 2004; Reischies, Baum, Bräu, Hedde, & Schwindt, 1988). In line with this, the domains most commonly affected in MS, in order of most to least frequent, include the following (Amato et al., 2001; Comi et al., 1995; Foong et al., 1997; Ruggieri et al., 2003; Ryan, Clark, Klonoff, Li, & Paty, 1996):

- Attention
- Information processing speed
- Working memory (WM)
- Verbal and visuospatial learning and memory
- Verbal fluency
- Visuospatial processing or perception
- Abstract reasoning
- Problem solving

Left cortical deficits such as aphasias, apraxias, and agnosias (DeSousa et al., 2002; Jeffery, Absher, Pfeiffer, & Jackson, 2000; Kujala, Portin, & Ruutiainen, 1996), as well as RH cortical deficits, such as unilateral spatial neglect (Gilad, Sadeh, Boaz, & Lampl, 2006; Graff-Radford & Rizzo, 1987), and/or difficulties with visuospatial construction (Asghar-Ali, Taber, Hurley, & Hayman, 2004), theory of mind (Banati et al., 2010; Ouellet et al., 2010) and emotion perception (Phillips et al., 2011) have also been noted in MS patients.

Neuropsychiatric sequelae. MS can also be associated with in a number of neuropsychiatric symptoms. Similar to cognitive impairment, the majority of these are considered to result from cerebral involvement (Fermo et al., 2010; Joffe, Lippert, Gray, Sawa, & Horvath, 1987; Minden & Schiffer, 1990; Rabins et al., 1986; Rodgers & Bland, 1996; Schiffer, Wineman, & Weitkamp, 1986). In addition, many can occur both early (Arnett, Barwick, & Beeney, 2008; Fermo et al., 2010) and late (Jannsens et al., 2006;

McIvor, Riklan, & Reznikoff, 1984; Zorzon et al., 2001) in the disease course, either with (Baretz & Stephenson,1981; Figved et al., 2005; Zorzon et al., 2001) or without (Gilchrist & Creed,1994; Zorzon et al., 2001) physical disability, as well as occurring either with (Arnett, Higginson, Voss, Randolph, & Grandey, 2002; Gilchrist & Creed, 1994; Simioni et al., 2007) or without (Korostil & Feinstein, 2007; Krupp, Sliwinski, Masur, Friedberg, & Coyle, 1994) cognitive impairment. Listed from most to least prevalent, the common disorders of mood, affect and behaviour include (Cummings et al., 2006; Jannsens et al., 2006; Joffe et al., 1987, Korostil & Feinstein, 2007; Patten, Svenson, & Metz, 2005; Schiffer et al., 1986; Simioni et al., 2007):

- Depression
- Anxiety
- Bipolar mood disorder
- Affective dysregulation (pseudobulbar palsy, pseudobulbar affect, pathological laughing and crying, emotional lability/incontinence, involuntary emotional expression disorder)
- Psychosis

The final of the most recognised symptoms of mood, affect and behaviour in MS, and the focus of this review, is that of euphoria. In the sections to follow, I shall present a review of the literature regarding these symptoms specifically within MS. Literature regarding the definitions, types of euphoria, and frequencies of those types will be presented first. What is known about the disease and cognitive correlates of the euphoric symptoms will then be presented, followed by literature on the causes of the euphoric symptoms.

Euphoria in Multiple Sclerosis

Since the hallmarks of MS include physical impairments such as motor and sensory abnormalities, visual impairment, bladder dysfunction and debilitating fatigue (Rich et al., 2008; Schapira et al., 2007), one may reasonably anticipate that people suffering from this disease would be likely to become depressed. However, although depression is a common neuropsychiatric symptom of MS, some patients appear cheerful, some optimistic about their recovery, and some unconcerned about their condition, claiming that they feel good (Cottrell & Wilson, 1926; Finger, 1998). This “happy state of mind”, a term coined by J. C. Morris in 1868 (Finger, 1998, p. 249), refers to the euphoria experienced by a subgroup of patients with MS. However, the constructs of these symptoms are not as simple as they may appear, and

the history of research into positive mood, unawareness of deficit and (unrealistic) optimism in MS is fraught with substantially differing ideas concerning their definitions, the rate at which they can be found amongst MS patients, their clinical correlates and their causes.

Definitions, types and incidence rates of euphoria. Before one can investigate something, a thorough understanding of the object of investigation is required. The review below, therefore, focuses on the historical development of the constructs relating to euphoria and the ways in which they have been described and defined.

The definitions and types of euphoria. Accounts of MS can be found dating back to the early 1800's, but most were based on autopsies and described the cerebral pathology of the disease, and, in some cases, its sensory and motor symptoms. From about the 1830's, however, descriptions of the emotional symptoms that accompany this disease began to appear. Before these can be discussed, it must be mentioned that no review of euphoria would be complete without highlighting the confusion between these symptoms and that of emotional lability, pathological laughing and crying and even bipolar mood disorder and mania. The difference between these symptoms was addressed at the beginning of the literature review, but there is often overlap and confusion of these concepts within the MS literature too. Thus, as the constructs are reviewed below, one may notice descriptions relating to these other symptoms being included in some definitions of euphoria and many authors present a picture of euphoria that includes quite clearly erroneous elements. The history presented below, however, focuses as closely as possible only on the elements relating to euphoria and literature on mania, pathological laughing and crying, and emotional lability or incontinence is not presented.

From as early as 1850 Wilhelm Valentiner noted the difficulty in evaluating the disease progression of MS patients who "den[y] their deteriorating condition and clearly overestimate… their abilities" (Finger, 1998, p. 242). William Moxon, in around 1875, echoed these concerns, but added a description of accompanying mood, by stating:

> The patients, who, as a rule, are cheerful and thankful for what is done on their behalf, are apt to declare themselves generally rather better, so that the report of the clinical clerk putting down their answers may read like a statement of continual good progress toward recovery. But the general result has been that, after many months stay in the hospital, the poor people are found to have grown steadily though slowly worse (Finger, 1998, p. 245).

The work of Jean-Martin Charcot, the physician most credited with making the medical community aware of the characteristics of MS, then began to emerge. In a famous quote, he noted that:

> There is marked enfeeblement of the memory; conceptions are formed slowly; the intellectual and emotional faculties are blunted in their totality. The dominant feeling in the patients appears to be a sort of almost stupid indifference in reference to all things. It is not rare to see them give way to foolish laughter for no cause, and sometimes, on the contrary, to melt into tears without reason. Nor is it rare, amid this state of mental depression, to find psychic disorders arise which assume one or other of the classic forms of mental alienation (Charcot, 1877, pp. 194-195).

While one may notice descriptions of pathological laughing and crying in this excerpt, the "stupid indifference" to which Charcot referred is often portrayed as the first description of euphoria (see, e.g., Carone, Benedict, Munschauer, Fishman, & Weinstock-Guttman, 2005; Sherman et al., 2008). Interest into euphoric symptoms then increased and in 1878 Samuel Wilks noted that "patients with MS often seem happy and are much more likely to laugh than cry spontaneously" (Finger, 1998, p. 244). In 1886 Alfred Vulpian observed a "morbid optimism" amongst patients with MS (Surridge, 1969, p. 749), and in 1893 William Gowers reiterated Wilks' notion of cheerful mood and noted, "an undue complacency and contentment, which, under the increasing disability, is distinctly unnatural" (Finger, 1998, p. 245). Gowers also went on to say that although MS patients may not overtly state an improvement in their symptoms, they will exaggerate any remission or cessation of symptoms (Finger, 1998). In 1904, interest into these phenomena continued with a review by Eduard Müller noting that one would be more likely to witness euphoria than depression in MS patients and that these patients often lacked insight into their physical state (Finger, 1998). However, these reports were still largely based on anecdotal case studies.

In the 1920's, these early descriptions were expanded upon and investigated using larger sample sizes. In 1922, Sanger Brown and Thomas Davis conducted a study on the emotional symptoms of MS patients and described their patients as having elevated mood and a tendency to, "not think of their condition as serious, nor… seem deeply concerned about it" (Brown & Davis, 1922, p. 629). They distinguished, however, between a "slight elevation of mood" and the "delusions of grandeur similar to those seen in patients with paresis… generally occur[ing] as a terminal stage [of MS] associated with considerable dementia" (Brown & Davis, 1922, p.630).

In 1926, Samuel Cottrell and Kinnier Wilson specifically studied euphoria amongst 100 patients with MS. They distinguished between three types and thereby provided by far the most comprehensive definition of euphoria. They operationalised them as follows:

(1) *Euphoria sclerotica* related to a state of emotional well-being, and was defined as "the mental state of cheerfulness, happiness, ease... in which the prevailing mood is one of serenity and cheerfulness".

(2) *Eutonia sclerotica* was used in the sense of a feeling of physical well-being, and was defined as feeling "physically well tuned up, [as though] the [patient] 'could do anything'" and where patients "are not conscious of physical disability".

(3) *Spes sclerotica*, by contrast, referred more to a cognitive state, defined as "an optimism as to the future and the prospects of ultimate recovery which is out of place and incongruous" (p. 8).

These constructs were viewed as separate symptoms that could occur independently of one another, and this distinction was maintained for a number of years until the focus of MS research began to shift. The cognitive, rather than affective, sequelae of MS began to receive attention and euphoria was dismissed as unimportant (Surridge, 1969). In addition, Lord Brain, in 1930, emphasised the lack of research on disorders of personality, as well as other psychological and psychiatric symptoms of MS, such as hysteria. As a result, these began to receive greater attention, and the few accounts of euphoria in MS that did surface during this time appeared to reflect this shift. The euphoric patient was, for example, defined as having "an unusually attractive personality" (Langworthy, Kolb, & Androp, 1941, p. 243). Further, euphoria was defined as "the upper end of a continuum, characterized by a mood of optimism and exuberance that may have a hypomanic flavour… in the most severe cases, it may be associated with overt psychotic symptoms such as delusions" (Baretz & Stephenson, 1981, p. 119), and, continuing with this manic reference point, as "a lesser degree of elation which does not impair the patient's judgement" (Ron and Logsdail, 1989, p. 888). These descriptions or definitions reflect ideas of personality disorders as well as of mood disorders such as mania and appear to focus only on positive mood, largely neglecting the ideas of optimism and unawareness of deficit.

A great renewed interest in the affective sequelae of MS returned in the mid to late 1990's and this resulted in a growth of contemporary literature on euphoria. However, the loss of conceptual clarity that occurred during the shift of research focus appears to have endured and few contemporary researchers continue to recognise the distinction between euphoria sclerotica, eutonia sclerotica and spes sclerotica described so clearly by Cottrell and Wilson (1926), an omission that has been noted by others (see, e.g., Rabins, 1990; Sherman

et al., 2008). Instead, there is a marked lack of clarity in the MS literature regarding what constitutes *euphoria* today.

Some appear to amalgamate all three types into a single symptom. This is evidenced by a number of recent reviews on the mood and affective disorders of MS which use all three of Cottrell and Wilson's constructs in one sentence to describe the term *euphoria*. For example, Ghaffar and Feinstein (2007) define euphoria as, "an overly optimistic state of mental and physical well-being in the presence of significant neurologic disability" (p. 280). Although somewhat confused regarding eutonia, Rodgers and Bland (1996) describe euphoria as, "a persistent cheerfulness and optimism about the future despite awareness of disability" (p. 442). And, Minden (2000) even quotes Cottrell and Wilson in his definition of euphoria, but instead of differentiating between the types, states that euphoria is present under all three conditions.

Others appear to have abandoned the ideas of both eutonia and spes sclerotica and describe euphoria in terms of positive mood alone. For example, Kesselring and Klement (2001) describe euphoria as "a type of mood characterised by inappropriate/inadequate serenity (in view of the patients' physical disability)" (p. 182).

Others still appear to acknowledge eutonia sclerotica but dismiss it (along with spes sclerotica) and measure only positive mood. For example, Diaz-Olavarrieta, Cummings, Velazquez, & de al Cadena (1999) define euphoria as an "unusual cheerfulness and lack of concern about disability" (p. 55), but measure it using only the Neuropsychiatric Inventory (NPI; Cummings et al., 1994), which solely asks informants about their loved-one's mood.

Still others appear to acknowledge both euphoria sclerotica and eutonia sclerotica (and at times spes sclerotica), but define and measure them in a way that is no longer the same as the classical descriptions of these phenomena. For example, Feinstein (2007) notes euphoric patients' "fixed state of well-being", their "conviction that all is well and that they will walk again", but goes onto describe this as a "lack of insight" (p.75). This latter description relating to insight may have different connotations to the former descriptions of well-being. Benedict et al. (2005) state that, "there is a sub-group of MS patients who are severely cognitively impaired yet cheery or indifferent to their circumstances, exemplified by the so-called euphoria sclerotica syndrome" (p. 32), substituting cognitive impairment for physical impairment. In addition, Benedict, Priore, Miller, Munschauer, and Jacobs (2001) state that euphoria "may be more accurately construed as a change in trait or character that includes rapid vacillations in mood (including anger, dysphoria, and euphoria), unrealistic optimism, denial, and/or inappropriate social behaviour" (p. 75) but somewhat astonishingly cite both Finger (1998) and Cottrell and Wilson (1926) as references for this statement,

despite a complete lack of mention of mood swings, anger or inappropriate behaviour in relation to euphoria within these articles. The same research group actually refer to the term euphoria sclerotica in a later article and call it "a syndrome characterized by euphoric mood state, social disinhibition, impulsivity, and emotional lability" (sic. Carone et al., 2005, p. 574) and this time, but again without basis, cite Brown and Davis (1922), Cottrell and Wilson (1926) and Surridge (1969) as references for this. They confuse the terminology even further by suggesting that patient/informant discrepancies on cognitive testing and/or tests of personality change could be used as predictors of "euphoric behavioural disinhibition" (Carone et al., 2005, p. 574). Here they are using patient/informant discrepancies as measures of unawareness, but instead of referring to the original domain of physical unawareness, they are referring to unawareness of cognitive and personality domains, thereby muddling the terminology related to eutonia sclerotica or unawareness. They also state that these discrepancies can predict "euphoric behavioural disinhibition". Firstly, this equates "euphoric behavioural disinhibition" with the original euphoria sclerotica, but their term was coined by performing a factor analysis on items of the NPI within a sample of MS patients, which grouped euphoria, disinhibition, agitation and irritability in one factor. This constitutes a different definition of this symptom than that of the original, again highlighting confusion of the terminology. Secondly, this implies that eutonia (unawareness) and euphoria are one and the same thing, which is also a confusion of the original terminology. This group of researchers go onto say that patients with this symptom are characterised as "impatient, inconsiderate, and quarrelsome" which they say "resemble[s] the syndrome as described in the classic literature" for which they again reference the 1998 article by Finger (Fishman, Benedict, Bakshi, Priore, & Weinstock-Guttman, 2004, p. 354). Since the definitions of euphoria within Finger's (1998) review do not include any mention of MS patients being impatient, inconsiderate or quarrelsome, this further highlights confusion of the constructs.

Therefore, not only does the distinction between the three classical euphoric types (in terms of them being regarded as separate and equally important symptoms) appear to have been lost by contemporary literature, but the way in which these symptoms are being described appears to have changed as well.

Another aspect concerning the definition of euphoria warrants discussion: that is whether it is an objective or subjective phenomenon. It has been noted that some euphoric patients appear happy and content when in fact they are subjectively very depressed (Baretz & Stephenson, 1981). Surridge (1969) even noted that euphoric patients may report subjective feelings of positive mood and optimism, but when provoked, or confronted with

reality, these emotions sometimes become less intense or even disappear completely. One of the first accounts of a discrepancy between inner feelings and outward expression of emotion was given by Barbellion in 1919 who, as a sufferer of MS himself, noted that despite an inner feeling of sadness he presented an "unforced and quite natural" picture of "almost constant gaiety" (Finger, 1998, p. 245). This poses a problem as some researchers, particularly the early ones, rely purely on objective observation of the patient's appearance, while others question the patient and rely on their subjective report. Surridge (1969) investigated this conundrum in depth and, remarkably similar to the idea of implicit versus explicit awareness described in relation to anosognosia above (Jenkinson et al., 2011), presented four states of euphoria. In the *mixed state*, patients appeared objectively euphoric, but were subjectively depressed. Those diagnosed with *slight euphoria* were initially euphoric (both objectively and subjectively) when interviewed, but their mood disappeared when confronted with the reality of their condition and it did not return. In *moderate euphoria*, patients were euphoric until confronted or provoked; at which time the euphoric mood disappeared, but then returned when provocation was stopped. Finally, in the *severe euphoria* state, patients were objectively and subjectively euphoric and remained that way even after confronted with their reality.

The incidence of euphoria in MS. Possibly even more controversial than the definitions of these symptoms, are the frequencies with which these symptoms can be found amongst patients with MS. Dating back to 1877, Charcot's famous description of the cognitive and affective sequelae of MS patients referred to "most of the patients" (Charcot, 1877, p. 194); and Paul Hoffman, in 1904, stated that euphoria was a "characteristic feature of the mental state" of MS patients (Surridge, 1969, p. 749). In the 1870's and '80's, Wilk's characterisation of MS patients also applied to "many patients" (Finger, 1998, p. 244), and the accounts of Moxon and Gowers, of the mood and optimism amongst MS patients, were "as a rule" and "especially frequent" (Finger, 1998, p. 245). These early case studies gave the impression that euphoria was the predominant mood state of patients with MS, and although they often gave examples from particular cases, the authors did not readily state the total number of patients on which these assumptions about the frequencies of euphoria were based. The 1920's saw larger sample sizes beginning to be reported, as well as the introduction of tests for syphilis which could mean the exclusion of these patients (who were likely to present with euphoria for non-MS reasons and confound the findings) and, hence, purer samples of patients with only MS (Reiser [1975] as cited in Baretz & Stephenson, 1981; Surridge, 1969). However the earlier suppositions continued to be confirmed. Brown

and Davis (1922), for example, found 71% (10/14) of their MS patients with "mental symptoms" to be euphoric (p. 629); while Cottrell and Wilson (1926) found 63% (63/100) of their MS patients to be euphoric, 84% (84/100) to be eutonic (i.e. to have a sense of physical well-being) and 84% (84/100) to be optimistic about their future. In 1938, in a review of the literature, David Arbuse also emphasised the high rates of euphoria that had been found until that point by stating that, "by far the most constant emotional state is one of euphoria or mild elation… It is present in the great majority of cases" (Finger, 1998, p. 248). By the 1940's the perception remained the same. Orthello Langworthy and colleagues, for example, wrote this of the MS patient's personality: it "is dependent largely upon the euphoric outlook and emotional instability which are so frequently encountered in the disease", and, in their review of clinical notes found at least 26 of 199 (13%) of patients where the euphoria was so marked that a note was specifically made in the medical folder (Langworthy et al., 1941, p. 243). In 1943, Carl Sugar and Raymond Nadell attempted to replicate the earlier findings of Cottrell and Wilson and found euphoria sclerotica in 53.6%, eutonia sclerotica in 50%, and spes sclerotica in 50% of their 28 MS patients (Sugar & Nadell, 1943). Although slightly lower than the original frequencies found by Cottrell and Wilson (1926), they still found high incidences of the euphoric types and maintained it was the prevailing mood state amongst MS patients (Sugar & Nadell, 1943).

In about the 1950's, however, things began to change. Braceland and Giffin, in 1950 for example, reported that euphoria was rare and found it in only in 10% of 75 patients (Pratt, 1951; Rabins, 1990). Thygesen contradicted this in 1953 by reporting that 77% of his 60 patients experienced euphoria (Rabins, 1990). But then Gall and colleagues, in 1958, again only reported four out of 40 patients (10%) as being euphoric (Salguero, Itabashi, & Gutierrez, 1969). Surridge (1969) then found rates of 25.9% (28/108) for euphoria, and 41.6% for eutonia (45/108). Baretz and Stephenson (1981) and Ron and Logsdail (1989) again echoed Braceland, Giffin and Gall et al. and found "elevated mood" and "elation" in only 10% (4/40) and 13.8% (16/116) of their MS patients respectively. But then, Rabins and colleagues measured both euphoria and eutonia and found either one or both of these in 48% (42/87) of their MS sample (Rabins et al., 1986).

Modern rates of euphoria, in contrast, are far less variable and the symptom is considered to be dramatically less common than in the literature described above. In fact the majority of authors report a frequency of between 9% and 13%, even though slightly higher rates have been found by some contemporary researchers.

All of the contemporary studies determined their incidence rates by using the NPI and refer to positive mood or euphoria sclerotica alone. With specific reference to the main

contemporary studies investigating frequency of euphoria in MS, Figved et al. (2005) found euphoria in 4.7% of their sample of 86 MS patients. Diaz-Olavarrieta et al. (1999), found a frequency of 13%, within a sample of 44 MS patients. And, Fishman et al. (2004) found euphoria, in terms of the NPI, to be present in 14.6% (11/75) of MS patients, but considered their euphoria/disinhibition factor, which they demonstrated in only 9% of their sample, to be more representative of euphoria sclerotica.

The correlates and causes of euphoria in MS. The review above focussed largely on the development of the constructs relating to euphoria. While this is important for our understanding of what the concepts of euphoria refer to, the symptoms themselves, as well as their correlates and causes are also of interest.

The correlates of euphoria. Early accounts such as those of Morris and Seguin in the late 1800's, referred to a positive state of mind even after the disease had progressed and the patients were severely disabled (Finger, 1998). This demonstrates that the mood persisted with a longer disease duration, but does not address the issue of when it began. Other early descriptions are equally vague, but information regarding the disease correlates of euphoria can be found from about the 1920's when more scientific investigations began to be conducted. Perhaps the first is that of Cottrell and Wilson (1926) who believed that (a) euphoria sclerotica, eutonia sclerotica and spes sclerotica could occur independently of one other, and (b) the three euphoric constructs could occur independently of the clinical type of MS, disease duration and/or disease severity, with these symptoms often preceding physical symptoms, or occurring early on in the disease course. Later, in the 1940's Sugar and Nadell appear to have agreed with the idea of euphoria occurring early in the disease course as they believed that the longer disease duration of their sample (10.5 years versus 6.6 years in that of Cottrell and Wilson's) accounted for the lower frequencies found within their sample (Sugar & Nadell, 1943). Had they believed that euphoria correlated with advanced disease, they would have expected a higher frequency within their sample. Further, Borberg and Zahle, in 1946, agreed that euphoria could occur early on, but went even further to say that it could change or even disappear as the disease progressed (Finger, 1998).

During this same time, contrasting opinions, however, also existed. For example, in 1924 Claude considered euphoria to be a relatively common feature of advanced MS (Finger, 1998), and Langworthy et al. (1941) and Surridge (1969) noted that it seemed to occur more readily in patients with severe physical disability. Later, Rabins et al. (1986) found it to correlate with a progressive course and greater physical disability.

Disagreement also existed surrounding the cognitive correlates of euphoria. Cottrell and Wilson (1926), for example, believed that the euphoric types did not co-occur with cognitive decline, finding intellectual deterioration in only 2% of their MS sample. Similarly, Sai-Halász, in 1956, only found intellectual deterioration in 10%, but emotional changes in nearly 50% of his MS sample and concluded that the two did not necessarily co-occur (Surridge, 1969). But cognitive impairment was measured as a patient's insight into changes in mood by Cottrell and Wilson (1926) and by the use of the Rorschach test by Sai-Halász (Surridge, 1969), neither of which may be appropriate measures of cognition, particularly (in the case of Cottrell and Wilson [1926]) when one considers that unawareness is a symptom of MS patients.

Meanwhile, during this time, experiments employing better measures of cognition, including tests of memory, logic and mathematics, were being conducted; and Brown and Davis, Runge, Ombredane, as well as Braceland and Giffin all found that euphoria was present predominantly in cognitively impaired MS patients and concluded that it was most likely secondary to cognitive deterioration (Brown & Davis, 1922; Finger, 1998; Surridge, 1969). Here again, however, problems emerge as Ombredane has been criticised for being too willing to link affective and cognitive symptoms, and for possibly overestimating the extent of cognitive impairment in his sample by including fatigue as a cognitive deficit (Finger, 1998).

Later, agreement appears to occur again and Surridge (1969) and Rabins et al. (1986) both found evidence of greater cognitive impairment amongst euphoric as opposed to noneuphoric MS patients. We know that discrepancies between classical and contemporary researchers existed, but it is clear from the above that disagreement regarding the disease and cognitive correlates of euphoria occurred even between classical researchers.

In contrast to a number of the classical investigators, today's authors are not of the opinion that euphoria can occur independently of clinical course or severity, and, also in contrast to classical times, are in general agreement. The majority appear to concur that it correlates with (a) a progressive course (Diaz-Olavarrieta et al., 1999; Fishman et al., 2004), (b) advanced physical disability (DeSousa et al., 2002, Diaz-Olavarrieta et al.,1999), and (c) significant cognitive involvement or dementia (DeSousa et al., 2002; Diaz-Olavarrieta et al.,1999; Fishman et al., 2004), characterised by executive dysfunction (Benedict et al., 2001; Benedict, Carone et al., 2004; Fishman et al., 2004).

The causes of euphoria in MS. While some classical authors, for example Braceland and Giffin, as well as the psychoanalyst Jelliffe, believed that euphoria could be due to

psychological factors, most agreed that these symptoms were the result of organic brain involvement (Brown & Davis, 1922; Cottrell & Wilson, 1926; Langworthy et al., 1941; Rabins et al., 1986; Surridge, 1969). Further evidence for this emerged in the 1950's when researchers began to include control groups. Surridge (1969), for example, found that patients with MS were significantly more likely to be euphoric than patients with muscular dystrophy (a degenerative muscular disease that does not affect the brain).

However, many of the early studies did not have the means to include measures of cerebral involvement, such as lesion load and atrophy, which are popular today, and Cottrell and Wilson (1926) even conceded that "the study of emotions has not advanced far enough to enable any conclusions to be drawn... that are other than purely hypothetical" (p. 28). But this did not stop them from hypothesising. Dercum, in 1912 for example, put forward a rather broad suggestion: that the euphoria in his patient was the result of lesions in both the cortical and subcortical areas of the frontal, temporal and parietal lobes (Salguero et al., 1969). Also early on, Barbu purported meningofibrosis and cortical atrophy as the underlying mechanisms of these types of symptoms (Sugar & Nadell, 1943). Cottrell and Wilson (1926) proposed a disruption or dysfunction of periventricular cortico-thalamic pathways, as well as some sort of invasion of the paleothalamus (which they believed was responsible for emotional expression), perhaps early on by an MS-related toxic process. Langworthy et al. (1941) suggested that euphoria may be the result of an interruption of the subcortical white matter (projection fibres) of the frontal lobes. Later, Rabins et al. (1986) found euphoria to correlate with enlarged ventricles, Reischies et al. (1988) with periventricular and frontal lesions, and Ron and Logsdail (1989) found it to correlate with a greater total lesion load. Lesion load and atrophy were therefore ideas that dominated the recent literature; however there was some disagreement as to the location of these processes.

Although it is now known that manic and euphoric episodes can also result from corticosteroid use (Brown, Khan, & Nejtek, 1999; Patten & Neutel, 2000), euphoria in MS today (as a persisting disorder of mood or affect and not simply a transient state related to treatment) is still found to occur with cerebral, and not spinal cord, involvement (Diaz-Olavarrieta et al., 1999). Therefore, in agreement with classical authors, it is typically regarded as an organic symptom of MS, and not a psychological reaction to the disease (Rodgers & Bland, 1996; Sanfilipo, Benedict, Weinstock-Guttman & Bakshi, 2006), although this assumption has not been proven unequivocally since the cause remains unknown. Modern authors also still report findings regarding both lesions and atrophy; however, instead of differing views regarding the location of these elements, they more often agree that euphoria is correlated with (a) periventricular atrophy and enlarged ventricles (Benedict,

Carone et al., 2004; Diaz-Olavarrieta et al., 1999), and (b) frontotemporal lesion load on MRI (Diaz-Olavarrieta et al., 1999). In addition, due to its correlations with executive dysfunction, some have proposed that euphoria may be due either to a disconnection of the frontal cortex and limbic structures by white matter lesions (Fishman et al., 2004), or to grey matter atrophy of the frontal cortex (Fishman et al., 2004; Sanfilipo et al., 2006).

Rationale, aims and hypotheses

It is clear from the review of the literature presented above that large discrepancies exist in the literature between classical and contemporary researchers concerning the definitions, types, frequencies and correlates and causes of the euphoric symptoms. The main aims of this study were therefore to address these obscurities and investigate the constructs of these symptoms, as well as to investigate the symptoms themselves within an adequate sample of MS participants.

I attempted this by dividing the research into three parts. The first part related to the definitions, types, and frequencies of euphoria, and investigated the constructs of the euphoric types by examining, amongst other things, some of the discrepancies in the literature. The second part aimed to gain a deeper understanding of the euphoric types identified by part one, and investigated the demographic, disease and cognitive correlates of these symptoms. Finally, the third part revolved around a very preliminary investigation of the causes of the euphoric types identified by this research, and comparisons were made between the MS participants and other patient control groups. The rationales, aims and hypotheses for each of these parts are presented below.

Part one. Addressing discrepancies and defining euphoria

Part one was concerned with the investigation of the constructs of the euphoric symptoms (i.e. positive mood, unawareness of deficit and optimism). A thorough investigation of the literature (and its discrepancies) and comparisons between the most popular measures used were conducted in order to examine issues regarding the number of types of euphoria, the definitions of those types, and the frequencies of those types. The rationale, aims and hypotheses related to part one are presented below.

Rationale for part one. The marked differences in definitions, types, and incidence rates of euphoria between the classical and contemporary researchers beg the questions: Why

did these discrepancies occur? Have they been incorrectly described? Do we currently have the correct understanding of the constructs? What is the real nature of these symptoms? The main way in which this study attempted to address these questions was to reinvestigate euphoria in terms of both the classical and contemporary view regarding these aspects.

Firstly, it is important to note that the loss of the classical definition of three types of euphoria, and the apparent discrepancies between classical and contemporary definitions, does not appear to have resulted from an inappropriateness or demonstrated invalidity of the classical constructs, as the distinction between Cottrell and Wilson's (1926) three euphoric concepts was maintained by authors such as Sugar and Nadell, Pratt, and Surridge for at least 40 years after they were first created. Thus, the classical definition may still be of value and worth including in an investigation of euphoria.

With regard to the rationale, reinvestigating euphoria in terms of both the classical taxonomy and contemporary definitions may be important both in terms of the number of types of euphoria described, and also in relation to the ways in which those types are defined. That is, changing the description of these symptoms may (a) alter the actual symptoms elicited and the euphoria measured today may not be the euphoria first described so many years ago, and (b) have an impact on the frequencies of euphoria found. For example, Cottrell and Wilson (1926) considered there to be three types of euphoria, described positive mood in terms of "cheerfulness, happiness, ease, serenity" (p. 8), and found high frequencies of this symptom amongst their sample. In contrast, contemporary researchers typically report only one type, describe it in terms of a persistent and abnormally good mood (Cummings et al., 1994), and find low frequencies of between approximately 4.7% and 14.6% (Diaz-Olavarrieta et al., 1999; Figved et al., 2005; Fishman et al., 2004).

While various reasons for these discrepancies have been put forward, differences in operational definitions (Baretz and Stephenson, 1981; Finger, 1998; Minden & Schiffer, 1990; Pratt, 1951; Rabins, 1990), the lack of objective, standardised measures of mood (Minden & Schiffer, 1990; Reischies et al., 1988), and different measurement instruments (Finger, 1998; Minden, 2000) may be the most relevant. If the way in which euphoria sclerotica is defined and/or measured today is more restrictive, it may account for the lower frequencies found today, and the demonstration of only one type. Conversely, approaching the investigation of euphoria from the perspective of the original definitions of these constructs (by Cottrell and Wilson, 1926) may result in larger frequencies being found, and more types of euphoria. A change in definition also means that we are no longer looking for or measuring what was originally deemed to be euphoria sclerotica, and the classical quality of this symptom may have been lost, which is also important. Thus, a re-investigation of the

symptoms, from both the classical and contemporary perspectives, may highlight important changes that may have occurred in the definition of these symptoms, as well as important characteristics regarding the constructs of positive mood, unawareness of deficit, and optimism that may, otherwise, have been lost. Moreover, all this can now be done using modern research methodologies and technologies.

Aims and hypotheses for part one. Given the above, the main aim of part one was to investigate the constructs of the symptoms in question to gain a deeper and clearer understanding of what they entail. The specific aims and hypotheses of part one revolved around the following:

Aim 1. To investigate the discrepancies found in the literature between classical and contemporary authors.

Proposition 1. A change in the number of types of euphoria has occurred.
Proposition 2. A change in definition has occurred and the euphoria measured today does not have the same quality as that of the classical literature.
Hypothesis 1. Using different measurement instruments (based on different definitions) will influence the incidence rates of euphoria found.
Hypothesis 2. High rates of euphoria will be replicated using the classical measure.
Hypothesis 3. Low rates of euphoria will be replicated using the NPI.

Aim 2. To investigate the constructs of euphoria from a modern perspective, using measures other than that of Cottrell and Wilson (1926) or the NPI.

Hypothesis 4. More than one type of euphoria exists.
Hypothesis 5. The incidence rates of euphoria found using these measures will be higher than those demonstrated today.

Part two. Describing and predicting positivity and unawareness

Part two was concerned with gaining a deeper understanding of the actual euphoric symptoms, within an MS population. The euphoric types identified by part one were described in more depth, and the ability to predict which MS participants might present with these types was investigated via an examination of the disease and cognitive correlates of the euphoric types. The rationale, aims and hypotheses related to part two are presented below.

Rationale for part two. Part two aimed to build on the understanding of euphoria gained in part one and to better define and predict these symptoms. Therefore, in addition to expanding the description of euphoria, the disease and cognitive correlates of the euphoric types were investigated. Similar correlates have been addressed by other recent research (see, e.g., Benedict et al., 2001; Diaz-Olavarrieta et al., 1999; Figved et al., 2005; Fishman et al., 2004; Sherman et al., 2008), but this study was different for two reasons. The first was that euphoria in the current research was defined differently from that of other modern investigations of these symptoms, and was approached from the classical perspective using more inclusive types and definitions of euphoria. This, therefore, provides a rationale for the inclusion of variables that have been investigated before, such as disease severity, disease course, duration of disease, and tests of executive functioning. Secondly, following a review of the literature, a number of factors were found to be missing from previous research of the various correlates, and a more comprehensive investigation of the disease and cognitive correlates was therefore undertaken.

A number of studies have investigated the disease correlates of euphoria, however few have included demographic variables in this investigation. Gender, however, may be a relevant variable to include based on the findings of low rates of euphoria amongst predominantly female MS samples (Figved et al., 2005) and high rates of euphoria amongst male MS patients (Fishman et al., 2004). Thus, gender was included in the current study as a potential demographic covariate.

In terms of the disease correlates, in addition to the variables explored by other research, current disease state was included based on Rabins et al.'s (1986) suggestion that disease state may be a reason for the discrepancy between the frequencies of euphoria found by various researchers. They were of this opinion based on the findings of Dalos, Rabins, Brooks and O'Donnell (1983) who demonstrated high rates (i.e. 90%) of emotional disturbances during exacerbating or progressing disease states, and a greater number of bodily complaints during remission. Furthermore, because an increase in cytokine production occurs during relapses, and because elevated levels of cytokines have been associated with mood disorders (Horrobin, & Bennett, 1999), a link may be present between euphoria and exacerbations. Therefore, it was thought that a more comprehensive investigation of the disease correlates of euphoria, in terms of the additional variable of current disease state, may be highly relevant and may aid considerably in our understanding of euphoria in MS.

Regarding additional cognitive variables, while most 21st century researchers have found that euphoria correlates with severe cognitive impairment (see, e.g., Benedict, Carone et al., 2004; DeSousa et al., 2002; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004), most have measured cognitive impairment by assessing the well-known dysexecutive MS picture reviewed earlier in this section (i.e. the domains of attention, information processing speed, WM, learning and memory, verbal fluency, and abstract reasoning), and have neglected to investigate the possible contributions made by additional cortical involvement. However, also as reviewed earlier in this section, grey matter involvement is increasingly being recognised in MS due to the advancement of MRI techniques (De Stefano et al., 2003; Pirko et al., 2007), and cortical deficits such as aphasia, apraxia, agnosia (DeSousa et al., 2002; Jeffery et al., 2000; Kujala et al., 1996) unilateral spatial neglect (Gilad et al., 2006; Graff-Radford & Rizzo, 1987), as well as deficits in visuospatial construction (Asghar-Ali et al., 2004; Beatty & Aupperle, 2002; Calabrese, 2006), and prosodic comprehension (Beatty, Orbelo, Sorocco, & Ross, 2003), have also been demonstrated in MS patients.

Furthermore, grey matter atrophy has been found to correlate with the modern definition of euphoria (Benedict, Weinstock-Guttman et al., 2004; Sanfilipo et al., 2006), and euphoric mood has been demonstrated in other patient groups with cortical involvement such as Alzheimer's disease, Wernicke's aphasia and neurosyphilis (Reiser [1975] as cited in Baretz & Stephenson, 1981). However, as far as I am aware, although measures of cortical executive functions have been included in past research, (see, e.g. Benedict et al., 2001; Fishman et al., 2004; Sherman et al., 2008), they have not specifically been differentiated from subcortical measures. Thus, a re-investigation of the euphoric constructs and the extent to which they correlate with cortical cognitive variables may contribute greatly to our understanding of these symptoms.

In addition, of those authors above who do include, but do not particularly emphasise, cortical variables, few appear to differentiate between left and right hemispheric functioning. However, a number of the cortical deficits mentioned above are known to be related to RH involvement in other patient populations (e.g. unilateral spatial neglect [Gilad et al., 2006; Graff-Radford & Rizzo, 1987], visuospatial construction difficulties [Asghar-Ali et al., 2004; Beatty & Aupperle, 2002; Calabrese, 2006], and impaired prosodic comprehension [Beatty, Orbelo, Sorocco, & Ross, 2003]).

The terminology used to describe the unawareness of deficit in today's form of euphoria may also reflect slightly different processes to what was originally meant by eutonia sclerotica. For example, phrases used in connection with ideas of eutonia sclerotica, such as "poor self-awareness" (Benedict et al., 2001, p. 74), and a "lack of insight" (Feinstein, 2007,

p. 75), have been found to correlate with executive dysfunction (Benedict et al., 2001), thereby "proving" an executive basis for euphoria. However, whilst these particular descriptions may refer to symptoms that are indeed moderated by executive dysfunction, the original descriptions, such as feeling "physically well tuned up", feeling as if the patient could "do anything" and "not [being] conscious of physical disability" (Cottrell & Wilson, 1926, p. 8) appear to be remarkably similar to the syndromes of anosognosia or anosodiaphoria for hemiplegia, which refer to a denial or unawareness, or an indifference to a physical deficit respectively (Amador et al., 1991; Devinsky, 2000; Jenkinson et al., 2011), and which are associated with damage to the RH (Devinsky, 2000; Jenkinson et al., 2011; Pia et al., 2004).

Further, Surridge's (1969) idea of there being different levels of euphoria that can disappear on provocation also resembles these syndromes. Finally, damage to the RH has also been demonstrated to result in euphoric (and sometimes manic) mood change (Devinsky, 2000; Gainotti, 1972; Starkstein et al., 1990), even though the valence hypothesis has largely been replaced now.

Despite the above, as far as I am aware, RH impairment, based on cognitive testing, has not specifically been included in research on euphoria. Thus, while I recognise that unawareness in MS may well be a different type of unawareness to that of anosognosia for hemiplegia, and not at all governed by damage to the RH, due to the emphasis on unawareness of physical deficits (as opposed to other types of unawareness) amongst this patient group, and to the additional apparent links to the RH, this aspect deserves attention and investigating the euphoric symptoms and the extent to which they correlate with RH impairment on neuropsychological testing may further contribute to our understanding of these symptoms.

Aims and hypotheses for part two. Given the above, the main aim of part two was to further describe and define, and to predict the euphoric types. The specific aims and hypotheses of part two were to:

Aim 1. Further describe and define the euphoric types

Aim 2. Investigate the demographic, disease and cognitive correlates of the euphoric types in the hopes of being able to predict which MS participants might develop these types of euphoria.

Hypothesis 1. The demographic and disease correlates of the euphoric types will differ.

Hypothesis 2. The cognitive correlates of the euphoric types will differ.

Hypothesis 3. The different types of euphoria will occur both early and late in the disease, with either little or severe physical disability

Hypothesis 4. At least one type of euphoria will correlate with gender

Hypothesis 5. At least one type of euphoria will correlate with current disease state

Hypothesis 6. At least one type of euphoria (most likely that of positive mood/euphoria sclerotica) will correlate with cortical involvement on neuropsychological testing

Hypothesis 7. At least one type of euphoria (most like that of unawareness/eutonia sclerotica) will correlate with RH involvement on neuropsychological testing

Part three. The causes of euphoria

Part three was also concerned with an investigation of the actual symptoms themselves. Despite a long history of interest concerning this symptom, the cause of euphoria in MS remains unclear. Thus, the MS participants were compared with control patients of other groups in order to attempt to investigate four hypotheses regarding the cause of these symptoms. However, I must draw attention to a very important point: These investigations were preliminary and provisional as the sample sizes of the patient control groups were extremely limited. Precise conclusions cannot be drawn from these analyses and any interpretations must be both made and received with caution. Thus, this section (i.e. part three) formed a pilot investigation that was supplementary to the main analyses of this research.

Two of the hypotheses investigated currently exist in the literature and were addressed in the literature review. These refer to euphoria being (a) a psychological reaction to a disabling disease (which was tested using a group of patients with MG), and (b) the result of executive dysfunction (which was tested using a group of patients with TBI as a result of a motor vehicle accident [MVA]). The second two hypotheses are new ideas. These refer to euphoria being the result of (a) immunological disease processes of auto-immune diseases affecting the CNS and brain (which was tested using a group of patients with neuropsychiatric systemic lupus erythematosus [NP-SLE]), and (b) RH dysfunction (which was tested using a group of patients with RH damage due to stroke).

A psychological reaction. Although general agreement exists that euphoria in MS is the result of cerebral involvement and not a psychological reaction to a chronic disabling disease (see Rabins et al., 1986; Rodgers & Bland, 1996; Sanfilipo et al., 2006), this has yet to be demonstrated empirically. To test this hypothesis a group of patients with MG (a chronic disease that does not affect the CNS) was included.

MG is an acquired autoimmune disorder, with a fluctuating course, where autoantibodies interrupt the signalling process at the neuromuscular junction, situated where the peripheral nerves meet the muscles, and cause a weakening or failure of muscle contraction by the nerve impulses. Sensory-motor deficits are therefore something MS and MG have in common, and MG is characterised by a progressive weakening of muscles during exercise followed by quick recovery when exertion is stopped (Cantor, 2010; Dönmez et al., 2004; Wolfe, Meriggioli, Ciafaloni, & Ruff, 2012).

In MG, the disease does not affect the CNS, and cognitive impairment is not generally regarded to be a feature (Bartel & Lotz, 1995). Some cognitive impairment has been reported, but results have been mixed and often discounted due to inadequate sample sizes, the use of non-standardised neuropsychological tests, and a lack of control of confounding factors such as effects of sleep apnea, depression, medication use and so on (Paul, Cohen, Zawacki, Gilchrist, & Aloia, 2001). Paul, Cohen, Goldstein, and Gilchrist (2000) have also documented increased cognitive fatigue amongst MG patients which may lead to a misdiagnosis of cognitive impairment.

Mood symptoms such as depression, anxiety and outbursts of rage and frustration are, however, common, although euphoria appears to be rare except as a reaction to corticosteroid treatment (Cantor, 2010; Kulaksizoglu, 2007).

Given that MG patients have a similar chronic, debilitating disease of unpredictable course, but that does not affect the CNS or brain, it was thought that a thorough investigation of their mood, awareness and outlook may yield important findings concerning the cause of euphoria (i.e. is it related to a psychological reaction to a chronic debilitating disease, or is it MS specific?) and may contribute to our understanding of these symptoms.

Executive dysfunction. Euphoria, in MS, is largely believed to be the result of executive dysfunction (Benedict et al., 2001; Benedict, Carone et al., 2004; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004). To test this hypothesis, a group of patients with motor vehicle accident traumatic brain injuries (MVA TBIs) was included. While it is recognised that the mechanism underlying the damage in these two patient groups differs, this group has damage to similar neuroanatomical areas (i.e. subcortical white matter), resulting in a similar

dysexecutive syndrome to patients with MS and were considered to be the closest or best representative group by which to test this hypothesis.

MVA TBIs most often involve diffuse damage to subcortical areas, due to the inertial forces of acceleration and deceleration which lead to widespread shearing or tearing of the axons (i.e. diffuse axonal injury) and, later, white matter atrophy (Bigler & Maxwell, 2012; Parizel et al., 1998). Thus, the neuroanatomical areas most often affected in MVA TBI include the subcortical white matter (particularly that of the frontal lobe), the grey-white matter interface, the corpus callosum, periventricular areas, the basal ganglia and thalamus, the brainstem and cerebellum (Flashman, 2002; Parizel et al., 1998; Smith, Meaney, & Shull, 2003).

Due to the largely subcortical damage involved, and similar to MS, TBIs are also often associated with executive dysfunction, affecting domains such as attention, WM, concentration, learning and memory, poor organisation, planning, sequencing, and set shifting (Hartman, Pickering, & Wilson, 1992; Rao & Lyketsos, 2000).

However, while they can present with cognitive anosognosia (Flashman, 2002; Toglia & Kirk, 2000), euphoria is not a prominent symptom, and symptoms of mood and behaviour in TBI are rather characterised by depression, mania, apathy, irritability, insomnia, anxiety disorders, psychosis, and disorders of behavioural control, sometimes leading to aggressive and violent behaviour (Fann, Katon, Uomoto, & Esselman, 1995; Rao & Lyketsos, 2000).

Given that MVA TBI patients have similar cerebral involvement and similar cognitive impairment to patients with MS, it was thought that a thorough investigation of their mood, awareness and outlook, may yield important findings concerning the cause of euphoria (i.e. is it related to executive dysfunction in general, or is it MS specific?) and contribute to our understanding of these symptoms.

Immunological processes affecting the brain. Although euphoria, in MS, is generally believed to be caused by cerebral involvement, research tends to focus on the area of involvement rather than the type of involvement. Issues of auto-immunity have been implicated in the MS disease process, in mood disorders such as euphoria, depression and bipolar mood disorder (Brietzke et al., 2009; Horrobin, & Bennett, 1999), as well as in unrealistic optimism (Segerstrom et al., 1998). However, to my knowledge they have not been addressed in relation to euphoria in MS. Furthermore, although considered to be rare and often associated with psychosis, euphoric mood has been demonstrated in systemic lupus erythematosus (SLE) involving the CNS (i.e. neuropsychiatric systemic lupus erythematosus

[NP-SLE]; Alao, Chlebowski, & Chung, 2009; Hanrahan, 1954). Thus, a group of patients with NP-SLE were included to test this hypothesis.

SLE is a chronic, relapsing-remitting, multisystem auto-immune disease of the central, peripheral, and autonomic nervous system, which affects many different tissues and organs. A sub-type of this disease includes that of NP-SLE, which affects the CNS (Benedict, Shucard, J., Zivadinov, & Shucard, D., 2008; Nived, Sturfelt, Liang, & De Pablo, 2003). Like MS, the neuroanatomical location of the cerebral pathology in NP-SLE is predominantly related to white matter changes (Benedict et al., 2008; Covey, Shucard, J., Shucard, D., Stegen, & Benedict, 2012); however the causes of damage are very different and advanced disease results in types of cerebral pathology that are quite different from MS, including an increased risk for cerebrovascular disease (Benedict et al., 2008; Jennekens & Kater, 2002).

While the physical symptoms of SLE, which can involve skin rashes and arthritis, are also different from MS, cognitive symptoms, which can occur in any form of SLE and not only NP-SLE, include a pattern of executive dysfunction similar to that of MS, affecting the domains of attention, judgement, WM, information processing speed, and, although with less consensus, the domains of learning and memory (Covey et al., 2012; Skeel, Johnstone, Yangco, Walker, & Komatireddy, 2000). Patients with NP-SLE also often experience psychiatric symptoms, including psychosis, anxiety disorders, and mood disorders, including depression, emotional lability, and, to a far lesser extent, bipolar mood disorder and euphoria (Alao et al., 2009; Benedict et al., 2008; Covey et al., 2012; Hanrahan, 1954).

Given that NP-SLE patients have a similar chronic, debilitating auto-immune disease that does affect the CNS or brain, it was thought that a thorough investigation of their mood, awareness and outlook, may yield important findings concerning the cause of euphoria (i.e. is it related to cerebral involvement within an auto-immune disease or is it something specific to MS?) and may contribute to our understanding of these symptoms.

Right hemispheric dysfunction. An extension of investigating the cognitive correlates of euphoria in terms of RH functioning is that of testing this hypothesis in a pilot study of patients with damage to only the RH. Earlier (see the rationale pertaining to the cognitive correlates of euphoria), it was suggested that RH involvement may, in some way, be implicated in euphoria. However, to my knowledge, RH involvement has not been investigated in this regard. A group of patients with RH damage, as a result of stroke, was therefore utilised to test this.

Much is known about the left hemisphere; however the RH largely remains a mystery. Patients with damage to this hemisphere, however, are known to present with symptoms such

as difficulties with spatial cognition and construction (Benowitz, Moya, & Levine, 1990), anosognosia or anosodiaphoria (Devinsky, 2000; Jenkinson et al., 2011; Pia et al., 2004), and, some believe, increased positive (or manic) mood (Devinsky, 2000; Gainotti, 1972; Starkstein et al., 1990). Similar symptoms of cognition and mood have been demonstrated in patients with MS (Asghar-Ali et al., 2004; Banati et al., 2010; Gilad et al., 2006).

Given that RH involvement has not been researched within MS and euphoria, but appears to perhaps have some relevance, it was thought that a thorough investigation of the mood, awareness and outlook of RH patients, may yield important findings concerning the cause of euphoria (i.e. is it related to RH dysfunction or is it something specific to MS?) and may contribute to our current understanding of these symptoms.

Aims and hypotheses of part three. Given the above, the main aim of part three was to gain a deeper understanding of the cause of euphoria, even though these were pilot investigations that could only yield limited preliminary results. The specific aims and hypotheses of part three were, therefore, to:

Aim 1. Preliminarily investigate the cause of the various types of euphoria in terms of the hypotheses regarding euphoria being (a) a psychological reaction to a chronic disease, (b) the result of executive dysfunction, (c) the result of an immunological disease process present in auto-immune diseases affecting the CNS, and (d) the result of RH dysfunction.

Hypothesis 1. The MG group will demonstrate better cognitive functioning than the MS group.

Hypothesis 2. The MVA TBI and NP-SLE groups will demonstrate similarly dysexecutive impairment to the MS group.

Hypothesis 3. The RH group will demonstrate similar impairment to the MS group on tests of RH functioning, but will not demonstrate impairment on tests of executive functioning.

Hypothesis 4. The euphoric types will not be as prominent amongst MG controls as amongst MS participants.

Hypothesis 5. At least one euphoric type will be demonstrated at similar levels within MVA TBI, NP-SLE and RH control groups, as within the MS group.

Methods

Research design

This study mainly gathered quantitative information. However, one of the questionnaires used (see the questionnaire of Cottrell and Wilson, 1926, [CWQ], described later under measurement instruments) gathered both open and closed ended questions which were analysed both quantitatively and qualitatively. Therefore, both quantitative and qualitative methods were employed within an exploratory, quasi-experimental between-subjects and cross-sectional design.

The study made use of an exploratory design as it sought to increase our knowledge on euphoria (Neuman, 1994) and addressed the topic from a number of angles, presenting an inclusive investigative approach. It was quasi-experimental because existing groups of predefined disease types were utilised. Furthermore, it was cross-sectional in design as data was collected, between January 2012 and November 2013, from participants of different ages and compared with one another instead of following same participants over a longer period as is the procedure in longitudinal research. This was done to examine what currently exists, rather than to observe a change, and because it was more time-efficient (Brink, 2006).

Procedure

Ethical approval was obtained from the Research Ethics Committee of the University of Cape Town (UCT; Faculty of Health Sciences; see Appendices A1 and A2), and Research Development and Support (University of Stellenbosch) for Tygerberg Hospital (TBH) patients (see Appendix A3).

Recruitment. Non-probability sampling techniques were employed to recruit the participants and controls of this study. Purposive sampling was used in order to select participants and controls with specific predetermined criteria, namely their disease, and controls with specific sociodemographic criteria (Wilson & Maclean, 2011). Further, convenience and snowball sampling were utilised to recruit participants and controls who were readily available for the study (Brink, 2006). Those who took part in face-to-face interviews were recruited from the Western Cape (WC). In order to access more participants, a number of additional participants were recruited from the greater SA, predominantly residing in the WC, Gauteng and KwaZulu-Natal.

Participants and controls were recruited from the databases of private neurologists and public hospitals (such as Groote Schuur Hospital [GSH] and TBH) in the WC, as well as via

Facebook and e-mail messages sent by Multiple Sclerosis South Africa (MSSA), a non-governmental organisation, the MG Facebook website, the Brain Injury Group, and private neuropsychologists in the WC.

A number of additional avenues were explored to increase the size of the population from which the participants were recruited. However, neurologists in private practise were unable to assist with the recruitment of the patient control groups, and those at GSH were concerned about research fatigue of patients, or did not have the resources to assist with additional recruitment of patients. The Muscular Dystrophy Foundation was also contacted, however they did not have any suitable patients and could not identify any additional appropriate foundations. Furthermore, no additional support groups for the patient groups could be found via Facebook or other hospitals such as the Panorama Medi-Clinic or Constantiaberg Medi-Clinic. A number of organisations and medical health practitioners were contacted with reference to the TBI group. These included the Panorama Memory Clinic, Cape Mental health, Community Mental Health and Psychiatry, the Western Cape Rehab Centre, Lentegeur Hospital, and a variety of neuropsychologists, occupational therapists, speech therapists, and road accident fund attorneys. However, none of these organisations or practitioners were able to assist.

Sample. One hundred MS participants and 100 HCs were recruited for this study. A number of patient control participants were also recruited to address specific, but very preliminary, research questions. As addressed in the section pertaining to the rationale and aims of part three, 20 MGs were recruited with the aim of investigating the hypothesis that euphoria in MS is a psychological reaction to a disabling disease; 19 MVA TBIs were recruited in relation to the hypothesis that euphoria in MS is the result of executive dysfunction; 10 NP-SLE were recruited to investigate the hypothesis concerning the immunological contributions to euphoria in MS; and 10 RH for the hypothesis concerning the contributions made by RH dysfunction to euphoria in MS. All required a confirmed diagnosis of their respective disease or condition, and the MVA TBIs and RHs were required to have experienced their brain trauma at least one year prior to involvement in this study, to allow for additional swelling (that may confound the results) to subside (Sbordone, Liter, & Pettler-Jennings, 1995). No distinction was made regarding the severity of the TBI, or the neuroanatomical cite of the RH damage as this would have resulted in very small sample sizes per group. Due to the limited number of patients available, exclusion criteria were not imposed on the abovementioned participants and were rather noted and controlled for statistically.

HCs were matched to the MS participants on the key sociodemographic variables of gender, age, highest level of education, and income, and these formed the inclusion criteria for this group. This group was included in order to better interpret the performance of the MS participants on tests that have been developed and standardised on populations of developed countries such as the United Kingdom and United States of America, as culture, language, and level of education, can influence performance on neuropsychological tests (Alcock, Holding, Mung'ala-Odera, & Newton, 2008; Roos et al., 2010). HCs were excluded from the study should they have experienced any of the following:

- A current or past infectious, immunological or neurological disease (e.g. human immunodeficiency virus [HIV]/acquired immune deficiency syndrome [AIDS], meningitis, Addisons disease, Huntington's disease, and Parkinson's disease)
- A history of other brain injury (e.g. brain tumour, head injury, stroke, epilepsy, or near drowning/heart attack due to their hypoxic/anoxic effects on the brain)
- A history, or current diagnosis of psychiatric disorder
- A history of developmental disorder or delay (e.g. attention deficit hyperactivity disorder, learning disability)
- A history, or current abuse of alcohol or other substances

Data collection. Data collection occurred between June 2012 and November 2013. All participants and controls were first contacted by someone in the medical field (or a family member or friend in the case of the HCs) and told about the research. Once verbal consent was attained, I contacted them and further explained the study, checked exclusion criteria (for HCs), and invited them to take part. Face-to-face interviews took place in (a) the homes of the participants, enabling participants to feel more relaxed and less inconvenienced (Neuman, 1994; Smith, Harré & Van Langenhove, 1995), and alleviating travelling difficulties for physically disabled participants; (b) the neuropsychology office (for some MS, HC and MVA TBI participants); (c) an office in the Rheumatology Clinic at GSH (for some NP-SLE participants); (d) an office in the Neurology department at TBH (for some MG participants); or (e) a quiet office, or boardroom, in the workplace of the participants (for some HCs).

Participants were given, or sent, an information sheet and written (informed) consent, pertinent to their group, was obtained (see Appendix B1 and B2). One MVA TBI participant was identified by his guardian as being unable to provide informed consent. Thus, consent was obtained from his guardian (see Appendix B2), and assent was obtained from the participant (see Appendix B3). Participants were assured that they could withdraw from the research at any time without experiencing any negative consequences.

All participants were questioned regarding the sociodemographic, medical and disease/condition specific information. All participants also completed the euphoria questionnaires described below. A subset of participants underwent cognitive testing, all of whom completed the tests in the same order, structured specifically to maintain the participants' attention and limit anxiety and (to as great a degree as was possible) fatigue, by administering more complex measures, interspersed by easier, less anxiety-provoking measures.

Visual representations of the final samples, as well as the composition of their interviews are presented in Figures 1 and 2.

Figure 1

Procedure for MS Participants

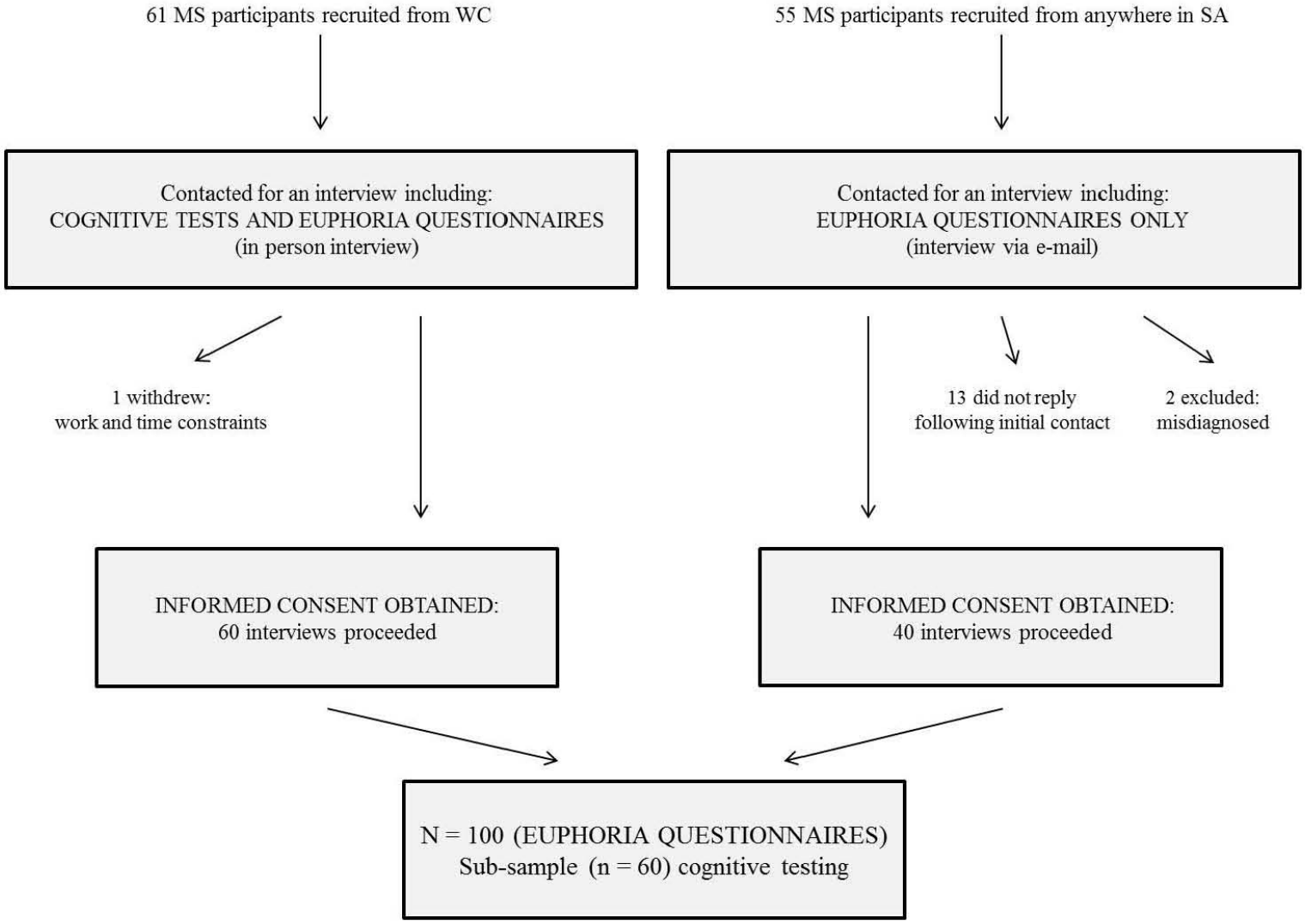
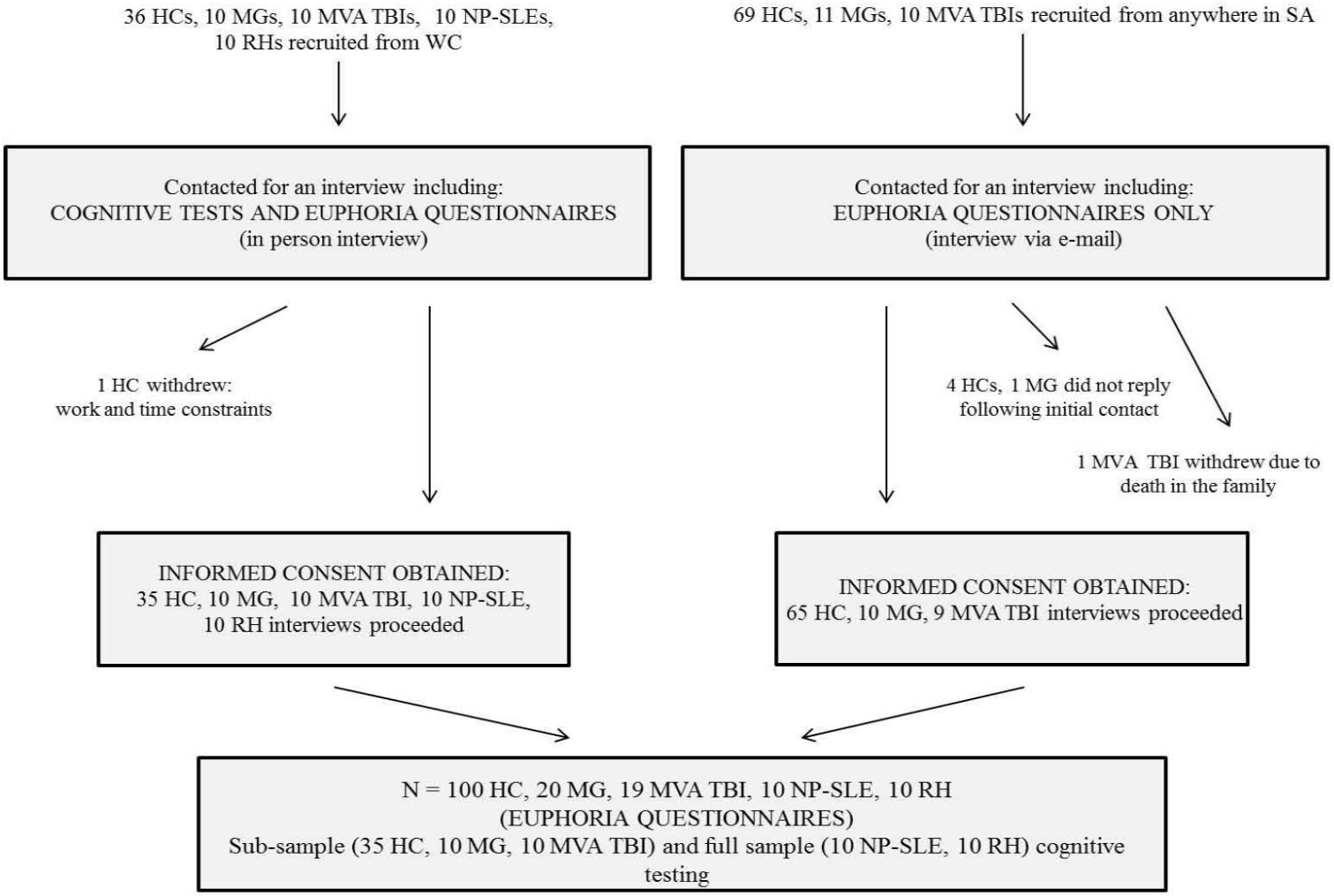


Figure 2

Procedure for All Control Participants



Both quantitative data, which was typed or written down, and (supplementary) qualitative data for the MS participants, which was either tape recorded or written down, was collected. To ensure confidentiality, a coding system was used whereby all participants' names were removed from their testing information and only a letter and number was used. Where excerpts were used to qualitatively describe the nature of the euphoric MS participants, any identifying data was changed or removed. All information from each interview and assessment was kept in a locked cupboard in the home of the researcher or on a password protected computer and was not be available to anyone other than the researcher. Besides the time invested, there were no known risks or costs for the participants. If a participant was feeling fatigued, breaks and refreshments were given.

