Antisocial Personality Disorder Comorbidity in Methamphetamine Use Disorder: Sociodemographic, clinical and childhood trauma correlates

By

Mr Edrich Rall

Student Number: RLLEDR001

Supervisor:

Assoc. Prof Debra Kaminer

Department of Psychology

University of Cape Town

Co-supervisor:

Prof Christine Lochner

SA MRC Unit on Risk and Resilience in Mental Disorders

Department of Psychiatry

Stellenbosch University

Submitted to the University of Cape Town

In partial fulfilment for the requirements of the award of the degree of Master of Clinical Psychology

February 2020

DECLARATION

I know that plagiarism is wrong. Plagiarism is to use another's work and pretend that it is one's own.

I, Edrich Rall, hereby declare that the work on which this thesis is based, is my own (original work) and that neither the whole work, nor a part of it, has been submitted in fulfilment of another degree.

I have used the APA 6th edition convention for citation and referencing. Each contribution to, and quotation in, this project from the work(s) of other people has been attributed, and has been cited and referenced.

This thesis titled "**Antisocial Personality Disorder comorbidity in Methamphetamine Use Disorder: Sociodemographic, clinical and childhood trauma correlates"** is my own work.

Signature _____Signed by candidate_____

Date: March 2021

DEDICATION

I wish to dedicate this writing to my parents, Andre and Daphne Rall, who unconditionally invested in my tertiary education for the past 10 years.

ACKNOWLEDGEMENTS

1. My profound gratitude goes to my primary supervisor, Prof Debra Kaminer, for her patient guidance and support with this thesis. Thank you.

2. To Prof Christine Lochner, thank you for your support in the completion of this thesis. Your guidance and support have been invaluable to me over the past years.

3. To Prof Martin Kidd, thank you for your assistance and guidance with the statistical analyses of this project. Your input was greatly appreciated.

4. To my father (Andrè), mother (Daphne) and brother (Divan), thank you for your support and patience in the time of completing this project. Thank you for your words of motivation in the times when the going got tough.

5. To my partner, Alarice Oosthuizen, thank you for your support, encouragement and motivation the past year of completing this thesis. You were a cornerstone in times when the going got tough and the nights turned into mornings.

6. I wish to thank the Stellenbosch University/University of Cape Town's Medical Research Council Unit on Risk and Resilience in Mental Disorders. This study would not have been possible without your help.

7. I wish to thank the South African National Research Foundation (NRF) that assisted financially to complete this project.

8. Lastly, I want to thank all the participants that participated in this research project. Without your participation and cooperation, this project would not have been possible.

ABSTRACT

Personality pathology, especially antisocial personality disorder (ASPD), often occurs in patients with methamphetamine use disorder (MAUD). However, little is known about potential risk factors for this dual diagnosis, and the impact of this comorbidity on both the severity of MAUD and levels of functional impairment. Casting light on such phenomena may aid in early identification of treatment targets, assist in the management of patients in this particular population, and contribute to development of treatment strategies. This cross-sectional study described and compared sociodemographic, clinical and childhood trauma correlates in patients with a dual diagnosis of MAUD and ASPD (MAUD+ASPD) and those with MAUD without ASPD (MAUD-ASPD). The contribution of sociodemographic and childhood trauma variables in predicting membership of the MAUD+ASPD group was also investigated.

A sample of 62 adult patients with a primary diagnosis of MAUD took part in the study. A sociodemographic questionnaire was completed and well established diagnostic measures of ASPD (The Mini-International Neuropsychiatric Interview; MINI) and MAUD (Structured Clinical Interview; SCID - 5) were used to determine diagnostic status. Illness severity was evaluated with the Yale-Brown Obsessive Compulsive scale (adapted for MAUD) (Y-BOCS-du) and functional impairment was assessed with the Sheehan Disability Scale (SDS). Histories of exposure and severity of childhood trauma (CT) were measured using the CTQ-SF.

Of the 62 participants, 14 (23%) had MAUD and had MAUD+ASPD whereas 48 (77%) had MAUD without ASPD (MAUD-ASPD). Bivariate analyses found significant group differences in terms of gender (df =1) = 8.05; p = <0.01), language (df = 2) = 7.12; p = 0.03), and level of physical neglect (F(1, 60) = 2.33; M = 9.85; SD = 4.23; p = 0.04). The MAUD+ASPD group members were mostly male (N = 9; 64%), English-speaking and with

histories of increased physical neglect. Logistic regression suggested that male gender (beta = 1.08; *OR* = 8.65; *p* = 0.01) and English language (beta = 1.55; *OR* = 11.38; *p* = 0.03) significantly predicted ASPD comorbidity. There were no significant differences in clinical severity or functional impairment between the MAUD+ASPD and MAUD-ASPD groups.

In conclusion, this study indicated that male gender and having English as a first language are associated with MAUD+ASPD but other sociodemographic variables, CT histories and clinical severity and impairment were not. Men who use MA are thus more prone to antisocial behaviour, which complicates their substance use condition. Treatment approaches for MAUD may benefit from developing adaptations that cater for challenges specific to comorbid ASPD. Additionally, the finding regarding first language warrants further investigation. Recommendations for future research are suggested.

Keywords: Antisocial personality disorder; methamphetamine use disorder; childhood trauma; illness severity; psychosocial functioning

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LIST OF ABBREVIATIONS

APA – American Psychological Association

ASPD – Antisocial Personality Disorder

CT – Childhood Trauma

CTQ-SF – Childhood Trauma Questionnaire (Short Form)

DSM 5 – The Diagnostic and Statistical Manual of Mental Disorders (fifth edition)

MA – Methamphetamine

MINI - The Mini-International Neuropsychiatric Interview (MINI)

MAUD – Methamphetamine Use Disorder

MAUD+ASPD – Methamphetamine Use Disorder with comorbid Antisocial Personality Disorder

MAUD-ASPD – Methamphetamine Use Disorder without Antisocial Personality Disorder

SCID – 5. The Substance Use Disorder module of the Structured Clinical Interview for DSM-5 Disorders (SCID-5)

SDS – Sheehan Disability Scale

SUD – Substance Use Disorder

Y-BOCS-du – Yale-Brown Obsessive Compulsive Scale (adapted for MAUD)

CHAPTER ONE

INTRODUCTION

In recent years, methamphetamine (MA) use has become a significant problem in South Africa (Dada et al., 2016; Plüddemann et al., 2013). In the Western Cape Province, MA use has reportedly reached epidemic proportions (Dada et al., 2017).

Methamphetamine use disorder (MAUD) is a psychiatric condition characterized by a pattern of MA use that results in significant distress or impairment on multiple levels of functioning (American Psychiatric Association (APA), 2013). Individuals with MAUD present with several symptoms which include tolerance, withdrawal when MA use is stopped or reduced, and craving for the substance (APA, 2013). In general and locally, MA use and MAUD have burdened public health and social services greatly, with demands ranging from a physical, psychological and psychiatric sequela, as well as social and intrapersonal in nature (Akindipe, Wilson, & Stein, 2014; Aronson, 2016; Kalechstein et al., 2000; Polcin, Buscemi, Nayak, Korcha, & Galloway, 2012; Richards & Laurin, 2017; Salo et al., 2011; Watt et al., 2014; Yen & Chong, 2006). Problems associated with MA use and MAUD are complicated, with varied treatment success (Polcin et al., 2012). Often treatment non-compliance, relapse rates, illness severity, and functional impairment are high (Cohen et al., 2007; Eslami-Shahrbabaki et al., 2015; Gonzales et al., 2011; Grant et al., 2010).

Comorbidity of personality pathology appears to be common in substance use disorder (SUD) patients (Verheul, 2001), with antisocial personality disorder (ASPD) being especially prevalent (Le Bon et al., 2004). There is also some evidence that personality pathology, and specifically ASPD, are highly prevalent in patients with MAUD (Zhang et al., 2018). Antisocial personality disorder is a psychiatric diagnosis classified among the personality disorders in the Diagnostic and Statistical Manual of Mental Disorders – fifth edition (DSM-5) and is characterized by a continuous disregard for, as well as violation of,

the rights and safety of others that often has its onset in childhood or adolescence (APA, 2013). It is often hallmarked with actions that are deceitful and presents with a pattern of lying, using aliases, or conning others for self-profit or pleasure (APA, 2013). Individuals with ASPD may also demonstrate a lack of remorse, as indicated by being indifferent to the realization of hurting, mistreating or stealing from others. Some of these characteristics and behaviours (e.g. being deceitful or untrustworthy, increased impulsivity, lack of obligation, lying and cheating, poor connection with others and aggression and violence) are similar to those that are often found in people with substance use disorder (Sommers, Baskin, & Baskin-Sommers, 2006; Watt et al., 2014; Watt, Guidera, Hobkirk, Skinner, & Meade, 2016).

To date most dual diagnosis research with MAUD patients has focused on mood and anxiety disorders, rather than personality pathology. In a few studies with both SUD and MAUD patients, ASPD has been associated with poorer prognosis and increased risk for treatment drop-out and relapse (Messina, Farabee, & Rawson, 2003; Zhang et al., 2018). The comorbidity of personality pathology has also been associated with increased severity of substance use (Zhang et al., 2018). However, the difference in clinical severity and functional impairment (and, hence, treatment needs and prognosis) between MAUD patients with and without ASPD comorbidity is not yet well understood.

Furthermore, it appears that there is limited research on risk factors for ASPD comorbidity in individuals with a primary diagnosis of MAUD. Sociodemographic factors may increase the risk for this dual diagnosis, but other than the well-established finding that both MAUD and ASPD are more common in men (Holzer & Vaughn, 2017), research on sociodemographic risk factors for MAUD+ASPD are limited.

Some circumstances may render people more vulnerable for developing psychopathology. Adversity during childhood is a global phenomenon that affects the lives of people worldwide (Stoltenborgh et al., 2015). Childhood adversity is often referred to as

childhood trauma (CT), which can broadly be defined as the exposure to traumatic events in childhood that may result in adverse developmental consequences (Busuttil, 2009; Gregorowski & Seedat, 2013). Also common in the South African context (Hobkirk et al., 2015; Kaminer et al., 2013; Williams et al., 2007), such histories place individuals at higher risk for acute and chronic physical, emotional or psychiatric problems compared to those with relatively trauma-free childhoods (Stoltenborgh et al., 2011).

Childhood trauma and adversity have been linked to several psychiatric conditions, including SUDs (Lieberman et al., 2011) as well as personality pathology (APA, 2013; Kounou et al., 2013). It appears that people with adverse childhood experiences have a significantly higher risk of both MAUD (Ding et al., 2014) and ASPD (Semiz et al., 2007). More specifically, some research has implicated CT in the development and onset of both MAUD and ASPD (Brown et al., 2003; Cohen et al., 2007; Kounou et al., 2013; Lopez-Patton et al., 2016; Messina et al., 2008; Semiz et al., 2007; Sher et al., 2015).

While there is some evidence that people with MAUD with histories of CT are at risk for comorbid ASPD (Lecomte et al., 2010), the role of CT in the risk for a dual diagnosis of MAUD and ASPD (MAUD+ASPD) remains unclear. It further appears that the role of CT in MAUD+ASPD has not been well explored in lower income countries like South Africa where rates of CT are high compared to higher income settings. This study was conducted in response to recent local pleas for more research on MA use as a matter of social development, safety, and public health (Mushanyu et al., 2015; Watt et al., 2014; Wyk & Stuart, 2011). Current and ongoing research on MAUD, specifically, conducted by the Medical Research Council's Unit on Risk and Resilience in Mental Disorders offered a cohort of South African adult patients with a primary diagnosis of MAUD and presented the opportunity to investigate the prevalence and correlates of comorbid ASPD. In the South African context, there is an exceptionally high prevalence of MA use, but research on

personality pathology in MAUD seems to be limited. A dual diagnosis of MAUD+ASPD may negatively impact illness severity and psychosocial functioning, which in turn, may create barriers to successful treatment, such as treatment dropout.. Understanding more about risk factors for MAUD+ASPD, and the impact of this dual diagnosis on severity and functioning, may allow for the development of more targeted treatment strategies that can enhance retention and outcome.

1.1 Research Aims and Objectives

The primary aim of this study was to describe and compare sociodemographic profiles, clinical correlates of illness severity and psychosocial impairment, and CT histories between patients with MAUD+ASPD and MAUD without ASPD (MAUD-ASPD). It also aims to determine the contribution of these variables in predicting the MAUD+ASPD dual diagnosis. Several objectives were identified:

Objective 1: To explore and compare sociodemographic variables, such as age, gender, ethnicity, and level of education, between MAUD+ASPD and MAUD-ASPD.

Objective 2: To compare rates of CT between patients with MAUD+ASPD and those with MAUD-ASPD.

Objective 3: To compare the severity of CT between patients with MAUD+ASPD those with MAUD-ASPD.

Objective 4: To compare illness severity and psychosocial disability between patients with MAUD+ASPD and those with MAUD-ASPD.

Objective 5: To determine whether MAUD+ASPD membership (as opposed to MAUD-ASPD) can be predicted by sociodemographic variables and different types and severity of CT.

1.2 Structure of Dissertation

In addition to Chapter One, this thesis comprises four chapters:

1. Chapter Two is a literature review that appraises both international and local research on MAUD and ASPD with associated illness severity and psychosocial functioning. It also reviews literature of CT in relation to MAUD and ASPD.
2. Chapter Three presents the methodology that was followed in conducting this research. It also includes a discussion of ethical considerations related to the study.
3. Chapter Four reports on the findings of the study.
4. Chapter Five presents a discussion of the findings by drawing on existing literature in the field. The chapter also concludes by exploring possible limitations of this research project and includes recommendations for future research.

CHAPTER TWO

LITERATURE REVIEW

This chapter will review exiting literature available on methamphetamine use disorder (MAUD) and antisocial personality disorder (ASPD), as well literature on the comorbidity of these diagnoses. By drawing on international and local research, this chapter will also explore illness severity and psychosocial impairment in patients with MAUD. The role of childhood trauma (CT) in both MAUD and ASPD will then be reviewed.

2.1 Methamphetamine Use Disorder (MAUD)

2.1.1 Methamphetamine

Methamphetamine (MA) is a synthetic substance that is also known as "speed", "meth", "ice", "crystal", "glass", (Aronson, 2016) or "tik", as it is most commonly referred to in South Africa (Plüddemann et al., 2013). It is a white odourless crystal-like substance (Plüddemann et al., 2013) and falls within the drug class of amphetamines (Yen & Chong, 2006). Methamphetamine is considered as a more potent form of amphetamine (Yen & Chong, 2006) and is a powerful psychoactive stimulant (Plüddemann et al., 2013). Usually, it is compounded in powder or pill form and can be taken orally (swallowing or smoking), intranasally (snorting), or intravenously (injecting) (Plüddemann et al., 2013). Locally, MA is relatively cheap and available – making it an attractive choice for users (Watt et al., 2014).

2.1.2 Methamphetamine Use Disorder

Methamphetamine use is increasing both globally (Meredith et al., 2005) and nationally (Plüddemann et al., 2013) and there is a need to understand both the causes and the impact of this fast-growing epidemic (Watt et al., 2014). Methamphetamine use disorder is a psychiatric condition characterized by a pattern of MA use that results in significant

impairment and/or distress on multiple levels of functioning (APA, 2013). Individuals with MAUD will often neglect major obligations such as occupational, family, recreational, and social responsibilities or activities. They also spend vast amounts of time obtaining, using, or recovering from the effects of MA use. Furthermore, patients often demonstrate a disregard for the negative consequences or problems that are caused or exacerbated by MA use and may even use MA in hazardous situations such as when they are driving (APA, 2013). Another hallmark of MAUD is repeated unsuccessful attempts to cut down or stop MA use (APA, 2013).

