Brain Mechanisms of Dreaming

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Abstract

This thesis comprises a series of six studies, aiming at clarifying some controversies surrounding the neuropsychological understanding of dreaming and the methodological issues of neuroanatomical investigation. The aim of the first study is to clarify whether or not recalling dream experience is difficult in nature. The frequency of dream recall in neurologically and psychiatrically healthy people was examined by using nonintrusive procedures. Guidelines for remembering dreams (Dream Recall Instruction) were established, based on a review of the existing literature on dream recall and its associated factors. The efficacy of the dream recall experience was explored using this procedure in neurologically and psychiatrically healthy individuals. One hundred and seventy Chinese subjects were included in the study: 100 received the dream recall instructions, and 70 did not. The dream recall instruction was shown to be effective in triggering dream recall in the subjects. The findings suggested that dream recall is not difficult in nature.

The second study examines the role of the posterior brain in the functional architecture of dreaming, and the controversy surrounding dream cessation caused by memory failure. Eight patients with posterior brain lesions were assessed on a daily basis, using neuropsychological assessment, and morning sleep and dream interviews. It was found that the patient with deficient dream experience was no more impaired in

memory than the seven patients who retained their dreaming capacity. Based on these findings, two arguments were underscored. Firstly, there is a clear distinction between memory deficits and cessation of dream experience. The inability to recall dreams and the loss of dream experience are rare in stroke patients, although memory disorders are not. Secondly, unilateral lesions to the supramarginal gyrus and its adjacent areas do not necessarily lead to cessation of dream experience.

According to the activation-synthesis hypothesis of dreaming, the conscious experience of dreaming involves an interplay between excitatory and inhibitory neurons in the pons. Contemporary research has cast doubt on this classical hypothesis by demonstrating that pontine lesions do not lead to a cessation of dream experience, implying that the pons may be unnecessary for dreaming. However, scrupulous human lesion studies are required in order to clarify the role of the pons in dreaming. Three case examples with lesions to various brainstem regions are reported in the third study to illustrate the paradox and difficulties of carrying out pontine lesion studies.

Solms's clincoanatomical studies found that damage to the ventromesial frontal pathway caused cessation of dream experience. However, most of the patients in Solms's clinical series were cases of tumour and diffuse injury. These conditions rendered the localization works difficult and imprecise. In view of this, the fourth

study investigated the association between dream deficiency and lesions to the ventromesial frontal region by using 21 patients who were diagnosed with infarctions. Results from this study were largely consistent with Solms's findings. In addition, the results indicated that compared to the other neural components in the ventromesial frontal pathway, the role of the caudate nucleus appeared to be particularly salient in the functional architecture of dreaming.

The fifth study compared the memory abilities of patients with deficient dream experience and those of patients with preserved dream experience, by using two widely-adopted measures for visuospatial and audioverbal memory. Thirty-two neurological patients were included in the analyses. The patients with preserved dream experience scored higher than the patient with deficient dream experience in the visuospatial memory functions. Nevertheless, the discrepancies in the visuospatial memory functions between the two groups did not hold statistical significance. Furthermore, there were no significant differences between the two groups in the audioverbal memory functions. The comparison analyses of the patients with ventromesial frontal region lesions and the patients with posterior brain lesions produced very similar results. These findings support the assertion that deficient dream experience does not seem to be the result of memory failure, even though it may be related to visuospatial and constructive dysfunctions.

Accumulated clinicoanatomical evidence suggests that the mesocortical-mesolimbic dopaminergic systems play a critical role in the functional architecture of dreaming, such that structural lesions to these systems result in dream deficiency. Nevertheless, the existence of human lesions only serves to provide indirect support to the neurochemical hypothesis that dopamine is one of the essential neurotransmitters that modulate dreaming. Moreover, while considerable empirical work has been done on the dreams of patients with schizophrenia, a condition associated with dopamine deregulation, few of these studies considered the effects of specific neuropharmacological agents that the subjects consumed. Therefore, the sixth study attempted to examine the dopamine hypothesis of dreams by investigating in detail the dream experience and medication regime of 55 patients with psychotic features. All of these patients were treated with therapies that demonstrated dopaminergic antagonism. A considerable number of the psychiatric subjects experienced a marked low frequency of dream experience. However, the neuroleptic treatment only suppressed dream recall and awareness in some cases. The differences in the dopamine antagonist consumption between the patients with different frequencies of dream experience were not substantial. Therefore, the present neurochemical findings were only partially consistent with the dopamine theory of dreaming. It can even be argued that the present neurochemical findings cast doubt on

the dopamine hypothesis. In addition, the study highlighted some confounding factors of conducting human neuropharmacological research in naturalistic and clinical settings.

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Chapter One

Background

Following several decades of scientific brain research, the brain mechanisms of dreaming appear to be established. The findings of modern researchers are for the most part consistent among different neurological methods, though a couple of uncertainties surrounding the brain mechanisms remain without being properly answered. One of the disagreements currently concerns the roles of the pons and the ventromesial frontal region pathway in the functional architecture of dreaming, which also underpins the underlying discrepancy between the classical REM-pons hypothesis and the latest forebrain models. By conducting clinicoanatomical and neuropharmacological analyses, this dissertation attempts to resolve some controversies in the field with respect to the brain mechanisms of dreaming which has played a pivotal role in psychological theorizing during the 20th century.

Specifically, the dissertation aims to:

1. assess the usefulness of subjective dream reports as a neuropsyhological tool to differentiate between normal population and brain damaged patients;

2. expand previous knowledge about the relationship between dreaming and the location of brain lesions, using high resolution brain imaging techniques now available;

3. investigate the correlation between dreaming and alterations in the central dopaminergic system in a population of psychiatric patients treated with different drugs affecting this neurochemical system.

In considering the above issues, a series of six studies were conducted and presented in this thesis. Details of each study including a specific review of the relevant literature are provided in latter chapters (Chapter Two to Chapter Seven). This chapter delineates the general background for the studies.

A. The Pontine Hypothesis

A.I. Associating Dreaming with REM Sleep and the Pons

The first major breakthrough of the neuroscientific study of dreaming was in 1953, when Aserinsky and Kleitman discovered a physiological state which occurs periodically in 90 minute cycles throughout sleep, and occupies 25% of the sleeping hours. This state is marked by heightened brain activation, bursts of rapid eye movement (REM), increased breathing and heart rate, genital engorgement and paralysis of bodily movement. It constitutes a paradoxical physiological condition in

which one is simultaneously highly aroused and fast asleep. Aserinsky and Kleitman (1955) and Dement and Klietman (1957a, 1957b) confirmed that the REM state is an observable and direct indicator of the subjective dream state. It is generally accepted that if someone is awakened from REM sleep and asked whether or not they have been dreaming, they will report that they were dreaming in approximately 70-95% of such awakenings. Non-REM (NREM) sleep, by contrast, yields equivalent dream reports at a rate of only 5-10% of awakenings. Therefore, according to many neurophysiologists, dreams are probably driven by automatic, physical mechanisms, rather than "wishes" or other psychological parameters.

By systematically ablating various brain structures, Jouvet (1962) was able to report that REM, and therefore dreaming, is produced by a small region of cells in a part of the brainstem, namely the "pons". He concluded that the higher levels of the brain, namely the forebrain, do not play any causal role whatever in the generation of dreaming. REM sleep occurs with monotonous regularity throughout sleep, as long as the pons remains intact, even if the great cerebral hemispheres are removed entirely (Figure 1.1).

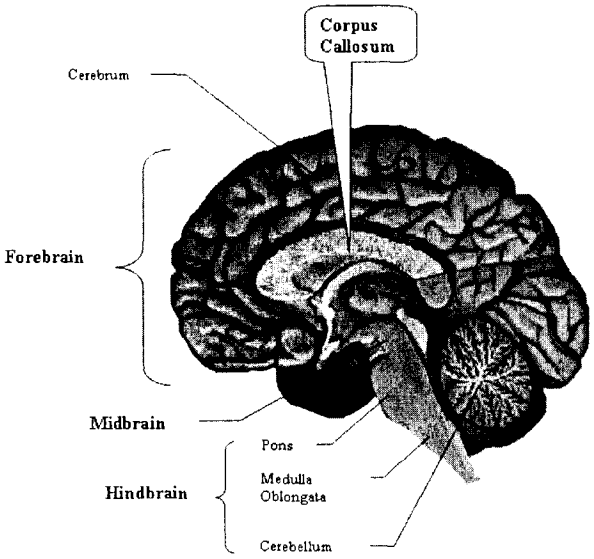


Figure 1.1 Divisions of the Brain: Forebrain, Midbrain and Hindbrain

Following this train of thought, Hobson and McCarley (Hobson, 1975; Hobson & McCarley, 1977; McCarley & Hobson, 1977) developed two anatomical and physiological models of dreaming sleep, namely the reciprocal-interaction and activation-synthesis models. The reciprocal-interaction model is characterized by the reciprocal on-off activity of two pontine neuronal populations (cholinergic and aminergic neuronal populations). The model proposed that REM sleep and dreaming are literally "switched on" by a small group of cells situated deep within the pons (principally in the mesopontine tegmentum) (Figure 1.2), which excrete a neurotransmitter called "acetylcholine" (ACh). This neurotransmitter activates the higher parts of the brain, which are thereby prompted to generate conscious images.

These images are nothing more than the higher brain making "the best of a bad job... from the noisy signals sent up from the brain stem" (Hobson & McCarley, 1977, p.1347) by attempting to synthesize into a coherent experiential episode the inherently random stimuli generated in the sleeping forebrain by an autoactivated pontine oscillator. After a few minutes of REM activity, the cholinergic activation arising from the brainstem is counteracted by another group of cells, also situated in the pons (but in the nucleus locus coeruleus and dorsal raphe nucleus), which excrete two other neurotransmitters: noradrenaline (NA) and serotonin (5-HT). These neurotransmitters "switch off" the cholinergic activation. Thereby, according to the theory, the conscious experience of dreaming is essentially operated by the interplay of the excitatory and inhibitory neurons in the pons.

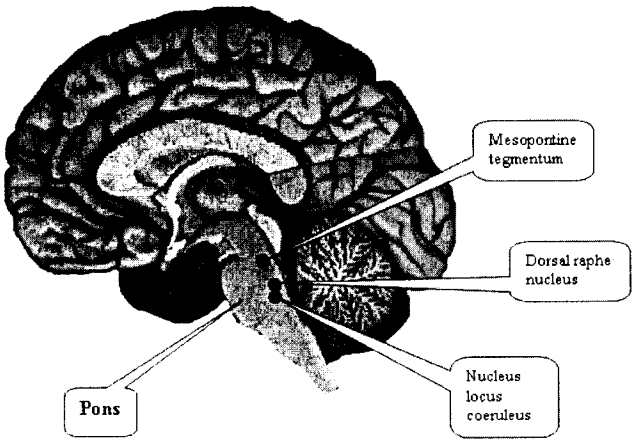


Figure 1.2 Sub-Structures in Pons

The activation-synthesis hypothesis (ASH) of dreaming was an attempt to provide an account of the psychophysiology of the mental state of typical REM sleep, and simultaneously to replace the Freudian theory of dreaming with a brain-based model. According to the ASH, dreams are actively generated by the brainstem but passively and non-specifically synthesized by the forebrain. This implies that the causal mechanisms underlying dreaming are "motivationally neutral" (Hobson & McCarley, 1977; McCarley & Hobson, 1977).

A.II. Separation of Dreaming from REM-Pons Hypothesis

Alongside the neurophysiological observations reviewed in the previous section, which provided an increasingly precise and detailed picture of REM sleep, a second body of evidence gradually began to accumulate, which has led some neuroscientists to suspect that perhaps REM sleep is not the physiological equivalent of dreaming after all (Solms, 1999, 2000a, 2000b). As pointed out by Solms (1999, 2000a), the notion that dreaming is "an epiphenomenon of REM sleep" (Hobson, Stickgold, & Pace-Schott, 1998) rested almost exclusively on the observation that arousal from the REM state yields dream reports on 70-95% of awakenings, whereas NREM awakenings yields such reports in only 5-10% of attempts. However, in one of the

studies, Foulkes awakened subjects from NREM sleep and asked them, "What was passing through your mind?" rather than, "Have you been dreaming?" (Foulkes, 1962). Dreams were elicited in more than 50% of these NREM awakenings. Although the NREM dream reports are more "thought-like" (less vivid) than the REM dream reports, this distinction holds only for the statistical average. The fact remains that at least 5-10% of NREM dream reports are "indistinguishable by any criterion (by blind raters) from those obtained from post-REM awakenings" (Hobson, 1988) and 5-30% of REM awakenings do not elicit dream reports. These findings "do not support a dichotomic distinction between REM and NREM mentation, rather they suggest the hypothesis of the existence of continuous dream processing characterized by a variability within and between sleep stages" (Cavallero, Cicogna, Natale, Occhonero, & Zito, 1992, p. 563).

The sharp demarcation between REM sleep and NREM sleep has further been eroded when it was found that dream reports can regularly be obtained even before the dreamer has entered the first REM episode. These dream reports, which are not significantly different from REM dreams in all respects except for length (i.e., they are vivid, bizarre, etc.), are obtainable from as many as 50-70% of awakenings during the sleep onset phase (descending NREM Stages 1 and 2) (Foulkes & Vogel, 1965; Foulkes, Spear, & Symonds, 1966; Vogel, Barrowclough, & Giesler 1972). This rate

is far higher than at any other point during the NREM cycle, and almost as high as the REM rate. Likewise, it was discovered that NREM dreams appear with increasing length and frequency towards the end of sleep, during the rising morning phase of the diurnal rhythm (Kondo, Antrobus, & Fein 1989). In other words, NREM dreams do not occur randomly throughout the sleep cycle. Dreaming during the NREM phases is apparently generated by specific NREM mechanisms (Solms, 1999, 2000a, 2000b).

The isomorphism between the neurophysiological phenomenon of the REM state and dreaming can not be retained. Accordingly, the role of the pons in dreaming is also questioned. Solms (1997) reviewed twenty-six cases which have been reported in the clinico-neurological literature, with damage to the pons that resulted in a total (or near-total) loss of REM sleep. However, surprisingly, the elimination of REM in these cases was not accompanied by cessation of dreaming. Only one of the 26 patients reported loss of dreaming (Feldman, 1971). By contrast, in all the other cases ever published in the neuroscientific literature in which focal damage to the brain did result in a reported cessation of dreaming, a completely different part of the forebrain was damaged; the pons was entirely spared. Moreover, it has been proved that REM sleep is preserved in some of the cases, despite their loss of dreaming (Benson & Greenberg, 1969; Bischoff & Bassetti, 2004; Efron, 1968; Jus, et al., 1973a; Kerr, Foulkes, & Jurkovic, 1978; Michel & Sieroff, 1981). According to Solms (1999, 2000a, 2000b),

this demonstrates that although the parts of the brain that are decisive for REM are in the pons, by contrast, the parts of the brain that are crucial for dreaming are located in the cerebrum.

In response to the data which challenged a direct parallelism between REM and dreaming, Hobson, Pace-Schott and Stickgold (2000) highlighted again the significant differences between average REM and NREM dreams. For instance, REM-NREM bizarreness differences may persist when report length is partialled out (Casagrande, Violani, Lucidi, Buttinelli, & Bertini, 1996; Nielsen, 1999; Waterman, Elton, & Kenemans, 1993), and NREM reports are far more likely than REM reports to be short, dull and undreamlike (Nielsen, 1999, 2000; Rechtschaffen, Verdone, & Wheaton, 1963). Notwithstanding these, it reveals a compelling need for revision and reconsideration of the authoritative model (ASH), which is unable to accommodate the latest neuroscientific findings.

B. The Forebrain Model

B.I. Deep Bifrontal Region

Deviating from the ASH, by using the human lesion method, which included a comprehensive review of the existing neurological literature, Solms (1997) concluded that the occurrence of dreaming is actively generated by the forebrain, but no the pons.

The evidence for this was found in the clinicoanatomical studies which demonstrated that global cessation of dreaming is associated with lesions in the inferior parietal lobule and in the white matter immediately surrounding the frontal horns of the lateral ventricles respectively.

The white matter of the frontal lobes of the brain just above the eyes contains a large fibre-pathway, which transmits a neurotransmitter named "dopamine" from the middle of the brain (the ventral tegmentum) to the higher parts of the brain (Figure 1.3). Bilateral damage to this pathway renders dreaming impossible but it leaves the REM cycle completely unaffected (Jus, et al., 1973a). According to Solms (1999, 2000a), these results suggest that dreaming is generated by a different mechanism than the one that generates REM sleep. This postulation is substantiated by the observation that chemical stimulation of this dopamine pathway (with drugs like L-DOPA, amphetamines and cocaine) leads to a massive increase in the frequency and vividness of dreams without having equivalent effects on the frequency and intensity of REM sleep (Hartmann, Russ, Oldfield, Falke, & Skoff, 1980; Klawans, Moskowitz, Lupton, & Scharf, 1978; Nausieda, Weiner, Kaplan, Weber, & Klawans 1982; Scharf, Moskowitz, Lupton, & Klawans, 1978). Conversely, the massive increase in dreaming caused by dopamine stimulants can be reversed by antipsychotic drugs ("chemical leukotomies") which block the transmission of dopamine in this

mesocortical-mesolimbic pathway (Sacks, 1985, 1990, 1991). Apparently, dreaming can be switched "on" and "off" by a neurochemical pathway which has nothing to do with the REM oscillator in the pons.

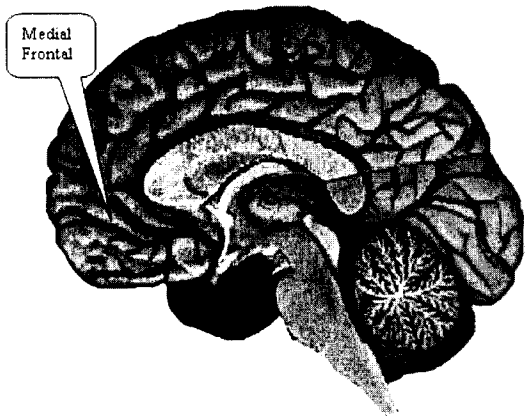


Figure 1.3 Location of Medial Frontal Cortex

From this, Solms (1995, 1997, 1999, 2000b) pointed out that the main function of this higher brain pathway which is crucial for the generation of dreams is to "instigate goal-seeking behaviours and an organism's appetitive interactions with the world" (Panksepp, 1985, 1998). Accordingly, damage to this pathway causes cessation of dreaming in conjunction with a dramatic reduction in motivated behaviour (Solms, 1997). On the basis of his findings, Solms (1999) asserted that contemporary neuroscientific evidence provided the reason to take seriously the hypothesis that dreams are motivated phenomena. This postulation is in contradiction

to the original ASH or REM-pons hypothesis in that the ACh mechanism which generates the REM state is "motivationally neutral", whereas the dopaminergic mechanism which generates the dream state is the appetitive, "seeking" or "wanting" command system of the brain (Berridge, 1999; Panksepp, 1985, 1998).

B.II. Inferior Parietal Lobule

As mentioned before, Solms (1997) concluded that cessation of dreaming is associated with lesions in the white matter immediately anterior to the frontal horns of the lateral ventricles and in the inferior parietal lobule. The second location, and in particular the supramarginal gyrus (BA40), is a portion of the grey cortex at the back of the brain (Figure 1.4). Right-sided lesions in the supramarginal gyrus cause complete cessation of dreaming in association with disorders of spatial cognition, whereas lesions in the same region of the left hemisphere convexity cause cessation of dreaming in association with disorders of quasi-spatial (symbolic) operations (Solms, 1997, 2000b). The supramarginal gyrus normally participates in the highest levels of perceptual information processing, including symbolic operations. This function is required for the conversion of concrete perception into abstract thinking, and for the retention of organized experience (Luria, 1973).

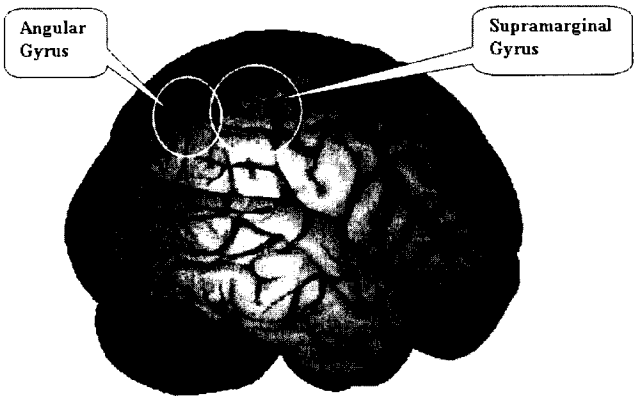


Figure 1.4 Sub-Divisions of Inferior Parietal Lobule

It is therefore suggested that in dreams abstract thoughts and memories are converted into concrete perceptions, if the theory that dream imagery is generated by a process which reverses the normal sequence of events in perceptual processing is correct. Solms (1999) further demonstrated that dreaming stopped completely with lesions circumscribed to this highest level of the perceptual systems, while only specific aspects of dream imagery were affected by damage at lower levels of the visual system, closer to the perceptual periphery (i.e., in the region of the ventral occipital cortex). It could therefore be concluded that in dreaming the contribution of the higher levels precedes that of the lower levels.

With the support of PET findings which display the striking deactivation of the dorsolateral frontal convexity during dreams, this picture of dreaming becomes more apparent. In waking ideational life, cerebral activity is concentrated in the dorsolateral

region at the front of the brain, "the upper end of the motor system - the gateway from thought to action" (Solms, 1997), while in dreaming, Solms (1997, 1999) suggested, it is concentrated in the inferior parietal cortex, in the memory and perceptual systems. This implies that whereas in waking life the normal course of mental events is directed towards action, in dreams this path is unavailable. The "gateway" to the motor systems is blocked in dreams (Braun, et al., 1997, 1998; Pompeiano, 1979; Solms, 1997). This sharp shift from the dorsolateral prefrontal cortex to the inferior parietal region defined a regressive path, away from the motor systems of the brain, towards the perceptual systems (Solms, 1997).