Benefits to participation, for all participants except the HC, included receiving a pamphlet, (see Appendix C1 for an example pamphlet) containing information on the common neuropsychological symptoms of each disease or condition, as well as feedback (see Appendix C2) following participation. All participants were also made aware that their participation would benefit the scientific community and increase our understanding about the cognitive and mood/affective symptoms of MS.

Participant characteristics

The characteristics of each of the control groups will be described in the relevant results sub-section in which they appear so as to orientate the reader during the appropriate sub-section rather than describe all groups upfront. However, relevant sociodemographic characteristics of the MS participants are represented in Table 2 as the majority of the results of this dissertation centre around this group. For the full list of group characteristics, see Table D1, in Appendix D.

Table 2

The Relevant Sociodemographic Characteristics of the MS Participants

Sociodemographic characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)
Gender – Male:Female	8:52	6:34	14:86
Age	43.35 (11.48)	46.20 (10.61)	44.49 (11.17)
Range	19-72	26-64	19-72
Race/ethnicity – White:Coloured[2]/Indian	34:26	37:3	71:29
Education[a]	13 (1.69)	13.45 (1.58)	13.18(1.65)
Range	8-15	8-15	8-15
Income[b]	R23,002.17 (R18,427.84)	R30,513.02 (R27,218.12)	R26,006.51 (R22,536.54)
Range	R1,200.50-R76,800.50	R4,800.50-R153,601.00	R1,200.50-R153,601.00
Informants			
Spouse/partner:Family member: Good friend	28:21:11	31:5:4	59:26:15
Living with participant Yes:No	44:16	35:5	79:21

Note. Categorical data are presented in ratios. The data on age, education, and income are presented as means with the standard deviations in parentheses, then minimum to maximum ranges below.
[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.
[b] = Combined monthly household income.

Two points of interest are that (1) although high numbers of female participants were expected, as MS is twice as prevalent amongst women as men (Mohr et al., 1999; Mohr et al., 2003), 86% of the 100 MS participants were female; and (2) in SA, MS is considered to be rare amongst the black, Coloured and Indian communities (Dean & Kurtzke, 1971; Dean et al., 1994), yet 29% of the MS group was Coloured or Indian.

The MS participants were also asked if they had ever been diagnosed by their doctor with a variety of medical conditions, or incidents, as well as any psychiatric disorders that could impact on neuropsychological functioning. As mentioned, although excluding participants based on these conditions would have been ideal, due to the scarcity of MS patients, and to the co-existing nature of many of these conditions with MS[3], these medical

[2] In South Africa, the term "Coloured" refers to individuals with a mixed ancestry of both black African and white/Caucasian.
[3] MS patients have an increased risk for other medical conditions either due to the neurological involvement or the auto-immune nature of the disease. These can include, for example, other auto-immune diseases, seizure disorders or epilepsy, vascular disease and stroke (Christiansen, 2012; Olafsson, Benedikz, & Hauser, 1999; Somers, Thomas, Smeeth, & Hall, 2009).

details (see Table 3) were not used as exclusion criteria but rather noted and controlled for statistically.

Table 3

The Medical Characteristics of the MS Participants

Medical characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)
Other neurological/ immunological disease			
Other auto-immune disease	3	5	8
Meningitis/encephalitis	2	1	3
Tuberculosis	2	2	4
Malaria	1	1	2
Other brain injury			
Head injury	8	1	9
Brain tumour	1	-	1
Stroke	1	-	1
Epilepsy	2	-	2
Near drowning/heart attack/loss of consciousness	1	3	4
Psychiatric disorder			
Depression	15	7	22
Bipolar mood disorder	2	-	2
Developmental disorder			
Complications at birth	8	1	9
Attention deficit hyperactivity disorder	1	1	2
Learning disability	1	1	2
Delay in walking/talking	3	2	5
Alcohol			
Number of participants who consumed alcohol	30	27	57
Mean quantity (*SD*)	14.03 (15.54)	20.70.34 (25.00)	17.19 (20.84)
Range	1-60	1-90	1-90
Marijuana	5	2	7
Number of participants with a medical history that can affect neuropsychological functioning	26	15	41

Note. The data on quantity of alcohol (per month) are presented as means with the standard deviations (*SD*) in parentheses.

Other concurrent auto-immune diseases included SLE, hypothyroidism, sarcoidosis, rheumatoid arthritis, psoriasis, antiphospholipid syndrome, rosacea, and Crohn's disease. None of the tuberculosis or malaria noted were of the cerebral form. In terms of other brain

injury, in four of the nine cases it was just a "bump to the head", but included loss of consciousness in five. A number of conditions were thought to have been confused with an MS relapse. These included one case of meningitis or encephalitis, one stroke, and one case of epilepsy. Diagnosed psychiatric disorders were limited to depression in 22% and bipolar mood disorder in 2% of the MS sample (with 66.6% [16/24] of these disorders occurring post onset of MS symptoms). Complications at birth involved being born premature or having their cord wrapped around their neck. Learning disabilities included only dyslexia. All participants had reached a high-school level of education and none reported having experienced any lasting effects from the incidents or conditions described above. Furthermore, no MS participant was deemed to abuse alcohol, however marijuana was used by 7% of the MS sample, regularly by some, in tea or "joint" form, but not within 48 hours of their being interviewed. Medications taken by the MS group are addressed in the part two of the results section, where their consideration is more pertinent.

Measurement instruments

Participant characteristics. Various sociodemographic details were recorded to describe the participants of the study. These included, but were not limited to (a) gender, (b) age, (c) race/ethnicity, (d) highest level of education, and (e) combined household income per month (for the full list, see Appendix E1).

A variety of medical questions were also asked. Most of these formed part of the exclusion criteria for HC participants, and were noted for the patient groups. Medical questions included, but were not limited to (a) a current or past infectious, immunological, or neurological disease such as HIV/AIDS or meningitis; (b) a history of other brain injury such as a brain tumour or stroke; (c) a history of diagnosed psychiatric disorders; and (d) a question concerning any other medical conditions (for full list, see Appendix E2).

Disease specific measures. Disease information, in accordance with previous MS studies of mood and cognition (see, e.g., Heaton et al., 1985; Peyser, Edwards, & Poser, 1980), were also obtained from the MS, MG, MVA TBI, NP-SLE, and RH groups. For the MS, MG and NP-SLE participants, these included: disease course or type (MS only), date of diagnosis, and current disease state (remission or relapse/exacerbation; see Appendices E3, E4, and E5). For the MVA TBI participants, these included: a brief description of what happened, where possible the Glasgow Coma Scale score at admission (usually obtained from the medical records), and the date of MVA TBI (see Appendix E6). For the RH

participants, these included a scan report or medical details (obtained from the medical records) of the type of stroke (see Appendix E7). Information on diagnosis, disease course (MS, MG, NP-SLE), type and severity of brain injury (MVA TBI) and type/location of brain injury (RH) were confirmed with the appropriate neurologist, neuropsychologist or neurosurgeon.

All participants, including HCs, were also questioned on their current medication use and asked whether or not they had undergone corticosteroid treatment within the last four weeks.

Much of the research investigating the correlates of mood and cognitive symptoms in MS includes Kurtzke's Expanded Disability Status Scale (EDSS; Kurtzke, 1983) as a measure of neurological disability. However, (a) due to time and cost considerations, (b) the fact that it was recommended that only a trained neurologist administer the test, and (c) the fact that many researchers actually use it as a measure of physical disability, it was decided to rather include a scale of physical ability, which is described in-depth in the next section.

Questionnaires pertaining to euphoria. Both self-report and informant-report measures were used. These related to euphoria sclerotica, eutonia sclerotica and spes sclerotica; however depression was also measured as there are some discrepancies in the literature regarding outward versus inward euphoric feelings (see Surridge, 1969).

For the informant measures (see Appendix F1), a loved-one or family member of each participant rated the MS participant on scales of euphoria/depression, optimism/pessimism and awareness/unawareness (created by myself) in order to obtain an objective view of these symptoms. They also answered the questions of the Physical Ability Scale (PAS; physical), the Awareness Interview (AI; cognitive) and the NPI (mood/behavioural), described below, which were re-worded, where necessary, to make it clear that the informant was reporting on their loved-one's deficits and not their own. This was done for the purposes of determining patient/informant discrepancies on these measures.

The self-report measures pertaining to euphoria (and depression) are also listed below. All participants and their informants were fluent in English, thus all questionnaires were presented in English. The majority of the measures originated in developed Western countries, and applying the measures to a multi-cultural context that is distinct from the Western culture may result in issues of applicability of the measures. However, the majority of participants (or at least those from the MS and HC groups) were white/Caucasian and therefore, such issues not be as pronounced within this sample. Where possible, cross-

cultural applicability of the measures will, never-the-less, be described.

With specific reference to the three types of euphoria, the CWQ was, first and foremost, utilised as this was the measure first used in connection with the classical definition of euphoria. The measure most often used in contemporary research, the NPI, was also included. These measures were then supplemented with additional measures pertaining to each of the three constructs (euphoria sclerotica or positive mood, eutonia sclerotica or unawareness of deficit, and spes sclerotica or optimism). Each measure is discussed, alphabetically, below, and the specific use of the measures is depicted below that in Table 4.

Awareness interview (AI). The AI[4] (Anderson & Tranel, 1989) is a questionnaire, originally developed to assess awareness of deficit in stroke, dementia and head injury patients. It consists of five specific questions, which are read out in full, pertaining to the cognitive domains of thinking, orientation, memory, language, and visual perception, as well as one question pertaining to motor impairments. Participants are required to respond with one of three answers that equate to *no impairment*, *mild impairment*, or *severe impairment*.

The additional questions pertaining to reason for hospitalisation and ability to return to work were removed as they were either not relevant to assess cognitive functioning, or were deemed inappropriate for the current study patient group. The question relating to motor impairment was used only for the feedback form. As is the accepted protocol in awareness research (Prigatano, Altman, & O'brien, 1990), both participants and informants were required to complete this questionnaire so that participant/informant discrepancies could be utilised in order to determine the participants' awareness of their potential cognitive impairment.

Inter-rater reliability of the standard AI is very high (Pearson r = .92; Anderson & Tranel, 1989). Although developed in North America, the AI has been used in a study with predominantly African American participants with an average of 10 years of education (LaBuda and Lichtenberg, 1999), as well as in a study based in Israel (Hartman-Maeir, Soroker, Ring, & Katz, 2002) indicating its cross-cultural applicability.

This measure was included based on its prior use among awareness of deficit research in MS (see Sherman et al., 2008), and because it was an appropriate measure of eutonia sclerotica. The dependant variable relating to the AI was defined via the discrepancy in terms

[4] Please note that although I requested permission to reproduce this questionnaire, I never received a reply from S. W. Anderson and rather did not include a copy of it in the Appendix.

of the difference in score between the participants' self-reports and the reports of their informants. Discrepancy scores could range from 0 to 10 where higher scores indicated greater unawareness.

Beck depression inventory-fast screen (BDI-FS). The BDI-FS (Beck, Steer, & Brown, 2000) is the most recent abbreviated version of the Beck Depression Inventory (BDI) and requires participants to provide self-reported answers to seven questions concerning symptoms of depression, independent of the features of medical illness, such as previous failure, self-dislike and self-criticalness. It is a four point scale measure, ranging from 0 to 3, with total scores ranging from 0 to 21.

The BDI-FS has been found to have high correlations with both self ($p < .001$) and informant reports of depression/dysphoria ($p < .01$) amongst MS patients (Benedict, Fishman, McClellan, Bakshi, & Weinstock-Guttman, 2003), and has been used extensively within MS research (see, e.g., Beatty et al., 1989; Savettieri et al., 2004). It has also been used successfully in countries such as Botswana (Lawler et al., 2011), and low income communities of Pietermaritzburg in SA (Pillay & Sargent, 1999), indicating its appropriateness within the SA cultural context.

The BDI is the gold standard amongst measures of depression for adults and particularly those in medical settings (Sharp & Lipsky, 2002) and was thus selected for inclusion to capture the level of depression amongst the various participant groups of this research. A shorter version was selected as, although it is important, depression is not the focus of this research. This particular version was selected as it was designed to screen for depression amongst medical populations. The dependant variable relating to the BDI-FS was defined by the total score, with higher scores indicating greater depressive symptomatology.

Comparative risk judgement rating form (CRJRF). A number of researchers have used variations of comparative risk judgement rating forms, where participants are asked to rate their chances of experiencing various items, relating to both their health and other aspects of their lives, whilst comparing themselves to a person of similar demographic (and illness) standing. Questions may include, for example, "compared with other (fe)males of your age, economic status and with similar health as you, what are the chances that you would break your arm or your leg?", or, "compared with other (fe)males that are similar to you, what are the chances that you would develop cancer?", or, "compared with other (fe)males that are similar to you, what are the chances you'd win R100,000 in the lottery?".

Participants are asked to rate their answers on a five point Likert-type scale from *extremely below average* to *extremely above average*. I employed this same rating technique and created my own form including questions that were considered relevant for this context, loosely based on the work of Fournier, de Ridder and Bensing (2003), Covey and Davies (2004), Weinstein (1983), and Warner, Schwarzer, Schüz, Wurm, & Tesch-Römer (2012) (see Appendix F2).

The CRJRF was selected based on its inclusion in a study concerning the role of unrealistic optimism among MS patients (see Fournier, de Ridder and Bensing, 1999). The dependant variable relating to the CRJRF was defined by the number of answers that fell within the "extremely below average" category for negative items (i.e. where participants stated they were less likely to experience negative events) and the "extremely above average" category for the positive items (i.e. where participants stated they were more likely to experience positive events). Possible answers ranged from 0 to 20 and higher scores indicated higher unrealistic optimism.

Cottrell and Wilson (1926) questionnaire (CWQ). Cottrell and Wilson (1926) asked a number of open and closed-ended questions, which require self-reported answers, regarding emotional and physical well-being as well as questions pertaining to outlook (see Appendix F3). These questions were included based on their use by these classical researchers to elicit and measure the presence of euphoria sclerotica, eutonia sclerotica and spes sclerotica. In-depth details of the procedures used in terms of the quantitative rating of this questionnaire will be described in part one of the results section; however the dependant variables relating to the CWQ were defined in terms of the average score given by three raters where "2" represented a *definite presence* of the symptom (i.e. euphoria sclerotica, eutonia sclerotica or spes sclerotica), "1" represented a *possible presence* of the symptom, and "0" signified an *absence* of the symptom.

Two questions were additionally used to supplement the quantitative data of this study and to aid in describing the quality of euphoria within MS. The first was an open ended question of this measure (i.e. "Describe in a few words your general or usual mood"). The second was a question that was added (the particulars of which will be addressed in greater detail in part one of the results section) and that related to the definition of Cottrell and Wilson (1926) (i.e. How do you feel about the future?). The answers of the MS participants were either tape recorded or typed by the participant and sent via e-mail. At a later stage these data were transcribed by the researcher for analysis.

Internal state scale (ISS). The ISS (Bauer et al., 1991) consists of four subscales: (a) depression, (b) activation (linked to symptoms of mania), (c) perceived conflict subscale (which has been used to determine psychopathy in patients), and (d) a well-being sub-scale which is the scale most relevant for euthymia and euphoria. The original rating scale of 0 to 100 was modified, for consistency and simplicity, to be in line with the system used in the Positive and Negative Affect Schedule (PANAS) which requires participants to rate their answers on a Likert-type scale from one, denoting *very slightly or not at all*, to five, signifying *extremely* (see Appendix F4).

There are very few self-report measures of euphoria available, thus, the ISS was included based on its euthymic/euphoric sub-scale. It was additionally included as the well-being sub-scale questions individuals about general well-being and subtle symptoms, which was in line with the original description and definition of the constructs in question. The dependant variable relating to the ISS was defined by the total score of the well-being sub-scale. Possible answers ranged between three and 15, where higher scores indicated greater positive mood/well-being (euphoria sclerotica). A participant was considered to have high well-being if their score fell within the 3rd quartile (i.e. 75% or more, or 12 or more) based on the minimum and maximum values of the scale.

Life orientation test-revised (LOT-R). The LOT-R (Scheier & Carver, 1985) requires participants to indicate the extent to which they agree, or disagree, with four positive, four negative and four filler items on a five point scale. This was adjusted to a four point scale, ranging from *strongly agree* to *strongly disagree*, so as to be consistent with the Optimism and Pessimism Scale (OPS) which requires a forced choice answer, thereby eliciting either optimism or pessimism rather than allowing for a neutral answer that does not indicate either outlook.

Moderate to high internal consistency (with Cronbach's alpha being between .74 and .77), and a test-retest reliability of .79 has been established (Scheier & Carver, 1985). It has also been utilised in countries such as Australia, Brazil, China, Estonia, Ghana, Israel, Japan, Korea and Turkey (Fischer & Chalmers, 2008), as well as an SA sample of English and Afrikaans speaking participants, predominantly with a Matric education (Rothmann & Essenko, 2007).

The LOT-R was selected for inclusion due to its common usage in optimism research (Fournier et al., 1999), the usage of its original form, the Life Orientation Test, in previous

MS research (see Sinnakaruppan, Macdonald, McCafferty, & Mattison, 2010), and because it is a relevant measure of spes sclerotica given the more subtle nature of the original definition and description of this symptom. Furthermore, Burke et al. (2000) describe it as being advantageous to include measures of both the more stable trait optimism, such as this one, and of the more transient state optimism, such as the OPS, in research concerning optimism. The dependant variable relating to the LOT-R was defined by the total score for the optimism sub-scale. Possible answered ranged from 3 to 12, where higher scores indicated greater optimism. A participant was considered to have high optimism if their score fell within the 3rd quartile (i.e. 75% or more, or 9 or more) based on the minimum and maximum values of the scale.

Neuropsychiatric inventory (NPI). Originally developed to assess neurobehavioural and psychiatric disturbances in dementia, the NPI (Cummings et al., 1994) requires participants' informants to provide information on twelve disturbances of mood and behaviour, including euphoria (in terms of only abnormally positive mood), in order to determine the prevalence of neuropsychiatric symptoms in the participant. A standardised script, for each domain, is read to the informant. Each symptom is rated based on its frequency, ranging from 1 (*occasionally-once a week*) to 4 (*very frequently-once a day*), and its severity 1 (*mild*) to 3 (*marked*), with total scores ranging from 0 to 144. Although usually administered only to the informant, it was also administered to the participants themselves in this research so as to ascertain their perspective on their mood and/or behavioural difficulties.

The NPI has well-established high content and concurrent validity and reliability (Cummings, 1997) and has been validated amongst MS patients (Benedict et al., 2001). Prior studies using the NPI have also been conducted using SA samples (see Feldman et al., 2010; Goldwurm et al., 2006; Rockwood, Mintzer, Truyen, Wessel, & Wilkinson, 2001), indicating the applicability of this measure within the current context.

It was included as a measure of euphoria sclerotica due to its common usage by the contemporary literature in identifying the presence of "euphoria" among patients with MS (see, e.g., Benedict, Carone et al., 2004; Figved et al., 2005; Sanfilipo et al., 2006). Additionally, it was included as a measure of eutonia sclerotica, or awareness of mood and/or behavioural abnormalities, by way of participant/informant discrepancies on the various items. The dependant variable relating to the NPI as a measure of euphoria was defined by the presence of euphoria in terms of a yes/no answer by the informant and participant. The dependant variable relating to the NPI as a measure of unawareness of mood and/or

behavioural abnormalities was defined via the discrepancy between the participants' self-reports of their mood and behaviour and the informants' perceptions of the participants' behaviour. Discrepancy scores could range from 0 to 144 where higher scores indicated greater unawareness.

Optimism and pessimism scale (OPS). The OPS (Dember, Martin, Hummer, Howe, & Melton, 1989) consists of 18 positive, 18 negative items, and 20 filler items and requires participants to indicate their agreement with each statement on a four point (forced choice) scale, ranging from *strongly agree* to *strongly disagree* (see Appendix F5).

The optimism sub-scale has been shown to be both valid and reliable, with a coefficient alpha of .83 (Dember et al., 1989). Although created in a developed country, it has been used to determine optimism in a culturally diverse sample from Queensland, Australia, with a high school education (Creed, Patton, & Bartrum, 2002) which may indicate its applicability to a diverse SA context.

It was included because it measures several optimistic areas relevant to the current investigation, including the participants' outlook on life and the future, as well as their expectations regarding their personal situation, which is line with the original classical description of the construct. Additionally, it was included based on its previous use within MS research on optimism (see Fournier et al., 1999). The dependant variable relating to the OPS was defined by the total score for the optimism sub-scale. Possible answers ranged from 18 to 72, with higher scores indicating greater optimism. A participant was considered to have high optimism if their score fell within the 3rd quartile (i.e. 75% or more, or 58 or more) based on the minimum and maximum values of the scale.

Physical ability scale (PAS). A simple scale of physical ability could not be located at the time of preparing this study. Therefore, one was created by the researcher loosely based on the physical items of the Patient Competency Rating Scale (PCRS; Prigatano & Fordyce, 1986; which is a 30-item self-reflexivity rating scale that assesses an individual's ability to perform a variety of physical, cognitive and behavioural tasks), and the physical items of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36; Ware & Sherbourne, 1992, a questionnaire regarding various aspects of health) (see Appendix F6). Participants and informants were asked to respond to the various items by answering *cannot do*, *a little problem*, or *no problem*.

As with the other measures of awareness, participants and informants completed this questionnaire in order to determine discrepancies between the two, but the informants'

ratings were also used as a measure of each participant's severity of disability. The dependant variable relating to the PAS in terms of disease severity was defined by the total score of the informants' report. Possible answers ranged from 0 to 28, with higher scores indicating greater physical disability. The dependant variable relating to the PAS in terms of unawareness of physical deficit was defined via the discrepancy between participants' self-reports of their abilities and the external criterion of the informants' perceptions of the participants' physical abilities. Discrepancy scores could range from 0 to 28, with higher scores indicating greater unawareness.

Positive and negative affect schedule (PANAS). The PANAS (Watson, Clark, & Tellegen, 1988) requires participants to respond to 10 positive and 10 negative questions by rating how they are currently feeling on a five point Likert-type scale, ranging from *very slightly or not at all* to *extremely*.

The positive sub-scale has high internal consistency, with a Cronbach's alpha of .89, and has established reliability and validity (Crawford & Henry, 2004). It has also been used within an SA context (see Getz, Chamorro-Premuzic, Roy, & Devroop, 2012; van Zyl & Rothmann, 2012).

The PANAS was selected as it has been used in previous MS research concerning affect (see, e.g., Christodoulou et al., 2009; Fournier et al., 1999) and was an appropriate measure of euphoria sclerotica, or positive affect, as it assesses more general or subtle positive mood which is in line with the original description or definition of euphoria sclerotica. The dependant variable relating to the PANAS was defined by the total score of the positive sub-scale of the PANAS. Possible answers ranged between 10 and 50, with higher scores indicating greater positive mood. A participant was considered to have high euphoria sclerotica if their score fell within the 3rd quartile (i.e. 75% or more, or 40 or more) based on the minimum and maximum values of the scale.

Table 4

The Neuropsychological Measures Pertaining to the Euphoria (and Depression)

Domain	Measure
Depression	BDI-FS
Euphoria sclerotica	CWQ
(positive mood)	NPI (euphoria question only)
	Positive sub-scale of the PANAS
	Well-being sub-scale of the ISS
Eutonia sclerotica	CWQ
(unawareness of deficit)	Participant/informant discrepancies on:
	• PAS (physical)
	• AI (cognitive)
	• NPI (mood/behavioural)
Spes sclerotica	CWQ
(optimism)	Optimistic sub-scale of the OPS
	Optimistic sub-scale of the LOT-R
	Number of unrealistic responses on the CRJRF

Note. BDI-FS = Beck Depression Inventory-Fast Screen; CWQ = Cottrell and Wilson (1926) questionnaire; NPI = Neuropsychiatric Inventory; PANAS = Positive and Negative Affect Schedule; ISS = Internal State Scale; PAS = Physical Ability Scale; AI = Awareness Interview; OPS = Optimism and Pessimism Scale; LOT-R = Life Orientation Test-Revised; CRJRF = Comparative Risk Judgement Rating Form.

Measures of cognition. In line with previous research as well as with the current aims of this research study, measures assessing the typical executive functioning domains found to be impaired in patients with MS were included. As an additional aim was to investigate the possibility of cortical versus subcortical involvement, as well as right versus left hemispheric involvement, measures pertaining to both left and right cortical involvement were also included.

All participants were fluent in English and were thus assessed in English. However, a number of participants were first language Afrikaans and three exceptions were made for measures heavily dependent on language: the Boston Naming Test Short Form (BNT-SF), the Controlled Oral Word Association Test (COWAT) and the Colour Word Interference Task (CWIT). The procedure followed in each case will be discussed under each relevant measure.

The measures were not being used for diagnostic purposes, but merely for comparison with various control groups, including the HC group which served as a normative group regarding performance on these tests. Thus, although the majority of the measures were developed in first world countries, this was not deemed to be problematic. The majority of participants (or at least those from the MS and HC groups) were, again, also white/Caucasian,

and therefore similar to the cultures in which the measures were produced, but cross-cultural applicability of the measures will be described where possible. The measures will be presented in alphabetical order.

Aprosodia battery (ApBat). The ApBat (Ross, Thompson, & Yenkosky, 1997) is a test of RH functioning. In it, participants are played pre-recorded audio clips and are required to either discern the appropriate emotion of the spoken speech on the audio clip, or to repeat the speech and affective prosody of the clip. Formal studies of the reliability and validity of the ApBat have not yet been conducted. The battery is, however, known to be sensitive to impairments associated with both left and right hemisphere stroke (Ross et al., 1997), as well as patients with MS (Beatty et al., 2003). This was, however, within an American population and since the test uses audio clips of an American accent, it may not be entirely appropriate for an SA context.

The ApBat was never-the-less included as a measure of RH cortical (language) functioning, in terms of the repetition and comprehension of the affective prosody of speech, as it is comparable to that of the left hemispheric structural language tests of repetition and comprehension, and because this is in line with the aim of investigating the right versus left/executive hypothesis. In addition, it has been used in other MS research (see, e.g., Beatty et al., 2003). The dependent variables 'prosodic repetition' and 'prosodic comprehension' were defined in terms of the total number of correct responses, with prosodic repetition being rated by three independent raters. Higher scores indicated a better performance.

Boston naming test- short form (BNT-SF). The BNT-SF (Mack, Freed, Williams, & Henderson, 1992) is a measure of left hemispheric functioning. The full measure requires patients to name 60 black and white line drawings; however, in order to reduce testing time, the short form (which includes 15 black and white line drawings and has been validated, and found to identify anomia equally as well as the longer version; Graves, Bezeau, Fogarty, & Blair, 2004) was selected. The short version has been found to correlate strongly with the original version (.97; Mack et al., 1992). Participants were asked to name each drawing. First language was taken into account and if the participant could not name the item in English, the Afrikaans name was accepted. If a participant was unable to name the item spontaneously in either language, this item was skipped until the end of the test when a choice of four words, one of which was the correct name, was given and participants were asked to select the correct name. This was done in order to ascertain, for the purposes of the feedback form for

each participant, whether they knew the word but could not name it, or whether they simply did not know the word.

The Boston Naming Test is a well-used and well recognised test of confrontational naming ability and was included based on its extensive previous use in research among patients with MS (see, e.g., Beatty, W., Goodkin, Monson, Beatty, P., & Hertsgaard, 1988; Kujala et al., 1996; Henry and Beatty, 2006). This version has also been used with success within an SA context (Baerecke, 2013). The dependent variable 'naming' was defined by the total number of correctly named items. Higher scores indicated a better performance.

Brief visuospatial memory test-revised (BVMT-R). Assessing visual memory (i.e. RH cortical), the BVMT-R (Benedict, 1997; Benedict, Schretlen, Groninger, Dobraski, & Shpritz, 1996) requires participants to recall a matrix of six geometric designs, presented in a 2x3 matrix for 10 seconds per trial, across three trials. Without re-presenting the designs, delayed recall and a forced choice yes/no recognition task of the six designs (with another six distractor designs) are assessed after a 25 minute delay interval. Because confounding variables such as weakness and incoordination may affect the drawings of the patients, no time limit was imposed, and, in accordance with the Minimal Assessment of Cognitive Function In MS (MACFIMS) recommendation, motor problems evident on a copy trial were taken into account when scoring design accuracy (Benedict et al., 2002). It has also been validated amongst MS patients as part of the MACFIMS (Benedict et al., 2006).

The BVMT-R was selected as a measure of visuospatial memory due to its recommendation over other visual memory tests and its inclusion in the MACFIMS (Benedict et al., 2002). It has also been used in a number of studies in sub-Saharan Africa (Kanmogne et al., 2010; Spies, Fennema-Notestine, Archibald, Cherner, & Seedat, 2012), indicating its applicability for diverse cultures similar to those found in SA. In addition, it was included as it, like the Rey Auditory Verbal Learning Test (RAVLT), includes both a measure of learning as well as of recognition and will, thus, not only provide a comprehensive measure of visuospatial memory, but will also allow for direct comparison of performance with that of audio-verbal memory. The dependent variables 'visual learning', 'visual memory' and 'visual recognition' were defined as the total learning score over the three trials, the total score in relation to correctly recalled designs on delayed recall, and the total number of correctly identified designs on recognition as rated by three independent raters. Higher scores indicated a better performance.

Controlled oral word association test (COWAT). The COWAT (Benton & Hamsher, 1989) is a measure of verbal fluency (i.e. subcortical executive functioning) and requires patients to generate as many words as possible, in one minute, that begin with each of the three specified letters (F, A, and S) which are presented individually. Although all participants were fluent in English, those who were first language Afrikaans were given the option of alternate letters (B, R, and S) which are considered to be more linguistically equivalent to the English letters in terms of frequency of use across the Afrikaans language and have been used in SA samples of Afrikaans participants (O'Leary, 2013). Patients are prohibited from using proper nouns or the same word with different endings (e.g. pot, pots, potter, potting). The COWAT has a reported reliability coefficient of approximately .70 (Lezak, Howieson, Loring, Hannay, & Fischer, 2004). It has also been validated amongst MS patients as part of the MACFIMS (Benedict et al., 2006).

Henry and Beatty (2006) demonstrated that tests of category or semantic fluency are able to distinguish MS patients from controls equally as well as tests of phonemic, or letter, fluency such as the COWAT. However, semantic measures are very often used in conjunction with, or secondary to, tests of phonemic fluency (Beatty, W., Goodkin, Monson, & Beatty, P., 1989; Kujala, Portin, & Ruutiainen, 1997). The COWAT was, therefore, selected for inclusion as a measure of verbal fluency or generativity, based on its use within MS research, often as the only measure of verbal fluency (see, e.g., Olivares et al., 2005; Nocentini et al., 2006), and because of its inclusion in the MACFIMS (Benedict et al., 2002). It is also a very popular measure of verbal fluency and in the same review of which tests neuropsychologists most often use, it was said to be used 81% of the time by the more than 200 Australian neuropsychologists involved in the study (Sullivan & Bowden, 1997). Furthermore, applicability for an SA context has been demonstrated (Mattson, Berk & Lucas, 1997). The dependent variable 'verbal fluency' was defined as the total number of permitted words generated across all three trials, with higher scores indicating a better performance.

Cube analysis (CA). CA or the block counting test (from the Stanford-Binet intelligence scale; Terman & Merrill, 1973), a measure of visuospatial ability (i.e. RH cortical) consists of fourteen two dimensional drawings representing blocks or cubes arranged in two or three dimensional patterns. Participants are asked to count the number of blocks or cubes in each design after attempting a practice item. It was explained to them that if a block should be there, but is not visible, they should include it.

The CA test was included as a measure of visuospatial perceptual ability based on its prior use within research in this area among MS patients (Vleugels et al., 2000). The dependent variable 'visuospatial perception 3D' was defined via the total number of correct responses. Higher scores indicated a better performance.

Delis-Kaplan executive function system (D-KEFS) sorting test (DST). The DST is a measure of functions sub-served by the dorsolateral prefrontal cortex, thus it was a measure of cortical executive functioning. Standard administration of the DST (Delis, Kaplan, & Kramer, 2001) requires patients to sort the cards into two groups, with three cards in each group, according to as many different concepts (either verbal-semantic or visuospatial) as possible, and to continue, in the recognition or cued condition, until all categories have been identified. However, in order to reduce testing time and to minimise anxiety and/or frustration that may impact on the remainder of the testing session, and in accordance with the MACFIMS recommendation (Benedict et al., 2002), only the free sorting condition was administered. The DST free sorting condition has good internal consistency, between .72 and .86 for adults, and moderate test-retest reliability, between .46 and .73 for adults (Delis et al., 2001). It has also been validated amongst MS patients (Parmenter et al., 2007b) and as part of the MACFIMS (Benedict et al., 2006). Furthermore it has been used previously within an SA context (Mosdell, 2013) indicating its appropriateness for the current sample.

The DST was selected as a measure of abstract reasoning because (a) it was revised from its predecessor, the California Card Sorting Test (CCST), to include 16 possible concepts or categories, instead of only 8 (Beatty, Jocic, Monson, & Katzung, 1994); (b) it has been shown to discriminate MS patients from controls better than comparative tests such as the Wisconsin Card Sorting Test (Parmenter et al., 2007b); (c) use of the DST, and its previous version, the CCST, has been demonstrated in MS research (see, e.g., Beatty, Hames, Blanco, Paul, & Wilbanks, 1995; Lovera et al., 2010); and (d) it was recommended for inclusion in the MACFIMS, the well-known and well-used measure of cognitive dysfunction among MS researchers (Benedict et al., 2002). Although numerous dependent variables are examinable, the dependent variable 'abstract reasoning' was defined in terms of the scaled score of total number of correct card sorts, with higher scores indicating a better performance.

D-KEFS colour word interference task (CWIT). The CWIT (Delis et al., 2001), a measure of functions sub-served by the orbitobasal frontal cortex (i.e. cortical executive functioning) is a modification of the Stroop test (Stroop, 1935) and is made up of four trials.

The first two control for visual or reading impairment. The third is an inhibition trial, and requires participants to inhibit the propensity for reading the word by naming the ink colour instead when presented with the words "red", "green" and "blue" printed incongruently in red, green or blue ink. The fourth is a set-shifting trial which requires participants to alternate between naming the ink colour as in the third trial, and reading the word when it is presented in a box. Afrikaans first language participants were given the option of completing this test in Afrikaans, however all participants chose to proceed in English. The CWIT has good internal consistency, between .72 and .86 for adults, and fairly good test-retest reliability, between .49 and .86 for adults (Delis et al., 2001).

It was included as a measure of inhibition, or the suppression of an overlearned verbal response, and switching or set-shifting due to its eminence as a measure of these domains (Spreen & Strauss, 1998), and because Fishman et al. (2004) found a correlation between dysexecutive disinhibition and euphoria in terms of the NPI but did not tested this cognitively. Its successful use has also been demonstrated in SA samples (Mattson et al., 1997; Mosdell, 2013). The dependent variables of 'disinhibition' and 'set-shifting' were defined both in terms of the scaled scores of time taken for each trial having taken the first two trials into account, as well as in terms of the scaled score error scores for both the inhibition and set shifting trials. Higher scores on all variables indicate a better performance.

Judgement of line orientation test (JLO). In the JLO (Benton, Sivan, Hamsher, Varney, & Spreen, 1994), (i.e. RH cortical) participants are presented with a visual array of numbered lines covering 180 degrees as well as two stimulus lines that correspond with two of the lines in the array. They are required to select a number from the array that correctly corresponds with each of the stimulus lines. The original JLO consists of 30 items, however in order to reduce testing time a short form was used. Various short forms are available, however many such as those using the first one to 15 items or those using only odd or even numbers have been criticised and excluded in favour of the Short Forms Q and S created by Qualls, Bliwise, and Stringer (2000). Short Form Q was utilised in the current study and has a reported internal consistency of .82 (Qualls et al., 2000).

The JLO was selected as a measure of visuospatial processing based on its (a) sensitivity to visuospatial perception and RH damage (Benton, Varney, & Hamsher, 1978); (b) extensive previous use, often as the primary or only measure of visuospatial processing, within MS patient groups (see, e.g., Benedict et al., 2000; Vleugels et al., 2000; Woolmore et al., 2008); and (c) recommendation by the MACFIMS expert panel (Benedict et al., 2002). It

is also considered to be a "culture-fair" test and has been used extensively in SA research (Venter & Bham, 2003, p. 34). The dependent variable 'visuospatial perception 2D' was defined via the total number of correct responses, and higher scores indicated a better performance.

N-back. The Paced Auditory Serial Addition Task (PASAT) is currently one of the most commonly utilised measures of cognitive dysfunction in MS, and is included in MS cognitive batteries such as the MACFIMS (Benedict et al., 2002) and the MS Functional Composite (Kalkers et al., 2000). However, it has been found to cause anxiety in patients with MS (Parmenter, Shucard, J., Benedict, & Shucard, D., 2006), sometimes resulting in them wishing to discontinue with testing (personal communication with Dr. D. Shucard, 15 March 2011). In addition, it does not include a measure of reaction time (Parmenter et al., 2006) and has been criticised for allowing for a "chunking strategy" that may aid or assist performance on the task (Fisk & Archibald, 2001). In contrast, the *n*-back task (Owen, McMillan, Laird, & Bullmore, 2005; Parmenter et al., 2006), (executive functioning) the primary measure within WM research, has been found to be less distressing and includes a measure of reaction time, which can be used to determine information processing speed (Parmenter et al., 2006). Furthermore, it has been demonstrated to discriminate MS patients from controls equally as well as the PASAT (Parmenter et al., 2006). Therefore, although it's psychometric properties of reliability are relatively poor (Jaeggi, Buschkuehl, Perrig, & Meier, 2010), it was included in the proposed study based on the aforementioned reasons.

While some MS studies have utilised the auditory version of the *n*-back (Form et al., 2007; Lengenfelder, Chiaravalloti, Ricker, & DeLuca, 2003), the standard visually presented *n*-back does not appear to be confounded by visuomotor abilities and the standard version of the *n*-back has been used within this patient group before (see, e.g., Parmenter et al., 2006; Sweet, Rao, Primeau, Durgerian, & Cohen, 2006). The same version has also been used as the sole measure of WM within other developing countries such as Korea (Chang et al., 2010), and within an SA context demonstrating its applicability for the current research (Human, 2010). The *n*-back usually involves three conditions (0-, 1-, and 2-back). The 0-back measures attentional abilities and also offers a reaction time for speed of information processing; while the 1- and 2-back conditions measure WM (and speed of information processing). However, the 2-back is more sensitive to WM impairments (Parmenter et al., 2006) and due to time constraints the 1-back was not included in this study. Patients were required to either identify a target letter (0-back, attention), or to compare each letter with the

letter presented two letters previously (2-back, WM), following a practice trial, by pressing one of two computer keys. Reaction time on the 0-back trial represented speed of information processing. The dependent variables 'attention' and 'WM' were defined as the total number of correct responses (on 0-back, out of 21, for attention and on 2-back, out of 27, for WM). A higher score indicated a better performance. The dependent variable 'speed of information processing' was defined as the total reaction time for all answered items, divided by the number of items answered (correct or incorrect). A higher score indicated a poorer performance.

Rey auditory verbal learning test (RAVLT). In the RAVLT (Lezak et al., 2004; Rey, 1964), (verbal memory, left cortical) participants are read a list of 15 unrelated words (List A) five separate times and are asked to recall the list in no particular order each time. Following an interference trial (List B), participants are required to recall the List A again. Without presenting the list again, delayed recall and a forced choice yes/no recognition of List A (with an equal number of distractor words) are assessed after a 20 minute delay interval. High internal reliability (that of .90) and high test-retest reliability (that of between .60 and .70) are reported by Straus et al. (2006). Test re-test reliability of this measure has also been reported as being between .60 and .86 (Lezak et al., 2004).

The RAVLT was selected as a measure of audio-verbal memory because it includes a measure of learning as well as of recognition which is important when considering executive dysfunction in memory. It is also a very popular measure of verbal memory and in a review of which tests neuropsychologists most often use, it was said to be used 77% of the time by the more than 200 Australian neuropsychologists involved in the study (Sullivan & Bowden, 1997). Furthermore, it has been used within an SA sample before (Mattson et al., 1997). The dependent variables 'verbal learning', 'verbal memory' and 'verbal recognition' were defined as the total learning score over the five trials, the total number of correctly recalled words on delayed recall, and the total number of correctly identified words on recognition. Higher scores indicated a better performance.

Rey-osterrieth complex figure (ROCF). The standard administration of the ROCF (Osterrieth, 1944; Rey, 1941), (i.e. RH cortical) requires participants to copy a complex geometric design, by drawing it freehand (the use of rulers is prohibited) directly below the original, to reproduce it from memory directly after the copy trial, and to then recall it again following a delay. However, in the current study, only the copy trial was administered and

timed, both in order to minimise any distress caused by motor or memory difficulties and because a second measure of visuospatial memory was deemed unnecessary for this study. The ROCF was selected based on its versatility as a test, measuring a number of different abilities, its use within studies of patients with MS (see, e.g., Benedict et al., 1996; Benedict et al., 2000; Schulz et al., 2006), and its prior use within SA samples of similar demographics (Mattson et al., 1997; Mosdell, 2013). Another popular measure, it was said to be used 88% of the time by the Australian neuropsychologists involved in the study concerning which tests are used most often by neuropsychologists (Sullivan & Bowden, 1997).

It was included in this study to assess visuospatial construction. Because confounding variables associated with motor difficulties can affect drawing, in line with the BVMT-R no time limit was imposed and evident motor problems were taken into account when scoring design accuracy. Copies were scored both according to structural accuracy and placement. The dependent variables 'visuospatial construction' was, therefore, defined by the total construction score (out of 36), as per the scoring criteria set out by Canham, Smith, and Tyrrell (2000), as rated by three independent raters. Higher scores indicated a better performance.

Western aphasia battery (WAB). The WAB (Kertesz, 1982) is a measure of language ability (i.e. left cortical functioning). In the auditory repetition test of the WAB, participants are read words, short phrases or long sentences and asked to repeat them using the same words, structurally. In the auditory comprehension test, participants are read sentences such as 'Is your surname are Brown?', and 'Do you eat a banana before you peel it?', and are asked to correctly answer yes or no by listening to the structure of the words.

These WAB sub-tests were included as they are comparable with the ApBat sub-tests described above. Additionally, there were included as recognised measures of left hemispheric cortical functioning and distinguish patients with left from those with right hemispheric damage (Lezak et al., 2004). They are often used by the speech therapists at GSH, and have been used in other SA research using similar sample demographics (Frankel, Penn, & Ormond-Brown, 2007; Penn, Jones, & Joffe, 1997).The dependent variables 'repetition' and 'comprehension' were defined in terms of the total number of correct responses. Higher scores indicated a better performance.

Data analysis. The majority of the data in this study was quantitative, but a small qualitative component was included to supplement the largely quantitative data. As different

approaches to analysis were used for these different types of data, they will be discussed separately below.

Quantitative data. All quantitative data analysis was run using the Statistical Package for the Social Sciences (SPSS), version 21.0 (SPSS Inc., 2012). Before beginning inferential analysis, I ensured that the data met the assumptions underlying each proposed statistical analysis, and unless specified, all of the required assumptions were upheld for each analysis.

Before discussing the relevant statistics, I would like to mention that for all analyses I set my significance level to $\alpha = .01$ due to the number of variables investigated in this research and to the increased risk for familywise error. In addition, I would like to acknowledge the risk of false discovery in this study due to the number of inferential tests included. However, due to the exploratory nature of this research, and to the in-depth and complex nature of its subject matter, the number and types of analyses included were deemed necessary. This issue is discussed further in the general discussion towards the end of this dissertation.

The statistical analyses used. Descriptive statistics were used to describe a number of variables. A variety of correlational analyses were also used. Pearson correlations were used when both variables were continuous, Phi correlation coefficients were calculated when both variables were dichotomous, and point-biserial correlation coefficients were used when one variable was dichotomous and the other continuous (Howell, 2004).

For all factor analyses, a principal components method was selected, using a promax rotation and the suppression of coefficients of .400 or below (Field, 2005). Two types of extraction methods were used based on the aims of the analysis: a fixed factor solution of either three or two factors, and an extraction criterion based on eigenvalues of greater than one. For each factor identified (made up of more than one variable), a Cronbach's α was calculated to determine the internal consistency of the factor.

Multiple regression analyses were used to determine which of a number of independent variables predicted one continuous dependent variable. Various aims meant that I used a hierarchical regression model and entered specific variables into the model first (Field, 2009). All variables were entered using the "enter" method. When an individual variable was found to significantly predict the particular type of euphoria being investigated, that variable was tested further in a separate linear regression model.

When group differences were expected, I reported 1-tailed *p* values. Independent samples *t*-tests were used to compare two groups on continuous data that was normally distributed. Mann Whitney *U*-tests were used to compare two groups on continuous data that was not normally distributed. Chi-squared tests of independence were used to compare two groups on categorical data. In terms of the independent samples *t*-tests, when Levene's test for homogeneity of variance was significant, the results for "equal variances not assumed" were reported. The relevant effect sizes (i.e. Cohen's *d* and Cramer's *V*) were calculated where appropriate.

When two groups were compared, while controlling for pre-existing group differences, Analysis of Covariance (ANCOVA) was used. While not all data was completely normally distributed across groups, it largely did not violate this assumption, and was used when all other assumptions were met as ANCOVAs are considered to be fairly robust (Levy, 1980; Lund Research Ltd, 2013). Eta-squared values were calculated using the corrected total, and represented the effect size for these analyses (Field, 2009).

Inter-rater reliability. Inter-rater reliability was determined via single measures intraclass correlation coefficients (ICC) for instances where continuous variables were rated by three raters. One measure was rated according to four categories by 15 raters, and for this, the average percentage of agreement was calculated for the category selected by the majority of the raters.

Creation of composite variables. A number of composite variables were created, both for some of the euphoric measures, in order to allow for analysis of the euphoric types identified by this research, and for the majority of the cognitive measures, in order to reduce the number investigated. In order to create these, a factor analysis was first run to identify which individual (continuous) measures loaded onto common factors. In order to further test their applicability to form one composite variable, Pearson correlations were run on the relevant individual variables for each factor, to compare each variable with the others. A composite variable was then created for well correlated variables by first adjusting the scales of all relevant individual variables for that factor/composite to begin at the same minimum value. The variance of each scale was then determined and the scales with smaller variance were adjusted to have the same variance as the scale with the largest variance. All scales were then added to form the composite. Rather than taking the Beta weights or the mean of the z-scores, which would have resulted in differing variances across the different groups, the

method just described was chosen in order to be able to obtain a standardised minimum and maximum score for the scale, and to compare different groups on the same scale, with the same degree of variance.

Calculation of moderate and high levels. Two cut-off points were imposed upon various continuous scales. For this, each scale was divided into quartiles and scores falling within the top quartile (i.e. above the 75% cut-off point), according to the full scale's minimum and maximum values, were considered to denote high levels of the symptom. Consequently, participants scoring within this range were termed *high-scorers*. Scores falling between the 50% cut-off point and the 75% (high) cut-off point were considered to denote moderate levels of the symptom, and participants scoring within this range were termed *moderate scorers*.

Qualitative data. A small sub-section of the results section was dedicated to a qualitative description of the euphoric nature of the MS participants in terms of an analysis of open-ended questions of, and relating to, the CWQ. These qualitative data were analysed using content analysis. This involved coding the qualitative data collected from the interviews and organising it into conceptual frameworks in order to identify common themes (Brink, 2006).

Verbatim transcription of the recorded interviews allowed for a greater efficiency of content analysis (Smith et al., 1995), and transcripts were read and re-read to identify and index the themes and categories. These were then examined by constant comparison where each item was checked or compared with the rest of the data to set up categories (Pope & Mays, 1999). The steps employed in this study included (Holloway, 2008):

1. Reading the data for meaning
2. Making sense of the data
3. Organising and ordering the data according to content
4. Describing and summarising the data
5. Dividing the data into segments
6. Coding (labeling or naming) sections of the data
7. Reducing (or collapsing) the codes to larger categories or themes

Results

In the following sub-sections I report the results of this research. Due to the scale and the complex nature of this study, I have divided this section into three parts. Part one pertains to the euphoric constructs and includes results based on the full sample of MS participants (n = 100). Part two better defines the symptom of euphoria in light of the findings regarding the constructs that underpin it. Here results are presented based on both the full sample of MS participants (n = 100) and the sub-sample who underwent cognitive testing (n = 60). The MS group is also compared with the full HC group (n = 100) and the sub-group of HCs who underwent cognitive testing (n = 35) in this sub-section. In part three, I present the provisional results concerning the causes of euphoria. First, the sub-samples of the patient control groups that underwent cognitive testing (i.e. 10 MGs, 10 MVA TBIs and 10 NP-SLEs) are compared with the sub-sample of MS participants who underwent cognitive testing (n = 60) to assist in evaluating the suitability of these control groups to test their relevant research questions. Then, the full MS group (n = 100) is compared with the full sample of each of these patient control groups to test the various hypotheses presented regarding the cause of euphoria via a limited pilot study: (a) a psychological reaction to a disabling disease, MG (n = 20); (b) executive dysfunction, MVA TBI (n = 19); (c) immunological disease processes, NP-SLE (n = 10); and (d) RH involvement, RH (n = 10).

Part one. Addressing discrepancies and defining euphoria

The main aim of part one was to investigate the constructs of euphoria further in order to gain a deeper and clearer understanding of what they entail. Differences between the classical and contemporary definitions of euphoria, in terms of the number of types, the definitions of those types, and the frequencies of those types was investigated by using a classical (i.e. the CWQ) and the popular contemporary measure (i.e. the NPI) of euphoria. Since, in the first sub-section I compared the descriptions that have been presented in the literature, I proposed, rather than hypothesised in the empirical sense, that a change in the number of types has occurred. I also proposed that a change in the definition of these types has occurred and that the euphoria measured today does not have the same quality as that described and measured by the classical literature. In the latter sub-section I was able to test my suppositions using data gathered in this study. Therefore, I hypothesised that differing measurement instruments, using these different definitions, would influence the rates of euphoria found in MS patients, and that high rates of euphoria would be replicated by using the classical

description/definition and measure, and that low rates of euphoria would be replicated by using the contemporary description/definition and measure.

An attempt was then made to determine how many types of euphoria really do exist. Aspects surrounding the definitions of those types of euphoria were then addressed and further issues regarding the frequencies of those types in a sample of 100 MS participants were addressed. As I approached this question from the original classical view, I hypothesised that more than one type of euphoria exists, and, that the frequencies of these types would be closer to that of Cottrell and Wilson (1926) than the frequencies found today.

Classical versus contemporary measures. First, the questions concerning the number of types of euphoria, the definitions of those types, and frequencies of those types will be addressed by using a classical and the contemporary measure.

Descriptions and definitions of euphoria can be found dating back to 1850, however the most comprehensive definition, and one that was maintained for a number of years after its conception, was that of Cottrell and Wilson (1926). The questionnaire used to measure these three types, published by Cottrell and Wilson (1926), was therefore used to represent the classical view of euphoria in terms of number of types of euphoria, the definitions of those types and the frequencies of those types.

The measure most often used today is the NPI. As it is the gold standard measure of euphoria in the 21st century, this measure was used to represent the contemporary view of euphoria in terms of the number of types of euphoria, the definitions of those types, and the frequencies of those types.

Number of types and definitions of the types of euphoria. A major discrepancy noticed in the literature relates to the definition of euphoria, both in terms of how many types it consists of, and in terms of the definitions of those types. Thus, this study aimed to address this discrepancy and I proposed that a change in the number of types has occurred since the original definition of Cottrell and Wilson (1926), and that the euphoria measured today does not have the same quality as that described/defined and measured by the classical literature. This was analysed both qualitatively and later quantitatively. The qualitative description of the popular measures used is presented first.

The classical view. Cottrell and Wilson (1926) described euphoria in terms of the following: (a) euphoria sclerotica, referred to "the mental state of cheerfulness, happiness,

ease... in which the prevailing mood is one of serenity and cheerfulness"; (b) eutonia sclerotica, referred to feeling "physically well tuned up, [as though] the [patient] 'could do anything'" and where patients "are not conscious of physical disability"; and (c) spes sclerotica, which referred to "an optimism as to the future and the prospects of ultimate recovery which is out of place and incongruous" (p. 8). From this it can be seen that they defined three types of euphoria.

Further definition of each of the types can be found by way of the measuring instrument used to measure these symptoms. For example, for euphoria sclerotica, Cottrell and Wilson (1926) asked their patients: "Describe in a few words your general or usual mood. Do you feel consistently cheerful or happy? Do you feel consistently sad or unhappy? Are you easily amused by what you see?" (p. 4-5).

Eutonia sclerotica could also be defined in terms of its questions: "Describe your bodily feeling as a whole. Are you conscious of any pleasant or unpleasant sensation in your body as a whole or a part? Is the feeling one of bodily ease? Is the feeling one of contentment? Is the feeling one of pleasure? Is your general feeling one of malaise?" (Cottrell & Wilson, 1926, p. 5-6).

Finally, spes sclerotica could be further defined via the questions used to measure this symptom, including, "Are you naturally optimistic? Are you naturally pessimistic? Are you optimistic or pessimistic in reference to your disease?".

The contemporary view. In contrast, researchers today present a number of differing views concerning euphoria. As addressed in the literature review, reviewers such as Ghaffar and Feinstein (2007) amalgamate all three of the classical types into one. Some researchers, like Carone et al. (2005), confuse euphoria sclerotica and eutonia sclerotica and state that measuring the one type means that the other type exists. Others, for example Diaz-Olavarrieta et al. (1999), acknowledge eutonia sclerotica but measure only positive mood, and some ignore all the other types of the classical definition and focus only on positive mood (the euphoria sclerotica type; see ,e.g. Kesselring & Klement, 2001).

Whether they acknowledge the other types or not, the dominant measure of euphoria today is the NPI. But this measure only measures the positive mood aspect (or the aspect most similar to the euphoria sclerotica of the classical definition).

While the classical definitions of each of the types of euphoria was put forward by the same team of researchers that created the three types, as highlighted above the NPI only addresses positive mood and thus definitions of the remaining types cannot be addressed

from the perspective of this measure alone. There are, however, many differing views among contemporary researchers regarding the definitions of euphoria and, despite the fact that this section was to be approached from the perspective of the two measures cited, these contemporary definitions need to be addressed. For consistency, I will approach the various definitions from the theoretical framework of the original three types.

Originally known as euphoria sclerotica, positive mood is now termed euphoria and definitions range from subtle or more mild mood states such as a "mental… well-being" (Ghaffar and Feinstein, 2007, p. 280), a "persistent cheerfulness" (Rodgers and Bland, 1996, p. 442), "a type of mood characterised by inappropriate/inadequate serenity (in view of the physical disability)" (Kesselring and Klement, 2001, p. 182), an "unusual cheerfulness" (Diaz-Olavarrieta et al., 1999, p. 55), and a "fixed state of well-being" (Feinstein, 2007, p. 75), to more extreme definitions including "a change in trait or character that includes rapid vacillations in mood (including anger, dysphoria, and euphoria)" **(**Benedict et al., 2001, p. 75), "a syndrome characterized by euphoric mood state, social disinhibition, impulsivity, and emotional lability" (Carone et al., 2005, p. 574), and descriptions of these euphoric patients being "impatient, inconsiderate, and quarrelsome" (Fishman et al., 2004, p. 354). The popular measure of euphoria, the NPI, also appears to focus more on the extreme end of the description and asks, "Does the patient seem too cheerful or too happy for no reason? I don't mean the normal happiness that comes from seeing friends, receiving presents, or spending time with family members. I am asking if the patient has a persistent and abnormally good mood or finds humour where others do not" (Cummings et al., 1994).

Originally known as eutonia sclerotica, this aspect is now defined in terms of a "lack of concern about disability" (Diaz-Olavarrieta et al., 1999, p.55), "denial" (Benedict et al., 2001, p. 75), a "conviction that all is well and that they will walk again" (Feinstein, 2007, p. 75), a "cheery indifferen[ce] to their circumstances" despite severe cognitive impairment (Benedict et al., 2005, p. 32), as well as in terms of patient/informant discrepancies on cognitive testing and/or tests of personality change (Carone et al., 2005, p. 574).

Finally, originally known as spes sclerotica, contemporary definitions of optimism include, "overly optimistic" (Ghaffar and Feinstein, 2007, p.280), an "optimism about the future despite awareness of disability" (Rodgers & Bland, 1996, p.442), and "unrealistic optimism" (Benedict et al., 2001, p. 75).

Further comparisons. To remind the reader, the aim of this sub-section was to address the discrepancies in the definitions of euphoria between classical and contemporary reports, both in terms of the number of types of euphoria, and the definitions of those types.

In addition to the differences that can be seen in the descriptions reported in the literature, further differences between classical and contemporary definitions become evident when comparing the various popular measures of the constructs of positive mood, unawareness of deficit and optimism. To again remind the reader, although contemporary descriptions and definitions relating to the other two classical types (i.e. eutonia sclerotica and spes sclerotica) were described above, the popular contemporary measure (the NPI), and the definition from which contemporary euphoria was compared with Cottrell and Wilson's classical definition of euphoria, only addresses positive mood.

Before I can report these results, however, some explanation on the measures included in this research is required. First, the NPI (contemporary measure) was administered to both the informants who were asked about their loved-ones' positive mood (standard administration process), and to the participants themselves who self-reported the symptom of euphoria. A yes/no response was required for this measure and, as such, participants were classified as either having or not having euphoria.