According to the South African Community Epidemiology Network on Drug Use (SACENDU), MA is a common substance of abuse locally and almost a third of all patients from addiction treatment centres in the Western Cape are patients who receive treatment for MA use-related problems (Dada et al., 2017). In general, it appears that locally substance use seems to be associated with contexts of historical oppression and economic marginalization (Chetty, 2015).

Internationally, different and inconsistent patterns of MA use between genders have been found (Cohen et al., 2007; Simpson et al., 2016), but locally it appears that MA is slightly more common among males (Watt et al., 2014). Sociodemographic research suggest that MA use is especially high among the 'coloured'[1] or mixed-race population and it is commonly used by younger individuals with lower levels of educational attainment (Cservenka & Ray, 2017; Polcin et al., 2012; Semple, Zians, Grant, & Patterson, 2005; Watt et al., 2014). Often users are separated or single, and occupation status varies with men more often having employment compared to women (Cohen et al., 2007). Female with MAUD often have lower levels of education, are unemployed or underemployed (Cohen et al., 2007).

[1] The term 'coloured' was used as a racial classification category under the Population Registration Act of the previous dispensation and is still commonly used in South Africa today to refer to individuals who are of mixed race (Adhikari, 2009).

In conclusion, MA is a powerful psychoactive stimulant with potent reinforcing effects and potential for misuse (Aronson, 2016). Over time and prolonged use may lead to pharmacological dependence that is characterized by (increased) tolerance to the effects of MA and withdrawal when reducing or stopping use (APA, 2013). Methamphetamine withdrawal is marked with more psychiatric manifestations, rather than somatic symptoms, and typically includes states of depression, severe dysphoria, anxiety, irritability and aggression, and paranoia (Meredith et al., 2005) that may exacerbate dysfunction and distress (APA, 2013).

2.1.3 Impact of Methamphetamine Use

The use of amphetamine-like substances, such as MA, is associated with a variety of physiological and medical sequela. When MA is administered, the initial physiological response includes increased physical functioning, reduced appetite, increased arousal, and restlessness (Watt et al., 2014). In contrast to the acute effects of MA intoxication, various medical sequela may arise from the prolonged use of MA. The most common are cardiac problems which include tachycardia, dysrhythmias, cardiomyopathy, cardiomegaly, and pulmonary oedema which have often been associated with inhalation (smoking) of MA (Aronson, 2016). Longstanding evidence suggests that the use of amphetamines like MA is associated with intracerebral haemorrhage and stroke (Aronson, 2016) which could be fatal. Changes in blood pressure and body temperature are common during use and in some cases may lead to hyperthermia that can result in convulsions, cardiovascular collapse, and death (Richards & Laurin, 2017). Other medical problems include increased risk for infections, skin problems, and immune-system disorders (Aronson, 2016) and severe dental decay, known colloquially as ‘meth-mouth’.

When MA is administered there is a surge in the release of dopamine from nerve terminals which results in central nervous stimulation that induces a state of euphoria (Aronson, 2016). The acute effects of intoxication (often called a 'high') produce a sense of exhilaration with increased self-esteem, improved mental functioning, violent and aggressive behaviour, and extended wakefulness (Watt et al., 2014). Amphetamine-like substances release monoamines in the brain and thereby stimulate noradrenergic, serotonergic, and particularly dopaminergic receptors (Aronson, 2016). In contrast to the euphoric and exhilarating affects of neurotransmitter release, chronic use of MA often leads to long-lasting neurological changes that may result in *amotivational* and psychiatric problems - even after use has stopped (Aronson, 2016). Neurological disorders in amphetamine and MA-using populations may include stereotypic movement disorders and motor-functional problems, chorea, and dyskinesia (Meredith et al., 2005). Stereotypic movement disorders are involuntary/automatic behaviours which may last for hours on end. These may include chorea or dyskinesia that includes strange facial and tongue movements or jerky motions of the arms and legs and a never-ending repetition of certain actions. Since significant reductions in dopamine transporters occur both with age and MA use, it is likely that MA use leads to a higher risk of Parkinsonian symptoms in abusers later in life (Aronson, 2016).

Some with MAUD may develop both acute and/or chronic psychosis – often referred to as MA-psychosis. These often include auditory and/or visual hallucinations that are similar to those experienced in paranoid schizophrenia (Aronson, 2016). Methamphetamine use has also been associated with secondary mental health problems. Psychiatric comorbidities may arguably be seen as a predisposition for, or perhaps a consequence of, continued drug use (Yen & Chong, 2006) and may include anxiety, depression, poor attention, and impaired executive functioning (Watt et al., 2014). Research to date has shown that depressive symptoms are frequently associated with MA use (Kalechstein et al., 2000;

Salo et al., 2011) and the prevalence of trauma- and stressor-related disorders [such as post-traumatic stress disorder (PTSD)] and anxiety disorders (social anxiety disorder, panic disorder, and agoraphobia) associated with MAUD may also be high (Akindipe et al., 2014).

Beyond the individual, MA use has been associated with various problems with inter-personal relationships and at community level (Polcin et al., 2012; Watt et al., 2014). Taking into account the psychological and behavioural effects and the lifestyle characteristics of individuals with MAUD, it has often been linked to relational problems, including violence, intimate partner or domestic abuse, crime, and community cohesion deficits (Watt et al., 2014). On a societal level, MA use places a significant financial burden on families and communities (Watt et al., 2014), as well as the health system (Polcin et al., 2012). Furthermore, MA use has a major impact on the economy as it fuels reduction in productivity, environmental damage, extra law enforcement, and additional healthcare expenses (Polcin et al., 2012). As in other countries, MAUD in South Africa is associated with a broad range of negative health issues, including HIV sexual transmission behaviours, HIV seroconversion and mental disorders (e.g. mood and psychotic disorders) (Okafor et al., 2020).

As mentioned earlier, MA is a potent psychoactive stimulant and experimental, recreational, or chronic use often results in the rapid development and onset of MA dependence/MAUD. Users are often caught in a cycle that is hallmarked by an inability to cut down or to stop MA use. Physical, as well as psychological dependence are often accompanied with discomfort and it is common for users to administer MA almost daily or even a few times a day to avoid distress (APA, 2013).

Methamphetamine use and MAUD often have a poor prognosis. Literature highlights varied treatment success, with high treatment drop out and relapse (Cohen et al., 2007; Polcin et al., 2012). As seen earlier, individuals who use MA often have comorbid physiological

(Aronson, 2016), psychological or emotional problems (Watt et al., 2015), as well as social constraints (Watt et al., 2014) that are caused and/or exacerbated by MA use which impacts functioning (APA, 2013).

2.1.4 Illness Severity and Psychosocial Disability

There are relatively few studies that investigate illness severity and psychosocial functioning in populations with a primary diagnosis of MAUD. However, it has been suggested that psychosocial functioning is negatively affected by MA use (Gonzales et al., 2011; Lecomte et al., 2010). Psychosocial functioning is often significantly impaired on and populations that use MA often have poor quality of life (Gonzales et al., 2011; Grant et al., 2010). One local study found that that people using MA are at high risk for problems related to psychosocial functioning (Berg et al., 2017). Grant et al. (2010) adds that moderate psychosocial dysfunction can be found among people with MAUD.

Methamphetamine use and MAUD may also lead to significant illness severity. One study suggests that people that use MA may present with marked illness severity (Grant et al., 2010). Another study stresses that illness severity in this population can be very high, and in some cases, MA use may result in mandatory hospital admission due to illness severity (Eslami-Shahrbabaki et al., 2015). Recent pleas have also highlighted the need for research on illness severity in patients with MAUD (Eslami-Shahrbabaki et al., 2015). Some authors suggest that there is little difference in illness severity between genders in populations that use MA (Grant et al., 2010) but findings are inconsistent (Simpson et al., 2016), with some studies suggesting that women have the highest MA use illness severity (Simpson et al., 2016).

2.2 Antisocial Personality Disorder (ASPD)

Antisocial personality disorder is a psychiatric diagnosis classified among the personality disorders in the Diagnostic and Statistical Manual of Mental Disorders – fifth edition (DSM-5) (Conti, 2016; APA, 2013). Personality disorders constitute a group of inflexible and pervasive mental health conditions that are characterized by an enduring pattern of inner experience and behaviour that distinctly differs from the cultural expectations of/for an individual (APA, 2013). More specifically, ASPD is characterized by a continuous disregard for, as well as the violation of, the rights and safety of others (APA, 2013). Individuals with ASPD often fail to conform to societal expectations of lawful behaviour. Often they are characterized as irresponsible in terms of work or financial responsibilities (APA, 2013). Furthermore, individuals with ASPD typically present with irritability, aggressiveness, and impulsivity. Other hallmarks of this disorder are being deceitful, lying, using aliases, or conning others for self profit or pleasure (APA, 2013). Individuals with ASPD may also demonstrate a lack of remorse, as indicated by being indifferent to the realization of hurting, mistreating or stealing from others (APA, 2013). According to the DSM-5 (APA, 2013), in order to meet a diagnosis of ASPD, one must be at least 18 years old, have a history of conduct disorder, and meet three of the following criteria: 1) failure to conform to social norms; 2) deceitfulness; 3) impulsivity; 4) irritability and aggressiveness; 5) reckless disregard for safety of self or others; 6) consistent irresponsibility; and 7) lack of remorse (Conti, 2016).

Psychiatric epidemiological studies in South Africa are limited and often do not report on the prevalence of personality disorders (Stein et al., 2008). Statistics on ASPD in South Africa's general population are also limited. International figures indicate that ASPD is present in around 3.5% of the general population (Salyer, 2007). Most studies that report on ASPD are conducted in special populations, such as prison settings (e.g. Loots & Louw,

2012), people with substance use disorder or psychiatric populations (Waumsly, 2007). In one small study done locally in a psychiatric hospital in the Western Cape, Waumsly (2007) found that ASPD is one of the most frequently diagnosed personality disorders among discharged psychiatric patients with figures indicating prevalence rates of 29%. This was notably higher compared to rates of other personality disorders in these patients, such as borderline personality disorder and histrionic personality disorder (Waumsly, 2007). Antisocial personality disorder is more common among males, younger age groups between the ages of 25-44 years, and individuals with low academic attainment (Holzer & Vaughn, 2017) and who are single (Salyer, 2007).

2.2.1. Comorbidity of Methamphetamine Use Disorder and Antisocial Personality Disorder

There is ample international research to suggest that ASPD is common among people with substance use disorders generally. In fact, ASPD is one of the two most consistently reported personality disorders in subjects with substance use disorders (SUDs) (Le Bon et al., 2004). One study found that ASPD is higher in populations with SUDs than compared to the general population (Compton et al., 2005).

Several models may explain ASPD comorbidity in SUDs. The comorbidity of MAUD and ASPD might be attributed to common underlying features, such as personality characteristics like impulsivity (APA, 2013; Dellazizzo et al., 2018), genetic, behavioural and cognitive factors (Rzhetsky et al., 2007; Smith et al., 2014), or shared risk markers for externalizing behaviours (Brook et al., 2016; Trull et al., 2000). It is also possible that the presence of personality pathology creates increased risk for substance use, for example as an emotion regulation strategy (Verheul, 2001). As mentioned earlier, locally MA is relatively cheap and an attractive substance of abuse. Individuals with ASPD may be more likely to

drop out from school, experience trouble with the law, and engage with peers that can expose them to illicit substance use. In a study by Meade et al. (2014) respondents linked tik use to increased rates of crime, violence and corruption, which undercut community cohesion, accompanied by antisocial behaviours (Cohen et al., 2007), which may be induced by the neurological and psychological impact of the substance.

In addition to the common comorbidity of ASPD in SUDs generally, it is well documented that ASPD often occurs comorbidly in populations that use MA (Fletcher & Reback, 2013; Lecomte et al., 2010; Plüddemann et al., 2013). However, if the onset of MA abuse is before the age of 15 years (the age by which ASPD symptoms need to have been present), it may be difficult to distinguish the effects of MA abuse from an emerging antisocial personality disorder.

Prevalence rates of this dual diagnosis seem to vary in the literature, with a prevalence range between five to 68% (Fletcher & Reback, 2013; Lecomte et al., 2010; Plüddemann et al., 2013). It appears that little is yet known about risk factors for the development of this dual diagnosis. There is some research on the clinical implications of MAUD+ASPD, but it is still quite limited. A comorbid diagnosis of ASPD in MAUD may be associated with heavier MA use (Lecomte et al., 2010) and reduced prosocial or health-related behaviours (Fletcher & Reback, 2013). Heavier MA use may also impact treatment-seeking efforts (Lin et al., 2004), which in return can result in increased psychiatric and physiological sequela (APA, 2013; Callaghan, Cunningham, Sykes, & Kish, 2012; Meredith et al., 2005). Where personality pathology such as ASPD is comorbid with MAUD, there may be greater clinical complexity and poorer prognosis (Kalechstein et al., 2000; Martens, 2000) which may often necessitate specialized assessment and intervention. It has been suggested that screening for deviant personality patterns like ASPD may be warranted in individuals with MAUD during admission for detoxification and rehabilitation as some research shows that people MAUD

with comorbid ASPD are more likely to relapse to heavy MA use after treatment (Fridell et al., 2006). Investigation of ASPD patterns in MAUD may improve our understanding of the development from MA use to dependence and addressing ASPD in MAUD and may help to decrease or even prevent development from MA use to MA dependence (Zhang et al., 2018).

2.3 Childhood Trauma (CT)

Childhood trauma is common in the South African context and high rates of at least one traumatic event during lifetime has been reported in local cohorts (Hobkirk et al., 2015; Kaminer et al., 2013; Williams et al., 2007). Childhood trauma can be defined as exposure to traumatic events during childhood that result in adverse developmental consequences (Busuttil, 2009; Gregorowski & Seedat, 2013). It is often conceptualized in terms of physical, sexual and emotional maltreatment or abuse that occurs within the context of a child and attachment or caregiver relationships (Bernstein et al., 2003; Norman et al., 2012). Trauma that occurs during childhood and adolescence can alter transition into adulthood due to social, behavioural, physiologic, and neurobiological changes that cascade from such adversity and is associated with a significantly increased risk of mental health difficulties (Anda et al., 2006; Hatcher et al., 2019).

2.4 Childhood Trauma, Methamphetamine Use Disorder and Antisocial Personality Disorder

Research to date has demonstrated that different types of CT frequently occur concurrently and that it confers the risk for multiple psychiatric diagnoses (Keyes et al., 2012), including substance use and personality disorders in adulthood (Machisa et al., 2016). More specifically, it has been associated with both MAUD (Lecomte et al., 2010; Lopez-Patton et al., 2016; Svingen et al., 2016) and ASPD (Berenz et al., 2013; Bierer et al., 2003; Haller &

Miles, 2004; Lecomte et al., 2010). Literature suggests that people with MAUD with a history of CT have increased risk for a comorbid diagnosis of ASPD (Lecomte et al., 2010) and Messina et al. (2008) found that populations who use MA and who have a diagnosis of ASPD report greater experiences of childhood abuse compared to those without ASPD. However, research that specifically explores CT in samples with a primary diagnosis of MAUD and comorbid ASPD seems to be scant and no South African research to date has examined this. This section provides an overview of current literature on the relationship that CT may have with MAUD and ASPD.

2.4.1 Childhood Trauma and Methamphetamine Use Disorder

Childhood trauma can profoundly affect mental health (Carliner et al., 2016; Hatcher et al., 2019) and substance use is often a mechanism or an attempt to cope with the lasting impact thereof (Berg, Hobkirk, Meade, & Joska, 2017; Watt, Myers, Towe, & Meade, 2015). Individuals with a history of CT are at greater risk of developing substance use problems during adolescence and in adulthood than those without such histories (Svingen et al., 2016).