B.III. Solms's Neuropsychological Model

Departing from traditional neurochemical theories, Solms (1995, 1997, 1999) therefore attempted to provide another alternative model based on the recent findings of neuroscience. In this neuropsychological model (Figure 1.5), frontal dopaminergic mesolimbic reward circuits produce an instigating impetus for dreaming when activated by arousing stimuli. The initial stimulus can be anything (external or internal and even REM); but only if it is sufficiently intense or persistent to activate the motivational mechanisms of the brain, does the dream process proper begin. The functioning of the motivational systems of the brain is normally channelled towards

goal-directed action but access to the motor systems is blocked during sleep. The purposive action which would be the normal outcome of motivated interest is thereby rendered impossible. Eventually, the process of activation assumes a regressive course. This involves a two-stage process. First, the higher parts of the perceptual systems (which serve memory and abstract thinking) are activated; then the lower parts (which serve concrete imagery) are activated. As a result of this regressive process, the dreamer does not actually engage in motivated activity during sleep, but rather imagines doing so. Due to inhibition during sleep of the reflective systems in the anterior limbic regions, the imagined scene is uncritically accepted, and the dreamer mistakes it for a real perception.

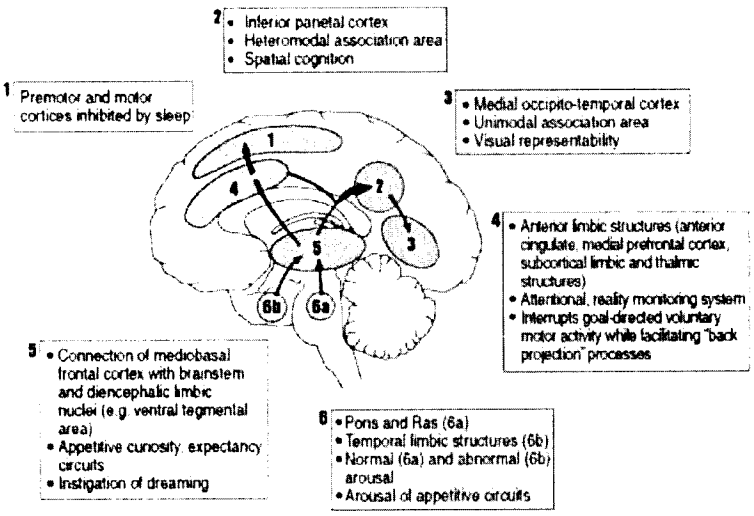


Figure 1.5 Forebrain Processes in Normal Dreaming (After Solms) Depicted by Hobson. Source: Hobson (1999)

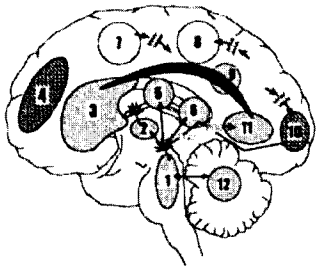
C. Revision of the ASH and Nielsen's Conclusion

The ASH emphasizes the randomness of dream imagery. According to the theory, dream images are generated because the representation systems of the brain are activated, that is, the brain-mind isomorphism. Yet the group which developed the ASH also developed the method of dream splicing, which shows how coherent dreams can be (Stickgold, Rittenhouse, & Hobson, 1994), and published on what the limits of such randomness are (Rittenhouse, Stickgold, & Hobson, 1994). For instance, in Stickgold, Rittenhouse and Hobson's study (1994), dream reports from college students were cut into segments, which were in turn randomly recombined to form spliced reports. After that, judges attempted to distinguish spliced reports from intact ones. Five judges correctly distinguished spliced and intact reports 82% of the time. This result demonstrated that dream reports contain sufficient *coherence* to allow people to distinguish intact from spliced reports. Corresponding to this, Flanagan's (2000) classic work put forth an intriguing argument that even though dreams are epiphenomenon and perform no function, they can have meaning. This proposition of dreams as "meaningful byproducts" was echoed by other researchers such as Blagrove (2000) and Domhoff (2000).

"While it could be that the dream is uninterpretable, or is meaningless as a narrative

construct, or that it has nothing like the meaning we are inclined to assign, but is nonetheless a good conversation starter for someone trying to figure out the shape of his or her life" (Flanagan, 2000, p. 150).

Furthermore, Hobson (1992, 1994, 1999, 2001) later elaborated the ASH into a new, more general theory of psychophysiological states, called AIM (Activation-Synthesis Integrated Model, Figure 1.6). In this model, Hobson (1999, 2001) has proposed a revision of the ASH that gives a greater role to forebrain mechanisms and allows for increased possibility that dreams are meaningful. Nevertheless, this has by no means changed his position concerning the leading role of the pons as an instigator of REM and therefore dreaming.



Subcortical and neocortical areas relatively activated during dreaming

Neocortical areas relatively deactivated during dreaming

Ascending activation systems

Sensory input/ motor blockade

Neocortical structures preferentially contributing to circuitry active during dreaming

1	• Pontine and midbrain RAS and nuclei • Ascending arousal of multiple forebrain structures • Dream: Consciousness, eye movement and motor pattern information via PGO system	2	• Diencephalic structures (hypothalamus, basal forebrain) • Autonomic and instinctual function, cortical arousal • Dream: Consciousness, instinctual elements
3	• Anterior limbic structures (amygdala, anterior cingulate, parahippocampal cortex, hippocampus, medial frontal areas) • Emotional labelling of stimuli, goal-directed behaviour, movement • Dream: Emotionally, affective salience, movement	4	• Dorsolateral prefrontal cortex • Executive functions, logic planning • Dream: Loss of volition, logic, orientation, working memory
5	• Basal ganglia • Initiation of motor actions • Dream: Initiation of fictive movement	6	• Thalamic nuclei (e.g. LGN) • Relay of sensory and pseudosensory information to cortex • Dream: Transmits PGO information to cortex
7 8 10	• Primary motor (7) and sensory (8, 10) cortices • Generation of sensory precepts and motor commands • Dream: Sensorimotor hallucinosis	9	• Inferior parietal cortex (BA 40) • Spatial integration of processed hetermodial input • Dream: Spatial organization
11	• Visual association cortex • Higher order integration of visual percepts and images • Dream: Visual hallucinosis	12	• Cerebellum • Fine tuning of movement • Dream: Fictive movement

Figure 1.6 Activation-Synthesis Integrated Model (Source: Hobson, 1999)

In his comprehensive review of the existing studies on NREM dreams, Nielsen (2000) ended the controversy with a conclusive remark that mentation can occur in NREM sleep with an overall average mentation recall rate of about 50%. REM episodes through the sleep period indeed correlate with the time-of-night dependent changes in the length and complexity of REM sleep dream reports, and the dream proper (termed "apex dream" by Nielson, 2000), distinguished by its high vividness, intensity and complexity, occurs in later REM episodes towards waking (Braun, et al., 1997; Cipolli & Poli, 1992; Kondo, Antrobus, & Fein 1989; Snyder, 1970). Nielsen (2000) calculated the probabilities of obtaining "covert REM sleep processes" (i.e., of recalling sleep mentation or dreams) within NREM sleep episodes. In line with the crescendo of dream intensity along the vicissitude of the REM sleep episodes over the night, the probabilities of retrieving NREM dreams increase progressively throughout the entire six consecutive NREM-REM cycles, and the highest probability occurs in the last NREM episode. This is consistent with Solms's (1999, 2000a, 2000b) proposition that NREM dreams occur steadily, rather than randomly, throughout the sleep cycle. In view of these, Nielsen (2000) claimed that "covert REM processes" may be operative during NREM sleep and responsible for producing NREM dreams.

There is now considerable evidence for this covert REM theory (e.g., Suzuki, et

al., 2004; Takeuchi, Miyasita, Inugami, & Yamamoto, 2001). Suzuki, et al (2004) found that although dream reports from NREM naps are less remarkable in quantity, vividness and emotion than those from REM naps, they are obtained more frequently during the rising morning hours when the occurrences of REM sleep are highest. Therefore, according to Suzuki, et al (2004), the EEG manifestations of REM sleep are not necessarily required for dream experiences. Yet the underlying mechanisms driving REM sleep appear to alter experiences during NREM sleep in the morning.

Contemporary understanding of the brain mechanisms of dreaming has undergone a paradigm shift. Contemporary research has cast considerable doubt on the classical assumptions that dreams are the subjective manifestation of the REM stage of normal sleep and therefore share the same physiological mechanisms as REM sleep. The revision proposed by Nielsen may well have ended this controversy. Accordingly, "covert REM processes" are perhaps necessary, albeit not sufficient, for dreaming. Facing a mounting body of evidence of the significant role played by the forebrain in dreaming and the evidence that dream experiences are not necessarily the subjective manifestation of the REM stage of sleep, Hobson (1999, 2001) has revised the original ASH in his AIM, though the pons is still posited as a crucial instigator of REM and dreaming in the AIM model.

D. Controversies

To reiterate, from the clinicoanatomical perspective, Solms's research has demonstrated that: (1) pontine brainstem lesions do not produce a loss of dreaming in human subjects (although they do, as in all mammals, produce a cessation REM sleep); (2) loss of dreaming is only produced in humans by lesions of the forebrain; (3) lesions producing a loss of dreaming are not associated with a concomitant cessation of REM sleep.

On the other hand, it has been argued that the data obtained by the human lesion methods should be interpreted cautiously vis-à-vis the potential methodological flaws (Hobson, 1999, 2001, 2002). Likewise, according to Pace-Schott, Solms, Blagrove and Harnad (2003), a number of areas of uncertainty and controversy remain without being adequately investigated.

D.I. Controversy I: Memory Problems

Almost all of Solms's (1997) conclusions were based on simple bedside methods of neurobehavioural investigation, and remain to be confirmed and qualified by more rigorous and systematic research methods. The primary methodological flaw of this neurobehavioural method, as far as Hobson (2001) concerned, is the possibility that patients' report of dream cessation is a secondary effect of memory failure, rather than

a direct consequence of neurological insults. There are two specific arguments within the memory controversy: first, dream recall is difficult per se, even in normal people, and second, stroke patients' memory is notoriously poor (especially patients with posterior brain lesions). With reference to Hobson:

"Although the question is easy to ask, the answer is not easy to interpret. Suppose the patient says that he stopped dreaming after his stroke? Should we take the answer seriously? Of course. But uncritically? Certainly not, because dream recall depends upon memory and memory is both notoriously poor for dreaming and notoriously subject to damage from stroke, especially if the damage is *in or near the temporal lobes*" (Hobson, 2001, p. 183, emphasis added).

D.II. Controversy II: Precision of Anatomical Localization

In addition to the memory controversy, there are other methodological issues concerning the human lesion approach. In practically most of the neuropathological insults, the precise anatomical definition of lesions is problematic, as is the functional impact of the lesion itself. A considerable number of cases in Solms's study sustained diffuse lesions, or had been diagnosed by tumour type (about one-third of the patients respectively). Both conditions render neuroanatomical analysis difficult and

unreliable (This will be elucidated in detail in Chapter Five).

D.III. Controversy III: REM-Pons Hypothesis

The classical REM-pons hypothesis was questioned by Solms's research (1997, 2000b) which demonstrated that "large" pontine lesions do not lead to a cessation of dreaming. Solms has not, however, been able to show that precise lesions to the target pontine nuclei (in the pontomesencephalic tegmentum and pontine peduncule), whose activity have been proved associated with REM sleep are compatible with preserved dreaming. Likewise, Pace-Schott, Solms, Blagrove and Harnad (2003) argued that further human lesion studies are required in order to prove that, as Solms (1997, 2000b) argued, the pons is not a crucial neural substrate for dream generation.

D.IV. Controversy IV: Posterior Cortex and Dream Formation

Most PET studies (see Yu, 2001a, for review) revealed that inferior parietal cortex, including the supramarginal gyrus (BA 40), deactivates significantly during REM sleep, whereas in contrast, Solms (1997, 1999) claimed that the lesion circumscribed to this specific part of brain, to which he attributed the important functions of dream formation (zone 2 in Figure 1.5; zone 9 in Figure 1.6), leads to the loss of dreaming. In reanalyzing Solms's clinical series, Yu (2001a) suggested that the dream cessation

effect could be alternatively attributed to the lesions circumscribed to the temporo-occipital junction (BA37) as opposed to the supramarginal gyrus. Additional clinical cases could help to further clarify if the inferior parietal lobule, and in particular the supramarginal gyrus, is necessary for dream formation.

D.V. Controversy V: Dopamine Theory

Solms (2000a, b) argued that the critical component of the ventromesial frontal region responsible for cessation of dreaming with anterior forebrain lesions is the mesocortical-mesolimbic dopamine system, but this hypothesis, as Hobson (2001) pointed out, is "entirely speculative" (p. 191) and not consistent with his laboratory's experimental observations.

"When we recorded from putative dopamine neurons in the substantia nigra, we were impressed with how little they changed their firing properties in any state! They tended to fire at the same high rates in NREM and REM sleep as they did in waking" (Hobson, 2001, p. 191).

"How could Solms account for the evanescence and intermittency of dreaming, given the apparent constancy of dopamine output? Why, for example, don't we dream as

frequently or as intensely in NREM sleep (or in waking, for that matter) if dopamine is playing more than an incidental role in the instigation of dreaming? It could be that dopamine abets the motivational aspects of both dreaming and waking cognition. This seems plausible and conforms to the observations in hand" (Hobson, 2001, p.192).

Dreaming abnormalities (vivid dreams, nightmares, night terrors) have been reported to precede the occurrence of hallucinations in Parkinson's disease, delusions and delirium are accepted to be induced by levo-dopa (Factor, Molho, Podskalny, & Brown, 1995; Pal, Calne, Smii, & Fleming, 1999), and REM abnormalities have been linked to drug-induced hallucinations in Parkinson's disease (Comella, Tanner, & Ristanovic, 1993). Those anti-Parkinsonian medications, namely dopamine agonists such as levo-dopa and pramipexole, were consistently found to be associated with increased dream intensity. Although this evidence demonstrating intensified dreaming in response to dopamine agonists seems to lend support to the role of dopamine in dreaming, surprisingly there have thus far been few empirical works on the systematic investigation of alterations in dreaming in cases of schizophrenia, given the context of its underlying neural pathology and dopamine antagonistic treatment. There are a couple of early studies investigating dream recall in schizophrenia (Chang, 1964; Dement, 1955; Julien, D'Agostino, & Balzamo, 1981; Jus, et al., 1973a, 1973b;

Kramer, Whitman, Baldridge, & Ornstein, 1970; Kramer, & Roth, 1973). However, these studies did not take the neuropharmacological mechanisms into account, and their results are far more contradictory than consistent.

E. Research Objectives

The present dissertation attempts to resolve the aforementioned outstanding questions currently facing sleep and dream science in the wake of the recent findings of clinicoanatomical and functional-imaging researchers as enumerated in the last section, by refining the neurobehavioral methods. The dissertation presents a series of six studies in the following six chapters (chapters 2 to 7), and summarizes the findings and implications of these studies in the last chapter (chapter 8). The three major objectives corresponding to the above controversies are as follows:

The first aim is to justify the legitimacy of subjective report of alterations in dream experience. In the same way that neuropsychological tests need to be established as possessing discriminatory power, the essential question underlying the human lesion method is whether subjective dream reports are a useful neuropsychological assessment tool for discriminating between the normal population and brain-damaged individuals. In relation to this is the methodological controversy of dream recall

problems. Chapter 2 will study the dream recall frequency of neurologically and psychiatrically healthy people, and examine the efficacy of the developed instrument (Dream Recall Instruction) for facilitating retrieval of dream experience. Along with these, the controversy as to whether or not dream recall is difficult in nature will also be clarified (corresponding to Controversy I). For further investigating the memory controversy, Chapter 3 examines whether or not memory dysfunction necessarily results in cessation of dream experience (including dream recall and awareness) (corresponding to Controversy I). Finally, Chapter 6 explores whether or not patients who have experienced deficient dream recall and awareness since their strokes differ from patients with preserved dream experience in their memory abilities (corresponding to Controversy I).

The second aim of this research is to identify the precise location of the neural pathways that are implicated in the generation of dreaming, corresponding to the neuroanatomical controversies. The dream experiences and neuropsychological parameters of neurological patients are studied by the refined human lesion method in Chapter 3 to 5. In particular, Chapter 3 clarifies if the inferior parietal lobule and supramarginal gyrus are necessary for dream formation (corresponding to Controversy II & IV). Chapter 4 discusses the role of the pons in dreaming, and

presents three rare neurological case examples of various brainstem lesions to illustrate the paradox and difficulties in carrying out pontine lesion studies (corresponding to Controversy II & III). Chapter 5 underpins the precise neural structures that are implicated in the generation of dreaming within the "ventromesial frontal region" by investigating patients diagnosed with infarctions (corresponding to Controversy II).

The third aim is to provide a tentative examination of the dopamine hypothesis. In Chapter 7, the dream experience and medication regime of patients with psychotic features are investigated thoroughly, along with a discussion of the difficulties in carrying out neuropharmacological studies (corresponding to Controversy V).

Chapter Two

A Study of Dream Recall Frequency in Neurologically and Psychiatrically Healthy People

A. Introduction

Previous clinicoanatomical studies on dreaming were largely based on unsystematic bedside methods (e.g., Benson & Greenberg, 1969; Boyle & Nielsen, 1954; Corda, 1985; Ettlinger, Warrington, & Zangwill, 1957; Farah, Levine, & Calviano, 1988; Lyman, Kwan, & Chao, 1938; Michel & Sieroff, 1981; Michel, Jeannerod, & Devic, 1965; Müller, 1892; Peña-Casanova, Roig-Rovira, Bermudez, & Tolosa-Sarro, 1985; Solms, 1995, 1997; Wapner, Judd, & Gardner, 1978; Wilbrand, 1887, 1892). A potential methodological flaw of the clinicoanatomical studies, as some researchers concerned (e.g., Hobson, 2001), is the possibility that patients' report of dream cessation is a secondary effect of memory failure, rather than a direct consequence of neurological insults. Furthermore, it can be argued that dream recall is difficult in nature, even in neurologically and psychiatrically healthy people (Hobson, 2001).

Much work has been devoted to the investigation of dream recall frequency in normal people and its associated factors. The average dream recall frequency, documented by several studies of western participants, is two to three times per week

(e.g., Görtelmeyer, 1986; Schredl, 2000a, 2000b, 2002a, 2003; Schredl, Ciric, Gotz, & Wittmann, 2003; Stepansky, et al., 1998; Zadra & Nielsen, 1999). Moreover, a number of personal characteristics have been found to be associated with dream recall frequency. These include, for instance, gender (Foulkes, 1977; Martinetti, 1989; Schredl, 2000a, 2003; Schredl & Piel, 2003; Schredl, Bozzer, & Morlock, 1999), age (Foulkes, 1977; Herman & Shows, 1984; Schredl, 2004a), Type A versus Type B personality (Koulack, Nesca, & Stroud, 1993), and openness to experience (Hartmann, 1989; Hartmann, Elkin, & Garg, 1991; Schredl, Ciric, Gotz, & Wittmann, 2003; Schredl, Kleinferchner, & Gell, 1996). Although most of the findings concerning these associations are far from conclusive, a few lines of hard evidence yield three comparatively reliable factors: the emotions experienced during dreams and waking, a capacity for visualization, and alteration of consciousness.

A.I. Emotionality

Perhaps the most obvious agreement about dreaming amongst different researchers is on the notion that dream experience is emotional in nature (e.g., Newell & Cartwright, 2000; Panksepp, 2003; Yu, 2001a, 2001b). Punamäki (1997) proposed two general rules that regulate the availability of dream recall. Firstly, the stronger the emotions that are experienced in dreams, the more likely it is that the dreams will be recalled.

Secondly, dreams are more likely to be recalled when the dream mood (i.e., atmosphere and feeling) is congruent with the waking mood. Furthermore, a wide range of evidence suggests that dream recall becomes more frequent when negative emotions are involved, regardless of whether such emotions arise from dreaming or waking (e.g., Cooper, 1999; De Gennaro, et al., 2003; McNamara, Andresen, Clark, Zborowski, & Duffy, 2001; Nielsen, Ouellet, Warnes, & Cartier, 1997; Wolcott, & Strapp, 2002).

A.II. Visualization

It has long been recognized that a global capacity for visualization may contribute to the quality of dream experience and thus to the ability to recall it (Hiscock & Cohen, 1973). A significant positive association between dream recall frequency and the vividness of voluntarily produced visual imagery has been repeatedly reported (e.g., Okada, Matsuoka, & Hatakeyama, 2000; Richardson, 1979). Many subfunctions that support the general ability to visualize also critically influence the frequency of dream recall. According to Fitch and Armitage (1989), those who recall a high frequency of dreams are more fluent in processing picture-completion tasks, suggesting that they adopt a more diverse approach in information processing than those who recall a low frequency of dreams. In addition to the scaffolding function of divergent processing,

the variability in dream recall frequency can be attributed to visual memory (Schredl, Frauscher & Shendi, 1995; Waterman, 1991), visual creative skills (Schredl, 1995), and frequent use of visual imagery (Okada, Matsuoka, & Hatakeyama, 2000). Corresponding evidence for the functional significance of visualization capacity in dream recall has also been found in clinical observations such as congenitally blind individuals (Bertolo, et al., 2003) and neurological patients (Bischof & Bassetti, 2004; Bonanni, Cipolli, Iudice, Mazzetti, & Murri, 2002; Murri, Arena, Siciliano, Mazzotta, & Muratorio, 1984; Murri, Massetani, Siciliano, Giovanditti, & Arena, 1985; Solms, 1995, 1997, 2000b; Yu, 2001a).