Second, the CWQ (classical measure) was administered to the participants who self-reported feelings of positive mood, physical well-being and optimism as to the future. While Cottrell and Wilson (1926) published their questionnaire, they did not describe how the answers to these questions were used to determine the frequencies of their three types or even which questions referred to which of the types. Instead of grouping them per type, they labelled them according to "emotional content", "physical determinants", and "affective conduct". While "affective conduct" appeared to refer to their other area of interest (i.e. pathological laughing and crying), and "physical determinants" appeared to refer to eutonia sclerotica, no distinction was made between euphoria sclerotica or spes sclerotica within the first group of questions. Sugar and Nadell (1943), who attempted to replicate the original study, set out their results section in the same way as Cottrell and Wilson (1926) but also did not objectively state how they determined the frequencies reported in their study. As I also wanted to use their measure within a modern day sample of 100 MS participants, I conducted a preliminary study whereby 15 independent raters rated the questions according to whether they referred to euphoria sclerotica, eutonia sclerotica, spes sclerotica or "other" (which was a question deemed to be relating to something other than positive/negative mood, bodily feelings, or optimistic/pessimistic outlook). Of the 50 questions, 14 were deemed to relate to

euphoria sclerotica, 11 to eutonia sclerotica, four to spes sclerotica, and 22 to "other", and the percentage of agreement between the 15 raters for the category selected by the majority of raters for each question, ranged from 46.67% to 93.33% (see Appendix F3 for the categories of questions selected by the raters and the percentage of agreement for each question).

The answers of the 100 MS participants to the 14 identified questions for euphoria sclerotica, 11 for eutonia sclerotica and four for spes sclerotica (questions falling into the "other" category were excluded) were then rated by three different raters, according to the definitions of Cottrell and Wilson (1926) described earlier. Each rater was required to give an answer a rating of "0" if the type of euphoria was *absent*, and a "1" if the type of euphoria was *present*. However, the raters voiced some uncertainty with a number of answers and the category "1" was changed to represent a *possible presence* of the symptom (i.e. the participant answered some questions in a manner that indicated the definitive presence of the symptom, but other questions in a manner that seemed as though the symptom was absent), and "2" became representative of a *definite presence* of the symptom. Following further disagreement, and uncertainty regarding the interpretation of the answers, a specific rating criterion was created (see Appendix G for a detailed description of the criteria for definite presence and definite absence of euphoria sclerotica, eutonia sclerotica and spes sclerotica). and this was used to determine definite and possible cases of euphoria sclerotica, eutonia sclerotica and spes sclerotica, of which only the definite cases were used for the analyses below.

Third, additional modern measures, the majority of which had good psychometric properties, and are recognised measures of positive mood, optimism and unawareness, were included. Both informant based questions and self-report questionnaires administered to the MS participants were used. These were described in detail in the methods section, but the informant measures included Likert-type scales for mood (ranging from very happy/euphoric to very sad/depressed) and outlook (ranging from very optimistic to very pessimistic), and Likert-types scales for unawareness where the informant was asked to rate how aware/unaware they thought their loved-one was regarding any physical, cognitive and/or mood/behavioural difficulties (all scales ranged from 1 *very aware*, to 10 *very unaware*).

In terms of self-reported measures of positive mood (euphoria sclerotica), the positive sub-scale of the PANAS and the well-being sub-scale of the ISS were included. For optimism (spes sclerotica), the CRJRF and the optimism sub-scales of the OPS and LOT-R were used. Due to the slightly complicated nature of the measures pertaining to unawareness, these will be described in more detail. Although this research used the classical definitions as

a framework, it adopted a more modern approach to the measurement of eutonia sclerotica, and negative differences, where the participants under-estimated their difficulties as compared to their informants' reports, were considered to represent unawareness, a technique that is considered to be the gold standard method in research of awareness (see, e.g. Prigatano et al., 1990). Furthermore, instead of restricting eutonia sclerotica to unawareness of physical deficit alone (measured by the PAS), as per the definition of Cottrell and Wilson (1926), some of the researchers investigating euphoria in the 21st century (see, e.g. Carone et al., 2005) have examined unawareness in terms of personality and cognitive impairment, thus participant/informant discrepancies on additional measures which addressed unawareness of cognitive (i.e. the AI) and mood/behavioural changes (i.e. the NPI) were also included. These measures did not only refer to severe disability though, and included questions that related to extremely mild impairment, such as an ability to walk but not to run, or the ability to orient oneself to place and time but not to remember the word for something, or the absence of hallucinations or delusions, but the presence of sadness or depression. Thus, any participant experiencing even mild problems had the potential to be unaware, if they underestimated these mild problems in comparison with their informant. However, the greater the disability of the MS participant, the greater the potential for unawareness of these deficits.

Returning to the differences between the classical and contemporary measures: In terms of euphoria sclerotica, self-reports of euphoria according to the NPI (modern measure) did not correlate well with definite cases of euphoria according to the classical measure, by means of a Phi correlation (Φ = -.02, p = .809), or with high-scorers[5] on other modern self-report measures of more subtle positive mood: the positive sub-scale of PANAS (Φ = .12, p = .220), and the well-being sub-scale of ISS (Φ = -.08, p = .413) [6]. Whereas, although definite euphoria sclerotica (according to the classical measure) did not correlate with self-reported NPI euphoria (modern measure), it did demonstrate better correlations with high-scoring cases on the other modern measures of more subtle positive mood: positive sub-scale of PANAS (Φ = .17, p = .086), and well-being sub-scale of ISS (Φ = .30, p = .003).

[5] Described briefly in the section on data analysis, high-scorers refer to those participants who scored within the top quartile (75% or more) according to the scale's minimum and maximum.

[6] It should be noted here that the other modern self-report measures of positive mood correlated well with each other (r_{pb} = .73, p=.0001) and that cases representing high-scores on the one correlated well with cases representing high-scores on the other (Φ = .38, p = .0001). Therefore, the poor correlations presented in this section are not just the result of generally poorly correlated measures.

As mentioned, informant-based administration of the NPI was also investigated, as the NPI is traditionally an informant-based questionnaire and self-reported euphoria may therefore not correlate well with other measures. Like self-reported NPI euphoria, however, the informant-reported NPI euphoria also did not correlate with definite cases of euphoria according to the classical measure, in terms of a Phi correlation (Φ = -.02, p = .808), or with cases of high-scorers on the modern self-report measures of more subtle positive mood: positive sub-scale of PANAS (Φ = .06, p = .523), and well-being sub-scale of ISS (Φ = .06, p = .523).

In addition, the informant-based NPI euphoria ratings did not correlate well with other informant ratings of positive mood (where informants were asked to rate their loved-ones on a scale of 1 = *sad/depressed*, to 10 = *very happy/euphoric*), based on a point-biserial correlation (r_{pb} = .02, p = .858). In contrast, the definite cases of euphoria, in terms of the classical measure, did correlate with informant ratings of positive mood (r_{pb} = .26, p = .010).

Thus, self-reported or informant reported euphoria according to the more extreme definition of the NPI did not correlate well with (a) the more subtly defined positive mood of the classical CWQ, (b) the more subtly defined positive mood of the other modern measures (i.e. the PANAS and ISS), or (c) the more subtly defined positive mood ratings of the informants. In contrast, the measures of less extreme and more subtle mood (i.e. the other modern measures, the informant ratings, as well as the CWQ) appeared to correlate well with each other, indicating a distinction between the NPI and the other measures of positive mood.

In terms of eutonia sclerotica, further differences between classical and contemporary eutonia sclerotica, are also highlighted by correlations between the various measures investigated in this study. Definite cases of eutonia sclerotica according to the classical measure did not correlate well, via point-biserial correlations, with cases where there were negative discrepancies indicated unawareness of cognitive deficits[7] (r_{pb} = .01, p = .963), or cases where unawareness of mood/behavioural changes was indicated (r_{pb} = .15, p = .124). However, definite cases of eutonia sclerotica according to the classical measure did not correlate well with cases where unawareness of physical deficits were indicated either (Φ = .03, p = .800). Although this research approached the study of euphoria from the classical perspective of Cottrell and Wilson (1926), eutonia sclerotica was measured in terms of unawareness of physical deficit, which could be different from a sense of physical well-

[7] Described in greater detail in part two, unawareness was calculated via participant/informant discrepancies on particular questionnaires and a negative discrepancy between participant and informant ratings denoted those participants who underestimated their deficits, and were, thus, considered to be unaware.

being. This could be why these two measures were poorly correlated, but it also highlights the difference between these measures, and the definitions that underpin them.

Finally, with reference to spes sclerotica, further evidence for changes in definitions are again evident when comparing the measures investigated in this study. Definite cases of spes sclerotica in terms the classical CWQ correlated well, via a Phi correlation, with cases representative of high-scores on the optimism sub-scale of the OPS (Φ = .26, p = .010), and the optimism sub-scale of the LOT-R (Φ = .28, p = .005), which are general measures of optimism and of feelings about the future and are, thus, similar in nature to the original definition. In contrast, definite cases of spes sclerotica (classical measure) were not found to correlate well, via a point-biserial correlation, with the CRJRF which is a measure of unrealistic optimism (r_{pb} = .11, p = .280). Further, high-scoring cases on the more extreme CRJRF (unrealistic optimism) did not correlate particularly well with high-scoring cases on the measures of more subtle optimism: the OPS (Φ = .09, p = .367), and the LOT-R (Φ = .17, p = .091).

From the above descriptions it appears evident that a change in not only the number of types of euphoria, but also in the definitions of those types appears to have occurred between the original definition of Cottrell and Wilson (1926) and the contemporary definitions and measurement instruments of these constructs.

Frequencies of euphoria. Possibly the most obvious discrepancy between the classical and contemporary literature is that of the incidence of the types of euphoria within MS patients. The aim of this sub-section was therefore to address this inconsistency and I hypothesised that the various measurement instruments used by classical and contemporary researchers would influence the rates of euphoria found in MS patients. It was furthermore hypothesised that high rates of euphoria would be replicated by using the classical description/definition and that low rates of euphoria would be replicated by using the contemporary description/definition.

The classical view. In their 1926 article, Cottrell and Wilson (1926) reported high incidence rates of euphoria sclerotica (63%), eutonia sclerotica (84%) and spes sclerotica (84%) in their sample of 100 MS participants. However, as mentioned in the previous sub-section, they did not specify the rating criteria imposed to determine these frequencies and I therefore created my own rating criteria. Initially a present or absent criterion was used, but after concern was raised by the raters regarding a mixed picture in some answers, I had each

of the three raters give each answer a "2" if they considered the symptom to be definitely present, a "1" if the symptom was possibly present, and a "0" if the symptom was absent.

This resulted in the following frequencies (see Table 5 below).

Table 5

Rater Frequencies of CWQ Euphoria Sclerotica, Eutonia Sclerotica and Spes Sclerotica, Amongst the MS Participants (n = 100)

	Euphoria sclerotica			Eutonia sclerotica			Spes sclerotica		
	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**
#1	23%	38%	**61%**	10%	39%	**49%**	38%	33%	**71%**
#2	21%	47%	**68%**	7%	27%	**34%**	15%	62%	**77%**
#3	6%	40%	**46%**	9%	40%	**49%**	12%	61%	**73%**

Note. Total frequencies are presented in bold font. Def. = definitely present; Pos. = possibly present; Tot. = total.

Inter-rater reliability of the three raters, according to a single measures intraclass correlation coefficient, was moderate, although still significant: (a) ICC = .50 for euphoria sclerotica, (b) ICC = .33 for eutonia sclerotica, and (c) ICC = .56 for spes sclerotica (all p values < .0001).

Raters again voiced their difficulties in interpreting the answers and it was discovered that each was using slightly different criteria. Consensus was then reached as to specific rating criteria (again, see Appendix G), and the following frequencies of the three euphoric types were found (see Table 6 below), with a much improved inter-rater reliability of: (a) ICC = .82 for euphoria sclerotica, (b) ICC = .60 for eutonia sclerotica, and (c) ICC = .90 for spes sclerotica (all p values < .0001).

Table 6 *Rater Frequencies of CWQ Euphoria Sclerotica, Eutonia Sclerotica and Spes Sclerotica (with Rating Criteria in Place), Amongst the MS Participants (n = 100)*

	Euphoria sclerotica			Eutonia sclerotica			Spes sclerotica		
	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**
#1	21%	39%	**60%**	10%	36%	**46%**	37%	32%	**69%**
#2	27%	38%	**65%**	7%	33%	**40%**	41%	34%	**75%**
#3	22%	43%	**65%**	10%	42%	**52%**	37%	37%	**74%**

Note. Total frequencies are presented in bold font. Def. = definitely present; Pos. = possibly present; Tot. = total.

The average of all three raters was then calculated and rounded up or down to the nearest whole number, with "0" again indicating an absence of the symptom, "1" again indicating a confused or mixed picture which led raters to select a possible presence, and "2" the definite

presence of the symptom. The following frequencies of the three types of euphoria, depicted below in Table 7, were therefore demonstrated in this sample of 100 MS participants.

Table 7

Frequencies of CWQ Euphoria Sclerotica, Eutonia Sclerotica and Spes Sclerotica, Amongst the MS Participants (n = 100)

Frequency	Euphoria sclerotica			Eutonia sclerotica			Spes sclerotica		
	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**
Average ratings	21%	42%	**63%**	6%	42%	**48%**	37%	33%	**70%**

Note. Total frequencies are presented in bold font. Def. = definitely present; Pos. = possibly present; Tot. = total.

In addition to disagreement on how to unequivocally determine the frequencies of euphoria, another problem with this measure was that Cottrell and Wilson (1926) defined spes sclerotica in terms of feelings toward the future and prospects of ultimate recovery, but included no questions relating to this. In order to fully investigate the symptom as per the original definition, questions such as, "How do you feel about the future?", "Do you think your MS will get better, stay the same, or get worse in the future?", and, "Do you believe one can ultimately recover from MS?" were included and asked of all MS participants. The three raters were then asked to re-rate spes sclerotica by taking both the answers to the old and the new questions into account. The following rates (depicted in Table 8) were demonstrated after averaging the raters' answers and again rounding the average up or down to the nearest whole number.

Table 8

Frequencies of CWQ Euphoria Sclerotica, Eutonia Sclerotica and Spes Sclerotica, Including Additional Questions of Spes Sclerotica, Amongst the MS Participants (n = 100)

Frequency	Euphoria sclerotica			Eutonia sclerotica			Spes sclerotica (original questions only)			Spes sclerotica (original and new questions)		
	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**	Def.	Pos.	**Tot.**
Average ratings	21%	42%	**63%**	6%	42%	**48%**	37%	33%	**70%**	27%	39%	**66%**

Note. Total frequencies are presented in bold font. Def. = definitely present; Pos. = possibly present; Tot. = total.

As one can see from the descriptive statistics above, taking the new questions into account reduced the incidence of spes sclerotica from 70% to 66%, or of definite spes sclerotica from 37% to 27%. However, in terms of reporting frequencies, since no guidance was given regarding the interpretation of this measure, if one presumes that my criteria for a definite presence of the symptom were too strict and one includes the unsure or possibly present cases, euphoria sclerotica was demonstrated in 63%, eutonia sclerotica in 48%, and spes sclerotica (in terms of what the original measure elicited) in 70% of the current sample of MS participants, by a measure that defines the euphoric concepts in a subtle way.

The contemporary view. In this sample, 11% were regarded as demonstrating euphoria sclerotica according to the standard informant-based administration of the NPI which regards euphoria as being a persistent and abnormally good mood. That is 11% of informants believed their loved-one, who had MS, to be euphoric as per the NPI description. By contrast, 16% self-reported the symptom of euphoria sclerotica when the same question was asked of them (i.e. the MS participants) instead of their informant.

As described above, the NPI asks only about a "persistent and abnormally good mood" (Cummings et al., 1994), and does not address aspects relating to eutonia sclerotica or spes sclerotica. Thus, frequencies of these other types cannot be reported with reference to the dominant contemporary measure.

Therefore, high rates were replicated by the classical measure (if one includes the possibly present cases) that defines euphoria in more subtle ways, and low rates were replicated by the modern measure which uses slightly more extreme definitions. Thus, evidence in support of the hypotheses was found. However, since it appears that incidence rates can be influenced by operational definitions, the findings further highlight the need for consistency regarding the number of types, and the definition of those types so that these symptoms can be better explored and the frequencies better described amongst MS participants.

Additional and different contemporary measures. Important questions relating to the constructs of euphoria, including questions surrounding the number of types of euphoria that exist, the definitions of these types, and the frequencies of these types was investigated above according to a classical and the popular contemporary measures. However, each measure appears to have its own limitations and were even thought to influence the rates of euphoria. Thus, additional and different popular measures, with good reliability and validity,

that are used today to assess positive mood, unawareness and optimism, were included to investigate these constructs further.

I gave a description of these earlier in part one. But, to remind the reader, these included informant based Likert-type scales of positive mood, optimism and unawareness of physical, cognitive and mood/behavioural deficits. In terms of the MS participants themselves, self-report measures were used, and the positive, well-being and optimistic sub-scales of the PANAS, ISS, LOT-R and OPS (respectively), as well as the unrealistic sub-scale of the CRJRF were included to represent positive mood (euphoria sclerotica) and optimism (spes sclerotica). For unawareness (eutonia sclerotica), both participants and their informants completed questionnaires regarding potential physical (PAS), cognitive (AI) and/or mood/behavioural difficulties (NPI). According to the accepted method of awareness research (see Prigatano et al., 1990), the MS participants' self-reports of physical, cognitive and mood/behavioural difficulties were compared with their informants' reports and the resulting discrepancy scores formed the scales for awareness, with negative discrepancies (where participants under-estimated their deficits) representing unawareness.

In terms of the aims of this sub-section, these measures were used to determine how many types of euphoria really do exist, and at what frequencies. As I approached this question from the classical perspective, I hypothesised that more than one type exists and that the frequencies of the types would be closer to that of Cottrell and Wilson (1926) than of the frequencies reported today.

Number of types and definitions of the types of euphoria. This section aimed to investigate whether three types of euphoria do in fact exist as per the classical definition, or whether there is only one type of euphoria, as is believed by some researchers today. Further, it aimed to present a description of these types to aid future research. As the contemporary definitions are characterised by confusion and the contemporary measure investigates only one type, the questions of this section were approached from the classical theoretical perspective. Thus, with regard to the number of types I hypothesised that more than one type of euphoria exists.

The first clinicians to describe euphoria in MS patients did so objectively. Thus, informant reports (i.e. the Likert-type scales) of their MS loved-one's mood, unawareness and optimism were analysed first to investigate the number of types of euphoria. Based on the theoretical framework of three types of euphoria, a principal components factor analysis, using promax rotation and suppression of coefficients of .400 or below, with an extraction

method based on 3 fixed factors was run. This yielded the following results (see Table 9 for the pattern matrix).

Table 9

Factor Analysis of Informant Measures Using a Three Factor Solution

	Component		
Informant rating	1	2	3
Euphoria sclerotica			
Positive mood	.84		
Eutonia sclerotica			
Unawareness of physical deficit			.99
Unawareness of cognitive deficit		.79	
Unawareness of mood/ behavioural difficulties		.97	
Spes sclerotica			
Optimism	.96		
Internal consistency (Cronbach's α)	.78	.77	

One factor relating to euphoria sclerotica and spes sclerotica was demonstrated, with the informant ratings of their loved-ones' positive/negative mood and optimism/pessimism loading onto this factor. The other two factors related to unawareness of deficit. Unawareness of physical deficit (with the informant ratings of their loved-one's awareness of physical symptoms) loaded onto one factor, while unawareness of cognitive and mood or behavioural deficits (with the informant ratings of their loved-one's awareness of cognitive and mood/behavioural symptoms) loaded onto the other factor.

The same variables and analysis were then used, but the extraction method was changed to the criterion of eigenvalues of greater than one, in order to determine the number of types of euphoria without forcing a particular factor solution (see Table 10 below for the pattern matrix results).

Table 10

Factor Analysis of Informant Measures Based on Eigenvalues of Greater Than One

	Component	
Informant rating	1	2
Euphoria sclerotica		
Positive mood		.85
Eutonia sclerotica		
Unawareness of physical deficit	.80	
Unawareness of cognitive deficit	.85	
Unawareness of mood/ behavioural	.79	

difficulties		
Spes sclerotica		
Optimism		.95
Internal consistency (Cronbach's α)	.78	.75

Two factors emerged. The first was a combined euphoria and spes sclerotica type (with informant ratings of their loved-one's mood and outlook loading onto this factor). The second factor was a eutonia sclerotica type (with informant ratings of their loved-one's unawareness of physical, cognitive, and mood/behavioural deficits loading onto this factor).

Euphoria sclerotica (in terms of positive mood), is sometimes, particularly by the classical literature, described and measured as an outward expression of positive mood. But it has been discovered that when pushed, the patient can acknowledge an inward feeling of depression, or of less positive mood than of how they appear to others (see Surridge, 1969, for a critique on relying on objective observation alone). Informant-based measures may, therefore, not be an appropriate way of measuring euphoria and its types. Therefore, the additional modern self-report measures discussed above, used in mood, awareness and outlook research today, were also investigated in terms of a factor analysis. Because Cottrell and Wilson (1926) believed there to be three types, a principal components factor analysis, with an extraction method initially based on 3 fixed factors was again run. A promax rotation was used and coefficients below .400 were suppressed. The results of the pattern matrix are represented in Table 11 below.

Table 11

Factor Analysis of Self-Report Measures Using a Three Factor Solution

	Component		
Measure/Variable	1	2	3
Euphoria sclerotica			
Positive sub-scale of PANAS	.83		
Well-being sub-scale of ISS	.82		
Eutonia sclerotica[a]			
Physical unawareness (PAS)		.60	
Cognitive unawareness (AI)		.78	
Mood unawareness (NPI)		.75	
Spes sclerotica			
Optimism sub-scale of OPS	.87		
Optimism sub-scale of LOT-R	.84		
Unrealistic optimism (CRJRF)			.95
Internal consistency (Cronbach's α)	.75	.22	-

Note. PANAS = Positive and Negative Affect Schedule; ISS = Internal State Scale; PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory; OPS = Optimism and

Pessimism Scale; LOT-R = Life Orientation Test-Revised; CRJRF = Comparative Risk Judgement Rating Form.
[a] = determined via patient/informant discrepancies.

Because a three factor extraction method was used, the analysis indicated three factors. The first revolved around positive mood (euphoria sclerotica) and optimism (spes sclerotica). The positive sub-scale of the PANAS and the well-being sub-scale of the ISS (both included as measures of positive mood), and the optimism sub-scale of the OPS and the optimism sub-scale of the LOT-R (both included as measures of optimism) loaded onto this factor. The second factor related to unawareness of deficits. Patient/informant discrepancies on the PAS (physical), the AI (cognitive) and the NPI (mood/behavioural) loaded onto this factor. The third factor related to unrealistic optimism, with only the CRJRF loading onto this factor.

A second factor analysis was performed, using the same variables. It was again a principal components factor analysis, with a promax rotation, and coefficients below .400 were suppressed. However, as with the informant based variables, the extraction method was again changed to the criterion of eigenvalues of greater than one. The results of this pattern matrix are presented in Table 12 below.

Table 12

Factor Analysis of Self-Report Measures Based on Eigenvalues of Greater Than One

	Component	
Measure/Variable	1	2
Euphoria sclerotica		
Positive sub-scale of PANAS	.84	
Well-being sub-scale of ISS	.84	
Eutonia sclerotica[a]		
Physical unawareness (PAS)		.70
Cognitive unawareness (AI)		.73
Mood unawareness (NPI)		.67
Spes sclerotica		
Optimism sub-scale of OPS	.86	
Optimism sub-scale of LOT-R	.85	
Unrealistic optimism (CRJRF)		
Internal consistency (Cronbach's α)	.75	.22

Note. PANAS = Positive and Negative Affect Schedule; ISS = Internal State Scale; PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory; OPS = Optimism and Pessimism Scale; LOT-R = Life Orientation Test-Revised; CRJRF = Comparative Risk Judgement Rating Form.
[a] = determined via patient/informant discrepancies.

Two factors emerged. One again related to euphoria sclerotica and spes sclerotica. The same measures loaded onto this factor (i.e. the positive sub-scale of the PANAS, the well-being sub-scale of the ISS, the optimism sub-scale of the OPS and the optimism sub-scale of the LOT-R). The second factor again related to eutonia sclerotica, and again the same measures loaded onto this factor (i.e. the patient/informant discrepancies on the PAS [physical], the AI [cognitive], and the NPI [mood/behavioural]). The measure of unrealistic optimism (i.e. the CRJRF) did not load onto either of these factors.

Additional measures, that were different from both the classical and contemporary measures, were specifically chosen to determine the number of types of euphoria. However, it was decided to test the two types of euphoria identified above in terms of the main popular measures in euphoria research. Since the NPI only refers to positive mood (euphoria sclerotica), this measure could not be investigated; however, a principal components factor analysis, with a promax rotation, a suppression of coefficients below .400 and an extraction criterion based on two fixed factors was run using only definite cases of the three types of euphoria identified from the data using the CWQ (which was also a self-report measure). The results of the pattern matrix are presented in Table 13 below.

Table 13

Factor Analysis of the CWQ Based on Eigenvalues of Greater Than One

	Component	
Measure/Variable	1	2
Euphoria sclerotica	.86	
Eutonia sclerotica		.93
Spes sclerotica	.68	
Internal consistency (Cronbach's α)	.35	-

Once again, the same two factors emerged: one relating to euphoria sclerotica and spes sclerotica. The definite cases of euphoria and spes sclerotica, according to the answers of the 100 MS participants to the CWQ, loaded onto this factor. The second factor related to eutonia sclerotica, and the definite cases of eutonia sclerotica, according to the answers of the 100 MS participants to the CWQ, loaded onto this factor.

The results, therefore, appear to suggest that two types of euphoria exist, even when data from the original measure that was designed to elicit three distinct types is used. In terms of defining these two types a little better, I shall name the first type *positivity*. It encompasses positive mood and optimism and, based on its component measures of more

subtle positive mood and optimism, is similar to the original definitions of euphoria sclerotica and spes sclerotica combined. I shall refer to the second type as *unawareness*. It is, in part, similar to the original definition of eutonia sclerotica in terms of unawareness of physical deficit, but it also includes unawareness of other domains.

Therefore, support for more than one type of euphoria was established with the finding of two latent constructs: positivity and unawareness. In terms of better defining these types, positivity appears to be based on something similar to the original euphoria sclerotica and spes sclerotica, while in contrast to the original definition, unawareness appears to relate to any one or a combination of the domains of physical, cognitive and/or mood/behavioural unawareness.

Frequencies of euphoria. The second aim of this sub-section was to address the issue regarding the frequency of these symptoms. Since Cottrell and Wilson (1926) demonstrated such high frequencies, and since I approached this section from the classical perspective, I hypothesised that the frequencies of the new types (i.e. those defined via factor analysis in the previous section) would be closer to that of Cottrell and Wilson (1926) than the frequencies found today.

Before the prevalence of these two types could be determined, an attempt needed to be made to create composite variables that represented the two new types. Because (a) self-reported euphoria may be more reliable than that of informant reports, and (b) the classical measure may have limitations, the additional modern self-report measures included in the factor analyses reported in Table 12, were used for this endeavour. These included the positive sub-scale of the PANAS, the well-being sub-scale of the ISS, the optimism sub-scale of the OPS, and the optimism sub-scale of the LOT-R, which represented positivity; and, participant/informant discrepancies on the PAS, the AI, and the NPI, which represented unawareness. Although these measures loaded onto the two factors, while positivity had a good internal consistency ($\alpha = .746$), unawareness did not ($\alpha = .224$), thus inter-correlations between the relevant variables were calculated, as an additional method of checking their suitability for creating composite variables before the composites were created. The results of these analyses are presented in Tables 14 and 15.

Table 14

Pearson Correlations Between the Positivity Variables (n = 100)

Positivity variable	PANAS (positive sub-scale)	ISS (well-being sub-scale)	OPS (optimism sub-scale)	LOT-R (optimism sub-scale)
PANAS (positive sub-scale)	-	.73	.51	.60
ISS (well-being sub-scale)	.73	-	.56	.65
OPS (optimism sub-scale)	.51	.56	-	.60
LOT-R (optimism sub-scale)	.60	.65	.60	-

Note. PANAS = Positive and Negative Affect Schedule; ISS = Internal State Scale; OPS = Optimism and Pessimism Scale; LOT-R = Life Orientation Test-Revised.
All p values < .001.

Table 15

Pearson Correlations Between the Unawareness Variables (n = 100)

Unawareness variable	Physical (PAS)	Cognitive (AI)	Mood/behavioural (NPI)
Physical (PAS)	-	.22 (p = .029)	.23 (p = .020)
Cognitive (AI)	.22 (p = .029)	-	.35 (p = .0001)
Mood/behavioural (NPI)	.23 (p = .020)	.35 (p = .0001)	-

Note. PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory.

The component measures of positivity were well correlated, indicating that those who scored high on measures of positive mood, also scored high on measures of optimism. In order to create a composite variable where descriptive statistics could still be obtained, the variance of each scale was calculated and all relevant scales were manipulated so that they fitted onto one scale, all with the same range of variance. For positivity, the composite correlated well with the original individual measures (all p values < .001; see Appendix H for the full results), and the composite was created, defined in terms of its more subtle component measures, similar in nature to the original definitions of euphoria sclerotica and spes sclerotica.

Patient/informant discrepancies on the PAS, the AI and the NPI (as per the factor analysis results of Table 12) were less well correlated with each other (explaining the poor internal consistency of this factor). Furthermore, when the actual participants classified as unaware were examined, although a certain amount of overlap did occur, of the 61 MS participants to demonstrate at least one type of unawareness, only two (3.3%) demonstrated unawareness of both cognitive and mood domains, six (9.8%) demonstrated unawareness of both physical and cognitive domains, eight (13.1%) presented with unawareness of both physical and mood domains, and four (6.6%) of MS participants presented with all three types of unawareness. This meant that having one type of unawareness did not necessarily mean that you were unaware in the other domains too. Therefore, although the various types of unawareness loaded onto one factor within the factor analysis, and clearly represent a second type of euphoria, it seems apparent that the components of this type need to be addressed separately.

Following the computation of the composite variable of positivity, the frequencies of this composite were calculated. However, neither the composite scale nor the original modern measures used to create the composite explicitly stated how to measure the presence of the symptoms. Therefore a method of analysis was created whereby the positivity composite scale was divided into quartiles and those participants who scored within the top quartile (i.e. 75% or more according to the scale's minimum and maximum scores) were considered to have scored high on that item. A description of these results are presented in Table 16, and according to this definition, 13% of the MS sample demonstrated high positivity, the new type of euphoria related to euphoria sclerotica and spes sclerotica, encompassing both positive mood and optimism.

Table 16

The Number of MS Participants Demonstrating Positivity (n = 100)

Variable	Scale min	Scale max	High positivity: 75% cut-off point	No. of MS participants demonstrating high positivity	Moderate positivity: 50% - 75% cut-off point	No. of MS participants demonstrating moderate positivity
Positivity composite	0	216	162	13	108-162	54

However, although the individual variables that made up the composite were well correlated, to impose a cut-off at 75% for a composite created from four variables may be a little strict. In addition, if one takes into account the subtle nature of the original definitions of Cottrell and Wilson (1926), as well as that of others such as Diaz-Olavarrieta et al. (1999) who view these patients as being unusually cheerful rather than demonstrating extremely high positive mood, this strict criterion may result in the exclusion of a large proportion of MS participants that are in fact demonstrating positivity. The only reason the 75% cut-off method was employed was because all other euphoric research used a present versus absent means of diagnosis. But, since this symptom was measured using continuous scales, presenting the symptom on a continuum may be more relevant. However, since scores on a continuum cannot be compared with past research, the number of MS participants who fell within the range between the halfway point and the top quartile cut-off point was also calculated and according to this criterion, 54% of the sample demonstrated moderate positivity.

The incidence rates of unawareness were also calculated. Table 17 depicts the results based on a similar analysis of the MS participants' answers, but for the variables relating to unawareness. The method of measurement and analysis was described in the previous section, but it is worth re-iterating that the greater the disability of the MS participant, the greater their chances of being unaware, in terms of this method of measurement. Therefore a certain degree of impairment is implied for high or moderate to high rates of unawareness, but no participant met the criteria for high unawareness when the cut-off was set at 75% of the scale's maximum score. Even at the 50% cut-off point, no participants were classified as demonstrating moderate unawareness.

When the intensity of unawareness was ignored and unawareness was defined only in terms of a negative discrepancy between participant and informant where the participant underestimated their deficits compared to the ratings made by their informant, it was found that 45% of the MS participants underestimated their physical deficits, 16% underestimated their cognitive deficits, and 24% underestimated their mood/behavioural difficulties. Thus, fairly large numbers of the MS group were unaware of their problems, but none demonstrated enough disability, or underestimated their problems significantly enough to be regarded as having high or even moderate unawareness.

Table 17

The Number of MS Participants Demonstrating Unawareness (n = 100)

Unawareness variable	Scale min	Scale max	High unawareness: 75% cut-off point	No. of MS participants demonstrating high unawareness (n = 100)	Moderate unawareness: 50% cut-off point	No. of MS participants demonstrating moderate unawareness (n = 100)	No. of unaware MS participants (n = 100)
PAS (physical)	0	-28	-21	0	-14	0	45
AI (cognitive)	0	-10	-7	0	-5	0	16
NPI (mood/behaviour)	0	-144	-108	0	-72	0	24

Note. PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory.

Thus, it may be appropriate for both positivity and unawareness to lie on a continuum, rather than to impose a cut-off point to denote the presence of absence of the symptoms. However, when cut-off points were imposed, low rates of high positivity and unawareness were demonstrated, while high rates of lower positivity and unawareness (defined by the moderate category for positivity and simply the unaware category for unawareness) were demonstrated. Thus mixed findings, which will be discussed further in the discussion section.

Furthermore, like the original definition of Cottrell and Wilson (1926), positivity was defined in more subtle terms; but unawareness was defined in terms of three domains: physical, cognitive and mood/behavioural deficits.

Summary of part one. The main aim of part one was to investigate the constructs of euphoria and to address the discrepancies evident in the literature. The results presented implied several changes in the types of euphoria and the definitions of those types, and the potential problems associated with the measurement instruments. Further, results showed that two types of euphoria, not three or one, appear to exist, that the type pertaining to the original eutonia sclerotica may include additional aspects, and, further, that the two types of euphoria appear to be better represented on a continuum than in a categorical diagnostic format.

Part two. Describing and predicting positivity and unawareness

The main aims of part two were to investigate the new types of euphoria (viz. positivity and unawareness), within the current MS sample, in order to better understand, and predict these symptoms. This was attempted by first expanding on the new types of euphoria, and by describing them further, the results of which are presented below. No hypotheses were presented in this regard. In order to be able to predict which MS participants might display the two types, the disease and cognitive correlates of these types were also investigated. Here, I hypothesised that the disease correlates of the different types of euphoria would differ, and that, due to the approach of this study from the classical perspective, the euphoric types would occur both early and late in the disease, with either little or severe physical disability. It was also hypothesised that the cognitive correlates of the euphoric types would differ, and that at least one of the euphoric types would correlate with impairment on neuropsychological tests of cortical domains of function.

Describing positivity and unawareness. From the previous section it appears that two types of euphoria exist within some MS patients that relate, at least in part, to the original types of euphoria described by Cottrell and Wilson (1926). The first is that of positivity which encompasses positive mood (euphoria sclerotica) and optimism (spes sclerotica). The second is unawareness and relates to unawareness of physical, cognitive and mood/behavioural deficits (which is, in part, similar to the original eutonia sclerotica). Although the types of euphoria identified were defined in terms of their component parts, they were not described in detail and, thus, I shall expand on their definitions in this section.

Do positivity and unawareness occur together or are they two separate symptoms?

One of the aims of part two was to better define the two types of euphoria, and the aim of this sub-section was to address that larger aim by determining whether the two types co-occur or whether they reflect distinct symptoms.

Therefore, first, a correlational analysis was run between positivity and unawareness. In order to include the full range of variance, the full scales of awareness were used. This means that the scores of all 100 participants were included and not only the negative scores of the unaware participants. Thus, higher scores indicated greater awareness and lower scores greater unawareness.

One might think that addressing the components of unawareness separately may impact on an analysis investigating the connectedness of the two types of euphoria.

However, this was found not to be the case, and all domains of unawareness, in terms of the full range of the awareness scales, were found to be negatively correlated with positivity (see Table 18 below). As the full sample was used, this negative correlation means that as positivity increases, so does unawareness.

Table 18

Pearson Correlations Between Positivity Scores and Awareness Scores (n = 100)

Variable	Physical (PAS)	Cognitive (AI)	Mood/behavioural (NPI)
Positivity	-.23 (p = .022)	-.29 (p = .003)	-.32 (p = .001)

Note. PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory.

Descriptive statistics were then used to determine how many MS participants, from the total sample of 100, demonstrated either or both symptoms, in order to determine if positivity and unawareness co-occur in the same MS participants. These are displayed in Table 19.

Table 19

Number of Participants Demonstrating Either of Both High Positivity and Unawareness

	Unawareness (n = 61)	High positivity (n = 13)			
Variable	Without high positivity	Without any unawareness	Plus 1 type of unawareness	Plus 2 types of unawareness	Plus all 3 types of unawareness
Number of participants	52 (85.2%)	4 (30.7%)	5 (38.7%)	2 (15.4%)	2 (15.4%)

Note. High positivity was defined in terms of the 75% cut-off point of the composite scale's minimum and maximum. Unawareness was defined by negative discrepancies between participant and informant where the participant under-estimated their deficits on various domains.

From the results above it can be seen that as many as 15.4% of the 13 MS participants demonstrating high positivity demonstrated this symptom in combination with unawareness of all three domains. When considering that each area of unawareness was treated separately, this is quite a high percentage of co-occurrence. Further, 69.3%, of the 13 MS participants demonstrating high positivity, demonstrated some form of unawareness in conjunction with their high positivity, also indicating a high rate of co-occurrence. However, these types did not necessarily co-occur, as 30.7% of the sub-group of MS participants to demonstrate high positivity did so without the presence of any unawareness. Equally, of the 61 MS participants to demonstrate at least one type of unawareness, 85.2% demonstrated this alone, without also scoring in the high range for positivity.

The same descriptive statistics were applied to those demonstrating positivity at the moderate level (i.e. between the 50% and 75% cut-off points) as it was thought that restricting positivity to only high levels may limit the potential for co-occurrence of these symptoms. These results, depicted in Table 20, also indicated a high rate of co-occurrence between positivity and unawareness, when positivity was defined more inclusively, at the moderate level.

Table 20

Number of Participants Demonstrating Either or Both Moderate Positivity and Unawareness

	Unawareness (n = 61)	Moderate positivity (n = 54)			
Variable	Without moderate or high positivity	Without any unawareness	Plus 1 type of unawareness	Plus 2 types of unawareness	Plus all 3 types of unawareness
Number of participants	17 (27.8%)	19 (35.2%)	23 (42.6%)	10 (18.5%)	2 (3.7%)

Note. Moderate positivity was defined in terms of scores falling between the 50% and 75% cut-off points of the composite scale's minimum and maximum. Unawareness was defined by negative discrepancies between participant and informant where the participant under-estimated their deficits on various domains.

In the above analysis, moderate positivity again occurred on its own (without unawareness) in 35.2% of the MS participants demonstrating moderate positivity, but unawareness occurred on its own (without moderate or high positivity) in only 27.8% of those MS participants demonstrating unawareness. This means that an MS patient can present with unawareness without positivity at the reduced moderate level. However, far fewer participants now demonstrated unawareness by itself, and when the entire sample is taken into account, of the 67 participants demonstrating moderate to high positivity, 44/67 (65.7%) did so in conjunction with some form of unawareness. Furthermore, far more participants presented with unawareness of all 3 domains in conjunction with high positivity (15.4%), than they did with moderate positivity (3.7%).

The above results therefore appear to suggest an association between positivity and unawareness and that, although these two symptoms can occur separately, they appear to have high rates of co-occurrence and most likely reflect two types of euphoria.

Does depression play a role in euphoria? Due to the idea of depressed patients being misdiagnosed as euphoric, based on their appearance (see Surridge, 1969), and the apparent lack of literature specifically examining a relationship between depression and unawareness, I wanted to investigate the association between depression and the two types of euphoria identified in this study with the aim of better describing the euphoric symptoms identified by the current research, viz. positivity and unawareness.

The level of depression in this sample was first determined by comparing the MS group with the HC reference group on the BDI-FS, via a Mann-Whitney *U* test as the data was not normally distributed across groups. It was found that the MS group were, on average, significantly more depressed than the HCs ($U = 2068.50$, $p = .0001$), and that, on average, the MS group was considered to be mildly depressed according to the BDI-FS cut-off point of four (*M* 4.75).

Pearson correlations between depression and positivity, and between depression and the various domains of unawareness (using the full scales of awareness from the full sample of 100 MS participants) were then run, the results of which are presented in Table 21.

Table 21

Pearson Correlations Between Depression and Positivity, and Depression and Awareness (n = 100)

		Awareness of		
Variable	Positivity	Physical domain	Cognitive domain	Mood/behavioural domain
Depression	-.65 (p = .0001)	.22 (p = .030)	.30 (p = .002)	.20 (p = .044)

The results of the above correlations indicate that positivity was significantly and negatively correlated with depression, which implies that as positivity increases, depression decreases.

For unawareness, the full scales were used including both aware and unaware participants in order to include the full range of variance (thus higher scores indicated greater awareness). Positive correlations with depression were seen for all domains of awareness and these reached statistical significance for the cognitive and approached significance for the physical domain. These results imply that as unawareness increases, depression decreases. These results therefore describe the two types of euphoria a little further, in that positivity and unawareness appear to have an inverse relationship with depression.

How euphoric is euphoria? How positive and unaware are MS patients? Are they observably so? Could one notice it with ease? Or would one consider them to be normal were they not experiencing a devastating, chronic and progressive disease? An attempt was made to answer these questions by comparing the MS participants with a sample of matched HCs, with the aim of increasing our understanding of and further describing these symptoms.

In terms of positivity, since such emphasis has been placed on this symptom by a whole history of literature, I hypothesised that the sub-group of MS participants who demonstrated high positivity would demonstrate it at similar levels to the HCs who demonstrated high positivity, and that the sub-group of MS participants who demonstrated moderate positivity would demonstrate it at similar levels to the HCs who demonstrated moderate positivity. As not all MS patients demonstrate these symptoms, however, I hypothesised that when the full MS sample's mood was compared with that of the full sample of HCs mood, the MS group would display levels of positivity that were lower than the levels displayed by the HCs.

Before these questions were addressed, however, the two samples were compared on key sociodemographic variables to ensure that the two groups were well matched and no significant pre-existing between-group differences existed that could contribute to differences

in positivity between the two groups. This was tested by using independent samples *t*-tests for the (normally distributed) continuous data and chi-squared tests of independence for the categorical data. The results of these analyses are presented in Table 22 (with the descriptive statistics of the full list of variables available in Appendix I).

Table 22

The Key Sociodemographic Characteristics of the MS Participants and Healthy Controls

Key variable	MS participants (n = 100)	Healthy controls (n = 100)	*t* (*df* = 198) / X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI *LL*	95% CI *UL*	Effect size *d* / *V*
Gender – Male:Female	14:86	14:86	.0001	1.000			0.00
Age	44.49 (11.17)	43.75 (11.02)	0.47	.638	-3.83	2.35	0.07
Race/ethnicity – White:Coloured/Indian	71:29	73:27	.10	.753			0.02
Education[a]	13.18 (1.65)	13.40 (1.50)	-0.98	.326	-0.22	0.66	-0.14
Income[b]	R26,006.51 (R22,536.54)	R26,993.51 (R21,480.21)	-0.32	.752	-5152.58	7126.58	-0.04

Note. Categorical data are presented in ratios. The data on age, education, and income are presented as means with the standard deviations in parentheses. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Combined monthly household income.

The characteristics of the 100 HCs did not differ significantly from the 100 MS participants on any of the key demographic variables listed above (all *p* values > .01). Thus, the groups were deemed to be similar and the sociodemographic variables explored were not thought to represent confounding factors.

The MS participants and HCs were then compared on positivity, at the various cut-off points, using either independent samples *t*-tests or chi-square tests of independence. Since hypotheses were made, directional one-tailed analyses were run (see Table 23).

Table 23

The Performance on Positivity of the MS Participants Compared with the Healthy Controls for Continuous Data

Level of positivity	MS participants (n = 100)	Healthy controls (n = 100)	*t* (*df* =198)	*p* (1-tailed)	95% CI *LL*	95% CI *UL*	Cohen's *d*
Composite (all participants)	122.12 (35.02)	151.14 (28.22)	6.45	**.0001**	20.15	37.89	-0.91
Moderate positivity scores (50% - 75% cut-off)	133.02 (15.26) (n = 54)	143.01 (13.92) (n = 56)	3.59 (*df* = 108)	**.001**	4.47	15.51	-0.68
High positivity scores (75% cut-off)	176.98 (9.24) (n = 13)	179.14 (13.03) (n = 35)	0.55 (*df* = 46)	.293	-5.78	10.11	-0.46

Note. All data are presented as means with standard deviations in parentheses. Significant results are presented in bold font. CI = confidence internal; *LL* = lower limit, *UL* = upper limit.

Table 24

The Performance on Positivity of the MS Participants Compared with the Healthy Controls for Categorical Data

Level of positivity	MS participants (n = 100)	Healthy controls (n = 100)	χ^2(*df* =1)	*p* (1-sided)	Cramer's *V*
Moderate-scorers (50%-75% cut-off)	54	56	0.08	.338	0.02
High-scorers (75% cut-off)	13	35	85.64	**.0001**	0.80

Note. Significant results are presented in bold font.

Results from the inferential statistics reported in Table 23 indicated that the total MS group, on average, demonstrated significantly less positivity than the HC reference group. Those participants who scored within the moderate range for positivity (i.e. between the 50% and 75% cut-off points on the scale, according to the scale's minimum and maximum) and within the high range (i.e. equal to or above the 75% cut-off point) were then identified. From Table 24, it can be seen that similar rates of MS participants and HCs were classified as moderate scorers, but significantly more HCs than MS participants were classified as high-scorers. In Table 23 one can see, however, that the average scores of moderately scoring HCs were significantly higher than that of the MS group. When just high-scorers were compared there were no significant differences between the average scores for high-scoring HCs and high-scoring MS participants. Since significant differences existed at the moderate level, the hypothesis, that the MS participants would demonstrate similar levels of positivity to the HCs (as defined by the two cut-off points denoting moderate to high positivity, and high positivity), was rejected.

While the measures of positivity were applicable to both groups, as they measured subtle mood and outlook and did not represent an extreme symptom that might only be appropriate for a patient group, the measures of unawareness were not, as HCs (by their healthy nature) cannot present with deficits and thus, cannot demonstrate unawareness of deficits. However, I did want to investigate the intensity or severity of the unawareness of the MS group. Thus, instead of comparing discrepancy scores between MS and HC groups, I analysed the difference between the MS participant and the MS informant ratings for the scales pertaining to physical, cognitive and mood/behavioural related deficits (a method that has been used by other researchers such as Benedict et al., 2001). I did this by using independent samples *t*-tests to determine if any significant differences between these two groups existed for the first two normally distributed variables, and a Mann Whitney *U*-test for the mood/behavioural variable as the data was not normally distributed. Since unawareness has also been emphasised throughout the literature, I hypothesised that the ratings of the MS participants would be significantly lower than the ratings of their informants, thus 1-tailed *p* values are reported. On average (i.e. taking the full sample into account), the analyses revealed significant differences between the ratings of the participants and their informants for the domains of cognition ($t(198) = 4.91$, $p = .0001$, $d = 0.70$, 95% CI [0.74, 1.72]) and mood ($U = 3855.00$, $p = .003$), but not for physical deficits ($t(198) = -0.60$, $p = .275$, $d = 0.08$, 95% CI [-2.83, 1.51]). Thus, the intensity or severity of the former two domains was greater in this sample than the intensity of unawareness of physical deficits. When just the ratings of

the unaware MS participants were compared with those of their informants, differences nearing significance were demonstrated between the two groups for physical ($t(88) = -2.34$, $p = .011$, $d = 0.49$, 95% CI [-6.09, -0.49]), and cognitive domains ($t(30) = -2.45$, $p = .011$, $d = 0.87$, 95% CI [-2.64, -0.24]), and significant differences were demonstrated for the mood/behavioural domain ($U = 173.00$, $p = .009$). Thus, the sub-sample of MS participants that were unaware, as defined by under-estimating their deficits in comparison with their informant, significantly (or almost significantly) under-estimated their deficits of all three domains. The hypothesis that the ratings of the MS participants would be significantly lower than the ratings of their informants was, therefore, largely accepted.

A qualitative characterisation. While quantitative analysis is very useful in helping to define and describe the symptoms of positivity and unawareness, statistics cannot tell us about what an unaware or positive MS participant sounds like, or what words they used to describe their feelings. For this reason, a qualitative content analysis was also performed on two open-ended questions.

Unawareness was difficult to analyse qualitatively, for reasons that will be discussed further in the next section. Thus, the questions analysed applied only to positivity and included the CWQ question, "Describe in a few words, your usual or general mood", as well as the question I added to their questionnaire to address the missing aspect of optimism as to the future, "How do you feel about the future?". A content analysis of these questions was completed for both the moderate and high scorers for positivity, and the following themes surrounding feelings emerged. The results of the moderately scoring group are presented first.

1. Positive. Some of the MS participants who were classified as demonstrating moderate positivity spoke about feeling positive. These feelings ranged from feeling "sometimes positive" (P79), to "quite positive" (P53), to "very positive" (P39, P98), to "extremely positive" (P35).

2. Happy. Feelings of happiness also ranged from mild to more extreme and included descriptions such as, "moody, but happy" (P21), "normally cheerful and happy" (P49), "most happy, fun-loving" (P76), to "generally happy" (P89).

3. Excited/upbeat. This theme referred to feelings of being "excited" (P49), and "mostly upbeat" (P69) or "upbeat" (P55, P63). P47, a female in her fifties who suffers from fatigue and is unable to work but is still active in her community, described herself as:

I'm… most of the time, full of joy and excitement to encourage others um … to, to really um … help other people to grab life and to live it to its fullest. It's such a gift we've received um … and, and that is really something.

4. Optimistic. Many of this group of MS participants also described feelings of optimism. Again a range of optimistic feelings were described, from "optimistic, but scared" (P34), to "quite optimistic" (P39), to "always an optimist" (P86).

5. Relaxed/at ease. Some moderate scorers on positivity described feelings of contentment, such as feeling "relaxed" (P42, P89), or "more relaxed than before my diagnosis" (P100) "content" (P98), "at ease" (P84), and "laidback" (P84).

6. Neutral. A number of this group, though, described their feelings in terms of more neutral terms. For example, some descriptions of mood included, "normal" (P31, P69) or "just normal" (P27), "easy" (P50), "cool and calm" (P77), or "not excessive mood" (P95).

7. General negative feelings. Others, of this same group, described more negative feelings, such as, feeling "apathetic" (P18), "generally positive with some downs" (P95), or "sometimes despondent" (P79). P64, a female in her forties who is also still able to work, described her feelings as follows:

I feel defeated easily– it takes longer after each of life's setbacks to get my bliss back. As if I cannot gather the energy to lift my head and go on like I usually could do. As if a sort of depression holds me back.

8. Worried/fearful/uncertain. A specific group of negative emotions was also identified within the descriptions of this group of moderate to high scoring MS participants on positivity. This theme referred to feelings such as, "worry about the future" (P22), feeling "uncertain for the future" (P36, P64), feeling "unsure of what the next day will be" (P67), of trying "to think positively, but worry[ing] at night" (P86), or of worrying that the participant won't "be around much longer" (P4).

Linked to this theme was one where the MS participants worried about future symptoms such as losing their vision (P31, P70), being unable to care for themselves (P39), the loss of independence and the process of death (P6). P77, a male in his late thirties who has been medically boarded due to his disability, states: "I try to remain positive but I'm always second guessing anything that could be a sign of a relapse."

9. Feeling/doing for others. Some of this group of MS participants also mentioned that despite how they felt on the inside, they tried to be, "upbeat around others" (P86), "always checking if others are happy" (P63).

10. Preoccupied/busy/don't think about it. Finally, the last theme pertaining to feelings was that of not having feelings. That is, the participants who mentioned this theme stated that they did not think about their mood, their future, or their MS. P44, for example, a home executive female, mentioned that she was so preoccupied during the day with planning of tasks etc., that she did not really notice her general or usual mood. P55 stated that she "do[es]n't look to the future". P1 and P76 echoed these sentiments by saying, "I try not to think about [my MS] too much" with P76 adding "as it can get me down". While for others, such as P19 and P69 who both have RRMS and have not experienced many relapses, it's not a conscious decision not to think about MS, they just "don't think of my MS that much" and act "maybe… like an ostrich, with my head in the sand. I just carry on and don't think about it".

A number of themes relating to feelings were also identified in the answers of MS participants who scored highly on positivity.

1. Positive and optimistic. Some of the MS participants who were classified as demonstrating high positivity also spoke about feeling positive and optimistic. These feelings ranged from feeling "positive, yet realistic" (P23) or "positive but uncertain" (P92), to "very positive" (P3, P5, P16), and these participants stated that they "look forward to the future" (P61), and have "naïve optimism, I don't see challenges" (P16).

2. Happy and upbeat. High-scoring MS participants on positivity also described feelings such as, “happy, content” (P5), “happy-go-lucky” (P61), “generally happy” (P8), “mostly upbeat”, and “always happy” (P28).

3. Neutral or negative. The only high scoring participants to note any neutral or negative feelings were P24 who described her mood as “passive, calm”, and P25 who voiced her concern of ending up in a wheelchair.

4. Feeling/doing for others. P8, a recently diagnosed female in her thirties, and a fairly new mother of 3 children, mentioned how she viewed taking her injections as being for her children rather than herself to prolong the time she has with them:

Every single time I take that interferon, every time with my injections I feel like I'm doing it for my children. I promise you, there’s sometimes, especially in winter you look like a pin cushion because you have to take injections like all over the place, and, at night, I’ll go to sleep, my arm will feel so sore that I can feel where I actually had my injection... It's just like slightly painful. But, I think, you know what, I know that I can’t stop what is there, but I can delay it.

5. Preoccupied/busy/don’t think about it. Finally, like P44 (a moderate scorer), P3, also a home executive female, mentioned that she did not really notice her general or usual mood.

It is clear from the results presented above that a number of different feelings emerged from the content analysis and that differences appeared to be present between those participants demonstrating positivity at moderate versus high levels.

Additional themes were also identified. Again, I will divide moderate and high scoring MS participants. Within moderately scoring participants, the first category pertained to one’s approach to life, and the first theme within this category referred to being grateful for what you have and taking something good from MS and was noted by a number of participants. P69, for example, a female in her fifties who has had MS since 1989 said that she “realise[s she is] blessed when [she] compare [her]self with others with MS”, and P5, a recently diagnosed female in her thirties, reported that:

I think what's come of this is, you know, doing the… different events and getting involved with [removed for anonymity]. I actually feel like I'm making a

> *difference, to change something and get the awareness out there. In a way, I wouldn't say I'm happy to have MS, but I am quite pleased that I can do something about it and I'll try and see where it'll take me.*

Linked to this idea of being grateful and seeing the positive side of MS was that of living life to the fullest. A number of pertinent quotes emerged here, so I will reproduce a few below:

> *I just…, I just feel I need to live. What I can do right now, I need to do it right now. I don't want to have regrets later on. That is what I feel.* (P10, a female in her thirties who suffers more from cognitive impairment than physical impairment).

> *I try to get the most out of every day, so that one day when I can't move anymore I can look back and say that I lived my life to the fullest.* (P32, a female in her forties who received a diploma but is now permanently unable to work).

> *Until the time comes when I have to use disability tools more prominently or move into a care centre, I want to enjoy every day as much as I can.* (P69, a female in her fifties who has had MS since 1989).

Others had a slightly less energetic or enthusiastic approach to life and rather took it one day at a time: P11 and P94 "take it one day at a time", P20 and P63 "focus on the now", P55 "live[s] for 24 hours", and P1 recommended to "take it one day at a time, otherwise you will end up crying every day".

Still others appeared to approach life with a more laissez-faire attitude, with either a "just get on with it" attitude or a "what will be, will be" approach (P14). For example, P63, a female in her thirties who was diagnosed with MS in 1995, told me:

> *I inject for three days of the week so I often pray for an end to it as I feel it is more disturbing for my family than me. Again, I have to do it so let's just get on with it.*

Planning one's life was also a prominent theme. Some participants mentioned planning their day around their MS. P35, for example, spoke of how she's learned to cope with her MS by planning her day and doing certain things in certain ways, and P86 remarked that "making notes has become a lifestyle".

The second aspect regarding planning referred to planning for the future and making provisions. P11 and P27 both planned ahead financially, providing for a future that may include an inability to work. P1 has had to plan for a future where she cannot have children; and P6 fostered her dogs with a friend as she would no longer able to take care of them.

The third aspect, which seems contradictory with all the planning above, is the idea of not making plans. For example, P18, a male in his fifties who has been experiencing RRMS since 1971 although it was only diagnosed in 2009, explained how he "basically take[s] each day as it comes" and has "long ago learned not to get too excited about plans made" as these can change suddenly due to a relapse. P55, a female in her late forties who was diagnosed with MS 13 years ago and who was one of the participants who advocate living day by day, stated:

> *I'm back to living 24 hours. But, the down side to that is, I actually don't plan for the future. So, if friends phone and say "Ag, let's have a braai next month" I say to them "That's great; but, can we talk closer to the day?" I'm very nervous about making any plans for the future. Because we've already done things like OK we'll go on a holiday in December, and in December I can't move.*

Religion also emerged as a theme. Many participants appeared to find meaning in their religion and stated ideas such as "with my belief system I'll be fine" (P50).

Finally, a theme that emerged from the data of MS participants who scored within the moderate range on positivity was that of control. P53, for example, noted her control over her own future and said that, "the future is up to me", while P1 noted her control over her life, and her MS, when she said that she "do[es]n't let MS interfere" with her life (even though she requires a wheelchair to get around outside). Finally, and this is my personal favourite quote, P100 indicated the control she has over her life and illness when she said "I have MS, but it does not have me".

Very few reactions to MS were identified by the highly positive MS participants. An equally unexpected and interesting finding was that most of the themes identified were of a more neutral or slightly negative quality. For example, P16 had a "just get on with it" approach to life, P3 had a "just live life" approach, and P23 had a "what will be will be" attitude. P90 was the most positive with a "live in the moment" approach.

This group also planned for their future and P24 noted how one needs to "readjust expectations" with MS and related how she plans her day around fatigue, but does not let this stop her from accomplishing what she needs to do.

One final theme emerged that was not present in the moderate scorers. This was the idea of a support network, and P61 said that she was "able to combat setbacks with help from [her] friends".

In conclusion, a number of additional interesting themes emerged that offer a little more insight into positivity. They all appeared to relate to reactions to MS, in one way or another, and moderate scorers identified far more themes, and unexpectedly (given that they noted negative feelings while the highly positive MS participants did not) appeared to be more positive in their reactions than high scorers.

Predicting euphoria. The next area of interest was that of the disease and cognitive correlates of euphoria. The aim was to investigate whether the two types of euphoria identified could be predicted in MS participants according to particular demographic, disease and/or cognitive variables. Again, because the investigation of the two types of euphoria was approached from the classical perspective, I hypothesised that the demographic, disease correlates of the two types would differ, and that positivity and unawareness would occur both early and late in the disease, with either little or severe physical disability, and that, due to factors highlighted by other studies, gender and current disease state would correlate with at least one type of euphoria. Furthermore, I hypothesised that the cognitive correlates of the euphoric types would differ, and that at least one of the euphoric types would correlate with impairment on neuropsychological tests of cortical domains of function, and that at least one of the euphoric types would correlate with impairment on neuropsychological tests of RH functioning.

Before this could be attempted however, the disease characteristics of the 100 MS participants, as well as their cognitive functioning, or impairment, needed to be described and/or interpreted. This description or interpretation will be presented in the beginning of each relevant section below, followed by an investigation of the correlates.

The demographic and disease correlates. The disease and demographic correlates of the two types of euphoria were investigated with the aim of predicting which MS participants may present with positivity and/or unawareness. I hypothesised that the demographic, disease correlates of the two types may differ and that the two types may occur early or late in the disease, with mild or severe disability, and that at least one type may correlate with gender and/or current disease state. First, however, the characteristics of the full MS sample will be described below in terms of the disease variables examined.

The disease characteristics of the MS sample. The demographic characteristics of the MS sample have been described in the methods section. However, the MS participants were also asked specific questions related to their MS and I will describe these here. In line with previous research investigating disease correlates in MS research, important variables such as disease course, duration of disease, current disease state, severity of disease, and use of medication were explored. Diagnosis and disease course were, where possible, confirmed with each participant's neurologist. Descriptions of these variables are presented, in Table 25.

Table 25

The Disease Specific Characteristics of the MS Participants

Medical characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)
A diagnosis of MS	60	40	100
Confirmed diagnosis	57	39	96
Disease course			
RRMS	46	29	75
PPMS	4	6	10
SPMS	10	5	15
Duration of disease since diagnosis (in years)	8.78 (7.88)	10.75 (6.83)	9.57 (7.50)
Mean (*SD*)			
Range	0-42	0-28	0-42
Current disease state			
Relapse	2	6	8
Remission	42	27	69
Progression	16	7	23
Disease severity			
Mean (*SD*)	10.98 (8.16)	11.75 (7.29)	11.29 (7.79)
Range	0-28	0-28	0-28
Corticosteroids within the last 4 weeks	11	3	14
Use of other medication that can affect mood	42	26	68

Note. The data on duration of disease since diagnosis and disease severity are presented as averages with the standard deviations (*SD*) in parentheses and the minimum to maximum range below. MS = multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; PPMS = primary progressive multiple sclerosis; SPMS = secondary progressive multiple sclerosis.