It has been suggested that between 40 and 90% of people with substance use disorders report a history of CT (Banducci et al., 2014; Kendler et al., 2000). Sexual abuse (Cuellar & Curry, 2007; Dong et al., 2004; Kendler et al., 2000; Vera et al., 2005), physical abuse and neglect (Dong et al., 2004; Mersky et al., 2013; Svingen et al., 2016), and emotional trauma (Svingen et al., 2016) during childhood have all been associated with substance use problems (Hogarth et al., 2019) and the development or onset of a SUD. Contextual factors such as the age when the trauma is experienced, or the frequency thereof, may also impact psychological functioning/development (van der Kolk, 2003) and increase the risk for substance abuse (Lieberman et al., 2011).

Childhood trauma is common in populations that use MA (Ding et al., 2014; Lanesman et al., 2019). However, there is a paucity of empirical studies investigating the relationship between CT and MA use in adulthood (Lopez-Patton et al., 2016). Some literature indicates that a wide range of childhood abuse, including sexual, emotional, and physical abuse, is significantly higher in patients who use MA compared to non-MA-users (Lopez-Patton et al., 2016). It has also been suggested that women, compared to men, report the most extensive histories of childhood abuse in MAUD populations (Messina et al., 2008). Little research that focuses on childhood physical trauma has been conducted in samples with a primary diagnosis of MAUD, warranting further exploration. There is evidence to suggest that childhood physical trauma is significantly more prevalent among substance-abusing males (Dong et al., 2004; Khoury et al., 2010; Svingen et al., 2016). This contrasts to the finding that MA using females are almost twice as likely as their male counterparts to report physical abuse during childhood and adolescence (Messina et al., 2008). In one study done with MA using participants, physical abuse was reported by 64% of women and 36% of men (Cohen et al., 2007).

Emotional trauma during childhood has been associated with substance use problems in both men and women (Hogarth et al., 2019; Dong et al., 2004). One study reports that 84% of women and 64% of men in their sample of participants who use MA reported histories of emotional abuse (Cohen et al., 2007).

Local studies that report on the prevalence of childhood sexual abuse among people with MAUD are limited. Nevertheless, it appears as if individuals with a history of MA use have increased histories of sexual abuse in comparison with the general population. In a review of lifetime abuse in patients with MAUD it was indicated that 29% of women and 7% of men reported sexual abuse (Cohen et al., 2007) during childhood. One local study with patients seeking treatment for problems associated with MA use suggested that childhood

sexual abuse was more than twice as prevalent in women who use MA compared to those who do not (Berg et al., 2017). The study also found histories of sexual abuse in 45% of women and 20% of men with MAUD (Berg et al., 2017).

2.4.2 Childhood Trauma and Antisocial Personality Disorder

Childhood trauma is associated with personality disorders in adulthood (Kounou et al., 2013) and has strong associations with ASPD in particular (Berenz et al., 2013; Semiz et al., 2007; Sher et al., 2015). Specific forms of trauma including a history of sexual abuse, physical abuse (Sher et al., 2015) and emotional abuse have all been associated with antisocial behaviour (Riggs & Kaminski, 2010). More specifically, a history of sexual abuse and physical abuse predicts ASPD in males, whereas sexual abuse, combined sexual and physical abuse, but not physical abuse alone, predict ASPD for females (Sher et al., 2015). Most of the research has focused on high-income countries and little is known about the relationship between CT and personality disorders in low and middle-income settings like South Africa (Kounou et al., 2013). Although CT is strongly associated with both MAUD and ASPD, the role of CT in creating risk for MAUD with ASPD comorbidity is vague. It is possible that specific types or increased severity of CT experiences may enhance the risk for this dual diagnosis.

2.5 Conclusion

Methamphetamine use is very common in South Africa with some authors suggesting that it has reached epidemic proportions. Methamphetamine use disorder holds devastating physiological, psychological and social sequela for the user and the community. Little is known about potential risk factors for the dual diagnosis of MAUD and ASPD, and the impact of this comorbidity on both the severity of MAUD and levels of functional

impairment and according to our knowledge South African research have not been conducted with these specific aims. The current study aimed to address these gaps in the research base.

CHAPTER THREE

METHODOLOGY

3.1 Research Design

This study has a cross-sectional and descriptive correlational design and formed part of a broader project which is largely quantitative in nature. The present study is a secondary analysis of data collected by the South African Medical Research Council's Unit on Risk and Resilience in Mental Disorders, a cross-university facility between Stellenbosch University (SU) and the University of Cape Town (UCT) (hereafter referred to as the SA MRC Unit). All the data analysed for this research project were sourced from the SA MRC Unit's on-going project, named "Gambling Disorder and Methamphetamine Use Disorder: A neurocognitive, genetic and neuroimaging study". The parent project was launched in September 2015 and was funded by the South African National Research Foundation (SA NRF).

The aim of the overarching project is to investigate the role of polymorphisms in specific candidate genes that account for differences in brain-imaging, cognitive-affective performance, and performance in behavioural tasks of patients with (primary diagnoses) of gambling disorder and methamphetamine use disorder (MAUD). It received ethics approval from SU (reference number N14/05/053) and UCT (reference number 770/2014). It must be noted that most of the methodological aspects, of the current research project, such as the recruitment of participants, data collection, and ethical considerations, were based on the overarching study's methodology and protocol.

The current research project was explorative and descriptive in nature. Exploratory and descriptive research is usually conducted when there is insufficient research available on a particular subject and aims to understand a phenomenon to develop preliminary ideas or to refine future research related to causality (Blaikie, 2003). For the current research study, the

researcher only included data from those measures relevant to the aim and objectives of the study and to my knowledge no research with the specific aims and objectives of this study have yet been conducted. It must be noted that the researcher and author of this study recruited participants and conducted interviews with such recruits.

3.2 Research Questions

As stated in Chapter One, the aim of the study was to compare sociodemographic variables and clinical severity, and histories of childhood trauma (CT) between MAUD with comorbid antisocial personality disorder (MAUD+ASPD) and MAUD without ASPD (MAUD-ASPD). Sociodemographic variables investigated here included age, ethnicity, gender, and level of education. Clinical severity included both illness severity and levels of psychosocial impairment. Childhood trauma history included exposure rates and severity of physical, sexual and emotional abuse, and emotional and physical neglect. The study aimed to answer the following research questions:

1. Are there sociodemographic differences between patients with MAUD+ASPD and patients with MAUD-ASPD?
2. Are there differences in illness severity and psychosocial disability between the two groups?
3. Are there differences in overall CT exposure, as well as the rates and severity of specific forms of trauma, between the two groups?
4. Can group membership (i.e. MAUD+ASPD vs. MAUD-ASPD) be predicted by any sociodemographic variables and CT history?

3.3 Sample

Recruitment of participants for the overarching study started in September 2015. Only individuals with a history of and/or current methamphetamine (MA) use were recruited. Males and females were recruited from the community through newspaper advertisements. In the advertisements, the researcher, who is the author of this dissertation, provided contact details for potential participants to respond to. Participants were also recruited from addiction treatment centres (inpatient and outpatient) or practitioners (private and governmental) who provide services to individuals with substance use problems (methamphetamine) in the Western Cape Province.

Individuals from the community who responded to newspaper advertisements were contacted by the research assistants that work on the overarching project. Participants that were recruited from local treatment centres or other treating professionals were screened by the referral practitioner prior to referral to the study. With patient permission, the treating professionals provided research assistants with contact details to contact their referrals. All prospective participants with a history of and/or current MA use were contacted either by telephone, e-mail, or WhatsApp to schedule a semi-structured interview to determine if they could be included in the research project. Inclusion criteria were 1) having a primary life-time diagnosis of MAUD, 2) aged between 18 and 65 years, 3) and residing in the Western Cape Province of South Africa. Because other psychiatric problems and poly-substance use are rife in MA using populations, individuals with a history of comorbid mental illnesses or additional substances were also allowed to participate in the study.

3.4 Instruments

All instruments used in this study were offered in both Afrikaans and English, depending on the participants' language preference. For measures that were not available in Afrikaans,

translation was done by the MRC from English to Afrikaans and these received approval by both ethics' committees at UCT and SU. For this study the following assessments were included in the data analysis:

Demographic characteristics. The sociodemographic questionnaire that was used in the SA MRC Unit's study was administered to each participant at the beginning of the interview. The questionnaire recorded the following sociodemographic information: the participant's age, level of education, occupational status, gender, and language. The questionnaire can be found in the appendices as "Appendix A".

SCID – 5. The Substance Use Disorder module of the Structured Clinical Interview for DSM-5 Disorders (SCID-5) was administered to all participants. It has often been used in research to diagnose substance use disorders (SUDs) such as MAUD (Lopez-Patton et al., 2016; Ogloff et al., 2015) and has also been used reliably in South African research (e.g. Mall et al., 2014). The SCID-5 (module E) measures symptoms of a wide variety of substance use that included stimulant-like substances (such as MA) on a severity scale comprising of 11 questions, with each item receiving a score out of three. The SCID-5's severity scale has demonstrated good internal consistency (Cronbach's $\alpha s > 0.80$), test–retest reliability, and concurrent, incremental and predictive validity (Shankman et al., 2018). The psychometric properties of the SCID-identified symptom scales have been shown to be far superior to other psychometric tests that consist of categorical diagnoses for both current and lifetime psychopathology (Shankman et al., 2018). The substance use disorder module of the SCID-5 can be found in the appendices as "Appendix B".

MINI. The Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1994) was used to assess the diagnostic status of ASPD. The MINI's ASPD module is divided into two sections based on the DSM-5 (American Psychiatric Association (APA), 2013) diagnostic criteria. Each section has six yes-no-questions relating to specific antisocial behaviours. The

first section focuses on specific behaviours prior to the age of 15 years. If two or more questions are answered as "yes" in this section, the interviewer continues with the second section of questions regarding antisocial behaviours after the age of 15 years. If three or more questions were answered as "yes" in this section, a diagnosis of ASPD is met. The MINI as a whole has good reliability and validity (Sheehan et al., 1998) and has been used in both international (Sulaiman et al., 2014) and local (Akindipe et al., 2014) research on MAUD. A copy of the ASPD module of the MINI can be found in the appendices as "Appendix C".

CTQ-SF. The Childhood Trauma Questionnaire Short Form (CTQ-SF) (Bernstein et al., 1994) was used to assess exposure to different forms of CT. The CTQ-SF is one of the most widely used and investigated measures of diverse forms of childhood maltreatment (Spinhoven et al., 2014). The CTQ-SF is a self-report measure used to assess both the nature and severity of CT. The CTQ-SF comprises of 28 Likert-type items, with five response options, ranging from "never true" to "very often true" and asks questions related to traumatic events in the childhood and adolescent years. The CTQ-SF is divided into dimensional scales to enhance reliability and maximize statistical power (Bernstein et al., 2003). Subscales of the CTQ-SF include measures of emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect (Bernstein et al., 2003; Oh et al., 2018; Spinhoven et al., 2014). Each scale consists of five items that are scored on the 5-point Likert-type scale ranging from five to 25 (Grassi-Oliveira et al., 2014; Spinhoven et al., 2014). The severity of abuse and neglect are determined according to cut-off scores: none to minimal, low to moderate, moderate to severe, and severe to extreme (Grassi-Oliveira et al., 2014). According to the manual the recommended cut off scores are emotional abuse: none to minimal = 5-8; low to moderate = 9-12; moderate to severe = 13-15; severe to extreme = 16+, physical abuse: none to minimal = 5-7; low to moderate = 8-9; moderate to severe = 10-

12; severe to extreme = 13+, sexual abuse: none to minimal = 5; low to moderate = 6-7; moderate to severe = 8-12; severe to extreme = 13+, emotional neglect: none to minimal = 5-9; low to moderate = 10-14; moderate to severe = 15-17; severe to extreme = 18+, and physical neglect: none to minimal = 5-7; low to moderate = 8-9; moderate to severe = 10-12; severe to extreme = 13+ (MacDonald et al., 2016). Total scores and severity of CT on the CTQ are interpreted as follows: none/minimal (< = 36), low to moderate (> 36 and < = 51), moderate to severe (> 51 and < = 68), and severe to extreme (> = 69) (MacDonald et al., 2016). To minimize socially desirable responses of false-negative trauma reports, three additional items are included in a minimization scale (Spinhoven et al., 2014).

The CTQ-SF can be used in adult populations (Bernstein et al., 2003; Oh et al., 2018). Reliability and validity of the CTQ-SF have been well established in both substance use populations and psychiatric populations with personality pathology (Bernstein et al., 2002), with good evidence of criterion-related validity in these subgroups (Bernstein et al., 2003; Spinhoven et al., 2014). It has been used in the South African context (e.g. Brooks et al., 2014; Hogarth et al., 2019; Lochner et al., 2005, 2008) with acceptable internal consistency (Cronbach's αs 0.70) (Brooks et al., 2014). Further, the CTQ-SF is quick to administer, usually not taking more than five minutes to complete (Bernstein et al., 2003), which made it ideal considering the extensive test battery of the overarching project. A copy of the CTQ-SF is attached in the appendices as “Appendix D”.

Y-BOCS-du. The Yale-Brown Obsessive Compulsive Scale adapted to reflect obsessions and compulsions related to drug use (Y-BOCS-du) (Goodman et al., 1989) was used to assess MA use severity. The Y-BOCS-du was adapted from the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Yale-Brown Obsessive-Compulsive Scale for Heavy Drinking (Y-BOCS-hd) and has been used in research with MA using participants (Eslami-Shahrbabaki et al., 2015). Similar to the Y-BOCS-hd, it measures obsessive-compulsive

characteristics of substance-using individuals (Friedman, Dar, & Shilony, 2000). The questionnaire specifically measures the severity of obsessionality and compulsivity related to substance use (Friedman et al., 2000). For this research project, the Y-BOCS-du was adapted to measure obsessionality and compulsivity of MA using individuals. The changes to Y-BOCS-du to assess MA use severity were limited, with only the words referring to alcohol use, adapted to refer to MA use.

The Y-BOCS-du is similar to the original Y-BOCS and comprises a 10-item clinician-rated scale. The scoring system is also identical to that of the original Y-BOCS. Each item is rated from 0 (no symptoms) to 4 (extreme symptoms). Items 1 to 5 comprise the obsessionality subscale and reflect MA-related thoughts; items 6 to 10 comprise the compulsivity subscale and reflect MA-related behaviours. The total score of the questionnaire is the sum of all 10 items with each subscale having a range of 0 to 20 and a total range of 0 to 40 (Friedman et al., 2000). The internal consistency of the Y-BOCS-du is good (Cronbach's αs 0.70) (Friedman et al., 2000). A total score of 10 to 20 indicates mild-, 21 to 30 indicates moderate-, and 31 to 40 indicates severe illness severity based on obsessive and compulsive symptoms (Boyette et al., 2011). A copy of the Y-BOCS-du can be found in the appendices as “Appendix E”.

SDS. The Sheehan Disability Scale (SDS) (Sheehan et al., 1996) is a self-report measure to assess the severity of psychosocial disability. The SDS comprises of three Likert style items on a discretized analogue scale to indicate the degree of impairment in the domains of work, family and social life (Olley et al., 2005; Sheehan & Sheehan, 2008). The higher the scores, the greater the psychosocial impairment and disability (Olley et al., 2005). Ranges of each domain are described as follow: zero = no impairment; one to three = mildly impaired; four to six = moderately impaired; six to nine = markedly impaired; and 10 = extremely impaired (Rush et al., 2008). The three items of the measure can be summed to provide a global score

(SDS total score) of functional impairment that ranges from zero (no impairment) to 30 (highly impaired) and converted into a total percentage (Rush et al., 2008). The psychometric properties have been found to be satisfactory (Hodgins, 2013) and it has been used in populations of MAUD and patients with psychiatric problems locally (Olley et al., 2005) and internationally (Glasner-Edwards et al., 2008). The SDS is attached in the appendices as "Appendix F".