A.III. Alteration of Consciousness

Braun (1999) postulated that the common phenomenon of poor memory for dreams results from a lack of contextual cues encoded simultaneously with the dream experience. Koukkou and Lehmann (1983; Lehmann and Koukkou, 2003) provided a comparable explanation that dream experiences are stored in a state of consciousness that is too remote from the later state in which attempts are made to recall dreams. In other words, dream recall may be difficult because of a deficiency caused by the shift in context. This postulation is reminiscent of the early theory that events experienced in one state are optimally available for recall when the same state is reinstalled (Eich,

1986).

In view of that, factors such as increased arousal and some personal traits (i.e., fantasy life, creativity, and visual memory) play a decisive part in the variability of dream recall (e.g., Schredl, 1998; Schredl & Montasser, 1997; Schredl, Bozzer, & Morlock, 1997). It is almost indisputable that individuals who are prone to absorption, imagination, and fantasy, are particularly good at remembering their dreams and more likely to report other vivid nocturnal experiences (Blagrove & Akehurst, 2000; Levin, Fireman & Rackley, 2003; Orlinsky, 1966; Schredl, Jochum, & Souguenet, 1997; Strunz, 1986; Tonay, 1993; Watson, 2003). Indeed, this scenario has been succinctly underscored by the early finding that frequency of dream recall correlates positively with fantasy predominance and associative productivity, and negatively with introspective constriction (Orlinsky, 1966). Accordingly, any manoeuvres that foster fantasy and associative productivity, and simultaneously free one from introspective constraints, can elevate the frequency of dream awareness.

A.IV. Techniques for Dream Recall: Focusing on Emotions, Visualization, and Reinstating a "Sleep" State

In view of the salient positive relationships between conscious arousal, visualization, and dream recall frequency, it is perhaps unsurprising that dream recall can be

significantly enhanced by relaxation techniques (Schredl & Doll, 1997), hypnosis (Stross & Shevrin, 1967), and increasing imagery abilities through activities such as introspection, daydreaming, and meditation (Martinetti, 1985, 1989; Reed, 1978). In line with the empirical evidence described above, it is conceivable that such an improvement in dream recall may result from the similarity in the nature of the cognitive processes underlying the dreaming state of sleep and the altered states of analogous conscious activities.

A.V. Asian Studies on Dreams

Some Asian studies on dreams have been conducted (e.g., Domhoff, Nishikawa, & Brubaker, 2004; Fiske & Pillemer, 2006; O'Nell & O'Nell, 1977; Shimizu & Inque, 1986; Takeuchi, Miyasita, & Inugami, 1996; Yamanaka, Morita, & Matsumoto, 1982). These mostly involved quantitative content analyses or laboratory experiments rather than a systematic investigation of dream recall frequency at a home setting. For instance, there is a Japanese study (Takeuchi, Miyasita, & Inugami, 1996), which correlated dream properties (e.g., bizarreness) with physiological variables (e.g., atonia index, REM density). It has also been reported that as compared with the norms for the American women, there are far fewer men in the dreams of Japanese women (Yamanaka, Morita, & Matsumoto, 1982) although the result could not be replicated

(Domhoff, Nishikawa, & Brubaker, 2004).

There is also a recent Chinese study about coloured dreaming (Schwitzgebel, Huang, & Zhou, 2006). The subjects in this study were asked: "How frequently do you dream?" and "Do you see colours in your dreams?" They were required to indicate their answers on a five-point scale (i.e., very frequently, frequently, occasionally, rarely, and never). Most subjects chose either occasionally or rarely dreaming in colour. However, no clear data was provided with regard to the question as to how frequently the subjects dream.

A.VI. Research Objectives

Frequency of dream recall has been investigated extensively in western countries. Overall, the average dream recall frequencies documented by many studies are around two to three times per week (e.g., Desroches & Kaiman, 1964; Paulsson & Parker, 2006; Schredl, 2002a; Schredl & Hofmann, 2003; Schredl, Wittmann, Ciric & Götz, 2003). Although it correlates with a variety of factors and some variations in the figures can be found in other studies (e.g., around once a week, Schredl, 2003; Schredl, Brenner & Faul, 2002), dream recall in general does not seem to be difficult, at least in western people.

Moreover, some of the previous studies on dream recall adopted a Likert scale.

Schwitzgebel, Huang and Zhou (2006) used the five-point scale in their Chinese study. Similarly, Schredl's group used a seven-point scale (Schredl, 2002b, 2002c, 2004a; Schredl & Fulda, 2005; Schredl, Brenner, & Faul, 2002). Specifically, for measuring dream recall frequency, Schredl's group used the question: "How often do you recall your dreams recently (several months)?" and applied the seven-point rating scale (0 = never to 6 = almost every morning) (Schredl, 2002c; Schredl, Brenner, & Faul, 2002). While the Likert scale is more ready for parametric statistical analyses, the responses triggered by this scale are relatively imprecise (e.g., very frequently, frequently, occasionally, rarely, and never).

The present study aims to provide a preliminary review of the dream recall frequency of Chinese in a relatively precise manner. Furthermore, the present study was geared towards developing nonintrusive procedures to facilitate dream recall based on the findings from previous studies on dream recall.

The four specific purposes of studying normal subjects are as follows:

1. To further clarify and confirm whether or not recalling dream experience is difficult in nature;
2. To develop an instrument (Dream Recall Instruction) for facilitating retrieval of dream experience in neurologically and psychiatrically healthy people, and to examine its efficacy;

3. To study frequency of *awareness* of dream experience (Most of the previous studies focused on dream *recall* frequency);
4. To provide a reference group for comparing with the dream experience of clinical populations.

B. Method

B.I. Design

The present study explored the four aforementioned issues by using survey and between-subject experimental methods. One hundred and seventy participants were included. Semi-structured interview was administered for collecting general information about dream experience. In addition, a between-subject experiment was carried out to test if dream recall can be improved by giving guidelines to the participants.

B.II. Subjects

A total of 170 Chinese participants from Hong Kong constituted the current sample, with a mean age of 23.5 years (SD = 7.5, range = 10-50). There was a predominance of female participants (males: N = 44 (25.9%); females: N = 126 (74.1%), binomial test, $p < 0.001$). They were all neurologically and psychiatrically healthy.

B.III. Procedure

All participants were first briefed on the questions and procedure before the initial interview. After the informed consent was obtained, the participants were interviewed for their general dream experience including dream recall frequency. After that, they were invited to participate in an experiment for facilitating dream recall (a between-subject intervention), and the dream and sleep diary was given to the participants. The participants then finished the diary on their own at home with the aid of the daily morning follow-up administered by the interviewers. All dream and sleep interviews and follow-ups were conducted by trained interviewers (employed research assistants) who were blind to the hypotheses of the current study.

The 170 participants were randomly allocated to one of two groups. An experimental group included 26 male and 74 female subjects, with a mean age of 24.7 years (SD = 7.3, range = 11-50). Most participants in this subsample reported more than one nocturnal experience subsequent to the initial interview (from one to three nights, dependent on their availability), and received instruction on dream recall techniques (Dream Recall Instruction). Seventy participants constituted a control group. Fifteen (21.4%) of these participants were male and 55 (78.6%) were female. The mean age was 21.9 years (SD = 7.2, range = 10-49). In contrast to the

experimental group, the participants in the control group were required to report one nocturnal sleep and dream experience after the initial interview, and did not receive any guidelines for facilitating dream recall.

B.IV. Materials

B.IV.1. Survey on Previous Dream Experience (for the Initial Interview)

Participants' dream recall frequency, frequency of dream awareness (i.e., participants were aware that they had dreams but did not necessarily remember the dream contents), and general concept and misunderstandings concerning dreams, were clarified in the initial interview (Appendix A). The primary predetermined questions included in the interview protocol were:

1. Can you tell me what a dream is?
2. How often do you recall your dreams for the past six months?
3. Some people know that they have dreamed at night even though they cannot remember the details of their dreams when they are awake. Do you ever think that you have dreamed even though you cannot remember any dreams in the morning?
4. People often forget the content of their dreams. However, on waking, they may know whether they have dreamed or not. How often did you dream in the past

six months (including both the dreams you remember clearly and the dreams whose contents you do not remember)? (Options were given if the participants could not tell spontaneously: "nightly", "1-6 times/week", "less than 1/week", "less than 1/month", and "uncertain").

5. Do you think that you did dream last night even though you no longer remember any dream details this morning?

By adopting the above questions as well as some follow-up questions, the interviewers tried to clarify participants' frequency of awareness of dream experience (i.e., frequency of dream experience with or without recalled dream contents).

B.IV.2. Dream Diary (for the Experiment)

All participants in both experimental and control groups were required to write down any dreams that they could remember each morning throughout the observation period (as far as possible immediately after waking up from sleep). The Most Recent Dream Report (Domhoff, 1996) was adopted as guidance for participants to report their dreams (Appendix B). In addition, questions about each human sensation were probed after participants describing their dream contents, for instance, "Did you *really see* anything in your dream?"

Again, in both the dream diary and the daily morning follow-up interviews

administered by the interviewers, the four conditions were clarified and distinguished as far as possible: (1) the participants had dreamed; (2) they claimed that they did not have any dreams; (3) they had dreamed but had forgotten the dream content; (4) they did not remember whether they had dreamed or not.

B.IV.3. Dream Recall Instruction (for the Experiment)

Guidelines were provided to the participants for aiding their dream recall and dream awareness. The literature has suggested a number of ways to recall dreams, but most procedures are similar. The guidelines to aid dream recall in the current study were established through the following process. Firstly, methods and procedures adopted in previous studies (e.g., Arena, Murri, Piccini, & Muratorio, 1984; Bonanni, et al., 2002; Cartwright & Lamberg, 1992; Murri, Arena, Siciliano, Mazzotta, & Muratorio, 1984; Murri, Massetani, Siciliano, & Arena 1985; Newell & Cartwright, 2000; Schredl, 2002a, 2002b, 2004b; Watson, 2003) were compared. Secondly, several procedures were selected and modified according to the two primary theoretical backgrounds and empirical evidence presented in the introduction: (1) dream experience is emotional in nature (e.g., Newell and Cartwright, 2000; Panksepp, 2003; Yu, 2001a, 2001b); (2) events experienced in one state are optimally available for recall when the same state is reinstalled (e.g., Eich, 1986; Koukkou & Lehmann, 1983, 1987; Lehmann &

Koukkou, 2003). Finally, the selected guidelines were simplified for practicality. Ultimately, seven steps were outlined to help the participants to remember their dreams, including, for instance, lying still while going over the dream, and hovering between sleeping and waking (Appendix C). Participants were only required to use the guidelines (i.e., step two to seven, and the asterisked item) if they were aware that they had dream experience.

C. Results

Not every participant in the 170-participant sample was subjectively aware of their dream experience every night, though a considerable number of participants were, according to their reports of their past experience (Table 2.1). In the initial interview, almost half the participants maintained that they dreamed between one and six times a week. This was generally consistent with the subsequent number of dreams triggered after the initial interview. This group, together with the nightly dream group, constituted over 80% of the entire sample. There were no noticeable differences between the experimental group and the control group in the frequency of dream experience, according to their reports of their past experience (Pearson chi-square (2) = 4.461, p = 0.107; Cramer's V = 0.163, p = 0.107 (the two categories with zero counts were excluded in calculation because they represented extremely small groups

of the population, i.e., "outliers") (Table 2.2).

Table 2.1 Frequency of Awareness of Dreaming from Past Experience

Dream Experience	Frequency	%	Cumulative %
Nightly	57	33.5	33.5
1-6 times/ week	81	47.6	81.1
Less than 1 time/ week	2	1.2	82.3
Less than 1 time/ month	1	0.6	82.9
Uncertain	29	17.1	100
Total	170	100	

Table 2.2 Frequency of Awareness of Dreaming from Past Experience between Experimental and Control Groups

Dream Experience	Frequency (Experimental)	Frequency (Control)
Nightly	37	20
1-6 times/ week	48	33
Less than 1 time/ week	2	0
Less than 1 time/ month	1	0
Uncertain	12	17
Total	100	70

The incidence rates of dream recall were high in the experiment. For the one-night self-observation, 44 (62.9%) of the 70 participants in the control group, which did not receive the dream recall instruction, reported dreaming (21.4% reported the content and 41.5% did not), while 26 (37.1%) participants reported no dreams. With the aid of the dream recall instruction, 79% of the 100 participants in the experimental group reported a dream experience immediately following the first

night's sleep. Seventy-three percent could provide detailed contents of their dreams, while six percent could not. The accumulating number of participants with dream awareness increased to 84% and 89% following the second and third nights, respectively. Of the 11 participants who did not recall a dream in the entire three-night experimental period, eight dropped out after the first night's report, and four of these were uncertain whether they had dreamed or not. The remaining three participants completed all three nights' recordings, and one of them was uncertain as to whether he had dreamed or not. The experimental group was significantly more likely to recall dream experience (i.e., dreams with content) than the control group (Pearson chi-square (1) = 5.36, $p < 0.05$; Cramer's V = 0.18, $p < 0.05$).

In the initial interviews with the experimental participants, 12 reported that they were uncertain about their dream experience (or dreamed sporadically, according to their daily report). Of these 12 participants, seven could recall their dreams during the three-night self-observation, four handed back only the last dream report, and one did not provide any dream report. All five participants who did not produce a dream report had participated in only one night's self-observation. Those participants who claimed that their frequency of dreaming was irregular often suggested that they tended to dream more frequently during particular highly predictable periods such as moving into a new apartment, travelling overseas, or preparing for examinations.

D. Discussion - Dream Recall is Not Difficult

Some western studies have demonstrated that very few non-neurological patients have no dream recall (e.g., Pagel, 2003). Moreover, when taking into account so-called "white" dreams (the certainty of having dreamed but not being able to recall specific dream content), the rate of dream "recall" is very high, up to 72.9% of spontaneous awakenings or an average of 5.1 dreams per week, for example (Schredl, Wittmann, Ciric & Götz, 2003). This suggests that people are regularly aware of their dream experiences irrespective of their ability to recall dream content. Similarly, the majority of the Chinese participants in the current study reported dream recall daily or several times a week in the initial interview. This frequency of dream recall is consistent with the normative data provided by most of the western studies (e.g., Görtelmeyer, 1986; Schredl, 2000a, 2000b, 2002a, 2003; Schredl, Ciric, Götz, & Wittmann, 2003; Webb & Kersy, 1967; Zadra & Nielsen, 1999). These results do not seem to suggest a cultural difference in dream recall frequency.

However, it should be cautious that the method of the current study is different from those of the previous studies. Firstly, the "dream recall frequency" that the present study intended to measure included dream experience with or without retrieved contents (i.e., frequency of dream awareness). Secondly, the dream recall

frequency was quantified in a more concrete way (instead of using a Likert scale). Thirdly, most of the scales used by the previous studies did not include an option "uncertain about dream recall frequency" for participants to choose. Therefore, the participants in those studies were forced to indicate their frequency of dream recall on a five- or seven-point scale, even if they found it difficult to quantify their dream experience.

The dream recall instruction and daily recording method were shown to be effective in triggering dream recall from neurologically and psychiatrically healthy individuals by utilizing an emotional approach and a conscious state that resembles dreaming. Although some participants claimed in the initial interview that they were uncertain about their dream experience and frequency, most were able to provide dream reports with the aid of the dream recall instruction. Perhaps, the internal affective texture of dreams and its derivatives constitute a core of associative memory networks and pathways that can be used to access the dream experience relatively directly. Nevertheless, it is worth noting that while keeping a dream diary increases dream recall in low and medium dream recallers, it may also decrease dream recall in high dream recallers (Schredl, 2002c).

It should be noted that the dream recall instruction involves some potential "suggestive" elements. This may limit its applications and may affect the current

findings, though the suggestibility of Chinese people is not particularly high, as compared to the western normative data (Yu, 2005). On the other hand, some precautionary measures can be taken to reduce the risks of false memory or secondary revision. For instance, participants are only required to use the guidelines (i.e., step two to seven, and the asterisked item) to retrieve the details of their dream experience if and only if they are aware that they have just been dreaming. Differences between dreaming and fantasy (or secondary revision) are clarified with the participants. The former is more involuntary, that is, it is relatively difficult for the dreamer to revise and control the narrative contents and experience during dreaming. By contrast, one can revise and control what to fantasize relatively easily. According to the interview reports, the participants in the current study did not find it difficult to distinguish their dream experiences and voluntarily created fantasies which have just happened to them.

More crucially, the entire design of the dream recall instruction is very much in line with the cognitive interview technique, which is based upon psychological principles of remembering and retrieving information from memory. The cognitive interview is an important technique that is used for forensic investigation and has been successfully evaluated both in the laboratory and the field setting (Geiselman & Fisher, 1989; Geiselman, et al., 1984; Köehnhen, Milne, Memon, & Bull, 1999; Milne

& Bull, 1996, 2002). It can increase the effectiveness of retrieving information in terms of quantity and accuracy rates without any apparent negative consequences. According to the basic principles of the cognitive interview technique, although memory is selective and reconstructed, *relaxation* and *concentration* can improve recall, especially when rapport is established (Bekerian & Dennett, 1996; Fisher, Geiselman, & Amador, 1989).

The central memory strategy of the cognitive interview is *context reinstatement.* This technique is based upon the encoding specificity hypothesis (Flexser & Tulving, 1978; Tulving & Thomson, 1973). Context reinstatement requires the subject to mentally reconstruct the physical and personal context (i.e., external and internal states) present during the target event. Context is mentally reinstated by instructing the subject to form an image of the scene of target event, and to describe thoughts, feelings, sounds, and other physical conditions present at the time of the event. All these are very much similar to the current approach of the dream recall instruction. Interestingly, some participants in the current study reported that they knew whether the recalled materials and images were accurate exactly because a piece of accurate material could help them recall more details (i.e., serving as a cue).

The sleep laboratory was once regarded as the best place to study the process of dreaming. Dreams are, however, something that are easily influenced by measurement

methodology (Schredl, 2003, 2004b; Schredl, Ciric, Gotz, & Wittmann, 2003). Laboratory experimentation is an intrusive method. For instance, Hobson, Goldfrank, and Snyder (1965) studied 10 subjects for four to six nights, with a total of 195 REM awakenings and 102 Non-REM awakenings. The large EEG machine, attachment of electrodes to the participant's head, numerous laboratory awakenings throughout the night, and adjustment to a new or laboratory sleep setting can substantially change the normal sleep-wake cycle of the participants as well as the content of their dreams (e.g., Domhoff & Schneider, 1999; Strauch & Meier, 1996). It is worth emphasizing that a reduction in sleep quality or a high number of nocturnal awakenings leads to heightened conscious arousal and thus higher dream recall frequency (e.g., Schredl, 2004b; Schredl, Bozzer, & Morlock, 1999). Collecting dream reports at a natural setting with appropriate guidelines for dream recall is therefore of value because of its comparatively low interference effect.

Every research method, especially experimental "intervention", can potentially bias the subject to behave in a particular way, and thus involve a certain degree of demand characteristics. Compared to the EEG awakening method, it seems that the application of the dream recall instruction, together with a relatively blind procedure, constitutes a less intrusive manoeuvre for investigating people's dream experience and perhaps reduces the possibility of demand characteristics.

All in all, the current results indicated that most people are frequently aware of their dream experience, even though they may not remember the details of their dreams. In the similar vein, dream recall and retrieval of dream content are not as difficult as some researchers predicted, and are indeed easily obtained within a few days by using some guidelines for dream recall facilitation. Therefore, memory of dream experience is not necessarily poor.

The current study combined several methods, namely, survey by thorough personal interview, between-subject experiment, and repeated measure, which required substantial inputs from the participants as well as considerable follow-ups by the interviewers. Therefore, a parsimonious approach was taken when designing the procedure of the study, in order to prevent lethargy and practice effects, which certainly threaten the validity of the study. Further studies that extend the sleep assessment period or obtain better baseline dream recall may complement the findings of the current study provided that the practice effects of a long repeated measure design can be properly tackled.

Chapter Three

A Clinicoanatomical Study of Dreaming in Patients with Posterior Brain Lesions

A. Introduction

According to the neuropsychological models of dreaming (Solms, 1995, 1999; Yu, 2003), the functioning of the motivational systems of the brain is normally channelled towards goal-directed action but access to the motor systems is blocked during sleep. This indicates a regressive course that reverses the normal process, which proceeds from the lower parts of the perceptual systems (which serve concrete imagery) to the higher parts (which serve memory and abstract thinking). Because of this regressive process away from the motor systems and towards the perceptual systems, dreamers do not actually engage in motivated activity during sleep, but rather imagines themselves to be doing so.

Such a mechanism of dream formation is supported by two main findings. Firstly, the dorsolateral frontal convexity, the motor gateway from thought to action, is deactivated during dreams (see Yu, 2003, for a review). Secondly, lesions in the inferior parietal lobule, and in particular the supramarginal gyrus (BA40), lead to global cessation of dreaming (Solms, 1995, 1997). The supramarginal gyrus (BA40), is a portion of the grey cortex at the back of the brain just behind and above the ears,

near the junction of occipito-temporo-parietal cortices (PTO). Right-sided lesions in the supramarginal gyrus cause cessation of dreaming in association with disorders of spatial cognition, whereas lesions in the same region of the left hemisphere convexity cause cessation of dreaming in association with disorders of quasi-spatial (symbolic) operations (Solms, 1997, 2000b). The supramarginal gyrus participates in the highest levels of perceptual information processing, including symbolic operations. This function is required for the conversion of concrete perception into abstract thinking, and for the retention of organized experience (Luria, 1973). Accordingly, a lesion circumscribed to this specific part of the brain, to which Solms (1997, 1999) attributes the important functions of dream formation and regression, leads to the loss of dreaming.