All 100 MS participants had received a diagnosis of MS and this was confirmed with their neurologist in 96 out of 100 cases (according to the McDonald criteria described in the literature review). Although non-probability sampling techniques were used to recruit the MS participants, participants were not selected based on any MS disease criteria, and one quarter of the 100 MS participants (25%) had a progressive type, and the remaining participants (75%) were experiencing RRMS at the time of their participation in this research. This was also confirmed with the relevant neurologist in 96% of the cases.

Disease duration was calculated since diagnosis, as is the accepted method in the literature. The majority of participants (69%) reported that they were in a state of remission at the time of their interview; however 8% self-reported that they were experiencing a relapse and 23% (all of whom were experiencing a progressive disease course) reported being in a state of progression. Two participants with a progressive course reported being in a state of relapse at the time of their interview.

As was mentioned in the methods section, the EDSS (Kurtzke, 1983) is the gold standard measure of physical disability, which is used as a representation of disease severity in MS. However, due to a number of factors addressed in the methods section, this measure was not used in the current study, and rather a scale of physical ability (i.e. the PAS) was included as a representation of disease severity (in terms of physical disability). As some patients with MS can be unaware of their deficits, informant reports of their physical ability (or disability) were used. Scores could range from 0 to 28. Thus, as is evident in Table 25, some MS participants' informants believed that their MS loved-ones were not impaired at all, while others believed their MS loved-ones were maximally disabled. On average though, the severity of disease, in terms of physical disability, was a little under 50% for the total sample of MS participants.

Finally, as was stated in the section pertaining to the exclusion criteria in the methods section, MS participants were not excluded based on corticosteroid use, even though it has been found to influence mood and, in some cases, cause a temporary state of euphoria (Brown et al., 1999; Patten & Neutel, 2000). Rather, use of this and other medication that could influence mood was noted and controlled for statistically in the analyses below. With this in mind, 14% had received some form of corticosteroid treatment within the last four weeks, and 68% were taking medication, such as anti-depressants, which may influence mood. In addition, medical history (reported in the methods section) was also controlled for, and 41% had a past medical history of a disease or condition (e.g. past diagnosis of depression) that could influence neuropsychological functioning.

The demographic and disease correlates of euphoria. Multiple regression analyses were run in order to determine the demographic and disease correlates of the types of euphoria identified in part one of the results section. Corticosteroids are known to induce a euphoric-like state (Brown et al., 1999; Patten & Neutel, 2000), and medications such as anti-depressants can lift or stabilise mood (Hewitt, Fraser, & Berger, 2000; Turner, Sharp, Folkes, & Chew-Graham, 2008). However, due to limitations regarding the accessibility of patients, these variables could not be excluded. Furthermore, participants could not be excluded on the basis of a medical history of diseases or conditions that could influence neuropsychological functioning for the same reason. Thus, I wanted to control for the potential effects of these variables in the following analyses and I, therefore, used hierarchical regression models.

'Corticosteroids' included the use of corticosteroids within four weeks prior to the participants' interview. This was a categorical variable where corticosteroid use was either present or absent. 'Medication' included any medication, such as anti-depressants, that specified a possible impact on mood as a side-effect. This was also a categorical variable, where medications that could potentially influence mood were either present or absent. Finally, the variable 'medical history' was created from the medical information provided by each participant, and which formed the exclusion criteria of the HC participants. This was also a categorical variable and any history of a disease or condition that could affect neuropsychological functioning (e.g. other neurological disease, brain tumour, epilepsy, previous psychiatric diagnosis, developmental delay) represented the presence of this symptom. Each of these three variables was entered into the hierarchical model first, in one step, using the "enter" method. This was followed by the selected demographic variables (gender, age and income) and disease variables (disease course, duration of disease, current disease state, and disease severity), all of which were entered as separate predictors, in a second step, also using the "enter" method.

For both positivity and unawareness, the full scales, within the full sample of 100 MS participants, were selected as the dependent variables, as analysing only those participants who were classified as highly positive, or unaware (in terms of negative discrepancy scores), would have restricted the range of positivity, rendering the multiple regression unusable. Thus, in this section, as in the section regarding the correlations between positivity and unawareness as well as between depression and unawareness, I will refer to the full scale as awareness when discussing the results, where higher scores indicate greater awareness and lower scores indicate greater unawareness. All assumptions were met prior to running the multiple regressions and the correlations between the variables investigated are reported in Tables J1 through J4, in Appendix J.

The aim was to investigate whether positivity and unawareness had distinct profiles in terms of these correlates. In line with the ideas of Cottrell and Wilson (1926), I hypothesised that the disease correlates of the different types of euphoria may differ, and that the euphoric types may occur both early and late in the disease, with either little or severe physical disability.

The model results. The results pertaining to all models tested are presented in Table 26.

Table 26

Model Summaries for Positivity and Unawareness

						Change statistics				
Model	R	R^2	F	*p*	SEE	Δ R^2	ΔF	*df*1	*df*2	Sig. ΔF
Positivity										
1	.26[a]	.07	2.36	.077	34.32	.07	2.36	3	96	.077
2	.39[b]	.15	1.55	.137	34.09	.08	1.18	7	89	.320
Unawareness of physical										
1	.23[a]	.05	1.72	.168	3.07	.05	1.72	3	96	.168
2	.48[b]	.23	2.63	**.008**	2.88	.18	2.91	7	89	.009
Unawareness of cognitive										
1	.18[a]	.03	1.08	.363	1.88	.03	1.08	3	96	.363
2	.25[b]	.06	.60	.810	1.92	.03	.42	7	89	.891
Unawareness of mood/behaviour										
1	.15[a]	.02	.71	.547	15.95	.02	.71	3	96	.547
2	.29[b]	.08	.82	.612	16.02	.06	.87	7	89	.537

Note. Significant results are presented in bold font.
[a] = Predictors: Corticosteroids, medication, and medical history.
[b] = Predictors: Corticosteroids, medication, medical history, gender, age, income, disease course, duration of disease, current disease state, and disease severity.

The only model found to significantly predict a type of euphoria was that of all demographic and disease variables and unawareness of physical deficits (p = .008). The results pertaining to the coefficients of all models (presented in Tables J5 through J8, in Appendix J), were, however, also analysed, and a number of individual predictors were identified.

The coefficient results. In terms of positivity, medical history was a significant individual predictor of positivity (β = -.28, p = .009) in the (second) total model, above not only the demographic and disease variables investigated, but also current corticosteroid and medication use which were expected to perhaps play a role. I had controlled for medical history because, due to the limited number of available patients, I was unable to exclude MS participants based on criteria such as having a brain tumour or a past psychiatric diagnosis. However, since this variable was found to be a significant predictor of positivity, I wanted to see how much variance of positivity it accounted for by itself. Therefore, I ran a linear regression with just this variable and positivity. On its own, previous medical history accounted for 7% of the variance in positivity (R^2 = .07, F(1, 98) = 7.11, p = .009), with a negative correlation which can be seen in the coefficient results below (see Table 27).

Table 27

Linear Regression Between Medical History and Positivity

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Constant	129.68	4.42		29.31	.0001	121.00	138.45
Medical history	-18.43	6.91	-.26	-2.67	**.009**	-32.14	-4.72

Note. Significant results are presented in bold font. Medical history = a previous diagnosis of a disease or condition, such as other neurological disease, brain tumour, epilepsy, previous psychiatric diagnosis or developmental delay, that may influence neuropsychological functioning. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Returning to the original set of models described, when the standardised Beta coefficients were examined in relation to unawareness of physical deficit, it was found that only disease severity significantly predicted awareness of physical deficits (β = -.45, p = .0001). Thus, disease severity was entered into a separate model, by itself, to assess how much of the variance of unawareness of physical deficits was explained just by the severity of the disease. However, it was found that alone it explained only 4.7% of the variance of awareness of physical deficits (R^2 = .05, F(1, 98) = 4.78), which was not significant at the .01 alpha level used throughout this study (β = -.22, p = .031). The negative correlation between these variables is presented below in Table 28.

Table 28

Linear Regression Between Disease Severity and Unawareness of Physical Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Constant	.25	.54		.47	.643	-0.82	1.32
Disease severity	-.09	.04	-.22	-2.19	.031	-0.16	-0.01

Note. Disease severity was measured in terms of informant ratings' of the MS participants' physical abilities. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

No individual disease or demographic variable was found to be a significant predictor of unawareness of cognitive deficits or unawareness of mood/behavioural deficits (all p values > .01).

Thus, in conclusion to this section, while no disease or demographic correlates were identified for unawareness of cognitive or mood/behavioural deficits, medical history was found to negatively correlate with positivity in this sample of 100 MS participants. Furthermore, the full model (including all medical, demographic and disease variables)

significantly predicted unawareness of physical deficits, with disease severity being negatively correlated with, and a significant individual predictor of, unawareness of physical deficits. I hypothesised that the disease correlates of the two types would differ, and support for this hypothesis was, therefore, largely found. I also hypothesised that positivity and unawareness would occur both early and late in the disease, with either little or severe physical disability. Disease duration was not found to correlate with either positivity or unawareness, however, disease severity (as measured by degree of physical disability) was found to correlate with unawareness of physical deficits. Thus, this second hypothesis was largely rejected. It was furthermore hypothesised that gender and/or current disease state would correlate with at least one type of euphoria, and this hypothesis was also rejected.

The cognitive correlates. The cognitive correlates of the two types of euphoria were then also investigated with the aim of predicting which MS participants may present with positivity and/or unawareness. I hypothesised that the cognitive correlates of the euphoric types would differ, that at least one of the euphoric types (most likely that of positivity) would correlate with impairment on neuropsychological tests of cortical domains of function, and that at least one of the euphoric types (most likely that of unawareness) would correlate with RH involvement on cognitive testing. First, however, the cognitive functioning (or impairment) of the sub-sample of MS participants (n = 60) that underwent cognitive testing will be described below. This was achieved by comparing them with the matched sub-sample of HCs (n = 35) who underwent cognitive testing in terms of the cognitive variables examined (as Western norms may not be appropriate for SA participants).

The cognitive functioning of the MS sample. The cognitive functioning of the MS sub-sample was compared with that of the HCs who underwent cognitive testing, and the results are presented in this section. I hypothesised that the MS group would demonstrate a significantly poorer performance on all measures than the HC group. Given indications in the literature reviewed at the beginning of this dissertation, it was further hypothesised that they would demonstrate impairment on cognitive functions sub-served by both cortical and subcortical domains, and that they would demonstrate impairment on measures of right cortical hemispheric functioning, but much less so on measures of left hemispheric functioning.

Although the HCs were matched as closely as possible to the MS participants, the 60 MS and 35 HC participants who underwent cognitive testing were first compared on the key

sociodemographic variables of gender, age, race/ethnicity, level of education and income, using independent samples *t*-tests for the continuous data (which was normally distributed) and chi squared tests of independence for the categorical data, in order to ensure that (a) they were well matched, (b) no significant group differences existed on these variables, and (c) none of these variables were confounding factors that could contribute to differences in cognition between the two groups. These results are presented in Table 29 (with the descriptive statistics of the full list of variables again available in Table H2, in Appendix H).

Table 29

The Key Sociodemographic Characteristics of the MS Participants and Healthy Controls That Completed Cognitive Testing

Key variable	MS participants (n = 60)	Healthy controls (n = 35)	*t* (*df* = 93) / X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI *LL*	95% CI *UL*	Effect size *d* / *V*
Gender – Male:Female	8:52	6:29	0.26	.613			0.05
Age	43.35 (11.48)	42.69 (11.35)	0.27	.785	-5.49	4.16	0.06
Race/ethnicity – White:Coloured/Indian	34:26	22:13	0.35	.554			0.06
Education[a]	13 (1.69)	13.49 (1.38)	-1.44	.152	-0.18	1.15	-0.31
Income[b]	R23,002.17 (R18,427.84)	R22,820.50 (R17,371.63)	0.05	.962	-7,804.88	7,441.55	0.01

Note. Categorical data are presented in ratios. The data on age, education, and income are presented as means with the standard deviations in parentheses. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Combined monthly household income.

The characteristics of the 35 HCs did not differ significantly from the 60 MS participants on any of the key demographic variables listed above (all *p* values > .01). Thus, the groups were deemed to be similar and the sociodemographic variables explored were not thought to represent confounding factors.

The main aim of this section was to investigate the cognitive correlates of the two euphoric types; however there were a number of cognitive variables, but only 60 MS participants who completed these tests. Thus, composite cognitive variables were created in order to reduce the number of cognitive variables investigated and to increase the power of the multiple regression. The procedure followed to determine these composites will be presented below, followed by an interpretation of the MS group's performance on these variables (as compared with that of the HCs).

First, it should be noted that a number of the cognitive measures required an interpretation of the participants' performance. These included the ROCF for visuospatial construction, the BVMT-R for visual learning and memory, and the ApBat for the repetition of prosody in spoken words. Three raters were therefore utilised for these measures and the average score (between all three) was used. Good to high inter-rater reliability was found for all measures after conducting a single measures intraclass correlation. The inter-rater reliability for the MS group was as follows: (a) ICC = .84 for visuospatial construction, (b) ICC =.99 for visual learning, (c) ICC = .98 for visual memory, and (d) ICC = .77 for prosodic repetition. Inter-rater reliability for the HC group was as follows: (a) ICC = .82 for visuospatial construction, (b) ICC = .99 for visual learning, and (c) ICC = .98 for visual memory (all *p* values < .001.). There was slightly less agreement between raters for the HC group on prosodic repetition, however the agreement was still statistically significant: ICC = .39 (*p* = .0001).

The average scores for the above measures, and the scores of the other variables were then entered into a factor analysis (with the extraction criterion of eigenvalues of greater than one) to determine which variables could be grouped together in order to reduce the number of variables included in the multiple regression analyses (see Table K1, in Appendix K, for the pattern matrix of this analysis). The variables speed of information processing, verbal fluency, and the two prosodic variables were removed as they were loading onto a number of variables, and another similar factor analysis was performed (see Table K2, in Appendix K, for these results). This analysis revealed clear factors for verbal memory, visual memory, language, and visuospatial processing and composites were created for these variables using the method outlined in the section on data analysis in the methods section. The remaining

executive functioning measures did not load clearly onto one single distinct factor. Thus, a number of composites were attempted for the measures of executive functioning.

Again, in order to create composite variables where descriptive statistics could still be obtained and the composites could be compared between groups, a composite was not computed by the creation and averaging of z scores. Rather, the variance of each scale[8] was calculated. The relevant individual scales that were to be combined to form each composite were then manipulated so that they all had the same range variance. Following this, all relevant (manipulated) individual scales were added together. Each composite was then tested using an inter-item correlation to test whether or not it correlated with the original individual component variables. Inter-item correlations are presented in Tables L1 through L12, in Appendix L, but all *p* values were < .001 for the MS participant data (except for WAB comprehension and the language composite, $p = .046$) and < .003 for the HC data (except for WAB comprehension and the language composite, $p = .421$, and attention and the dorsolateral prefrontal functioning composite, $p = .038$).

The MS participants and HCs were then compared on these composites, and the individual variables of speed of information processing, verbal fluency and prosodic repetition and comprehension, which were removed from the factor analysis. This was achieved via independent samples *t*-tests. The significance level was again set at $\alpha = .01$. As the MS participants were hypothesised to perform more poorly than the HCs; directional one-tailed *p* values are reported with the results (see Table 30).

[8] All cognitive variables were measured on continuous scales.

Table 30

The Cognitive Performance of the MS Participants Compared with the Healthy Controls

Measure	MS participants (n = 60)	Healthy controls (n = 35)	*T* (*df* = 93)	*p* (1-tailed)	95% CI *LL*	95% CI *UL*	Effect size *d* / *r*
Subcortical (executive functioning)							
Speed of information processing[b]	630.74 (232.36)	543.23 (199.66)	-1.86	.033	-180.84	5.82	0.40
Verbal fluency	35.27 (12.44)	40.60 (10.62)	2.12	.018	0.35	10.32	0.22
Cortical							
Executive functioning							
Dorsolateral prefrontal functioning composite[c]	59.36 (7.11) (n = 45)	64.44 (6.32) (n = 30)	3.17 (*df* = 73)	**.001**	1.88	8.28	-0.74
Orbitobasal composite[a]	34.45 (9.27)	35.97 (5.72)	0.88	.192	-1.92	4.96	-0.19
Memory							
Verbal memory composite (left)	169.75 (24.06)	189.51 (18.52)	4.19	**.0001**	10.39	29.14	0.40
Visual memory composite (right)	85.14 (16.86)	93.74 (11.52)	2.67	**.005**	2.21	14.99	-0.57
Language composite (left)	272.14 (18.34)	278.11 (15.17)	1.63	.054	-1.32	13.25	0.17
Visuospatial composite (right)[a]	93.16 (9.86)	97.45 (6.12)	2.62 (*df* = 92.58)	**.005**	1.04	7.55	-0.49
Prosody (right)							
Prosodic repetition[a c]	127.10 (13.06) (n = 56)	133.88 (6.03) (n = 32)	3.31 (*df* = 83.17)	**.001**	2.70	10.84	-0.62
Prosodic comprehension	56.05 (8.21)	58.51 (10.32)	1.28	.102	-1.35	6.28	-0.27

Note. All data are presented as means with standard deviations in parentheses. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning. Orbitobasal composite = disinhibition and set shifting. Verbal memory composite = verbal learning, memory and recognition. Visual memory composite = visual learning, memory and recognition. Language composite = naming, repetition and comprehension. Visuospatial composite = visuospatial perception 2D, visuospatial perception 3D and visuospatial construction.

[a] = Levene's test for homogeneity was significant, therefore the results for "equal variances not assumed" were reported along with the degrees of freedom next to the statistic.

[b] = a lower value indicates a better performance.

[c] = incomplete data set, relevant sample numbers are presented in parentheses.

In terms of descriptive statistics, the MS group performed more poorly than the HC reference group on every measure (composite or individual) of cognitive functioning. However, from the inferential statistics, one can see that they performed significantly more poorly than the HC group on measures of verbal memory composite (verbal learning, memory and recognition), visual memory composite (visual learning, memory and recognition), dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), and repetition of prosodic information (all p values < .01). Variables that almost reached statistical significance at the .01 level included verbal fluency (p = .018). Thus, the only variables that did not reach, or very nearly reach, statistical significance were speed of information processing, orbitobasal composite (disinhibition and set shifting), language composite (naming, repetition and comprehension), and the comprehension of prosodic information.

Since I hypothesised that when compared to the HCs, the MS participants would perform significantly more poorly, the evidence largely supports this hypothesis. The variables investigated were also delineated in terms of the neuroanatomical area by which the domain was sub-served and a subcortical versus cortical hypothesis and a right versus left hypothesis was tested. Firstly, the results presented above largely appeared to provide support for the cortical/subcortical hypothesis, as the MS group performed near to significantly more poorly than the HCs on the subcortical variable of verbal fluency, and importantly performed significantly more poorly than the HCs on the cortical variables of dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), verbal memory composite (verbal learning, memory and recognition), visual memory composite (visual learning, memory and recognition), visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), and the repetition of prosody. Secondly, using these same measures, but now separating them in terms of which were sub-served by left versus right areas, the MS group performed significantly (or very nearly significantly) more poorly than the HCs on the majority of measures of RH functioning, but did not perform significantly more poorly than the HCs on measures of left cortical hemispheric functioning.

The cognitive correlates of euphoria. The cognitive correlates of positivity and unawareness were then examined and multiple regression analyses were run in order to determine if each symptom has a separate, distinct cognitive profile and if one could predict

which MS participants would present with which symptom based on their type and severity of cognitive impairment. As only a sub-sample of the MS participants took part in cognitive testing, the multiple regression analyses run were conducted using the sub-sample of 60 MS participants, and individual cases that did not complete the prosodic repetition or the measures making up the dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning) were excluded pair-wise.

As predictions were made regarding particular variables, two hierarchical regression models were used. In the first, the cortical variables pertaining to (a) executive functioning (i.e. the dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), and orbitobasal composite (disinhibition and set shifting)); (b) memory (i.e. the verbal memory composite (verbal learning, memory and recognition), and visual memory composite (visual learning, memory and recognition)); (c) the language composite (naming, repetition and comprehension); (d) the visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction); and (e) the repetition and comprehension of prosody were entered first. This was followed by the subcortical variables of verbal fluency and speed of information processing.

In the second hierarchical model, measures of RH functioning were entered first. These included (a) the visual memory composite (visual learning, memory and recognition), (b) the visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), and (c) the two measures of prosody. These were followed by the remaining measures of left hemispheric functioning or executive functioning, as described above in relation to the first model.

The full scales of positivity and unawareness, within the sub-sample of MS participants who underwent cognitive testing (n = 60), were selected as the dependent variables, as including only those participants demonstrating high positivity, or those participants demonstrating unawareness would again limit the range of these variables, thereby precluding covariance analysis. Again, I will refer to awareness to denote the full scale of this variable, as I have done previously. All assumptions were met prior to running the multiple regressions and the correlations between the variables investigated are reported in Tables M1 through M4, in Appendix M.

The aim was to investigate whether positivity and unawareness had distinct profiles in terms of these correlates. In line with the ideas of Cottrell and Wilson (1926), I hypothesised that the cognitive correlates of the euphoric types may differ. Furthermore, based on the literature presented at the beginning of this dissertation, I hypothesised that at least one of the

euphoric types (most likely that of positivity) would correlate with impairment on neuropsychological tests of cortical domains of function, and that at least one of the euphoric types (most likely that of unawareness) would correlate with RH involvement on cognitive testing.

The model results. The results pertaining to all models testes are presented in Tables 31 and 32.

Table 31

Model Summaries for Positivity and Unawareness (Cortical and Subcortical Cognitive Correlates)

						Change statistics				
Model	R	R^2	F	*p*	SEE	ΔR^2	ΔF	*df*1	*df*2	Sig. ΔF
Positivity										
1	.37[a]	.14	.65	.734	36.33	.14	.65	8	32	.734
2	.39[b]	.15	.54	.847	37.22	.01	.25	2	30	.783
Unawareness of physical										
1	.55[a]	.31	1.76	.123	2.89	.31	1.76	8	32	.123
2	.58[b]	.33	1.52	.182	2.92	.03	.69	2	30	.509
Unawareness of cognitive										
1	.46[a]	.21	1.07	.407	1.87	.21	1.07	8	32	.407
2	.49[b]	.24	.93	.524	1.90	.02	.48	2	30	.623
Unawareness of mood/behaviour										
1	.37[a]	.14	.64	.740	16.48	.14	.64	8	32	.740
2	.41[b]	.17	.62	.788	16.70	.03	.59	2	30	.559

Note. [a] = Predictors: Dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), orbitobasal composite (disinhibition and set shifting), verbal memory composite (verbal learning, memory and recognition), visual memory composite (visual learning, memory and recognition), language composite (naming, repetition and comprehension), visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), prosodic repetition, and prosodic comprehension.

[b] = Predictors: Dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), orbitobasal composite (disinhibition and set shifting), verbal memory composite (verbal learning, memory and recognition), visual memory composite (visual learning, memory and recognition), language composite (naming, repetition and comprehension), visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), prosodic repetition, prosodic comprehension, speed of information processing and verbal fluency.

Table 32

Model Summaries for Positivity and Unawareness (Right and Left/Executive Cognitive Correlates)

						Change statistics				
Model	R	R^2	F	*p*	SEE	ΔR^2	ΔF	*df*1	*df*2	Sig. ΔF
Positivity										
1	.24[a]	.06	.57	.687	35.80	.06	.57	4	36	.687
2	.39[b]	.15	.54	.847	37.22	.09	.55	6	30	.766
Unawareness of physical										
1	.46[a]	.21	2.45	.063	2.90	.21	2.45	4	36	.063
2	.58[b]	.34	1.52	.182	2.92	.12	.91	6	30	.499
Unawareness of cognitive										
1	.40	.16	1.70	.171	1.82	.16	1.70	4	36	.171
2	.49	.14	.93	.524	1.90	.08	.50	6	30	.802
Unawareness of mood/behaviour										
1	.33	.11	1.10	.373	15.80	.11	1.10	4	36	.373
2	.41	.17	.62	.788	16.70	.06	.37	6	30	.891

Note. [a] = Predictors: Visual memory composite (visual learning, memory and recognition), visuospatial construction (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), prosodic repetition and prosodic comprehension.
[b] = Predictors: Visual memory composite (visual learning, memory and recognition), visuospatial construction (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction), prosodic repetition, prosodic comprehension, dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning), orbitobasal composite (disinhibition and set shifting), verbal memory composite (verbal learning, memory and recognition), language composite (naming, repetition and comprehension), speed of information processing and verbal fluency.

None of the models tested were found to significantly predict either type of euphoria. The results pertaining to the coefficients (presented in Tables M5 through M12, in Appendix M), were, however, also analysed.

The coefficient results. No individual cognitive variable was found to significantly predict any of the types of euphoria (i.e. positivity or unawareness of physical, cognitive or mood/behavioural deficits) in either the cortical versus subcortical model or the right versus left/executive model (all *p* values >.01).

Although not significant, two variables that were close to significant were tested further via a linear regression to investigate their ability to predict euphoria. These were the orbitobasal composite (disinhibition and set shifting) for unawareness of physical deficits, when all (i.e. right and left) cortical (but no subcortical) measures were included (β = .45, *p* = .056), and the visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction) for unawareness of cognitive deficits, in all models (cortical variables only: β = .47, *p* = .032; RH variables only: β = .38, *p* = .056; all cognitive variables: β = .48, *p* = .032).

The orbitobasal composite was found to significantly predict awareness of physical deficits, explaining 23% of the variance on its own (R^2 = .23,F(1, 58) = 17.72, *p* = .0001). The coefficient results are presented below, in Table 33.

Table 33

Linear Regression Between the Orbitobasal Composite and Unawareness of Physical Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Constant	-6.30	1.37		-4.59	.0001	-9.05	-3.55
Orbitobasal composite	.16	.04	.48	4.21	**.0001**	0.09	0.24

Note. Significant results are presented in bold font. Orbitobasal composite = disinhibition, set shifting. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

The results pertaining to the analysis of the visuospatial composite demonstrated that, on its own, visuospatial ability significantly predicted 12% of the variance of awareness of cognitive deficits (R^2 = .12, F(1, 58) = 7.66, *p* = .008). The coefficient results are presented in Table 34.

Table 34

Linear Regression Between the Visuospatial Composite and Unawareness of Cognitive Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Constant	-4.85	2.21		-2.20	.032	-9.28	-0.43
Visuospatial composite	.07	.02	.34	2.77	**.008**	0.02	0.11

Note. Significant results are presented in bold font. Visuospatial composite = visuospatial perception 2D, visuospatial perception 3D, visuospatial construction. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Thus, in conclusion to this section, while no cognitive correlates were identified for positivity, or for unawareness of mood/behavioural deficits, disinhibition and problems with set shifting were significant predictors of unawareness of physical deficits, and poor visuospatial abilities significantly predicted unawareness of cognitive deficits. In terms of the first hypothesis of this section, namely that the cognitive correlates of the euphoric types would differ, support was largely found for this hypothesis. It was, furthermore, hypothesised that at least one of the euphoric types (i.e. positivity) would correlate with cortical impairment on cognitive testing, and that at least one (i.e. unawareness) would correlate with measures of RH functioning on neuropsychological testing. As a cortical variable was found to be significant in two cases of unawareness, and a measure of RH functioning was found to be significant in one case of unawareness, support for these hypotheses also appeared to be found.

Summary of part two. The main aims of part two were to further describe and be better able to predict the newly identified types of euphoria (viz. positivity and unawareness). The results appeared to indicate an association between positivity and unawareness implying that they are two types of euphoria that often co-occur. Both were demonstrated to have an inverse relationship with depression. The positivity of the MS participants was found to be comparable to that of the HCs only at the high level; and MS participants were found to significantly (or near to significantly) under-estimate their deficits, compared with their informants, across all domains. Few demographic, disease or cognitive correlates were identified; however, positivity was predicted by the lack of a prior medical history of conditions that could influence neuropsychological functioning. Unawareness of physical deficits was predicted by all demographic and disease variables included as well as by a

greater disease severity and problems with disinhibition and set shifting, individually. Unawareness of cognitive deficits was predicted only by visuospatial impairment. No correlates were identified for unawareness of mood/behavioural deficits.

Part three. The cause of euphoria

The main aim of part three was to explore some intriguing ideas about potential causes of euphoria. Due to limited sample sizes and unequal sizes between the patient control groups and the MS group, the findings of this section are very preliminary. However, because these are interesting and exciting hypotheses, and because they may perhaps shed some light on which lines of investigation show promise for future investigation with full research protocols, they are presented despite these limitations. But, great caution is required with regard to any interpretations of this data.

As was described in detail in the literature review, two main hypotheses have existed in the literature: that euphoria in MS is (a) a psychological reaction to a disabling disease, or (b) the result of executive dyscontrol. In terms of the first hypothesis, the literature largely regards euphoria as being caused by cerebral involvement (see, e.g. Rabins et al., 1986), but this has not been unequivocally proven, and the psychological reaction hypothesis is still a possibility. Thus, a group of MG patients were used to examine this idea, as MG is similarly a chronic disease, but does not affect the CNS (Cantor, 2010; Dönmez et al., 2004; Wolfe et al., 2012).

Regarding the second hypothesis, the contemporary literature, and even some of the classical literature, regards euphoria in MS to be the result of executive dysfunction (largely due to the white damage so prevalent in MS, or to focal grey matter damage of the frontal lobes; Benedict et al., 2001; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004). However, this has not yet been proven. Thus, a group of patients who had experienced a TBI as a result of an MVA were included to examine this hypothesis, as MVA TBI results in damage to neuroanatomical areas and causes a dysexecutive cognitive picture that is similar to that of MS.

There may, however, be other factors at play regarding the cause of euphoria in MS. For example, possible contributions made by the immunological nature of the disease or RH dysfunction have not (to my knowledge) been addressed before. Thus, two further patient control groups (i.e. NP-SLE patients and patients with damage to only their RH) were also included to test these third and fourth hypotheses.

The diagnoses of all of the participants in the above patient control groups were confirmed prior to analysis. All groups were then analysed in the same way. First, an attempt was made to assess the suitability of each patient control group to address their relevant research question. This was done by comparing each patient control group with the MS group on key demographic variables, via chi-squared tests of independence for the categorical

variables and independent samples *t*-tests for the normally distributed continuous variables, to determine the influence of variables such as gender, age, race, education and income on the other variables in question (i.e. the cognitive and euphoric variables). In addition, the sub-samples of each patient control group that underwent cognitive testing[9] were compared with the 60 MS participants who underwent cognitive testing, via ANCOVAs, which controlled for any significant pre-existing between-group differences on the abovementioned key demographic variables, while investigating the cognitive performance of the group. This was done in an attempt to test the hypotheses that the MGs would demonstrate a better cognitive performance in relation to the MS group, and that the MVA TBIs and NP-SLEs would demonstrate similar executive dysfunction to the MS group. All assumptions were checked prior to performing this test and although unequal sample sizes were present, the ANCOVA was never-the-less performed as the remaining assumptions were met and it is considered to be fairly robust test (Levy, 1980; Lund Research Ltd, 2013).

The hypotheses to be tested included that, when significant pre-existing group differences were controlled for, the MGs would demonstrate better cognitive functioning than the MS group, and that the MVA TBI and NP-SLE groups would demonstrate similar cognitive functioning to the MS group. As group differences were expected, 1-tailed *p* values are reported.

First, however, two of the cognitive measures (i.e. BVMT-R, part of the visual memory composite, and the ROCF for visuospatial construction) required an interpretation. Therefore three raters scored these particular tests and the average between all three was used. A single measures intraclass correlation was calculated for each of the measures, for each group of participants. Inter-rater reliability for the MS group has already been reported in part two of the results section, and fairly high inter-rater reliability was found for all measures in the patient control groups: (a) visual learning - MG: .96, MVA TBI: .99, NP-SLE: .96; (b) visual memory - MG: .99, MVA TBI: .99, NP-SLE: .85; and (c) visuospatial construction - MG: .76, MVA TBI: .82, NP-SLE: .98 (all p values < .001).

Composite variables were then created for these and the remaining cognitive variables included in this study. The method of creation of these cognitive composites has been described in part two of the results section, and the correlations between the individual component measures and their composites reported for the MS group. The individual

[9] Note: The RH control participants did not undergo cognitive testing in this study due to research fatigue of this patient group. However, their cognitive functioning was described in detail from their participation in a similar study conducted in the same year.

component measures and their composites for the patient control groups were, on the whole, well correlated, with the majority of *p* values < .01 (please see Tables N1 through N12, in Appendix N, for the results of these analyses).

All patient control groups were then compared with the full MS group (n = 100) on the measures pertaining to positivity and unawareness, via ANCOVAs, to determine whether group differences occurred between the MS and patient control groups for these variables, while taking any significant pre-existing group differences on the key demographic variables into account. For positivity, the participants were compared using the scores of the full sample, those participants presenting with moderate positivity, and those participants presenting with high positivity. For unawareness, the scores of only unaware participants (i.e. those with negative discrepancy scores where participants under-estimated their deficits when compared to their informants) were compared.

The above comparison (i.e. between the groups for positivity and unawareness) was made in order to test the main hypotheses of this section: that the euphoric types would not be prominent amongst participants with MG (or would not be as prominent as in the other groups), and that at least one euphoric type would be present in participants with MVA TBI, NP-SLE, and participants with RH damage. As group differences were again expected, 1-tailed values are reported.

The results of the four hypotheses will be presented below. To remind the reader, these hypotheses regarded euphoria in MS as being the result of: (a) a psychological reaction to the disease, (b) executive dysfunction, (c) immunological processes, and (d) RH damage. To further remind the reader, the results presented below are from preliminary analyses, using very small patient control groups, and must be interpreted with caution.

A psychological reaction. An attempt was made to test the first potential cause for euphoria (i.e. a psychological reaction to the disease) using the participants with MG. Ten MG participants underwent a cognitive assessment and completed the questionnaires pertaining to euphoria, while a further 10 only completed the euphoria questionnaires.

Assessing the suitability of the group to address the research question. MS and MG participants were compared on the key demographic variables first (see Table 35) to determine if any pre-existing group differences existed that may influence their performance on the other variables investigated.

Table 35

The Key Sociodemographic Characteristics of the MS Participants and MG Controls

Key variable	MS participants (n = 100)	MG controls (n = 20)	*t* (*df* = 118) / X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI		Effect size *d* / *V*
					LL	*UL*	
Gender – Male:Female	14:86	4:16	0.47	.493			0.06
Age	44.49 (11.17)	39.95 (13.39)	1.60	.111	-1.07	10.15	0.04
Race/ethnicity – White:Coloured/Indian	71:29	8:12	7.12	**.008**			0.24
Education[a b]	13.18 (1.65)	11.65 (2.58)	2.545 (*df* = 22.22)	.018	0.29	2.77	0.84
Income[c]	R26,006.51 (R22,536.54)	R22,200.53 (R37,983.85)	0.61	.546	-8,640.72	16,252.68	0.15
Duration of illness	9.57 (7.50)	7.45 (7.19)	1.16	.248			0.28
Number of participants with a medical history that can affect neuropsychological functioning	41 (41%)	10 (50%)	0.55	.457			0.07
Use of medication that can affect mood	68 (68%)	15 (75%)	0.38	.536			0.06

Note. Categorical data are presented in ratios or percentages. The data on age, education, income, and duration of illness are presented as means with standard deviations in parentheses. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Levene's test for homogeneity was significant, therefore the results for "equal variances not assumed" were reported along with the degrees of freedom next to the statistic.

[c] = Combined monthly household income.

The only significant pre-existing group difference between the MS and MG groups occurred for the variable of race or ethnicity. Highest level of education was almost, but not quite, significant (p = .018). Education, however, had a large effect size (d = 0.84) and while well-matched on the other variables, these differences in race and education could impact negatively on performance on neuropsychological tests and, therefore, were controlled for in the following analyses.

The MG group who underwent cognitive testing (n = 10) was then compared with the MS group who underwent cognitive testing (n = 60), to assess their cognitive functioning while controlling for the significant pre-existing between-group differences for race/ethnicity and close to significant differences for education. This was done in order to attempt to assess the MG's suitability as a control group and to assist in indicating whether their cognitive functioning was better than that of the MS group. Descriptive results are presented first in Table 36, followed by results of the inferential statistics in Table 37.

Table 36

The Cognitive Performance of the MS Participants and MG Controls

Measure	MS participants (n = 60)	MG controls (n = 10)
Subcortical (executive functioning)		
Speed of information processing	630.74 (232.36)	634.15 (179.26)
Verbal fluency	35.27 (12.44)	27.60 (9.69)
Cortical		
Executive functioning		
Dorsolateral prefrontal[a]	59.36 (7.11)	55.35 (8.29)
functioning composite	(n = 45)	(n = 6)
Orbitobasal composite	34.45 (9.27)	33.10 (11.51)
Memory		
Verbal memory composite (left)	169.75 (24.06)	151.35 (30.24)
Visual memory composite (right)	85.14 (16.86)	73.10 (16.62)
Visuospatial (right)		
Visuospatial construction	30.56 (3.09)	29.10 (3.26)

Note. All data are presented as means with standard deviations in parentheses.
[a] = incomplete data set, relevant sample numbers are presented in parentheses.

Table 37

ANCOVA Between-Subjects Effects (Between MS Participants and MG Controls) for the Cognitive Variables, Controlling for Race and Education

	Adjusted means							
Source	MS	MG	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Subcortical (executive functioning)								
Speed of information processing	640.46	610.10						
Corrected model			173,288.19	4	43,322.05	0.85	.497	0.05
Intercept			802,048.52	1	802,048.52	15.79	.0001	0.23
Type of participant			4,989.59	1	4,989.59	0.10	.755	0.00
Error			3,301,569.96	65	50,793.38			
Total			31,365,933.68	70				
Corrected total			3,474,858.15	69				
Verbal fluency	34.25	31.43						
Corrected model			2,304.74	4	576.19	4.59	.003	0.22
Intercept			57.94	1	57.94	0.46	.500	0.01
Type of participant			43.08	1	43.08	0.34	.560	0.00
Error			8,169.20	65	125.68			
Total			92,212.00	70				
Corrected total			10,473.94	69				
Cortical								
Executive functioning								
Dorsolateral prefrontal functioning composite	58.91	56.21						
Corrected model			459.53	4	114.88	2.41	.063	0.17
Intercept			440.40	1	440.40	9.24	.004	0.17
Type of participant			33.06	1	33.06	0.69	.409	0.12
Error			2,192.33	46	47.66			
Total			179,509.21	51				
Corrected total			2,651.86	50				

Source	Adjusted means MS	Adjusted means MG	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Cortical								
Orbitobasal composite	33.28	39.53						
Corrected model			2,537.22	4	634.30	11.02	.0001	0.40
Intercept			1.55	1	1.55	0.03	.870	0.00
Type of participant			211.49	1	211.49	3.68	.060	0.03
Error			3,740.16	65	57.54			
Total			88,426.00	70				
Corrected total			6,277.37	69				
Memory								
Verbal memory composite (left)	167.76	155.52						
Corrected model			12,495.20	4	3,123.80	6.19	.0001	0.28
Intercept			7,017.62	1	7,017.62	13.91	.0001	0.15
Type of participant			810.00	1	810.00	1.61	.210	0.02
Error			32,786.02	65	504.40			
Total			2,000,351.25	70				
Corrected total			45,281.22	69				
Visual memory composite (right)	83.33	78.91						
Corrected model			8,085.42	4	2,021.36	10.58	.0001	0.02
Intercept			128.09	1	128.09	0.67	.416	0.00
Type of participant			105.74	1	105.74	0.55	.220	0.00
Error			12,417.89	65	191.05			
Total			507,670.56	70				
Corrected total								

Source	Adjusted means MS	Adjusted means MG	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Cortical								
Visuospatial (right)								
Visuospatial construction	30.36	30.03						
Corrected model			93.73	4	23.43	2.61	.044	0.00
Intercept			637.38	1	637.38	70.92	.0001	0.03
Type of participant			0.59	1	0.59	0.07	.798	0.00
Error			584.20	65	8.99			
Total			65,146.39	70				
Corrected total			20,503.32	69				

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning; Orbitobasal composite = disinhibition and set shifting; Verbal memory composite = verbal learning, memory and recognition; Visual memory composite = visual learning, memory and recognition.

Descriptive statistics appear to imply that the MG participants performed a little more poorly than the MS participants on all measures of cognition. However, the ANCOVA results above (see Table 37), suggest that when race and education were controlled for, no significant differences existed between the MS and MG groups, with very small eta-squared values indicating a very small effect size within these analyses.

These are limited results and are based on a small sample of only 10 MG controls. However, they appeared to suggest that the cognitive performance of the MG group was not better than that of the MS group. However, they did not appear to perform significantly more poorly on any of the measures. Thus, the MG group were tentatively accepted to be a possibly appropriate reflection of a similar chronic disease to MS that does not affect the brain, or cognitive functioning. Thus, I proceeded with an analysis of the euphoric variables.

Addressing the research question. The 20 MG controls were then compared with the 100 MS participants on the two types of euphoria identified by this study: positivity and unawareness, while controlling for the significant group differences described above. This was done in order to provisionally investigate whether the MGs would demonstrate these two types of euphoria at lower levels than the MS participants. Descriptive results are presented first in Table 38, followed by results of the preliminary inferential statistics, based on limited and unequal sample sizes, in Table 39.

Table 38

The Performance on Measures of Positivity and Unawareness of the MS Participants and MG Control Group

Self-report measure	MS participants (n = 100)	MG controls (n = 20)
Positivity		
Composite (all participants)	122.12 (35.02)	138.94 (28.49)
Moderate positivity scores (50%-75% cut-off)	133.02 (15.26) (n = 54)	139.33 (15.01) (n = 13)
High positivity scores (75% cut-off)	176.98 (9.24) (n = 13)	174.21 (5.33) (n = 4)
Unawareness (negative discrepancies only)		
Physical domain (PAS)		
Unawareness scores (all unaware participants)	3.42 (2.30) (n = 45)	4.00 (2.41) (n = 10)
Moderate unawareness scores (50%-75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Cognitive domain (AI)		
Unawareness scores (all unaware participants)	1.44 (.81) (n = 16)	1.00 (n = 1)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Mood/behavioural domain (NPI)		
Unawareness scores (all unaware participants)	9.21 (8.94) (n = 24)	12.00 (9.43) (n = 7)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-

Note. All data are presented as means with standard deviations in parentheses. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale. AI = Awareness Interview. NPI = Neuropsychiatric Inventory.

Table 39

ANCOVA Between-Subjects Effects (Between MS and MG Participants) for Positivity and Unawareness (Controlling for Race and Education)

	Adjusted means							
Source	MS	MG	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Positivity								
Composite (all participants)	125.72	138.97						
Corrected model			12,067.62	4	3,016.91	2.68	.035	0.09
Intercept			26,233.82	1	26,233.82	23.30	.0001	0.19
Type of participant			2,616.75	1	2,616.75	2.33	.130	0.02
Error			129,457.93	115	1,125.72			
Total			2,014,201.28	120				
Corrected total			141,525.55	119				
Moderate positivity scores (50%-75% cut-off)	134.20	142.05						
Corrected model			1,304.52	4	326.13	1.427	.235	0.08
Intercept			17,424.15	1	17,424.15	76.27	.0001	1.13
Type of participant			548.37	1	548.37	2.40	.126	0.04
Error			14,165.11	62	228.47			
Total			1,222,867.15	67				
Corrected total			15,469.63	66				
High positivity scores (75% cut-off)	174.39	183.00						
Corrected model			327.82	4	81.96	1.22	.353	0.29
Intercept			4,630.26	1	4,630.26	68.97	.0001	4.09
Type of participant			87.42	1	87.42	1.30	.276	0.08
Error			805.61	12	67.13			
Total			529,680.84	17				
Corrected total			1,133.43	16				

Source	Adjusted means MS	Adjusted means MG	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Unawareness (unaware participants only)								
Physical domain (PAS)	3.45	3.88						
Corrected model			16.68	4	4.17	0.77	.552	0.06
Intercept			48.78	1	48.78	8.97	.004	0.17
Type of participant			1.05	1	1.05	0.19	.662	0.94
Error			277.25	51	5.44	0.001	.975	
Total			994.00	56				
Corrected total			293.93	55				
Cognitive domain (AI)	1.46	0.06						
Corrected model			3.19	3	1.06	1.99	.165	0.32
Intercept			4.95	1	4.95	9.29	.009	0.49
Type of participant			1.24	1	1.24	2.32	.152	0.12
Error			6.93	13	0.53			
Total			44.00	17				
Corrected total			10.12	16				
Mood/behavioural domain (NPI)	9.25	12.31						
Corrected model			284.41	4	71.10	0.87	.496	0.12
Intercept			313.80	1	313.80	3.83	.061	0.13
Type of participant			48.43	1	48.43	0.59	.449	0.02
Error			2,129.79	26	81.92			
Total			5,415.00	31				
Corrected total			2,414.19	30				

Note. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale. AI = Awareness Interview. NPI = Neuropsychiatric Inventory.

Descriptive statistics suggested that, on average, the MG control participants appeared to demonstrate higher rates of positivity, than the MS participants. When the sample was divided and moderate and high scorers were examined, MGs appeared to demonstrate greater positivity at the moderate level, but not at the high level. In terms of the unaware participants, the MGs appeared to be slightly more unaware of physical and mood/behavioural deficits, but slightly more aware of cognitive deficits.

Inferential statistics controlling for the pre-existing group difference in race and education, however, appeared to suggest that no significant differences existed between these two groups for any analysis of positivity or unawareness. Not only were all *p* values > .01, but the eta-squared values were all low (the majority being $\eta^2 < 0.13$), indicating small effect sizes and a lack of statistical significance.

The above results therefore appeared to imply that the MG and MS participants, in this sample, performed similarly on all variables relating to the two types of euphoria: that is, the MGs could be described as being as positive/optimistic and as unaware of potential deficits as the MS participants. This was unexpected as the hypothesis was that MGs would not demonstrate positivity and unawareness at the same levels as the MS participants. Since they did, this hypothesis was rejected.

Executive dysfunction. Executive dysfunction is often considered to be the cause of euphoria, particularly by contemporary researchers (see, e.g. Benedict et al., 2001; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004). Thus, this was the second potential cause to be investigated, and an attempt was made to examine this using the participants with MVA TBI. Ten MVA TBI participants underwent a cognitive assessment and completed the questionnaires on euphoria, while a further nine completed only the euphoric questionnaires.

Assessing the suitability of the group to address the research question. The MS and MVA TBI participants were compared on the key demographic variables first (see Table 41) to determine if any pre-existing group differences existed that may influence their performance on the other variables investigated.

Table 40

The Key Sociodemographic Characteristics of the MS Participants and MVA TBI Controls

Key variable	MS participants (n = 100)	MVA TBI controls (n = 19)	*t* (*df* = 117) / X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI *LL*	95% CI *UL*	Effect size *d* / *V*
Gender – Male:Female	14:86	12:7	22.60	**.0001**			0.44
Age	44.49 (11.17)	32.58 (10.57)	4.30	**.0001**	6.42	17.40	1.07
Race/ethnicity – White:Coloured/Indian	71:29	7:12	8.25	**.004**			0.26
Education[a]	13.18 (1.65)	11.11 (1.88)	4.90	**.0001**	1.24	2.91	1.23
Income[b]	R26,006.51 (R22,536.54)	R14,274.18 (R16,168.59)	2.16	.033	987.52	22,477.12	0.54
Number of participants with a medical history that can affect neuropsychological functioning	41 (41%)	10 (52.6%)	0.88	.348			0.09
Use of medication that can affect mood	68 (68%)	4 (21.1%)	14.73	**.0001**			0.35

Note. Categorical data are presented in ratios or percentages. The data on age, education, and income are presented as means with the standard deviations in parentheses. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Combined monthly household income.

The inferential statistics appeared to suggest that these groups were not particularly well matched. Significant pre-existing group differences existed for gender, age, race, highest level of education and current use of medication, in this limited sample. Since group differences were implied, these variables were controlled for in future analyses, but additional caution should be taken with the interpretations made.

The MVA TBI group that underwent cognitive testing (n = 10) was then compared with the MS group that underwent cognitive testing (n = 60), to assess their cognitive functioning while controlling for the significant pre-existing between-group differences for gender, age, race, education and use of medication. This was done in order to attempt to assess the MVA TBIs suitability as a control group and to assist in signifying whether their cognitive functioning was similar to that of the MS group. Descriptive results are presented first in Table 41, followed by results of the inferential statistics in Table 42.

Table 41

The Performance on Cognitive Measures of the MS Participants and MVA TBI Controls

Measure	MS participants (n = 60)	MVA TBI controls (n = 10)
Subcortical (executive functioning)		
Speed of information processing[a]	630.74 (232.36) (n = 60)	547.64 (137.31) (n = 9)
Verbal fluency	35.27 (12.44)	27.20 (9.99)
Cortical		
Executive functioning		
Dorsolateral prefrontal functioning composite[a]	59.36 (7.11) (n = 45)	50.09 (11.32) (n = 8)
Orbitobasal composite	34.45 (9.27)	35.50 (4.67)
Memory		
Verbal memory composite (left)	169.75 (24.06)	132.80 (31.24)
Visual memory composite (right)	85.14 (16.86)	69.67 (20.96)
Visuospatial (right)		
Visuospatial construction	30.56 (3.09)	31.28 (2.45)

Note. All data are presented as means with standard deviations in parentheses.
[a] = incomplete data set, relevant sample numbers are presented in parentheses.

Table 42

ANCOVA Between-Subjects Effects (Between MS Participants and MVA TBI Controls) for the Cognitive Variables (Controlling for Gender, Age, Race, Education and Current Medication Use)

	Adjusted means							
Source	MS	MVA TBI	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Subcortical (executive functioning)								
Speed of information processing	657.31	603.15						
Corrected model			994,552.43	13	76,504.03	1.76	.075	0.29
Intercept			38,685.50	1	38,685.50	0.89	.350	0.01
Type of participant			20,377.17	1	20,377.17	0.47	.497	0.01
Error			2,395,876.47	55	43,561.39			
Total			29,905,179.02	69				
Corrected total			3,390,428.89	68				
Verbal fluency	31.93	30.19						
Corrected model			3,243.89	13	249.53	1.90	.049	0.31
Intercept			75.06	1	75.06	0.57	.452	0.01
Type of participant			3.40	1	3.397	0.03	.873	0.00
Error			7,337.20	56	131.02			
Total			92,046.00	70				
Corrected total			10,581.09	69				
Cortical								
Executive functioning								
Dorsolateral prefrontal functioning	59.45	52.04						
Composite								
Corrected model			1,827.32	12	152.28	3.25	.002	0.49
Intercept			144.48	1	144.48	3.08	.087	0.04
Type of participant			393.21	1	393.21	8.39	**.006**	0.11
Error			1,874.63	40	46.87			
Total			181,762.03	53				
Corrected total			3,701.96	52				

Source	Adjusted means MS	Adjusted means MVA TBI	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Cortical								
Orbitobasal composite	32.34	39.03						
Corrected model			2,380.89	13	183.15	3.54	.0001	0.45
Intercept			2.77	1	2.77	0.05	.818	0.00
Type of participant			97.44	1	97.44	1.886	.175	0.02
Error			2,893.91	56	51.68			
Total			89,076.00	70				
Corrected total			5,274.80	69				
Memory								
Verbal memory composite (left)	159.28	124.05						
Corrected model			29,576.30	13	2,275.10	5.08	.0001	0.54
Intercept			2,595.48	1	2,595.48	5.80	.019	0.05
Type of participant			3,618.80	1	3,618.80	8.09	**.006**	0.07
Error			25,061.65	56	447.53			
Total			1,948,197.50	70				
Corrected total			54,637.94	69				
Visual memory composite (right)	82.17	64.40						
Corrected model			12,775.36	13	982.72	5.50	.0001	0.56
Intercept			64.93	1	64.93	0.36	.549	0.00
Type of participant			1,791.87	1	1,791.87	10.03	**.002**	0.08
Error			10,007.63	56	178.71			
Total			504,239.19	70				
Corrected total			22,783.00	69				

Source	Adjusted means MS	Adjusted means MVA TBI	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Cortical								
Visuospatial (right)								
Visuospatial construction	30.55	31.37						
Corrected model			220.34	13	16.95	2.36	.014	0.35
Intercept			327.52	1	327.52	45.57	.0001	0.53
Type of participant			2.01	1	2.01	0.28	.599	0.00
Error			402.46	56	7.19			
Total			66,423.25	70				
Corrected total			622.80	69				

Note. Significant results are presented in bold font. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning; Orbitobasal composite = disinhibition and set shifting; Verbal memory composite = verbal learning, memory and recognition; Visual memory composite = visual learning, memory and recognition.

The descriptive statistics above (see Table 41) suggest that the MVA TBI group performed more poorly than the MS group on the majority of variables.

However, the ANCOVA results above (see Table 42) indicated that when gender, age, race, education and current medication use were controlled for, the MVA TBIs appeared to perform significant more poorly than the MS participants only on the dorsolateral prefrontal functioning composite (attention, WM, abstract reasoning), the verbal memory composite (verbal learning, memory, recognition), and the visual memory composite (visual learning, memory, recognition).

The results above, although not without notable associated limitations, therefore appeared to demonstrate that the MVA TBI group performed similarly to the MS group on the majority of variables, but significantly more poorly on one variable of executive functioning and the two variables of memory (where they performed more poorly on recall than recognition memory). This was largely expected and since impairment in recall memory, comparative to recognition memory, is considered to be representative of a dysexecutive, rather than an axial-type memory impairment, the performance on the memory tasks, along with the remaining performance on executive tasks, implied possible support for the tentative hypothesis regarding their similar dysexecutive picture of cognitive impairment. This group was, therefore, tentatively accepted as a possible reflection of a group with similar executive dysfunction, and I proceeded with an analysis of the euphoric variables.

Addressing the research question. The 19 MVA TBI control participants were then compared with the 100 MS participants on the two types of euphoria identified by this study: positivity and unawareness, while controlling for the significant group differences described above. This was done in order to attempt a preliminary investigation of the hypothesis that MVA TBI participants would demonstrate at least one of these two types of euphoria at the same levels as the MS participants. Descriptive results are presented first in Table 43, followed by results of the inferential statistics in Table 44.

Table 43

The Performance on Self-Report Measures of Mood and Outlook of the MS Participants Compared with the MVA TBI Control Group for Continuous Data.

Self-report measure	MS participants (n = 100)	MVA TBI controls (n = 19)
Positivity		
Composite (all participants)	122.12 (35.02)	122.65 (30.53)
Moderate positivity scores (50%-75% cut-off)	133.02 (15.26) (n = 54)	128.10 (14.41) (n = 13)
High positivity scores (75% cut-off)	176.98 (9.24) (n = 13)	172.80 (13.79) (n = 2)
Unawareness (negative discrepancies only)		
Physical domain (PAS)		
Unawareness scores (all unaware participants)	3.42 (2.30) (n = 45)	3.50 (1.05) (n = 6)
Moderate unawareness scores (50%-75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Cognitive domain (AI)		
Unawareness scores (all unaware participants)	1.44 (.81) (n = 16)	2.10 (1.60) (n = 10)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Mood/behavioural domain (NPI)		
Unawareness scores (all unaware participants)	9.21 (8.94) (n = 24)	20.70 (13.88) (n = 10)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-

Note. All data are presented as means with standard deviations in parentheses. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale. AI = Awareness Interview. NPI = Neuropsychiatric Inventory.

Table 44

ANCOVA Between-Subjects Effects (Between MS Participants and MVA TBI Controls) for Positivity and Unawareness, Controlling for Gender, Age, Race, Education and Current Medication Use

	Adjusted means							
Source	MS	MVA TBI	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Positivity								
Moderate positivity scores (50%-75% cut-off)	129.87	121.86						
Corrected model			2,701.72	14	192.98	0.81	.655	0.18
Intercept			9,480.45	1	9,480.45	39.79	.0001	0.63
Type of participant			259.47	1	259.47	1.09	.302	0.02
Error			12,390.32	52	238.28			
Total			1,183,595.90	67				
Corrected total			15,092.04	66				
High positivity scores (75% cut-off)	176.02	180.42						
Corrected model			596.52	8	74.57	0.69	.695	0.48
Intercept			649.72	1	649.72	6.01	.050	0.53
Type of participant			0.92	1	0.92	0.01	.930	0.00
Error			648.73	6	108.12			
Total			468,105.50	15				
Corrected total			1,245.25	14				
Unawareness (unaware participants only)								
Physical domain (PAS)	3.03	2.83						
Corrected model			32.87	12	2.74	0.51	.898	0.14
Intercept			9.04	1	9.04	1.69	.204	0.04
Type of participant			0.05	1	0.05	0.01	.922	0.00
Error			205.64	38	5.41			
Total			839.00	51				
Corrected total			238.51	50				

Source	Adjusted means: MS	Adjusted means: MVA TBI	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Unawareness (unaware participants only)								
Cognitive domain (AI)	1.42	1.83						
Corrected model			27.09	12	2.26	3.47	.017	0.76
Intercept			2.20	1	2.20	3.38	.089	0.62
Type of participant			0.12	1	0.12	0.19	.671	0.00
Error			8.45	13	0.65			
Total			110.00	26				
Corrected total			35.54	25				

Note. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale. AI = Awareness Interview.

Descriptively, on average, the MS and MVA TBI groups appeared to demonstrate similar levels of positivity. When moderate and high scorers for positivity were examined, the MVA TBIs demonstrated slightly lower levels of positivity at the two different cut-off points, than the MS group. When the participants classified as unaware were examined, the MVA TBIs seemingly demonstrated greater unawareness of all three domains.

ANCOVAs (see Table 46) suggested that no group differences were present for any of the variables relating to positivity or unawareness represented above. Effect sizes (via eta-squared results) were again small (all $\eta^2 < 0.03$); thus, the lack of statistical significance may not just be due to the small sample sizes. Positivity (for all participants) and unawareness of mood/behavioural deficits both violated an assumption of ANVOCA. Thus, hierarchical multiple regression analyses were run, including the controlled for variables first, and then using the "type of participant" grouping variable as a predictor variable. The grouping variable did not appear to be a significant predictor of either positivity ($\beta = -.02$, $p = .846$, 95% CI [-23.45, 19.35]) or unawareness of mood ($\beta = -.21$, $p = .087$, 95% CI [-21.10, 1.46]). Thus, significant group differences were tentatively considered not to be present for these variables either.

The above results therefore appear to indicate that the MVA TBI and MS participants performed similarly on all variables relating to the two types of euphoria: that is, the MVA TBIs were as positive/optimistic and as unaware of potential deficits as the MS participants. This was expected as the hypothesis was that MVA TBIs would demonstrate at least one of the euphoric types at the same level as the MS participants. Thus, tentative, provisional support for this hypothesis may have been demonstrated.

Immunological processes affecting the brain. An attempt was made to investigate the third potential cause for euphoria (i.e. the result of immunological processes) using the participants with NP-SLE. Ten NP-SLE participants underwent the cognitive assessment and completed the mood questionnaires.

Assessing the suitability of the group to address the research question. The MS and NP-SLE participants were compared on the key demographic variables first (see Table 45) to determine if any pre-existing group differences existed that may influence their performance on the other variables investigated.

Table 45

The Key Sociodemographic Characteristics of the MS Participants and NP-SLE Controls

Key variable	MS participants (n = 100)	NP-SLE controls (n = 10)	*t* (*df* = 108) / X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI		Effect size *d* / *V*
					LL	*UL*	
Gender – Male:Female	14:86	1:9	0.12	.725			0.03
Age	44.49 (11.17)	45.60 (9.54)	-0.30	.762	-8.37	6.15	-0.10
Race/ethnicity – White:Coloured/Indian	71:29	0:10	20.03	**.0001**			0.43
Education[a b]	13.18 (1.65)	9.40 (4.33)	2.74 (*df* = 9.27)	.022	0.68	6.88	1.88
Income[c]	R26,006.51 (R22,536.54)	R11,040.50 (11,493.30)	2.07	.041	614.24	29,317.77	0.69
Duration of illness[b]	9.57 (7.50)	10.90 (13.21)	-0.31 (*df* = 9.59)	.761	-10.84	8.18	-0.16
Number of participants with a medical history that can affect neuropsychological functioning	41 (41%)	7 (70%)	3.11	.078			0.17
Use of medication that can affect mood	68 (68%)	7 (70%)	0.02	.897			0.01

Note. Categorical data are presented in ratios or percentages. The data on age, education, income, and duration of illness are presented as means with the standard deviations in parentheses. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Levene's test for homogeneity was significant, therefore the results for "equal variances not assumed" were reported along with the degrees of freedom next to the statistic.

[c] = Combined monthly household income.

The only significant pre-existing between-group difference that appeared to exist was for race or ethnicity, which was controlled for in the following analyses.

The NP-SLE group was then compared with the MS group who underwent cognitive testing (n = 60), while controlling for the significant pre-existing between-group differences for race. This was done in order to attempt to assess the suitability of the NP-SLE group to investigate their research question, and to assist in indicating whether their cognitive functioning was similar to that of the MS group. Descriptive results are presented first in Table 46, followed by results of the inferential statistics in Table 47.

Table 46

The Cognitive Performance of the MS Participants and NP-SLE Controls

Measure	MS participants (n = 60)	NP-SLE controls (n = 10)
Subcortical (executive functioning)		
Speed of information processing	630.74 (232.36)	777.98 (428.92)
Verbal fluency	35.27 (12.44)	30.10 (14.26)
Cortical		
Executive functioning		
Dorsolateral prefrontal functioning composite[a]	59.36 (7.11) (n = 45)	53.15 (8.25) (n = 8)
Orbitobasal composite	34.45 (9.27)	33.20 (9.99)
Memory		
Verbal memory composite (left)	169.75 (24.06)	151.75 (29.77)
Visual memory composite (right)	85.14 (16.86)	69.33 (17.86)
Visuospatial (right)		
Visuospatial construction	30.56 (3.09)	27.58 (9.64)

Note. All data are presented as means with standard deviations in parentheses.
[a] = incomplete data set, relevant sample numbers are presented in parentheses.