3.5 Procedures

After recruitment, each participant was asked to attend a semi-structured interview for psychometric evaluation with research assistants working for the SA MRC Unit. On arrival, each participant provided informed consent before data collection started. Subsequently, each participant (together with the researcher) completed psychometric tests and self-reports. The majority of data collection was conducted at the SA MRC Unit sites, based in the Department of Psychiatry at SU or UCT. Participants recruited from the community selected which site they preferred to attend (based on distance from home, ease of access, the availability to travel, etc.). To meet the needs of participants who were recruited from local treatment centres or other practitioners, they were either seen at the respective facility/organization or at a SA MRC Unit site. All interviews took place in a private consultation room and refreshments such as coffee, tea, or water were offered when the participant arrived. The researchers are fluent in Afrikaans and English and the interviews were conducted in the language preferred by the participant.

The researchers received training to administer the battery of psychometric tests and worked under the supervision of a clinical psychologist to discuss assessment results of diagnostic measures such as with the SCID 5 and MINI. Most of the interviews lasted for three hours, however, breaks were provided as needed.

3.6 Data Analysis

After data collection ended, all data were entered into an electronic database (SPSS software). Any identifying information of the participants was removed and an anonymized database was used for data mining. A total of 110 participants were included when data collection for this study ended. However, only 62 participants were included in the analysis. Reasons for exclusion were an absence of MAUD as a primary diagnosis.

During data analysis, the scores of each assessment were calculated and entered in the database. Sub-scale-scores of the CTQ-SF were calculated by applying syntax developed for the measure in the electronic database. The rates of CT (i.e. absence vs. presence) were manually calculated by examining total scores of the CTQ-SF. The minimum score that could be obtained on the CTQ-SF was 25 (absence). If a score greater than 25 was obtained, a history of CT was inferred. The different sub-scales with minimum scores of five were examined to determine the absence versus the presence of different types of childhood abuse. For the SDS and the Y-BOCS-du, individual scores were calculated by the researcher based on participant response.

Assistance with data analysis was sought from the Centre of Statistical Consultation of the Department of Statistics and Actuarial Sciences at SU. For objectives one to four (see page 16), bivariate analyses were conducted. For comparisons of sociodemographic variables (e.g. age, gender, level of education, etc.), clinical variables (SDS and Y-BOCS-du) and CT histories between the two groups (MAUD+ASPD and MAUD-ASPD), cross tabulation was used for categorical predictors (e.g. gender, language, employment status), with the Fisher exact test, while for ordinal/continuous data (e.g. age, level of education, and years of education) one-way analysis of variance (ANOVA) was conducted to compare means between the two groups. The accepted level of significance was < 0.05. For objective

five, a logistic regression was conducted to examine sociodemographic and CT predictors of diagnostic group membership, yielding adjusted odds ratios.

3.7 Ethics

As mentioned earlier, at the time of conducting this study, the overarching study already had approval from both the SU Health Research Ethics Committee and the UCT Human Research Ethics Committee. The project was conducted in accordance with the ethical guidelines and principles of the international Declaration of Helsinki and the South African Guidelines for Good Clinical Practice. This researcher also received ethics approval from the Department of Psychology at UCT on 30 April 2019 (reference number: PSY2019-017). Ethics, with specific reference to informed consent, confidentiality, and risks and benefits, are discussed below.

3.8 Informed Consent

Before the interview started, the participant received a consent form. The participant was instructed to thoroughly read the consent form. The researcher allowed enough time for the reading of the consent form and verbally explained the study procedures in layperson's terms thereafter. The researcher allowed for and answered any questions that arose. Only participants who provided signed consent were included in the study. Informed consent forms were available in Afrikaans as well as English. Participation in the study was voluntary and participants had the right to withdraw at any stage. Participants were clearly informed about their right to voluntary participation prior to data collection. The English version of the consent form can be found in the appendices as "Appendix G".

3.9 Anonymity and Confidentiality

To ensure the anonymity of participants, the researcher assigned a study number to each participant (e.g. MA 001). The participant numbers were kept on a separate database from the original identifying information. Both databases were stored on a password-protected computer in a locked office at the SA MRC Unit. The hard copies of completed questionnaires were stored in a file for each participant in a locked drawer in the same office. All data were only available to the researcher and his supervisors. All information that was obtained in the study remains confidential and is not discussed outside of the research team.

3.10 Risks and Benefits

Due to the length of the interview, there was a minimal risk that participants may have felt tired by their participation. Participants were allowed to take breaks during the interview, as needed.

All participants were offered psychological or emotional support or referral for treatment of MA dependence and associated problems. If requested, appropriate referrals were made to registered health care facilities/practitioners (e.g. The South African National Council on Alcoholism and Drug Dependence (SANCA), Narcotic Anonymous (NA), day hospitals with outpatient psychiatric services and/or private practice psychologists/psychiatrists). Participants that experienced emotional distress as result of sharing their histories, were offered appropriate referrals to psychologists or counsellors.

3.11 Incentives

Each participant received a R75 Checkers gift card to compensate for the time spent on the research project.

CHAPTER FOUR

RESULTS

This chapter presents the results of the study. It first presents the demographic characteristics of each group and the sample as a whole. It further presents associations of each group with illness severity, psychosocial impairment, and childhood trauma (CT). Lastly, it presents findings of a logistic regression of sociodemographic and CT variables in predicting comorbid antisocial personality disorder (ASPD) in methamphetamine use disorder (MAUD).

4.1 Demographic Characteristics

The demographic features of the total sample are depicted in Table 1. Sixty-two adults with a primary diagnosis of MAUD were included in the study. The sample was predominantly female (*N* = 42; 68%) and aged between 18 and 44 years (*M* = 30.14 years; *SD* = 6.64). The majority of participants were of mixed-race ancestry (coloured) (*N* = 56; 90%), reported their first language as a combination of Afrikaans and English (*N* = 27; 44%), had educational attainment between grade eight and 10 (*N* = 30; 48%) and were unemployed (*N* = 45; 73%).

Table 1: Demographic features of the total sample

	N	**%**	***M***	**Std Dev**
Gender:				
Male	20	32		
Female	42	68		
Age:	-	-	30.14	6.14
Population:				
White	2	3		
Black	2	3		
Coloured	56	90		
Other	2	3		
First Language:				

Afrikaans	19	31		
English	14	23		
Combined Afrikaans and English	27	44		
African Language	2	3		
Level of Education:				
Grade 1 - 7	3	5		
Grade 8 - 10	30	48		
Grade 11 - 12	23	37		
College/Technicon	4	6		
University	2	3		
Years of Education:	-	-	10.80	2.01
Occupation:				
Professional	2	3		
Business owner, business director, manager	2	3		
Homemaker	1	2		
Sales, administrative, clerk, technician	4	6		
Labourer, cleaner	5	8		
Unemployed	45	73		
Other	3	5		

4.2 Associations Between Diagnostic Group and Demographic Variables

Of the 62 participants, 14 (23%) had MAUD and comorbid ASPD (MAUD+ASPD) whereas 48 (77%) had MAUD without ASPD (MAUD-ASPD). Table 2 depicts the demographic correlates of MAUD+ASPD and MAUD-ASPD.

Significant gender differences (df =1) = 8.05; p = <0.01) were found between the two diagnostic groups, with the MAUD+ASPD mostly being male (N = 9; 64%), and MAUD-ASPD mostly female (N = 37; 77%). No statistically significant differences were found between groups in terms of age (F(1, 60) = 0.83; M = 30.15; SD = 6.64; p = 0.37), level of education (F(1, 60) = 0.23; M = 5.55; SD = 0.82; p = 0.50) and number of years of education (F(1, 60) = 3.22; M = 10.81; SD = 2.02; p = 0.07). With regard to employment status, both groups had comparable high levels of unemployment (71% of MAUD+ASPD, 73% of

MAUD-ASPD); (p = 1.00). There was a significant difference between the two diagnostic groups with regard to their first language (df = 2) = 7.12; p = 0.03), with patients with English as a first language being more common in the MAUD+ASPD group.

Table 2: Comparison of the demographic features of the two diagnostic groups

	MAUD-ASPD	**MAUD+ASPD**	**p-value**
Total	48	14	
Percentages %	77	23	
Gender:			
Male	11 (23%)	9 (64%)	<0.01
Female	37 (77%)	5 (36%)	
Age:			
Mean	29.73	31.57	
Std. Dev	6.55	7.01	
First Language:			
Afrikaans	17 (37%)	2 (14%)	
English	7 (15%)	7 (50%)	<0.01
Combined Afrikaans and English	22 (48%)	5 (36%)	
Years of Education:			
Mean	10.56	11.64	0.07
Std. Dev	2.03	1.78	
Occupation:			
Employed	27%	29%	1.00
Unemployed	73%	71%	

4.3 Association between Diagnostic Group and Illness Severity

As summarized in Table 3, the total sample presented with moderate illness severity (M = 23.76; SD = 10.54). There was no significant difference in levels of illness severity between the two diagnostic groups (F(1, 60) = 0.00; M = 23.76; SD = 10.54; p = 0.90).

Table 3: Comparison of illness severity of the two diagnostic groups

	Y-BOCS Mean	Std. Dev	p-value	Y-BOCS-du Description
MAUD-ASPD	23.71	10.44	0.90	Moderately ill
MAUD+ASPD	23.93	11.30		
Overall	23.76	10.54		

4.4 Association between Diagnostic Group and Psychosocial Functioning

As depicted by Table 4, the total sample presented with moderate overall psychosocial impairment and disability (M = 17.16; SD = 9.38). There were no significant differences between the two diagnostic groups in the overall SDS score ($F(1, 60) = 0.40$; M = 17.16; SD = 9.38; p = 0.92) or on the specific dimensions of work ($F(1, 60) = 0.01$; M = 4.82; SD = 3.45; p = 0.97), social ($F(1, 60) = 0.09$; M = 5.68; SD = 3.49; p = 0.71) or family ($F(1, 60)$ = 0.13; M = 6.47; SD = 3.80; p = 0.89) functioning.

Table 4: Comparison of psychosocial functioning of the two diagnostic groups

	SDS Range	SDS Mean	Std. Dev	SDS Description	p-value
Work					
All cases	0-10	4.82	3.45	Moderately impaired	0.97
MAUD-ASPD		4.79	3.42		
MAUD+ASPD		4.93	3.69		
Social					
All cases	0-10	5.68	3.49	Moderately impaired	0.71
MAUD-ASPD		5.75	3.53		
MAUD+ASPD		5.43	3.44		
Family					
All cases	0-10	6.47	3.80	Markedly impaired	0.89
MAUD-ASPD		6.56	3.70		
MAUD+ASPD		6.14	4.28		

Total					
All cases	0-30	17.16	9.38		
MAUD-ASPD		17.29	9.31	Moderately impaired	0.92
MAUD+ASPD		16.71	9.96		

4.5 Childhood Trauma

The differences in rates and severity of exposure to CT between the diagnostic groups are depicted in Table 5. Overall, 98% (N = 61) of the total sample reported a history of CT. The severity of CT reported in the total sample was moderate to severe (M = 56.56; SD = 22.49). There was no significant difference in severity of overall Childhood Trauma Questionnaire – Short Form (CTQ-SF) scores between the two diagnostic groups (F(1, 60) = 0.72; M = 56.56; SD = 22.49; p = 0.30).

Eighty-seven percent (N = 54) of the sample reported a history of emotional abuse. The rates of emotional abuse in the two diagnostic groups did not differ significantly (df =1) = 0.03; p = 0.86). The severity of emotional abuse in the total sample ranged from moderate to severe (M = 12.85; SD = 5.69). There was no significant difference in severity of emotional abuse between the diagnostic groups (F(1, 60) = 0.73; M = 12.85; SD = 5.69; p = 0.43).

Seventy-three percent (N = 45) of the total sample indicated a history of physical abuse. The rates of physical abuse both diagnostic groups did not differ significantly between the diagnostic groups (df =1) = 1.73; p = 0.18). The severity of physical abuse in the total sample was moderate to severe (M = 11.10; SD = 6.20). There was no significant difference between the diagnostic groups in terms of severity of physical abuse (F(1, 60) = 1.35; M = 11.10; SD = 6.20; p = 0.19).

With regards to sexual trauma, 56% (N = 35) of the total sample reported a history of this type of adversity. The rate of exposure to sexual abuse did not differ significantly between diagnostic groups (df =1) = 0.00; p = 0.95). The severity of sexual abuse in the total

sample was moderate to severe (*M* = 11.15; *SD* = 7.47). Severity of sexual abuse were not significantly different between the two diagnostic groups (*F*(1, 60) = 0.006; *M* = 11.15; *SD* = 7.47; *p* = 0.96).

Eighty-four percent (*N* = 52) of the total sample reported a history of emotional neglect. The rate of exposure to emotional neglect did not differ significantly between diagnostic groups (*df* =1) = 1.25; *p* = 0.26). The severity of emotional neglect in the total sample was low to moderate (*M* = 11.61; *SD* = 5.44). Severity of emotional neglect between the two groups was not significantly different (*F*(1, 60) = 0.59; *M* = 11.61; *SD* = 5.45); *p* = 0.70).

Seventy-nine percent (*N* = 49) of the total sample reported histories of physical neglect. The rate of exposure to physical neglect did not differ significantly between diagnostic groups (*df* =1) = 2.49; *p* = 0.11). The severity of physical neglect across the total sample was borderline moderate to severe (*M* = 9.85; *SD* = 4.23). Statistical significance was reached for differences in physical neglect between the two diagnostic groups (*F*(1, 60) = 2.33; *M* = 9.85; *SD* = 4.23; *p* = 0.04), with the MAUD+ASPD group reporting higher levels of childhood physical neglect.

Table 5: Comparison of rates and severity of exposure to CT between the two diagnostic groups

	CTQ-SF Range	**Mean**	**Std. Dev**	**Rate**	**p-value (rate)**	**CTQ-SF Description**	**p-value (severity)**
Emotional abuse							
All cases	5-25	12.85	5.69	87%	0.86	Borderline moderate to severe	0.43
MAUD-ASPD		12.52	5.56	87%		Borderline moderate to severe	
MAUD+ASPD		14,00	6.16	85%		Moderate to severe	
Physical abuse							
All cases	5-25	11.1	6.2	73%		Moderate to severe	

MAUD-ASPD		10.6	6.07	68%	0.18	Moderate to severe	0.19
MAUD+ASPD		12.79	6.55	85%		Borderline severe and extreme	
Sexual abuse							
All cases	5-25	11.15	7.47	56%	0.95	Moderate to severe	0.96
MAUD-ASPD		11.19	7.71	56%		Moderate to severe	
MAUD+ASPD		11,00	6.87	57%		Moderate to severe	
Emotional neglect							
All cases	5-25	11.61	5.45	84%	0.26	Low to moderate	0.70
MAUD-ASPD		11.52	5.54	81%		Low to moderate	
MAUD+ASPD		11.93	5.3	92%		Low to moderate	
Physical neglect							
All cases	5-25	9.85	4.22	79%	0.11	Borderline moderate to severe	0.04
MAUD-ASPD		9.42	4.4	75%		Low to moderate	
MAUD+ASPD		11.36	3.25	92%		Moderate to severe	
CTQ total							
All cases	25-125	56.56	22.49	98%		Moderate to severe	0.30
MAUD-ASPD		55.25	22.88	-		Moderate to severe	
MAUD+ASPD		61.07	21.28	-		Moderate to severe	

4.6 Predicting Group Membership

The bivariate analyses suggested significant group differences in terms of gender, language, and physical neglect, with MAUD+ASPD group members significantly more likely than the MAUD-ASPD group to be male, to be English-speaking and to have higher rates of childhood physical neglect.