Most PET studies, however, have revealed that the inferior parietal cortex, which includes the supramarginal gyrus, deactivates significantly during REM sleep (Braun, et al., 1997; Braun, et al., 1998; Heiss, Pawlik, Herholz, Wagner, & Wienhard, 1985; Hong, Gillin, Dow, Wu, & Buchsbaum, 1995; Madsen, Holm, et al., 1991; Madsen, Schmidt, et al., 1991; Maquet, et al., 1990; Maquet, et al., 1996; Nofzinger, Mintun, Wiseman, Kupfer, & Moore, 1997; see Yu, 2001a, for a review). Global cessation of dreaming as a consequence of posterior brain lesions has long been recognized in the neurological literature (Benson & Greenberg, 1969; Bischof & Bassetti, 2004; Boyle

& Nielsen, 1954; Corda, 1985; Ettlinger, Warrington, & Zangwill, 1957; Farah, Levine, & Calviano, 1988; Lyman, Kwan, & Chao, 1938; Michel, Jeannerod, & Devic, 1965; Michel & Sieroff, 1981; Müller, 1892; Nielsen, 1955; Peña-Casanova, Roig-Rovira, Bermudez, & Tolosa-Sarro, 1985; Wapner, Judd, & Gardner, 1978; Wilbrand, 1887, 1892). Not every reported case involved lesions to the supramarginal gyrus (Yu, 2001a). For instance, Bischof and Bassetti (2004) documented a case of complete dream loss (a 73-year-old woman) following bilateral posterior cerebral artery thrombosis in the absence of REM sleep abnormalities. No dreaming was elicited by repeated awakenings from REM sleep. Bischof and Bassetti also assessed the memory functions of this case to show that memory was not deficient. In reanalyzing Solms's clinical series, Yu (2001a) suggested that the dream cessation effect could alternatively be attributed to lesions circumscribed to the temporo-occipital junction (BA37). Further clinical investigation is therefore required to clarify whether lesions to the inferior parietal lobule and supramarginal gyrus necessarily lead to cessation of dream experience. This is the first purpose of this study.

In diagnosing cessation of dreaming by the semi-structured dream interview, Solms (1997) asked directly patients whether or not their dreams had changed since the onset of their neurological illness:

"If the response was negative, the patient was carefully questioned to determine whether or not this had also been the case prior to the onset of the illness.... Subsequently changes from a patient's personal baseline were then determined. Patient were classified under three headings, namely, (a) those who continued to dream, (b) those in whom all dreaming had ceased, and (c) those who were unsure as to whether or not they were still dreaming" (Solms, 1997, p.84).

Over and above the anatomical uncertainty, more fundamentally, Hobson (1999, 2001, 2002) questioned the validity of the human lesion methods on the grounds that patients' reports of dream cessation can be conceived as a secondary effect of memory failure, rather than as a direct consequence of neurological insults. There are two arguments within Hobson's criticism: that dream recall is difficult per se, even in normal people (as has been explored in the last chapter), and stroke patients' memories are "notoriously poor". Associating cessation of dream experience with posterior cerebral lesions is particularly alarming because the important neural substrates of memory are situated in the parietal and temporal lobes, namely, the posterior brain. The second purpose of the present study was to examine whether or not memory dysfunction necessarily results in cessation of dream experience.

B. Method

B.I. Design

Considering the clinical evidence that memory is affected by many neuropathologies, and is even considered to be a "fragile" system, it is perhaps unsurprising to find that most patients who have ceased dreaming also experience memory deficits. Yet, patients who have memory deficits but a preserved ability to dream provide equally important evidence for the dissociation between the two syndromes. In the same vein, patients' reports of preserved dream experience (i.e., no cessation of dream experience) after posterior brain insults cannot be ignored. To clarify the memory and anatomical issues, the study included eight patients who had posterior brain lesions as a consequence of cerebrovascular insults. Their sleep and dream experience before and after stroke was compared, using Solms's (1997) protocol for dream alterations. In addition, they were investigated systematically on a daily basis from initial hospital admission to discharge. Patients were classified as deficiency of dream experience if and only if cessation of dream recall and awareness occurred since their strokes as compared to their premorbid baselines of dream awareness frequency and this was further confirmed by daily testing during the period at the hospital. The precise locations of brain lesions were strictly charted and coded according to Brodmann's

system (Brodmann, 1909; Damasio & Damasio, 1989).

In particular, there are four essential differences in the methodology between the present clinicoanatomical study and Solms's previous ones:

1. Different from Solms's previous studies which included patients with a variety of neuropathologies, with a few exceptions only patients with cerebrovascular insults and specifically the non-hemorrhagic type were included in the present study. Non-hemorrhagic infarctions provide good specimens for clinicoanatomical study investigating correlations between behavioural dysfunction and site of brain destruction, because they entail actual destruction of brain parenchyma (Damasio & Damasio, 1989) and their symptomatologies were clear. (This will be explained thoroughly in Chapter Five "A Clinicoanatomical Study of Dreaming in Patients with Ventromesial Frontal Region Lesions").
2. The present study also distinguished itself by adopting a *daily* neuropsychological assessment (including memory functions) as well as *morning* sleep and dream interviews. Instead of using the single interview method, the current study investigated patients systematically on a daily basis from initial hospital admission to discharge.
3. The functional anatomy of the brain lesions was determined and coded more

precisely by using standard CT and MRI methods.

4. Each case was interviewed by at least two separate investigators (the author and at least one trained interviewer).

B.II. Subjects

Eight patients who were drawn from the relevant clinical populations in the neurological ward of the hospital associated with the University of Cape Town formed the sample. These were patients with focal posterior brain lesions as a consequence of cerebrovascular accidents (CVA). Six were males, and two were females. The average age was 45.8 years (S.D. = 14.0, range = 27-72). The pre-stroke frequency of dream experience of all patients included in the study was within the regular range (i.e., the frequency of dream awareness was three times per week or more). A pathophysiological classification divides cerebrovascular disease or stroke into two main subtypes of cerebral haemorrhage and cerebral ischaemia, and subdivides each of these (Appendix D). Some cases were ultimately excluded due mostly to inadequacy of data for accurate interpretation (e.g., type or nature of pathology, but not based on the locations of their lesions or dream alteration experiences).

B.III. Procedure

Patients were transferred to the neurological ward of the hospital mostly within a week after cerebrovascular accidents, and all patients were interviewed within two weeks after cerebrovascular accidents. Therefore, all patients in the current study had experienced a recent cerebrovascular accident. All potential patients at the stroke unit of the neurological ward were interviewed. Those patients who had initially presented with symptoms of sudden cerebrovascular accidents but upon neuroimaging were diagnosed as other neuropathologies were excluded. In addition, some cases with a diagnosis of cerebrovascular disease were ultimately excluded due to mostly inadequacy for accurate interpretation. For instance, Case No. 11, a patient experienced a cessation of dream experience (including both dream recall and awareness) since stroke suffered from a glioblastoma multiform in addition to a cerebrovascular disease, involving almost the entire left hemisphere with distorting features. His lesions were too diffuse to make any accurate neurobehavioral interpretations. Similarly, patients who could not provide clear pre-stroke dream experience (i.e., "uncertain" about the frequency of dream recall and awareness) were also excluded.

According to Schredl and Fulda (2005), although day-to-day variability of dream recall may be high, a time period of two weeks is sufficient to obtain reliable measurements. They also suggested that the diary method is well suited for measuring

interindividual differences in dream recall frequency reliably. To obtain a comprehensive clinical picture of each patient, they were investigated systematically on a daily basis from initial hospital admission to discharge. The length of the hospitalization (and mostly the investigation) period ranged from two weeks to more than a month. Each patient was interviewed by at least two separate investigators (the author and at least one trained interviewer). The trained interviewers (students in Master degree programmes) were blind to the hypotheses of the current study and the diagnoses of the subjects. In the first interview, information about pre-stroke sleep and dream experience (e.g., dream recall frequency, frequency of dream awareness, recurrent dreams or nightmares, etc.) was obtained, and neuropsychological examination including assessing patients' memory functions was administered. Most information was reconfirmed by different investigators in latter interview sessions.

After the first interview, the patients' sleep and dream experience as well as neuropsychological and memory functions were closely monitored on a daily basis by using morning sleep and dream interview as well as follow-ups during the other time of the day. All patients were interviewed in the morning for their sleep and dream experience. Additional follow-ups and behavioural observation were administered during the daytime, primarily for more thorough neuropsychological assessments and investigating their sleep and dream experience during the daytime (they were

investigated immediately after naps to confirm whether they had dream experience during napping). Post-stroke capacity and frequency of dream experience (including dream recall and awareness) were assessed. The dream recall instruction was provided (in the initial interview) to the patients to increase their ability to remember their dream experience (see Chapter Two). If the patients reported no dream recall, it was distinguished carefully whether the patients did not have any dream experience/awareness or they had dreamed but had forgotten the dream content.

After investigation, consistency of the findings collected by the different interviewers was checked. Each patient's dream experience or dream alteration was characterized by using Solms's (1997) protocol, the information about their dream experiences preceding and following strokes, and the results of the daily assessments during the hospitalization.

The functional anatomy of the neuropathologies was determined precisely by using standard CT and MRI methods. In order to make a comparison with the data between the patients, the precise locations of brain lesions based on the same systems were strictly charted and coded in detail according to the cytoarchitectonic maps developed by Brodmann (1909) and the templates by Damasio and Damasio (1989) for precise and specific localization, following the standard lesion method in humans (Damasio & Damasio, 1989) (Appendix E). In addition, the patients' background

information and full medical history were traced including all diagnostic reports made by neurologists and neuroradiologists. The precise locations of brain lesions between the patients were then compared and analyzed together with all clinical information including alterations in dream experience.

B.IV. Materials

The protocol of the present study comprised three primary components: 1) assessment of dream and sleep experience, 2) neuropsychological assessment, and 3) assessment of brain lesions.

B.IV.1. Assessment of Dream and Sleep Experience

B.IV.1.i. Interviews for Premorbid Dream and Sleep Experience

Solms's (1997) protocol for dream alterations (Appendix F) was adopted in the interviews for dream experiences before and after stroke. Besides Solms's protocol, a set of probing and core questions were designed to facilitate thorough and in-depth discussions about premorbid dream and sleep experience, with reference to the measures adopted by the previous dream studies (e.g., Erlendur, 2003; Foulkes, Spear, & Symonds, 1966; Kemp, Burt, & Sheen, 2003; Klosch, et al., 1999; Punamäki, 1998; Schredl, 2002a, 2004a, 2004b; Schredl, Bozzer, & Morlock, 1999; Schredl &

Frauschier, 1995; Zadra & Nielsen, 1999) (Appendix A). Specifically, the patients' general concepts of dream, and pre-stroke frequency of dream experience including dream recall and awareness were clarified. In addition, the patients were required to provide the latest dream/s that they could remember before their strokes with the aid of the Most Recent Dream Report (Domhoff, 1996) (Appendix G).

B.IV.1.ii. Daily Dream and Sleep Assessments

All patients were required to provide any dreams that they could remember each morning throughout their hospitalization. The Most Recent Dream Report (Domhoff, 1996), with modifications for some neuropsychological purposes (Appendix H), was adopted as guidance for participants to report their dreams. For neuropsychological and prompting purposes, questions about each human sensation were probed after participants describing their dream contents, for instance, "Did you *really see* anything in your dream?" It should be noted that quantitative content analysis is not the focus of the current study. The Most Recent Dream Report Form was primarily used for 1) facilitating dream reporting, 2) exploring any qualitative changes in their dreams (e.g., non-visual dreaming), and 3) drawing patients' interest and attention to their dream experience.

By using some predetermined questions, the four conditions were clarified and

distinguished as far as possible: (1) the subjects had dreamed; (2) they claimed that they did not have any dreams; (3) they had dreamed but had forgotten the dream content; (4) they did not remember whether they had dreamed or not (see Chapter Two, for details).

Dream recall instruction (Appendix C) was provided to the patients to increase, as far as possible, their ability to remember their dreams. The dream recall instruction had seven guidelines (see Chapter Two, for details). In addition to dream experience, the patients were also assessed for their sleeping quality (Jacobs, 1998; Appendix I).

B.IV.2. Assessment of Neuropsychological Functions

The neuropsychological battery used in this study was composed of three primary parts, which measured the executive functions, visual memory, and verbal memory, respectively. All neuropsychological tests and scoring systems in the battery are widely adopted standard measures. Assessing these functions could help establishing a diagnostic consistency between anatomical pathology and clinical observation. In particular, these three components constitute a critical test for the potential association between cessation of dream experience and memory dysfunction. The two major assessments for memory were the Rey-Osterrieth Complex Figure (ROCF; Rey, 1941; Osterrieth, 1944; Guyot & Rigault, 1965) and the Rey Auditory-Verbal Learning Test

(RAVLT; Rey, 1964; Taylor, 1959).

B.IV.2.i. Executive Functions

Tests were chosen based upon their capacity to measure distinct subcategories of executive functions. These included semantic fluency/category naming (animals and fruits) (Morris, et al., 1989; Spreen & Strauss, 1991), story recall (Babcock, 1930; Babcock & Levy, 1940), digit span (WAIS-III; Wechsler, 1997a), matrix reasoning (WAIS-III; Wechsler, 1997a), motor sequencing (Christensen, 1979; Luria, 1966), repeated pattern drawing (Christensen, 1979; Luria, 1966), tapping rhythm (Christensen, 1979; Luria, 1966), and Go/No-Go test (Christensen, 1979; Luria, 1966).

B.IV.2.ii. Visual Memory

Rey-Osterrieth Complex Figure (ROCF; Rey, 1941; Osterrieth, 1944) was used to investigate both perceptual organization skills and visual memory in participants. The ROCF includes a copy trial, an immediate recall trial and finally a delayed recall trial. The present study adopted the widely used scoring system developed by Guyot and Rigault (1965). In this system, the scoring units refer to specific areas or details of the figure that have been numbered for scoring convenience. There are 18 units in total

and the highest possible number of points is 36. Two points are given for each unit that is drawn correctly and placed properly. One point is given if the unit is drawn correctly but placed poorly, or if the unit is distorted or incomplete, but recognizable and placed properly. Half a point is given if a unit is distorted or incomplete and placed poorly, but still recognizable. No points are given if the unit is absent or unrecognizable.

B.IV.2.iii. Verbal Memory

Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964; Taylor, 1959) was used to measure both short- and long-term verbal retention. In addition, the test measures immediate verbal span, reveals a learning curve, exposes learning strategies, elicits retroactive and proactive interference tendencies, and finally exhibits tendencies to confusion or confabulation on memory tasks. The test consists of five presentations with recall of a 15-word list, one presentation of a second 15-word list, and a sixth recall trial. The maximum score for each trial is 15. A recognition trial is administrated in specific cases where severe amnesia makes free recall impossible.

Further details of the neuropsychological battery are provided in Appendix J. A more thorough introduction to the memory tests, the ROCF and the RAVLT, is

provided in Chapter Six, which also includes analyses of the memory functions of different groups of neurological patients.

B.IV.3. Assessment of Brain Lesions (Neuroimaging)

The brain images of the patients in the current neurological series were traced and analyzed. These images were obtained using either computerized X-ray tomography (CT) or magnetic resonance imaging (MRI), which are the only two current scanning techniques for the identification of structural neuropathological changes.

The variance of angles of incidence in CT and MRI is a factor to be taken into consideration. In transverse cuts, CT is mostly obtained in relation to the inferior orbitomeatal line, with angulations varying between 10 degrees and 30 degrees. MRI is generally obtained parallel to the orbitomeatal line and at a 90-degree angle in coronal cuts. Due to the variability of angles of incidence in CT and MR, it is necessary to use different sets of brain templates to localize the cerebral lesions. Hence, a total of six sets of templates covering incidence ranges of 0 to 90 degrees [based on those developed by Damasio and Damasio (1989)] were used in this research. The chosen angles correspond to those most frequently used. This standard series of templates was prepared with reference to the classical cytoarchitectonic maps of Brodmann (1909) and anatomical information available in standard atlases

(DeArmond, Fusco & Dewey, 1976; Hanaway, Scott, & Strother, 1977; Matsui & Hirano, 1978; Palacios, Fine, & Henghton, 1980; Schnitzlein & Murtagh, 1985).

Furthermore, templates for the analysis of vascular territories based on current knowledge of vascular anatomy (Lazorthes, Gouaze & Slamon, 1976; Salamon & Huang, 1976; Waddington, 1974), the pre-existing templates of Damasio (1983, 1987), and the neuroanatomical atlas of Montemurro and Bruni (1988) were used in order to maximize the accuracy of cytoarchitectonic mapping.

B.V. Interviewer-Interviewee Relationship

A cooperative relationship between the interviewers and the patients, and genuine responses from the patients were regarded as essential. Rapport was established through, for example, presenting administration of the tasks in a professional but unhurried manner, elaborating as needed to help put the patients at ease, showing sincere interest in what the patients were saying and doing, etc. It was emphasized that the accuracy of the information the patients provided was important for the investigation.

B.VI. Research Ethics

Ethical approvals from relevant bodies were obtained. Ethical considerations are

provided in Appendix K.

C. Neuroanatomical Analysis and Case Reports

No patients reported premorbid absence of dream experience (including both dream recall and awareness). The average premorbid frequency of dream awareness was 4.2 per week (ranged from three times per week to nightly). In the clinical series of eight cases presenting with posterior cerebral lesions, one subject had ceased awareness of dreaming experience (i.e., no dream recall and awareness) since infarction and no dream could be recalled during hospitalization (Table 3.1), while the other seven subjects had experienced no evident alteration in their dream experience based upon Solms's (1997) protocol for dream alterations and their post-CVA dream recall during hospitalization (Table 3.2). Of these seven dreaming patients, five had sustained lesions to the parietal lobule, and a range of posterior lesions covering almost all parietal regions was detected (BA40, BA39, insula, cortices S). Five of the seven dreaming patients showed memory deficits. More detailed neuroanatomical analysis, and corresponding neuropsychological assessment of some of the cases, is presented in the following passage.

Table 3.1 A Case of Deficient Dream Experience with Posterior Brain Lesions

No.	Sex	Age	Pathology	Lesion Sites

7	M	58	Large artery infarct	R. BA22, 41, 42, 21, S, 4, 6, 39, 19, insula

Note. R: Right.

Case No. 7 (Deficient Dream Recall and Awareness with Posterior Brian Lesions Excluding BA40)

Mr. JL was a 58-year-old, right-handed, ex-building constructor. He presented with headaches, left-sided weakness of the leg and arm, slurred speech, visual disturbance, and difficulty swallowing.

He was alert, orientated, and clear, and was not distressed about his stroke during the neuropsychological investigation. A relatively good memory for his age range was demonstrated by his scores from the RAVLT (Trial I: 5, II: 6, III: 8, IV: 8, V: 9; B: 2, VI: 9), which was carried out under noisy conditions. No episodic memory deficit was noted, nor did Mr. JL personally have any problem with his memory. In contrast, his ROCF performance (Copy: 5.5, Immediate Recall: 2.5) was affected by his constructional apraxia, and his mild left-sided neglect and hemianopia, which were evidenced by the line bisection test and bilateral visual stimulation. Anton's syndrome was possible considering that, although he admitted his stroke and movement problem, he showed no awareness of his visual disorders. His pre-stroke frequency of dream awareness was around five times per week. He ceased having dream recall and awareness after stroke. No dream was reported throughout two weeks of daily

investigation and intermittent follow-ups, with the use of the dream recall instruction.

At first glance, the distribution of lesion sites was anatomically inconsistent in that almost all regions surrounding the right BA40 were damaged, except the BA40 itself, including BA4, BA6 and cortices S (anterior to BA40), BA39 and BA19 (posterior to BA40), and BA22, BA21, BA41, and BA42 (inferior to BA40). Indeed, the lesions involved primarily the temporal lobule, along with a separate single lesion in the inferoposterior parietal region.

Table 3.2 Cases of Dream Preservation with Posterior Brain Lesions

No.	Sex	Age	Pathology	Lesion Sites
10	F	39	Lacunar infarct	L. BA40
15	M	46	Large artery infarct	B. BA28, globus pallidus, red nucleus
22	F	27	Large artery infarct	L. BA40, 39, 22, 7
27	M	46	Large artery infarct	L. BA28, 36, 20, 37, 18, 19, petrous apex
33	M	72	Lacunar infarct	L. BA4, 6, S, insula
41	M	35	Infarct	L. BA4, 6, S, R. BA 41, 42, insula
42	M	43	Lacunar infarct	B. BA 44, 45, 46, 8, 9, 10, 4, 6 & 23, L. BA40, R. BA 23, 31, cerebellar region next to pyramis

Note. R: Right; L: Left; B: Bilateral.

Case No. 10 (Dream Preservation with BA40 Lesion)

Ms. BA (39 years old) had been admitted to the hospital due to a third stroke, which resulted in hemiparesis to the right. She obtained high scores in the ROCF (Copy: 35, Immediate Recall: 18). Although she did not have any sensory loss, further investigation by bilateral stimulation showed finger agnosia on the right side without

tactile neglect. Her RAVLT scores were substantially deviant from the norms for her age range, with only six words in the final trial (Trial I: 3, II: 4, III: 5, IV: 7, V: 7, B: 2, VI: 6). Her ability to memorize was measured using the digit span test (WAIS-III), in which she experienced difficulty holding five digits (as opposed to forgetting), and it was obviously impossible for her to manipulate six or more digits, even with a considerable amount of practice. She was surprised and frustrated with her "failure" in these remarkably "easy" tasks. Her memory deficit belonged to the short-term and working type, and the clinical signs were clearly left parietal.