Table 47

ANCOVA Between-Subjects Effects (Between MS Participants and NP-SLE Controls) for the Cognitive Variables, Controlling for Race

	Adjusted means							
Source	MS	NP-SLE	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Subcortical (executive functioning)								
Speed of information processing	637.03	777.98						
Corrected model			317,154.23	2	158,577.12	2.26	.113	0.63
Intercept			21,030,604.29	1	2,103,0604.29	299.16	.0001	4.18
Type of participant			63,466.13	1	63,466.13	0.90	.345	0.01
Error			4,709,970.27	67	70,298.06			
Total			34,763,441.76	70				
Corrected total			5,027,124.51	69				
Verbal fluency	34.72	30.10						
Corrected model			1,205.10	2	602.55	4.05	.022	0.11
Intercept			51,020.13	1	51,020.13	342.58	.0001	4.56
Type of participant			2.22	1	2.22	0.02	.903	0.00
Error			9,978.34	67	148.93			
Total			94,639.00	70				
Corrected total			11,183.44	69				
Cortical								
Executive functioning								
Dorsolateral prefrontal functioning composite	59.00	53.15						
Corrected model			376.10	2	188.05	3.64	.034	0.13
Intercept			115,613.87	1	115,613.87	2236.03	.0001	39.04
Type of participant			94.29	1	94.29	1.82	.183	0.03
Error			2,585.24	50	51.71			
Total			183,864.55	53				
Corrected total			2,961.34	52				

Source	Adjusted means MS	Adjusted means NP-SLE	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Cortical								
Memory								
Verbal memory composite (left)	169.33	151.75						
Corrected model			3,364.18	2	1,682.09	2.71	.074	0.07
Intercept			1,193,371.77	1	1,193,371.77	1924.78	.0001	26.58
Type of participant			1,502.40	1	1,502.40	2.42	.124	0.03
Error			41,540.34	67	620.01			
Total			2,001,311.75	70				
Corrected total			44,904.52	69				
Visual memory composite (right)	84.63	69.33						
Corrected model			3,021.09	2	1,510.54	5.39	.007	0.14
Intercept			282,581.27	1	282,581.27	1008.79	.0001	12.97
Type of participant			944.52	1	944.52	3.37	.071	0.04
Error			18,768.00	67	280.12			
Total			502,692.00	70				
Corrected total			21,789.09	69				

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning; Verbal memory composite = verbal learning, memory and recognition; Visual memory composite = visual learning, memory and recognition.

According to the descriptive statistics above (see Table 46), the NP-SLE group appeared to perform more poorly than the MS group on all variables of cognition. However, neither the ANCOVA results (presented in Table 47), nor the hierarchical multiple regression analyses that were conducted for the orbitobasal composite (disinhibition and set shifting) and visuospatial construction (which violated an assumption of the ANCOVA) implied significant group differences (orbitobasal composite {$\beta = .07$, $p = .455$, 95% CI [-1.00, 2.21]}; visuospatial construction {$\beta = .16$, $p = .099$, 95% CI [-0.14, 1.61]}).

These preliminary results, therefore, appeared to imply that the NP-SLE group performed similarly to the MS group on all variables of cognition. These findings were largely expected and the NP-SLE group, as a whole, was tentatively accepted to be possibly representative of a similar auto-immune disease to MS that does affect the brain and cognitive functioning. Thus, I proceeded with an analysis of the euphoric variables.

Addressing the research question. The 10 NP-SLE control participants were then compared with the 100 MS participants on the two types of euphoria identified by this study: positivity and unawareness, while controlling for the significant pre-existing between-group differences for race. This was done in an attempt to provisionally investigate whether NP-SLEs would demonstrate at least one of the two types of euphoria at the same levels as the MS participants. Descriptive results are presented first in Table 48, followed by results of the inferential statistics in Table 49.

Table 48

The Performance on Self-Report Measures of Mood and Outlook of the MS Participants Compared with the NP-SLE Control Group for Continuous Data

Self-report measure	MS participants (n = 100)	NP-SLE controls (n = 10)
Positivity		
Composite (all participants)	122.12 (35.02)	145.98 (15.01)
Moderate positivity scores (50%-75% cut-off)	133.02 (15.26) (n = 54)	141.11 (12.34) (n = 8; 80%)
High positivity scores (75% cut-off)	176.98 (9.24) (n = 13)	165.45 (3.61) (n = 2)
Unawareness (negative discrepancies only)		
Physical domain (PAS)		
Unawareness scores (all unaware participants)	3.42 (2.30) (n = 45)	2.25 (1.50) (n = 4)
Moderate unawareness scores (50%-75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Cognitive domain (AI)		
Unawareness scores (all unaware participants)	1.44 (.81) (n = 16)	- (n = 0)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Mood/behavioural domain (NPI)		
Unawareness scores (all unaware participants)	9.21 (8.94) (n = 24)	3.00 (0.00) (n = 1)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-

Note. All data are presented as means with standard deviations in parentheses. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory.

Table 49

ANCOVA Between-Subjects Effects (Between MS Participants and NP-SLE Controls) for Positivity and Unawareness, Controlling for Race

	Adjusted means							
Source	MS	NP-SLE	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Positivity								
Composite (all participants)	125.67	145.98						
Corrected model			11,059.03	2	5,529.52	5.03	.008	0.09
Intercept			888,859.54	1	888,859.54	809.28	.0001	6.91
Type of participant			1,044.32	1	1,044.32	0.95	.332	0.01
Error			117,522.10	107	1,098.34			
Total			1,827,824.30	110				
Corrected total			128,581.13	109				
Moderate positivity scores (50%-75% cut-off)	134.14	141.11						
Corrected model			800.78	2	400.39	1.81	.173	0.06
Intercept			696,284.06	1	696,284.06	3,143.41	.0001	50.20
Type of participant			93.94	1	93.94	0.42	.517	0.01
Error			13,068.84	59	221.51			
Total			1,128,133.44	62				
Corrected total			13,869.62	61				
High positivity scores (75% cut-off)	177.12	165.45						
Corrected model			275.91	2	137.96	1.67	.229	0.22
Intercept			270,357.13	1	270,357.13	3,269.52	.0001	213.18
Type of participant			275.40	1	275.40	3.33	.093	0.22
Error			992.28	12	82.69			
Total			462,956.10	15				
Corrected total			1,268.20	14				

Source	Adjusted means MS	Adjusted means NP-SLE	Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
Unawareness (unaware participants only)								
Physical domain (PAS)	3.38	2.25						
Corrected model			8.35	2	4.18	0.81	.450	0.03
Intercept			184.34	1	184.34	35.87	.0001	0.75
Type of participant			2.42	1	2.42	0.47	.496	0.97
Error			236.42	46	5.14			
Total			787.00	49				
Corrected total			244.78	48				
Mood/behavioural domain (NPI)	9.25	3.00						
Corrected model			37.34	2	18.67	0.22	.802	0.02
Intercept			258.43	1	258.43	3.09	.092	0.14
Type of participant			36.13	1	36.13	0.43	.518	0.02
Error			1,837.63	22	83.53			
Total			3,882.00	25				
Corrected total			1,874.96	24				

Note. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale; NPI = Neuropsychiatric Inventory.

Descriptive statistics appeared to suggest that, on average, the NP-SLEs were more positive/optimistic than the MS group. When the scores of the moderately and highly scoring participants were compared, the NP-SLE group seemingly demonstrated greater levels of moderate positivity, but lower levels of high positivity than the MS participants. In terms of the unaware participants, the MS group appeared to demonstrate greater unawareness than the NP-SLEs, for all three domains.

Results from the ANCOVAs (presented in Table 49 above), however, implied that, when race was controlled for, no significant differences existed between these two groups for any analysis of positivity or unawareness. In addition, unawareness of cognitive deficits, tested via a hierarchical multiple regression by inserting the controlled for demographic variable first, and then including type of participant as a predict variable (because it violated as assumption of ANCOVA), was also non-significant (β = -.05, p = 6185, 95% CI [-1.66, 0.99]), implying no between-group differences for this variable.

In support of this, the majority of eta-squared values, for the ANCOVAs were found to be less than 0.23 (except for unawareness of physical deficits which was high; η^2 = 0.97). Thus, small effect sizes were largely indicated for these analyses and the non-significant differences may, exist despite the small sample sizes.

The above results therefore suggested that the NP-SLE and MS participants performed similarly on all variables relating to the two types of euphoria. This was expected and appears to provide possible support for the hypothesis that the NP-SLEs would demonstrate at least one of the euphoric types at the same level as the MS participants.

Right hemispheric dysfunction. The fourth and last potential cause for euphoria (i.e. RH involvement) was provisionally investigated using the participants with RH damage. As this was also a pilot investigation, 10 participants with RH damage as a result of a previous stroke were recruited. As they had recently taken part in another neuropsychological study (see Mosdell, 2013), to minimise research fatigue and to maximise their willingness to take part in the current research, the RH control participants only completed the questionnaires pertaining to euphoria.

Assessing the suitability of the group to address the research question. MS and RH participants were compared on the key demographic variables first (see Table 53) to determine if any pre-existing group differences existed that may influence their performance on the other variables investigated.

Table 50

The Key Sociodemographic Characteristics of the MS Participants and RH Controls

Key variable	MS participants (n = 100)	RH controls (n = 10)	*t* (*df* = 108)/ X^2 (*df* = 1)	*p* (2-tailed / 2-sided)	95% CI		Effect size *d* / *V*
					LL	*UL*	
Gender – Male:Female	14:86	5:5	8.25	**.004**			0.27
Age	44.49 (11.17)	46.90 (8.82)	-0.66	.510	-9.64	4.82	-0.22
Race/ethnicity – White:Coloured/Indian	71:29	1:9	14.96	**.0001**			0.37
Education[a b]	13.18 (1.65)	11.00 (2.83)	2.40 (*df* = 9.63)	.038	0.14	4.22	1.23
Income[c]	R26,006.51 (R22,536.54)	R9,360.50 (R11,604.14)	2.30	.023	2,291.03	31,000.99	0.76
Number of participants with a medical history that can affect neuropsychological functioning	41 (41%)	5 (50%)	0.30	.582			0.05
Use of medication that can affect mood	68 (68%)	3 (30%)	5.74	.017			0.23

Note. Categorical data are presented in ratios or percentages. The data on age, education, income, and duration of illness are presented as means with the standard deviations in parentheses. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Levene's test for homogeneity was significant, therefore the results for "equal variances not assumed" were reported along with the degrees of freedom next to the statistic.

[c] = Combined monthly household income.

Significant pre-existing between-group differences appeared to be present for gender and race. Use of medication that can affect mood was close to significant (p = .017) with far more MS participants using such medications than RH participants (68% versus 30%). While well-matched on the other key variables, these differences could impact negatively on neuropsychological functioning and, thus, were controlled for in the comparisons between these groups to follow.

As discussed previously, due to research fatigue, the RH participants did not undergo cognitive testing as they had just taken part in an extensive neuropsychological study. In private correspondence with the principal investigator, however, Ms Jill Mosdell described the cognitive performance of her RH group, of which the participants in the current study formed 50%. The RH patients of the Mosdell et al. (2013) study performed similarly to well-matched HCs on all measures of executive functioning (all p values > .01). These measures included the digit span forwards and backwards test from the Wechsler Memory Scale, 3rd edition (for attention and WM; Wechsler, 1997), and the same CWIT (for disinhibition and set shifting) and DST (for abstract reasoning) used in the current study. Although intelligence quotients (IQ) were not assessed in the current study, the RH group also performed similarly to the HCs on these measures. However, they performed significantly more poorly than the HCs on RH measures of perspective taking and theory of mind tasks, as well as on measures of spatial cognition, including the construction and rotation subsets of the Stick Test (Benson & Barton, 1970; Lezak et al., 2004), and the ROCF (which was also used in the current study to assess visuospatial constructional ability; all p values < .01).

This description largely appears to be in line with what was expected for this group, and the RH group, as a whole, was therefore tentatively accepted to be a possible appropriate reflection of a control group with damage to the RH only. I thus proceeded with an analysis of the euphoric variables.

Addressing the research question. The 10 RH control participants were then compared with the 100 MS participants on the two types of euphoria identified by this study: positivity and unawareness, while controlling for the significant group differences described above. This was done in order to provisionally investigate whether the RHs would demonstrate at least one of these two types of euphoria at the same levels as the MS participants. Descriptive results are presented first in Table 51, followed by results of the inferential statistics in Table 52.

Table 51

The Performance on Self-Report Measures of Mood and Outlook of the MS Participants Compared with the NP-SLE Control Group for Continuous Data

Self-report measure	MS participants (n = 100)	RH controls (n = 10)
Positivity		
Composite (all participants)	122.12 (35.02)	107.36 (29.80)
Moderate positivity scores (50%-75% cut-off)	133.02 (15.26) (n = 54)	125.71 (11.52) (n = 6)
High positivity scores (75% cut-off)	176.98 (9.24) (n = 13)	- (n = 0)
Unawareness (negative discrepancies only)		
Physical domain (PAS)		
Unawareness scores (all unaware participants)	3.42 (2.30) (n = 45)	7.43 (5.38) (n = 7)
Moderate unawareness scores (50%-75% cut-off)	- (n = 0)	17.00 (0.00) (n = 1)
High unawareness scores (75% cut-off)	-	-
Cognitive domain (AI)		
Unawareness scores (all unaware participants)	1.44 (.81) (n = 16)	1.00 (0.00) (n = 2)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-
Mood/behavioural domain (NPI)		
Unawareness scores (all unaware participants)	9.21 (8.94) (n = 24)	3.00 (2.83) (n = 2)
Moderate unawareness scores (50% - 75% cut-off)	-	-
High unawareness scores (75% cut-off)	-	-

Note. All data are presented as means with standard deviations in parentheses. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R. Unawareness = negative discrepancies between participant and informant ratings. PAS = Physical Ability Scale; AI = Awareness Interview; NPI = Neuropsychiatric Inventory.

Table 52

ANCOVA Between-Subjects Effects (Between MS Participants and RH Controls) for Positivity and Unawareness, Controlling for Gender, Race and Current Medication Use

Source	Adjusted means		Type III Sum of Squares	*df*	Mean Square	F	*p*	η^2
	MS	RH						
Positivity								
Composite (all participants)	125.33	100.62						
Corrected model			17,220.00	12	1,435.00	1.22	.281	0.13
Intercept			270,663.40	1	270,663.40	230.03	.0001	2.06
Type of participant			5,951.62	1	5,951.62	5.06	.027	0.05
Error			114,135.97	97	1,176.66			
Total			1,735,958.53	110				
Corrected total			131,355.98	109				
Moderate positivity scores (50%-75% cut-off)	129.59	121.81						
Corrected model			2,071.44	11	188.31	0.81	.635	0.16
Intercept			320,463.75	1	320,463.75	1.40	.243	24.09
Type of participant			326.83	1	326.83	0.10	.754	0.02
Error			11,228.83	48	233.93			
Total			1,063,255.13	60				
Corrected total			13,300.27	59				

Note. Positivity = Positive sub-scale of PANAS, well-being sub-scale of ISS, optimism sub-scale of OPS, optimism sub-scale of LOT-R.

Descriptively, on average, the RHs appeared to demonstrate less positivity than the MS participants. When just moderate and high scorers were examined, no RHs scored within the high range and RH moderate scorers demonstrated slightly less positivity than the MS moderate scorers. The RHs appeared to be more aware of their deficits, except for physical deficits.

No RHs scored within the high range for positivity, thus no inferential statistics were run on this variable. However, ANCOVAs were run on the scores of the majority of other variables. An assumption was violated for unawareness of physical and unawareness of mood/behavioural deficits. Thus, hierarchical multiple regression analyses were run, including the controlled for variables first, and then using the 'type of participant' grouping variable as a predictor variable. The grouping variable was found to be a significant predictor of unawareness of physical deficits (β = -.27, p = .010, 95% CI [2.60, 8.88]), which implied that the RHs were significantly more unaware of their physical deficits than were the MS group. However, unawareness of cognitive deficits (β = .07, p = .622, 95% CI [-0.95, 1.82) and unawareness of mood/behavioural deficits (β = .02, p = .844, 95% CI [-10.30, 12.58]) were non-significant. All ANCOVA results for all of the remaining variables associated with positivity and unawareness (presented above in Table 52), also appeared to be non-significant (with small effect sizes of $\eta^2 < 0.05$).

The above results therefore suggest that the RH and MS participants did not perform similarly on the majority of variables relating to the two types of euphoria, as there were significant differences in their performance on unawareness of physical deficits (where the RHs appeared to be significantly more unaware of their physical deficits than the MS participants), and positivity at the high level (where no RHs scored within this range). Since group differences were demonstrated for both positivity and unawareness (i.e. both of the euphoric types), the hypothesis that RHs would demonstrate at least one of the euphoric types at the same level as the MS participants was tentatively rejected.

Summary of part three. The aim of part three was to explore four hypotheses regarding the cause of euphoria in MS, via preliminary analyses. The MG, MVA TBI and NP-SLE groups all demonstrated as much positivity and unawareness as the MS group. The RH group, in comparison, did not demonstrate positivity at the high cut-off point, and demonstrated significantly more unawareness of physical deficits than did the MS group. Implications of these results will be discussed further in the next section.

Discussion

This study was the first of its kind to approach euphoria in MS comprehensively. Not only did it include both classical and contemporary understandings, which allowed for a more broad and comprehensive investigation; it also investigated both the symptoms of euphoria, and the constructs that define them, in order to gain a greater understanding of these phenomena. It additionally included a preliminary investigation of new hypotheses regarding the possible cause of euphoria in MS. The results of these investigations will be discussed in the following sub-sections.

This section will follow the same format as the results section. In part one I discuss the results presented on the constructs of euphoria. In part two I discuss the findings pertaining to a better description of the types of euphoria; and, in part three, I discuss the provisional results presented on the various hypotheses concerning the etiology of euphoria. These will be followed by a general discussion where I will summarise the study and further discuss some important issues raised by this research.

Part one. Addressing discrepancies and defining euphoria

The main aim of part one was to critically examine the constructs of euphoria in order to better understand what euphoria involves before investigating it within the sample. The discrepancies between classical and contemporary literature in terms of the number of types, the definitions of each type and the frequencies of the various types were investigated via an analysis of the literature and the use of the original (classical) CWQ, and the popular modern measure, the NPI; and I proposed that a change in the number of types, and in the definition of those types has occurred since the description presented by Cottrell and Wilson (1926), resulting in the euphoria measured today having a different quality to that of the classical measure/description. I also hypothesised that the different measurement instruments, which are based on the different definitions, could influence the incidence rates of euphoria found and that high rates of euphoria could be replicated by using the classical measure (and definition) and that low rates of euphoria could be replicated by using the modern measure (and definition).

These ideas (that of the number of types, definitions of the types and frequencies of the types) were then addressed using additional, different measures (i.e. not the CWQ or NPI) with good psychometric properties, that are popular measures in the study of positive mood, awareness and optimism today, to investigate the symptoms of euphoria from a modern

perspective. As I approached this largely from a framework using the classical definitions, I hypothesised that more than one type of euphoria exists and that the frequencies of these types would be higher than those found today and more comparable to that of Cottrell and Wilson (1926).

Classical versus contemporary measures. First, the euphoric constructs were investigated using the classical CWQ and the modern measure of the NPI. Discrepancies between authors using these measures regarding the number of types of euphoria, the definitions of those types, and the frequencies or incidence rates of those types were investigated and results pertaining to the analysis of these discrepancies were presented.

Number of types and definitions of the types of euphoria. As has been noted, a number of discrepancies between the classical and contemporary literature regarding euphoria exist. One of the most obvious is a difference in the number of types and in the definitions of those types. Results from an investigation of these differences were presented first and I proposed that a change in the number of types has occurred since the original definition of Cottrell and Wilson (1926), and that the euphoria described and measured today does not reflect the same euphoria of the original classical definition.

The classical and contemporary views. First, the classical descriptions and definitions of Cottrell and Wilson (1926) were presented. These reflected three types of euphoria: euphoria sclerotica, eutonia sclerotica, and spes sclerotica. The contemporary descriptions and definitions were then presented. As the NPI only addresses something similar to euphoria sclerotica, reporting findings of the NPI alone implies that only one type of euphoria exists. Thus, it appears clear that a change in the number of types of euphoria recognised has occurred. While Cottrell and Wilson (1926) included three types, authors today often fail to differentiate between these types, and even when they do, the majority report euphoria only in terms of the NPI which measures only one type (something similar to euphoria sclerotica).

It is also clear, from reading the descriptions of the types, that a change in the definition of these types appears to have occurred. In terms of the definitions of the various types, euphoria sclerotica appears to have changed from cheerfulness, happiness and serenity to unusual or persistent cheerfulness, inappropriate serenity, rapid mood changes, and social disinhibition. In terms of the two main measures investigated in this study (i.e. the CWQ and NPI), fairly general questions referring to what could be called normal mood or a subtle or

mild positive mood (in the classical CWQ) seem to have been replaced by a single question referring to persistent and abnormally good mood (in the modern NPI).

Even greater changes in definition are evident when it comes to eutonia sclerotica. Original definitions included a sense of physical well-being, with or without disability, and a lack of awareness of physical disability. These seem to have been replaced by an unawareness of physical deficit in the presence of severe physical impairment, as well as by definitions that include cognitive impairment and unawareness of cognitive or personality changes. With the classically described lack of awareness may have indeed occurred alongside physical impairment, Cottrell and Wilson (1926) did not maintain that physical disability needed to be present for these patients to experience a sense of physical well-being. Furthermore, although they defined eutonia sclerotica in terms of an unawareness of physical disability, as well as in terms of physical well-being, the questions of their original questionnaire related far more to the latter than they did to the former. Thus a change appears to have occurred here as contemporary researchers place a far larger emphasis on unawareness of disability rather than on a feeling of physical well-being; and patient/informant discrepancies are the dominant means of measuring this symptom. With regard to the object of unawareness, the classical definition referred only to that of the physical domain, but contemporary researchers broaden this to include cognitive and personality changes.

Spes sclerotica, in contrast, does not appear to have undergone as much of a change; although general optimism regarding the future and recovery that is elevated or out of place when considering the MS patient's situation appears to have been intensified to reflect an optimism that is considered to be unrealistic. Therefore, euphoria sclerotica and spes sclerotica appear to have become more extreme or abnormal, while eutonia sclerotica has morphed from a feeling of physical well-being or lack of awareness of physical deficit, to an unawareness of physical, cognitive and/or personality changes or deficits.

Further comparisons. Results from a variety of correlational analyses between the various measures investigated were also presented. In terms of euphoria sclerotica and spes sclerotica, the classical CWQ did not correlate well with the current popular measures of extreme mood and outlook such as the NPI ($p = .809$), which measures a persistent and abnormally good mood, and the CRJRF ($p = .280$), which measures unrealistic optimism. However, it did correlate well with other modern measures of more subtle mood and outlook,

including the positive sub-scale of the PANAS, the well-being sub-scale of the ISS, and the optimism sub-scales of the OPS and LOT-R (all *p* values < .01, except for PANAS, *p* = .086).

In contrast, in addition to poorly correlating with the classical measure (CWQ), the more extreme modern measures – the NPI and CRJRF (which are often used to measure the constructs of euphoric mood and unrealistic optimism today) - did not correlate well with the other modern measures of more subtle mood and outlook – the PANAS, ISS, OPS and LOT-R (all *p* values > .05). This provides compelling evidence that the NPI and the CRJRF seem to be measuring something other than positive mood and optimism; perhaps as the questions suggest: something more, something abnormal, something unrealistic. But, it also appears to imply that the more general, subtle measures of positive mood and optimism (i.e. the PANAS, ISS, OPS and LOT-R), which perhaps have greater reliability and validity than the original CWQ, appear to better reflect (than the NPI and CRJRF) what was originally described by Cottrell and Wilson (1926) to represent euphoria sclerotica and spes sclerotica.

The fact that the quality of euphoria elicited by these measures appears to be different from that which is elicited by the NPI (and CRJRF) suggests that a change in definition appears to have taken occurred. The subtle symptoms described by the classical literature appear to now be defined in a slightly more extreme manner and no longer measure the same symptoms.

In terms of the correlational analysis concerning eutonia sclerotica, the CWQ did not correlate well with the modern measures of awareness used to represent this type of euphoria. Not only did it correlate poorly with unawareness of cognitive and mood/behavioural deficits (*p* values > .100), but the original measure of eutonia sclerotica also correlated fairly poorly with the modern measure of unawareness of physical deficits (*p* = .800). This, again, provides evidence that the current measures of unawareness of deficit are measuring something other than the physical well-being originally described by Cottrell and Wilson (1926), and that a change in definition has taken place.

But then are euphoria sclerotica and spes sclerotica meant to be abnormal positive mood and unrealistic optimism? Or just subtle positive mood and optimism that appear abnormal when one considers the plight of the MS patient? And, is eutonia sclerotica meant to be a state of physical well-being or rather an unawareness of physical deficit? In terms of the definition of Cottrell and Wilson (1926), it would appear that euphoria sclerotica and spes sclerotica reflect a more subtle quality, and that modern measures that are similar to the original constructs are better reflectors of these symptoms than more popular, extreme, measures such as the NPI (and CRJRF). In reference to eutonia sclerotica, however, Cottrell

and Wilson (1926) were not clear on which aspect (i.e. physical well-being or unawareness of physical deficit) deserved more attention, and included both in their definition, but measured only well-being. However, although they may not reflect the same construct, unawareness of deficit may be more important than a feeling of physical well-being in terms of treatment and rehabilitation. Therefore, a greater emphasis on unawareness than on physical well-being may be more appropriate.

These are, however, difficult questions to answer. What can be addressed here, though, is that a change in the conceptual definition of euphoria, since the definition provided by Cottrell and Wilson (1926), appears to have taken place. While reviews of the literature on euphoria, such as that of Finger (1998), exist that note some of these discrepancies, to my knowledge no one has addressed them specifically, or closely investigated whether a change in definition has actually taken place, or investigated why this has occurred. However, clarifying the differences that exist and the confusions that have crept into the literature is of great importance as the operational definitions, and the measurement of a symptom depends on the construct and conceptual definition underpinning that symptom. If the questions or measures used today are based on definitions that are different from that of the original descriptions, we may be missing out something important or excluding a number of patients that could benefit from treatment or intervention. As I proposed that a change in definition (in terms of the number of types and the definitions of those types) has occurred, support for this proposition has been demonstrated.

Frequencies of euphoria. Cottrell and Wilson (1926) found high rates of euphoria amongst their sample of 100 MS participants: 63% euphoria sclerotica, 84% eutonia sclerotica and 84% spes sclerotica. Today, however, researchers such as Diaz-Olavarrieta et al. (1999), Figved et al. (2005), and Fishman et al. (2004), using the popular NPI, report much lower rates of around 4.7% to14.6 % of euphoria (of the euphoria sclerotica type). Thus, the aim of this section was to investigate these discrepancies in incidence rates of euphoria. I hypothesised that the measurement instruments used may influence the rates of euphoria found, and that high rates of euphoria would be replicated using the classical measure (and definition) and that low rates of euphoria would be replicated using the modern measure (and definition).

In accordance with the aims and hypotheses above, I used these same measures as those used with reference to the rates reported above (i.e. the CWQ for the classical measure and the NPI for the contemporary measure) as I wanted to investigate, among other things,

the incidence of euphoria within a sample of 100 MS participants. In terms of the classical measure (i.e. the CWQ), Cottrell and Wilson (1926) did not specify how to determine rates of euphoria from the answers to their questionnaire. Nor did they explicitly state which of their questions referred to which types of euphoria. Thus, 15 raters assigned each of the questions to a category (i.e. euphoria sclerotica, eutonia sclerotica, spes sclerotica, other), some with fairly low agreement. I then asked three different raters to rate each answer to the relevant questions identified by the provisional study according to whether they thought the symptom (i.e. only euphoria sclerotica, eutonia sclerotica or spes sclerotica; "other" questions were not rated) was definitely present, or definitely absent. Raters, however, stated that a number of answers appeared to be mixed, some of the answers pertaining to the euphoric type indicating a definite presence, and some an apparent absence of the symptom. They thus requested that a possibly present category be included. Following this, the three raters again rated the answers and determined whether the type of euphoria was definitely present, possibly present or absent. After additional concerns were raised regarding the interpretation of the answers and after uniform rating criteria were created, using a lenient criterion (i.e. including both definite and possible cases) I demonstrated similar rates to that of others using this questionnaire. I found euphoria sclerotica in 63% of participants, eutonia sclerotica in 48%, and spes sclerotica in 70%. This was comparable to the 63% euphoria sclerotica, 84% eutonia sclerotica, and 84% spes sclerotica found by Cottrell and Wilson (1926) and the 53.6% euphoria sclerotica, 50% eutonia sclerotica, and 50% spes sclerotica found by Sugar and Nadell (1943) who later attempted to replicate the original study.

This appears to demonstrate that high frequencies of the euphoric types were found by this study when these symptoms were defined more subtly, which provides support for the hypothesis that high rates of euphoria could be replicated by using the classical description/definition and measure. However, the fact that a possibly present category was needed by the raters, and the fact that a lack of consensus existed between the 15 raters who initially assigned each question a category of euphoria illuminates the highly interpretable nature of the CWQ, and this demonstrated a major limitation of the CWQ.

In contrast, similar low rates of euphoria (in terms of abnormal positive mood, a symptom that is most similar to the euphoria sclerotica of the classical types of euphoria) to those found by other modern authors were demonstrated by this study when using the NPI: 11% according to the standard informant-based administration of the measure, and 16% when the euphoria question of the NPI was asked of the participants themselves, which is similar to the 13% found by Diaz-Olavarrieta et al. (1999) and the 14.6% found by Fishman et al.

(2004). Support for the hypothesis that low rates of euphoria could be replicated by using the contemporary description/definition and measure was, therefore, also found, and the results indicated that low rates of euphoria (sclerotica) were demonstrated when the symptom was defined in a more extreme, abnormal manner.

However, only rates relating to euphoria sclerotica could be reported as the NPI does not address the other types, which revealed a major limitation of this popular measure.

As a number of limitations of each of these measures was uncovered, a discussion of these is required. In terms of the modern measure, the NPI addressed only a symptom that related to euphoria sclerotica and no results could be provided regarding eutonia sclerotica or spes sclerotica. Thus, in terms of the classical framework, this measure could be described as being too specific, restrictive and/or lacking in content validity. Furthermore, although a limitation associated more with the researchers using the NPI rather than with the NPI itself, reviewers of the contemporary literature may regard modern investigators as being biased against detecting this aspect of euphoria in MS patients (see, e.g. Fishman et al., 2004; Kesselring & Klement, 2001). This could also influence the definitions they use to describe it and, consequently the rates at which they find euphoria.

The classical CWQ, on the other hand, could be described as being too inclusive and lacking specificity, if one presumes that the rating criteria used were lenient and included the definite and unsure cases that were identified by the current study. In addition, as they did not objectively state their rating criteria, as they were fixed on the idea of there being three types, and as they believed euphoria to be the predominant mood state of MS patients, experimenter bias may have played a role in the high frequencies they found.

Furthermore, the fact that unsure or possibly present cases were identified at all is a limitation, and indicates that their measure was highly subjective and potentially arbitrary. This was evident not only when rating the answers for the presence of euphoria (where inter-rater agreement was between .327 and .555), but also in determining which questions referred to which type of euphoria (where the percentage of inter-rater agreement per question was between 46.67% and 93.33%).

Finally, Cottrell and Wilson (1926) operationalised spes sclerotica to include prospects of recovery, but no questions were included in their measure that related to this issue. When questions relating to their description were included (along with the original questions), the rates of definite spes sclerotica dropped from 37% to 27%, and the rates of definite as well as possibly present spes sclerotica from 70% to 66%. The fact that important questions pertaining to their definition were not included in their questionnaire is noteworthy

enough; but the fact that the inclusion of these questions negatively influenced rates of optimism again indicates that the original questions were not specific enough.

The results concerning these two measures, however, also revealed interesting findings pertaining to the incidence rates of euphoria within this sample. As low rates were demonstrated when the NPI was administered, and as relatively high rates were found when the CWQ was used, albeit with some interpretation of the findings, support for the hypotheses concerning the replication of either high or low frequencies was largely demonstrated. As the same MS participants were tested on both measures at the same time, this implies that high frequencies of euphoria were demonstrated when the associated symptoms were defined more subtly.

However, these findings also provide support for the hypothesis that different measuring instruments (along with their different operational definitions of euphoria), can influence the rates of euphoria found within MS patients. Again, reviews of euphoria, such as that of Finger (1998), have highlighted vast differences in rates. Furthermore, reasons for these differences have been postulated, including differences in disease duration across samples (Minden, 2000; Minden & Schiffer, 1990), inadequate screening to rule out other diseases such as neurosyphillis (Ombredane, 1929, as cited in Finger, 1998; Rabins, 1990), as well as differences in definitions and measurement instruments (Baretz and Stephenson, 1981; Finger, 1998; Minden, 2000; Minden & Schiffer, 1990; Pratt, 1951; Rabins, 1990) and the lack of standardised measurement instruments (Minden & Schiffer, 1990; Reischies et al., 1988). However, to my knowledge, no-one has addressed the issue of differing incidence rates specifically, or investigated factors which may directly impact on this problem. Prior to this study, it could be argued that the rates of these symptoms had somehow changed and that MS patients are no longer predominantly euphoric. However, if this change could be due to the instruments and definitions used to measure these symptoms, rather than a change in the MS patient, an interrogation of these factors is important in illuminating the real facts concerning the constructs of euphoria as well as the frequencies with which these symptoms can be found in MS patients. Since the operational definition of these symptoms and the ways in which they are measured is entirely dependent on how these symptoms are conceptualised, it seems clear that both the conceptual and operational definitions of euphoria have changed. As a result, the main measures of this study (i.e. the NPI and the CWQ), and their associated definitions of euphoria, appear to have impacted on the incidence rates and typing of euphoria within MS patients via artefact of these measures (American Psychiatric Association, 2001; DeSteno, Bartlett, Braverman, & Salovey, 2002), which refers to a

specific error that occurs due to the influence of the measurement instrument and is a serious threat to validity. Therefore, the findings of this section both provide support for the associated hypothesis (i.e. that the measurement instruments used will influence the rates of euphoria found, and, by association, that high rates of euphoria will be replicated using the classical measure and low rates using the modern measure), as well as highlight the need for a better definition regarding the number of types of euphoria, the definition of those types and better measurement instruments that reliably measure these constructs.

Additional and different contemporary measures. Since I hypothesised that the main measures investigated in this study would impact on the definitions and incidence rates of euphoria, the true number of types and frequencies of these types were also investigated using different modern measures, with well-established psychometric properties. These consisted of either informant reports of their MS loved-one's mood, or of well-known modern self-report measures of positive mood, unawareness of deficit and optimism. Given the weaknesses demonstrated for both the most-used classical and contemporary measurement instruments, this was a very important line of investigation.

Number of types and definitions of the types of euphoria. The first aim was to investigate the true number of types of euphoria, and to describe these types. As contemporary definitions are characterised by confusion, I approached this research question from the classical theoretical perspective of there being three types of euphoria. Thus, I hypothesised that more than one type of euphoria exists.

The results from the informant based factor analyses were reported first, based on the classic objective descriptions of euphoric patients put forward in the literature review. A principal components factor analysis, using promax rotation and the suppression of coefficients of .400 or below was run using the informants' ratings of their loved-ones' mood, outlook and awareness. As the classical framework suggests three types, a solution with three forced factors was run. This revealed one factor consisting of euphoria sclerotica and spes sclerotica (with the informants' ratings of their loved-ones' mood and outlook loading onto this factor). The second factor related to unawareness of cognitive deficits and unawareness of mood deficits (with the informants' ratings of their loved-ones' awareness of any deficits present in these domains loading onto this factor). The third factor only included unawareness of physical deficits (with the informants' ratings of the MS loved-ones' awareness of their physical difficulties loading onto this factor). However, when these

variables were not forced into three factors, two clear factors emerged: one relating to euphoria sclerotica and spes sclerotica (i.e. positive mood and optimism), and one on which all forms of unawareness loaded (i.e. eutonia sclerotica).

The factors relating to unawareness in these two analyses deserve a special mention. The original definition of eutonia sclerotica is circumscribed to unawareness of physical deficit alone, and based on our neuropsychological understanding of unawareness, and particularly the difference between unawareness of physical and cognitive disability which may have unique underlying mechanisms, it was not unexpected to find them separated (as in the first analysis). However, given that these additional elements were included based on contemporary descriptions of unawareness in MS, it is of particular interest to find that they did, in fact, all load onto one factor (along with unawareness of physical deficit) when the variables were not forced into particular factors (as in the second analysis). In the latter analysis each domain or type of unawareness could have loaded onto its own distinct factor, but did not. This, therefore, suggests some underlying commonality between them which is an important finding. Unawareness in MS may, therefore, include a wider spectrum than just that of physical deficits.

Due to the issues raised by researchers such as Surridge (1969) addressed in the literature review, we know that objective reports of euphoria (in terms of physicians determining the mood state of the patient without asking for their subjective opinion) may be unreliable. Thus, the modern self-report measures were also analysed via principal components factor analyses, using promax rotation and suppression of coefficients of .400 or below. When the variables were not forced onto three factors, the factor analysis again revealed two types of euphoria: one relating to positive mood and optimism (a combined euphoria and spes sclerotica, with self-report measures of positive mood [PANAS and ISS] and of optimism [OPS and LOT-R] loading onto this factor), and one relating to unawareness of deficit (or eutonia sclerotica, with self-report measures of unawareness in terms of participant/informant discrepancies on the PAS, AI and NPI loading onto this factor). Importantly, the latent factor structure revealed was the same for informant based and self-reported measures, and again revealed an underlying commonality between the types of unawareness.

I then tested this two factor structure using the classical measure of euphoria (it was not possible to test the NPI as it measures only one type of euphoria). A two fixed factor analysis was run as (a) I already knew that the CWQ and classical definition included three types, and (b) I was rather interested in determining whether even this measure (which was

designed to elicit three types of euphoria) might actually only elicit two types. The same principal components analysis was run, using the CWQ, and the forced two factor solution demonstrated the same two factors as the previous analyses using the additional measures described above: one encompassing euphoria sclerotica and spes sclerotica, and one onto which eutonia sclerotica loaded.

Therefore, it would almost certainly appear that two types of euphoria exist: (a) a type that I referred to as positivity, that is defined in terms of both positive mood (euphoria sclerotica) and optimism (spes sclerotica); and (b) a type characterised by unawareness and defined in terms of physical, cognitive and mood/behavioural domains (eutonia sclerotica). This interesting finding has mixed implications. It contradicts of both Cottrell and Wilson (1926) and contemporary researchers, such as Carone et al. (2005), Kesselring and Klement (2001), and Minden (2000), in that it suggests that two and not three or one type exists.

However, it also supports the findings of Cottrell and Wilson (1926) in terms of a type being present that relates to unawareness, which is sometimes ignored by contemporary researchers. But, again in contrast to Cottrell and Wilson (1926), the unawareness is not circumscribed to the physical domain, but supports more modern ideas of, for example, Benedict et al. (2005) and Carone et al. (2005), who include cognitive and affective domains in their descriptions of unawareness in MS.

Because this finding, in terms of unawareness is in support of previous literature, it not only provides support for the measures of unawareness included in the current study (some of which, e.g. the PAS and NPI, had either not been used before or had not been used in this context), in that they appear to be measuring something similar to that of other studies. It further provides support for the idea that MS patients in general may be unaware of domains other than purely the physical.

In conclusion, evidence in support of the hypothesis that more than one type of euphoria exists was demonstrated, and the characteristics of two types of euphoria were defined.

Frequencies of euphoria. The second aim of this section was to determine how prevalent these symptoms really are in MS patients. Since high rates of euphoria were described by Cottrell and Wilson (1926) and since I approached this section from the classical perspective, I hypothesised that the frequencies of the new types (i.e. positivity and unawareness) would also be high.

Results from correlational analyses indicated that although the different types of unawareness clearly shared some underlying commonality and were appropriately considered to represent one type of euphoria, they were poorly correlated and a composite measure could not be created. Thus, each type of unawareness was addressed individually.

The component measures of positivity, on the other hand, appeared to be well correlated and instead of using a z-score approach to create a composite, the variance of each component scale (relating to positivity) was calculated, and each scale was manipulated to lie on the same range (i.e. all were manipulated to range from 0 to the maximum score of the scale with the largest variance). This was done so that the composite could be treated as a variable with descriptive statistics that would allow for it to be compared across groups.

Thus, results were presented that defined positivity in terms of its component subtle measures of positive mood and optimism. Unawareness was similarly defined in terms of its related parts of physical, cognitive and mood/behavioural domains.

Following the above procedure, rates of positivity and unawareness within the sample of 100 MS participants were reported. While high positivity (defined in terms of scoring within the top quartile of the scale's minimum and maximum) was determined to be present in 13% of the sample, moderate rates (defined by scoring between the top half and the top quartile of the scale's minimum and maximum) were present in 54% of the sample.

Although this type of euphoria was defined in terms of its components, how to interpret the incidence and intensity of this symptom is not straightforward. Unlike the CWQ, however, where differing interpretations could lead to different rates of the symptoms, positivity (as measured in this research) was measured on a continuous scale and MS participants could present with different degrees of positivity without there having been a misinterpretation of the answers. While previous research has used a dichotomous present/absent means of diagnosis, perhaps rating euphoria on a continuum is more appropriate. With this view, a large number of MS participants (67%) demonstrated moderate to high positivity, but only a handful of those (19.4% of moderate to highly positive participants, or 13% of the total sample) demonstrated high positivity.

This poses slight problems when relating these results to previous research as, due to their present/absent approach, levels or grades of euphoria are not addressed in the literature: Euphoria is simply reported as either being present or absent.

Rates of unawareness within the sample were also presented. These were determined via participant/informant discrepancies on measures of physical, cognitive and mood/behavioural symptoms or disabilities, and a negative difference (where participants

underestimated their deficits as compared with the ratings of their informant) denoted unawareness. The MS participants did not need to present with severe disability to have unawareness, as the scales ranged from mild impairment to severe disability. What was important was that they had a potential for impairment, due to the nature of their disease, and that they considered themselves to be less impaired than their informant did. Although each domain was examined separately (due to their poor inter-correlation, which most likely explains the poor internal consistency found for the unawareness factor), the level or degree of unawareness was calculated in the same way as the rates of positivity.

The levels were not as high for unawareness as they were for positivity. In fact, no participant scored within the top quartile of the scale's minimum and maximum (denoting high unawareness) or even between the top half and top quarter of the scale's minimum and maximum (denoting moderate unawareness). However, as with the research on euphoria, those studies who have examined unawareness in MS do not distinguish between mild and high rates of unawareness, they simply note its presence or absence (see, e.g. Benedict et al., 2001; Carone et al., 2005; Sherman et al., 2008). This might imply that results simply pertaining to the number of participants showing any unawareness may be sufficient. In this regard, almost half (45%) of the MS participants were considered to be unaware of physical deficits, a little under one fifth (16%) were unaware of cognitive deficits, and just under one quarter (24%) were unaware of mood/behavioural difficulties (in terms of an under-estimation of deficits by the MS participant compared to the rating of their loved-one). Thus, in terms of the most popular method of determining rates of unawareness used in research today, fairly high rates were demonstrated in this sample.

Lower rates of physical unawareness were found in the current study than were presented in Cottrell and Wilson's (1926) paper; thus, the present results could be said to differ from or contradict the classical findings. However, in this study, unawareness (which relates to the original eutonia sclerotica) was measured in terms of patient/informant discrepancies and did not address the issue of physical well-being, while in their paper, although they defined eutonia sclerotica in terms of an unawareness of physical deficit, Cottrell and Wilson (1926) predominantly measured it in terms of a feeling of physical well-being. Thus, comparing my results with theirs is problematic and likely reflects the difference in definition, rather than a contradiction of results in terms of the incidence rates demonstrated.

A number of contemporary researchers, however, have looked at unawareness in MS. Benedict et al. (2001), for example, found that on average, their MS group was significantly

more likely to over-estimate their capacity for empathy and conscientiousness than their HC sample. However, they did not report the actual frequencies of unaware participants. In contrast, in Carone et al.'s (2005) study unawareness was measured in terms of overestimating one's cognitive ability and frequencies of unaware MS participants were reported. Just over 18% (18/98) of the MS participants were reportedly unaware; thus the results of the current study are in support of these. Likewise, Sherman et al. (2008) found 31.1% of their MS sample to be unaware of cognitive deficits (slightly higher than the frequencies demonstrated in the current study, that is 16%), and 35.1% to be unaware of physical deficits (slightly lower than the frequencies demonstrated in the current study, that is 45%). Interestingly though, Sherman et al. (2008) found that 16% of their sample were unaware of both cognitive and physical domains, whereas the overlap between these two domains in the current study was present in only 6%.

However, although (a) simply reporting the rates of unaware participants may be sufficient, and (b) no high or even moderate rates of unawareness were reported within this sample (according to the criteria imposed), a range of unawareness still existed. Thus, unawareness, like positivity, might also be better represented on a continuum (albeit with less variance), and ideas relating to the appropriateness of using a continuum to measure the euphoric symptoms as well as of what denotes the pathological presence of these symptoms will be discussed in greater detail in the general discussion to follow towards the end of this dissertation.

Since such low intensities of unawareness were demonstrated, factors that may influence this (as well as the rates of unawareness as a whole) should be addressed. The first issue is the influence of the informant, as unawareness could only be present if the informant rated the participant as being more impaired than the participants rated themselves. As much as the participants might be unaware of their deficits as a symptom of their disease, their informants may be equally unaware due to their own denial, avoidance, or to the participants hiding their disease and putting on a brave face.

The CWQ includes the question, "Is your outward expression a reliable gauge of your inward feeling?". This refers to pathological laughing and crying and the incongruence that can occur between hysterical laughter, for example, on the outside without the accompanying internal affect of amusement. But when this question was asked of the MS participants of this sample, the majority answered "no" and explained that they put on a brave face, created a happy mask, and generally preferred hide their feelings and symptoms from their loved-ones so as not to add to their burden. Additionally, many participants noted that they preferred not

to talk to their spouses or partners about their MS and rather asked a family member or best friend (who they spoke to more often about their problems) to complete their informant form. This occurred in 41% of the sample, and 21% of informants did not live with their MS loved-one. Thus, while these informants knew their MS loved-ones very well, it is possible that they only knew the symptoms which the MS participants wanted them to know, and not being around them in the same way as a spouse might be, might have lead them to under-report impairment as they may not have been aware of some symptoms that they did not see themselves. Thus, rates of unawareness, and particularly the level or intensity of unawareness could be higher than reported here and although participant/informant discrepancies is the recognised method of determining awareness, this method is not without limitations, and the resulting finding, should therefore be approached and interpreted with care.

Another factor that may have influenced the level or degree of unawareness, (again, as well as the rates of unawareness as a whole) is the idea of disability. Given that greater discrepancies denote greater unawareness, a certain degree of disability is required for greater discrepancies to occur. For example, the mood/behavioural scale on which unawareness of this domain is based, ranges from 0 to 144, but only 12% of informants noted an impairment of more than 20/144 in their loved-ones, thus very few MS participants demonstrated extreme levels of disability in this area, according to their informants, which would be required for extreme unawareness. This lack of severe impairment within the current sample could explain why no moderate or high unawareness was found.

Therefore, this study evidenced low rates of high positivity, but high rates of lower positivity (defined by the moderate cut-off point). Further, it demonstrated no moderate or high unawareness amongst MS participants (in terms of the criteria used in the current research), but demonstrated fairly high rates of unawareness when the most often used method of determining the frequency of unawareness (i.e. using only negative discrepancy scores) were employed.

Summary of part one. In terms of the main aim of part one, that of investigating the constructs of euphoria, a clearer understanding has been gained by this research. The results appear to suggest that due to demonstrated changes in conceptual and operational definitions the types of euphoria and definitions of those types have changed. Furthermore, discrepancies in incidence rates may be indicative of artefact of measure.

Following extensive analysis with additional measures of the euphoric symptoms, (measures with strong psychometric properties that are often used today in research in these fields), it was also demonstrated that the original three constructs described appear to rather represent two constructs (viz. positivity and unawareness). Unawareness was developed even further to show that different aspects of unawareness could exist within the same patient group. Ideas regarding a continuum as opposed to a cut-off point for positivity and unawareness were also addressed and varying degrees of these symptoms were demonstrated depending on where one imposed the cut-off.

Part two. Describing and predicting positivity and unawareness

The main aims of part two were to further describe and define the two types of euphoria, viz. positivity and unawareness, within this sample of 100 MS participants in order to better understand these symptoms. No hypotheses for this former part of the section were made.

Following this, the disease and cognitive correlates of positivity and unawareness were investigated in the hopes of being able to predict which MS participants might develop these types of euphoria, and the results of the multiple regression analyses were presented. Here, I hypothesised that the disease correlates of positivity and unawareness may differ, and, because I approached this study from the classical perspective, that these symptoms may occur both early and late in the disease, with either little or severe physical disability. I also hypothesised that the cognitive correlates of positivity and unawareness may differ, and that at least one of these euphoric types would correlate with impairment on neuropsychological tests of cortical domains of function, and that at least one type would correlate with RH impairment on cognitive testing.

Describing positivity and unawareness. It was established in the previous section that there appear to be two types of euphoria: positivity (which involves positive mood, or euphoria sclerotica, and optimism, or spes sclerotica) and unawareness (which includes unawareness of physical, cognitive and mood/behavioural domains and refers in part to the original eutonia sclerotica). The aim of this section was to further expand on these two types by describing them and defining them in more detail.

Do positivity and unawareness occur together or are they two separate symptoms?

The first question relating to a better description of the identified types of euphoria was that of whether they represent interdependent symptoms that invariably co-occur, or whether they reflect two distinct symptoms that can be seen in (different) patients with MS.

Results pertaining to a correlational analysis between positivity and each domain of awareness (using the full scale) indicated a negative correlation for every domain, which means that as positivity increases, awareness decreases. Put another way, as positivity increases, unawareness increases. This indicates that each domain of unawareness, although treated separately, forms part of a similar symptom as the direction of the correlations were the same no matter which domain was tested. It also indicates an association between positivity and unawareness and a tendency to co-occur.

Although we know that inconsistencies exist regarding the definitions of euphoria, this finding does appear to support a large amount of the literature that positions euphoric mood and unawareness (of at least physical deficit), as being symptoms that appear to occur together (Finger, 1998).

Results were also presented in terms of the number of participants demonstrating both an area of unawareness and positivity at the high level. These appeared to demonstrate a co-occurrence between the two, as 9% of the total MS sample, and 69.3% of the 13 participants demonstrating high positivity, did so in conjunction with least one type of unawareness. However, 30.7% of this same sub-group (demonstrating high positivity) did so without any unawareness, and 85.2% of the sub-group demonstrating unawareness did so without high positivity.

In this comparison, though, positivity and unawareness were measured at two different levels. High positivity reflected scores that were within the top quartile of the composite scale's minimum and maximum values. While, because unawareness did not have the same extensive range, the intensity of unawareness was not measured and unawareness was represented by merely the presence of any negative discrepancy scores between the participants and their informants. This may, therefore, have affected the number of participants displaying both, as positivity was defined in a more stringent way (i.e. by including only the high level), thus preventing a number of participants from displaying this symptom, which, in turn, restricted the potential to display both.

Thus, results of the same type of correlational analysis were presented, but between unawareness and positivity at the moderate cut-off point. These results demonstrated that 35% of the total sample, and 64.8% of the MS participants scoring in the moderate range for positivity demonstrated at least one type of unawareness along with moderate positivity. Furthermore, only 27.8% of the sub-group to demonstrate unawareness, did so without also demonstrating at least moderate positivity. This implied that there was a greater co-occurrence between these two symptoms when both were measured in a more inclusive way.

However, as there were greater numbers of MS participants presenting with all three types of unawareness and high positivity than there were with all three types of unawareness and moderate positivity, and as positivity was shown to be negatively correlated with awareness, an association between these two symptoms was also implied, where an increase in positivity appears to be associated with an increase in unawareness. It was therefore concluded that positivity and unawareness likely represent two types of euphoria that are

appear to be positively associated with one another. But, it was noted that these two types could also occur independently of one another.

These results appear to contradict some of the somewhat confusing contemporary approaches to euphoria. For example, Carone et al. (2005) acknowledge that both euphoric mood and eutonic unawareness exist. They define euphoric mood as "euphoric behavioural disinhibition" and measure it in terms of the NPI, and they measure unawareness via patient/informant discrepancies on cognitive testing and tests of personality change. But, they suggest that these aforementioned patient/informant discrepancies on cognitive or personality measures can predict the "euphoric behavioural disinhibition", which is their conceptualisation of euphoria sclerotica. This implies that patients displaying unawareness will also display euphoria. Even though a co-occurrence was demonstrated in the current study, 17 MS participants in this study still demonstrated some form of unawareness without the presence of even moderate positivity (which was measured at the more inclusive, lower cut-off level). Thus, these two types, although related, do not represent the same symptom, and determining the presence of the one does not mean that the other automatically exists.

The complete opposite was stated by Cottrell and Wilson (1926). They believed their triad of euphoric symptoms (i.e. euphoria sclerotica, eutonia sclerotica and spes sclerotica) to be independent of each other, and that each of the three symptoms could occur on its own. But, since they found that 63% of their sample had euphoria sclerotica, 84% eutonia sclerotica and 84% spes sclerotica, there must have been considerable overlap between these symptoms. Thus, the results of this research support both the suppositions of Cottrell and Wilson (1926), and their findings, as it has been demonstrated that positivity and unawareness can occur independently of one another, but that they are associated and, more often than not, co-occur, with a considerable overlap between the two symptoms being evident in their study.

Although this section did not have an associated hypothesis, the aim of expanding on the definition and description of the two types was addressed, broadening our knowledge on these symptoms a little further.

Does depression play a role in euphoria? We know that, although euphoric mood was considered to be the prevailing mood state of MS patients for many years, depression is considered to be the most common symptom of mood in MS patients today, with a lifetime prevalence rate of up to 50% (Joffe et al., 1987; Sadovnick, Dyment, Ebers, & Risch, 1996). We also know, however, that some researchers have noted an inconsistency relating to

euphoria, where an outward display of emotion is not necessarily a reflection of inward subjective feeling, and Surridge (1969) even went so far as to create four different degrees of euphoria from mixed state (objective euphoria but subjective depression), to severe euphoria (objective and subjective euphoria). Furthermore, we know that outsiders can, at times, be misled to believe that anosognosic (for hemiplegia) patients are happy, even though they can experience intense sadness, because the reality that they create is almost always more positive than their actual reality at the time (Fotopoulou et al., 2004; Turnbull et al., 2002). However, these inconsistencies noted by Surridge, as well as Turnbull and colleagues, are often found when objective and subjective descriptions are compared, so when only subjective or self-reported data is used, do euphoric MS patients still demonstrate some degree of depression?

Furthermore, while unawareness in MS has historically been associated with euphoric mood (Cottrell and Wilson, 1926; Finger, 1998), less has been investigated in terms of awareness or unawareness and depression. Questions regarding the association of depression with the two euphoric types were, therefore, asked in the hopes of addressing the main aim of part two: to better describe and define the symptoms of positivity and unawareness.

Results indicated a significant negative correlation between depression and positivity, a significant positive correlation between depression and awareness of cognitive deficits (in terms of the full scale), and a trend towards a positive association between depression and awareness of physical and mood/behavioural deficits.

In terms of positivity, this implies that as self-reported positivity increases, depression decreases. Thus, although some negative mood may be present, it appears to be unlikely that an MS patient would demonstrate profoundly depressed mood alongside positivity, and even less so at the higher ends of the positivity scale. While previous research has investigated both self-reported euphoric mood and depression in the same sample, to my knowledge, no studies have specifically investigated the relationship between these two variables, thus I cannot comment on these findings in terms of previous research.

However, the significant inverse relationship identified between positivity and depression does further imply that, at least in this sample, positivity does not appear to mask an underlying depression and that self-reported positivity appears to be an accurate way of measuring euphoric mood. This goes some way to address the concerns of Surridge (1969) as well as Turnbull and colleagues (Fotopoulou et al., 2004; Turnbull et al., 2002) who have noted a discrepancy between outward and inward feelings, or the feelings portrayed and the feelings truly felt, by patients with euphoria and/or anosognosia (for hemiplegia).

For unawareness, the results demonstrated a largely significant positive relationship between depression and awareness (indicating that as unawareness increases, depression decreases). This finding is consistent with previous research. Sherman et al. (2008), for example, found that depressed MS patients were more aware of their physical impairments, but those who were unaware of physical impairments appeared to be less concerned about them. Furthermore, Carone et al. (2005) found that over-estimators of cognitive ability (i.e. MS participants unaware of cognitive deficits) were more likely to be characterised by less depression. In conclusion, depression does not appear to play a role in euphoria and appears, in contrast, to be negatively correlated with both positivity and unawareness. These findings address the associated aim, by better defining and describing the euphoric symptoms.

How euphoric is euphoria? As we know, some MS patients demonstrate positivity and unawareness, albeit, perhaps, in differing degrees. Contemporary literature (and the popular measure used) would have us believe that the symptoms demonstrated are abnormal and unrealistic. But, although defined in less extreme terms, even the classical literature regarded these symptoms as being unusual or striking enough to warrant comment, description and study. Thus, an aspect of positivity and unawareness that required further interpretation was that of how positive the MS participants that scored in the moderate or high ranges for this variable were, and how unaware the unaware MS participants were. The intensity or severity of unawareness will be discussed in the latter half of this section; however, an attempt to answer the first part of this question was made by comparing the MS participants with the HC group as a reference point denoting "normal" levels of positivity.

Since the literature has noted positive mood and optimism in MS patients for years and the intensity of the symptom has been implied by the emphasis placed on it within the literature, I felt that it must be relatively prominent to warrant this notice. Thus, I hypothesised that those MS participants who demonstrated high positivity would demonstrate similar levels of this mood/outlook variable to the HCs demonstrating high positivity. That is, no significant differences between these two groups would be demonstrated for high positivity. Furthermore, I hypothesised that those MS participants who demonstrated positivity at the moderate cut-off point (i.e. between 50% and 75% of the scale's minimum and maximum) would demonstrate similar levels of this mood/outlook variable to the HCs at the same cut-off point. Further, as not all MS participants demonstrate positivity and as depression is quite a prominent mood symptom within MS, I hypothesised that on average

(i.e. when all scores were taken into account) the MS group would demonstrate levels of positivity that would be lower than those demonstrated by the HC group.

As expected, the results indicated that, on average, the total MS group was significantly less positive than the HCs, with a large effect size of 0.91. Furthermore, at the high level of positivity the MS group presented with similar levels of positivity to the HC group. Although expected, this is an incredibly interesting finding. Individuals with MS can experience a wide variety of debilitating symptoms (Jones, 2011; Rich et al., 2008; Schapira et al., 2007), and suffer from a highly unpredictable disease (Lublin & Reingold, 1996) that, as I was told from the participants themselves, limits their ability to plan for the future and severely impacts on their day. Yet, some experience a high level of positive mood and optimism that is as high as HCs demonstrating high levels. This appears to be completely out of keeping with their diagnosis and current disease state and clearly demonstrates the euphoria demonstrated by some MS patients.

In contrast, and unexpectedly, at the moderate cut-off point the MS group demonstrated significantly less positivity than the HC group, again with a fairly large effect size of 0.68. This finding is important for two reasons. First, it implies that moderate positivity, although positive by nature, is not at the same level as the moderate positivity of HCs. While I cannot comment on the construction of this affect/outlook according to the statistics presented, evidence of a more mild positive mood with the inclusion of some negative feelings was provided in the section referring to the quality of positivity. This further appears to imply that positivity is only truly reflective of euphoria at higher levels, and that moderate positivity may be representative of more normal mood and outlook including both positive/optimistic and negative/pessimistic feelings and attitudes.

Secondly, this finding is important since an increase in positivity was associated with an increase in unawareness (thereby implying a development of these symptoms), although positivity was not found to correlate with disease duration in this sample, and although this was beyond the scope of this cross-sectional study, this finding is important as moderate positivity may develop into high positivity later in the disease course. Thus, identifying patients with moderate positivity may help to predict and better serve patients who might benefit from treatment or management protocols later in their disease course.

In terms of this section however, I hypothesised that the MS group would demonstrate positivity at the same levels of the HC group at both the moderate and high cut-off points, and as such, this hypothesis was rejected.

With regard to unawareness, I hypothesised (again because these symptoms have received so much attention in the literature), that the MS participants would significantly under-estimate their deficits when their ratings were compared with those of their informants. The results revealed that when the scores of all aware and unaware participants were analysed, significant differences between participant and informant ratings were demonstrated for cognitive (p = .0001) and mood/behavioural deficits (p = .003), but not for physical deficits (p = .275). Thus, on average (in the whole sample), the intensity or severity of unawareness for cognitive and mood/behavioural difficulties was greater than for physical difficulties. The former two findings were expected, but this latter finding was unexpected, particularly considering that the physical domain had the greatest number of unaware participants (i.e. 45 as opposed to 16 for cognitive and 24 for mood/behavioural).

However, these scores were based on the full sample which included both aware and unaware participants, and while there were large numbers of unaware MS participants for this domain, the participants who over-estimated their physical deficits may have done so at such an extreme level that it cancelled out the unawareness displayed by the unaware participants.

Furthermore, over-estimators of deficits may have been more likely to severely over-estimate their physical deficits as opposed to their cognitive or mood/behavioural deficits as physical symptoms and difficulties appeared to be uppermost in the minds of the majority of participants and were mentioned far more often than cognitive or mood/behavioural symptoms. A few MS participants did not even appear to know that cognitive and mood/behavioural symptoms could form part of the symptoms experienced by MS patients.