Standard logistic regression was performed to explore the simultaneous contribution of these three variables in predicting group membership. First, a test of all effects (indicated in Table 6) was performed on the variables (i.e. gender, language, and physical neglect) that reached statistical significance with bivariate analysis. Gender ($p = 0.01$) and language ($p = 0.03$) were predictors of diagnostic group.

As shown in Table 7, odds ratios were then calculated, with the male gender being a significant predictor of being diagnosed with comorbid ASPD (beta = 1.08; *OR* = 8.65; p =

0.01). Male gender increased the probability to be diagnosed with comorbid ASPD more than eight times. Language was also a significant predictor ($p = 0.03$) of group membership, with English as first language increasing the odds more than 11 times to be diagnosed with comorbid ASPD (beta = 1.55; *OR* = 11.38; $p = 0.01$). However, severity of physical neglect was not a significant predictor of a diagnosis of comorbid ASPD ($p = 0.10$) when considered simultaneously with gender and language.

Table 6: Test of all effects for predicting group membership

	Wald Statistic	***p*-value**
Gender	6.87	0.01
Language	7.34	0.03
Physical neglect	2.74	0.10

Table 7: Odds ratios of predictors for MAUD+ASPD

	Odds ratio	Regression coefficient	CL lower	CL upper	*p*-value
Gender: Male	8.65	1.08	1.72	43.39	0.01
Language: English	11.38	1.55	1.65	78.61	0.01
Physical neglect	1.17	0.15	0.97	1.40	0.10

4.7 Conclusion

This chapter presented the results of this study. Bivariate analyses found that there were significant differences between the MAUD+ASPD group and the MAUD-ASPD group in terms of gender, language, and histories of severity of physical neglect. The logistic regression showed that MAUD+ASPD were predicted only by male gender and English as a first language.

CHAPTER FIVE

DISCUSSION

The aim of this study was to describe and compare sociodemographic, childhood trauma (CT) and clinical severity variables between patients with a primary diagnosis of methamphetamine use disorder (MAUD) with and without antisocial personality disorder (ASPD) and without ASPD, and to determine the contribution of these variables in predicting MAUD+ASPD. This chapter will discuss the study findings in light of existing literature, consider the limitations of the study, and propose some recommendations for future research.

5.1. Rates of Methamphetamine Use Disorder with comorbid Antisocial Personality Disorder

Of the 62 participants that were included in the study, almost a quarter (23%) were diagnosed with comorbid ASPD. Substance use disorders (SUDs) and ASPD often co-occur (Sakai et al., 2004) and it has widely been accepted that ASPD has strong associations with stimulant use disorders (APA, 2013). International research in MA-using populations has shown that patients often present with antisocial traits, but varying prevalence rates for this dual diagnosis have been reported (Cohen et al., 2007; Fletcher & Reback, 2013). . In this study MAUD+ASPD was markedly lower than what was found in international works by Lecomte et al. (2010) who reported rates of 68% and Fletcher and Reback (2013) who found prevalence rates of 34%. The high rates found in these studies may be accounted for by the sampling methods used. Lecomte and colleagues sampled patients from emergency rooms at local hospitals, who presented with MA psychosis and who were homeless. The authors highlighted that ASPD was prevalent among patients with severe mental illness (such as schizophrenia/psychosis) and individuals with housing instability (Lecomte et al., 2010). Similar to Lecomte et al. (2010), Fletcher and Reback (2013) sampled only male participants

who were homeless and did not seek treatment for MA abuse. The lower rates found in our study might be accounted for by the predominance of female participants in this sample.

As discussed in Chapter 2, there are a number of possible reasons for the high prevalence of ASPD in MAUD. Chronic use of MA often leads to long-lasting neurological changes that may result in psychiatric problems even after use has stopped (Aronson, 2016) and a dual diagnosis of MAUD+ASPD can be accounted for by diagnostic similarity of both disorders. In general, SUDs and ASPD share common underlying diagnostic features (Brook et al., 2016; Dellazizzo et al., 2018; Rzhetsky et al., 2007; Smith et al., 2014; Trull et al., 2000). These may include genetic, behavioural or cognitive factors (Rzhetsky et al., 2007; Smith et al., 2014) which accompany antisocial behaviours, such as criminality and violence (Cohen et al., 2007) and are often implicated in a diagnosis of ASPD and seen in MAUD (APA, 2013).

In conclusion, this study found that a substantial minority of the sample has MAUD+ASPD, although the rate was lower than has been reported in previous international studies. However, this finding should be interpreted as preliminary as the sample size was small and the use of larger and more representative South African cohorts may yield a different prevalence rate.

5.2 Demographic Features of the Sample

The majority (93%) of participants from this study were of mixed-ancestry. The high rates of participants that were of mixed ancestry may be accounted for by the catchment areas of the referral sites (e.g. non-governmental organizations that specifically provide services to people with substance use disorders who can not afford private healthcare fees) and location of such referral sites, treatment-seeking patterns, and there may be several other reasons related to the sampling procedures for this study. Further, ethnicity was not associated with

MAUD+ASPD and did not pose an increased risk for the relevant dual comorbidity in this sample.

International research on gender and MA use has revealed mixed results (e.g. Cohen, Greenberg, Uri, Halpin, & Zweben, 2007; Simpson et al., 2016). However, local research indicates that the majority of patients who use MA are male (e.g. Watt et al., 2014). In contrast, in this South African study, the majority of participants were female. This discrepancy could be explained by our recruitment strategy, i.e. interviewing a large cohort of patients from an inpatient-treatment-centre that provided care only for females with substance use and associated problems.

The mean age of the participants in this sample was 30 years and was slightly higher than what has been found in other South African studies (Akindipe et al., 2014). In line with other research, it appears that MA use and MAUD are common among younger individuals (e.g. Akindipe et al., 2014). The finding that almost half the sample in the current study were persons with lower levels of education (48% of participants only had an educational level between grades eight to 10 and only nine percent of the sample had education further than high school) may again reflect the sampling bias of the study (recruiting mainly from state services and non-governmental organizations), but is in line with much previous international and local research that indicates lower educational attainment among populations with MUAD (e.g. Akindipe et al., 2014; Cservenka & Ray, 2017; Harker et al., 2008; Lecompte et al., 2010; Meade et al., 2012; Polcin et al., 2012; Semple et al., 2005; Watt et al., 2014). By contrast, Eslami-Shahrbabaki et al. (2015) reported a higher level of education an Iranian sample of psychiatric patients diagnosed and hospitalized for MA-psychosis, where the majority had education on diploma level. One local study highlighted that MA use often led to school dropout (Watt et al., 2014). However, it must be highlighted that the current study did not investigate at which stage/level of schooling MA use was

initiated. Thus, we can not infer that MA use lead to lower levels of educational attainment in this sample.

A large majority of the patients (almost three quarters) were unemployed. South Africa is known to have one of the highest levels of unemployment in the world (Burger & Fourie, 2019) and our finding may simply reflect the high levels of unemployment in the country. However, considering the psychosocial impact of stimulants (APA, 2013) such as MA, it is also possible that users may have difficulty to successfully obtain or maintain employment. One of the hallmarks of MAUD is a failure to fulfil major role obligations at work which, perhaps, in some cases, may have lead to dismissal of employment (APA, 2013). Methamphetamine use may often interfere and limit future career prospects (Watt et al., 2014). Furthermore, South African laws on substance use and the work place may also be a contributing factor that impacts unemployment in this sample. South African labour law implemented processes that ultimately can lead to dismissal of employees that test positive on routine drug tests at work (The South African Labour Guide, 2019). As the sample was predominantly female, it might also explain the general high rates of unemployment, as previous works have found that women who use MA are often unemployed or underemployed (Cohen et al., 2007). It is also possible that the high level of unemployment in the sample reflects the referral sources from which the participants were drawn as most referrals were from government rather than private settings.

5.3 Demographic Factors Associated with Comorbid Antisocial Personality Disorder

The study found that there were few significant sociodemographic differences between the two diagnostic groups. An expected finding was the significant difference in gender between the two diagnostic groups. The MAUD+ASPD group was predominantly male and the MAUD-ASPD group predominantly female. The MAUD+ASPD group had almost double

the number of males (N = 9) compared to females (N = 5). The link between ASPD and male gender has repeatedly been reported in the literature (e.g. Yang & Coid, 2007) and the predominance of males in the ASPD group is moreover consistent with recent findings that men who use MA are more likely to present as antisocial compared to women who use MA (Chun et al., 2017; Polcin et al., 2012). Other authors have suggested that ASPD may be underdiagnosed in females, due to the emphasis on aggressive items in the definition of conduct disorder, for which traits have to be prominent since childhood to be able to make a diagnosis of ASPD (APA, 2013). The sex-paradox or group resistance hypothesis suggests that females may have a higher etiological threshold for the development of ASPD as females are often raised with a gender-role that minimizes acts of violence (Yang & Coid, 2007). Additionally, other research on gender in ASPD has implicated neurological factors to account for the increased prevalence among males (Raine et al., 2011). This may also account for the predominance of males in the MAUD+ASPD group.

There was a significant difference between the two diagnostic groups with regards to language, with English-only speakers being significantly more prevalent in the MAUD+ASPD group. This finding should, however, be interpreted with caution as it might not hold an accurate reflection of the participant's proficiency in home language or mother tongue. Many of these participants may have come from homes that spoke Afrikaans only or both Afrikaans and English, but for reasons that were not explored further chose to indicate English as their mother tongue in the interview.

No difference was found between the two diagnostic groups with regard to age, ethinicity, or education. The findings on age and ethnicity were not unexpected, as the study-sample had a relatively narrow age range (18-44 years) and a large majority (90%) of patients were of mixed-ancestry.

The unemployment rates in both groups were similarly high. Thus, the study suggests that a comorbid diagnosis of ASPD does not result in an increased risk to be unemployed, probably because the comorbid diagnosis of ASPD was not associated with greater illness severity and psychosocial disability. Overall, other than male gender and English as first language, sociodemographic factors were not significantly correlated with the MAUD+ASPD dual diagnosis, suggesting that other factors may better account for the presence of this comorbidity in the current sample.

5.4 Association of Childhood Trauma with Methamphetamine Use Disorder

In line with other works, this study showed that, in general, exposure to childhood trauma in the MAUD population is high. Ninety-eight percent of the participants in this study reported a history of exposure to CT. This rate is notably higher when compared to local research by Slopen et al. (2010) who found that only 41% of their adult participants from the general South African population reported a history of childhood adversity. It was also markedly higher than the rates of 50% reported in a study by Ding and colleagues (2014) who investigated CT in patients with a history of MA use. In the current sample, the highest rates of adversity were reported for emotional abuse (87%) and emotional neglect (84%). These are notably higher than what has been reported in general population studies of both adolescents (Ward, Artz, Leoschut, Kassanjee, & Burton, 2018, 2018) and adults (Machisa et al., 2016) in South Africa. It was also almost double the rate found in international works that investigated emotional adversity in MA using patients (Ding et al., 2014). Similarly, high rates were reported in terms of exposure to physical abuse (73%) and physical neglect (79%). Physical abuse was also greatly higher than what has been reported in retrospective studies done with nationally representative samples of adolescents (18%; Ward et al, 2018) and adults (a rate of 19% was reported in the South African Stress and Health Study) (Kaminer et

al., 2008; Slopen et al., 2010). Sexual abuse, although high (56%), was lower compared to the other forms of abuse in the total MAUD sample. It was notably higher than what has been reported in other local research that explored childhood sexual abuse in MA using (Berg et al., 2017) and general populations (12%; Ward et al., 2018). Some authors have suggested that disclosure of sexually related trauma or abuse is more likely in research using confidential and self-completed questionnaires (Ward et al., 2018). The CTQ-SF was a self-report questionnaire and perhaps this may account for the high rates that were found in this study.

In general, the findings of the current study suggest that histories of childhood trauma may be particularly prevalent in South Africans with MAUD compared to the general South African population. The severity of overall CT reported in the sample was moderate to severe. Moderate to severe levels were reported for physical abuse, sexual abuse and physical neglect. Emotional abuse reached borderline scores of moderate to severe levels. Emotional neglect also had lower levels compared to the other abuse and was only low to moderate. Overall, the severity of CT and the specific forms thereof were higher that what has been reported in a multinational (including South Africa) study that included community and clinical participants (MacDonald et al., 2016). Additionally, the mean scores of the severity of overall CT and specific forms thereof were greater in our study than what has been reported in previous international samples of substance-using participants (Bernstein et al., 2002). Thus, the findings from our study suggest that this sample may have had both greater exposure and more severe histories of overall CT and of specific forms of childhood trauma than what has been found in other works. Some studies have shown that, in general, people with substance use disorders are likely to have significant histories and higher rates of CT (Ekinci & Kandemir, 2015) compared to non-using populations (Bernstein et al., 2003; Hogarth et al., 2019). It has been suggested that women, compared to men, report the most

extensive histories of childhood abuse in MAUD populations (Messina et al., 2008). The predominance of females in this sample may account for the high rates of trauma reported.

It has been suggested that a better understanding of the association of CT between SUDs and psychiatric comorbidity may inform treatment intervention strategies and medical treatment programs to enhance positive health outcomes for users who are living with psychological consequences of childhood abuse (Lopez-Patton et al., 2016). Our findings emphasise that there is a need for further research, with larger and more gender-balanced local-samples, to explore and recognise the prominence of CT histories in populations with MAUD and factor this into treatment approaches.

5.4.1 Childhood Trauma and Group Membership

This study explored differences in CT between the diagnostic groups. Literature suggests that people with MAUD with a history of CT have increased risk to have a comorbid diagnosis of ASPD (Lecomte et al., 2010) and Messina et al. (2008) found that populations who use MA and who have a diagnosis of ASPD report greater experiences of childhood abuse compared to those without ASPD. However, this study found no significant differences in rates of exposure to overall CT, physical abuse and neglect, sexual abuse, and emotional abuse between the MAUD+ASPD and MAUD-ASPD groups.

Similarly, there was no difference between the diagnostic groups in overall severity of CT, with both diagnostic groups reporting moderate to severe overall histories. Further, this study found no diagnostic group differences in severity of CT for emotional abuse and neglect, physical abuse, or sexual abuse between the two diagnostic groups. However, statistical significance was reached in differences between the two diagnostic groups for the severity of physical neglect. The MAUD+ASPD group reported higher levels of childhood physical neglect. Some works have highlighted associations between physical maltreatment

and both MAUD (Lopez-Patton et al., 2016) and ASPD (Sher et al., 2015). While bivariate analyses in the current study suggest that (increased) severity of physical neglect was associated with a comorbid diagnosis of ASPD in this sample, this relationship was not sustained when physical neglect was considered simultaneously with other variables in a regression analysis. In the bivariate analysis, physical neglect may therefore have been a proxy for one of the other variables that were later included in the regression analysis, such as gender.

Overall, this study found no significant association between CT exposure or severity and comorbid ASPD in participants with MAUD, suggesting that other unexplored factors may account for the MAUD+ASPD comorbidity in this sample.

5.5 Illness Severity and Psychosocial Disability

Another objective of this study was to compare illness severity and psychosocial disability between MAUD+ASPD and MAUD-ASPD. This study found that the overall sample described their illness severity as mild and with moderate psychosocial impairment. A noteworthy finding was that the patients in this sample presented with lower illness severity compared to other works that used similar measures to investigate illness severity in people with MAUD (Grant et al., 2010). This was an unexpected finding, as research has demonstrated that individuals with lower levels of education, like that found in our sample, may be at more risk for increased negative sequela associated with MA use (Eslami-Shahrbabaki et al., 2015). Additionally, there was no difference in illness severity of MA use between the diagnostic groups. Our findings were consistent with other works that also found no significant difference in illness severity between patients with MA use only and patients with MA use and psychiatric comorbidities (Eslami-Shahrbabaki et al., 2015).