According to her most recent MRI head scan, a single focal area of FLAIR hyperintensity was present in the left high parietal region (a small lesion in the white matter of BA40). She dreamed every night, and this had not changed since her stroke. She had no difficulty remembering whether she had dreamed or not, nor recalling the dream content, even with the aforementioned working memory disorders and spatial dysfunctions. She produced a very clear and detailed dream report each day without any difficulty during the investigation period.

Case No. 27 (Dream Preservation with Occipital Lobe Lesions)

Mr. LK (46 years old) experienced an acute onset of "tunnel-vision". Symptoms also included headache in the left temporal area, vomiting, convulsions, and decreased

memory. The CT brain scan identified a 4.5 x 3 cm, low-density, ovoid-shaped lesion in the left cerebropontine angle. It was associated with destruction of the petrous apex.

Mr. LK was clearly oriented during neuropsychological assessment, and was able to answer all questions in the MMSE flawlessly. He obtained 31 in ROCF Copy, and 11.5 in Immediate Recall, and in the subsequent 10-day delayed recall his score was 12. Visual performance was good with no higher-perceptual dysfunction or object agnosia, although his visual memory was lower than expected. His RAVLT scores, however, were well below the expected performance for his age range (Trial I: 3, II: 4, III: 3, IV: 5, V: 5, B: 3, VI: 2) and, after the second interview, he could not remember a single word. Clinically, he presented with low-level perceptual dysfunction, along with a certain degree of visual and verbal memory deficits of the encoding type. This did not affect his recall of his dream experience. During the neuropsychological investigation, dreams were reported in detail once every other day.

Case No. 41 (Dream Preservation with Sensorimotor Area and Insular Lesions)

Mr. JJ was 35 years old. His verbal memory was clearly below the average for his age range (RAVLT Trial I: 5, II: 1, III: 4, IV: 6, V: 6, B: 5, VI: 4), and he made 14 confabulation errors throughout the seven trials. No constructional apraxia was

apparent in the ROCF, though some kind of organizational problem was apparent and his visual memory was compromised (Copy: 31, Figure 3.1). Although Mr. JJ scored relatively highly in the ROCF copy trial, he misplaced the interior mainstay, and the gestalt, although not entirely lost, deteriorated quickly in the subsequent immediate and delayed recall trial.

Cases No. 33 and 41 continued to have regular dream experience after CVA, and had sustained lesions to similar regions, the insula and sensory cortex, but on different sides. The clinical picture of these two patients, whose BA40 and BA39 were intact, resembled those of the patients with BA40 lesions. This was particularly clear when considering their spatial disorders, which were attributable to the destruction of the insula, which is situated just under the BA40.

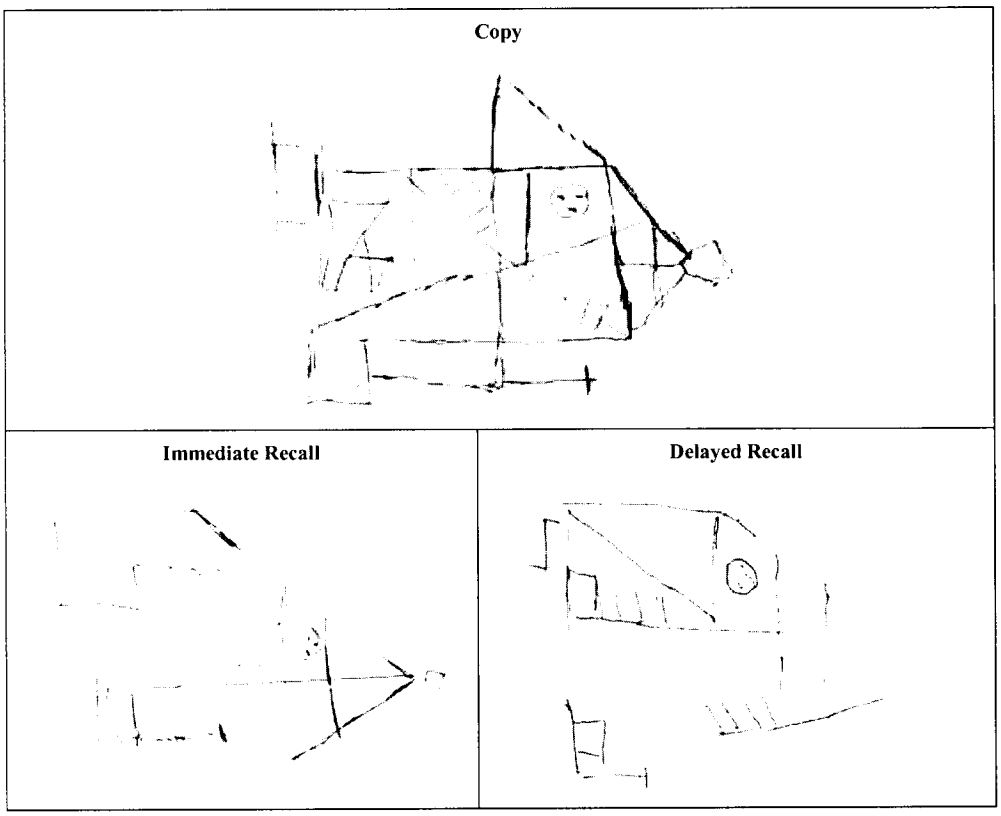


Figure 3.1 Case No. 41's ROCF

Case No. 42 (Dream Preservation with Diffuse Bilateral Posterior Brain Lesions)

Mr. NM was a 43-year-old chronic alcohol abuser. He suffered from left homonymous hemianopia (without visual ataxia or neglect), partial object agnosia, and simultanagnosia. During the neuropsychological interviews, he exhibited substantial difficulty in concentration and mental tracking, especially on visual tasks. Although he did not seem to have dyscalculia, he took more than a minute for each subtraction in the Serial 7 test. He managed to finish seven subtests of the WAIS-III block design

with much encouragement from the investigator, though he took much longer than the standard limits. In the WAIS-III picture completion task, he was able to identify the objects in the pictures without any difficulties. However, he could not find any single missing part of the objects in Figures 1 to 6. He exhibited substantial difficulty in completing the memory tasks (e.g., ROCF, RAVLT, digit-span test) due to his profound attention and visual deficits.

The MRI images demonstrated fairly extensive, but scattered, deep white matter and periventricular hyperintensities, involving both frontal and both parietal regions, and the left occipital lobe. There was a more extensive area of hyperintensity in the right occipital lobe, related to the posteromedial aspect of the occipital horn of the right lateral ventricle, and extending to the midline (specifically, the right splenium of the corpus callosum, or BA23 and BA31). The optic tracts might have been involved at this point. There was also a previous right medial cerebellar infarct.

The neuroradiological findings were consistent with his neuropsychological presentation of mild executive impairment, and relatively low level perceptual dysfunction. Mr. NM was frequently aware of his dream experiences before coming to the hospital, and this did not change after admission, despite the limited memory capacity associated with the fundamental attention problem, and the extensive damage to his prefrontal, parietal, and occipital cortices. He had a happy dream at the hospital:

"I am at home. See many people drinking".

D. Discussion

D.I. Memory Loss is Not Equal to Loss of Dream Experience

Two points of interest are highlighted in this Chapter, corresponding to the memory and anatomical controversies. Firstly, a post-stroke failure of dream recall or loss of dream experience is uncommon and not as prevalent in stroke patients as some researchers have predicted, although memory dysfunctions are frequently observed. Almost all patients in the current study presented with some degree of memory difficulty, and included visual, verbal, and short- and long-term memory spectrums. Nonetheless, these patients were able to report their dream experiences. A single case with post-stroke deficient dream experience was no more impaired in memory than seven similar patients who retained dreaming capacity. This provides clear evidence of the distinction between memory deficits and cessation of dream experience (This argument will be further explored in Chapter Six).

Echoing the findings reported in Chapter Two, recalling dream experience is not difficult, even in some neurologically-compromised patients. Therefore, as Hobson correctly pointed out, although stroke patients' memory is poor, and dream contents may be easily forgotten, impaired memory by no means provides a sufficient

explanation for a total lack of awareness of dream experiences.

D.II. Multiple Pathways of Dream Formation

Secondly, unilateral lesions to BA40 (Cases 10, 22, and 42) and its adjacent areas, including the sensorimotor cortices (BA1–6, anterior to BA40) (Cases 33, 41, and 42), the angular gyrus (BA39, posterior to BA40) (Case 22), Wernicke's area (left posterior BA22, inferior to BA40) (Case 22), and the insula (underneath BA40) (Cases 33 and 41), do not necessarily lead to cessation of dream experience. This has two implications for the neuropsychological understanding of dreaming: multiple pathways of dream formation, and loss of attentional consciousness.

Solms (1999, 2000b) found a bridge between the motivational system and the visual hallucinatory apparatus in the supramarginal gyrus. The role of this structure, however, was shown to be insignificant, and the contemporary replicated findings by different neuroimaging techniques do not provide convincing evidence for its active operation during dreaming. Other parietal regions, such as the sensory cortex, do not seem to play an essential part in dreaming either.

The supramarginal gyrus, together with its neighbour, the angular gyrus, performs a critical function in associating and organizing cross-modal perceptions, which allows complex concepts to be understood. From a functional point of view,

this high-order associative cross-modal region is not implicated in the formation of dreaming for a number of reasons (see Yu, 2001a). For instance, to a large extent, dreaming is visually based, and primarily unimodal, rather than transmodal.

From an anatomical perspective, there seem to be multiple pathways for connecting the motivational systems and the visual cortex. The inferior mesial temporal lobe (including BA37), for instance, has been identified as one of the crucial pathways, other than the supramarginal gyrus, for the formation of dreaming (Yu, 2001a). Ample evidence has shown that the inferotemporal cortex has intense afferent and efferent connections to both the visual representation cortex and the limbic motivational system (e.g., Akert, Gruesen, Woolsey, & Meyer, 1961; Creutzfeldt, 1995; Prelevic, McIntyre-Burnham, & Gloor, 1976; Turner, Mishkin, & Knapp, 1980; Whitlok & Nauta, 1956).

D.III. Loss of Attentional Consciousness

Unilateral spatial neglect is common after unilateral damage to the supramarginal gyrus. It is characterized by a lack of awareness for sensory events, and is located towards the contralesional side of space, together with a loss of orienting behaviors that would normally be directed towards that side. However, considerable residual processing can still take place for neglected stimuli, without reaching the patient's

awareness (see Driver & Vuilleumier, 2002, for a review). Similar to "preattentive" processing in normal people, such residual processing can modulate what enters the patient's awareness.

Although prefrontal regions have long been regarded as the pivotal substrate for selective attention and working memory, neurons in the parietal lobule also exhibit sustained activity in latter periods of working memory tasks (e.g., Andersen, Essick, & Siegel, 1985; Andersen, Snyder, Bradley, & Xing, 1997). Indeed, parietal regions may represent the current contents of working memory, with frontal areas manipulating what enters the proposed store (D'Esposito et al., 1998; Shallice, 1988; Ungerleider, Courtney, & Haxby, 1998). Accordingly, the relatively insignificant role of the parietal lobule in dream formation may underscore the dynamics of how the attentional consciousness and orientation, high level body awareness, space for selective working memory, and analytical computation are substantially undermined during dreaming, whereas the "preattentive" or unconscious processing remains. This is congruent with the phenomenological attributes of the aforementioned inferotemporal pathway, which appears to be more primitive but incisive, in contrast to the relatively sophisticated pathway constituted by the supramarginal gyrus (Yu, 2001a).

D.IV. A Limitation of Clinicoanatomical Studies

To reduce demand characteristics and support intensive investigation, students in Master degree programmes were trained to conduct some interview sessions. Employing completely naive interviewers is unfeasible because clinicoanatomical studies require some basic counselling, neuropsychological and clinical skills. Importantly, patients' welfare and safety should be considered and ensured.

E. Conclusion

Cessation of dream experience or awareness does not appear to be a secondary symptom of memory dysfunction. Even patients who suffer from profound memory deficits due to strokes are able to report their dream experiences. Although the current study was unable to replicate earlier findings on the cessation of dream experience based on inferior parietal lobe injuries, this is by no means conclusive. The present study encourages further detailed work, considering that the earlier claims by Solms were based on a large number of cases. Moreover, some of the cases in Solms's study reported recovery of dreaming. A comparison study of bilateral and unilateral posterior lesions (in particular involving the inferior parietal lobules on both sides) may further identify the necessary components in the neural pathway of dream formation.

Chapter Four

A Clinicoanatomical Study of Dreaming in Patients with Pontine Lesions

A. Introduction

By systematically ablating various brain structures, Jouvet (1962) identified that rapid eye movement (REM), and therefore dreaming, is produced by a small region of cells in a part of the brainstem, namely the "pons". He asserted that the forebrain, on the other hand, does not play any causal role in the generation of dreams. Even when the great cerebral hemispheres are entirely removed, as long as the pons remains intact, REM sleep occurs with monotonous regularity throughout sleep.

REM sleep is manifested by EEG desynchronization, which results from a net tonic increase in reticular thalamocortical and cortical neuronal firing. The firing signals were termed PGO waves by Jouvet (1962) because they originate in the pons (P), radiate rostrally to the geniculate bodies in the thalamus (G), and then to the occipital cortex (O). PGO waves are claimed to be the consequences of tonic disinhibition and phasic excitation of burst cells in the lateral pontomesencephalic tegmentum (i.e., neurons of the reticular formation and the pedunculopontine region).

Following this train of thought, Hobson and McCarley (Hobson, 1975; Hobson & McCarley, 1977; McCarley & Hobson, 1977) developed two anatomical and

physiological models of dreaming, namely the reciprocal-interaction model and the activation-synthesis hypothesis. The reciprocal-interaction model is characterized by the reciprocal on-off activity of two pontine neuronal populations: the cholinergic and the aminergic neuronal populations. The model proposed that REM sleep and dreaming are literally "switched on" by a small group of cells situated deep within the pons (principally in the mesopontine tegmentum), which secrete acetylcholine (ACh). This neurotransmitter activates the higher parts of the brain, which are thereby prompted to generate conscious images. These images are nothing more than the higher brain making "the best of a bad job... from the noisy signals sent up from the brain stem" (Hobson & McCarley, 1977, p. 1347). These inherently random stimuli generated in the sleeping forebrain by an autoactivated pontine oscillator are thereby synthesized into a coherent experiential episode. After a few minutes of REM activity, the cholinergic activation arising from the brainstem is counteracted by another group of cells, also situated in the pons (but in the nucleus locus coeruleus and dorsal raphe nucleus). The two neurotransmitters released, namely noradrenaline (NA) and serotonin (5-HT) "switch off" the cholinergic activation. Thereby, according to the theory, the conscious experience of dreaming involves essentially the interplay of the excitatory and inhibitory neurons in the pons.

The activation-synthesis hypothesis (ASH) of dreaming is, on the other hand, an

attempt to provide an account of the psychophysiology of the mental state of typical REM sleep, and simultaneously to replace the psychoanalytic theories of dreaming with a brain-based model. According to the ASH, dreams are actively generated by the brainstem but passively and non-specifically synthesized by the forebrain. This implies that the causal mechanisms underlying dreaming are "motivationally neutral" (Hobson & McCarley, 1977; McCarley & Hobson, 1977). Hobson (1992, 1994, 1999, 2001) gradually elaborated this model into a newer, more general theory of psychophysiological states, called AIM (Activation Level, Input Source, and Mode of Processing). In this newer theory, Hobson (1999, 2001) proposed a revision of the ASH that assigns a greater role to the forebrain mechanisms and allows for a higher possibility that dreams are psychologically meaningful. Nevertheless, this has by no means changed his position concerning the leading role of the pons as an instigator of REM and therefore dreaming.

The classical REM-pons hypothesis has been questioned by Solms's research (1997, 2000b) which demonstrated that "large" pontine lesions do not lead to a cessation of dreaming. Solms has not, however, been able to show that precise lesions to the target pontine nuclei (in the pontomesencephalic tegmentum and pontine peduncule), the activity of which has been proved to be associated with REM sleep, are compatible with preserved dreaming. Likewise, Pace-Schott, Solms, Blagrove and

Harnad (2003) argued that further human lesion studies are required in order to prove that the pons is not crucial in dream generation. Along with a brief discussion of the role of the pons in dreaming, the follow passage presents three neurological case examples of various brainstem lesions to illustrate the paradox and difficulties in carrying out pontine lesion studies.

B. Method

In considering the aforementioned issue, three rare cases with pontine lesions were analyzed thoroughly. The present study followed the entire methodological design delineated in the last chapter (see Chapter Three). Detailed clinical presentations and neuroanatomical pathologies of the patients were provided in order to underscore the clinical limitations of studying pontine lesions.

C. Neuroanatomical Analysis and Case Reports

In the clinical series of patients with neurological insults, three cases sustained pontine lesions (Table 4.1). Their pre-stroke frequency of dream experience ranged from three times per week to nightly. Two cases lacked dream recall and awareness since CVA (Case No. 19 & 20), and one reported no dream alteration (Case No. 13).

Table 4.1 Cases with Pontine Lesions

No.	Sex	Age	Pathology	Primary Lesion Sites
19	F	24	Neurosarcoidosis & infarct	L. ventral pons, parasellar regions, BA20, 28 & 36
13	M	54	Lacunar infarct	R. dorsal pons
20	F	44	Infarct	L. dorsal pons, F01, F09, F02, F03, F05, & F04

Note. R: Right; L: Left.

First Case – Ventral Pontine Lesions with Deficient Dream Recall and Awareness

BV (Case No.19), a 24-year-old, left-handed, female patient was in the hospital because the left side of her face had been aching and had become numb as a consequence of the recent CVA. Her left eye hurt, and she was not able to close it properly. Tears came out of her eyes uncontrollably. Her nose ran whenever she looked down. At the beginning she also complained of diplopia, but this was later resolved. The patient had no sensation in the left half of her face and the left half of her tongue, and her mouth drooped on the left side. She could move her limbs normally and there were no other signs of weakness.

She had a neurological history of mild maxillary sinusitis, which was more pronounced on the left side. A MRI scan 2 years ago indicated an enhancing lesion in the left parasellar region and medial to the left temporal lobe, which extended laterally to the cavernous sinus and inferiorly to the region of Meckel's cave (left internal auditory canal). Lesions included BA20, BA28 and BA36. There was no other

obvious evidence of dural enhancement.

A CT head scan 3 months later found hypodensity in the right basal ganglia and fronto-parietal regions, which kept enhancing as shown in the subsequent CT head scans done later in the same year. This was in keeping with areas of sub-infarction. There was no midline shift or hydrocephalus. An angiogram indicated irregularity of the proximal right internal carotid artery consistent with atheroma.

The most recent MRI axial and coronal brain scans replicated the finding that there was an enhancing T1 and T2 hypointense mass which involved the left cavernous sinus extending into the left internal auditory canal Meckel's cave and to the left foramen ovale. There was marked asymmetry of the parotids and muscles of mastication. The right parotid and hypertrophied were consistent with the muscles of mastication. The maxillary antra and ethmoid air cells were opacified in keeping with chronic pansinusitis. No other intra or extra axial lesions were present. There was no significant change in the lesion previously described on the left when compared with the previous MRI scans 2 years earlier.

Anatomically, the pituitary gland lies within a bony depression called the sella turcica located in the sphenoid bone at the base of the brain. The sphenoid sinus is immediately below the sella turcica. The pituitary stalk transverses the suprasellar cisterns. The optic chiasm and nerves are located superiorly and anteriorly to the stalk,

and the supraclinoid carotid arteries are positioned laterally. The cavernous sinuses lie within the dura on either side of the pituitary gland, and contain a meshwork of venous channels. The carotid arteries course through the middle of the sinuses. Cranial nerves III and IV and the 1st (ophthalmic) and 2nd (maxillary) divisions of the V cranial nerve are located within the lateral walls of the cavernous sinuses. The VI cranial nerve lies more medially within the sinus just below the cavernous carotid artery.

Considering the neurobehavioral presentation and the findings of the brain imaging series, the most recent symptomatological diagnosis is neurosarcoidosis, involvement evidenced by left II (Optic: located at the thalamus, responsible for vision), V (Trigeminal: located at the pons and medulla, responsible for chewing and facial sensations), VI (Abducens: located at the pons, responsible for lateral eye movements), and VII (Facial: located at the pons and medulla: responsible for the control of facial muscles and taste sensation of the front part of the tongue, salivation and the control of lacrimation) cranial nerves. This patient's lesions are restricted to the ventral dimension of the brainstem and pons, possibly extending up to the basal forebrain and some temporal lobe areas.

The patient stayed at the ward for three weeks. The investigation was a week delayed due to her physical conditions. Although the patient said that she quite often

dreamed normally and sometimes remembered her dreams well, she was unable to retrieve a single dream experience during the daily investigation in the ward, even with the aid of guiding dream recall. She did not have dream awareness except for one night (she claimed that she either did not dream or failed to recall her dreams). When she was confronted with the fact that she used to dream every night before the onset of her neurological illness, the patient explained that she could not sleep due to her condition. She was clearly orientated, and performed very well in both visual and verbal memory tests (both the short- and long-term dimensions), albeit sustaining temporal lobe lesions (which seemed to involve the ventral surface instead of the medial aspect or hippocampus). No episodic memory deficit was evident. The deficient dream/sleep experience was therefore attributable to the anterior pons as well as the parasellar regions (including the ventromesial frontal areas).