Further evidence for this explanation was obtained when the scores of only the unaware participants were compared: Significant differences between participant and informant ratings were demonstrated for mood/behavioural deficits (p = .009), and close to significant differences were demonstrated for physical (p = .011) and cognitive deficits (p = .011). This means that, amongst those participants who were unaware the intensity of unawareness was relatively high or strong, and roughly the same across all domains for unaware MS participants. Thus, evidence was demonstrated for the hypothesis that MS participants would significantly underestimate their deficits when compared with their informants.

A qualitative characterisation. In order to further address the main aim of this section (that is to better describe and define the symptoms of positivity and unawareness), the results of a content analysis were presented.

Qualitative description of unawareness was unfortunately not possible as MS participants were not specifically asked questions about their physical, cognitive or mood/behavioural symptoms, other than the ones included in the questionnaires on these domains. Had they been asked such questions though, it would still have been difficult to describe the quality of their unawareness as I did not know them particularly well, and did not meet some of them in person. Thus, descriptions such as those given in terms of anosognosia for hemiplegia would have been very difficult for physical deficits and virtually impossible for cognitive and mood/behavioural deficits as I could not know or objectively rate what deficits to question or point out in the hopes of eliciting unawareness, and would not necessarily know when their answers were reflective of unawareness.

However, results from a content analysis of data pertaining to the mood and outlook of only those participants scoring in the moderate and high ranges for positivity revealed some interesting findings regarding the quality of moderate versus high positivity. A number of themes were identified. These were centred around two main topics: feelings and reactions to MS.

With regard to feelings, although relaxed feelings, as well as positive, happy, optimistic, and excited feelings might be expected from participants who scored within the moderate to high range on positivity, it is of interest to note that asides from P25 who noted concern about possibly having to use a wheelchair in the future, only moderately scoring MS participants demonstrated negative feelings such as apathy, despondence, defeat, fear, worry and uncertainty.

This might appear to be in contradiction to the bulk of the literature on euphoria, as the majority of articles written on this topic would have us believe that euphoric MS patients demonstrate highly positive or abnormally positive mood with an implication that they do not also experience negative mood symptoms. However, this finding may not imply that euphoric MS patients experience negative mood, but rather that positivity measured at the moderate level reflects normal mood, and that mood and outlook at the higher level (where only one participant identified a negative feeling) is more indicative of true euphoria.

In addition to themes surrounding feelings, the content analysis revealed themes regarding reactions to MS. These encompassed aspects such as approach to life, planning, religion and control. When considering that these themes emerged from questions relating to one's general mood and outlook (and not about how one feels about MS or views one's MS in the future), it is clear that, for many of the MS participants, the disease has greatly

impacted on their life and even their general mood and outlook is viewed through the lens of MS.

It is also interesting to note that although a number of negative feelings were identified, very few negative reactions to MS were present in the descriptions given. The closest representation of a negative reaction was that of needing to live in the now or take things one day at a time, perhaps the need to make provisions for one's future, and the inability to plan too far ahead in case a relapse prevents the participant from completing the plan. However, many of these were viewed in a more realistic than negative light and many of the participants gave the sense that you just adjust and life goes on. Even for the theme of control, no MS participant related relinquishing their control to MS, or ideas of life being out of their control (except perhaps for the "what will be will be" approach to life of P14 and P23), and the participants who mentioned this theme framed it in a positive light.

Following from this, a number of participants related taking something positive from MS, or gaining something good from it. Although they may truly feel such positive feelings, an interpretation of this could be something similar to that of Turnbull and colleagues, who noticed that anosognosic (for hemiplegia) patients often create a new reality that is very often more positive than their actual reality at the time (Fotopoulou et al., 2004; Turnbull et al., 2002). While I'm not suggesting that, like anosognosic-hemiplegic patients, this is masking an underlying depression, there may be some psychodynamic aspect to the way in which they frame their experience of their disease.

Further to this, another interpretation may be that the unconscious of a euphoric MS patient is faced with positive feelings that are incongruent to its reality, and reframing the illness in a positive light is a way of defending against the harsh reality. These interpretations are beyond the scope of the current study, but are never-the-less interesting inferences to consider.

Finally, it was of interest to note that very few themes relating to reactions to MS were identified by the group who scored high on positivity, and that the moderate scorers appeared to report more positive experiences. Since unawareness increases with an increase in positivity, one might speculate that the moderate scorers were more able to make sense of their experience and to report a variety of reactions to MS, while the high scorers for positivity were less able to do so, being less aware of their experience of MS or the ways in which they have dealt with it.

Although no hypotheses were presented for this section, these findings help to illuminate the quality of the types of euphoria in question and the aim of better describing and defining these symptoms was addressed.

Predicting euphoria. The final section of part two included the results pertaining to the disease and cognitive correlates of the two types of euphoria. The aim was to determine if these types could be predicted, within a sample of 100 MS participants, according to particular disease and/or cognitive variables, and this formed part of the larger aim of part two, which was to better describe these symptoms. I hypothesised that at least one type of euphoria may correlate with gender and/or with current disease state. Furthermore, because I approached the investigation of the two types of euphoria identified from the classical perspective, I hypothesised that the disease correlates of the two different types may differ, and that positivity and unawareness may occur both early and late in the disease, with either little or severe physical disability. Additionally, I hypothesised that the cognitive correlates of the euphoric types may differ, and that at least one of the euphoric types would correlate with impairment on neuropsychological tests of cortical domains, and that at least one type of euphoria would correlate with impairment on neuropsychological tests of RH functioning.

The demographic and disease correlates. Results were first presented describing the various disease variables in question. In line with previous literature, disease variables investigated included: disease course (i.e. RRMS or a progressive type), duration of disease (from diagnosis), current disease state (i.e. relapse/progression or remission), and severity of disease (in terms of physical disability). As numbers were limited, MS participants were not excluded based on current medication use or past history of a disease or condition that could potentially influence neuropsychological functioning, even though these variables could influence their performance on the measures pertaining to positivity and/or unawareness. Thus, these factors were noted and controlled for in the multiple regression analyses that followed.

Predicting positivity and unawareness: results from the models tested. Hierarchical multiple regression analyses were run in order to control for the abovementioned variables of corticosteroid use, use of other medications that could affect mood, and a previous history of a disease or condition that may affect neuropsychological functioning. These three covariates were entered into the model first, followed by the demographic predictor variables of gender,

age and income, and the disease predictor variables of disease course, duration of disease, current disease state, and disease severity.

For both positivity and unawareness, the full scales, using the full sample of 100 MS participants, were selected as the dependent variables to avoid restricting the range of these variables, thereby rendering the analysis impossible. Thus, when referring to awareness I am referring to all 100 MS participants, and not only unaware participants.

Only one model was found to be significant. When all demographic and disease variables were included, they significantly predicted awareness of physical deficits, and accounted for 23% of the variance, 18% more variance than the variance explained by factors relating to medical history or medication use alone. Gender, current disease state and disease severity were all negatively correlated, while age, income, disease course and duration of disease were positively correlated with awareness of physical deficits. Because the full scale of awareness was used, this means that greater unawareness of physical deficits was more likely to be present in females, of a younger age, and lower income, with RRMS course, but in a relapse, exacerbation or a progressive state, with a shorter disease duration, but with greater disease severity. This describes a female patient with fairly early onset MS that is still in the early stages, but who has experienced a number of relapses or exacerbation of the disease that has resulted in physical disability early on.

Few researchers have specifically investigated unawareness of physical deficit, but these findings do appear to be in contradiction to what was believed by classical researchers such as Cottrell and Wilson (1926) and Sugar and Nadell (1943): that eutonia sclerotica (unawareness of physical deficit) could occur early or late in the disease with mild or severe physical disability. The findings are also in contradiction with those of Langworthy et al (1941) and Surridge (1969) who noted that euphoria tends to occur later in the disease course with greater physical disability. Furthermore, the findings appear to contradict what is believed regarding euphoria, in general, today: that is tends to occur later in the disease, along with a progressive course (Diaz-Olavarrieta et al., 1999; Fishman et al., 2004), and advanced physical disability (Rabins et al., 1986).

This finding further means that the demographic and disease variables included in this study together did not significantly account for the variance seen in positivity, or the majority of domains of unawareness. This may imply that something other than those variables investigated could be responsible for these symptoms, but the findings may have also been influenced by the number of variables included, particularly if they were not adding to the variance. Thus, the coefficient results were also analysed and a number of individual

predictors were identified, which will be discussed individually according to each type of euphoria.

Predicting positivity: coefficient results of individual predictors. Only one individual variable was found to predict positivity: medical history was negatively correlated with, and significantly predicted, positivity ($p = .009$). This means that the fewer previous diseases or conditions that could influence neuropsychological functioning a participant had, the greater the positivity they would demonstrate, although it should be noted here, that this finding denotes an association and not necessarily a causal relationship. This was an interesting finding as, not only did medical history predict positivity over the MS disease variables that were investigated, but it also predicted positivity over and above the use of corticosteroids or other medications such as anti-depressants which are known to affect mood (Brown et al., 1999; Hewitt et al., 2000; Patten & Neutel, 2000; Turner et al., 2008).

In this sample of 100 MS participants, previous diseases or conditions classified as having a potential influence on neuropsychological functioning included (a) other auto-immune diseases, present in 8% of the sample; (b) previous meningitis/encephalitis, present in 3%; (c) previous TB or malaria, present in 4% and 2% respectively; (d) previous head injury, present in 9%; (e) brain tumour, present in 1%; (f) previous stroke, in 1%; (g) epilepsy, present in 2%; (h) some form of loss of consciousness, in 4%; (i) a diagnosis of depression or bipolar mood disorder, present in 22% and 2% respectively; (j) complications at birth, present in 9%; (k) attention deficit hyperactivity disorder in childhood, in 2%; (l) learning disability, in 2%; (m) delay in walking/talking, in 5%; and (n) use of marijuana, present in 7%. While the use of marijuana might be expected to have a positive influence on mood (Clark, Ware, Yazer, Murray, & Lynch, 2004), some of the other conditions, such as depression, may negatively affect mood (Arnett et al., 2008). Thus, the fewer of these negatively impacting conditions a patient has, the greater their potential for experiencing positive mood and outlook.

Furthermore, the mere experience of one of these diseases or conditions, or even worse – a combination of them – may indirectly result in a more negative outlook as the individual may be presented with additional stressors and problems with which they are required to cope. However, this interpretation refers more to general mood than to something that is caused by an organic process, and euphoria is, in fact, thought to increase with disease progression. To my knowledge, though, no researchers have investigated co-morbidity

between euphoria and other illness, and the extent to which euphoria in MS endures in the face of, or can override, other stressors remains to be seen.

Predicting unawareness: coefficient results of individual predictors. Even though the relationship did not maintain its significance when the association between disease severity and awareness of physical deficits was investigated ($p = .031$), disease severity (measured by means of physical disability) was found to be a significant individual predictor of awareness of physical deficits when included in the full model ($\beta = -.45$, $p = .0001$). Since it was negatively correlated, an association was demonstrated between greater disease severity (or physical disability) and greater unawareness of physical deficits.

Unawareness of physical deficits refers, at least in part, to what was originally described as eutonia sclerotica, and Cottrell and Wilson (1926) believed that eutonia sclerotica could occur independently of the disease type or course of MS and with or without physical impairment. Thus, the finding that unawareness of physical deficit is associated with greater physical disability is in contradiction to their findings. However, they defined eutonia sclerotica in terms of physical well-being (as well as unawareness of physical deficits), but measured only the former, which could very well be experienced by MS patients who either are, or are not, experiencing physical disability. But, the measure referring to eutonia sclerotica in the current study referred to unawareness of physical deficits and not to feelings of physical well-being, and unawareness of physical deficits in this study (i.e. discrepancies between the scores of the participants and the scores of their informants), required a certain degree of physical disability to be present in order for the participant to under-estimate their deficits in comparison with the ratings of their informant and be classified as unaware of physical deficits. Thus, these variables may be associated due to artefact of measure.

Of course, degree of physical disability, in this research, represented degree of disease severity, in place of the EDSS which also largely relies on physical dysfunction to represent the progression and severity of the disease. Thus, unawareness of physical deficit may actually have had an association with the severity of the disease, in terms of degree of cerebral involvement, represented by greater physical disability in the participant. This is in support of previous research such as that of Sherman et al. (2008) who found that disease severity (in terms of EDSS score) was significantly and positively correlated with unawareness of physical deficits.

No individual variables were found to be significant predictors of unawareness of cognitive or of mood/behavioural deficits.

A discussion of the hypotheses. A number of hypotheses were considered in this sub-section that were not specifically addressed by the findings discussed above and require further discussion. In terms of the first hypothesis, that the disease correlates of the two types of euphoria (i.e. positivity and unawareness) may differ, as different disease correlates appeared to be demonstrated for the various types of unawareness, this hypothesis was largely confirmed.

However, very few disease correlates were actually identified in total, and some euphoric types (i.e. unawareness of cognitive and mood/behavioural difficulties) did not have any significant disease, or demographic, correlates. This could indicate that these variables simply are not associated with positivity and/or unawareness; which may, further, mean that positivity and unawareness can, as Cottrell and Wilson (1926) suggested, occur independently of disease variables. This further implies that different mechanisms may underpin positivity and unawareness, and that the different domains of unawareness may be accounted for by different underlying mechanisms. However, this finding may also mean that the disease variables investigated may have been associated with positivity and unawareness, but this association was not revealed due to the sample size being too small, or the sample size to variable number ratio being too poor, or due to the measures not being sensitive enough. The issue of sample size to variable number ratio was somewhat addressed by exploring the significant individual variables in a model by themselves, as then the sample size remained at 100, but the number of variables investigated was reduced from 10 to only one. However, the issue regarding sensitivity of the measures may still be relevant.

The second hypothesis stated that positivity and unawareness may occur both early and late in the disease, with either little or severe physical disability. Disease duration was not found to correlate with either positivity or unawareness, however, disease severity was found to correlate with unawareness of physical deficits, with greater disease severity (in terms of physical disability), being associated with greater unawareness of physical deficits. Thus, this hypothesis was largely rejected.

However, the fact that disease severity correlated with only one type of unawareness, and that disease duration did not correlate with either type of euphoria may reflect support for Cottrell and Wilson's (1926) suppositions that these symptoms can occur independently of the disease variables of MS. It also, however, supports an interesting finding put forward by

Peyser et al. (1980), who noted the difference between euphoric MS patients, and those MS patients who have only had the disease for a short period of time, and who, therefore, have minimal cognitive and physical disability, but who yet demonstrate positive mood and a sense of physical well-being. Peyser et al. (1980) describe the emotional and physical well-being in these patients as being in proportion to their physical state as they are not disabled, and explain this in terms of denial and "coping mechanism[s] rather than the pathologic state implied by Sugar and Nadell" (p. 440). Of the 13 MS participants to demonstrate high positivity, although 4/13 (30.8%) were rated by their informants as falling within the top quartile of physical disability (i.e. were severely physically disabled), with one even rating their loved-one as being 100% impaired according to the items included in the PAS, 6/13 (46.1%) were rated as being 50% or less impaired physically. Thus well-being was demonstrated amongst MS participants in this study who had both minimal and severe physical disability, which raises an interesting question regarding the pathological nature of euphoria and whether (a) all MS patients should be expected to present with negative feelings and thus any positive feelings are abnormal; (b) positive mood and outlook in early patients, or patients not severely affected, is still abnormal given the unpredictability of the disease, or (c) true euphoria is only possible once the disease has progressed.

Finally, the third hypothesis related to the influence of gender and current disease state. These variables were included due to the apparent higher rates of euphoric mood amongst male MS participants (Figved et al., 2005; Fishman et al., 2004), and greater emotional disturbances occurring around periods of disease exacerbation (Dalos, et al., 1983; Rabins et al., 1986). Although, neither variable emerged as a significant predictor of either positivity or unawareness, a female gender and a state of exacerbation or progression were included in the model that was found to significantly predict unawareness of physical deficit. This was unexpected, however, as the rationale for their inclusion centred more around the euphoric symptom relating to mood, than unawareness, and, as a result, this finding cannot be compared with that of previous research. However, since disease activity in the brain is more active during relapse or a progressive state, it seems plausible that this may be related to greater unawareness.

The cognitive correlates. As with the disease and demographic correlates, results were first presented describing the cognitive performance of the sub-sample of MS participants who underwent cognitive testing (n = 60), and the cognitive variables in question. In line with previous research, subcortical and executive variables were included,

but due to the aims of this particular study I also included additional cortical variables, as well as measures of right versus left hemispheric functioning. As expected, it was found that the MS group performed more poorly than the HCs (and significantly more poorly in the majority of cases) on both variables of subcortical and cortical functioning, and, furthermore, significantly more poorly on recognised measures of RH functioning (i.e. the visuospatial composite [visuospatial perception 2D, visuospatial perception 3D and visuospatial construction], and at least one measure of prosody) than on recognised measures of left hemispheric functioning (i.e. the language composite [naming, repetition and comprehension]).

Thus, the picture of cognitive impairment demonstrated was typical of MS patients, as executive dysfunction, and visuospatial processing deficits amongst other deficits of RH functioning, with a lack of left hemispheric deficits, are commonly demonstrated amongst patients with MS (Amato et al., 2001; Comi et al., 1995; Foong et al., 1997; Ruggieri et al., 2003), and support for the hypothesis was largely found as impairment was demonstrated in the predicted domains, and the domains central to the investigation of the cognitive correlates to follow.

Predicting positivity and unawareness: results from the models tested. As questions regarding cortical versus subcortical and right versus left/executive functioning were important, results pertaining to two hierarchical multiple regression models per type of euphoria were presented. In the cortical versus subcortical regression model, the cortical predictor variables (i.e. the dorsolateral prefrontal functioning composite [attention, WM and abstract reasoning], orbitobasal composite [disinhibition and set shifting], the verbal memory composite [verbal learning, memory and recognition], visual memory composite [visual learning, memory and recognition], the language composite [naming, repetition and comprehension], the visuospatial composite [visuospatial perception 2D, visuospatial perception 3D and visuospatial construction], and the repetition and comprehension of prosody) were entered into the model first. This was followed by the subcortical variables of verbal fluency and speed of information processing. In the right versus left/executive regression, measures of RH functioning (i.e. the visual memory composite [visual learning, memory and recognition], the visuospatial composite [visuospatial perception 2D, visuospatial perception 3D and visuospatial construction], and the two measures of prosody) were entered into the model first, followed by the remaining measures. The full scales for positivity and unawareness, using the full sample of 100 MS participants, were again selected

as the dependent variables. Thus, when referring to awareness, I am referring to all 100 MS participants, and not only aware or unaware participants.

Not one of the models was found to be significant. This means that the cognitive variables included in this research together did not significantly account for the variance seen in positivity or any of the domains of unawareness. The coefficient results were also analysed to determine if any individual predictors existed.

Predicting positivity and unawareness: coefficient results of individual predictors. No individual cognitive variable was found to significantly predict any of the types of euphoria (i.e. positivity or unawareness of physical, cognitive or mood/behavioural deficits) in either the cortical versus subcortical model or the right versus left/executive model (all *p* values >.01). This may imply that something other than the variables included in this study could be responsible for the variance of these symptoms; or that the symptoms can occur independently of cognitive impairment; or it may imply that they number of variables to participant ratio may have impacted on the results.

Two variables were found to be close to significant predictors and these were investigated further via a linear regression. First, the orbitobasal composite (disinhibition and set shifting) was a close to significant predictor of unawareness of physical deficits, when all (i.e. right and left) cortical (but no subcortical) measures were included ($\beta = .45$, $p = .056$). On its own, the orbitobasal composite (disinhibition and set shifting) significantly accounted for 23.4% of the variance, and was positively correlated with awareness of physical deficit in the full sample of MS participants. This means that as performances improve for inhibition and set shifting, awareness increases, and conversely, the more disinhibited a participant is, and the more they struggle to shift between cognitive sets, the more unaware they will be of physical deficits. That is not to say that disinhibition or problems with set shifting cause unawareness of physical deficits, but they appear to be associated in some way, and this deserves some discussion.

Despite descriptions of eutonia sclerotica throughout the literature, little research has been conducted on unawareness of physical deficits in particular, amongst MS patients and Sherman et al. (2008), who did research this domain, found that no cognitive variable predicted this type of unawareness. Considering the similarities to anosognosia for hemiplegia, it was thought that unawareness of physical deficit might correlate with a cortical measure of RH functioning, and not a cortical measure of executive functioning, thus, this association was particularly interesting. However, if one assumes that disinhibition,

measured by the CWIT, can represent behavioural disinhibition as well as an inability to inhibit a natural response, perhaps the association makes sense, as caring less about what one says or does, or the way one behaves may be related to caring less about, and therefore underestimating, physical difficulties that one may be experiencing.

Second, the visuospatial composite (visuospatial perception 2D, visuospatial perception 3D and visuospatial construction) was found to be a close to significant predictor of unawareness of cognitive deficits, in all models (cortical variables only: $\beta = .47$, $p = .032$; RH variables only: $\beta = .38$, $p = .056$; all cognitive variables: $\beta = .48$, $p = .032$). This means that an association was found between decreasing or worsening visuospatial ability and increasing unawareness of cognitive deficits. Again, this was particularly interesting, as although unawareness (in terms of the hypothesis) of cognitive deficits was predicted to possibly correlate with a measure of cortical functioning, it was thought that it might correlate with a cortical measure of executive functioning, and not a cortical measure of RH functioning, as a lack of insight into cognitive performance has been related to executive dysfunction (Benedict et al., 2001; Flashman, 2002).

Although this result was unexpected, it has been demonstrated before. Sherman et al. (2008), for example, found that visuospatial functioning, in terms of the JLO, was moderately and inversely related to unawareness of cognitive deficits ($r = -.42$). This means that, like the current finding, as performance on the JLO worsened, unawareness increased. However, they did demonstrate that the cognitive variable with the best association was their executive functioning composite, which, similar to this study, was comprised of verbal fluency (COWAT), disinhibition (CWIT), a measure of abstract reasoning, and a measure of set shifting.

Although there may be a true association between visuospatial difficulties and unawareness of cognitive deficits, a possible explanation for this finding, could be that neuropsychological tests can often tap into additional (and often executive) functions, even though they are meant to assess a different domain such as that of visuospatial functioning. To this end, the CA task, for example, is sometimes used as a test of reasoning (executive functioning) rather than a test of 3-D visuospatial ability (Lezak et al., 2004).

A discussion of the hypotheses. A number of hypotheses were again connected to this sub-section that were not specifically addressed by the findings discussed above and require further discussion. Since different correlates were identified for the different types of euphoria, support for the first hypothesis (that the cognitive correlates of the euphoric types

may differ) was largely demonstrated. Although, as with the disease correlates, very few cognitive correlates were again actually identified. I created this hypothesis with the assumption that the euphoric types would correlate with cognitive impairment, as based on the extensive findings of researchers such as Surridge (1969), Rabins et al. (1986), Diaz-Olavarrieta et al. (1999), DeSousa et al. (2002), and Fishman et al. (2004). Although the MS group demonstrated significant cognitive impairment in comparison with the HC group on a number of variables, none of the cognitive models were significant predictors of positivity or unawareness in their totality, and significant individual predictors were few and far between. This was an interesting finding and implies that the cognitive variables assessed may simply not be associated with positivity and unawareness in this study. However, it may also mean that the association between these variables was not revealed in this research due to factors such as inadequate sample size, too many cognitive variables being assessed in the current sample, or to a lack of sensitivity of the measures. The variable to sample ratio was, once again, addressed by investigating those individual variables which were significant or very nearly significant predictors of the two types of euphoria. However, the other limitations could not be addressed and may still have played an influential role.

It was, furthermore, hypothesised that at least one of the euphoric types (most likely that of positivity) would correlate with cortical impairment on cognitive testing, and that at least one (most likely that of unawareness) would correlate with measures of RH functioning on cognitive testing, and support for this hypothesis was also largely demonstrated. Although only two cognitive correlates were identified in relation to two types of unawareness (with one correlate being identified per type), and thus the results should perhaps be interpreted with care, the findings did reveal that cortical cognitive variables, as well as a variable of RH functioning, are important in euphoria, and particularly in relation to unawareness.

Previous research has not specifically compared cortical and subcortical or right and left/executive measures of cognitive functioning, and although some have found euphoric mood to correlate with grey matter atrophy (see Benedict, Weinstock-Guttman et al., 2004; Sanfilipo et al., 2006), I cannot relate this finding, in terms of unawareness, to that of others. However, I believe it is an important result which further describes and defines the types of euphoria investigated in this study. In terms of cortical involvement, it may implicate the influence of grey matter damage in euphoria to greater extents than it is currently considered; and, in terms of RH involvement, it may implicate the influence of RH damage in euphoria. However, since only one aspect of euphoria correlated with this variable and since limitations associated with this neuropsychological measure as a sole measure of RH dysfunction were

addressed above, this finding is slightly less clear and I recognise that unawareness in MS may be a different type of unawareness to that of anosognosia for hemiplegia.

Summary of part two. The main aims of part two were to further describe and define the two types of euphoria identified by part one (viz. positivity and unawareness), as well as to investigate their correlates with the aim of better predicting these symptoms. An association between positivity and unawareness was established, and these symptoms were considered to represent two types of euphoria with high rates of co-occurrence. Depression was found to be negatively correlated with both positivity and unawareness; thus euphoric mood was found to represent an inward feeling experienced by the MS patient and not an outward façade.

Although no high or moderate levels of unawareness were demonstrated in this sample, the MS participants significantly (or near to significantly) under-estimated their deficits in comparison with their informants which described the intensity of unawareness amongst unaware participants. Further, those MS participants demonstrating high levels of positivity did so at levels that were comparative to high scoring HCs, indicating the intensity of positivity amongst highly positive MS participants.

While few demographic, disease or cognitive correlates were identified, positivity and each domain of unawareness appeared to have different correlates and these types appeared to be independent of the majority of the variables investigated. However, limitations associated with these findings were also discussed and definite conclusions could not be drawn.

Part three. The cause of euphoria

The main aim of part three was to explore some heuristic ideas about potential causes of euphoria via a preliminarily investigation of a number of hypotheses. Although these investigations were tentative due to a number of limitations, they had the additional aim of perhaps identifying which hypotheses show promise for larger research, with full research protocols, in the future. The hypotheses investigated included euphoria in MS being the result of: (a) a psychological reaction to the disease (investigated via MG controls who have a similar disease that does not affect the CNS), (b) the result of executive dyscontrol (investigated via MVA TBI controls who demonstrate similar executive dysfunction to MS participants), (c) immunological disease processes (investigated via NP-SLE controls who have an auto-immune disease affecting the CNS), and (d) involvement of the RH (investigated via stroke patients with damage to the RH).

The related hypotheses were, therefore, that the MG group would demonstrate better cognitive functioning than the MS group, given that their disease does not affect the CNS, and that, therefore, the euphoric types identified by this research would not be as prominent amongst MG controls as it was in MS participants. For the MVA TBI and NP-SLE groups, I hypothesised that they would demonstrate similar executive dysfunction to the MS group, given that their diseases affect the CNS and brain, and that at least one euphoric type would be demonstrated, at similar levels, within the MVA TBI and NP-SLE control groups, as within the MS participants. Finally, in terms of the RH group, I hypothesised that they would demonstrate good performance on tests of executive functioning, but would perform similarly poorly to the MS group on tests of functions sub-served by the RH, given their particular cerebral pathology, and that at least one euphoric type would be demonstrated, at similar levels, within the RH control group, as within the MS participants.

I would again like to remind the reader of the small sample sizes included in this section, and the risks associated with inferring any definite conclusions, and caution the reader when interpreting the findings. However, I would like to rationalise the preliminary nature of these hypotheses in light of the unavoidable limitations associated with control patient recruitment, within this research, and emphasis the value of pilot studies in planning future research.

A psychological reaction. Results pertaining to the first potential cause of euphoria (i.e. a psychological reaction to the disease) were presented.

Assessing the suitability of the group to address the research question. The cognitive functioning of the sub-group of MG participants (n = 10) who underwent cognitive testing was presented and compared with that of the sub-group of MS participants (n = 60) who underwent cognitive testing. This was done in order to assist in indicating whether their cognitive functioning was better than that of the MS group and to attempt to assess their suitability as a control group to address their particular research question.

When the significant pre-existing between-group differences for race and education were controlled for, the MG participants were found to perform similarly to the MS group on all domains of cognitive functioning. This result was somewhat unexpected given that the MS group was compared with the HCs in part two of the results section and were found to perform significantly more poorly than the HCs on the majority of cognitive variables.

However, the analyses were based on a small sample of MG participants, and this could possibly have negatively influenced the potential for statistically significant results. Even though the effect sizes showed very small effects, implying that even with larger sample sizes a lack of statistically significant differences between these two groups may have been found, the power analyses revealed a very small statistical power of between 0.01 and 0.09 for these analyses. Thus, there may not have been enough statistical power within these analyses to determine whether MG controls really do perform at the same level as MS participants.

Furthermore, even though the significant between-group differences for race and education were controlled for, since the group on which cognitive performance was based was small, these key differences may have played an influential role. With this in mind, the MG group had almost double the number of Coloured and Indian participants (60%) that were included in the MS group (29%). While ethnic background does not influence one's cognitive capacity per se, in SA due to the Apartheid regime, people of Coloured and Indian backgrounds were marginalised and did not receive the same quality of education or access to resources as white SA citizens (Case & Yogo, 1999). The average age of the MG sample was just under 40 years and 60% were over the age of 33. Thus, only 40% of this sample would have received their high-school education post-Apartheid (which occurred 20 years ago, pre-1994) when new educational policies were adopted. Their background may, therefore, have negatively impacted their education and thus their cognitive functioning.

Level of education has also been found to correlate with performance on cognitive testing, particularly IQ tests (Heaton & Pendleton, 1981), and the difference between these

two groups on these variables may therefore have played an influential role in the cognitive performance demonstrated.

Mild cognitive impairment, and particularly that of executive dysfunction, has, however, been noted in patient groups whose chronic illness does not affect the CNS, due to secondary factors such as fatigue, increased anxiety and stress (Grosshans, Meyers, Allen, Davenport, & Komaki, 2008; Kurella, Chertow, Luan, & Yaffe, 2004). Thus, even though the MG group appeared to perform at a similar level to the MS participants, their performance does not necessarily reflect CNS involvement.

Furthermore, the MGs did not perform significantly more poorly than the MS participants on any variable. Thus, although the MGs appeared to demonstrate some compromise of cognitive functioning, as this may not have been a direct result of CNS involvement, they were very tentatively thought to be an appropriate reflection of a similar disease to MS that does not affect the brain. An attempt was, therefore, made to address the question concerning a psychological reaction to a disease with reference to euphoria.

Addressing the research question. The full MG (n = 20) and MS groups (n = 100) were then compared on variables relating to positivity and unawareness, while controlling for significant pre-existing between-group differences for race and education. This comparison was made in an attempt to investigate whether or not the MGs would demonstrate positivity and unawareness at a lower level to the MS participants. Unexpected results were, however, found, and the MG group appeared to perform similarly to the MS group on all variables relating to the two types of euphoria. This meant that the MGs were just as positive and unaware as the MS participants, and implied that euphoria (in terms of both positivity and unawareness) may be caused by something both MG and MS patients have in common.

On relating these findings to previous research, it was found that these results are in contradiction to previous literature as little has been documented regarding positive mood in MG, and negative mood such as depression is regarded as being common (Cantor, 2010; Kulaksizoglu, 2007).

Since the MGs unexpectedly appeared to demonstrate as much positivity and unawareness as the MS group, and since the hypothesis was, therefore, tentatively rejected, possible reasons for this finding require discussion. First, again, the analyses were based on a small sample of MG participants, and this could possibly have negatively influenced the potential for statistically significant results. Even though the effect sizes showed very small effects, the power analyses revealed a very small statistical power of between 0.01 and 0.20

for these analyses. Thus, there may not have been enough statistical power within these analyses to determine whether MG controls really do perform at the same level as MS participants.

One may also conclude that the null hypothesis was correct and that euphoria (in terms of positivity and unawareness) may be caused by a psychological reaction to a chronic disease (and not necessarily by brain involvement), which these groups have in common. But this seems unlikely since euphoric mood has not been demonstrated in other non-neurological patient groups, such as muscular dystrophy, and impaired awareness of physical deficits has also been found to be significantly less common amongst patients with muscular dystrophy than that of MS (30.5% for MS versus 5.1% for muscular dystrophy, $p < .001$; Surridge, 1969). Further, euphoria in MS has been found to be more likely following cerebral rather than spinal cord involvement (Rabins et al., 1986). Thus, cerebral involvement, rather than a psychological reaction, appears to be a more likely cause of euphoria.

Further, the measures used to determine positivity in this research were in line with the classical description of euphoria sclerotica and spes sclerotica and defined these symptoms in a more subtle way. If studies concerning positive mood have taken place, perhaps investigations defined in more subtle terms have not, and this may account for these seemingly contradictory findings.

Disease severity may have, however, played a role. The PAS used in this study was related more to physical abilities rather than specific symptoms such as diplopia (from which both groups can suffer; Cantor, 2010; Rich et al., 2008; Schapira et al., 2007), and, thus, I did not compare the two groups on this variable. But, a number of the MGs mentioned that they didn't even think they had MG anymore as, provided they take their medication, they had not experienced a relapse or any symptoms for a few years, and this may have positively influenced their outlook and possibly resulted in them under-estimating their symptoms.

The nature of the disease of these control participants may too have played an influential role. While MG might appear to be an appropriate control disease, as it is a disease similar in nature to MS, with an unpredictable pattern and chronic disability, but without an effect on the CNS, it is, however, similar to MS as it is also an auto-immune disease. Since effects of immunological processes on mood (particularly that of depression and bipolar) have been found (Horrobin & Bennett, 1999), it is possible that the auto-immune nature of MG could be influencing the mood of the patients affected by it, and that euphoria may be caused by some form of immunological disease process related to auto-immune

diseases in general. To my knowledge, however, this has not been researched before in MS, thus hypotheses as to this relationship at this stage remain just that.

Finally, even though it was argued that executive dysfunction may have been demonstrated in this group without there having been CNS involvement, the MG group never-the-less demonstrated similar cognitive functioning to that of the MS group, and, thus, similar executive dysfunction. As will be addressed in the sub-section to follow, executive impairment has been hypothesised to play a causative role in euphoria, in MS (Benedict et al., 2001; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004), and further investigation regarding executive dysfunction due to cerebral involvement versus executive dysfunction relating to secondary factors in non-neurological patients may be of significant relevance. However, as was noted earlier in this sub-section, patients with muscular dystrophy (another disease that does not affect the CNS) who are just as likely as MGs to present with executive impairment due to similar secondary disease processes, such as fatigue (Grosshans et al., 2008; Kurella et al., 2004), have been found to not demonstrate positive mood or unawareness of physical deficit (Surridge, 1969). Thus, a further investigation of immunological disease markers may also be relevant.

Executive dysfunction. Results pertaining to the second pilot study, and potential cause of euphoria (i.e. executive dysfunction), were presented.

Assessing the suitability of the group to address the research question. The cognitive functioning of the sub-group of MVA TBI participants (n = 10) who underwent cognitive testing were presented and compared with that of the sub-group of MS participants (n = 60) who underwent cognitive testing. This was done in order to attempt to assist in identifying whether their cognitive functioning was similar to that of the MS group, and to assess the suitability of this control group to answer its relevant hypothesis.

This control group was particularly ill-matched on a number of key demographic variables, but when the significant pre-existing between-group differences for gender, age, race, education and current medication use were controlled for, the MVA TBI participants appeared to perform similarly to the MS group on the majority of variables but significantly more poorly than the MS group on three variables that can be considered tests of executive functioning (i.e. the dorsolateral prefrontal functioning composite [attention, WM, abstract reasoning], the verbal memory composite [verbal learning, memory, recognition], and the visual memory composite [visual learning, memory, recognition]). This apparent

performance of the MVA TBI group was consistent with previous literature which has demonstrated a picture of predominantly executive dysfunction, and memory retrieval difficulties (Hartman et al., 1992; Rao & Lyketsos, 2000).

Although they were expected to demonstrate some impairment, it was thought that they would perform within a similar range on variables of executive functioning to the MS group. They, however, performed significantly more poorly on three variables, and although significant between-group differences on key demographic variables such as age, race and education were controlled for, these variables may have played an influential role in their cognitive performance due to the aforementioned legacy of Apartheid and its effects on marginalised minority groups (Case & Yogo, 1999; Heaton & Pendleton, 1981).

Since the MVA TBIs, however, did not demonstrate a significantly better performance than the MS group on any cognitive measure, and did appear to demonstrate executive impairment, they were tentatively accepted to be an appropriate representation of a condition with similar executive dysfunction (and white matter involvement). Thus, the hypothesis surrounding the association between executive impairment and euphoria was addressed.

Addressing the research question. The full MVA TBI (n = 19) and MS groups (n = 100) were then compared on the variables pertaining to positivity and unawareness, while controlling for the significant pre-existing between-group differences for gender, age, race, education and current medication use. This comparison was made in an attempt to investigate whether or not the MVA TBIs would demonstrate at least one of these two types of euphoria at the same levels as the MS participants.

Results appeared to imply that no significant differences existed between these two groups for either positivity or unawareness, meaning that the MVA TBIs were just as positive and unaware as the MS participants. Even taking the small sample sizes into account, the effect sizes of $\eta^2 < .02$ imply that had greater sample sizes been used, these non-significant results may have remained. Thus, these findings appear to suggest that euphoria (in terms of both positivity and unawareness) may be caused by something both MVA TBI and MS patients have in common.

In terms of unawareness, these results largely support what has been found in the literature as poor insight into cognitive and behavioural changes post TBI is a common symptom of these patients (Flashman, 2002; Toglia & Kirk, 2000). However, euphoric mood is not a common symptom, and this finding was in contradiction to previous research. Fann

et al. (1995), for example, describe the mood of TBI patients as predominantly including depression and anxiety, while Rao and Lyketsos (2000) describe a picture of depression, mania at times, anxiety, psychosis, apathy and behavioural dyscontrol. However, the measures used to determine positivity in this research were, again, in line with the classical description of euphoria sclerotica and spes sclerotica and defined these symptoms in a more subtle way. Thus, more subtle descriptions of positive mood/outlook may not have been investigated in reference to TBI and this may account for these seemingly contradictory findings.

Significant between-group differences, furthermore, existed between the MVA TBIs and the MS participants. Although these were controlled for, more MVA TBIs were Coloured or Indian and the group had a lower level of education than the MS group. While these two variables don't have an obvious effect on mood, due to the aforementioned legacy of Apartheid, economic deprivation (as an indirect result of a lower level of education), might be thought to impact on mood. However, this would likely have a negative and not a positive effect (Bassuk, E., Buckner, Perloff, & Bassuk, S., 1998). Thus, the differences between these groups on these variables are unlikely to have accounted for the MVA TBIs unexpected positivity.

Furthermore, use of particular medications such as corticosteroids or anti-depressants were controlled for as these can also influence mood (Brown et al., 1999; Hewitt, Fraser, & Berger, 2000; Patten & Neutel, 2000; Turner, Sharp, Folkes, & Chew-Graham, 2008). However, although significant group differences existed for this variable, significantly fewer MVA TBIs were taking these medications and, thus, group differences on this variable were also unlikely to account for their unexpected mood and outlook.

Therefore, tentative support for this hypothesis may have been demonstrated, and the results may provisionally suggest that the null hypothesis was incorrect and the MVA TBI group appeared to demonstrate similar levels of euphoria due to the executive dysfunction that these two groups have in common. Since euphoria in MS has been hypothesised to be the result of executive dysfunction (see, e.g. Benedict et al., 2001; Benedict, Carone et al., 2004; Diaz-Olavarrieta et al., 1999; Fishman et al., 2004), even though euphoric mood is not readily reported in MVA TBI patients (Fann et al., 1995; Rao & Lyketsos, 2000), this dysfunction may be, in some way, associated with the symptoms of euphoria demonstrated in this study. This was, however, a provisional investigation, and small sample sizes were used. Thus, bigger studies are needed to better test this worthwhile hypothesis.

Immunological processes affecting the brain. Preliminary results pertaining to the third potential cause of euphoria to be investigated (i.e. effects of immunological disease processes in auto-immune disease affecting the CNS and brain) were presented.

Assessing the suitability of the group to address the research question. Results pertaining to the cognitive functioning of the NP-SLE participants (n = 10) were presented and compared with that of the sub-group of MS participants (n = 60) who underwent cognitive testing. This was done in order to assess their suitability as a control group to investigate their associated research question and to assist in indicating whether the cognitive functioning of the NP-SLE group was similar to that of the MS group.

When the significant pre-existing between-group differences for race were controlled for, no significant differences were apparent between the NP-SLE and MS groups. These findings, therefore, appeared to be in support of previous research that indicates a cognitive picture of NP-SLE patients similar to that of MS patients, predominantly characterised by executive dysfunction and including impairment in the domains of attention, WM, information processing speed, learning and memory (Benedict et al., 2008; Covey et al., 2012; Skeel et al., 2000).

Additionally, the findings appeared to provide cautious support for the hypothesis that NP-SLEs would demonstrate similar cognitive functioning when compared with the MS participants. This patient control group was, thus, tentatively considered to be an appropriate reflection of a similar auto-immune disease to MS that does affect the brain and cognitive functioning. The question pertaining to the effect of immunological disease processes on the cause of euphoria was, therefore, addressed.

Addressing the research question. The 10 NP-SLEs and 100 MS participants were then compared on the two types of euphoria (i.e. positivity and unawareness), while controlling for the significant pre-existing between-group differences for race. This was done in an attempt to preliminarily investigate whether or not the NP-SLEs would demonstrate at least one of these two types of euphoria at similar levels to the MS participants. Results of these pilot investigations appeared to demonstrate no significant differences between the NP-SLE and MS participants for any variables pertaining to positivity or unawareness. This meant that the NP-SLEs were just as positive and unaware as the MS participants, and possibly implied that euphoria (in terms of both positivity and unawareness) may be caused by something both NP-SLE and MS patients have in common.

Again, these results are based on analyses conducted within groups of unequal sample sizes, and small sample sizes on the part of the control group. However, effect sizes were also small (all except for high positivity were $\eta^2 < .03$), and this may indicate that even with larger sample sizes results may remain non-significant.

Although little appears to have been described regarding unawareness in NP-SLE, this result was largely in support of previous literature which has noted euphoria as a neuropsychiatric symptom of NP-SLE (Alao et al., 2009; Benedict et al., 2008; Covey et al., 2012; Hanrahan, 1954).

Since support for the hypothesis was suggested and the NP-SLEs appeared to demonstrate at least one type of euphoria at a similar level to the MS group, the results could, tentatively and provisionally, therefore suggest that euphoria may, in some way, be associated with an immunological disease process, which both groups have in common.

However, the NP-SLE group seemingly demonstrated similar executive dysfunction to the MS group, which (as has been discussed in the previous sections above) has been hypothesised to be involved in the cause of euphoria in MS patients (Benedict et al., 2001; Fishman et al., 2004). Thus, one could argue that it was the executive dysfunction and not the immunological nature of the disease that resulted in positivity and unawareness being demonstrated within this group.

However, even though the MGs also appeared to demonstrate executive impairment, euphoria in MS has been linked not only to executive dysfunction, but to cerebral involvement (Rabins et al., 1986), and the MGs, by way of their disease, do not suffer from cerebral damage but never-the-less demonstrated just as much positivity and unawareness as the MS group. Thus, immunological disease processes, such as fatty acid regulation and levels of cytokines (addressed in the rationale of part three, following the literature review) may still be worth further investigation.

Right hemispheric dysfunction. Preliminary results pertaining to the fourth and last potential cause of euphoria to be investigated (i.e. the effects of RH involvement) were presented.

Assessing the suitability of the group to address the research question. The cognitive functioning of the RH participants (n = 10) was described, according to a personal communication with Ms Mosdell who personally interviewed each of these participants as part of her neuropsychological study (see Mosdell et al., 2013). The description of the RH

participants was in line with what was expected as the RHs appeared to demonstrate similar impairments of RH functioning to the MS participants, but no executive dysfunction. This description was also in line with previous literature on deficits due to RH stroke, who found that RH damage was associated with difficulties in spatial cognition and construction (Benowitz et al., 1990) as well as less executive dysfunction than damage to the left hemisphere (Nys et al., 2007).

While significant differences existed between the MS and RH groups for gender, race/ethnicity and combined household monthly income, these were not thought to account for the cognitive functioning of the RH group as they demonstrated only RH deficits and no differences on IQ or tests of executive functioning when compared with matched HCs (see Mosdell et al., 2013), which would be more common if their cognitive deficits were the result of impoverished or under-privileged conditions (Heaton & Pendleton, 1981).

Thus, the RH group was tentatively considered to be an appropriate reflection of a control group with damage only to the RH. The question pertaining to the effect of RH involvement on the cause of euphoria was, therefore, addressed.

Addressing the research question. The 10 RHs and 100 MS participants were then compared on the two types of euphoria (i.e. positivity and unawareness), while controlling for significant pre-existing between-group differences for gender, race and current medication use. This was done in an attempt to investigate whether or not the RHs would demonstrate at least one of the euphoric types at the same level as the MS participants.

Although significant differences were not apparent for the majority of variables, two findings of interest emerged. The first was that no RHs demonstrated positivity at the high level. The second was that the RH group appeared to be significantly more unaware of their physical (but not their cognitive or mood/behavioural) deficits than the MS participants.

The findings in terms of unawareness of physical deficit appears to be in support of previous research in this field (see, e.g., Hartman-Maeir et al., 2001; Jenkinson et al., 2011; Vocat & Vuilleumier, 2010). Equally, the findings in terms of low positive mood also appear to be in support of more recent theories concerning the neuroanatomical location of positive mood in the brain (see, e.g., Davidson et al., 1990; Hartman-Maeir et al., 2001; Jenkinson et al., 2011; Vocat & Vuilleumier, 2010).

However, these findings appeared to suggest that the RHs did not demonstrate positivity and unawareness at the same levels as the MS participants. In fact, they were not positive at the high level, and were significantly more unaware of physical deficits than the

MS group, which may imply that euphoria (in terms of both positive and unawareness) may not be caused by RH involvement.

Thus, although many similarities appeared to exist between the original descriptions of eutonia sclerotica and anosognosia for hemiplegia, and although the original theories such as the RH hypothesis held that positive mood could result from damage to the RH (Borod, 1992; Borod et al., 2002; Tondowski et al., 2007), RH impairment does not appear to be related, in this limited preliminary analysis, to euphoria in MS.

Summary of part three. The aim of part three was to explore four hypotheses regarding the cause of euphoria in MS, via preliminary analyses. While the MVA TBIs and NP-SLEs expectedly demonstrated similar levels of positivity and unawareness to the MS participants, significant between-group differences were also absent between the MG and MS groups. These findings implied a potential role played by executive dysfunction, due to the cognitive performance of the groups, as well as possibly immunological disease processes in euphoria. RH dysfunction did not appear to be implicated in the etiology of euphoria in MS.

General discussion

Being unaware of one's difficulties, displaying positive mood that seems out of place, and having an optimism regarding recovery in the future that is unlikely to occur, are all symptoms experienced by sub-groups of MS patients. Since notable disagreement concerning these symptoms, collectively known as euphoria, has appeared throughout the literature, improving our understanding of (a) the euphoric symptoms; (b) their underlying causes and mechanisms; (c) the definitions which underpin them; (d) the ways in which they should be measured; and (e) at what level they should be considered pathological symptomatology, rather than representations of normal beliefs and feelings, are all areas of significant value.

The risk of false discovery

Before I begin to summarise and discuss the abovementioned points which form the crux of this dissertation, special attention must be given to the number of inferential statistics included in this study. Firstly I would like to acknowledge that including so many analyses is problematic and that I am aware of the risk of false discovery. I, thus, urge caution in the interpretation of the findings and do not claim these results to be unequivocal fact. However, I would also like to justify the use of the analyses used, as the complex nature of euphoria necessitated the use of a comprehensive, exploratory approach. With such vastly differing opinions and findings on what constitutes euphoria, in which patients it presents, and what causes this interesting phenomenon, a small concise study would not have adequately addressed the important questions which this research attempted to answer. Moreover, I attempted to compensate for this problem to some extent by adopting a more conservative alpha cut-off level of .01, rather than the conventional .05.

A change in the constructs

As we now know, an abundance of literature on the topic of euphoria in MS exists, dating all the way back to the early 1800's. However, great differences in opinion appear to exist between authors researching and reporting on these phenomena. Contemporary investigators appear to disagree with classical authors, and even classical researchers disagreed with each other regarding the definitions, types, and incidence rates of euphoria. Although a number of excellent review articles exist that note, or imply, such discrepancies in the literature, or even go so far as to hypothesise a possible reason for the change, this study is the first empirical

investigation of the actual changes that appear to have crept into the literature. Although a renewed interest in euphoria in MS has taken place in recent times, resulting in a number of contemporary studies of these symptoms, well-grounded research cannot take place without a substantial understanding of the constructs that underpin those symptoms. Thus, in addition to investigating the inconsistencies as well as the root of the inconsistencies present in the literature, a further strength of this research was that it re-investigated the euphoric constructs themselves in order to better define, and therefore better study euphoria.

Prior to this study, it seemed as though the rates of euphoria had just changed, and that MS patients are no longer predominantly euphoric as they once were. However, this study demonstrated that instead of three types, only one type is typically measured today, and that instead of more subtle definitions of cheerfulness, happiness, ease, and optimism (euphoria and spes sclerotica), today researchers report the presence of more abnormal, unrealistic and extreme mood and optimism. Furthermore, eutonia sclerotica appears to have morphed from a sense of physical well-being (and unawareness of physical deficit) to largely only an unawareness, but not just of the physical domain. Using the CWQ to represent the classical definition and measure, I demonstrated that replication of relatively high rates of euphoria according to the more subtle definition (along with an interpretation of the results) was possible. Using the NPI as the popular modern definition and measure, I demonstrated that lower rates of euphoria (in the same sample) according to the more extreme definition were possible. This highlighted that the high rates of Cottrell and Wilson's (1926) three types, and the low rates of the modern researchers' predominantly one type, reflect an artefact of measure and the different operational definitions used; which implies that the nature of the MS patient has not undergone the shift apparent in the literature. It further seems possible that a bias amongst researchers exists where the majority of classical investigators (i.e. not just Cottrell and Wilson) appeared to be biased towards finding euphoria and described it as the predominant mood state of MS patients (Charcot, 1877; Finger, 1998; Surridge, 1969), while the modern investigators appear to be biased against finding euphoria and consider it to be rare (Figved et al., 2005; Kesselring & Klement, 2001). This bias may further have influenced the ways in which euphoria was or is defined, measured, and the rates at which it is found. These discoveries regarding the altering definitions, are a significant finding and may influence our understanding of these constructs moving forward.

Towards the beginning of this dissertation, I stated that the change in definition that appears to have occurred does not appear to have resulted from a demonstrated inappropriateness of the definition provided by Cottrell and Wilson (1926). Since euphoria

sclerotica, eutonia sclerotica and spes sclerotica were all demonstrated within this sample (even if one only accepts the definite presence of these symptoms), and since using the more inclusive, subtle definition identified a number of euphoric MS participants that were not identified by the more extreme NPI, it appears that this supposition is correct.

Furthermore, it highlights that by using modern definitions that are different from the classical definitions described as "cogent" (Minden & Schiffer, 1990), we are likely losing important characteristics that were present in the original definitions that may assist us in the diagnosis and treatment of MS patients (and perhaps translate into better treatment for other patients too).

Thus, this re-investigation of euphoria from a classical perspective has broadened our knowledge of the constructs underlying the symptoms of euphoria. However, now that we know a change appears to have taken place, it is important to understand the real nature of these symptoms.

The quality of euphoria

Despite the above noted disagreement regarding the characteristics and definitions of euphoria, many studies exist that have investigated the symptoms of positive mood, optimism and unawareness of deficit, within MS. However, contemporary researchers predominantly use different measures from those used in classical research and appear to approach the topic from a slightly different perspective. A strength of this study was, therefore, that it combined both classical and contemporary views, thereby addressing potential missing components from both perspectives. It also included additional demographic and disease variables that have previously not specifically been assessed in relation to euphoria. Furthermore, this research attempted to investigate the cortical contributions to euphoria, as well as to investigate euphoria from the perspective of RH dysfunction, which has not been done before, and some of these avenues yielded useful and interesting results that enabled me to better describe and define the symptoms associated with euphoria.

From the results of this study, it appears that two types of euphoria exist within this sample. Relating to Cottrell and Wilson's (1926) original euphoria sclerotica and spes sclerotica, the first type, which I termed positivity, includes feelings of positive mood and an optimistic outlook. It is not defined in terms of abnormal positive mood or unrealistic optimism, but rather involves a more subtle definition that exists on a continuum of milder to more intense presentations of this symptom.

The second type, in part referring to the original eutonia sclerotica as defined by Cottrell and Wilson (1926), I called unawareness. Rather than focussing on the aspect of physical well-being from the original definition, I focussed on the idea of unawareness of physical deficit (which also formed part of the original definition); but results revealed that unawareness, in MS, may extend to more domains than just the physical, and MS patients appear to demonstrate unawareness of, at least, cognitive and mood or behavioural deficits too. Results did, however, reveal that an MS patient does not necessarily present with unawareness of all domains concurrently, and while overlap did occur, of the 61 MS participants to demonstrate unawareness, 41/61 (67.2%) did so in only one domain.

An association between positivity and unawareness was demonstrated, where an increase in the one is associated with an increase in the other, and fairly high rates of co-occurrence between these two symptoms appeared to exist. This appeared to demonstrate that positivity and unawareness are not mutually exclusive. However, some participants demonstrated one without the other, and, as such, I concluded that, although associated, positivity and unawareness are also not one and the same symptom, and that measuring one does not mean that the other automatically exists.

In relation to discrepancies between definitions of inward and outward euphoria, positivity was found to be negatively correlated with depression. This finding not only implied that the two symptoms are unlikely to co-occur, but that self-reported positivity (i.e. positive mood and optimism) is a symptom experienced by the patient themselves, and not just a façade or persona that they project, as MS participants reporting moderate to high rates of positivity did not also report depression. This further implies that the self-report measures included in this study are accurate ways of eliciting or measuring this type of euphoria identified.

Awareness was positively correlated with depression, which meant that as unawareness increased, depression decreased. As this finding supported that of previous research, I concluded that the measures and method used (i.e. participant/informant discrepancy scores) for this type of euphoria, were also appropriate and accurate ways of determining unawareness.

While no cognitive correlates, of the domains of cognitive functioning that were assessed in the current study, were found to significantly predict positivity, a previous medical history of diseases or conditions that could impact on one's neuropsychological functioning was found to negatively correlate with and significantly predict positivity. This appeared to imply that positivity can (at least in this sample) occur independently of cognitive

impairment, gender, age, income, disease course, disease duration, current disease state, and severity of disease (in terms of physical disability). Furthermore, it appears to be independent of medication. However, the fewer medical conditions a patient has had in the past, the more positive s/he will be, in terms of the findings of this research.

For unawareness, no correlates were identified for the domain of mood and/or behavioural difficulties. No demographic or disease correlates were identified for unawareness of cognitive deficits either; however, poor visuospatial ability (a cognitive predictor) was found to be associated with greater unawareness of cognitive deficits. Unawareness of physical deficits had the greatest number of correlates and the full model of demographic and disease variables significantly predicted unawareness of physical deficits. Two individual variables were also significant predictors: Greater disease severity (in terms of physical disability; a disease predictor) and increased disinhibition and difficulties in set shifting (a cognitive predictor) were found to be associated with greater unawareness of physical deficit. Few demographic, disease and/or cognitive correlates were thus identified in general and, apart from the correlates addressed above, unawareness too, appears to be largely independent of the variables assessed in this research.

Although overall, relatively few correlates were identified, there did appear to be different correlates not only for positivity and unawareness, but for the different domains of unawareness too. While this may imply that different mechanisms may underpin positivity and unawareness, and that the different domains of unawareness may be accounted for by different underlying mechanisms, limitations such as sample to variable ratio or sensitivity of the measures were also discussed in relation to those findings, and definitive conclusions cannot yet be drawn.

In the process of investigating the origin of a change in definition, as well as of better describing and defining what euphoria really appears to involve, I uncovered an exceptionally important aspect: What is the most appropriate way to measure positivity and unawareness, and at what point are they no longer characteristic of normal beliefs and feelings, but rather something that one can consider to be pathological?

How best to measure euphoria and what is pathological?

As stated, this research has produced important findings in terms of the influence of artefact of measure and differing conceptual and operational definitions on the frequencies of euphoria demonstrated throughout the literature. In addition, it has contributed to a better understanding of euphoria. However, it has also raised two additional important issues, that

of: (a) how best to measure euphoria, and (b) at what point the feelings and beliefs of MS patients should be considered outside the normal range, or strong enough to be considered pathological or indicative of a symptom.

A major strength of this research, and one that assisted in answering these difficult questions, was that it included different types of measurement instruments (both classical and modern, as well as other well-known subtle [e.g. PANAS, OPS] and more extreme [e.g. CRJRF] modern measures), and that it approached euphoria from both the classical and contemporary views.

I will discuss the idea of how best to measure euphoria first. Researchers investigating euphoric mood predominantly use a yes/no diagnosis, and those investigating unawareness largely just distinguish between aware and unaware patients based on whether they over or under-estimate their deficits. Although, continuous scales are often used in unawareness research, the researchers generally do not acknowledge the different degrees of unawareness; and although a wide range of unawareness was not demonstrated in this research, a range was never-the-less found.

Determining whether or not a patient has euphoric mood, or is unaware, is important, but since a range does exist, it may be beneficial and appropriate to represent both positivity and unawareness on a continuum, instead of imposing cut-off points or a yes/no diagnosis. One benefit may be that patients with differing degrees of positivity and unawareness require, and may benefit from, different types of intervention or treatment options. As such, identifying at what level a patient is experiencing these symptoms may assist practitioners to develop tailor-made treatment programs, specific to their patient, rather than treating all euphoric patients in the same way.

Another benefit is associated with the finding that an increase in positivity was associated with an increase in unawareness, and an increase in unawareness (of physical impairment) was associated with, and significantly predicted by, an increase in disease severity. If unawareness, and thus positivity, increase as the disease worsens, identifying those participants who fall within a more moderate category, but who may progress to present with more severe euphoria at a later stage, may assist clinicians and caregivers to provide such patients with timeous and appropriate care.

Representing an individual's mood and/or outlook on a scale of euphoria may also lessen any sense of stigma that may be attached to an abnormal symptom. When asking a number of participants in this study whether they experience a "persistent and abnormally good mood" (Cummings et al., 1994), many replied that they may be happy but they are not

crazy, and are not abnormal, and one related that she had been called euphoric by her neurologist and spoke of this label in a very negative light. If these patients feel that their support networks (i.e. their families and doctors) think they are not normal, they may be less likely to share their concerns or ask for help when they need it.

Although a range of unawareness may exist and although it may be beneficial to identify patients with differing degrees of unawareness, determining which patients are pathologically unaware is relatively easy if one assumes that those who underestimate their deficits are unaware.

In contrast, although the same benefits (as related to unawareness) of conceptualising positivity on a continuum exist, positivity is more difficult to diagnose and the majority of patients demonstrating positivity may not necessarily have euphoria. Thus, the idea of what denotes a pathological presence of positivity is of equal, or even greater, importance.

This idea, though, is an even more difficult one to address, particularly given the inconsistencies present in the literature, as well as the limitations identified regarding the measures most often used to determine whether or not euphoric mood exists. It is further complicated by ideas such as those raised by Peyser et al. (1980) who noted a difference between early MS patients who have minimal impairment, but who (in their opinion) realistically demonstrate well-being (due to their lack of disability), and MS patients who have had the disease for longer, are more disabled, and who (in their opinion) unrealistically demonstrate well-being (due to their severe impairment). Similar findings were noted in this sample, where 46.1% of the participants scoring within the high range for positivity were rated, by their informants, as being 50% or less impaired physically. Thus, like the early MS patients in Peyser et al.'s (1980) study, almost half of the participants classified as displaying high positivity in the current study were not severely physically impaired and may have (due to their lack of disability) been entitled to demonstrate positive mood and optimism without it being considered abnormal. However, even early MS patients have an unpredictable, chronic, degenerative, disabling disease, and displaying euphoric mood in the face of this reality, even with minimal symptoms initially, may be considered pathological.

The above complexity aside, participants in the present study displaying moderate positivity still noted some negative mood, as per the themes identified in the qualitative analysis. This means that it was only towards the higher level of positivity that the symptom resembled pathological euphoria. Furthermore, when the MS participants were compared with the control groups of this research, they generally demonstrated slightly, but not significantly, lower levels, than the other patient control groups, of positivity on average (i.e.

when the full sample was included) and demonstrated significantly lower levels than the well-matched HCs (p = .0001). They also largely demonstrated slightly, but not significantly, lower levels of positivity than the other patient control groups at the moderate cut-off point (i.e. when all scores between the 50% and 75% cut-off points were included) and again demonstrated significantly lower levels than the HCs (p = .001). But, they demonstrated similar levels of positivity to the HCs (p = .293) and slightly, but not significantly, higher levels of positivity than all patient control groups at the high cut-off point (i.e. when all scores within the top quartile were included). This appears to demonstrate not only that high positivity is likely to represent the level at which this symptom may be deemed pathological, but also that there appears to be a fairly steep increase in the curve of positivity at this end of the continuum, and that, in general, MS patients are not obviously euphoric, but those that do present with euphoria demonstrate it at very high levels.

However, positivity was measured on a continuum, and the moderate and high cut-off points imposed were perhaps as arbitrary as believing a yes/no answer can address the complexities of this symptom. Thus, these interpretations should be received with caution, and a 65% cut-off point may have differentiated euphoric patients from non-euphoric patients just as well as the 75% cut-off point. My recommendation is, therefore, that one acknowledges that a large percentage of MS patients experience some form of positive mood and optimistic outlook, as 67% of the participants of this study fell within the moderate to high range; but that this mood and outlook only becomes pathological at a higher level, and, thus (in this sample at least) is relatively uncommon.