It has been widely accepted that MA use affects global functioning (APA, 2013). A recent South African study (Lanesman et al., 2019) showed that individuals with MAUD experience problems on various levels of functioning. Lanesman and colleagues (2019) suggested that individuals with MAUD report negative effects on social, work and family functioning at an interpersonal, intrapersonal, and community level (Lanesman et al., 2019). Overall, the patients in this study presented with moderate impairment and disability. However, overall psychosocial functioning did not differ between the MAUD+ASPD and MAUD-ASPD groups and there were also no differences in specific domains of functioning (work, family, and social). These findings were unexpected as ASPD has often been associated with problems that can have a negative impact on family, social, occupational, and global functioning (APA, 2013). For example, individuals with ASPD often present with irritability, aggressiveness, and impulsivity (APA, 2013) which may negatively affect relationships with family members, in social situations, or with co-workers. Other hallmarks of ASPD are being deceitful, lying, using aliases, or conning others for self profit or pleasure (APA, 2013) and are traits that arguably may lead to impairment on multiple levels of functioning.

An explanation that may account for the lower levels of illness severity and psychosocial impairment reported here is the fact that most participants of this study were recruited from an inpatient treatment centre, where they have received treatment that may have resulted in reduced illness severity and improved psychosocial functioning already.

5.6 Predicting Comorbid Antisocial Personality Disorder in Methamphetamine Use Disorder

The final objective of this study was to determine whether MAUD+ASPD can be predicted by sociodemographic variables and different types and or severity of CT when these are

considered simultaneously. Lawrie and colleauges (2019) suggest that it may be vital to identify risk factors in patients as it could be used to inform patients, carers, and health professionals about how to improve prevention or treatment of psychiatric disorder (Lawrie et al., 2019).

The regression analysis included only those variables found to be significantly associated with MAUD+ASPD in bivariate analyses: gender, language and severity of physical neglect. It must be noted that logistic regression analysis with small samples, such as this study, need to be interpreted with caution as they may result in an overestimation of the odd's ratios. In the regression analysis, language was a predictor for comorbid ASPD, with English-only-speakers having 11 times greater odds of being in the MAUD+ASPD group. Although this may be an interesting finding, we are of the opinion that this should be interpreted with caution. It must be emphasized that the study mainly consisted of three language groups and had a relatively small sample size and, further, professed first language at the interview may not always be participants' actual home language. Disseminating possibly false-positive results may potentially hold deleterious consequences related to prejudice and discrimination in this population (Lawrie et al., 2019). Further exploration in future research is needed for optimal and reliable prediction and to rule out a false-positive result. Additionally, further research is warranted on the role of language as a predictor of MAUD+ASPD as preferred language may be a proxy for other factors linked to ethnicity and class in South Africa.

Another predictor of dual MAUD+ASPD diagnosis was male gender. Being male increased the odds of a comorbid diagnosis of ASPD more than eight times compared to females. This finding was not unexpected, as ample research supports the link between ASPD and the male gender (APA, 2013; Chun et al., 2017; Holzer & Vaughn, 2017; Loots & Louw, 2012; Salyer, 2007). However, during the investigation with bivariate tests it was

found that almost a quarter (23%) of the MAUD-ASPD was male, indicating that not all men with MAUD will have comorbid ASPD. Lawrie and colleagues (2019) emphasize that diagnostic tests normally generate binary outcomes (disease present or absent) and there may be a need for further investigation that will promote individualized predictions (Lawrie et al., 2019) and the identification of specific risk factors for ASPD in males with a primary diagnosis of MAUD.

Moreover, the findings from the logistic regression suggested risk factors that are historically determined and "fixed" (i.e. male gender and English as first language). It is not possible to say which diagnosis (MAUD or ASPD) preceded the other. Nevertheless, comorbid ASPD has been associated with reduced prosocial or health-related behaviours (Fletcher & Reback, 2013), such as less treatment-seeking efforts (Lin et al., 2004), and/or increased psychiatric and physiological sequela (APA, 2013; Callaghan, Cunningham, Sykes, & Kish, 2012; Meredith et al., 2005). Patients with MAUD+ASPD are also more likely to relapse to heavy MA use after treatment (Fridell et al., 2006) and it has been suggested that specialized treatment is needed for patients with a comorbid diagnosis of ASPD (Fletcher & Reback, 2013). Identifying male gender as a significant predictor of MAUD+ASPD in a South African sample suggests that screening of male MAUD patients for ASPD may be indicated during treatment intake. This may ultimately facilitate the selection and the development of prevention and treatment plans to address ASPD comorbidity in MAUD and thus improve outcomes.

5.7 Limitations and Recommendations

This study had several limitations. First, this research project was based on a cross-sectional study design which is particularly suitable for estimating the prevalence of a behaviour or disease in a population (Sedgwick, 2014) and cannot draw firm conclusions about causality

of MAUD and ASPD. Second, it has been recommended that findings in small samples such as that in the current study should only be interpreted as preliminary (Lanesman et al., 2019). The study may have been under-powered to detect significant other differences in sociodemographic variables, CT histories, severity and impairment between the diagnostic groups. Third, together with the small sample size, the use of a clinician-referred, treatment-seeking, volunteer sample also limits the generalizability of the findings to MA dependent individuals within the general (non-treatment seeking) population. Most of the participants of the study were recruited from drug treatment centres, psychiatric institutions, and other health care practitioners. Moreover, as previously mentioned, polysubstance use is rife within populations with MAUD and the findings should also be interpreted with caution as no analysis examined the role of polysubstance in this sample. Finally, this study did not collect data on treatment response in the two groups. This would have yielded valuable information about whether MAUD+ASPD predicts treatment drop-out and treatment outcome in this South African sample, as it has been shown in international studies (Öhlin et al., 2011).

Future research should use larger and more representative samples that, for example, include a broader range of age, ethnic groups, languages, and educational histories, to explore the risk factors and outcomes associated with comorbid ASPD or other personality disorder in MAUD. Such research may hold valuable implications in prevention, treatment, and maintenance of MAUD and MAUD+ASPD. A better understanding of demographic and other risk factors, and of clinical features, may potentially guide the selection of treatment targets, harm reduction strategies, and relapse prevention in MAUD.

5.8 Conclusion

This study examined factors associated with a comorbid diagnosis of ASPD in a treatment-seeking sample of participants with MAUD. Although the presence of comorbid ASPD

(23%) was lower in this sample than in some previous studies, this rate is higher than would be expected in a predominantly female sample and highlights the need for a better understanding of this dual diagnosis. Gender and language differed significantly between the MAUD+ASPD and MAUD-ASPD group, with those in the MAUD+ASPD group more likely to be male and having English as a first language. Men who use MA are thus more prone to antisocial behaviour, which complicates their substance use condition. Lack of motivation, disruptiveness, impulsivity, and general disregard for others, typical of ASPD, may all contribute to lower rates of engagement, retention, and poorer outcomes for individuals undergoing substance abuse treatment, and thus present increased challenges to the treatment setting. The language finding should be treated with some caution and warrants further investigation. Other sociodemographic factors and most aspects of CT history were not associated with MAUD+ASPD in this sample. Severity of physical neglect, while associated with diagnostic group in bivariate analysis, did not maintain significance when considered with gender and language in a regression analysis. Finally, there was no difference in levels of clinical severity of MAUD or psychosocial impairment between the two diagnostic groups. Given the use of a small, treatment-seeking sample, future research using larger, more representative samples may allow for more robust investigation of the correlates of ASPD comorbidity in MAUD.

Acknowledgements

This study was supported by a grant from the South African National Research Foundation (NRF) and Prof Christine Lochner by the SA MRC. I also wish to acknowledge Prof Martin Kidd from the Centre for Statistical Consultation, Department of Statistics and Actuarial Sciences, Stellenbosch University, for assistance with the data analyses.

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Appendix A - Demographics Questionnaire

Participant number: _____Date of Interview _____

DEMOGRAPHICAL QUESTIONNAIRE

Full names: _____ **Surname:** _____

Sex: 1 – male, 2 – female

Interviewer:

Date of Birth: _____

1 – Christine

Participant's Age: _____

2 – Other

Contact Details :

Phone (H): _____ Phone (W): _____

Cell: _____ e-mail: _____

Postal Address: _____

_____

_____

_____

Name & contact number of family member or friend:

_____

_____

Population:

1 – White SA, Afrikaans speaking
2 – White SA, mixed Afrikaans and English
3 – White SA, English-speaking
4 – Coloured
5 – Malaysian

_____

Language (mother tongue):

1 – Afrikaans
2 – Mixed Afrikaans and English
3 – English
4 – African Language
5 – Other Language (German, etc.)

6 – Black

6 – Mixed Afrikaans and other

_____

7 – Indian

8 – Persons from other Asian decent

9 – Jewish

10 –Other: _____

Highest Level of Education (completed):

1 – No School

2 – Grade 1-7

3 – Grade 8-10

4 – Grade 11-12

5 – College / Technicon

6 – University

Occupation:

1 – Professional

2 – Business Owner, Business Director / Manager

3 – Homemaker

4 – Sales, Admin, Clerical, Technician

5 – Laborer / Cleaner

6 – Student

7 – Artist / Musician / Writer

8 – Pensioner

9 – Disability Pensioner

10 – Unemployed

11 – Other: _____

Health:

0. Do you have any known physical or neurological disease? Yes / No. If yes, please specify.

_____

_____

_____

2. What is the date of your last doctor's (GP) visit?

_____

3. Are you currently using any medication? If yes, please specify.

_____

_____

_____

_____

4. Do you have any metal prosthesis (e.g. pacemaker or metal clips)?

_____

5. Name and contact details of physician / psychiatrist

_____

_____

_____

Diagnosis – Current **Diagnosis – Past**

_____ Onset: _____ _____ Onset: _____ End: _____

_____ Onset: _____ _____ Onset: _____ End: _____

_____ Onset: _____ _____ Onset: _____ End: _____

_____ Onset: _____ _____ Onset: _____ End: _____

Appendix B - SCID-RV (for DSM-5®) Module E for Substance Use Disorders

PAST-12-MONTH NON-ALCOHOL SUBSTANCE USE DISORDER

REVIEW HISTORY OF DRUG USE ON PAGES 7-8 OF PATIENT OVERVIEW (OR PAGES 5-6 OF NON-PATIENT OVERVIEW). IF DENIES ANY LIFETIME DRUG USE IN OVERVIEW, CHECK HERE____AND GO TO NEXT MODULE. E38

FOR DRUGS USED IN PAST 12 MONTHS: CODE "3" FOR EACH DRUG CLASS BELOW BASED ON CODING IN RIGHT HAND COLUMN OF OVERVIEW DRUG ASSESSMENT (PATIENT OVERVIEW PAGES 7-8 OR NON-PATIENT OVERVIEW PAGES 5-6). OTHERWISE, CODE "1" FOR THAT DRUG CLASS.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOIDS	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
1	1	1	1	1	1	1	1
E39	E40	E41	E42	E43	E44	E45	E46

IF ALL DRUG CLASSES CODED "1" FOR PERIOD OF PAST 12 MONTHS, CHECK HERE____AND GO TO ****PRIOR-TO-PAST-12-MONTH NON-ALCOHOL SUBSTANCE USE DISORDER**** *E.26.* E47

FOR ALL CLASSES CODED "3" ABOVE, CIRCLE THE APPROPRIATE COLUMN HEADERS (DRUG CLASS NAMES) ON PAGES E.11 TO E.18, BASED ON ONE OF THE FOLLOWING OPTIONS: (Indicate option used with a check mark in front of option)

____***OPTION #1: DETERMINE THE PRESENCE OF SUBSTANCE USE DISORDER IN PAST 12 MONTHS (SINGLE MOST PROBLEMATIC SUBSTANCE).*** E48

Which drug or medication caused you the most problems over the past 12 months, since (1 YEAR AGO)**? Which one did you use the most? (Which was your "drug of choice?")**

START WITH THE DRUG CLASS THAT WAS MOST PROBLEMATIC OR USED THE MOST. RETURN HERE IF CRITERIA ARE NOT MET FOR INITIAL DRUG CLASS AND THERE IS ALSO EVIDENCE OF CLINICALLY SIGNIFICANT USE OF OTHER DRUG CLASSES. ASK ABOUT EACH DRUG CLASS IN SEQUENCE UNTIL EITHER THE CRITERIA ARE MET FOR A SUBSTANCE USE DISORDER IN THE PAST 12 MONTHS OR ELSE NONE OF THE DRUG CLASSES MEET CRTERIA.

____***OPTION #2: DETERMINE PRESENCE OF THE THREE SUBSTANCE CLASSES MOST HEAVILY USED OR MOST PROBLEMATIC IN THE PAST 12 MONTHS.*** E49

Which drugs or medications caused you the most problems over the past 12 months, since (1 YEAR AGO)**? Which ones did you use the most? (Which were your "drugs of choice?")**

____***OPTION #3: DETERMINE PRESENCE OF SUBSTANCE USE DISORDER IN THE PAST 12 MONTHS FOR ALL DRUG CLASSES ABOVE SCREENING THRESHOLD.*** E50

NON-ALCOHOL SUBSTANCE USE DISORDER CRITERIA

Now I'd like to ask you some more questions about your use of (DRUG CLASS[ES] CIRCLED IN COLUMN HEADERS) **in the past 12 months, since** (1 YEAR AGO)**.**

A. A problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by at least two of the following occurring within a 12-month period:

FOR EACH CRITERION, ASK QUESTIONS FOR CIRCLED DRUG CLASS(ES) ONLY:

During the past year, have you found that once you started using (DRUG) **you ended up using much more than you intended to? For example, you planned to have** (SMALL AMOUNT OF DRUG) **but you ended up having much more. (Tell me about that. How often did that happen?)**

IF NO: **What about using** (DRUG) **for a much longer period of time than you were intending to?**

1. The substance is often taken in larger amounts OR over a longer period than was intended.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E51	E52	E53	E54	E55	E56	E57	E58

During the past year, have you wanted to stop or cut down using (DRUG), **or control your use of** (DRUG)**?**

IF YES: **How long did this desire to stop, cut down, or control your use of** (DRUG) **last?**

IF NO: **During the past year, did you ever try to cut down, stop, or control your use of** (DRUG)**? How successful were you? (Did you make more than one attempt to stop, cut down, or control your use of** [DRUG]**?)**

2. There is a persistent desire OR unsuccessful efforts to cut down or control substance use.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E59	E60	E61	E6	E63	E64	E65	E66

During the past year, have you spent a lot of time getting (DRUG) **or using** (DRUG) **or has it taken a lot of time for you to get over the effects of** (DRUG)**? (How much time?)**

3. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E67	E68	E69	E70	E71	E72	E73	E74

Have you had a strong desire or urge to use (DRUG) **in between those times when you were using** (DRUG)**? (Has there been a time when you had such strong urges to use** (DRUG) **that you had trouble thinking about anything else?)**

IF NO: **How about having a strong desire or urge to use** (DRUG) **when you were around people with whom you used** (DRUG)**?**

4. Craving, or a strong desire or urge to use the substance.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E75	E76	E77	E78	E79	E80	E81	E82

During the past year, have you missed work or school or often arrived late because you were intoxicated, high, or recovering from the night before?

IF NO: **How about doing a bad job at work or school, or failing courses or flunking out of school because of your use of** (DRUG)**?**

IF NO: **How about getting into trouble at work or school because of your use of** (DRUG)**?**

IF NO: **How about not taking care of things at home because of your use of** (DRUG)**, like making sure there is food and clean clothes for your family and making sure your children go to school and get medical care? How about not paying your bills?**

IF YES TO ANY: **How often?**

5. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home [(e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)].

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1

IF NOT ALREADY KNOWN: **During the past year, has your use of** (DRUG) **caused problems with other people, such as with family members, friends, or people at work? (Have you found yourself regularly getting into arguments about your** [DRUG] **use? Have you gotten into physical fights when you were taking** [DRUG]**?)**

IF YES: **Have you kept on using** (DRUG) **anyway?**

6. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance [(e.g., arguments with spouse about consequences of intoxication, physical fights)].