Second Case – Dorsal Pontine Lesion without Dream Alteration

KR (Case No.13), a 54-year-old man had just experienced a stroke when he consulted a doctor. First his throat felt dry. Then he felt dizzy, and fell over a chair. There was a sudden onset of right-sided weakness, headache, as well as speech and swallowing problems. Notwithstanding hemiparesis in the right arm and leg, sensory functions appeared to be normal. The patient was diagnosed with a lacunar CVA and diabetes.

A CT scan was administered 45 minutes after the onset of the right hemiparesis. Within the posterior fossa, there was a calcific ectatic basilar artery, almost certainly dolicho-ectatic (i.e., a distorted, dilated, and elongated artery commonly compressing a neural structure). Above the tent, there was no evidence of recent infarction. A focal lesion was identified in the right anterior pons, covering the basis peduncle and interpedunclar fossa, near the hypothalamus. Another small lesion was found in the right tegmentum, involving the right pontine reticular formation and medial lemniscus. The presenting symptoms of swallowing and speech impairment (cranial nerves IX, X, and XII) as well as hemiparesis were consistent with the injuries to the pons and medulla oblongata.

This patient claimed that he normally dreamed five days within a week before CVA. His most recent dream was on the night after his stroke. In this dream the patient remembered: "I was looking at a window, (making windows is his profession) and suddenly I had a sausage in my hands and in it was a piece of metal that I use in my work". He did not notice any unusual alteration to his dream experience after his stroke. During the neuropsychological investigation, dreams were reported almost daily. He was clearly orientated with no apparent symptoms of changes in consciousness. On the contrary, he could answer the questions, and finish the required tasks correctly during the neuropsychological assessment.

Third Case – Dorsal Pontine Lesions with "Dream Alteration"

CD (Case No. 20), a right-handed, 44-year-old, married female with four daughters, felt well until she suddenly fell and lost consciousness for a few minutes. When she regained consciousness, she was confused and unable to talk or move either of her right limbs. Her speech returned to normal within an hour and she gradually regained movement in her right hand, while the dense hemiplegia in her right leg remained unchanged. There was no sign of facial palsy.

According to the CT brain scan, V4 and cerebral hemisphere were normal. There was a small low density lesion in the upper left dorsal pons. Above the tent, there was no midline shift, and the ventricular system was of normal size. There was, however, slightly more opercular atrophy than expected for her age. The neuroradiological diagnosis based on the CT findings was left pontine peduncle infarct.

According to a follow-up MRI scan, an abnormally high signal was detected in the left parafalcine cortex and white matter of the centrum semiovale, extending to the cortex of the convexity. This distribution involved at least the left ACA vascular territory but the area may, in part, also be supplied by the left MCA branches. The follow-up MRA showed marked attenuation of the signal from the left internal carotid artery and the left MCA artery branches. The left P1 and A1 segments (vascular

territories) also showed decreased signal. This may be due to hypoplasia of these vessels as there appeared to be a prominent A1 segment on the right and a prominent posterior communicating artery on the left. The neuroradiological comment was a decreased flow in the left internal carotid artery and MCA with resultant ischaemia infarction involving the left ACA and possibly a branch of the left MCA territory. To summarize: the lesions were localized, in the small region restricted to the left superior dorsal part of the brainstem, and the deep frontal white matter surrounding the upper frontal horn of the lateral ventricle (F01, F09, F02, F03, F05 & F04).

The patient was assessed for her neuropsychological functions. The RAVLT reflected acceptable short- and long-term verbal memory (trial I: 5, II: 6, III: 8, IV: 8, V: 7, B: 3, VI: 15; by recognition in the last trial) albeit below the average of her age range. She obtained a perfect score in the copy trial of the ROCF, which implied that her perceptual abilities were functioning fully. Interestingly, her immediate and delayed ROCF recalls were dramatically lower (scored of 7 in both). This was certainly the result of poor organization and strategic planning. For instance, the interior configuration lines were not tightly linked in the copy production (Figure 4.1).

In the first interview, the patient stated that she had not been sleeping at all since her stroke, and therefore could not answer the questions about dreams. After her persistent request, she was finally prescribed sleeping pills, which however only

"worked" for two nights. Before her stroke, she used to sleep well and dream regularly. Her pre-stroke dream recall frequency was three times per week. Yet since her stroke, she had not been able to have dream experience, even with the aid of the guiding dream recall. The patient insisted that she had not been sleeping at all in the hospital, and therefore she had not had the opportunity to dream. Though she suffered from severe primary insomnia, which was characterized by inability to fall asleep and frequent awakenings during the night, she did not feel sleepy and did not sleep during the day. Neither did she nap nor have any trouble concentrating.

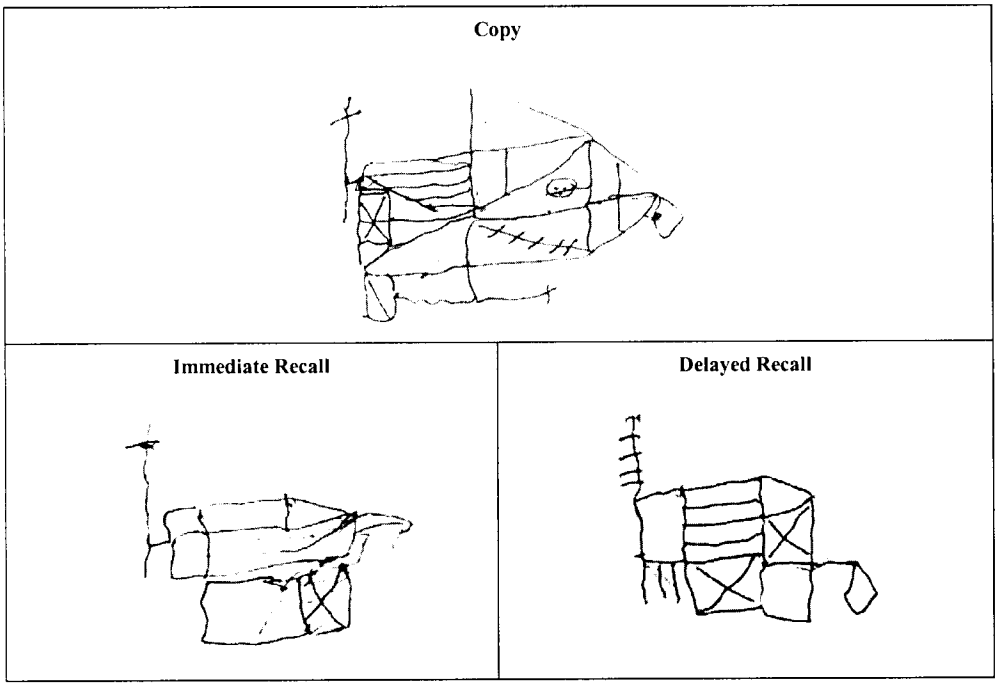


Figure 4.1 Case No. 20's ROCF

D. Discussion - A Paradox of Studying Dream Alteration in Patients with Pontine Lesions

Cases of cessations of REM with preserved communication ability were repeatedly reported throughout the clinical literature (Adey, Bors & Porter 1968; Chase, Moretti & Prensky 1968; Cummings & Greenberg 1977; Lavie, Pratt, Scharf, Peled & Brown 1984; Markand & Dyken 1976; Solms, 1997; see also Solms, 1997, 2000b for reviews). One of the possible explanations for this phenomenon is that REM processes are not localized in narrow, circumscribed areas of the brainstem, but take place through groups of concertedly working reticular thalamocortical structures. It appears that pontine brainstem lesions large enough to disrupt REM processes do not necessarily render patients unconscious or incommunicative, if certain critical regions remain intact or functionally intact.

In Solms's (1997) series of cases which included 61 patients with broadly-defined brainstem lesions (i.e., from the pons up to the thalamus), 53 were able to provide clear information about their dream experience. Amongst these patients, 43 reported a preservation of dreaming and 18 of them were focal cases. It should, however, be noted that almost all these 18 patients suffered from tumours, which do not necessarily entail actual destruction of the brain parenchyma or inoperative brain structure. Moreover, in at least 11 of the 18 cases, the "lesions" were

localized in the ventral part of the brainstem, sparing the dorsal aspect (e.g., 6 cases were with pituitary adenoma).

Neuroanatomically, the brainstem tegmentum contains distinct nuclei, each of which has a set of chemical, physiological and anatomical features. The reticular formation which includes the pontine reticular nuclei, raphe nuclei and locus coeruleus, the crucial neural substrate of consciousness, is a diffuse set of nuclei, which run through the dorsal part of the brainstem in the paramedian tegmental zone, from the medulla to the midbrain. The ascending reticular activating system is a core of grey matter continuous caudally with the reticular intermediate grey lamina of the spinal cord and rostrally with the subthalamus, hypothalamus and thalamic nuclei.

The three cases reported in this chapter were presented with lesions to various pontine regions. The first case experienced changes in dream experience after the ventral pontine lesions. The ventral aspect is, however, not a critical area according to the REM-pons hypothesis, and the dream alteration in this case was probably attributable to the parasellar axis including the ventromesial frontal regions. Lesions to the critical region, the medial dorsal aspect of the pons, were instead noted in the second and third cases. The second patient was, nevertheless, clearly orientated with no apparent symptoms of changes in dream experience and consciousness, and therefore the targeted system can be considered as functionally intact. Indeed, this

patient's pontine tegmental lesions were unilateral and relatively small, that is, not involving the whole reticular activating system. In the third case, "alteration" in dream experience may be due to a collapsed sleep-wake cycle (dyssomnias). Alternatively, similar to the first case, it may be the direct effect of the medial frontal white matter lesions. In the instance of collapsed sleep-wake cycle, which is frequently associated specifically with dorsal pontine lesions, nevertheless, dream experience cannot be studied properly due to a fundamental disruption of consciousness (viz., dyssomnias or conversely coma).

Clinically, pontine lesions appear to be related to a wide range of disorders of consciousness and sleep, such as the circadian rhythm sleep disorder with excessive daytime sleepiness (Kenichi, Koji, & Toshikiyo, 1999), horizontal and vertical smooth pursuit deficit (Deleu, Michotte, & Ebinger, 1997), and REM without atonia (Morrison, Sanford, & Ball, 1995). The brainstem tegmentum, in particular the ascending reticular activating system, plays a unique role in mediating the levels of consciousness and REM-NREM oscillation, and in Hobson's dreaming model. In addition, damage to the pontine tegmentum is known to cause comas, the most radical disturbance of general consciousness (and even loss of life), and has been considered as a "Neuroantomical Correlate of Coma" (Parvizi & Damasio, 2003). Any kind of dream report or investigation from this kind of patient with full pontine tegmental

lesion is ipso facto almost impossible even if they "survive". In a study of MRIs obtained from 47 patients with brainstem stroke, Parvizi and Damasio (2003) found that in the 38 patients who did not experience comas, brainstem damage was either located outside the tegmentum or produced a very small and unilateral compromise of the tegmentum. In contrast, in patients who sustained a coma, the lesions in the tegmentum were mostly bilateral and were located either in the pons alone or in the upper pons and the midbrain. The maximum overlapping territory of the lesions coincided with the location of the rostral raphe complex, locus coeruleus, laterodorsal tegmental nucleus, nucleus pontis oralis, parabrachial nucleus and the white matter in between these nuclei. Note that according to Hobson's model, the phenomenon of dreaming is the result of the interplay between the first three nuclei.

Furthermore, the speed of onset, site, and size of a brainstem lesion determine whether it results in coma. Brainstem *infarction* or hemorrhage often causes comas, while other brainstem conditions such as multiple sclerosis or tumour rarely do so (Bateman, 2001). Likewise, lesions below the level of the pons do not normally result in coma, while the specific nuclei within the tegmentum and specifically the ascending reticular activating system are without doubt crucial for the maintenance of general consciousness in humans. Mostly, these specific pontine infarcts (including the three nuclei implicated in the ASH) result in poor physical and mental conditions,

which render routine clinical neuropsychological assessment difficult.

"The critical role of the brain stem in the synchronous activation of the distributed forebrain circuits via thalamocortical activation is strongly evidenced by the fact that the most devastating and irreversible impairments of consciousness occur as deep and often irreversible comas following brainstem trauma or stroke" (Hobson, 2001, p.177).

The paradox is that a patient with a completely damaged tegmentum or with lesions to the critical nuclei should accordingly be unable to answer any question (i.e., comatose) or cannot be properly studied (e.g., dyssomnias), while a patient who does not suffer from the symptoms of coma (e.g., the second case) is considered atypical, or deemed to have a lesion that is so insignificant that the compromised region more or less continues to function. Therefore, investigating dreams of patients with ponto-tegmental lesions is clinically impractical in that such precise lesions which lead to REM cessation in particular, should, by definition, also result in severe disturbance of consciousness.

Notwithstanding the clinical unfeasibility, this sort of lesion study is, when taking the neuro-functional perspective, unnecessary. It has even been argued that the

elimination of observable REM sleep is not proof that no REM mechanisms are active (Ogilvie, Takeuchi, & Murphy, 2003). Is the pons (not REM) necessary for dream formation? As mentioned above, the reticular activating system is crucial to maintain a certain level of consciousness, which in Parvizi and Damasio's (2003) term, "core consciousness", refers to the simplest form of consciousness, insomuch as it provides the most basic energy for all consciousness and cognitive activities. When taking this functional point of view, the answer is definite yes. Indeed, the core consciousness can be conceived as a general conscious background constituted, at least partly, by the body state at the lower level, and perhaps by the body schema at the higher level (Parvizi & Damasio, 2003). It is a stage upon which life's drama (i.e., more complicated thoughts, dream vignettes, etc.) is played out.

Chapter Five

A Clinicoanatomical Study of Dreaming in Patients with Ventromesial Frontal Region Lesions

A. Introduction

Cessation of dream experience has long been observed in patients with frontal lobe lesions (Corda, 1985; Epstein & Simmons, 1983; Gloning & Sternbach, 1953; Piehler, 1950). By using the clinicoanatomical method, Solms (1997) further suggested that cessation of dreaming was associated with lesions in the white matter immediately surrounding the frontal horns of the lateral ventricles. The white matter of the frontal lobes of the brain just above the eyes contains a large fibre-pathway, which transmits dopamine from the ventral tegmentum to the higher parts of the brain. From this finding, Solms (1995, 1997, 1999, 2000a, 2000b) underscored that the primary function of this brain pathway, which is crucial for the generation of dreams, is to "instigate goal-seeking behaviours and an organism's appetitive interactions with the world" (Panksepp, 1985, 1998). In other words, the function of this important brain pathway is to motivate the subject to seek out and engage with external objects which in turn can satisfy his inner biological needs. Accordingly, damage to this pathway causes cessation of dreaming along with a dramatic reduction in motivated behaviour

(Solms, 1997).

The lesion method by means of clinical neuropsychological interviews in conjunction with structural imaging techniques has played a dominant role in the history of understanding the relationship between the brain and behaviours. The power of this method is, however, limited by the lesion's size (Damasio & Damasio, 1989). The smaller the lesion probe, the more discriminatory effects are generated. Another major methodological consideration is the choice of pathological specimen. Neuropsychological manifestations of infarctions, intraparenchymal hemoarrhages, or different types of tumours are distinct, even with apparently similar lesion loci. Non-hemorrhagic infarctions provide good specimens for neuroanatomical and neuropsychological study investigating the correlations between behavioural dysfunctions and sites of brain destruction, because they entail actual destruction of brain parenchyma. Lacunar infarct is the best fit for human lesion studies of all types of neuropathology. With a few exceptions, tumour material is unsuitable (Damasio & Damasio, 1989).

Most of the patients in Solms's clinical series (1997) were cases of diffuse injury. Despite the large sample size, only nine patients had definite frontal lesions. Four of these patients suffered from tumours (specifically, two glioblastoma multiforme, one meningioma, one prolactinoma-macroadenoma), two had abscess, and three presented

with intracerebral hemorrhage. None of these cases were good specimens for neurobehavioral establishment due to complicated nature and characteristics of their neuropathology. Such conditions rendered neuroanatomical analysis difficult and imprecise. For instance, one of the patients (Case No. 181) sustained deep left frontal abscess and intracerebral hemorrhage, and right medial frontal intracerebral hemorrhage as well as subdural empyema. The precise site of the brain destruction could not be pinned down confidently, nor could any inoperative brain structure be determined. In view of these, the present study aims to: 1) reconsider the association between alterations in dream experience and lesions to the ventromesial frontal region by investigating patients diagnosed with infarctions, and 2) identify the precise neural structures that are implicated in the generation of dreaming within the "ventromesial frontal region".

B. Method

A total of 21 neurological patients (males: N = 11; females: N = 10) were included in the current series. The average age was 58.0 years (S.D. = 17.4, range = 21-88). They all suffered from medial frontal lobe lesions as a consequence of recent cerebrovascular insults (one case had repeated cerebrovascular accidents). The majority of the cases were diagnosed with lacunar infarct. Some cases were excluded

due to inadequacy for accurate interpretation (e.g., inability to provide clear pre-stroke dream experience, neuropathologies not suitable for accurate neurobehavioral interpretations or precise localization).

The 21 patients were investigated systematically on a daily basis from initial hospital admission to discharge. All patients were examined within two weeks after cerebrovascular accidents. The daily investigation period ranged from two weeks to a month, with some intermittent follow-ups. Sleep and dream experiences before and after neurological impairments, as well as neurocognitive functions were assessed. The dream recall instruction was provided to patients to increase their ability to remember their dreams. By adopting the cytoarchitectonic maps developed by Brodmann (1909) and the templates by Damasio and Damasio (1989) for precise and specific localization, the neuropathological changes noted by CT and MRI scans were charted and coded. The precise locations of brain lesions between patients were then compared.

The present chapter focuses on neuroanatomical analyses and precise localization. The memory issues are addressed in the next chapter (Chapter Six). The whole design of this study was in line with the two previous clinicoanatomical studies reported in Chapter Three and Chapter Four. Detailed information of the methodology is provided in Chapter Three.

C. Neuroanatomical Analysis and Case Reports

C.I. Cases of Deficient Dream Experience with Focal Lesions

No patients reported premorbid absence of dream experience (including both dream recall and awareness). The average premorbid frequency of dream awareness was 3.8 per week (ranged from three times per week to nightly). Of the 21 cases with lesions to the medial frontal lobes, 17 experienced a deficiency of dream experience since CVA and had no single report of dream recall or awareness of dream experience during hospitalization, while four reported no evident dream alterations. Seven (41%) of the 17 patients with deficient dream experience had bilateral subcortical lesions. Thirteen patients with deficient dream experience whose lesion sites were relatively precise are provided in Table 5.1. All 13 focal cases had lesions involving ventromesial frontal regions. Lesions to the head of the caudate nucleus (including the ventral striatum and nucleus accumbens) were the most common subcortical regions involved, implicated in nine (70%) of the focal cases (Figure 5.1). This was followed by lesions to the corona radiata and internal capsule (six patients for each). Lesions to the frontal white matter (especially the critical area F09 in Damasio & Damasio's classification) were evident in five cases. All except two cases had pure subcortical or basal forebrain insults, sparing the entire frontal convexity, and four patients' lesions

were precisely circumscribed to the critical region of the head of the caudate nucleus (Case No. 1, 6, 12, & 45) (Figure 5.2). With the exception of two cases, all patients with dream alterations had lesions in either the head of the caudate nucleus or F09 or both (Cases No. 9 & 44).

Case No. 9, a 60 year-old patient, presented with full hemiplegia, and bladder and bowel dysfunctions. His RAVLT score was 7 in the last trial. This was roughly within normal limits according to his age. There was no clear evidence of short or long-term memory deficits. He exhibited good autobiographical memory and clear speech during the interviews. He had no problems with comprehension and sentence repetition, nor did he have difficulty naming in spontaneous speech. Bilateral tactile stimulations were performed, and no sensory problem was found. No visuospatial deficits were indicated, with a ROCF score of 34 in the copy trial. There were no signs of ideomotor or ideational apraxia. The overall symptomatology did not suggest any deficits in the patient's higher functions.

The patient was assessed daily for almost a full month. He could remember his previous dreams before the stroke quite well, although at the beginning he claimed that he only dreamed around once a week. After some discussion, it became clear that he did dream every night and quite frequently during the daytime as well. However, he tended to have a dream once a week that was so vivid and impressive as to cause

him to consider and remember it. Despite this, the patient did not report a single vivid or non-vivid dream during either night sleep or day napping for his entire stay in the ward.

Case No. 44 (78 years old) managed to complete various tests designed to measure dorsolateral frontal functioning (e.g., Luria's motor sequencing). However, on those tests designed for assessing ventromesial frontal functioning, the patient's performance was consistently poor. For instance, she was unable to shift cognitive set to a new set of rules, and so repeatedly exhibited stereotyped responses in the Go/No-Go task. Her approach to problem solving was also inadequate (e.g., the Eighteen Books problem). In the second trial of the Story Recall Test, she could identify the main theme of the story, but her version was contaminated by confabulation. At times, the patient's performance was compromised by her deficit in attention. Neither dream recall nor awareness could be elicited during her 25 days in the hospital.

Table 5.1 Cases of Deficient Dream Experience with Focal Ventromesial Frontal Region Lesions

No.	Sex	Age	Pathology	Lesion Sites
1	F	21	Infarct	L. head of caudate nucleus, internal capsule, putamen, corona radiate
6	M	69	Lacunar infarct & chronic schizophrenia	R. head of caudate nucleus, L. anterior internal capsule
9	M	60	Lacunar infarct	L. corona radiata

12	M	61	Lacunar infarct	B. head of caudate nucleus, F01, F09
16	M	65	Hemorrhage	L. head of caudate nucleus, internal capsule, corona radiata, thalamus
18	M	60	Large artery infarct	L. head of caudate nucleus, internal capsule, external capsule, putamen, globus pallidus, insula
21	F	88	Lacunar infarct	B. globus pallidus, L. head of caudate nucleus, external capsule, thalamus
26	M	-	Large artery infarct	R. head of caudate nucleus, internal capsule, external capsule, putamen, F01, F09, BA4, 6, S
30	F	67	Infarct	B. corona radiate, anterior cingulate gyrus, L. F01, F04
31	F	29	Large artery infarct	B. head of caudate nucleus, R. external capsule, insula, F09, BA45, 44, 6, 9, 46, S, 4, 5
37	F	68	Lacunar infarct	L. corona radiate, F01, F09, F10
44	F	78	Lacunar infarct	L. internal capsule, putamen, corona radiata
45	M	64	Large artery infarct	B. head of caudate nucleus, F01, F09

Note. R: Right; L: Left; B: Bilateral.