What is the cause of euphoria?

Many researchers have hypothesised as to what may be causing euphoria in MS, and a number of (particularly contemporary) investigations have brought us a little closer to an answer to this question. However, the absolute etiology of euphoria in MS remains unclear. A strength of this study, therefore, was that it tested a number of existing hypotheses, and that it introduced a pilot investigation of two new hypotheses that, despite a strong rationale for their inclusion/consideration, had not been investigated before. However, I will remind the reader again of the unequal sample sizes between groups and the small sample sizes of the patient control groups, and emphasise that only tentative speculations regarding the causes of euphoria could be made and that absolute conclusions could not be drawn from the preliminary findings provided by these analyses.

Although the euphoric symptoms may be better represented on a continuum, in terms of the above understanding, the level at which positive mood and optimistic outlook becomes pathological and may be considered to represent euphoria appears to be around the higher cut-off point, rather than the more modest cut-off point of moderate positivity. Thus, an examination of the underlying cause of euphoric mood should perhaps be made by comparing the MS group with the patient control groups at this high level, as it is likely here that we may see some trends with regard to the various groups (whereas scores in the lower quartiles may present more 'normal' mood states).

However, except for the RHs where statistics could not be calculated due to a lack of any RHs scoring highly on positivity, inferential statistics appeared to reveal no significant differences between the MS group and any of the patient control groups for high positivity. Sample sizes were small though, and this limitation could likely have influenced these results. However, an examination of the effect sizes appeared to reveal very small effects for the majority of these analyses (all $\eta^2 < .21$). Thus, what these provisional results may imply is that as executive dysfunction, in terms of, in this research, at least, the dorsolateral prefrontal functioning composite (attention, WM and abstract reasoning) as well as dysexecutive-type memory deficits appeared to be demonstrated in all patient control groups (except for the RHs), this form of cognitive impairment may, as has been theorised, be imperative in the etiology of euphoria.

However, since intriguing findings were unveiled with regard to the MG group, who, even though they appeared to present with executive impairment, did not have a disease that affects the CNS, executive dysfunction, in terms of cerebral involvement, might not be the only causative factor in euphoric mood/outlook and immunological disease processes could play a potentially influential role. Furthermore, the results may suggest that RH involvement may not be a causative factor in positivity.

In terms of unawareness, a distinction was not made regarding the level or degree of unawareness, and participants were merely classed as being aware or unaware. Thus, an investigation of the underlying cause of unawareness could possibly be made by comparing the scores of unaware MS participants with those of unaware patient controls for the different domains. For unawareness of physical deficits, no significant differences appeared to be demonstrated between the unaware MS participants and the unaware control participants of any group, except for that of the RHs. But since the RHs were significantly more unaware of their physical deficits than the MS participants and did not present their unawareness at the same level as the MS participants, this may imply that RH unawareness of physical deficit is

something different from MS unawareness of physical deficit. Further, since the effect sizes regarding the analyses between the MS and the MG, NP-SLE and MVA TBI groups were all small (all $\eta^2 < .01$) these findings may again implicate both executive dysfunction as well as, potentially, immunological factors in the etiology of euphoria.

Regarding unawareness of the remaining two domains (that of cognitive and mood/behavioural deficits), no significant differences were found in the limited analyses conducted for any of the groups for these variables. Furthermore, even though sample sizes were small, since all effect sizes were less than .15, this lack of significant differences may be somewhat representative of larger groups. While these findings do not implicate a particular group, and, thus, underlying cause, for unawareness of these domains, the lack of significant differences also does not rule out any of the hypotheses as a potential cause, which is also an important finding.

However, although the findings of this study, in terms of the demographic, disease and cognitive correlates of positivity and the different domains of unawareness, implied that differing correlates between these aspects of euphoria may exist, associated limitations (such as sensitivity of measures and sample size to variable ratio) with this interpretation have been discussed. Furthermore, an association was demonstrated between positivity and unawareness in this research, and indeed much of the literature before this (see, e.g. Finger, 1998). In addition, a number of participants were found to demonstrate unawareness of more than one domain concurrently, and many in conjunction with moderate to high positivity. Furthermore, all domains of unawareness loaded onto one factor, in the factor analysis conducted to determine the number of types of euphoria, indicating some underlying commonality between them. Moreover, even Sherman et al. (2008), who stated that different mechanisms may underlie different aspects of unawareness, found an overlap of 16% of participants experiencing both physical and cognitive unawareness. Therefore, it seems likely that one mechanism underlies not only both types of euphoria identified in this research, but all domains of unawareness. In terms of the provisional studies conducted, executive dysfunction appears to be the most likely avenue to explore. However, immunological disease processes should not be discounted as other non-neurological diseases, such as muscular dystrophy, which also presumably have the potential for executive impairment according to studies such as that of Grosshans et al. (2008) and Kurella et al. (2004), have not been found to present with euphoric mood or unawareness of physical deficits (Surridge, 1969). Thus, auto-immunity, along with executive impairment, both appear to require further investigation.

Limitations of the study

Although every attempt was made to address these, I recognise that a number of limitations were present in this study. I will address each limitation below in separate sections pertaining to the participants, their medical records, and the measures included in this research.

Inaccessibility of patients. Not one of the patient groups included in this study was easily accessed. Firstly, there were not many of these patients in the WC (or SA), and secondly a lack of motivation and resources, as well as time constraints, existed for neurologists in private practise, support groups, speech therapists, neuropsychologists and/or rehabilitation centres, which impacted on the identification and recruitment of patients. In addition, research fatigue of patients in public hospitals led to my being unable to interview a number of MG patients that were identified, as well as to my being unable to cognitively test the RH patients that were included in this study.

As addressed in the methods section, every attempt was made to address these problems and I explored every avenue of patient recruitment available to me, including adapting the research to include only the euphoric questionnaires and broadening the research population to the whole of SA in order to be able to post or e-mail the questionnaires to participants that were too far away to see in person. However, despite this, patient numbers remained low and this led to a number of limitations in this research. The first is that it resulted in small sample sizes, particularly of the patient control groups (i.e. the groups of MG, MVA TBI, NP-SLE and RH patients), which may have influenced the generalisability of the results as well as the reliability of the data.

The second is that inaccessibility of patients resulted in my not being able to exclude any MS or patient control participant according to the exclusion criteria imposed upon the HC group. This resulted in the potential for confounding variables that could influence neuropsychological functioning being present in groups that should otherwise have had clean pathology (i.e. only the disease or condition in question being present), which may, in turn, have influenced the results. Severe cerebral pathology within the samples (for instance, stroke or current epilepsy) was, however, rare and the kinds of conditions reported were a loss of consciousness in childhood with no lasting effects, or malaria, but not of the cerebral kind). Furthermore, a medical history of factors that could influence neuropsychological functioning was controlled for statistically.

Thirdly, inaccessibility of patients resulted in my inability to match groups according to one on one, or even aggregate matching. Thus, some of the groups were mis-matched on certain key demographic variables, although this was controlled for statistically.

Finally, the issue of research fatigue led the RH patient control group to be excluded from cognitive testing. Here, I used the thorough description of the cognitive performance of these patients that was available to me and they were still regarded as being appropriate controls for the hypothesis in question.

Access to medical information. Accessing MS patients via neurologists and private practise and at public hospitals accounted for approximately one quarter of the total participants included in this research. The majority were recruited via MSSA or MS support groups, and, due to time constraints and limited numbers of patients being available, these participants were often interviewed before their neurologist could be reached. Thus, a confirmed diagnosis of MS and current disease course could not be obtained in four cases, despite my sending numerous e-mails and making numerous phone-calls to the relevant neurologists. Although this was a small percentage, it may, never-the-less, have influenced the results.

The measures. A number of limitations associated with the measures included in this research were also present. Firstly, the majority of measures were only available in English. Thus, although provisions were made for certain cognitive tests (addressed in the methods section), all participants had to be fluent in English in order to be able to answer the remaining measures. This did not, however, result in the exclusion of any participants as all participants were fluent in English, and were able to answer all the questions.

The majority of the measures were also created in developed countries and, thus, cross-cultural applicability issues may have played an influential role in the interpretation of the performance of the patient groups. I addressed this issue by including matched HCs as a reference group for the MS patients and rather than comparing their performance with standardised international norms, they were compared with HCs from similar sociodemographic (where possible) and geographic areas.

Self-reported measures were included for a particular reason: to address the discrepancies between objective and subjective displays of emotion noted by Surridge (1969). But since (at least some) MS and TBI participants are known to present with issues of unawareness, self-report measures may present their own limitations in accurately measuring

the euphoric symptoms in question. I addressed this by including informant ratings which supplemented the self-reported findings (for example when determining how many types of euphoria exist).

Furthermore, as was addressed in part one of the discussion, although informants were used to determine the degree of unawareness amongst the MS participants, factors relating to the informants themselves, such as not knowing the extent of the participants' deficits, may also have affected the results obtained. However, as was further addressed in part two of the discussion, forming true objective opinions regarding the physical, cognitive and mood/behavioural deficits of the participants would have been near to impossible as I did not know them well enough, and I followed the procedure that is considered to be standard practice in unawareness research (see Prigatano et al., 1990).

Another limitation associated with the measures of the study was that of including the PAS as a measure of disease severity rather than the EDSS. While it was not possible to include this measure (the reasons for which were addressed in the methods section), the fact that these measures are not directly comparable does influence the extent to which the current results relating to disease severity could be compared with that of previous research results relating to disease severity.

Another factor that has also been addressed previously but should never-the-less be mentioned here, is that many neuropsychological measures are not as domain specific as we would like them to be. For example, it was noted in part two of the discussion that the CA, for example, may tap into executive functioning in addition to RH visuospatial abilities. Thus, basing a study that aims to differentiate between cortical and subcortical, as well as right versus left neuroanatomical areas solely on neuropsychological testing may not be the most scrupulous form of methodology. Differentiating between these areas was, however, an exploratory investigation, and it was not deemed essential to include these additional techniques (such as MRI) in this initial study.

Finally, the number of measures included may also have impacted on the results. While all were considered to be necessary, the number of measures included resulted in a full testing session (for the MS and HC participants who took part in both the cognitive assessment and the interview including the euphoric questionnaires) of between 2.5 and 3 hours; and patient control interviews, which included the euphoric questionnaires and the tests of executive functioning, of up to 2 hours. This may have resulted in fatigue or loss of concentration. A number of attempts were made to address these concerns. Participants were given breaks and refreshments, and the interview schedule was structured in such a way that

difficult, complicating or tiring tasks were interspersed with easier, less taxing tasks. However, fatigue is a common symptom of at least MS and MG (Cantor, 2010; Jones, 2011; Rich et al., 2008), thus may have influenced the performance of these patients.

Directions for future research

There are a number of factors that could be addressed by future researchers to minimise the limitations described above. For example, future research should consider larger sample sizes for each of the patient control groups addressing the hypotheses concerning the cause of euphoria. If availability and/or accessibility of patients still poses a problem with the groups included in this study, perhaps future investigators might consider other patient groups that are appropriate to answer the various questions. Someone else may, for example, have better access to muscular dystrophy patients and will, thus, be better equipped to investigate the psychological reaction/cerebral involvement hypothesis. Obtaining greater sample sizes will also allow for more stringent/rigorous exclusion criteria.

Future researchers should also ensure that all diagnoses of participants obtained via support groups are confirmed with the patients' neurologists prior to their inclusion in the study. Or, if patients are readily available, they should include only patients referred by a neurologist, neurosurgeon, neuropsychologist, or medical practitioner who has access to the medical records of the patient. This will ensure that 100% of the sample has clean and confirmed pathology.

In addition, one of the aims of this research was to determine if one could predict either of the euphoric types identified, based on cortical versus subcortical and/or right versus left hemispheric involvement. But, this involvement was measured by means of neuropsychological tests which can tap into more than the specific domain one is wanting to investigate (Lezak et al., 2004). Because of this limitation, and because this study revealed some interesting results regarding the cortical correlates of unawareness, future research may want to consider measuring this more objectively by including MRI scans to examine, in more depth, the contributions made by these neuroanatomical areas to the euphoric types.

A number of interesting and important findings, however, also emerged from this study that could be further investigated and addressed by research studies to come. For example, researchers investigating euphoria might consider approaching this topic from the perspective of a longitudinal study. Past research, like the current study, appears to have consistently investigated euphoria from a cross-sectional methodological approach; however given that positivity and unawareness could be appropriately measured by a continuum, it

would be interesting to see if these symptoms change or develop over time. A longitudinal study would also help to address the association found between positivity and unawareness, by seeing if this relationship (i.e. an increase in positivity is associated with an increase in unawareness) endures, or increases over time.

I would like to add, in addition, that future researchers investigating euphoria should be cognisant of the varying degrees of positivity and unawareness, and should be cautious and pay particular attention to the question surrounding what is considered to be a pathological presentation of these symptoms.

In addition, although three domains of unawareness were included in the present research, based on prior literature and the aims and objectives of the current study, and also limited by time constraints and the length of the interview, that is not to say that they are the only objects of unawareness in MS. Additional domains, or additional aspects of the current domains, could be included to better describe and define unawareness in MS.

Future research may also consider incorporating premorbid characteristics, for example concerning coping strategies, of the MS patients, and investigate how these are associated with positivity (and unawareness) post MS. Although not addressed in-depth in the findings of this study, I, like Cottrell and Wilson (1926), found that many participants noted a change since their MS to a more positive and optimistic state. Some who were positive and optimistic before their disease reported becoming more so, while others who were slightly negative and/or pessimistic reported a change to being more positive and optimistic. A study investigating whether premorbid personality can affect which participants develop positivity (and unawareness) and which develop these symptoms in higher rates of intensity may reveal interesting findings regarding these concepts.

Following on from this, the investigation of positivity and unawareness from a psychodynamic or psychoanalytic approach would also be of great interest. Concepts such as denial and avoidance would be interesting to pursue within this subject matter. Further, some MS participants related ways in which they have gained something or taken something positive from their MS. However, did this positive outcome and the accompanying mood and outlook result from an acceptance of the disease, or did the organic euphoria experienced by the participant create an incongruence between mood/outlook and the reality of their situation that their unconscious addressed by reframing the participants' experience of the disease into something more positive? These are interesting questions that deserve further attention.

Finally, further research is required to investigate the etiology of euphoria. Since (a) the results concerning these analyses were preliminary, (b) an association between positivity

and unawareness and a high co-occurrence of these two symptoms was demonstrated, but (c) no one clear cause of euphoria was identified by this research, researchers may want to explore this question further. In addition, due to the interesting (but very provisional) findings that were revealed in relation to the contributions made by the immunological nature of the disease, future researchers should additionally explore this area further, with both bigger sample sizes and perhaps the inclusion of immune disease markers such as cytokine levels.

Conclusion

This exploratory study demonstrated that a change in the definition of euphoria appears to have occurred since the first comprehensive definition was provided, in 1926, by Cottrell and Wilson. It further put forward a new definition and described two associated types of euphoria (viz. positivity and unawareness), of which positivity was defined in more subtle terms, and unawareness was defined in terms of a variety of domains (including unawareness of physical, cognitive and mood or behavioural deficits), and both of which were elicited by self-report measures (which were compared with the answers of informants, in the case of unawareness). Although a range was present and both symptoms appeared to be represented on a continuum, any under-estimation of deficits was deemed representative of pathological unawareness, while positivity was considered pathological around the high cut-off point. Although associated, each symptom appeared to have different disease and cognitive correlates, and, although both executive dysfunction and immunological disease processes may possibly be implicated in euphoria, no single indisputable underlying cause for both symptoms was identified in terms of the very preliminary analyses conducted.

This study has thus added substantially to our understanding of both the constructs that underpin euphoria in MS as well as the symptoms of euphoria themselves. These results may, therefore, shape research in this area going forward. In addition, they might assist clinicians in the diagnosis of patients that may benefit from, either currently, or in the future, both direct treatment and management of these symptoms as well as from taking these symptoms into account when treating the patient's disease in general.

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Appendix A: Letters of Ethical Approval

Appendix A1: University of Cape Town Health Sciences Faculty Approval

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 [illegible] • Facsimile [021] [illegible]
e-mail: [illegible]@uct.ac.za

30 November 2011

HREC REF: 548/2011

Ms A Northam
c/o Prof M Solms
Humanities
Psychology
Graduate School Building

Dear Ms Northam

PROJECT TITLE: EUPHORIA: A CONTEMPORARY INVESTIGATION OF CLASSICAL CONSTRUCTS.

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year till the 30th December 2012.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010) if the study is completed within the approval period.

Please note that there is a UCT [illegible] Insurance Policy which covers research related injuries. Information about the availability of this policy should be included in the relevant informed consent forms. Please obtain permission from Dr [illegible] Patel, Chief Operating Officer at GSH, to access medical patients for research purposes.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA000[illegible]

[illegible]

Appendix A2: University of Cape Town Health Sciences Faculty Renewal

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA[illegible]; IRB[illegible])			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	15/12/2014
☐ Not approved	[illegible]		
Signature Chairperson of the HREC		Date Signed	6/2/2013

Principal Investigator to complete the following:

1. Protocol Information

Date form submitted	15/01/2013		
HREC REF Number	048/2011	Current Ethics Approval was granted until	15/12/2012
Protocol title	Euphoria: A contemporary investigation of a classical construct		
Protocol number (if applicable)	N/A		
Principal Investigator	Miss Amy Northam [illegible]		
Department / Office Internal Mail Address	c/o Prof M Solms, Humanities, Psychology, PD Hahn Building		

1.1 Does this protocol receive US Federal funding?	☐ Yes	☒ No
1.2 Has sponsorship of this study changed? If yes, please attach a revised summary of the budget	☐ Yes	☒ No

2. List of documentation

RESEARCH ETHICS COMMITTEE
2013 -02- 04
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

26 July 2012 Page 1 of 1 FHS016

[illegible]

Appendix A3: University of Stellenbosch Ethical Approval

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot · your knowledge partner

14 February 2013

MAILED

Ms A Northam
Dept of Psychology
UCT

Dear Ms Northam

Euphoria: A contemporary investigation of classical constructs

ETHICS REFERENCE NO: UCT 14

RE : ETHICS APPROVAL

We acknowledge receipt of documents pertaining to the above study and the approval letter from the UCT Human Research Ethics Committee, for this project.

The approval of the UCT HREC is recognised by the Stellenbosch University Health Research Ethics Committee for this particular project. However please continue to keep us informed of the progress of the project, by submitting annual progress reports.

Please note that research that will be conducted at any tertiary academic institution also requires approval from the relevant hospital manager.

Yours faithfully

MR FRANKLIN WEBER
RESEARCH DEVELOPMENT AND SUPPORT
Tel: +27 (0)21 938-9657 / E-mail: fweb@sun.ac.za
Fax: +27 (0)21 931-3352

Fakulteit Gesondheidswetenskappe · Faculty of Health Sciences

Verbind tot Optimale Gesondheid · Committed to Optimal Health
Afdeling Navorsingsontwikkeling en -steun · Division of Research Development and Support
Posbus/PO Box 19063 · Tygerberg 7505 · Suid-Afrika/South Africa
Tel.: +27 21 938 9075 · Faks/Fax: +27 21 931 3352

Appendix B: Consent and Assent Forms

Appendix B1: Multiple Sclerosis Participants, Healthy Controls, Myasthenia Gravis, Neuropsychiatric Systemic Lupus Erythematosus, Stroke, Traumatic Brain Injured Controls Able to Provide Informed Consent and Guardians of Traumatic Brain Injured Controls Unable to Provide Informed Consent: Full Interview (Consent Form)

The cognitive and affective symptoms of Multiple Sclerosis

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Invitation to take part in this research study
We would like to invite you to participate in a neuropsychological study conducted by researchers of the University of Cape Town (see above).

Purpose and description
The purpose of the study is to investigate the cognitive and mood, or affective, symptoms associated with multiple sclerosis (MS). Cognitive, or cognition, refers to one's mental processes of, for example, perception, attention, and memory. Mood, or affect, refers to one's state of mind, or quality of feeling or emotion. Examples might include depression or cheerfulness.

[For MS participants] You are invited to participate because 1) you have been diagnosed with MS, and 2) you either contacted me, or gave consent for the researcher to contact you.

[For HCs] You are invited to participate because 1) your demographic details match those of an MS participant, 2) you are a healthy person, and 3) the study requires control participants who have no neurological disease.

[For MG controls] You are invited to participate because 1) have received a diagnosis of myasthenia gravis, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For MVA TBI controls] You are invited to participate because 1) you have experienced a head injury, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For NP-SLE controls] You are invited to participate because 1) you have received a diagnosis of systemic lupus erythematosus, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For RH controls] You are invited to participate because 1) you have experienced a stroke, and 2) you either contacted us, or gave consent for the researcher to contact you.

Participants will be recruited for this study from Groote Schuur and Tygerberg Hospitals, private neurologists/neurosurgeons/neuropsychologist in the Western Cape, organisations such as Multiple Sclerosis South Africa, and by word of mouth.

Procedures
I [and/or your neurologist] will have already briefly explained the study to you via telephone, letter or e-mail. [For HC controls] I asked you a number of questions relating to the exclusion criteria of the study (e.g. prior brain injury). [For all participants] You agreed to give a loved-one a questionnaire for this research. If you decide to participate in this study, you will be asked to take part in a one-on-one interview with the researcher and will be encouraged to answer all the questions and give as much detail as possible, where required. You will be asked to answer a number of questionnaires regarding your mood and to complete a number of tasks assessing your cognition, for example your attention, memory, spatial and language abilities. As mentioned, your loved-one will also be asked to answer some questions. Your answers will be marked down [For MS participants] as well as tape-recorded. These recordings will be kept until the research study has been submitted. They will then be destroyed. There will only be one interview. It may take up to 3 hours to complete, but you may request a break at any point during the interview. Your interview will take place in an office at either Groote Schuur or Tygerberg Hospital, or in your own home.

Access to medical records
[For MS participants] This study requires information such as when your MS was diagnosed and the type of MS you are experiencing. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For MG controls] This study requires information such as when your MG was diagnosed. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For MVA TBI controls] This study requires information such as the date of your head injury. As some participants might not be sure of this information, we may need to check the above information with their neurosurgeon, or in the medical folder.

[For NP-SLE controls] This study requires information such as when your lupus was diagnosed. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For RH controls] This study requires information such as the location of your stroke. As some participants might not be sure of this information, we may need to check the above information with their neurologist, or in the medical folder.

Risks and benefits
There are no foreseeable risks for you as a participant of this study. However, the interview may take up to [For MS participants and HC controls] 3 hours to complete [For MG, MVA TBI, NP-SLE and RH controls] 2 hours to complete, and should you experience increased mental and/or physical fatigue, or any form of psychological distress, please inform the researcher immediately. Breaks can be taken at any point during the interview. Besides your time, there are no costs for taking part in this study.

Participation in this study will benefit you in the following ways:

1) You will receive an information pamphlet on the common cognitive and affective symptoms of MS/MG/MVA TBI/NP-SLE/RH. This will include information about each of the symptoms as well as ways of coping with them.
2) You will receive a full [for MS participants] / brief [for MG, MVA TBI, NP-SLE and RH controls] feedback form following participation in this study. This will outline any potential cognitive or mood symptoms you may be experiencing and help you to understand them better. It can also be used in conjunction with the information pamphlet to learn more about possible impairments in cognition and mood.
3) Should you travel to the interview, you will be compensated for travel costs and will receive refreshments during a break, during the interview.
4) In addition, we hope to gain information about the cognitive and affective symptoms of MS, the publication of which will broaden the scientific knowledge on the topic, and your answers will be invaluable in this respect.

Voluntary participation and withdrawal

Participation in this research study is voluntary. It is your choice to decide whether or not to take part. If you agree to take part you will be given this form to keep and will be asked to sign the declaration of consent at the bottom. You will still be free to withdraw from the study at any time.

Debriefing following participation and end of study

You will be debriefed following your interview. Any additional questions you may have following participation in this study may then be asked and will be answered to the best of the researcher's ability. Should you wish to receive the results of the study and/or any journal articles, please indicate this to the researcher.

Confidentiality

The confidentiality of your answers and identity will be protected. All interviews will be coded in such a way that your name and all identifying features will be removed and your answers will be given a participant number rather than a name, known only to the researcher. Only this will appear when the results of this study are published, and your name, contact details and other identifying data will not be included. All your answers will be confidential.

They will be combined with the answers from the other participants and it will be impossible to identify you from the responses you give. All paper-based answers will be kept in a locked cupboard at the researcher's home, will only be accessible to the researcher, and will be destroyed following completion of the study. [For MS participants] Tape-recorded information will be transcribed, will be kept in the same locked cupboard as the written answers, and the tape-recordings and transcribed notes will be destroyed following the completion of the study. Computer-based information will be available only to the researcher and will be password protected.

Research ethics approval

The Human Research Ethics Committee of the University of Cape Town (Faculty of Health Sciences) has reviewed this project for the protection of human participants in research. If you have any questions or concerns regarding your rights and welfare as a research participant, please contact Lamees Emjedi at one of the following details:

Contact details:

E52, Room 24, Old Main Building, Groote Schuur Hospital, Observatory, 7925
Tel: 021 406 6338; Fax: 021 406 6411

Declaration of consent

I recognise that I was contacted by my neurologist, an organisation, by word of mouth, or contacted the researcher directly and I was invited to take part in this study. I gave my consent for a loved-one to answer a questionnaire about me. I have read the information above. I have had the chance to ask questions and have received satisfactory answers to my questions. I understand that my involvement in this study is voluntary and that I may withdraw from the study at any time. [For all but HC controls] I understand that my neurologist may be contacted for medical information and give my permission for this to take place. I understand that my answers will be written down and tape recorded, but that neither my name, nor any identifying information will be included; and I consent to the confidential use of these recordings for scientific purposes. I understand that I will be given a copy of this form to keep, and that by signing this form I am agreeing to take part in a once-off interview for this research study.

Signed: _____ Date: _____

(Name in block letters) _____

If you have any questions or concerns regarding the study, or would like to be informed of the results when the study is completed, please feel free to contact the researcher.

Thank you.

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Appendix B2: Multiple Sclerosis Participants, Healthy Controls, Myasthenia Gravis, Neuropsychiatric Systemic Lupus Erythematosus, Stroke, Traumatic Brain Injured Controls Able to Provide Informed Consent and Guardians of Traumatic Brain Injured Controls Unable to Provide Informed Consent Euphoria Questionnaires Interview via E-mail or Post (Consent Form)

The cognitive and affective symptoms of Multiple Sclerosis

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Invitation to take part in this research study
We would like to invite you to participate in a neuropsychological study conducted by researchers of the University of Cape Town (see above).

Purpose and description
The purpose of the study is to investigate the cognitive and mood, or affective, symptoms associated with multiple sclerosis (MS). Cognitive, or cognition, refers to one's mental processes of, for example, perception, attention, and memory. Mood, or affect, refers to one's state of mind, or quality of feeling or emotion. Examples might include depression or cheerfulness.

[For MS participants] You are invited to participate because 1) you have been diagnosed with MS, and 2) you either contacted me, or gave consent for the researcher to contact you.

[For HCs] You are invited to participate because 1) your demographic details match those of an MS participant, 2) you are a healthy person, 3) the study requires control participants who have no neurological disease, and 4) you gave consent for the researcher to contact you.

[For MG controls] You are invited to participate because 1) have received a diagnosis of myasthenia gravis, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For MVA TBI controls] You are invited to participate because 1) you have experienced a head injury, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For NP-SLE controls] You are invited to participate because 1) you have received a diagnosis of systemic lupus erythematosus, and 2) you either contacted us, or gave consent for the researcher to contact you.

[For RH controls] You are invited to participate because 1) you have experienced a stroke, and 2) you either contacted us, or gave consent for the researcher to contact you.

Participants will be recruited for this study from Groote Schuur and Tygerberg Hospitals, private neurologists/neurosurgeons/neuropsychologist in the Western Cape, organisations such as Multiple Sclerosis South Africa, and by word of mouth.

Procedures
I [and/or your neurologist] will have already briefly explained the study to you via telephone, letter or e-mail. [For HC controls] I asked you a number of questions relating to the exclusion criteria of the study (e.g. prior brain injury). [For all participants] You will now be asked to take part in an e-mail interview with the researcher, or to complete a number of forms posted to you, where you will be asked to answer a number of questionnaires regarding your mood and outlook. You are encouraged to answer all the questions and give as much detail as possible, where required. Your loved-one will also be asked to answer some questions about you. Your answers will be kept until the research study has been submitted. They will then be destroyed. There will only be one interview.

Access to medical records
[For MS participants] This study requires information such as when your MS was diagnosed and the type of MS you are experiencing. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For MG controls] This study requires information such as when your MG was diagnosed. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For MVA TBI controls] This study requires information such as the date of your head injury. As some participants might not be sure of this information, we may need to check the above information with their neurosurgeon, or in the medical folder.

[For NP-SLE controls] This study requires information such as when your lupus was diagnosed. As some participants might not be sure of this information, we may need to check the above information with their neurologist.

[For RH controls] This study requires information such as the location of your stroke. As some participants might not be sure of this information, we may need to check the above information with their neurologist, or in the medical folder.

Risks and benefits
There are no foreseeable risks for you as a participant of this study. Besides your time, there are no costs for taking part in this study. Participation in this study will benefit you in the following ways:

1) You will receive an information pamphlet on the common cognitive and affective symptoms of MS/MG/MVA TBI/NP-SLE/RH. This will include information about each of the symptoms as well as ways of coping with them.
2) You will receive a brief feedback form following participation in this study. Unfortunately as this aspect does not include cognitive testing I cannot comment on your cognition, but I can comment on your mood/behaviour and may make recommendations regarding these.
3) In addition, we hope to gain information about the cognitive and affective symptoms of MS, the publication of which will broaden the scientific knowledge on the topic, and your answers will be invaluable in this respect.

Voluntary participation and withdrawal
Participation in this research study is voluntary. It is your choice to decide whether or not to take part. If you agree to take part you will be given this form to keep and will be asked to sign the declaration of consent at the bottom. You will still be free to withdraw from the study at any time.

Debriefing following participation and end of study
You will be debriefed following your interview via e-mail. Any additional questions you may have following participation in this study may then be asked and will be answered to the best of the researcher's ability. Should you wish to receive the results of the study and/or any journal articles, please indicate this to the researcher.

Confidentiality
The confidentiality of your answers and identity will be protected. All interviews will be coded in such a way that your name and all identifying features will be removed and your answers will be given a participant number rather than a name, known only to the researcher. Only this will appear when the results of this study are published, and your name, contact details and other identifying data will not be included.
All your answers will be confidential. They will be combined with the answers from the other participants and it will be impossible to identify you from the responses you give. Computer-based information will be available only to the researcher and will be password protected.

Research ethics approval
The Human Research Ethics Committee of the University of Cape Town (Faculty of Health Sciences) has reviewed this project for the protection of human participants in research. If you have any questions or concerns regarding your rights and welfare as a research participant, please contact Lamees Emjedi at one of the following details:
Contact details:
E52, Room 24, Old Main Building, Groote Schuur Hospital, Observatory, 7925
Tel: 021 406 6338; Fax: 021 406 6411

Declaration of consent
I recognise that I was contacted by my neurologist, an organisation, by word of mouth, or contacted the researcher directly and I was invited to take part in this study. I also gave my consent for a loved-one to fill in a questionnaire about me. I have read the information above. I have had the chance to ask questions and have received satisfactory answers to my questions. I understand that my involvement in this study is voluntary and that I may withdraw from the study at any time. I understand that my neurologist may be contacted for medical information such as my date of diagnosis and give my permission for this to take place. I understand that my answers will be recorded, but that neither my name, nor any identifying information will be included in these; and I consent to the confidential use of these recordings for scientific purposes. I understand that I will be given a copy of this form to keep, and that by signing this form I am agreeing to take part in a once-off interview for this research study.

Signed: _____ Date: _____

(Name in block letters) _____

If you have any questions or concerns regarding the study, or would like to be informed of the results when the study is completed, please feel free to contact the researcher.

Thank you.

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Appendix B3: Traumatic Brain Injured Controls Un-able to Provide Informed Consent Full Interview (Assent Form)

The cognitive and affective symptoms of Multiple Sclerosis

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Invitation
We would like to invite you to participate in a research study looking at cognition (things to do with your mind like memory and attention) and mood (feelings like happiness and depression).

Procedure
You will be asked to take part in an interview with the researcher. This will include answering some questionnaires about your mood and playing some games that look at your memory and attention. Your loved-one will also be asked to answer some questions about your mood. The interview might take 2 hours. Please let me know if you get tired and we will take a break.

After the interview you and your loved-one will receive a pamphlet that will tell you about some of the symptoms you might experience and ways of coping with them. You will also get some feedback on your interview.

If at any time you don't want to take part anymore, please let me know and we will stop. If you would like to ask any questions at any time, I will do my best to answer them.

Confidentiality
Your answers will be kept confidential. That means that only a number will appear next to your answers and your name will not be next to your answers. Written information will be kept in a locked cupboard. Computer information will be available only to the researcher and will be password protected.

Declaration of consent
I agree to take part in this study.
Signed: _____ Date: _____
(Name in block letters) _____

Thank you.

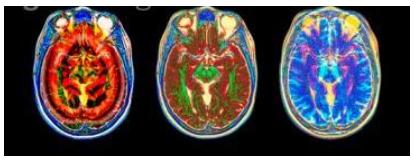
Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Appendix C: Materials for Participants

Appendix C1: Example of Information Pamphlet for Participants

Multiple Sclerosis



MS is a chronic, inflammatory degenerative disease of the central nervous system. Its main disease processes involve:

- Demyelination - an inflammatory response whereby the body's own immune system attacks the myelin sheath surrounding the axons in the central nervous system
- Reactive gliosis - the formation of plaques, or lesions
- Atrophy - the loss of neurons and the connections between them

These disease processes can occur anywhere in the central nervous system. Therefore, MS can produce a wide variety of neurological, cognitive and affective (or mood) symptoms. You (or your loved-one) may not experience any of the following cognitive and/or mood symptoms, or you may experience just one, or a few in varying combinations. Symptoms may also change and new ones may develop throughout the course of the disease, so it is important to be aware of the possible (cognitive and affective) symptoms of MS.

Common cognitive symptoms of MS

Domain	Symptom
Attention	Difficulty following a conversation, tv program or book; forgetting what one has just read or been told
Speed of information processing	A longer time is needed to think about what one wants to say or to process what one has just heard or read
Working memory	Difficulty holding information in mind to use it
Visuo-spatial and verbal learning and memory	Difficulty remembering information one has seen or been told
Verbal fluency/generativity	A longer time is needed to think of and produce words
Visuo-spatial processing/perception	Difficulty in understanding visual patterns, navigating unfamiliar environments, or accurately perceiving lengths and angles
Abstract reasoning	Difficulty in perceiving abstract categories and connections between concepts
Problem solving	Difficulty in working one's way around a problem

Planning	Difficulty in formulating a strategy to reach a goal

Strategies to help cope with the cognitive symptoms of MS

Attention (and working memory)

1. Take breaks – if you are required to concentrate on something for an extended period of time, allow yourself to move around and take a break in between periods of paying attention.
2. Change things up and reduce concentration time – try changing your working environment every 30min to give you renewed focus. Or alter what you're paying attention to (e.g. reading a book, then watching tv).
3. Use signals – get your family members or care-giver to use a signal when you have "tuned out". For example, they could tap you on the shoulder to bring you back or prompt you when you need to pay attention by saying, "I'm going to tell you something important now".
4. Minimise other distractions – when you need to pay attention, try to minimise noise and distractions. For example, turn off the radio or tv, or close the door.
5. Get organised – the use of notebooks, lists, check-lists, diaries and calendars may help you to plan and structure your day. You might also find colour-coding helpful (e.g. red = 'things I still need to do', blue = 'completed tasks').
6. Get instructions in different forms – ask your family members or care-giver to give you information in a number of different ways. For example, they could tell you about a lunch invitation and then also add it to your diary to remind you.

Speed of information processing

1. Understand the problem – realise yourself, and educate your family members/care-giver, that this is not a behavioural or emotional problem, but is a cognitive symptom of MS and not something you are doing on purpose.
2. Establish a routine – understand the sequence of activities that makes up your day. Try not to alter the routine too much as you might have trouble processing and adjusting.
3. Slow down instructions – if you're having trouble keeping up, ask the person you're speaking to, to simply slow down or repeat the instruction. Family members – be patient, speak slowly, and repeat where needed.
4. . Use non-verbal supports – verbal material may be presented too quickly to process. Request additional instructions in the form of writing, pictures, symbols, and checklists that you can go through in your own time.
5. More time – allow yourself additional time to complete a task or work through a piece of information. Don't pressurise yourself. Reduce the amount of activities in your day.
6. Speak to your doctor – slowed information processing can be a result of medication. See if this can be adjusted.

Memory

1. Use rhymes/acronyms – try to simplify something you need to remember with a catchy phrase. For example, when leaving the house you need to remember to 1) **T**ake

your wallet/bag/car keys, 2) **R**eason for going out? (do you need a shopping list? notes for a meeting?), 3) turn off dangerous **A**ppliances (stove/iron), 4) check the **W**eather (take a warm jacket?), 5) **L**ock the door behind you. This could become: TRAWL .

2. Use cues/structure – always keep your keys in the same place. Get rid of confusing clutter. Make use of alarms and reminders to remind you to do something. Keep your lists in a visible place (such as on the fridge) and don't move them.
3. Stay healthy - get enough exercise, relaxation, sleep, and eat a balanced diet.
4. Reduce anxiety – relax and be patient with yourself. Don't be critical or fearful of forgetting. Educating one's family members about your areas of difficulty and ways they can help will also reduce your anxiety.
5. Determine the important items - get help in determining which tasks or pieces of information are most important so you don't end up paying attention to and remembering unimportant tasks and forgetting the important ones.

Verbal fluency

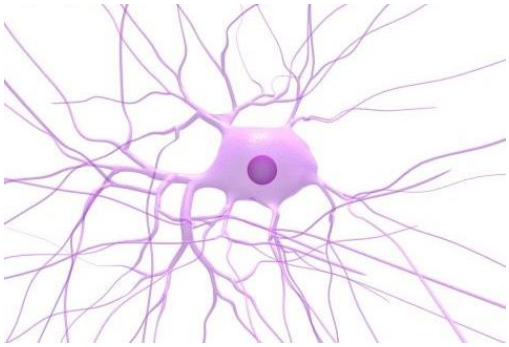
1. Patience - take your time. Think about what you want to say and speak slowly. Family members – have patience while your loved-one tells you what they want to say. Try not to interrupt or finish their sentence for them.
2. Encouragement and support – family members - encourage conversation by speaking about things your loved-one is interested in.

Visuo-spatial processing

1. Minimise change - keep items in regular places. Moving them may cause confusion.
2. Accident proof your home – keep breakable items away from the edges of surfaces where they could be knocked off accidentally. Separate items such as sharp knives from other cutlery.
3. Ask for help - family members or care-givers can assist in locating items or guiding you around unfamiliar locations. You could also ask people to visit you rather than you having to travel to them.

Abstract reasoning/problem-solving/planning

1. Fatigue – avoid carrying out tasks when you are tired, stressed or in pain. These internal distractions will limit your ability to pay attention, plan and carry out the task.
2. Time to plan – schedule a time in your diary for planning ahead. This will allow you enough time to process, think about and prepare for upcoming tasks.
3. Keep it simple – ask your family members/care-giver to give you easy, straight-forward instructions. Family members – do not assume your loved-one knows what you are thinking or feeling, state things explicitly.
4. Alarms and reminders – alarms and reminders may again be useful to remind you or help you to initiate a task.
5. Check-lists/diaries etc – the use of lists, check-lists, diaries etc can also help you plan for upcoming activities.
6. Use notes – notes and signs dotted around the house may help you through your day and avoid problems such as over-flowing baths or stoves being left on.



The disorders of mood and affect associated with MS

Disorder of mood or affect
Depression
Bipolar affective disorder
Euphoria
Disorders associated with affective dysregulation
Psychosis

Definitions of the disorders of mood and affect associated with MS

Depression: a mood disorder characterised by intense feelings of sadness, feelings of helplessness or worthlessness, social withdrawal, a loss of interest, changes in appetite and weight, disturbance of sleep and loss of sex drive.

Bipolar affective disorder: a mood disorder in which depression is accompanied by mania (elevated or irritable mood, accompanied by intrusive thoughts, a lack of attention, uninhibited behaviour such as impulsive sexual activity, increased energy and a reduced need for sleep). Characteristically, individuals cycle between the two.

Euphoria: a mood disorder characterised by cheerfulness, happiness and ease. Some also consider it to include a denial of physical disability and an optimism regarding the future that is disproportionate to the individual's situation.

Disorders associated with affective dysregulation: a group of mood disorders characterised by rapid mood changes, exaggerated expression of emotion, and an inability to control one's expression of emotion. These are also known as emotional lability, pseudobulbar affect, pathological laughing and crying, or involuntary emotional expression disorder.

Psychosis: a disorder characterised by impairment in thinking and perception. This may be accompanied by confused speech, incorrect beliefs or delusions (e.g. false ideas about what is taking place or who one is), hallucinations, (e.g. seeing or hearing things that aren't there)

and emotions or feelings that are inappropriate. In MS, psychosis can include syndromes resembling schizophrenia, delusional disorders, affective psychoses, and delirium.
In addition to mood disorders, one can experience avariety of other difficulties, including apathy, fatigue, irritability and sleep disturbances (to name a few).

Strategies to help cope with the mood symptoms of MS

General tips for most symptoms

1. Education and understanding – educate your family and loved-ones/care-giver about your mood and behavioural symptoms to avoid unrealistic expectations. It is not your fault, it's part of the disease. Ask a family member to join you at doctor's appointments – this will help them to learn more and give them the opportunity to ask questions.
2. Take care of yourself – aim for 8 hours of sleep per night; spend a bit of time in the sun each day; try relaxation techniques to keep stress levels down; eat a healthy balanced diet. Exercise can also help to lift your spirits, and exercising with a friend can also double up as a social activity. Avoid alcohol and drugs as these can trigger your symptoms. Be careful when taking over-the-counter medications – these can interfere with your mood and/or your mood medications.
3. Ask for help – take advantage of any resources available to you. Initially you may require medication, but sharing your experiences can also be beneficial. There are also therapists that could give you skills to cope with your symptoms and change the way you think. If your symptoms are persisting or getting worse, seek professional help. If you have seen a doctor but you're experiencing side-effects of medication, report these as you may need to change the dosage or type of medication.
4. Exercise – regular exercise can have a positive effect on mood. Try to include at least 30min of exercise 5 times per week. You also tend to think about your worries less when you are out exercising.
5. Relax – Try relaxation techniques such as deep breathing, tai chi or yoga. Don't rely on the television, drugs or alcohol to relax you – these can often have the opposite effect. Do things you enjoy and try to keep stress to a minimum.
6. Connect/socialise - isolation and loneliness can cause depression. Make use of the energy you have by going for a short walk, going to the movies, or calling or e-mailing a loved-one. Try to do these, even if you don't feel like it, this will help you to feel supported and secure. Try to socialise with positive people that will enhance your life. Share what you're going through with loved-ones or join a support group.
7. Keep busy – if you can, spend time with positive people. If you would rather be alone, fill your time with things you enjoy doing and things that will take your mind off your troubles and prevent negative thinking.

Depression

1. Start small and take things one day at a time – decide on a few small goals and build from there, each small step adds up.
2. Help someone else – volunteer and help others. This can give you a purpose and a sense of accomplishment.
3. Reward yourself – Celebrate the baby steps!
4. Get a pet – animals and pets can bring joy and companionship and help you feel less isolated. It may also help you to feel needed.

5. Challenge negative thinking – ask yourself if you'd say what you're thinking about yourself to someone else.

Bipolar disorder

1. Get involved in your treatment – keep in contact with your health professional. Talk to them if your symptoms change and be honest about your experiences.
2. Take your medication as instructed – don't skip or change your dosage without talking to your doctor, even if you're feeling better. This can have detrimental effects on your symptoms.
3. Monitor your moods and symptoms – know your triggers and the early warning signs and watch for them.
4. Develop a daily routine – structure can help stabilise mood swings. Include set times for sleeping, eating, socialising, exercising, working and relaxing. Try to keep to this pattern, even through ups and downs.
5. The right amount of sleep – too little sleep can trigger mania and too much sleep can lower your mood. Try to go to bed and wake up around the same time each day.
6. Develop a crisis plan – create a plan with a loved-one in case you become manic or suicidal. For example, your family might want to take away your credit card when you're in a manic state to avoid unnecessary spending.
7. Have hope – in most cases bipolar can be treated and stabilised. Have hope that a solution will be found.

Euphoria

Most professionals don't offer advice on how to deal with euphoria because it usually doesn't bother the patient or their family, but it can be frustrating for a caregiver when their loved-one is indifferent to their symptoms. Try to remember that it's a symptom of their disease; this may help to lessen your frustration.

Disorders associated with affective dysregulation

1. Recognising there's a problem – crying can be misinterpreted as depression and laughter as happiness. Both can also be embarrassing. It is important to know when these outward displays of emotion are real and when they are manageable pathological symptoms (that don't reflect one's inner feelings).
2. Medication – out of all the mood disorders, medication can help to control this one the most effectively, so speak to your health professional.
3. Know your triggers – sometimes an episode of laughing or crying can be set off by a trigger such as stress or a particular topic. Try to avoid these.
4. Watch out for isolation – because it can sometimes be embarrassing, people tend to isolate themselves which can lead to depression and other symptoms of mood. If you'd like to avoid large groups or public places, then rather invite a few close friends to your home.

Psychosis

1. Family members take control – try to keep your loved-one calm. Take them to the nearest hospital if you think they might be a danger to themselves or others. If your

loved-one is experiencing hallucinations due to sleep deprivation try to get them to sleep.
2. Avoid violent movies – watching violent or visually busy television can be detrimental.
3. Use soft lighting – this may aid sleep.
4. Avoid being alone – family members: talk to your loved-one in a calming voice and stay with them. Find a quiet room to talk to them without distractions.
5. Don't take offence/care for your loved-one – family members - try not to take things your loved-one says personally. Talk to them about things other than their mistaken beliefs. Don't go along with their delusions or hallucinations, but try not deny or dismiss them either. When recovering, they may need your help in making decisions. Try to be caring and non-judgemental. Give your loved-one extra time to process what you've said as they might not be able to think clearly.

Apathy

1. Try doing things you think you would enjoy – even if you don't enjoy them at first, give it a bit of time before you give up.
2. Have people around you, you might find you have less apathy when you are around others than when you are alone.
3. Create some healthy competition. Whether it's video games or a work related goal. And it doesn't have to be against another person, you could just aim to better your last attempt.
4. Identify the areas on which apathy is impacting most and make active plans to deal with it. For example, if apathy is keeping you from taking care of your household, create a specific schedule for doing the necessary chores.
5. Break tasks down into manageable chunks and reward yourself when you achieve them.
6. Use self-talk. When you don't feel like doing anything, ask yourself, "Do I really want to let this rule my life?", or "What can I do to motivate myself?".
7. Know the difference between apathy, fatigue and depression and seek medical help if necessary.

Fatigue

1. Know the difference between fatigue and depression.
2. Avoid stress wherever possible.
3. Do things that boost your energy – talking with friends, a stroll around the garden etc.
4. Eat often (and healthily) – this will help to keep your energy levels up throughout the day.
5. Exercise if you can.
6. Get enough sleep. Try relaxation techniques in the evening, or a hot bath. Keep to regular sleeping patterns.
7. Drink less alcohol and caffeine and more water.

Irritability

1. Find your triggers - the things that make you irritable and try to avoid them or diffuse them before they set you off.
2. Count to five. Try to relax before responding.

3. Think about what you want to say before responding.
4. Try relaxation techniques and spending a little time each day doing something just for you – something that you enjoy.
5. Don't wait until you are annoyed with someone before breathing and trying to relax – attempt to avoid the annoyance altogether by relaxing before you encounter a potential trigger.

Sleep disturbances

1. Seek medical assistance and fine the right treatment.
2. Keep a regular sleep schedule – go to bed at the same time, get the same number of hours of sleep per night.
3. Create a happy sleep environment – make sure your room is dark, cool and quiet.
4. Try not to combine working areas with sleeping areas. Keep your bedroom for sleeping only.
5. Turn off all TV's, radio's, iPod's and computers etc.
6. Wind down close to bed. Don't do anything too stimulating.
7. Consciously relax. Try a warm bath or warm drink before bed.
8. Don't force sleep. The more you try to fall asleep, the more anxious you'll become.
9.

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Appendix C2: Example of Feedback Form

FEEDBACK FROM RESEARCH STUDY

Name: Ms X

DOB: 01/01/1981 (age 31)

Assessment date: 26 June 2012

Assessed by: Mrs Amy Duncan (researcher)

Thank you for participating in this study. Below is some feedback from your interview/assessment on 26 June 2012. If you have any questions, please contact me at the details provided below.

MS Background:

You were diagnosed with MS in 2009, around the time that your symptoms first started. Your MS currently follows a relapsing-remitting pattern and you have experienced about 7 relapses. You describe yourself as having minimal (as opposed to significant or no) motor impairment and you rated yourself 6/34 (17.6%) impaired on the physical ability scale. You noted some difficulties with thinking or concentration, memory, language or speech and visual perception on the cognitive ability scale.

Cognition

Memory

This refers to your ability to remember information. Audio-verbal memory mainly refers to memory for spoken words and visuo-spatial memory refers to memory for pictures or visual information in relation to space.

Your audio-verbal memory was assessed with the Rey Auditory-Verbal Learning Test (the word list I read five times). You demonstrated learning across trials, and you were able to retain 10 of the 15 words on delayed recall. You correctly identified 28 out of 30 words on the recognition trial, which implies that your recognition memory is better than your unprompted recall memory.

Your visuo-spatial memory was assessed with the Brief Visuospatial Memory Test-Revised (BVMT-R; the one where you had to remember the six designs). You again demonstrated some learning across trials, and were able to retain the majority of details on delayed recall (scoring 11/12). You correctly identified 12 out of 12 pictures on the

recognition trial. Although your visual memory was slightly better than your verbal, this performance did not indicate any obvious impairments in memory.

Attention, working memory and speed of information processing

Attention refers to your ability to attend to information (or concentrate). For this we did the 0-back task (where you had to identify all the "X's" on the computer screen). You achieved an accuracy rating of 100% on the *n*-back task, implying no obvious problems with attention.

Working memory is required when you need to hold some information in mind in order to use it in some way. For this, we used the 2-back, where you had to remember the letter that was presented two letters ago and then decide whether or not it was a match. For this task you achieved a score of 96.3% which is above average and indicates no problems with working memory.

Speed of information processing refers to how long it takes you to process new incoming information and answer the question, perform a task, push a button etc. You performed well on most timed tests (such as the Colour Word Interference Test and Sorting Test, described below) and didn't demonstrate any obvious slowing of information processing speed.

Executive functioning

This refers to higher cognitive functions such as planning, the ability to think abstractly (i.e. to see relationships between items and not just the items themselves), to inhibit an automatic response (inhibition), to switch between ideas or rules (set shifting) and to voluntarily generate words or ideas without prompts or clues (generativity).

Planning was assessed with the Rey-Osterrieth Complex Figure (where you had to copy the geometric design using coloured pens) and you did not demonstrate any obvious difficulties.

Inhibition and set shifting was assessed with the Colour Word Interference Test (where you had to name the ink colour or read the word). You completed the task quickly and made only a few errors, which you corrected yourself. You therefore do not appear to have any difficulties in inhibiting an automatic response and switching between different rules or ideas.

Abstraction was assessed using the Sorting Test (where you had to sort the cards into two sets of three) and you identified 7/16 possible ways to sort the cards. Taking your age

into account, you performed within the normal range and demonstrated an ability to see abstract relationships between objects.

Your generativity was assessed using the Controlled Oral Word Associated Test (where you had to say lots of words starting with a particular letter). You produced 40 words across the three letters and have no difficulties in generating words spontaneously (also sometimes known as verbal fluency).

Language

This refers to both output (i.e. your ability to produce sounds, words and sentences) as well as understanding incoming information. The ability to name various items and repeat spoken words also falls under the category of language.

Your ability to name objects was assessed with the short form of the Boston Naming Test (where you had to give names to the pictures I showed you). You were able to name all except one of the drawings. Therefore you did not demonstrate any difficulties in naming.

Repetition was assessed using the repetition task of the Western Aphasia Battery (where you had to repeat the phrases I read) and you were able to repeat all phrases correctly, implying no deficits in repetition.

Finally, comprehension was also assessed with the Western Aphasia Battery (where you had to answer questions and point to a variety of objects and pictures) and you achieved a perfect score, implying no difficulties in understanding or comprehension.

Therefore, at present, you do not appear to have any impairments in language.

Emotion in language

While language is considered a “left hemisphere” function, the ability to produce, repeat or understand emotion in language is considered a “right hemisphere” function.

Your ability to identify emotion in spoken language was assessed with the Aprosodia Battery (where you listened to the speaker on the CD and then identified the emotion he was using). You achieved slightly below the average American norms on this test (SA norms are not yet available), but never-the-less do not appear to have any gross deficits in this domain.

Visuospatial processing

This refers to your ability to perceive spatial relationships and construct images correctly in space. This was assessed using the copy trials of the BVMT-R and the ROCF and there were

elements of the ROCF that were not constructed perfectly, although you didn't demonstrate major difficulties in visuo-spatial construction.

Your visuo-spatial perception was also assessed using the Judgement of Line Orientation (JLO) test (where you had to choose the corresponding number in the array of lines below), and the Cube Analysis test (where you had to count the number of blocks in each design). You performed well on both of these tasks (scoring 29/30 for the JLO and 14/14 for the Cube Analysis). You therefore have no difficulties with visuo-spatial perception.

Mood and behaviour

Fairly self-explanatory, this refers to happy, sad and other possible mood states, as well as a variety of behaviours, such as apathy or aggression. In terms of mood, you noted some symptoms of low mood, and scored in the moderate range on the Beck Depression Inventory-Fast Screen. You also demonstrated slightly more negative than positive mood and slightly more pessimism than optimism on other scales.

On the Neuropsychiatric Inventory, which is a questionnaire regarding mood and behavioural disturbances, in addition to the low mood, you noted some anxiety, euphoria or positive mood at times, apathy or loss of interest, disinhibition or impulsivity, irritability, aberrant motor behaviour or repetitive movements, some difficulty sleeping and some changes in eating habits. These were all extremely frequent and appear to cause you quite a bit of distress at present.

Impression and Conclusion

Your primary functions were intact. You were able to attend, your working memory was intact, and you didn't appear to have any difficulties in speed of information processing. You did not demonstrate any obvious impairments in memory, language or identifying emotion in language. In addition, you could inhibit a natural response, switch between rules, generate words spontaneously and think abstractly. Your visual processing was also intact.

In terms of your mood and behavior, you are experiencing some low mood as well as a number of other mood and behavioural symptoms. As these behaviours are worrying you, I would recommend your seeking help with these, particularly if they worsen, as your doctor will be able to help limit their impact on you.

Therefore at present, asides from the behavioural symptoms addressed above, you do not appear to demonstrate any neuropsychological difficulties. I am happy to do a follow up with you in 1 year (or more) to track any changes, on your request.

Thank you once again for participating in this study.

Yours sincerely,

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Appendix D: The Sociodemographic Characteristics of the Multiple Sclerosis Participants

Sociodemographic characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)
Gender – Male:Female	8:52	6:34	14:86
Age	43.35(11.48)	46.20 (10.61)	44.49 (11.17)
Range	19-72	26-64	19-72
Race/ethnicity – White:Coloured/Indian	34:26	37:3	71:29
Marital status			
Never married	12	4	16
Widowed/divorced/separated	12	8	20
Married/living with partner	36	28	64
Number of children	1.48 (1.45)	1.38 (1.56)	1.42 (1.51)
Range	0-5	0-6	0-6
Education[a]			
High school (up to 12 years)	21	12	33
Certificate / diploma (up to 14 years)	26	15	41
Degree (15 years)	13	13	26
Average mean (*SD*)	13 (1.69)	13.45 (1.58)	13.18 (1.65)
Average range	8-15	8-15	8- 15
Employment status			
Full time/part time/self employed	31	25	56
Homemaker	7	4	11
Student	1	-	1
Retired/unemployed/disabled	21	11	32
Medical aid – Yes:No	46:14	36:4	82:18

Sociodemographic characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)
Income[b]			
R801 – R6400 (ave R3600.50)	4	2	6
R6401 – R51 200 (ave R28 800.50)	52	34	86
R51 201 – R204 800 (ave R128 000.50)	4	4	8
Mean (*SD*)	R23,002.17 (R18,427.84)	R30,513.02 (R27,218.12)	R26,006.51 (R22,536.54)
Range	R1,200.50 – R76,800.50	R4,800.50 – R153,601.00	R1,200.50 – R153,601.00
Number of people in household	2.87 (1.6)	2.70 (1.35)	2.80 (1.51)
Range	1-8	1-7	1-8
Informant – Spouse/partner:Family member:Good friend	28:21:11	31:5:4	59:26:15
Living with participant – Yes:No	44:16	35:5	79:21

Note. Categorical data are presented in ratios. The data on age, education, and income are presented as means with the standard deviations (*SD*) in parentheses, then minimum to maximum ranges below.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Combined monthly household income.

Appendix E: Sociodemographic, Medical and Disease/Condition Specific Questionnaires

Appendix E1: Sociodemographic Information (For All Participants and Controls)

Gender	(mark with an "X")
Male	
Female	
Date of birth	
Age	
Race/ethnicity	(mark with an "X")
Caucasian/white	
Coloured	
Indian	
Black	
Other	
Preferred language	(mark with an "X")
English	
Afrikaans	
Other	
Marital status	(mark with an "X")
Never married	
Widowed	
Divorced	
Separated but not divorced	
Married	
Living with partner	
Children	(mark with an "X")
No	
Yes	
Number of children	
Level of education	(mark with an "X")
Grade 8/Std. 6	
Grade 9/Std. 7	
Grade 10/Std. 8	
Grade 11/Std. 9	
Grade 12/Matric	
Trade/Apprenticeship	
Certificate from college	
Diploma	
Degree	
Other	
Employment status	(mark with an "X")
Full time employed	
Part time employed	
Self-employed	
Homemaker	

Full time student	
Part time student	
Retired	
Unemployed	
Permanently unable to work	
Disabled	
Other	
Current occupation (if retired, past occupation)	
Do you have medical aid?	(mark with an “X”)
Yes	
No	
Socioeconomic status (household income per month)	(mark with an “X”)
No income	
Disability grant (plus value)	
R1 – R400	
R401 – R800	
R801 – R1600	
R1601 – R3200	
R3201 – R6400	
R6401 – R12 800	
R12 801 – R25 600	
R25 601 – R51 200	
R51 201 – R102 400	
R102 401 – R204 800	
More than R204 801	
Number of people in household (including you)	

Appendix E2: Medical Information (For All Participants and Controls) /Exclusion Criteria (For Healthy Controls)

	Mark with an "X"	
Have you ever had/do you currently have any of the following?	**Yes**	**No**
A diagnosis of multiple sclerosis		
A diagnosis of myasthenia gravis		
A head injury		
A diagnosis of systemic lupus erythematosus		
A stroke		
If you have **not** received a diagnosis of any of the above, has your doctor ever been concerned that you might have one of the above?		
Which one? (type/write out)		
Any other infectious, immunological or neurological disease? For example:	(mark with an "X")	
HIV/AIDS		
Meningitis/encephalitis		
TB		
Malaria		
Addisons disease		
Huntington's disease		
Parkinson's disease		
Any other brain injury? For example:	(mark with an "X")	
Brain tumour		
Epilepsy		
Near drowning/heart attack/loss of consciousness (other than head injury)		
A diagnosis of psychiatric disorder? For example:	(mark with an "X")	
Depression		
Bipolar mood disorder		
Psychosis/hallucinations/delusions		
Schizophrenia		
Obsessive/compulsive disorder		
A developmental disorder or delay? For example:	(mark with an "X")	
Complications at birth		
Attention deficit hyperactivity disorder		
Learning disability		
A delay in walking or talking		
A generalized developmental delay		
A delay in school readiness		
Did you reach high school by age 16 in a mainstream school?		
Do you drink alcohol?		
What do you drink? (type/write out)		
How much to do you drink? (type/write out)		
Do you take any other substances (i.e. recreational drugs, not medication)?		
What do you take? (type/write out)		
How much do you take? (type/write out)		

Do you have any other medical conditions (other than the ones listed above)?		
If yes, please list them here:		

Appendix E3: Multiple Sclerosis Specific Information

Disease course (type of multiple sclerosis)	
Date (year) of symptom onset	
Date (year) of diagnosis	
Number of relapses	
Date of last relapse	
Current disease state (remission or relapse/exacerbation)	
Do you take any medication specifically for MS?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Have you ever had corticosteroid treatment?	(mark with an "X")
Yes	
No	
When last did you have corticosteroid treatment? (was it within the last 4 weeks?)	(mark with an "X")
Yes	
No	
Other than all medications listed above (i.e. for MS and/or other reasons), are you taking any other medication?	
Name and dosage	
Name and dosage	
Name and dosage	

Appendix E4: Myasthenia Gravis Specific Information

Date (year) of symptom onset	
Date (year) of diagnosis	
Number of relapses	
Date of last relapse	
Current disease state (remission or relapse/exacerbation)	
Do you take any medication specifically for your myasthenia gravis?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Have you ever had corticosteroid treatment?	(mark with an "X")
Yes	
No	
When last did you have corticosteroid treatment? (was it within the last 4 weeks?)	(mark with an "X")
Yes	
No	
Other than all medications listed above (i.e. for the myasthenia gravis and/or other reasons), are you taking any other medication?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	

Appendix E5: Neuropsychiatric Systemic Lupus Erythematosus Specific Information

Date (year) of symptom onset	
Date (year) of diagnosis	
Number of relapses	
Date of last relapse	
Current disease state (remission or relapse/exacerbation)	
Do you take any medication specifically for your lupus?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Have you ever had corticosteroid treatment?	(mark with an "X")
Yes	
No	
When last did you have corticosteroid treatment? (was it within the last 4 weeks?)	(mark with an "X")
Yes	
No	
Other than all medications listed above (i.e. for the lupus and/or other reasons), are you taking any other medication?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	

Appendix E6: Traumatic Brain Injury Information

What happened? (brief description)	
Date of head injury (month and year)	
Did you lose consciousness?	
How long were you unconscious? (approximately)	
Do you take any medication specifically as a result of your head injury?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Have you ever had corticosteroid treatment?	(mark with an "X")
Yes	
No	
If yes, briefly explain why	
Other than all medications listed above (i.e. for your head injury and/or other reasons), are you taking any other medication?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	

Appendix E7: Stroke information

Date of stroke (month and year)	
Which side of your body was affected?	
Do you take any medication specifically as a result of your head injury?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Have you ever had corticosteroid treatment?	(mark with an "X")
Yes	
No	
If yes, briefly explain why	
Other than all medications listed above (i.e. for your head injury and/or other reasons), are you taking any other medication?	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	
Name and dosage	

Appendix F: The Less Well-known Questionnaires

Appendix F1: The Informant Questionnaire

The questionnaire given to each informant, reproduced below, included four parts. The first part included Likert-type scales, created by myself, to measure euphoria sclerotica, eutonia sclerotica and spes sclerotica. The second part included the PAS (which was loosely based on the PCRS, by Prigatano and Fordyce [1986] and the SF-36, by Ware & Sherbourne [1992]). The third part included the items of the AI[10] included in this research, and the fourth, the NPI (which is readily available).