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E91	E92	E93	E94	E95	E96	E97	E98

Have you had to give up or reduce the time you spent at work or school, with family or friends, or on your hobbies because you were using (DRUG) **instead?**

7. Important social, occupational, or recreational activities given up or reduced because of substance use.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E99	E100	E101	E102	E103	E104	E105	E106

During the past year, have you ever gotten high before doing something that requires coordination and concentration like driving, boating, climbing on a ladder, or operating heavy machinery?

IF YES: (FOR SUBSTANCES OTHER THAN STIMULANTS): **Would you say that your use of** (DRUG) **affected your coordination or concentration so that it was more likely that you or someone else could have been hurt?**

IF YES: (FOR STIMULANTS ONLY): **Would you say that your being high on** (STIMULANT) **made you drive recklessly like driving very fast or taking unnecessary risks?**

IF YES TO EITHER AND UNKNOWN: **How many times?**

8. Recurrent substance use in situations in which it is physically hazardous [(e.g., driving an automobile or operating a machine when impaired by substance use)].

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E107	E108	E109	E110	E111	E112	E113	E114

Has your use of (DRUG) **during the past year caused you any problems like making you very depressed, irritable, anxious, paranoid, or extremely agitated? What about triggering panic attacks, making it difficult for you to fall or stay asleep, putting you into a "mental fog," or making it so you couldn't recall what happened while you were using** (DRUG)**?**

Has your use of (DRUG) **caused physical problems, like heart palpitations, coughing or trouble breathing, constipation, or skin infections?**

IF YES TO EITHER OF ABOVE: **Have you kept on using** (DRUG) **anyway?**

9. Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance [(e.g., recurrent cocaine use despite recognition of cocaine-related depression)].

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E115	E116	E117	E118	E119	E120	E121	E122

Have you found that you needed to use much more (DRUG) **in order to get the feeling you wanted than when you first started using it?**

IF YES: **How much more?**

IF NO: **What about finding that when you used the same amount, it had much less effect than before?**

IF PRESCRIBED MEDICATION: **Were you taking** (DRUG) **exactly as your doctor told you to? (Did you ever take more of it than was prescribed or run out of your prescription early? Did you ever go to more than one doctor in order to get the amount of medication you wanted?)**

10. Tolerance, as defined by either of the following:

    a. A need for markedly increased amounts of the substance to achieve intoxication or desired effect.

    b. Markedly diminished effect with continued use of the same amount of the substance.

    Note: If opioids, sedative/hypnotic/anxiolytic medications, or stimulant medications are taken solely under appropriate medical supervision, this criterion is not considered to be met.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCINOGENS	OTHER/ UNKNOWN
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
?	?	?	?	?	?	?	?
E123	E124	E125	E126	E127	E128	E129	E130

THE FOLLOWING ITEM DOES NOT APPLY TO INHALANTS, PCP, OR HALLUCINOGENS.

During the past year, have you had any withdrawal symptoms, in other words felt sick when you cut down or stopped using (DRUG)**?**

IF YES: **What symptoms did you have?** *REFER TO LIST OF WITHDRAWAL SYMPTOMS ON E.28.*

IF NO: **After not using** (DRUG) **for a few hours or more, did you sometimes use it or something like it to keep yourself from getting sick with** (WITHDRAWAL SXS)?

11. Withdrawal, as manifested by either of the following:

a. The characteristic withdrawal syndrome for the substance (see page E.28).

b. The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

Note: This criterion does not apply to inhalants, PCP, or hallucinogens.

Note: If opioids, sedatives/hypnotics/anxiolytics medications, or stimulant medications are taken solely under appropriate medical supervision, this criterion is not considered to be met.

SEDATIVE/ HYPNOTIC/ANX	CANNABIS	STIMULANTS	OPIOID	OTHER/ UNKNOWN
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?
E131	E132	E133	E134	E135

PAST-12-MONTH NON-ALCOHOL SUBSTANCE USE DISORDER CODING

	SEDATIVE/ HYPNOTIC ANXIOLYTIC	CANNABIS	STIMULANTS	OPIOID	INHALANTS	PCP	HALLUCIN-OGENS	OTHER/ UNKNOWN
AT LEAST TWO SUBSTANCE USE DISORDER ITEMS CODED "3" FOR THE PAST 12 MONTHS	3 1 E136	3 1 E138	3 1 E140	3 1 E142	3 1 E144	3 1 E146	3 1 E148	3 1 E150
*Indicate **Severity**:* 1 – **Mild**: 2-3 sxs. 2 – **Moderate:** 4-5 sxs. 3 – **Severe:** 6+ sxs.	1=mild 2=mod 3=sev E137	1=mild 2=mod 3=sev E139	1=mild 2=mod 3=sev E141	1=mild 2=mod 3=sev E143	1=mild 2=mod 3=sev E145	1=mild 2=mod 3=sev E147	1=mild 2=mod 3=sev E149	1=mil 2=mo 3=sev E151

IF SELECTED OPTION #1 (MOST PROBLEMATIC SUBSTANCE):

*IF THERE IS EVIDENCE OF CLINICALLY SIGNIFICANT USE OF ANOTHER DRUG CLASS IN PAST 12 MONTHS (OTHER THAN THOSE ALREADY ASSESSED), GO BACK TO E.11 AND RE-ASSESS CRITERIA FOR THAT DRUG CLASS. OTHERWISE, GO TO ***PRIOR-TO-PAST-12-MONTH NON-ALCOHOL SUBSTANCE USE DISORDER*** E.26.*

IF SELECTED OPTION #2 (THREE MOST HEAVILY USED) OR OPTION #3 (ALL DRUG CLASSES AT USE THRESHOLD):

*IF NO DRUG CLASSES CODED "3" (I.E., NO CURRENT [PAST YEAR] SUBSTANCE USE DISORDER), GO TO ***PRIOR-TO-PAST-12-MONTH NON-ALCOHOL SUBSTANCE USE DISORDER*** E.26.*

INDICATE SPECIFIC NAME(S) OF SUBSTANCE(S) FOR WHICH CRITERIA WERE MET (I.E., CODED "3" ABOVE):

Sedatives, Hypnotics, or Anxiolytics _____ E152

Cannabis _____ E153

Stimulants (including cocaine) _____ E154

Opioids _____ E155

Inhalants _____ E156

Phencyclidine and Related Substances _____ E157

Hallucinogens _____ E158

Other or Unknown _____ E159

LIST OF WITHDRAWAL SYMPTOMS (FROM DSM-5 CRITERIA)

Listed below are the characteristic withdrawal syndromes for those classes of psychoactive substances for which a withdrawal syndrome has been identified. (NOTE: A specific withdrawal syndrome has not been identified for PCP, HALLUCINOGENS, OR INHALANTS). Withdrawal symptoms may occur following the cessation of prolonged moderate or heavy use of a psychoactive substance or a reduction in the amount used.

SEDATIVES, HYPNOTICS, AND ANXIOLYTICS:

Two (or more) of the following, developing within several hours to a few days after cessation of (or reduction in) sedative, hypnotic, or anxiolytic use, that has been prolonged:

1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 bpm).
2. Hand tremor.
3. Insomnia.
4. Nausea or vomiting.
5. Transient visual, tactile, or auditory hallucinations or illusions.
6. Psychomotor agitation.
7. Anxiety.
8. Grand mal seizures.

CANNABIS:

Three (or more) of the following signs and symptoms developing within approximately one week after cessation of cannabis use that has been heavy and prolonged (i.e., usually daily or almost daily use over a period of at least a few months):

1. Irritability, anger, or aggression.
2. Nervousness or anxiety.
3. Sleep difficulty (e.g., insomnia, disturbing dreams).
4. Decreased appetite or weight loss.
5. Restlessness.
6. Depressed mood.
7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors,sweating, fever, chills, or headache.

STIMULANTS/COCAINE:

Dysphoric mood AND two (or more) of the following physiological changes, developing within a few hours to several days after cessation of (or reduction in) prolonged amphetamine-type substance, cocaine, or other stimulant use:

1. Fatigue.
2. Vivid, unpleasant dreams.
3. Insomnia or hypersomnia.
4. Increased appetite.
5. Psychomotor retardation or agitation.

OPIOIDS:

Three (or more) of the following, developing within minutes to several days after cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer) or after administration of an opioid antagonist after a period of opioid use:

1. Dysphoric mood.
2. Nausea or vomiting.
3. Muscle aches.
4. Lacrimation or rhinorrhea (runny nose)
5. Pupillary dilation, piloerection ("goose bumps"), or sweating.
6. Diarrhea.
7. Yawning.
8. Fever.
9. Insomnia.

Appendix C - MINI – Antisocial Personality Disorder

(" ▸ ▸ MEANS : GO TO THE DIAGNOSTIC BOX AND CIRCLE NO.)

P1 **Before you were 15 years old, did you:**

a. repeatedly skip school or run away from home overnight? NO YES

b. repeatedly lie, cheat, "con" others, or steal? NO YES

c. start fights or bully, threaten, or intimidate others? NO YES

d. deliberately destroy things or start fires? NO YES

e. deliberately hurt animals or people? NO YES

f. force someone to have sex with you? NO YES

ARE **2** OR MORE **P1** ANSWERS CODED **YES**? NO ▸ ▸ YES

DO NOT CODE **YES** TO THE BEHAVIORS BELOW IF THEY ARE EXCLUSIVELY POLITICALLY OR RELIGIOUSLY MOTIVATED**.**

P2 **Since you were 15 years old, have you:**

a. repeatedly behaved in a way that others would consider irresponsible, like failing to pay for things you owed, deliberately being impulsive or deliberately not working to support yourself?

NO YES

b. done things that are illegal even if you didn't get caught (for example, destroying property, shoplifting, stealing, selling drugs, or committing a felony)?

NO YES

c. been in physical fights repeatedly (including physical fights with your spouse or children)?

NO YES

d. often lied or "conned" other people to get money or pleasure, or lied just for fun?

NO YES

e. exposed others to danger without caring?

NO YES

f. felt no guilt after hurting, mistreating, lying to, or stealing from others, or after damaging property?

NO YES

ARE **3** OR MORE **P2** QUESTIONS CODED **YES**?

NO **YES = *ANTISOCIAL PERSONALITY DISORDER* LIFETIME**

Appendix D - Childhood Trauma Questionnaire

Instructions: These questions ask about some of your experiences growing up **as a child and a teenager**. For each question, circle the number that best describes how you feel. Although some of these questions are of a personal nature, please try to answer as honestly as you can. Your answers will be kept confidential.

When I was growing up, …	**Never True**	**Rarely True**	**Sometimes**	**Often True**	**Very Often**
1. I didn't have enough to eat.	**1**	**2**	**3**	**4**	**5**
2. I knew there was someone to take care of me and protect me	**1**	**2**	**3**	**4**	**5**
3. People in my family called me things like "stupid", "lazy", or "ugly".	**1**	**2**	**3**	**4**	**5**
4. My parents were too drunk or high to take care of me.	**1**	**2**	**3**	**4**	**5**
5. There was someone in my family who helped me feel important or special.	**1**	**2**	**3**	**4**	**5**
6. I had to wear dirty clothes.	**1**	**2**	**3**	**4**	**5**
7. I felt loved.	**1**	**2**	**3**	**4**	**5**
8. I thought that my parents wished I had never been born.	**1**	**2**	**3**	**4**	**5**
9. I got hit so hard by someone in my family that I had to see a doctor or go to the hospital.	**1**	**2**	**3**	**4**	**5**
10. There was nothing I wanted to change about my family.	**1**	**2**	**3**	**4**	**5**
11. People in my family hit me so hard that it left bruises or marks.	**1**	**2**	**3**	**4**	**5**
12. I was punished with a belt, a board, a cord, or some hard object.	**1**	**2**	**3**	**4**	**5**
13. People in my family looked out for each other.	**1**	**2**	**3**	**4**	**5**
14. People in my family said hurtful or insulting things to me.	**1**	**2**	**3**	**4**	**5**
15. I believe that I was physically abused.	**1**	**2**	**3**	**4**	**5**
16. I had the perfect childhood.	**1**	**2**	**3**	**4**	**5**
17. I got hit or beaten so badly that it was noticed by someone like a teacher, neighbour, or doctor.	**1**	**2**	**3**	**4**	**5**

18. I felt that someone in my family hated me.	**1**	**2**	**3**	**4**	**5**
19. People in my family felt close to each other.	**1**	**2**	**3**	**4**	**5**
20. Someone tried to touch me in a sexual way, or tried to make me touch them.	**1**	**2**	**3**	**4**	**5**
21. Someone threatened to hurt me or tell lies about me unless I did something sexual with them.	**1**	**2**	**3**	**4**	**5**
22. I had the best family in the world.	**1**	**2**	**3**	**4**	**5**
23. Someone tried to make me do sexual things or make me watch sexual things.	**1**	**2**	**3**	**4**	**5**
24. Someone molested me.	**1**	**2**	**3**	**4**	**5**
25. I believe that I was emotionally abused.	**1**	**2**	**3**	**4**	**5**
26. There was someone to take me to the doctor if I needed it.	**1**	**2**	**3**	**4**	**5**
27. I believe that I was sexually abused	**1**	**2**	**3**	**4**	**5**
28. My family was a source of strength and support.	**1**	**2**	**3**	**4**	**5**

Appendix E – Yale Brow Obsessive Compulsive Scale (adapted for drug use)

Obsessive subscale – Questions 1 to 5

1. How much of your time (when you've gone without using meth for 1 or 2 days) is occupied by ideas, thoughts, impulses or images related to meth/tik use? How frequently do these thoughts occur?

   ☐ **0 = None**

   ☐ **1 = Mild (Less than 1 hour** a day), or occasional intrusion (occur no more than 8 times a day)

   ☐ **2 = Moderate (1-3 hours** a day), or frequent intrusion (occur more than 8 times a day, but most hours of the day are free of these thoughts)

   ☐ **3= Severe (4-8 hours** a day), or very frequent intrusion (occur more than 8 times a day and occur during most hours of the day)

   ☐ **4 = Extreme (Greater than 8 hours** a day), or near constant intrusion (too numerous to count and an hour rarely passes without several such thoughts occurring

2. How much do the thoughts, impulses or images related to meth use interfere with your social or work (or role) functioning (1 to 2 days after the last time you used)? Is there anything you don't do because of them?

   ☐ **0 = None**

   ☐ **1 = Mild**, slight interference with social or occupational activities, but overall performance not impaired

   ☐ **2 = Moderate**, definite interference with social or occupational performance, but still manageable

   ☐ **3 = Severe**, causes substantial impairment in social or occupational performance

   ☐ **4 = Extreme**, incapacitating

3. How much distress do these ideas, thoughts, impulses or images related to meth use cause you (when you've done without using meth for 1 to 2 days)?

   ☐ **0 = None**

   ☐ **1 = Mild**, infrequent and not too disturbing

   ☐ **2 = Moderate**, frequent and disturbing, but still manageable

   ☐ **3 = Severe**, very frequent and very disturbing

   ☐ **4 = Extreme**, near constant, and disabling distress

4. How much of an effort do you make to resist these thoughts (when you've gone without using meth for 1 to 2 days)? How often do you try to disregard or turn your attention away from these thoughts as they enter your mind (when you've done without using meth for 1 to 2 days)? *(Only rate effort made to resist, not success or failure in actually controlling these thoughts.)**

   ☐ **0** = Makes an **effort to always resist**, or symptoms are so minimal, **doesn't need to actively resist**

   ☐ **1** = Tries to **resist most of the time**

   ☐ **2** = Makes **some effort to resist**

   ☐ **3** = **Yields to all** such thoughts without attempting to control them, but does so with some **reluctance**

   ☐ **4** = **Completely and willingly yields** to all such thoughts

5. How much control do you have over these thoughts (when you've gone without using meth for 1 to 2 days)? How successful are you in stopping or diverting such thinking?