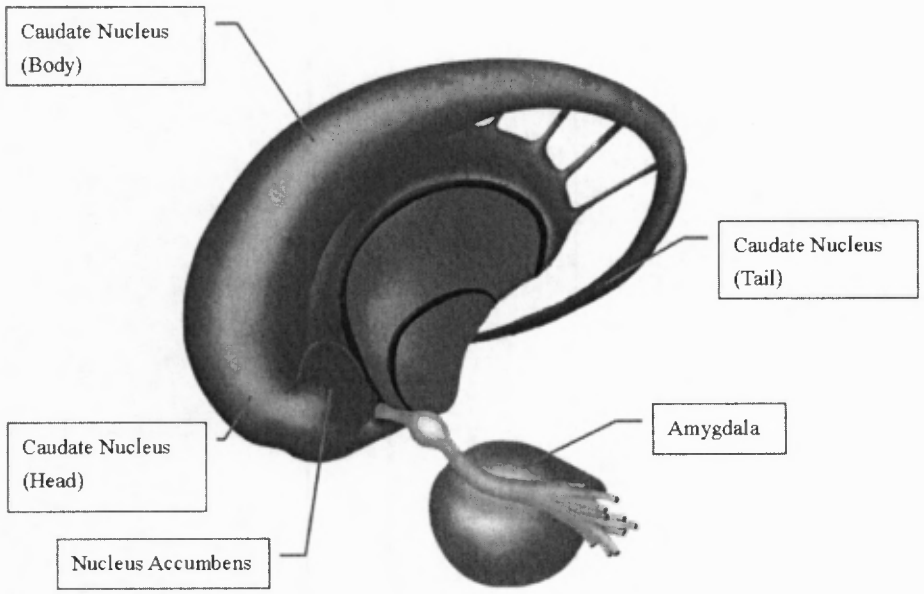


Figure 5.1 Caudate Nucleus and Nucleus Accumbens

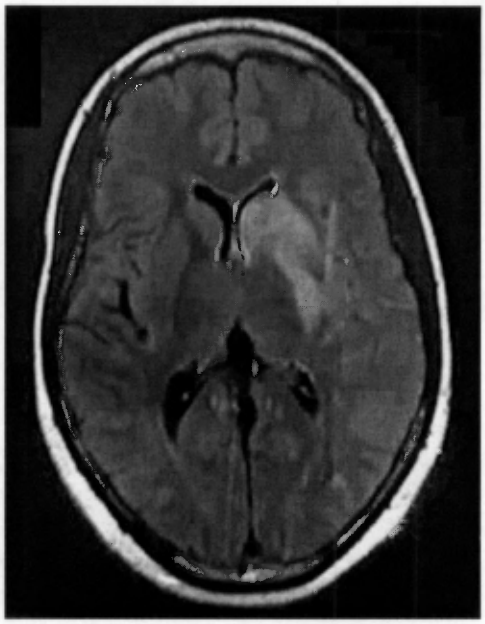


Figure 5.2 Case No.1's MRI Scan (Hyperintensity in the Head of the Left Caudate Nucleus)

C.II. Cases of Deficient Dream Experience with Diffuse Lesions

In addition to the 13 focal cases outlined above, there were four cases with lesions that were relatively diffuse but otherwise well-defined (Table 5.2). These patients similarly experienced a deficiency of dream recall and awareness post CVA. All of them demonstrated lesions in either the head of the caudate nucleus or frontal white matter F09, along with evident frontal dysfunctions. For instance, early symptoms of Parkinson's disease were noticed in Case No. 8. Case No. 25's confabulation was indicated in the RAVLT. He articulated four confabulated words in addition to the five correct words in the delayed recall trial administered during the third interview. Case No. 4 had obvious difficulty inhibiting his desire to peek when he was supposed to

close his eyes during the stimulation testing. His slowed responses and lack of energy were observed during the drawing tasks (e.g., ROCF). He appeared unconcerned about his condition throughout the neuropsychological assessment.

Table 5.2 Cases of Deficient Dream Experience with Diffuse Ventromesial Frontal Region Lesions

No.	Sex	Age	Pathology	Lesion Sites
4	M	54	Large artery infarct	R. external capsule, insula, F09, BA22, 44, 6, 4, S, 40
8	M	74	Large artery infarct	R. head of caudate nucleus, posterior internal and external capsule, putamen, corona radiate, F01, F09, BA22, 21, 44, 45, 6
17	F	68	Large artery infarct	B. head of caudate nucleus, internal capsule, L. external capsule, putamen, R. globus pallidus, thalamus, BA40, 39
25	M	42	TIA	R. conrona radiata, F09, BA 23, 24

Note. R: Right; L: Left; B: Bilateral.

C.III. Cases of Preservation of Dream Experience

While the majority of patients with ventromesial frontal region lesions (in particular the head of the caudate nucleus and frontal white matter F09) exhibited deficiency of dream recall and awareness, four patients reported no changes in their dream experience (Table 5.3). They could provide dream reports almost daily during hospitalization (except Case No. 2). Except for one case (Case No. 2), all of these four dreaming patients' unilateral lesions spared the head of the caudate nucleus and the ventromesial frontal white matter (Figure 5.3).

Case No. 2 had suffered two previous CVAs with good recovery. She presented with sudden dysarthria, dysphonic and right-sided weakness. According to the CT scan, a previous infarct was present in the posterior aspect of the left cerebellum. Cerebellar atrophy was evident, but V4 was central. Above the tentorium, there were infarcts in the anterior limb of the left internal capsule and lentiform nucleus, as well as in the white matter of the deep right parietal and left posterior parietal regions. The lesions also involved the left inferior caudal aspect of the head of the caudate nucleus. No lesion was detected in F01 or F09. The patient recalled only one dream during her time in the hospital. The dream was about her father. In her dream, she said to her father, "You must come out to me", but he did not respond. She felt sad in the dream. She burst into tears when talking about her dream and father.

Table 5.3 Cases of Dream Preservation with Ventromesial Frontal Region Lesions

No.	Sex	Age	Pathology	Lesion Sites
2	F	65	Lacunar infarct	L. head of caudate nucleus, internal capsule, external capsule, putamen, BA40, 41, 42, S, 22
5	F	32	Large artery infarct	L. internal capsule, putamen, corona radiata, globus pallidus, BA22, 44, 45, 47, 6, S
43	M	58	Lacunar infarct	R. internal capsule, putamen, corona radiate
50	F	36	Lacunar Infarct	L. internal capsule, putamen, body of caudate nucleus, insula

Note. R: Right; L: Left; B: Bilateral.

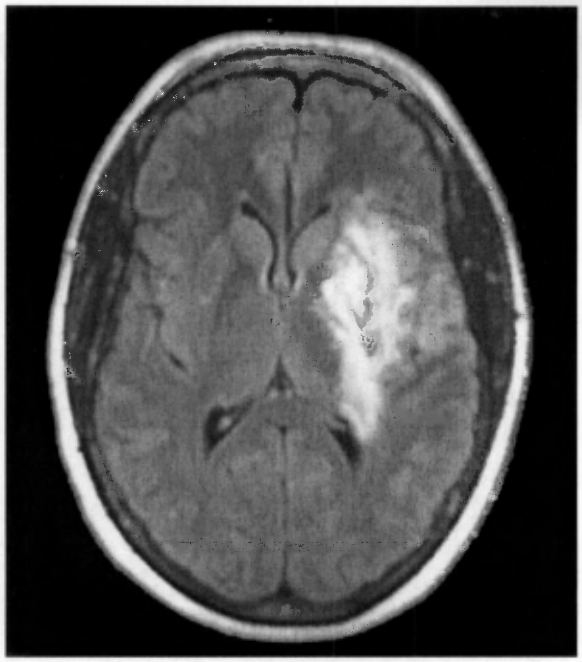


Figure 5.3 Case No. 5's CT Scan (Hyperintensity in the Basal Ganglia Excluding the Head of the Left Caudate Nucleus)

D. Discussion – Association between Dream Experience and the Head of the Caudate Nucleus in the Ventromesial Frontal Region

The weight of the evidence obtained from the present study lies in favour of a causal link between lesions of the ventromesial frontal region and deficiency of dream experience. Over eighty percent of the patients in the present study who sustained the ventromesial frontal region lesions as a consequence of infarctions experienced a deficiency of dream recall and awareness. In most of these cases the lesions were circumscribed to the deep medial frontal regions, sparing the prefrontal convexity, the inferior parietal lobule, the diencephalic areas, and the medial temporal regions (i.e.,

the neural substrates of memory). These findings were established using the best specimens of the human lesion method, and were consistent with the results drawn from the previous studies using the non-infarct samples (Solms, 1997; Yu, 2001b, 2003).

Moreover, the current findings suggested that both unilateral and bilateral lesions can result in deficiency of dream experience notwithstanding the undeniable fact that a significant proportion of the patients with dream deficiency sustained bilateral ventromesial frontal region lesions. These findings were in contrast with Solms's proposition that only bilateral ventromesial frontal region lesions cause cessation of dream experience. Indeed, functional presentation suggestive of bilateral lesions on the basis of a unilateral injury has long been acknowledged in the practice of clinical neuropsychology (Baldwin 1956; Penfield & Milner, 1958; Serafetinides & Falconer, 1962; Walsh, 1987). On the other hand, the evidence of an inherent asymmetry in striatal function is provided by both experimental and clinical studies of unilateral lesions to the caudate nucleus (Apicella, Legallet, & Nieoullon, 1991; Benke, Delazer, & Bartha, 2003; Budilin & Mats, 2002; Glick & Cox, 1976, 1978; Hansing, Schwartzbaum, & Thompson, 1968; Rothman & Glick, 1976; Saji, Endo, & Miyanishi, 1997). For instance, left caudate lesions induce marked and long-lasting behavioural and neuropsychological impairments comprising predominantly drive and

executive control (Benke, Delazer, & Bartha, 2003). According to these studies, the effects of a unilateral striatal lesion as well as the compensatory processes depend on whether the lesion is placed in the more or less active striatum. In particular, the extent of lesion in the head of the caudate nucleus is the critical factor for the severity and the outcome of the syndrome, whereas damage to the putamen and pallidum is less crucial for the corresponding functions (Benke, Delazer, & Bartha, 2003).

In the same way, the present study indicated that the head of the caudate nucleus in the ventromesial frontal region appeared to be a particularly crucial component of the neural network of dreaming. Lesions to the head of the caudate nucleus were common amongst the patients with dream deficiency. Cases with focal infarct lesions circumscribed precisely to this region were documented. Although two of these patients' (Case No. 9 & 44) lesions did not seem to involve the head of the caudate nucleus or the frontal white matter F09, their neurological and neurocognitive presentation indicated basal ganglia symptoms (e.g., bladder and bowel dysfunction, motor disorders, dysarthria, along with relatively intact memory and visuospatial functions).

In the light of the present findings and the recent rehabilitation of the study of motivational determinants in dreaming processes (e.g., Peterson, Henke, & Hayes, 2002; Smith, et al., 2004), it appears that the experience of dreaming is motivational.

It is worth noting that the caudate nucleus is one of the key loci for reward-based behavioural learning (Aron, Fisher, & Mashek, 2005; Delgado, 2003; Eagle, Humby, & Dunnett, 1999; Kawagoe, Takikawa, & Hikosaka, 2004; Kimura, Yamada, & Matsumoto, 2003; Popova, Gneushev, & Dereviagin, 1982; Uslaner, Pengwei, & Robinson, 2005; Watanabe, Lauwereyns, & Hikosaka, 2003; Yamada, Matsumoto, & Kimura, 2004), for it playing a pivotal role in encoding motivational contexts for goal-directed action planning and learning (Yamada, Matsumoto, & Kimura, 2004). By using the fMRI technique, Aron, Fisher and Mashek (2005) demonstrated that activation in the right anteromedial caudate was correlated with the intensity of romantic passion. Their results suggest that romantic love relies on the ventral striatal reward and motivation systems to focus on a specific individual.

Neuroanatomically, the caudate nucleus can be divided into three portions: The head, located within the frontal lobe; the body, located deep in the parietal lobe; and the tail, which goes into the temporal lobe. The nucleus accumbens is situated immediately beneath the head of the caudate nucleus, just before the ventral part of the putamen, and in the ventral striatum (the ventral striatum is below the ventral part of the putamen). Therefore, the nucleus accumbens is located within the frontal lobe, more precisely, in the ventromesial frontal region, attached to the inferior caudal part of the frontal horn of the lateral ventricle and surrounded by the white matter (F09)

around the frontal horn of the lateral ventricle.

The head of the caudate, together with the ventral striatum and the nucleus accumbens, is one of the most important constituents of the motivational mesolimbic dopaminergic pathway, the "instinctual motor brain" (Panksepp, 1998). Many of the psychobehavioral routines, including all the basic instinctual functions and gratifications, are governed by interactions with the basal ganglia, in particular the ventral striatal areas. Accordingly, the significant role of this neural structure in dreaming encourages further investigation of motivational determinants in dreaming processes.

Chapter Six

A Study of Memory in Neurological Patients

A. Introduction

The validity of the human lesion methods has been questioned on the grounds that neurologically compromised patients' reports of dream deficiency can be conceived as a secondary effect of memory failure, rather than as a direct consequence of neurological insults. Chapter Two considered the issue as to whether or not dream recall is difficult per se. Chapter Three examined if memory dysfunction necessarily results in cessation of dream experience. This chapter proceeds to explore whether or not patients who have experienced a deficiency of dream recall and awareness since their strokes (as reported through chapters 3 to 5) differ from patients with preserved dream experience in their memory abilities.

While memory functions can be classified according to different taxonomies, the dichotomy of short-term memory and long-term memory is probably the most popular classification. In clinical practice, long-term memory disorder refers primarily to a disorder of recent memory, a difficulty in acquiring new information. On the other hand, short-term memory disorder refers to a difficulty in immediate memory. In assessing short-term memory dysfunction, the cutoff score of 7±2 is often applied. Both long-term and short-term memory disorders can be limited to a specific modality

or material. In other words, a patient with difficulty remembering pictorial materials can be completely free of audioverbal memory deficits or vice versa (see case examples in Chapter Three). Along with the categories of short-term memory and long-term memory, cognitive psychology research also suggests an additional category, "sensory memory". However, in clinical practice, neuropsychological conceptualizations of memory do not consider sensory memory; rather, it is thought of as a component of sensory processing, namely perception. From the neuroanatomical perspective, testing visuospatial and audioverbal memory functions constitutes a parsimonious modus operandi, which provides clues to lateralization, with verbal memory predominantly processed by the left hemisphere and pictorial memory by the right hemisphere.

There are a variety of clinical tests for assessing memory functions, such as the Hidden Object Test (Strub & Black, 1985), the Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964), the Rey-Osterrieth Complex Figure (ROCF; Rey, 1941; Osterrieth, 1944), the Babcock's Story Recall Test (Babcock, 1930; Babcock & Levy, 1940), the Benton's Visual Retention Test (Benton, 1974), the Wechsler Memory Scale III (Wechsler, 1997b), and the subtests of the Wechsler Adult Intelligence Scale III (Wechsler, 1997a). Not all these tests are suitable for measuring short- and long-term memory spectrums simultaneously. The Rey-Osterrieth Complex Figure

(ROCF; Rey, 1941; Osterrieth, 1944) and the Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1964) were two classical neuropsychological tests, which were developed to assess both spectrums. Quantitative and qualitative analyses of the performance of these two tests are clinically informative.

The ROCF and the RAVLT have been used extensively in clinical practice and research. For instance, the ROCF has been applied but not limited to the studies of patients with temporal lobe epilepsy (e.g., McConley, Martin, & Baños, 2006), hippocampal atrophy (e.g., Ariza, et al., 2006), posterior cortical atrophy (e.g., Charles & Hillis, 2005), Alzheimer's disease and vascular dementia (e.g., Golden, Bouvier, & Selden, 2005), severe traumatic brain injury (e.g., Serra-Grabulosa, Junqué, Verger, Salgado-Pineda, Mañeru, & Mercader, 2005), cerebral infarction (e.g., Okuda, Matsui, Fujita, & Seishin, 1995), as well as children with cerebral palsy (Katz, Cermak, & Shamir, 1998). Similarly, the RAVLT has been applied to the investigation of hippocampal atrophy (e.g., Ariza, et al., 2006), temporal lobe epilepsy (e.g., Grammaldo, et al., 2006), posterior cortical atrophy (e.g., Charles & Hillis, 2005), traumatic brain injury (e.g., Schopp, Shigaki, Bounds, Johnstone, Stucky, & Conway, 2006), multiple sclerosis (e.g., Tong, Yip, Lee, & Li, 2002), and Parkinson's disease (e.g., Singh & Behari, 2006).

The ROCF is used to investigate both perceptual organization skills and visual

memory. The ROCF includes a copy trial (for measuring perception), an immediate recall trial (for measuring short-term memory performance) and finally a delayed recall trial (for measuring long-term memory performance). The most widely used scoring system was developed by Guyot and Rigault (1965). In this system, the scoring units refer to specific areas or details of the figure that have been numbered for scoring convenience. There are 18 units in total and the highest possible number of points is 36. Two points are given for each unit that is drawn correctly and placed properly. One point is given if the unit is drawn correctly but placed poorly, or if the unit is distorted or incomplete, but recognizable and placed properly. Half a point is given if a unit is distorted or incomplete and placed poorly, but still recognizable. No points are given if the unit is absent or unrecognizable.

The performance of the ROCF very much depends on the strategy used by subjects. Generally, subjects who approach the ROCF copying task conceptually, dealing first with the overall configuration of the design and then with the details, recall the figure much better than subjects who copy the details one by one, even if they do so in a systematic manner (Ogden, Growden, & Corkin, 1990). Copy organization is henceforth crucial for good recall (Sullivan, Mathalon, Ha, Zipursky, & Pfefferbaum, 1992).

The RAVLT was used to measure both short- and long-term verbal retention. In

addition, the test measures immediate verbal span, reveals a learning curve, exposes learning strategies, elicits retroactive and proactive interference tendencies, and finally exhibits tendencies to confusion or confabulation on memory tasks. The test consists of five presentations with recall of a 15-word list, one presentation of a second 15-word list, and a sixth recall trial. The first trial reveals short-term memory capacity, and the subsequent trials measure long-term memory performance. The maximum score for each trial is 15.

The current study examined the memory abilities of patients with deficient dream recall and awareness on the one hand and patients with preserved dream experience on the other, by using the two widely-adopted measures, namely the ROCF and the RAVLT. The specific question is whether or not there are significant differences in their memory capacities between the two groups of patients.

B. Method

B.I. Design

A total of 32 neurological patients who were initially reported in Chapter Three, Four and Five formed the current sample. Twenty patients experienced deficient dream recall and awareness subsequent to their strokes whereas dream experience was preserved in 12 patients. Three cases had pontine lesions, 21 cases had ventromesial

frontal region lesions, and eight patients were posterior brain cases. Eighteen (56.3%) were males, and 14 (43.7%) were females. The average age was 54.1 (S.D. = 17.0, range = 21-88). The ROCF and the RAVLT were used to test the patients' memory.

B.II. Axial (True) Amnesia

In addition to the visuospatial and audioverbal memory, the patients were examined for amnesic features. The neuroanatomical correlate of axial or true amnesia involves bilateral lesions to the posterior brain (This will be elucidated in the discussion). Neurological diagnosis of each case was administered by at least two professionals (i.e., neurologist and neuroradiologist) who were blind to the hypotheses of the current study. All neurological, neuroradiological and neuropsychological diagnostic reports and other medical reports produced by different professionals were included for investigation. The patients were observed for their daily behaviours which may indicate amnesic symptoms or features (e.g., constantly forgetting their experiences, inability to recognize the nurses or people whom they regularly contacted, etc.). Clinically, axial amnesia is diagnosed primarily based on the following symptomatological criteria:

1. Presence of anterograde amnesia;
2. Presence of retrograde amnesia for recent events;

3. Awareness of deficit;

4. Defective episodic memory;

5. Inability to benefit from prompting.

C. Results

C.I. Visuospatial and Audioverbal Memory

The patients with preserved dream experience scored higher than the patient with deficient dream recall and awareness across all ROCF copy and recall trials (Table 6.1). In the ROCF copy trial, the patients with deficient dream recall and awareness obtained 20.3 on average, while the mean score of the patients with preserved dream experience was 27.9. The ROCF immediate (short-term) recall mean scores for the patients with deficient dream experience and the patients with preserved dream experience were 8.3 and 17.1. The ROCF delayed (long-term) recall mean scores on the first day were 7.2 and 12.8 respectively. Nevertheless, the discrepancies between the patients with deficient dream experience and the patient with preserved dream experience in the ROCF performance did not hold statistical significance: the ROCF copy scores ($z = 1.39$, $p = 0.17$), the ROCF immediate recall scores ($z = 1.96$, $p = 0.05$), and the ROCF delayed recall scores ($z = 1.92$, $p = 0.06$).