The cognitive and affective symptoms of Multiple Sclerosis

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Description of study

Your loved-one is participating in a neuropsychological research study investigating the cognitive and mood symptoms of multiple sclerosis. In terms of the study we need to know some things about your loved-one and ask you to answer the questions below. You will only need to fill in one questionnaire and it shouldn't take you more than about 15 minutes to complete. There are no risks to you and your information will be kept confidential and your identity protected.

Declaration of consent

I recognise that I was contacted by my loved-one and asked to complete this questionnaire. I understand that my involvement in this study is voluntary. I understand that my answers will be recorded, but that neither my name, nor any identifying information will be included in these; and I consent to the confidential use of these recordings for scientific purposes. I understand that by signing this form I am agreeing to take part in this research study.

Signed: _____ Date: _____

(Name in block letters) _____

[10] The AI has not been reproduced as I didn't receive a reply from S. Anderson regarding permission to reproduce his questionnaire.

Informant Form

Below are a number of questions relating to your loved-one. Please be as honest as possible in answering these questions and don't let anyone else influence your answers (i.e. it might be better to answer the questions below on your own, without your loved-one being present). There are **four** parts to this questionnaire. Instructions will be given at the beginning of each section. If you are unclear about anything or would like to ask a question, please contact me.

Section One:

Please rate your answers to the following questions from 1 – 10 and place an "X" next to the correct option.

1. **On average** (i.e. most of the time), how optimistic/pessimistic is your loved-one?
   For example, if on average, they tend toward being optimistic, you would rate them between 1 and 4, with 1 being **very** optimistic and 4 being **slightly** optimistic; but if they tend toward being pessimistic most of the time, you would rate them between 6 and 10, with 10 being **very** pessimistic and 6 being **slightly** pessimistic.

Very optimistic Neither/both Very pessimistic

1 2 3 4 5 6 7 8 9 10

2. **On average** (i.e. most of the time), how happy/depressed is your loved-one?
   For example, if on average, they are usually happy, you would rate them between 1 and 4, with 1 being **very** happy/euphoric and 4 being **slightly or mildly** happy; but if they tend to be unhappy or depressed most of the time, you would rate them between 6 and 10, with 10 being **very** unhappy/depressed and 6 being **slightly or mildly** unhappy.

Very happy/euphoric Neither/both Very unhappy/depressed

1 2 3 4 5 6 7 8 9 10

3. How aware do you think your loved-one is of any physical problems they might have?
   For example, if they deny any deficits and continue as if nothing were wrong, they would be "unaware". If they acknowledge their limitations, have to adjust, or mention their disabilities, they would be "aware".

Very aware Average Very unaware

1 2 3 4 5 6 7 8 9 10

4. How aware do you think your loved-one is of any problems with cognition they might have (e.g. memory, ability to concentrate, slowed thinking etc)?
   For example, if they deny any deficits and do not realise they have any problems with memory or thinking, would be "unaware". If they acknowledge their limitations, have to adjust, or mention their impairments, they would be "aware".

Very aware Average Very unaware

1 2 3 4 5 6 7 8 9 10

5. How aware do you think your loved-one is of any problems with mood/behaviour they might have (e.g. depression, unrealistic happiness, apathy, aggression etc)? For example, if they deny any deficits and do not realise they have any problems with mood, would be "unaware". If they acknowledge changes or problems with mood and/or behaviour, have to adjust, or mention their symptoms, they would be "aware".

Very aware Average Very unaware

1 2 3 4 5 6 7 8 9 10

Section Two:

The following items are about activities your loved-one might do during a typical day. Please read each item carefully, and then rate how capable your loved-one is of performing these activities **currently**. Use the following scale to record your answers:

"No problem" = He/she has no problems performing these activities
"A little problem" = He/she has a little problem performing these activities
"Cannot do it" = He/she cannot perform these activities on his/her own

Please indicate the appropriate response by placing an "X" in the correct block (either "no problem", "a little problem" or "cannot do it") next to each item. Choose only **one** per item (the one that fits the best). For example, if they currently have no problems performing vigorous activities such as running, lifting heavy objects or participating in strenuous sports, then you would place an "X" in the "no problem" block.

No	Question	No problem	A little problem	Cannot do it
1	Running or participating in sport			
2	Doing the dishes			
3	Doing the laundry			
4	Moving a table, pushing a vacuum cleaner			
5	Lifting or carrying shopping bags			
6	Making lunch/dinner			
7	Climbing several flights of stairs			
8	Climbing one flight of stairs			
9	Dressing yourself			
10	Bathing/showering			
11	Bending, kneeling, getting onto the ground			
12	Walking more than a kilometre			
13	Walking several blocks			
14	Walking one block			

Section Three:

The following items are about your loved-one's cognition (their way of thinking, memory etc.). Please read each item carefully, and then rate your loved-one on each item. There will be three options per item. Please indicate your response by placing an "X" next to the appropriate option. Choose only **one** per item (the one that fits the best).

(This has been removed, please see footnote above).

Section Four:

This last section concerns your loved-one's mood and behaviour. Please read each item carefully, and then rate your loved-one on each item. For each item, you will need to answer "yes" or " no". If "yes" (i.e. your loved-one does demonstrate this mood/emotion or behaviour), you also need to rate the frequency of this emotion/behaviour (i.e. how often it occurs) and the severity of this emotion/behaviour (i.e. how disturbing or disabling this emotion/behaviour is for your loved-one).

1. Delusions

   Does your loved-one have beliefs that you know are not true? For example, does he/she insist that people are trying to harm him/her or to steal from him/her? Has he/she said that family members are not who they say they are or that the house is not their home? I'm not asking about mere suspiciousness: I am interested if the patient is convinced that these things are happening to him/her.

   Yes No (mark an "X" next to the appropriate response)

   If yes…

   How often do these things occur? (mark an "X" next to the appropriate response)
   1 – Occasionally (less than once a week)
   2 – Often (about once a week)
   3 – Frequently (several times a week but less than every day)
   4 – Very frequently (daily or essentially continuously present)

   How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
   1 – Mild (produce little distress in loved-one)
   2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
   3 – Severe (very disturbing for my loved-one)

2. Hallucinations

   Does your loved-one have hallucinations such as false visions or voices? Does he/she seem to see, hear or experience things that are not present? By this question I do not mean just mistaken beliefs such as stating that someone who had died is still alive; rather I am asking if the patient actually has abnormal experiences of sounds, or visions.

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

3. Agitation/Aggression

Does your loved-one have periods when he/she refuses to co-operate or won't let people help him/her? Is he/she hard to handle?

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

4. Depression/Dysphoria

Does your loved-one seem sad or depressed? Does he/she feel sad or depressed?

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)

3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

5. Anxiety

Is your loved-one very nervous, worried, or frightened for no apparent reason? Does he/she seem very tense or fidgety? Is he/she afraid to be apart from you?

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

6. Elation/Euphoria

Does your loved-one seem too cheerful or too happy for no reason? I don't mean the normal happiness that comes from seeing friends, receiving presents, or spending time with family members. I am asking if he/she has a persistent and <u>abnormally</u> good mood or finds humour where others do not.

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

7. Apathy/Indifference

Has your loved-one lost interest in the world around him/her? Has he/she lost interest in doing things or does he/she lack motivation for starting new activities? Is he/she more difficult to engage in conversation or in doing chores? Is he/she apathetic or indifferent?

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

8. Disinhibition

Does your loved-one seem to act impulsively without thinking? Does he/she do or say things that are not usually done or said in public? Does he/she do things that are embarrassing to you or others?

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their

family/friends)
3 – Severe (very disturbing for my loved-one)

10. Irritability/Lability

Does your loved-one get irritated and easily disturbed? Are his/her moods very changeable? Is he/she abnormally impatient? I do not mean frustration over memory loss or inability to perform usual tasks; I am interested to know if the patient has abnormal irritability, impatience, or rapid emotional changes different from his/her usual self.

Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

10. Aberrant motor behaviour

Does your loved-one pace, do things over and over such as opening closets or drawers, or repeatedly pick at things or wind string or threads?
Yes No (mark an "X" next to the appropriate response)

If yes…

How often do these things occur? (mark an "X" next to the appropriate response)
1 – Occasionally (less than once a week)
2 – Often (about once a week)
3 – Frequently (several times a week but less than every day)
4 – Very frequently (daily or essentially continuously present)

How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
1 – Mild (produce little distress in loved-one)
2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
3 – Severe (very disturbing for my loved-one)

11. Night-time behaviours

    Does your loved-one have problems sleeping at night? By this I do not mean getting up to go to the bathroom. What I mean is difficulty in achieving and maintaining sleep.

    Yes No (mark an "X" next to the appropriate response)

    If yes…

    How often do these things occur? (mark an "X" next to the appropriate response)
    1 – Occasionally (less than once a week)
    2 – Often (about once a week)
    3 – Frequently (several times a week but less than every day)
    4 – Very frequently (daily or essentially continuously present)

    How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
    1 – Mild (produce little distress in loved-one)
    2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
    3 – Severe (very disturbing for my loved-one)

12. Eating disorders

    Have your loved-one's eating habits changed? By this I mean eating less or overeating different from his/her usual self.

    Yes No (mark an "X" next to the appropriate response)

    If yes…

    How often do these things occur? (mark an "X" next to the appropriate response)
    1 – Occasionally (less than once a week)
    2 – Often (about once a week)
    3 – Frequently (several times a week but less than every day)
    4 – Very frequently (daily or essentially continuously present)

    How disturbing or disabling are these behaviours for your loved-one? (mark an "X" next to the appropriate response)
    1 – Mild (produce little distress in loved-one)
    2 – Moderate (more disturbing to my loved-one but can be redirected by their family/friends)
    3 – Severe (very disturbing for my loved-one)

Thank you very much for taking the time to fill out the above questions. If you have any questions, please feel free to contact me.

Regards,

Amy Duncan

Mrs Amy Duncan
Researcher
Department of Psychology
University of Cape Town
083 653 3048
E-mail: amynortham@gmail.com

Prof Mark Solms
Supervisor
Department of Psychology
University of Cape Town
021 650 3437
E-mail: Mark.Solms@uct.ac.za

Appendix F2: Comparative Risk Judgement Rating Form

This questionnaire was loosely based on the Forms of Fournier et al. (2003), Covey and Davies (2004), Warner et al. (2012), and Weinstein (1983).

Compared to an average person of the same sex, age and form of illness as you, what are the chances that …

No	Question	Very much below average	Below average	The same	Above average	Very much above average
1	Your purchase of an expensive TV will turn out to be a mistake					
2	You'll get a fractured limb					
3	You'll make and keep good friends on whom you can trust					
4	You'll experience financial problems					
5	You'll be offered an interesting position with flexible working hours (You'll be offered an interesting position which allows for a career move)					
6	You'll contract HIV					
7	You'll need to stay in hospital at least once sometime next year					
8	You'll be unable to go on holiday					
9	You'll experience a drinking problem					
10	You'll fall ill and will have to stay in bed for at least one week next year					
11	You'll find affordable and handicap compliant housing (You'll find affordable housing)					
12	You'll develop cancer					
13	You'll be considered a show-off by people close to you					
14	You'll win R100 000 in the lottery					
15	You'll need to ask for help as you can't cope on your own anymore					
16	You'll have a heart attack					
17	You'll be deceived by a good friend					
18	You'll not have to stay in hospital next year					
19	You'll be able to spend your holidays abroad every year					
20	Your health will worsen					

Appendix F3: Cottrell and Wilson (1926) Questionnaire

Category selected by majority of raters	Question	Percentage of agreement for category rated by majority
Euphoria sclerotica	Describe in a few words your general or usual mood	73.33%
Euphoria sclerotica	Do you feel consistently cheerful or happy?	93.33%
Euphoria sclerotica	Do you feel consistently sad or unhappy?	93.33%
Spes sclerotica	Are you naturally optimistic?	86.67%
Spes sclerotica	Are you naturally pessimistic?	93.33%
Euphoria sclerotica and spes sclerotica	Are you aware of any alteration in either respect since the onset of the illness?	53.33%
Spes sclerotica	Are you optimistic or pessimistic in reference to your disease?	73.33%
Euphoria sclerotica	Do you change readily from a feeling or cheerfulness to one of sadness, and vice versa?	60%
Euphoria sclerotica	Are you easily amused by what you see?	93.33%
Euphoria sclerotica	Are you easily amused by what you hear?	93.33%
Euphoria sclerotica	Are you easily amused by what you read?	93.33%
Euphoria sclerotica	Are you easily depressed by what you see?	80%
Euphoria sclerotica	Are you easily depressed by what you hear?	80%
Euphoria sclerotica	Are you easily depressed by what you read?	80%
Other	Are you moods fleeting or apt to last for some time?	73.33%
Other	Any change in this respect from formerly?	86.67%
Other	Are you naturally phlegmatic or indifferent?	80%
Other	Are you anxious or worried?	86.67%
Other	Are you irritable?	86.67%
Other	Do you easily lose your temper?	86.67%
Other	Are you different in mood in any of these respects from what you were one, two, five, ten, twenty years ago, or before the commencement of the illness?	60%
Euphoria sclerotica	Are your thoughts consistently pleasant?	73.33%
Other	Are your thoughts amusing?	80%

Other	Are you inclined to daydream, to live in the future, to live in an ideal world, or to live in the past?	46.67%
Euphoria sclerotica	Are your thoughts consistently unpleasant, serious, sombre?	60%
Euphoria sclerotica	Are you inclined to ruminate on unpleasant subjects?	60%
Euphoria sclerotica	Are your thoughts depressing?	73.33%
Other	Are you inclined to worry about yourself?	80%
Other	Do you dream?	93.33%
Other	Are the dreams pleasant or unpleasant?	80%
Eutonia sclerotica	Describe your bodily feeling as a whole.	60%
Eutonia sclerotica	Are you conscious of any pleasant or unpleasant sensation in your body as a whole or a part?	60%
Eutonia sclerotica	Do you feel tired or fatigued?	60%
Eutonia sclerotica	Do you feel relaxed?	46.67%
Other	Do you feel sleepy?	66.67%
Eutonia sclerotica	Is the feeling one of bodily ease? Is the feeling one of contentment?	80%
Eutonia sclerotica	Is the feeling one of pleasure?	53.33%
Eutonia sclerotica	Is your general feeling one of malaise?	60%
Eutonia sclerotica	Do you feel tense?	60%
Other	Do you feel nervous or jumpy?	66.67%
Eutonia sclerotica	Have you any feeling or pain, aching, soreness?	60%
Eutonia sclerotica	Are you restless?	53.33%
Eutonia sclerotica	Does the performance of normal bodily functions produce pleasant or unpleasant sensations?	60%
Other	Do you laugh easily?	86.67%
Other	Do you laugh without adequate cause?	73.33%
Other	Do you cry easily?	80%
Other	Do you cry without adequate cause?	86.67%
Other	Is your outward expression a reliable gauge of your inward feeling?	80%
Other	Can you control the expression of your feeling?	80%
Other	Are you different in any of these respects from what you were one, two, five, ten, twenty years ago, or before the commencement of the illness?	86.67%

Appendix F4: Internal State Scale (Bauer et al., 1991)

This questionnaire is readily available. The original questionnaire requires participants to rate how they feel with an 'x' on a 100mm line from 0 to 100. I adapted this rating criteria to a Likert-type scale from 1-5. Items from the well-being sub-scale are produced in bold.

No	Question	Very slightly/ not at all	A little	Moderately	Quite a bit	Extremely
1	My mood is changeable					
2	I feel irritable					
3	**I feel like a capable person**					
4	I feel like people are out to get me					
5	**I actually feel great inside**					
6	I feel impulsive					
7	I feel depressed					
8	My thoughts are going fast					
9	It seems like nothing will ever work out for me					
10	I feel overactive					
11	I feel as if the world is against me					
12	I feel "sped up" inside					
13	I feel restless					
14	I feel argumentative					
15	**I feel energized**					

Appendix F5: Optimism and Pessimism Scale (Dember et al., 1989)

This questionnaire is reproduced with the permission of S. Howe, on behalf of the late B. Dember.

The following 56 statements represent individual differences in viewpoint. Please read each item carefully, and then, using the scale shown below, please respond with your own point of view to all of the statements. Do not spend a lot of time thinking about each one; just indicate your first impression. Remember, respond to these statements according to how you feel about them right now.

No	Question	Strongly agree	Agree	Disagree	Strongly disagree
1	I like people I get to know				
2	It is best not to set your hopes too high since you will probably be disappointed				
3	There is so much to be done and so little time to do it in				
4	I have a tendency to make mountains out of molehills				
5	Rarely do I expect good things to happen				
6	Everything changes so quickly these days that I often have trouble deciding which are the right rules to follow				
7	All in the world is a good place				
8	When it comes to my future plans and ambitions in life, I expect more to go wrong than right				
9	My hardest battles are with myself				
10	I believe there's not much hope for the human race				
11	It does not take me long to shake off a bad mood				
12	If you hope and wish for something long and hard enough, you will eventually get it				
13	People get ahead by using 'pull' and not because of what they know				
14	Even when things in my life are going okay, I expect them to get worse soon				
15	With enough faith, you can do almost anything				
16	I enjoy myself most when I am alone, away from other people				
17	When I undertake something new, I expect to succeed				
18	Honesty is the best policy in all cases				
19	I generally look at the brighter side of life				

20	If I make a decision on my own, I can pretty much count on the fact that it will turn out to be a poor one				
21	I generally make light of my problems				
22	It is always good to be frank				
23	Where there's a will, there's a way				
24	I have a tendency to blow up problems so they seem worse than they really are				
25	All in all, it is better to be humble and honest than important and dishonest				
26	As time goes on, things will most likely get worse				
27	It is the slow, steady worker who usually accomplishes the most in the end				
28	When I go to a party I expect to have fun				
29	Times are getting better				
30	Everyone should have an equal chance and an equal say				
31	Better to expect defeat; then it doesn't hit so hard when it comes				
32	It is wise to flatter important people				
33	I expect to achieve most of the things I want to in life				
34	It seems the cards of life are stacked against me				
35	What is lacking in the world today is the old kind of friendship that lasted for a lifetime				
36	When the weatherman predicts 50% chance of rain, you might just as well count on seeing rain				
37	Before an interview, I am usually confident that things will go well				
38	Sometimes I feel down, but I bounce right back again				
39	The future seems too uncertain for people to make serious plans				
40	When I have undertaken a task, I find it difficult to set it aside even for a short time				
41	Tenderness is more important than love				
42	When gambling, I expect to lose				
43	Anybody who is willing to work hard has a good chance for success				
44	The future looks very dismal				
45	If I had to choose between happiness and greatness, I'd choose greatness				
46	Minor setbacks are something I usually ignore				
47	In general, things turn out all right in the end				
48	It is better to be a dead hero than a live coward				
49	Give me 50/50 odds and I will choose the wrong answer every time				

50	It is hard to get ahead without cutting corners here and there				
51	If I were in competition and contestants were narrowed down to myself and one other person, I would expect to be runner-up				
52	April showers bring May flowers				
53	I can be comfortable with nearly all kinds of people				
54	The worst defeats come after the best victories				
55	In the history of the human race there have probably been just a handful of really great thinkers				
56	Every cloud has a silver lining				

Appendix F6: Physical Ability Scale

This questionnaire was loosely based on the PCRS of Prigatano and Fordyce (1986) and the SF-36 of Ware and Sherbourne (1992).

Please indicate to what extent you are able or unable to perform the following physical activities

No	Question	No problem	A little problem	Cannot do it
1	Running or participating in sport			
2	Doing the dishes			
3	Doing the laundry			
4	Moving a table, pushing a vacuum cleaner			
5	Lifting or carrying shopping bags			
6	Making lunch/dinner			
7	Climbing several flights of stairs			
8	Climbing one flight of stairs			
9	Dressing yourself			
10	Bathing/showering			
11	Bending, kneeling, getting onto the ground			
12	Walking more than a kilometre			
13	Walking several blocks			
14	Walking one block			

Appendix G: Rating Criteria for Definite Presence and Definite Absence of Euphoria Sclerotica, Eutonia Sclerotica and Spes Sclerotica (in terms of the CWQ)

Euphoria sclerotica

2 = mood described as generally positive, yes to consistently happy, no to consistently unhappy, yes to easily amused, no to easily depressed, yes to thoughts are pleasant, no to thoughts are unpleasant

1 = confused/mixed answer

0 = indifferent or depressed (no to consistently happy, yes to consistently unhappy)

Eutonia sclerotica

2 = body feels good/great, not aware of any unpleasant feelings, yes to bodily ease, yes to feeling of pleasure, no to malaise

1 = confused/mixed answer

0 = aware of negative feelings (no to bodily ease, yes to malaise)

Spes sclerotica

2 = yes to naturally optimistic, no to naturally pessimistic, yes to optimistic about MS

1 = confused/mixed answer

0 = pessimistic (no to optimistic, yes to pessimistic, yes to pessimistic about MS)

Appendix H: Pearson Correlations Between the Positivity Composite and its Component Measures

	Component variables			
Composite variable	PANAS (positive sub-scale)	ISS (well-being sub-scale)	OPS (optimism sub-scale)	LOT-R (optimism sub-scale)
Positivity	.66 (p = .001)	.46 (p = .029)	.44 (p = .041)	.66 (p = .001)

Note. PANAS = Positive and Negative Affect Schedule. ISS = Internal State Scale. OPS = Optimism and Pessimism Scale. LOT-R = Life Orientation Test-Revised.

Appendix I: The Sociodemographic Characteristics of the MS Participants and Healthy Controls

	MS participants			Healthy controls		
Sociodemographic characteristic	Cognitive and euphoria questionnaires (n = 60)	Euphoria questionnaires only (n = 40)	Total (n = 100)	Cognitive and euphoria questionnaires (n = 35)	Euphoria questionnaires only (n = 65)	Total (n = 100)
Gender – Male:Female	8:52	6:34	14:86	6:29	8:57	14:86
Age	43.35 (11.48)	46.20 (10.61)	44.49 (11.17)	42.69 (11.35)	44.32 (10.88)	43.75 (11.02)
Range	19-72	26-64	19-72	19-69	21-67	19-69
Race/ethnicity – White:Coloured/Indian	34:26	37:3	71:29	23:12	53:12	76:24
Education[a]	13 (1.69)	13.45 (1.58)	13.18(1.65)	13.49 (1.38)	13.35 (1.58)	13.40 (1.50)
Range	8-15	8-15	8-15	11-15	8-15	8-15
Marital status						
Never married	12	4	16	8	6	14
Widowed/divorced/separated	12	8	20	6	10	16
Married/living with partner	36	28	64	21	49	70
Income[b]	R23,002.17 (R18,427.84)	R30,513.02 (R27,218.12)	R26,006.51 (R22,536.54)	R22,820.50 (R17,371.63)	R29,240.51 (R23,211.18)	R26,993.51 (R21,480.21)
Range	R1,200.50-R76,800.50	R4,800.50-R153,601.00	(R1,200.50-R153,601.00	R1,200.50-R76,800.50	R2,400.50-R153,601.00	R1,200.50-R153,601.00
Informants – Spouse/partner:Family member:Good friend	28:21:11	31:5:4	59:26:15	24:6:5	50:7:8	74:13:13
Living with participant – Yes:No	44:16	35:5	79:21	25:10	52:13	77:23

Note. Categorical data are presented in ratios. The data on age, education, and income are presented as means with the standard deviations in parentheses, then minimum to maximum ranges below.

[a] = Highest level of education obtained, presented in years; it excluded pre-school and grade R and presumed a certificate to be a one year course, a diploma to be a two year course, and capped "degree" at three years.

[b] = Combined monthly household income.

Appendix J: Tables Relating to the Demographic and Disease Correlates of Euphoria

Table J1

Pearson Correlations Between Positivity and the Medical, Demographic and Disease Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Positivity	1.00	-.26*	.04	-.05	.03	-.08	.04	.10	-.09	-.18	-.16
2. Medical history		1.00	-.10	.09	-.07	.24*	-.10	.13	.07	.09	-.09
3. Corticosteroids			1.00	.28*	-.00	-.01	-.10	-.26*	.09	.15	.06
4. Medication				1.00	.22	.09	.08	-.13	.08	.11	-.14
5. Gender					1.00	.05	-.05	.00	-.06	-.08	-.15
6. Age						1.00	-.12	.44**	.23	.38**	.33**
7. Income							1.00	-.07	.00	-.03	-.09
8. Duration of disease								1.00	.08	.09	.15
9. Disease course									1.00	.86**	.45**
10. Current disease state										1.00	.56**
11. Disease severity											1.00

Note. * $p < .01$. ** $p < .001$.

Table J2

Pearson Correlations Between Unawareness of Physical Deficit and the Medical, Demographic and Disease Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of physical deficits	1.00	.16	.13	.01	-.09	.08	.01	.06	.20	.12	-.22
2. Medical history		1.00	-.10	.09	-.07	.24*	-.10	.13	.07	.09	-.09
3. Corticosteroids			1.00	.28*	-.00	-.01	-.10	-.26*	.09	.15	.06
4. Medication				1.00	.22	.09	.08	-.13	.08	.11	-.14
5. Gender					1.00	.05	-.05	.00	-.06	-.08	-.15
6. Age						1.00	-.12	.44**	.23	.38**	.33**
7. Income							1.00	-.07	.00	-.03	-.09
8. Duration of disease								1.00	.08	.09	.15
9. Disease course									1.00	.86**	.45**
10. Current disease state										1.00	.56**
11. Disease severity											1.00

Note. * $p < .01$. ** $p < .001$.

Table J3

Pearson Correlations Between Unawareness of Cognitive Deficit and the Medical, Demographic and Disease Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of cognitive deficits	1.00	.17	-.08	-.01	-.01	.01	-.04	-.03	-.02	.05	-.02
2. Medical history		1.00	-.10	.09	-.07	.24*	-.10	.13	.07	.09	-.09
3. Corticosteroids			1.00	.28*	-.00	-.01	-.10	-.26*	.09	.15	.06
4. Medication				1.00	.22	.09	.08	-.13	.08	.11	-.14
5. Gender					1.00	.05	-.05	.00	-.06	-.08	-.15
6. Age						1.00	-.12	.44**	.23	.38**	.33**
7. Income							1.00	-.07	.00	-.03	-.09
8. Duration of disease								1.00	.08	.09	.15
9. Disease course									1.00	.86**	.45**
10. Current disease state										1.00	.56**
11. Disease severity											1.00

Note. * $p < .01$. ** $p < .001$.

Table J4

Pearson Correlations Between Unawareness of Mood/Behavioural Deficit and the Medical, Demographic and Disease Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of mood/behavioural deficits	1.00	.10	.09	.01	-.13	.02	-.11	-.02	-.13	-.07	-.11
2. Medical history		1.00	-.10	.09	-.07	.24*	-.10	.13	.07	.09	-.09
3. Corticosteroids			1.00	.28*	-.00	-.01	-.10	-.26*	.09	.15	.06
4. Medication				1.00	.22	.09	.08	-.13	.08	.11	-.14
5. Gender					1.00	.05	-.05	.00	-.06	-.08	-.15
6. Age						1.00	-.12	.44**	.23	.38**	.33**
7. Income							1.00	-.07	.00	-.03	-.09
8. Duration of disease								1.00	.08	.09	.15
9. Disease course									1.00	.86**	.45**
10. Current disease state										1.00	.56**
11. Disease severity											1.00

Note. * $p < .01$. ** $p < .001$.

Table J5

The Demographic and Disease Correlates of Positivity

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	130.79	6.54		20.01	.0001	117.82	143.76
Corticosteroids	1.92	10.39	.02	0.19	.854	-18.70	22.53
Medication	-2.23	7.72	-.03	-0.29	.773	-17.55	13.09
Medical history	-18.09	7.07	-.26	-2.56	.012	-32.13	-4.06
Step 2							
Constant	131.93	18.50		7.13	.0001	95.17	168.69
Corticosteroids	9.62	10.90	.10	0.88	.380	-12.04	31.27
Medication	-2.516	8.21	-.03	-0.31	.760	-18.83	13.80
Medical history	-19.87	7.48	-.28	-2.66	**.009**	-34.74	-5.01
Gender	-2.57	10.37	-.03	-0.25	.805	-23.17	18.04
Age	0.07	0.40	.02	0.18	.860	-0.73	0.87
Income	1.37	0.00	.01	0.09	.931	0.00	0.00
Disease course	9.97	9.56	.21	1.04	.300	-9.03	28.97
Duration of disease	0.83	0.54	.18	1.54	.127	-0.24	1.90
Current disease state	-11.36	9.45	-.27	-1.20	.233	-30.14	7.42
Disease severity	-0.75	0.57	-.17	-1.30	.196	-1.88	0.39

Note. Significant results are presented in bold font. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table J6

The Demographic and Disease Correlates of Unawareness of Physical Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-1.15	0.59		-1.96	.053	-2.31	0.02
Corticosteroids	1.47	0.93	.17	1.59	.116	-0.37	3.32
Medication	-0.37	0.69	-.06	-0.54	.592	-1.74	1.10
Medical history	1.15	0.63	.18	1.82	.072	-0.10	2.41
Step 2							
Constant	-0.16	1.56		-0.10	.918	-3.26	2.94
Corticosteroids	1.67	0.92	.19	1.82	.072	-0.15	3.50
Medication	-0.80	0.69	-.12	-1.15	.254	-2.17	0.58
Medical history	0.54	0.63	.09	0.85	.397	-0.72	1.79
Gender	-1.05	0.88	-.12	-1.20	.234	-2.79	0.69
Age	0.04	0.03	.13	1.05	.298	-0.03	0.10
Income	2.63	0.00	.02	0.20	.843	0.00	0.00
Disease course	1.61	0.81	.38	2.00	.049	0.01	3.22
Duration of disease	0.03	0.05	.06	0.55	.582	-0.07	0.12
Current disease state	-0.18	0.80	-.05	-0.23	.819	-1.77	1.40
Disease severity	-0.18	0.05	-.45	-3.67	**.0001**	-0.27	-0.08

Note. Significant results are presented in bold font. CI = confidence internal; *LL* = lower limit, *UL* = upper limit.

Table J7

The Demographic and Disease Correlates of Unawareness of Cognitive Deficits

Model	Coefficients						
						95% CI	
	b	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	1.04	0.36		2.89	.005	0.33	1.75
Corticosteroids	-0.34	0.57	-.06	-0.59	.557	-1.47	0.80
Medication	-0.02	0.42	-.01	-0.05	.961	-0.86	0.82
Medical history	0.62	0.39	.16	1.60	.112	-0.15	1.39
Step 2							
Constant	1.74	1.04		1.67	.099	-0.34	3.82
Corticosteroids	-0.54	0.62	-.10	-0.87	.386	-1.76	0.69
Medication	-0.08	0.46	-.02	-0.16	.872	-1.10	0.85
Medical history	0.62	0.42	.16	1.47	.146	-0.22	1.46
Gender	0.06	0.59	.01	0.11	.915	-1.10	1.23
Age	-0.01	0.02	-.07	-0.49	.623	-0.06	0.03
Income	-2.52	0.00	-.03	-0.28	.777	0.00	0.00
Disease course	-0.75	0.54	-.29	-1.39	.167	-1.82	0.32
Duration of disease	-0.01	0.03	-.05	-0.40	.694	-0.07	0.05
Current disease state	0.81	0.53	.37	1.53	.131	-0.25	1.87
Disease severity	-0.01	0.03	-.06	-0.43	.672	-0.08	0.05

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table J8

The Demographic and Disease Correlates of Unawareness of Mood/Behavioural Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	4.65	3.04		1.53	.129	-1.37	10.68
Corticosteroids	5.26	4.83	.12	1.09	.278	-4.32	14.84
Medication	-1.24	3.59	-.04	-.35	.730	-8.36	5.88
Medical history	3.64	3.29	.11	1.11	.270	-2.88	10.17
Step 2							
Constant	13.73	8.70		1.58	.118	-3.55	31.01
Corticosteroids	4.48	5.12	.10	.88	.384	-5.70	14.66
Medication	-.28	3.86	-.01	-.07	.942	-7.95	7.39
Medical history	2.16	3.52	.07	.61	.542	-4.83	9.14
Gender	-7.04	4.87	-.16	-1.45	.152	-16.73	2.64
Age	.06	.19	.04	.30	.764	-0.32	0.43
Income	-6.98	.0001	-.10	-.95	.347	0.00	0.00
Disease course	-5.29	4.49	-.25	-1.18	.242	-14.22	3.64
Duration of disease	0.00	.25	.00	.01	.994	-0.50	0.50
Current disease state	3.23	4.44	.17	.73	.469	-5.60	12.06
Disease severity	-.29	.27	-.14	-1.09	.278	-0.83	0.24

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Appendix K: Factor Analyses of the Cognitive Variables

Table K1

Factor Analysis of the Cognitive Variables

	Component						
Measure	1	2	3	4	5	6	7
Attention							.80
WM	.78						
Speed of information processing			-.41				
Verbal learning				.71			
Verbal memory				.76			
Verbal recognition				.84			
Visual learning			.93				
Visual memory			.90				
Visual recognition			.65				
Naming	.42						
Repetition					.43	.50	
Comprehension	.78						
Visuospatial perception 2D		.86					
Visuospatial perception 3D		.83					
Visuospatial construction	.55	.44					
Verbal fluency		.41				-.45	
Abstract reasoning		.46					
Disinhibition (time)							-.66
Disinhibition (errors)	.82						
Set shifting (time)						.82	
Set shifting (errors)	.61						
Prosodic repetition					.82		
Prosodic comprehension		.40			.62		
Internal consistency (Cronbach's α)	.68	.68	-.04	.58	.52	.43	.07

Table K2

Factor Analysis of the Cognitive Variables, Without Speed of Information Processing, Verbal Fluency, Prosodic Repetition and Prosodic Comprehension

	Component					
Measure	1	2	3	4	5	6
Attention						.61
WM	.79					
Verbal learning				.70		
Verbal memory				.81		
Verbal recognition				.84		
Visual learning		.95				
Visual memory		.93				
Visual recognition		.71				
Naming	.54					
Repetition	.41					
Comprehension	.74					
Visuospatial perception 2D			.84			
Visuospatial perception 3D			.91			
Visuospatial construction			.51			
Abstract reasoning						
Disinhibition (time)						-.82
Disinhibition (errors)	.76					
Set shifting (time)					.86	
Set shifting (errors)	.50					
Internal consistency (Cronbach's α)	.54	.67	.72	.58	-	.07

Appendix L: Inter-Item Correlations for MS and HC Groups

Table L1

Inter-Item Correlations Between the Language Composite and its Component Variables for MS Participant Data

Composite	Naming	Repetition	Comprehension
Language composite	.83**	.84**	.26

Note. Language composite = naming, repetition and comprehension.
** $p < .001$.

Table L2

Inter-Item Correlations Between the Verbal Memory Composite and its Component Variables for MS Participant Data

Composite	Verbal learning	Verbal memory	Verbal recognition
Verbal memory composite	.91**	.96**	.67**

Note. Verbal memory composite = verbal learning, memory and recognition.
** $p < .001$.

Table L3

Inter-Item Correlations Between the Visual Memory Composite and its Component Variables for MS Participant Data

Composite	Visual learning	Visual memory	Visual recognition
Visual memory composite	.97**	.97**	.70**

Note. Visual memory composite = visual learning, memory and recognition.
** $p < .001$.

Table L4

Inter-Item Correlations Between the Visuospatial Composite and its Component Variables for MS Participant Data

Composite	Visuospatial perception 2D	Visuospatial perception 3D	Visuospatial perception construction
Visuospatial composite	.83**	.86**	.74**

Note. Visuospatial composite = visuospatial perception 2D, visuospatial perception 3D and visuospatial construction.
** $p < .001$.

Table L5

Inter-Item Correlations Between the Dorsolateral Prefrontal Functioning Composite and its Component Variables for MS Participant Data

Composite	Attention	WM	Abstract reasoning
Dorsolateral prefrontal functioning composite	.47**	.85**	.60**

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning.
** $p < .001$.

Table L6

Inter-Item Correlations Between the Orbitobasal Composite and its Component Variables for MS Participant Data

Composite	Disinhibition (time)	Disinhibition (errors)	Set shifting (time)	Set shifting (errors)
Orbitobasal composite	.61**	.84**	.73**	.79**

Note. Orbitobasal composite = disinhibition and set shifting.
** $p < .001$.

Table L7

Inter-Item Correlations Between the Language Composite and its Component Variables for HC Participant Data

Composite	Naming	Repetition	Comprehension
Language composite	.68**	.81**	.14

Note. Language composite = naming, repetition and comprehension.
** $p < .001$.

Table L8

Inter-Item Correlations Between the Verbal Memory Composite and its Component Variables for HC Participant Data

Composite	Verbal learning	Verbal memory	Verbal recognition
Verbal memory composite	.86**	.93**	.65**

Note. Verbal memory composite = verbal learning, memory and recognition.
** $p < .001$.

Table L9

Inter-Item Correlations Between the Visual Memory Composite and its Component Variables for HC Participant Data

Composite	Visual learning	Visual memory	Visual recognition
Visual memory composite	.97**	.96**	.48*

Note. Visual memory composite = visual learning, memory and recognition.
* $p < .01$. ** $p < .001$.

Table L10

Inter-Item Correlations Between the Visuospatial Composite and its Component Variables for HC Participant Data

Composite	Visuospatial perception 2D	Visuospatial perception 3D	Visuospatial construction
Visuospatial composite	.67**	.76**	.70**

Note. Visuospatial processing composite = visuospatial perception 2D, visuospatial perception 3D and visuospatial construction.
** $p < .001$.

Table L11

Inter-Item Correlations Between the Dorsolateral Prefrontal Functioning Composite and its Component Variables for HC Participant Data

Composite	Attention	WM	Abstract reasoning
Dorsolateral prefrontal functioning composite	.35	.74**	.62**

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning.
** $p < .001$.

Table L12

Inter-Item Correlations Between the Orbitobasal Composite and its Component Variables for HC Participant Data

Composite	Disinhibition (time)	Disinhibition (errors)	Set shifting (time)	Set shifting (errors)
Orbitobasal composite	.63**	.81**	.59**	.57**

Note. Orbitobasal composite = disinhibition and set shifting.
** $p < .001$.

Appendix M: Tables Relating to the Cognitive Correlates of Euphoria

Table M1

Pearson Correlations Between Positivity and the Cognitive Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Positivity	1.00	-.05	.02	.23	.15	-.08	-.03	-.15	.04	-.12	-.02
2. Language comp.		1.00	.42**	.35*	.33*	.40*	.58**	.24	.50**	-.09	.45**
3. Visuospatial comp.			1.00	.48**	.44**	.30	.50**	.20	.59**	-.18	.41*
4. Verbal memory comp.				1.00	.61**	.32	.40*	.22	.44**	-.30	.52**
5. Visual memory comp.					1.00	.15	.46**	.22	.49**	-.35*	.30
6. Dorsolateral prefrontal functioning comp.						1.00	.40*	.20	.23	-.06	.28
7. Orbitobasal comp.							1.00	.01	.58**	-.04	.53**
8. ApBat repetition								1.00	.31	-.25	.10
9. ApBat comprehension									1.00	-.30	.46**
10. Speed of info. processing										1.00	-.06
11. Verbal fluency											1.00

Note. * $p < .01$. ** $p < .001$.

Table M2

Pearson Correlations Between Unawareness of Physical Deficits and the Cognitive Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of physical deficits	1.00	.25	.39*	.24	.37*	.14	.48**	.14	.37*	-.03	.38*
2. Language comp.		1.00	.42**	.35*	.33*	.40*	.58**	.24	.50**	-.09	.45**
3. Visuospatial comp.			1.00	.48**	.44**	.30	.50**	.20	.59**	-.18	.41*
4. Verbal memory comp.				1.00	.61**	.32	.40*	.22	.44**	-.30	.52**
5. Visual memory comp.					1.00	.15	.46**	.22	.49**	-.35*	.30
6. Dorsolateral prefrontal functioning comp.						1.00	.40*	.20	.23	-.06	.28
7. Orbitobasal comp.							1.00	.01	.58**	-.04	.53**
8. ApBat Repetition								1.00	.31	-.25	.10
9. ApBat Comprehension									1.00	-.30	.46**
10. Speed of info. processing										1.00	-.06
11. Verbal fluency											1.00

Note. * $p < .01$. ** $p < .001$.

Table M3

Pearson Correlations Between Unawareness of Cognitive Deficits and the Cognitive Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of cognitive deficits	1.00	.08	.34*	.07	.21	-.06	.03	.20	.13	-.07	-.16
2. Language comp.		1.00	.42**	.35*	.33*	.40*	.58**	.24	.50**	-.09	.45**
3. Visuospatial comp.			1.00	.48**	.44**	.30	.50**	.20	.59**	-.18	.41*
4. Verbal memory comp.				1.00	.61**	.32	.40*	.22	.44**	-.30	.52**
5. Visual memory comp.					1.00	.15	.46**	.22	.49**	-.35*	.30
6. Dorsolateral prefrontal functioning comp.						1.00	.40*	.20	.23	-.06	.28
7. Orbitobasal comp.							1.00	.01	.58**	-.04	.53**
8. ApBat Repetition								1.00	.31	-.25	.10
9. ApBat Comprehension									1.00	-.30	.46**
10. Speed of info. processing										1.00	-.06
11. Verbal fluency											1.00

Note. * $p < .01$. ** $p < .001$.

Table M4

Pearson Correlations Between Unawareness of Mood/Behavioural Deficits and the Cognitive Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Unawareness of mood/behavioural deficits	1.00	.11	.14	-.04	-.14	.00	-.09	.18	.06	.07	-.14
2. Language comp.		1.00	.42**	.35*	.33*	.40*	.58**	.24	.50**	-.09	.45**
3. Visuospatial comp.			1.00	.48**	.44**	.30	.50**	.20	.59**	-.18	.41*
4. Verbal memory comp.				1.00	.61**	.32	.40*	.22	.44**	-.30	.52**
5. Visual memory comp.					1.00	.15	.46**	.22	.49**	-.35*	.30
6. Dorsolateral prefrontal functioning comp.						1.00	.40*	.20	.23	-.06	.28
7. Orbitobasal comp.							1.00	.01	.58**	-.04	.53**
8. ApBat Repetition								1.00	.31	-.25	.10
9. ApBat Comprehension									1.00	-.30	.46**
10. Speed of info. processing										1.00	-.06
11. Verbal fluency											1.00

Note. * $p < .01$. ** $p < .001$.

Table M5

The Cortical and Subcortical Cognitive Correlates of Positivity

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	165.84	103.42		1.60	.119	-44.82	376.49
Language composite	-0.06	0.42	-.03	-0.13	.894	-0.90	0.79
Visuospatial composite	-0.24	0.78	-.07	-0.31	.760	-1.82	1.34
Verbal memory composite	0.47	0.32	.32	1.46	.154	-0.19	1.13
Visual memory composite	0.18	0.47	.09	0.38	.708	-0.78	1.13
Dorsolateral prefrontal functioning composite	-0.36	0.95	-.07	-0.38	.706	-2.30	1.58
Orbitobasal composite	-0.64	0.05	-.17	-0.67	.505	-2.58	1.30
Prosodic repetition	-0.64	0.50	-.24	-1.27	.212	-1.66	0.38
Prosodic comprehension	0.42	1.04	.10	0.40	.690	-1.70	2.53
Step 2							
Constant	162.59	116.02		1.40	.171	-74.36	399.54
Language composite	-0.02	0.43	-.01	-0.04	.969	-0.89	0.86
Visuospatial composite	-0.21	0.80	-.06	-0.27	.792	-1.84	0.86
Verbal memory composite	0.55	0.36	.38	1.52	.140	-0.19	1.29
Visual memory composite	0.09	0.50	.04	0.17	.866	-0.93	1.11
Dorsolateral prefrontal functioning composite	-0.40	0.98	-.08	0.41	.688	-2.39	1.60
Orbitobasal composite	-0.43	1.02	-.11	-0.42	.679	-2.52	1.66
Prosodic repetition	-0.66	0.52	-.25	-1.28	.211	-1.71	0.40
Prosodic comprehension	0.43	1.10	.10	0.39	.697	-1.81	2.67
Speed of information processing	-0.01	0.03	-.05	-0.28	.784	-0.07	-0.05
Verbal fluency	-0.40	0.64	-.14	-0.62	.540	-1.70	0.91

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M6

The Right and Left/Executive Cognitive Correlates of Positivity

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	163.27	70.38		2.32	.026	20.53	306.01
Visuospatial composite	-0.18	0.73	-.05	-0.25	.805	-1.66	1.30
Visual memory composite	0.41	0.40	.20	1.04	.307	-0.39	1.21
Prosodic repetition	-0.53	0.46	-.20	-1.16	.256	-1.46	0.40
Prosodic comprehension	0.14	0.92	.03	0.16	.878	-1.73	2.01
Step 2							
Constant	162.59	116.02		1.40	.171	-74.36	399.54
Visuospatial composite	-0.21	0.80	-.06	-0.27	.792	-1.84	1.41
Visual memory composite	0.09	0.50	.04	0.17	.866	-0.93	1.11
Prosodic repetition	-0.66	0.52	-.25	-1.28	.211	-1.72	0.40
Prosodic comprehension	0.43	1.10	.10	0.40	.697	-1.81	2.67
Language composite	-0.02	0.43	-.01	-0.04	.969	-0.89	0.86
Verbal memory composite	0.55	0.36	.38	1.52	.140	-0.19	1.29
Dorsolateral prefrontal functioning composite	-0.40	0.98	-.08	-0.41	.688	-2.39	1.60
Orbitobasal composite	-0.42	1.02	-.11	-0.42	.679	-2.52	1.66
Speed of information processing	-0.01	0.03	-.05	-0.28	.784	-0.07	0.05
Verbal fluency	-0.40	0.64	-.14	-0.62	.540	-1.70	0.91

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M7

The Cortical and Subcortical Cognitive Correlates of Unawareness of Physical Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-8.97	8.24		-1.09	.285	-25.74	7.81
Language composite	-0.02	0.03	-.10	-0.51	.612	-0.08	0.05
Visuospatial composite	0.06	0.06	.18	0.94	.355	-0.07	0.18
Verbal memory composite	-0.01	0.03	-.08	-0.39	.698	-0.06	0.04
Visual memory composite	0.03	0.04	.16	0.77	.445	-0.05	0.11
Dorsolateral prefrontal functioning composite	-0.04	0.08	-.08	-0.46	.652	-0.19	0.12
Orbitobasal composite	0.15	0.08	.45	1.98	.056	-0.00	0.31
Prosodic repetition	0.03	0.04	.13	0.77	.447	-0.05	0.11
Prosodic comprehension	-0.01	0.08	-.02	-0.07	.943	-0.17	0.16
Step 2							
Constant	-8.38	9.11		-0.92	.365	-26.99	10.22
Language composite	-0.02	0.03	-.13	-.066	.517	-0.09	0.05
Visuospatial composite	0.06	0.06	.17	0.87	.390	-0.07	0.18
Verbal memory composite	-0.02	0.03	-.16	-0.73	.474	-0.08	0.04
Visual memory composite	0.04	0.04	.22	1.04	.307	-0.04	0.12
Dorsolateral prefrontal functioning composite	-0.03	0.08	-.07	-0.39	.698	-0.19	0.13
Orbitobasal composite	0.12	0.08	.37	1.52	.138	-0.04	0.29
Prosodic repetition	0.03	0.04	.14	0.82	.418	-0.05	0.12
Prosodic comprehension	-0.01	0.09	-.02	-0.10	.920	-0.18	0.17
Speed of information processing	0.00	0.00	.07	0.42	.675	-0.00	0.01
Verbal fluency	0.05	0.05	.21	1.06	.299	-0.05	0.16

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M8

The Right and Left/Executive Cognitive Correlates of Unawareness of Physical Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-13.52	5.70		-2.37	.023	-25.09	-1.96
Visuospatial composite	0.07	0.06	.21	1.14	.264	-0.05	0.19
Visual memory composite	0.04	0.03	.21	1.22	.231	-0.03	0.10
Prosodic repetition	0.00	0.04	.01	0.07	.943	-0.07	0.08
Prosodic comprehension	0.05	0.08	.14	0.69	.494	-0.10	0.20
Step 2							
Constant	-8.38	9.11		-0.92	.365	-26.99	10.22
Visuospatial composite	0.06	0.06	.17	0.87	.390	-0.07	0.18
Visual memory composite	0.04	0.04	.22	1.04	.307	-0.04	0.12
Prosodic repetition	0.03	0.04	.14	0.82	.418	-0.05	0.12
Prosodic comprehension	-0.01	0.09	-.02	-0.10	.920	--0.18	0.17
Language composite	-0.02	0.03	-.13	-0.66	.517	-0.09	0.05
Verbal memory composite	-0.02	0.03	-.16	-0.73	.474	-0.08	0.04
Dorsolateral prefrontal functioning composite	-0.03	0.08	-.07	-0.40	.698	--.19	0.13
Orbitobasal composite	0.12	0.08	.37	1.52	.138	-0.04	0.29
Speed of information processing	0.00	0.00	.07	0.42	.675	-0.00	0.00
Verbal fluency	0.05	0.05	.21	1.06	.299	-0.05	0.15

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M9

The Cortical and Subcortical Cognitive Correlates of Unawareness of Cognitive Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-5.80	5.32		-1.09	.284	-16.65	5.05
Language composite	0.00	0.02	.03	0.15	.880	-0.04	0.05
Visuospatial composite	0.09	0.04	.47	2.24	.032	0.01	0.17
Verbal memory composite	-0.01	0.02	-.16	-0.77	.450	-0.05	0.02
Visual memory composite	0.02	0.02	.20	0.91	.369	-0.03	0.07
Dorsolateral prefrontal functioning composite	-0.04	0.05	-.15	-0.79	.435	-0.14	0.06
Orbitobasal composite	-0.02	0.05	-.10	-0.42	.680	-0.12	0.08
Prosodic repetition	0.02	0.03	.17	0.93	.361	-0.03	0.08
Prosodic comprehension	-0.04	0.05	-.15	-0.65	.521	-0.14	0.07
Step 2							
Constant	-5.91	5.93		-1.00	.327	-18.02	6.20
Language composite	0.01	0.02	.06	0.28	.785	-0.04	0.05
Visuospatial composite	0.09	0.04	.48	2.25	.032	0.01	0.18
Verbal memory composite	-0.01	0.02	-.10	-0.40	.690	-0.05	0.03
Visual memory composite	0.02	0.03	.14	0.60	.554	-0.04	0.07
Dorsolateral prefrontal functioning composite	-0.04	0.05	-.16	-0.83	.415	-0.14	0.06
Orbitobasal composite	-0.01	0.05	-.03	-0.10	.925	-0.11	0.10
Prosodic repetition	0.02	0.03	.16	0.85	.403	-0.03	0.08
Prosodic comprehension	-0.03	0.06	-.15	-0.62	.543	-0.15	0.08
Speed of information processing	-0.00	0.00	-.08	-0.43	.669	-0.00	0.00
Verbal fluency	-0.03	0.03	-.18	-0.84	.407	-0.09	0.04

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M10

The Right and Left/Executive Cognitive Correlates of Unawareness of Cognitive Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-6.93	3.58		-1.94	.061	-14.20	0.33
Visuospatial composite	0.07	0.04	.38	1.98	.056	-0.00	0.15
Visual memory composite	0.01	0.02	.10	0.57	.572	-0.03	0.05
Prosodic repetition	0.02	0.02	.16	1.00	.326	-0.02	0.07
Prosodic comprehension	-0.05	0.05	-.20	-0.99	.330	-0.14	0.05
Step 2							
Constant	-5.91	5.93		-1.00	.327	-18.02	6.20
Visuospatial composite	0.09	0.04	.48	2.25	.032	-0.01	0.18
Visual memory composite	0.02	0.03	.14	0.60	.554	-0.04	0.07
Prosodic repetition	0.02	0.03	.16	0.85	.403	-0.03	0.08
Prosodic comprehension	-0.03	0.06	-.15	-0.62	.543	-0.15	0.08
Language composite	0.01	0.02	.06	0.28	.785	-0.04	0.05
Verbal memory composite	-0.01	0.02	-.10	-0.40	.690	-0.05	0.03
Dorsolateral prefrontal functioning composite	-0.04	0.05	-.16	-0.83	.415	-0.14	0.06
Orbitobasal composite	-0.01	0.05	-.03	-0.10	.925	-0.11	0.10
Speed of information processing	-0.00	0.00	-.08	-0.43	.669	-0.00	0.00
Verbal fluency	-0.03	0.03	-.18	-0.84	.407	-0.09	0.04

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M11

The Cortical and Subcortical Cognitive Correlates of Unawareness of Mood/Behavioural Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-57.55	46.93		-1.23	.229	-153.13	38.03
Language composite	0.15	0.19	.17	0.80	.432	-0.23	0.53
Visuospatial composite	0.40	0.35	.25	1.13	.268	-0.32	1.12
Verbal memory composite	-0.02	0.15	-.03	-0.13	.899	-0.32	0.28
Visual memory composite	-0.23	0.21	-.25	-1.10	.280	-0.67	0.20
Dorsolateral prefrontal functioning composite	-0.13	0.43	-.06	-0.30	.764	-1.01	0.75
Orbitobasal composite	-0.33	0.43	-.19	-0.76	.451	-1.21	0.55
Prosodic repetition	0.18	0.23	.15	0.81	.426	-0.28	0.65
Prosodic comprehension	0.08	0.47	.04	0.18	.862	-0.88	1.04
Step 2							
Constant	-34.44	52.06		-0.66	.513	-140.76	71.87
Language composite	0.14	0.19	.16	0.74	.468	-0.25	0.54
Visuospatial composite	-0.25	0.22	-.27	-1.12	.270	-0.71	0.21
Verbal memory composite	-0.07	0.16	-.11	-0.43	.668	-0.40	0.26
Visual memory composite	-0.25	0.22	-.27	-1.12	.270	-0.71	0.21
Dorsolateral prefrontal functioning composite	-0.13	0.44	-.06	-0.30	.767	-1.03	0.77
Orbitobasal composite	-0.32	0.46	-.19	-0.70	.492	-1.26	0.62
Prosodic repetition	0.17	0.23	.14	0.72	.480	-0.31	0.64
Prosodic comprehension	-0.05	0.49	-.02	-0.09	.927	-1.05	0.96
Speed of information processing	-0.01	0.01	-.18	-0.97	.342	-0.04	0.01
Verbal fluency	0.17	0.29	.13	0.58	.564	-0.42	0.75

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Table M12

The Right and Left/Executive Cognitive Correlates of Unawareness of Mood/Behavioural Deficits

	Coefficients						
						95% CI	
Model	*b*	*SE b*	β	*t*	*p*	*LL*	*UL*
Step 1							
Constant	-35.55	31.07		-1.14	.260	-98.55	27.45
Visuospatial composite	0.36	0.32	.22	1.11	.277	-0.30	1.01
Visual memory composite	-0.27	0.17	-.29	-1.57	.125	-0.63	0.08
Prosodic repetition	0.24	0.20	.20	1.18	.245	-0.17	0.65
Prosodic comprehension	0.03	0.41	.01	0.06	.950	-0.80	0.85
Step 2							
Constant	-34.44	52.06		-0.66	.513	-140.76	72.87
Visuospatial composite	0.40	0.36	.25	1.13	.269	-0.33	1.13
Visual memory composite	-0.25	0.22	-.27	-1.12	.270	-0.71	0.21
Prosodic repetition	0.17	0.23	.14	0.72	.480	-0.31	0.64
Prosodic comprehension	-0.05	0.49	-.02	-0.09	.927	-1.05	0.96
Language composite	0.14	0.19	.16	0.74	.468	-0.25	0.54
Verbal memory composite	-0.07	0.16	-.11	-0.43	.668	-0.40	0.26
Dorsolateral prefrontal functioning composite	-0.13	0.44	-.06	-0.30	.767	-1.03	0.77
Orbitobasal composite	-0.32	0.46	-.19	-0.70	.492	-1.26	0.62
Speed of information processing	-0.01	0.01	-.18	-0.97	.342	-0.04	0.01
Verbal fluency	0.17	0.29	.13	0.58	.564	-0.42	0.75

Note. CI = confidence interval; *LL* = lower limit, *UL* = upper limit.

Appendix N: Inter-Item Correlations for the Patient Control Groups

Table N1

Inter-Item Correlations Between the Verbal Memory Composite and its Component Variables for MG Participant Data

Composite	Verbal learning	Verbal memory	Verbal recognition
Verbal memory composite	.95**	.98**	.58

Note. Verbal memory composite = verbal learning, memory and recognition.
** $p < .001$.

Table N2

Inter-Item Correlations Between the Visual Memory Composite and its Component Variables for MG Participant Data

Composite	Visual learning	Visual memory	Visual recognition
Visual memory composite	.93**	.96**	.65

Note. Visual memory composite = visual learning, memory and recognition.
** $p < .001$.

Table N3

Inter-Item Correlations Between the Dorsolateral Prefrontal Functioning Composite and its Component Variables for MG Participant Data

Composite	Attention	WM	Abstract reasoning
Dorsolateral prefrontal functioning composite	.15	.93*	-.01

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning.
* $p < .01$.

Table N4

Inter-Item Correlations Between the Orbitobasal Composite and its Component Variables for MG Participant Data

Composite	Disinhibition (time)	Disinhibition (errors)	Set shifting (time)	Set shifting (errors)
Orbitobasal composite	.70	.86*	.80*	.90**

Note. Orbitobasal composite = disinhibition and set shifting.
* $p < .01$. ** $p < .001$.

Table N5

Inter-Item Correlations Between the Verbal Memory Composite and its Component Variables for MVA TBI Participant Data

Composite	Verbal learning	Verbal memory	Verbal recognition
Verbal memory composite	.89*	.98**	.89*

Note. Verbal memory composite = verbal learning, memory and recognition.
* $p < .01$. ** $p < .001$.

Table N6

Inter-Item Correlations Between the Visual Memory Composite and its Component Variables for MVA TBI Participant Data

Composite	Visual learning	Visual memory	Visual recognition
Visual memory composite	.92**	.98**	.99**

Note. Visual memory composite = visual learning, memory and recognition.
** $p < .001$.

Table N7

Inter-Item Correlations Between the Dorsolateral Prefrontal Functioning Composite and its Component Variables for MVA TBI Participant Data

Composite	Attention	WM	Abstract reasoning
Dorsolateral prefrontal functioning composite	.40	.90*	.95**

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning.
* $p < .01$. ** $p < .001$.

Table N8

Inter-Item Correlations Between the Orbitobasal Composite and its Component Variables for MVA TBI Participant Data

Composite	Disinhibition (time)	Disinhibition (errors)	Set shifting (time)	Set shifting (errors)
Orbitobasal composite	.80*	.52	.52	.38

Note. Orbitobasal composite = disinhibition and set shifting.
* $p < .01$.

Table N9

Inter-Item Correlations Between the Verbal Memory Composite and its Component Variables for NP-SLE Participant Data

Composite	Verbal learning	Verbal memory	Verbal recognition
Verbal memory composite	.95**	.99**	.85*

Note. Verbal memory composite = verbal learning, memory and recognition.
* $p < .01$. ** $p < .001$.

Table N10

Inter-Item Correlations Between the Visual Memory Composite and its Component Variables for NP-SLE Participant Data

Composite	Visual learning	Visual memory	Visual recognition
Visual memory composite	.99**	.95**	.76

Note. Visual memory composite = visual learning, memory and recognition.
** $p < .001$.

Table N11

Inter-Item Correlations Between the Dorsolateral Prefrontal Functioning Composite and its Component Variables for NP-SLE Participant Data

Composite	Attention	WM	Abstract reasoning
Dorsolateral prefrontal functioning composite	.60	.78	.78

Note. Dorsolateral prefrontal functioning composite = attention, WM and abstract reasoning.

Table N12

Inter-Item Correlations Between the Orbitobasal Composite and its Component Variables for NP-SLE Participant Data

Composite	Disinhibition (time)	Disinhibition (errors)	Set shifting (time)	Set shifting (errors)
Orbitobasal composite	.90**	.76	.63	.69

Note. Orbitobasal composite = disinhibition and set shifting.
* $p < .01$. ** $p < .001$.