☐ **0** = **Complete control**

☐ **1** = **Much control**, usually able to stop or divert such thoughts with some effort and concentration

☐ **2 = Moderate control**, sometimes able to stop or divert such thoughts

☐ **3** = **Little control**, rarely successful in stopping such thoughts, can only divert such thoughts with difficulty

☐ **4** = **No control**, experienced as completely involuntary, rarely able to divert thinking even momentarily

Compulsive Subscale – Questions 6 to 10

6. How much time per day do you spend using meth? (i.e. time spent getting and smoking tik *[the clinician should take into account the amount of time as well as the frequency of the behavior per day]*)

☐ **0 = None**

☐ **1 = Mild (Spend less than 1 hour** a day), or occasional use

☐ **2 = Moderate (1-3 hours** a day), or frequent use

☐ **3= Severe (4-8 hours** a day), or very frequent use

☐ **4 = Extreme (Greater than 8 hours** a day), or near constant use

7. How much does your meth use interfere with your social or work (or role) functioning? Is there anything you don't do because of your meth use? *(If currently not working, determine how much performance would be affected if subject were employed.)*

☐ **0 = None**

☐ **1 = Mild**, slight interference with social or occupational activities, but overall performance not impaired

☐ **2 = Moderate**, definite interference with social or occupational performance, but still manageable

☐ **3 = Severe**, causes substantial impairment in social or occupational performance

☐ **4 = Extreme**, incapacitating

8. How would you feel if prevented from using meth when you wanted to use? How anxious or upset would you become? *(Rate degree of distress subject would experience if meth use were suddenly interrupted without reassurance offered.)*

☐ **0 = None**

☐ **1 = Mild**, only slightly anxious or irritated if meth use prevented

☐ **2 = Moderate**, reports that anxiety or irritation would mount but remain manageable if meth use prevented

☐ **3 = Severe**, prominent and very disturbing increase in anxiety or irritation if meth use interrupted

☐ **4 = Extreme**, incapacitating anxiety or irritation from any intervention aimed at modifying meth use

9. How much of an effort do you make to resist using meth?

*(Only rate effort made to resist, not success or failure in actually controlling meth use.)**

☐ **0** = Makes an **effort to always resist**, or meth use is so minimal, **doesn't need to actively resist**

☐ **1** = Tries to **resist most of the time**

☐ **2** = Makes **some effort to resist**

☐ **3** = **Yields to all** meth use without attempting to control it, but does so with some **reluctance**

☐ **4** = **Completely and willingly yields** to all meth use

10. How strong is the drive to use meth? How much control do you have over the meth use?

☐ **0** = **Complete control**

☐ **1** = **Much control**, experiences pressure to use meth, but usually able to exercise voluntary control over it

☐ **2 = Moderate control**, strong pressure to use meth, can control it only with difficulty

☐ **3** = **Little control**, very strong drive to use meth, must be carried to completion, can only delay with difficulty

☐ **4** = **No control**, drive to use meth experiences as completely involuntary and overpowering, rarely able to delay meth use even momentarily

Appendix F - Sheehan Disability Scale (SDS)

Please circle the number that best describes the way you have felt over the **past month**

1.) Work

These symptoms have disrupted your work

Not at all Mildly Moderately Markedly Extremely

0 1 2 3 4 5 6 7 8 9 10

2.) Social Life

These symptoms have disrupted your social life

Not at all Mildly Moderately Markedly Extremely

0 1 2 3 4 5 6 7 8 9 10

3.) Family life/Home responsibilities

These symptoms have disrupted your family life/home responsibilities

Not at all Mildly Moderately Markedly Extremely

0 1 2 3 4 5 6 7 8 9 10

Appendix G - SA MRC Unit's Consent Form

PARTICIPANT INFORMATION AND INFORMED CONSENT FORM

(PATIENTS)

TITLE OF RESEARCH PROJECT: Gambling disorder and methamphetamine use disorder: A neurocognitive, genetic and neuroimaging study

REFERENCE NUMBERS: **SU HREC:** N14/05/053

UCT HREC: 770/2014

PRINCIPAL INVESTIGATORS: **SU:** Prof Christine Lochner

UCT: Prof Dan Stein

ADDRESS: MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University

CONTACT NUMBERS: Lochner: 021 – 938 9179; Stein: 021 – 404 2174

We would like to invite you to participate in a research study that involves genetic analysis and possible long-term storage of blood or tissue specimens. Please take some time to read the information presented here which will explain the details of this project. Please ask the study staff any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part initially.

This research study has been approved by the **Health Research Ethics Committee at Stellenbosch University and the Human Research Ethics Committee at the University of Cape Town** and it will be conducted according to international and locally accepted ethical guidelines for research, namely the Declaration of Helsinki, and the SA Department of Health's 2004 Guidelines: *Ethics in Health Research: Principles, Structures and Processes.*

What is Genetic research?

Genetic material, also called DNA, is usually obtained from a small blood sample. Occasionally genetic material is obtained from other sources such as saliva. Genes are found in every cell in the human body. Our genes determine what we look like and sometimes our susceptibility to certain kinds of diseases. Worldwide, researchers in the field of genetics are continuously discovering new information. This information may be of great benefit to both future generations and people today, who suffer from particular diseases or conditions.

What does this particular research study involve?

This study is part of a research project we are conducting to learn more about gambling disorder and methamphetamine use disorder.

Doctors and scientists at the MRC Unit on Risk and Resilience in Mental Disorders, University of Stellenbosch, and the Department of Psychiatry, University of Cape Town, are collaborating with researchers from other research institutions worldwide to investigate the structure and functioning of selected brain areas in 40 individuals with gambling disorder and 40 individuals with methamphetamine use disorder. This study also aims to identify the genes that may increase the risk for the development of these conditions. Information from patients will be compared with 40 age- and gender-matched healthy controls.

This is not a treatment study. Information is being collected for research purposes only.

Why have you been invited to participate?

You have been invited to participate because you have indicated (either to your doctor, or to the National Responsible Gambling Programme's telephone counselling line which is affiliated with UCT's Addiction division) that you excessively gamble or use methamphetamine ("tik") to the extent that it affects your functioning.

Gambling disorder (GD) or pathological gambling can be defined as the inability to resist the urge to gamble despite severely negative personal or social consequences. Similarly, methamphetamine use disorder (MAUD) refers to the inability to resist taking the drug, and is often associated with repeated unsuccessful attempts to cut down, resulting in a failure to fulfill major obligations at work, school or home.

What procedures will be involved in this research?

If you decide to participate, we will ask you to attend 2-4 sessions, each with a different study focus.

The first session will comprise an interview with a researcher and the drawing of bloods. These procedures will last approximately 3-4 hours (with a break in-between, if need be). Depending on the preferences of your treatment centre, this session may be broken up into two sessions and the drawing of bloods and completion of questionnaires may be conducted in a group setting. The clinical interview will, amongst other things, include a number of questions related to gambling or methamphetamine use and your prior psychiatric history. Approximately 20 ml (4 teaspoons) of blood will be drawn from your arm. We may need to contact you again to

get another blood sample should we fail to get a DNA sample (the genetic material) from your blood. The blood sample you give may be used to create a cell line. A cell line is living tissue that can be used to make more of your DNA at any time in the future. Genetic material previously found to be associated with gambling disorder which may also play a role in brain activity, will also be investigated. This process will take place at the Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, at the University of Stellenbosch. Should you not wish to provide us with a blood sample, you may provide us with a saliva sample instead.

The second session will involve 2 hours of brain scanning followed by neuropsychological testing (i.e. computer based tasks to test abilities such as decision making) of approximately 1.5 hours' duration. This session may also be broken up into two sessions, depending on your or your treatment centre's preference, as well as transport availability. MRI (brain scanning) makes use of magnetic fields and radio waves to examine internal structures of the body. The procedure is non-invasive and completely harmless. No 108onizing radiation (such as X-rays) or radio-active material are used during the study. MRI is particularly useful for imaging soft tissue such as the brain. It is capable of measuring certain characteristics of brain function. The procedure requires that you lie on your back with your head in a "tunnel" which is very similar to a CAT scan machine. The tunnel is open on both sides and is well lit and ventilated. You will at all times be in intercom contact with the radiographer, who will also be able to see you at all times. The examination will take about 90 minutes (with breaks if needed) and will be accompanied by a series of loud knocking sounds. There are no moving parts within the scanner, and the knocking sounds occur due to vibration of the machine in the magnetic fields. In some instances, the intravenous administration of contrast agent is also necessary, but you

will be notified in advance about this. Finally, it is important that you do not move at any stage during the examination as this makes the images blurry.

The initial screening and assessment of GD or MAUD patients as well as the drawing of bloods will take place either at the National Responsible Gambling Programme (NRGP) offices in Kenilworth, at the Faculty of Medicine and Health Sciences at the Tygerberg Campus of Stellenbosch University, or at the rehabilitation centre where you are currently being treated, depending on your preference for either location. The brain imaging will proceed at the recently established scanning centre at Groote Schuur Hospital (UCT). The computer-based tasks will proceed at the Faculty of Medicine and Health Sciences at the Tygerberg Campus of Stellenbosch University. You will receive grocery vouchers for participation and refreshments will be provided if requested. Where necessary, transport will also be provided.

We may contact you later for further information, or request you to complete another interview at a later date, in order to obtain follow-up information that may be of use in our genetic analyses. This may involve an assessment similar to the current assessment, including a series of interviews and/or another blood sample. Your current participation is in no way binding to your future participation.

Are there any risks involved in participation?

There are no more than minimal medical or psychological risks associated with this study. If you feel fatigued, uncomfortable, or in any way upset during any part of the session(s), you may ask to stop for a rest break or have the interview or scanning discontinued. The research interview does not take the place of a full psychiatric evaluation. You may experience some emotional discomfort when answering some questions. If any particular question makes you

feel uncomfortable, you may discuss its importance with the specially trained interviewer. You may choose not to answer any question should you feel uncomfortable.

You may feel some pain associated with having blood drawn from a vein. You may experience discomfort, bruising and/or other bleeding at the site where the needle is inserted. Occasionally, some people experience fleeting dizziness or feel faint when their blood is drawn. Some insurance companies may mistakenly assume that your participation in this study is an indication that you are at higher risk of a genetic disease, and this could hurt your access to health or other insurance. We will not share any information about you, or your family, with an insurance company. It is the opinion of the investigators that participation in this study does not constitute genetic testing. Therefore, participation in this study should not be reported as genetic testing.

You may feel some discomfort or fatigue associated with being in the brain scanner or while undergoing neuropsychological testing.

Are there any benefits to your taking part in this study? Will the results of your participation be discussed with you?

This study will hopefully provide useful data about the nature of problem gambling in South Africa, potentially filling gaps in the current body of knowledge regarding gambling. Individuals who might develop one of these conditions in the future, their family members, and future generations may benefit from the project if we can locate the genes and brain structures or functions that may have led to these symptoms. That knowledge may then be used for prevention or treatment planning and policy purposes

Individuals who choose not to partake in this study are free to do so at no consequence and will be referred for treatment, if requested.

How long will your blood/DNA sample be stored and where will it be stored?

Samples will be safely stored at -80 degrees Celsius at the Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, at the University of Stellenbosch, and de-identified (identified by a code number), and access will be limited to authorised scientific investigators. We also collaborate with researchers abroad; this means we may in future share DNA samples and anonymous (clinical or imaging) information with these sites to study your condition.

Your DNA will be maintained permanently, unless you request to have it removed. If at any time in the future you wish to have your DNA or clinical data removed from the storage site, you may do so by contacting the researchers conducting this study.

Will your clinical and genetics information be used for other research?

You can choose to share your clinical and DNA information with other scientists through a central database. In other words, the data that have been collected may be used for future investigations. Other researchers would be able to learn from your data and would be able to conduct studies that include DNA from many countries. This can lead to larger and better studies related to gambling disorder, methamphetamine use disorder and other health conditions.

An “online database” is a database that is created from the central database. Researchers all over the world have access to this database (this is called “data sharing”). The DNA stored in this online database will be used for research into general medical conditions OR psychiatric

illnesses. If South African researchers wish to use your stored blood/DNA for additional research in this field, they will be required to apply for permission to do so from the Health Research Ethics Committee at Stellenbosch University and the Human Research Ethics Committee at the University of Cape Town. If researchers from abroad wish to use your DNA information that has been stored on the online database, they will be required to apply for permission to do so from the National Institute of Health in the United States of America. If you wish to withdraw your data or your sample in the future, this is possible. However, please note that by the time we withdraw your data or your sample, it may already have been shared with other researchers. The United States National Institute for Mental Health (NIMH) Repository would, however, then instruct researchers to destroy your data and your sample if requested.

Will your brain imaging data be shared with other researchers?

In the same way as above, you can also choose to share your brain imaging data with researchers from other research institutions worldwide, to investigate, the structure and functioning of selected brain areas (anonymously).

How will your confidentiality be protected?

If you consent to participate in this study, your identity will be kept confidential. Your answers will not be shared with other family members or anyone else except for staff members involved in this study. All research information and laboratory samples obtained from you will be safely stored and identified by code number. This means that no identifying information will be shared. Access will be limited to authorised scientific investigators. Any publications resulting from this study will not identify you by name.

Because some of your DNA/cells are going to be stored in the United States, there is a very small chance the United States government might forcibly gain access to it using one of their laws called "The Patriot Act". This Act is used when the United States government judges that access to DNA is important for security purposes.

Will you or the researchers benefit financially from this research?

You will not be paid to take part in this study although your travel expenses will be reimbursed. In addition to this, you will have the opportunity of winning some money in a monetary reward task. The exact amount you will receive is dependent on your performance on the task.

Is there anything else that you should know or do?

You can contact the principal investigator at Stellenbosch University, Christine Lochner, on 021 – 938 9179 or CL2@sun.ac.za, or the principal investigator at the University of Cape Town, Dan Stein, on 021 – 404 2164 or dan.stein@uct.ac.za , if you have any further queries or encounter any problems. You can contact the UCT Faculty of Health Sciences Human Research Ethics Committee at 021 – 406 6346 if you have any concerns or complaints that have not been adequately addressed by study staff.

Declaration by participant

By signing below, I ……..……. agree to take part in a genetic research study entitled **Gambling disorder and methamphetamine use disorder: A neurocognitive, genetic and neuroimaging study**.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I have received a signed duplicate copy of this consent form for my records.

Tick the options that apply:

☐ I agree to take part in the study and consent to my blood being drawn. My anonymized information and blood sample will be stored and used for the current research project. Please destroy my DNA sample as soon as the current research project has been completed.

☐ I agree that my anonymized information and blood or DNA sample can be stored**,** but I can choose to request at any time that my stored sample be destroyed. I have the right to receive confirmation that my request has been carried out.

☐ I agree that my anonymized information and blood or DNA sample can be made available on an online database for use by other researchers, but I can choose to request

that my stored sample be destroyed. I have the right to receive confirmation that my request has been carried out.

☐ I agree that my anonymized brain imaging information can be made available for use by other researchers.

Signed at (*place*) ..... on (*date*) .....

....

Signature of participant **Signature of witness**

Declaration by investigator

I *(name)* …… declare that:

- I explained the information in this document to ……..……...
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research as discussed above.
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below).*

Signed at (*place*) .....….....…….. on (*date*) ……...…….. .

....

Signature of investigator **Signature of witness**

Declaration by interpreter

I *(name)* …… declare that:

- I assisted the investigator (*name*) ……. To explain the information in this document to (*name of participant*) …….. using the language medium of Afrikaans/Xhosa.
- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) .....…..…….. on (*date*) ……...…….. .

....

Signature of interpreter Signature of witness