As indicated by the RAVLT mean scores, there were no significant differences

between the two groups in the audioverbal memory functions (Table 6.2): RAVLT Trial I (short-term memory span) ($z = 0.30$, $p = 0.77$), Trial II (long-term performance) ($z = 1.04$, $p = 0.30$), Trial III ($z = 0.07$, $p = 0.94$), Trial IV ($z = 0.15$, $p = 0.88$), Trial V ($z = 0.074$, $p = 0.94$), and Trial VI after interference ($z = 0.44$, $p = 0.66$). Likewise, no significant differences between the two groups in the ROCF delayed recall scores ($z = 1.74$, $p = 0.08$) and the RAVLT delayed trial scores were detected during the retest on the seventh day ($z = 0.09$, $p = 0.93$).

Table 6.1 ROCF Mean Scores between Patients with Deficient Dream Experience and Patients with Preserved Dream Experience

ROCF	Deficient Group (N = 20)	Preserved Group (N = 12)	Total (N = 32)
Copy	20.3±12.6	27.9±7.4	23.2±11.4
Immediate Recall	8.3±6.4	17.1±9.2	12.4±8.9
Delayed Recall	7. 2±4.9	12.8±5.9	9.3±5.8
7th Delayed Recall	6.4±5.9	12.5±6.4	9.0±6.7

Note. 7th Delayed Recall: Retest on the 7th day.

Table 6.2 RAVLT Mean Scores between Patients with Deficient Dream Experience and Patients with Preserved Dream Experience

RAVLT	Deficient Group (N = 21)	Preserved Group (N = 8)	Total (N = 32)
Trial I	3.8±2.7	3.8±0.8	3.8±2.1
Trial II	4.8±2.5	4.2±1.1	4.5±2.1
Trial III	6.3±3.9	5.8±2.9	6.1±3.5
Trial IV	6.1±3.9	6.4±2.9	6.2±3.5
Trial V	6.8±4.3	7.0±3.2	6.8±3.8
Trial VI	5.8±3.9	4.8±3.3	5.4±3.6
7th Trial	4.0±3.4	3.8±3.5	3.9±3.3

Note. 7th Trial: Retest on the 7th day.

There seemed to be differences between the patients with ventromesial frontal region lesions and the patients with posterior brain lesions in the ROCF visual performance (Table 6.3), although not all of the differences reached the significant level: the ROCF copy scores ($z = 1.39$, $p = 1.65$), the ROCF immediate recall scores ($z = 1.64$, $p = 0.10$), the ROCF delayed recall scores ($z = 2.41$, $p < 0.05$), and the ROCF delayed recall scores ($z = 2.35$, $p < 0.05$) on the seventh day. There were no significant differences in all RAVLT trials (all $p > 0.05$).

Table 6.3 ROCF Mean Scores between Frontal, Posterior and Pontine Patients

ROCF	Frontal (N = 21)	Posterior (N= 8)	Pontine (N= 3)	Total (N= 32)
Copy	19.4±11.5	25.6±10.3	34.3±2.1	23.2±11.4
Immediate Recall	7.7±5.9	16.2±9.0	17.8±11.6	12.4±8.9
Delayed Recall	6.5±4.6	13.9±5.4	10.8±5.3	9.3±5.8
7^{th} Delayed Recall	5.4±5.8	13.6±5.5	10.5±5.7	9.0±6.7

Note. 7^{th} Delayed Recall: Retest on the 7^{th} day.

Four examples of ROCF productions are provided in figures 6.1-6.4. The patents with ventromesial frontal region lesions had considerable problems in organizing details (Figure 6.1 and 6.2). For instance, the ROCF copy produced by Case No. 17 showed that while she managed to hold the primary gestalt (contour) of the figure, she lost its interior configuration (Figure 6.1). The internal components were misplaced and disorganized. Another frontal patient (Case No. 9) gave up drawing the

components (Figure 6.2). He found it very difficult to organize and draw the internal components in the appropriate places because they were organized in such a complex fashion, although the patient was able to see all the segments and details of the figure clearly.

The ROCF productions of the patients with posterior cerebral lesions unveiled a different type of perceptual dysfunction from the frontal patients. They demonstrated relatively less serious organizational deficits in drawing the complex figure (Figure 6.3 and 6.4). Instead, in their ROCF copies, the interior mainstay was distorted possibly due to a difficulty in estimation of relative length and size.

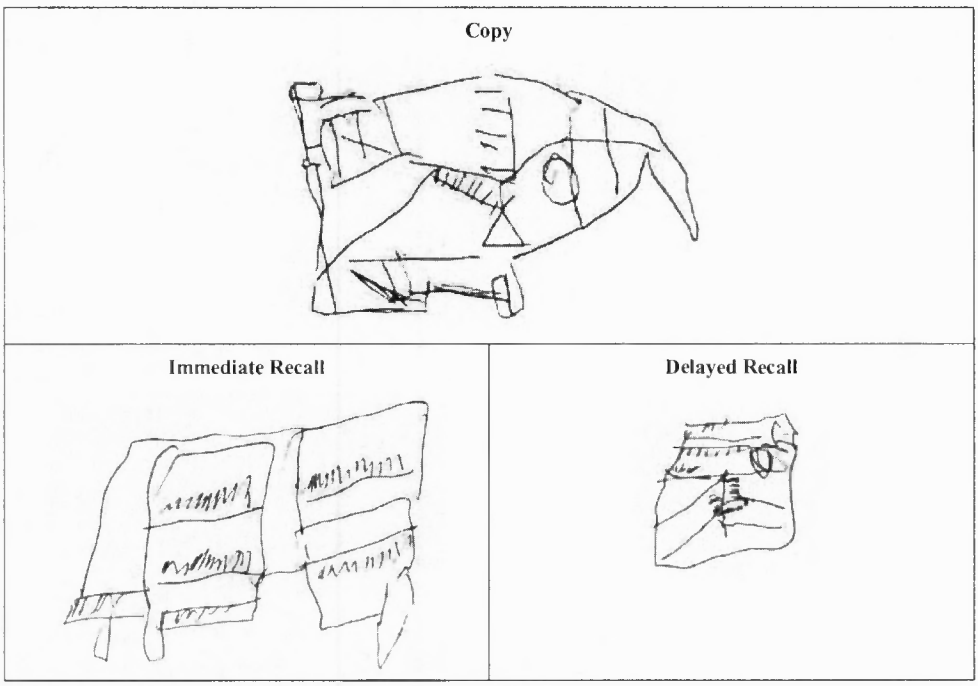


Figure 6.1 Frontal Patient Case No. 17's ROCF

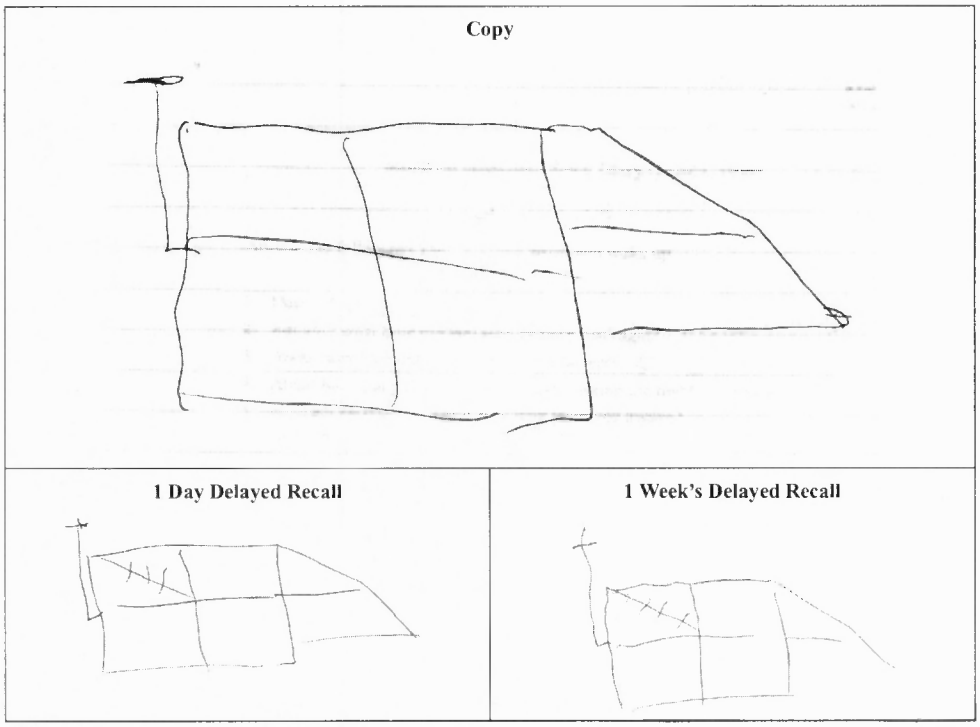


Figure 6.2 Frontal Patient Case No. 9's ROCF

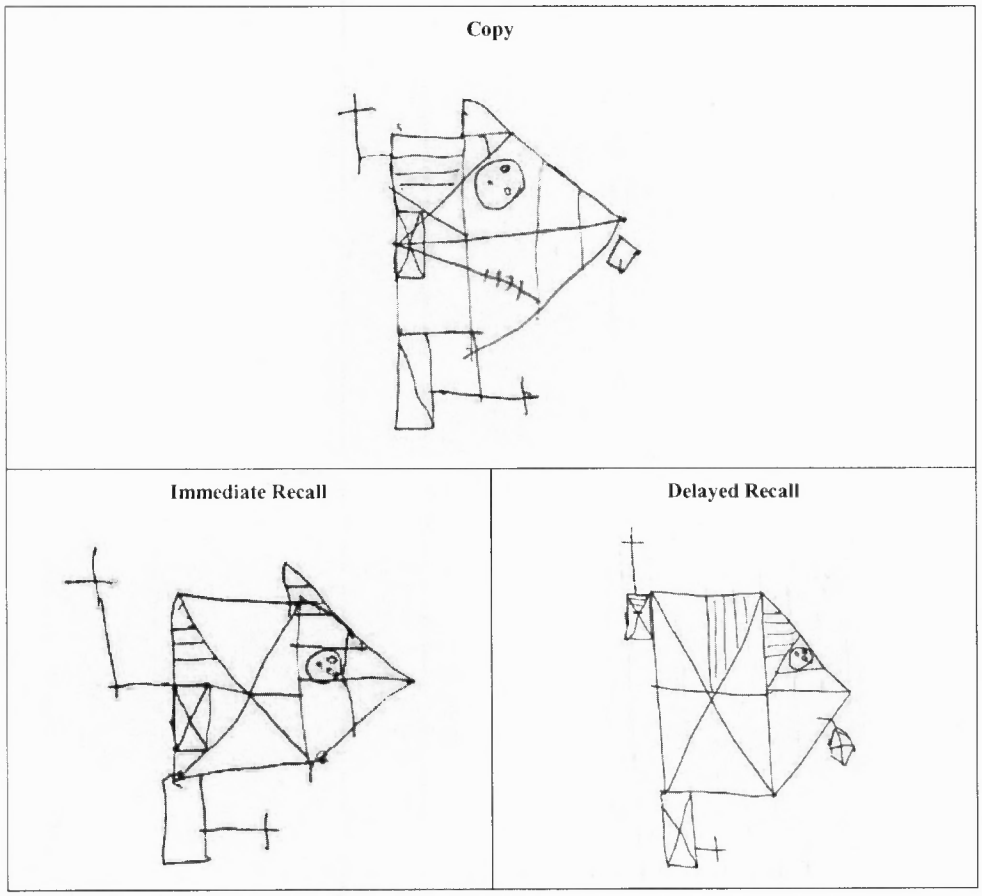


Figure 6.3 Posterior Patient Case No. 22's ROCF

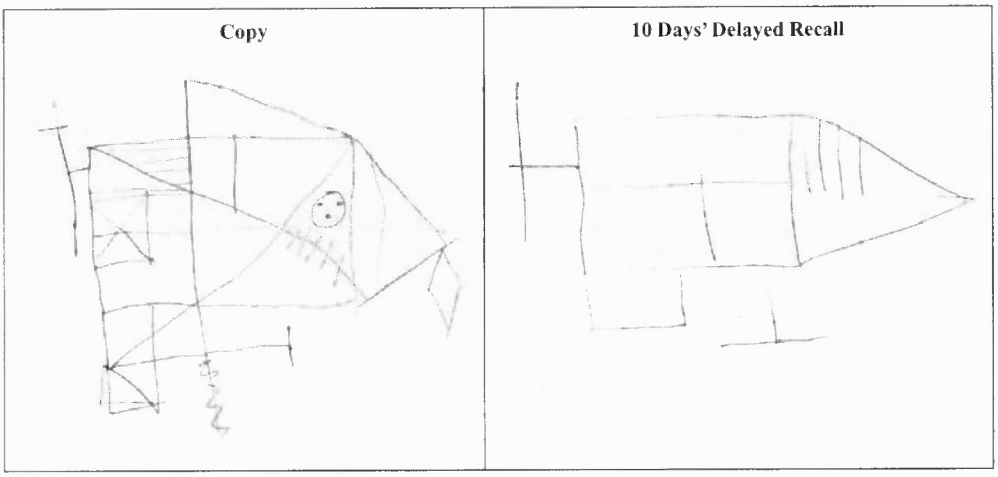


Figure 6.4 Posterior Case No. 27's ROCF

C.II. Axial Amnesia

None of the 32 patients were diagnosed as axial amnesia. One case (Case No. 2) showed amnesic features. Two cases (Case No. 27 & 42) among the 32 patients suffered infarctions involving the posterior cerebral arteries. One of them was bilateral case (Case No. 42). Dream experience was preserved in all three cases.

D. Discussion

D.I. Differences in Memory between Patients with Deficient Dream Experience and Patients with Preserved Dream Experience

Considering the clinical evidence that memory is affected by many neuropathologies, and is even considered to be a "fragile" system, it is perhaps unsurprising to find that most patients who were no longer aware of their dream experience since their strokes simultaneously sustained memory deficits. However, the discrepancies between the patients with deficient dream experience and the patients with preserved dream experience in their visual and verbal memory functions did not hold statistical significance. Although the patients with deficient dream experience (or ventromesial frontal region lesions) performed worse than the patients with preserved dream experience (or posterior brain lesions) in the ROCF short- and long-term recall trials,

they also obtained lower scores in the ROCF *copy* trial. This indicated that their poorer visual recall resulted from lacking in skills in strategy and organization. As mentioned in the introduction section, the ROCF is used to investigate both perceptual organization skills and visual memory, and the performance of the ROCF very much depends on the strategy used by patients. Therefore, the poor performance of the patients in the ROCF recall trials were not necessarily due to memory disorders per se, but instead were the consequence of the other cognitive disorders such as deficits in organization and strategic planning. This conclusion was further supported by the finding that the performances of the patients with dream deficiency (or ventromesial frontal region lesions) and the patients with preserved dream experience (or posterior brain lesions) were similar in the RAVLT, a far less "complex" task than the ROCF. It is worth noting that the RAVLT is a straightforward audioverbal memory test, which requires a least degree of strategic planning. Perhaps, collecting more cases with different lesion sites can improve the current statistical analyses by exploring a possible interaction effect between lesion sites and dream experiences on memory functions. For instance, it may be that people with frontal lesions who have cessation of dreaming do not differ in RAVLT memory scores from those with frontal lesions and who continue dreaming.

It has previously been demonstrated in Solms's study (1997) that most memory

spectrums did not discriminate significantly between "nondreaming" subjects and dreaming patients. The only significant difference was found in relation to visuospatial short-term memory performances. On the basis of their studies, both Solms (1997) and Doricchi and Violani (1992) made a similar conclusion that the cessation of dream experience may be correlated with visuospatial and visuoconstructive deficits (visual working memory), but is not a consequence of amnesia. The current results are very much reminiscent of the previous findings, and provide further substance to their assertion.

D.II. Why Are Patients with Memory Disorders Able to Recall Their Dream Experience?

The differentiation between memory disorders and deficient dream experience is highly consistent with the clinical neuropsychological understanding of memory organization, and the memory principles of investigative psychology. Specifically, the cognitive interview technique that is frequently used for forensic investigation is based upon the three primary principles (Geiselman & Fisher, 1989):

1. The memory for a piece of information can be retrieved through several paths. Therefore, information that is not accessible with one cue or technique may be accessible using another cue or technique (Tulving, 1974).

2. A memory trace is made up of several properties, including for example the size, shape, colour of the to-be remember material, and even the sound, feelings, or emotions associated with it.
3. The efficacy of a particular retrieval cue in eliciting retrieval is dependent upon the extent of the overlap or the number of similarities between the encoded information and the retrieval cue (Flexser & Tulving, 1978).

Accordingly, although many neurological patients display profound memory disorders which are always specific to a certain modality (e.g., visuospatial vs. audioverbal), they are still able to retrieve personal or dream experience via many other channels or cues. This is perhaps also one of the reasons why many neurological patients are free of autobiographical memory deficits.

D.III. Axial Amnesia

Amnesia is not uncommon. Damage to the temporal lobe, and especially the anterior temporal cortex including the hippocampus is associated with various degrees of amnesia. Another important structure in the posterior brain is diencephalon. Damage to the diencephalon causes amnesia. A common disease associated with this region is Korsakoff's syndrome following long-term alcoholism.

However, only *bilateral* lesions circumscribed to the medial temporal lobe

(Steinvorth, Levine, & Corkin, 2005), and in particular to the hippocampal region (Bayley & Squire, 2003) result in axial or true amnesia. There are even findings that remote memories are associated with distributed activation along the rostrocaudal axis of the hippocampus whereas activation associated with recent memories is clustered precisely in the anterior portion of the hippocampus (Gilboa, Winocur, & Grady, 2004). Therefore, even lesions to the hippocampus only disproportionately affect recent memories and do not necessarily result in severe amnesia.

Unlike the relatively mild material specific memory losses (i.e., visuospatial vs. audioverbal memory deficits) caused by unilateral lesions, the memory difficulties of patients with bilateral lesions affecting the medial temporal regions are profound, pervasive and generally lasting. The most famous example of hippocampal amnesia is patient HM, who suffered a profound amnesia for most ongoing events (Iversen, 1977; Keane, Gabrieli, Mapstone, Johnson, & Corkin, 1995; Milner, 1970; Milner, Corkin, & Teuber, 1968; Scoville & Correll, 1973; Scoville & Milner, 1957).

Some common causes of bilateral medial temporal or hippocampal damage are epilepsy, infections like necrotic encephalitis of herpetic origin, and degenerative illnesses such as Alzheimer's disease. Medial temporal amnesia can also result from bilateral compromise of the posterior cerebral arteries. Typically, the onset is so sudden and dramatic that term "amnesic stroke" is used. Infarction due to

compromised posterior cerebral arteries is not uncommon since both posterior cerebral arteries arise from the single parent vessel, namely the basilar artery. Because of the anatomical proximity, cases of vascular origin with axial amnesia, as documented in the clinical neurological literature, almost invariably suffered a cerebral blindness (Benson, Marsden, & Meadows, 1974; Boudi, Barbizet, Derouesené, & Van Amerongen, 1967; Boudin, Brion, Pepin, & Barbizet, 1968, De Jong, Itabashi, & Olson, 1968, 1969; Dide & Botcazo, 1902; Trill, Fischer, Serclerat, & Schott, 1980; Van Buren & Borke, 1972; Victor, Angevine, Mancall, & Fisher, 1961; Whitty & Lishman, 1966).

For some anatomical reasons, however, the middle cerebral arteries are far more likely the origin of infarctions than the posterior cerebral arteries. Only two cases included in the current neurological series suffered infarctions due to compromised posterior cerebral arteries, and only one of them was bilateral case. Dream recall was preserved in both patients. Furthermore, none of the 32 patients was diagnosed with axial amnesia. There was one patient who presented with amnesic features. This patient was able to report dream experience.

D.IV. Frontal "Amnesia"

Some prominent clinicians consider that there is no true amnesia in frontal patients,

that is, no inability to register or to retrieve material given the proper conditions (e.g., Luria, 1971, 1973, Luria, Sokolov, & Klimkowski, 1967). In their views, the memory disorder is only apparent and superficial, and the poor performance of frontal patients on some memory tasks is better understood as a disruption of complex forms of behaviour which reflects itself in numerous ways (e.g., attention deficits, pathological inertia). Patients with frontal lobe lesions have difficulty with learning or memory through a true axial type of amnesia is indeed rare.

D.V. Confabulation

Clinically, pathological confabulation is more related to frontal abnormalities than to posterior brain lesions. Some cases with ventromesial frontal region lesions in the current study exhibited symptoms of confabulation. Confabulatory recollections and materials involve distorted *additions* and *elaborations* which are thought to be based on actual events. They typically consist of exaggerated, grandiose, impossible, or loosed verbalizations. When confabulators attempt to answer questions about events, it is as though they respond with the first association that comes to mind no matter how loosely or inappropriately it might be linked to the questions (Lezak, 1995; Lezak, Howieson, & McGavin, 1983; Lhermitte & Signoret, 1972). Similar to "positive symptom", confabulation therefore involves fabricating something that does

not exist, rather than erasing something that exists. The *absence* of dream recall and awareness does not therefore appear to be properly explained by spontaneous, impulsive confabulation.

Finally, it can be argued that even if there is no relationship between dream cessation and waking life memory deficits, it is still possible that those *patients* with dream cessation have a *deficit* in memory during sleep, but not when awake. *Normal* memory problems have been proposed for non-REM sleep, as an explanation of why non-REM sleep has lower dream recall than REM sleep (see Conduit, Crewther, & Coleman, 2004, for a review). However, a periodic manifestation of *deficits* appears to be clinico-anatomically impossible in infarct patients whose lesions entail actual destruction of brain parenchyma and therefore relatively permanent neuropsychological dysfunctions. Moreover, such a *hypothetical neuropathological* memory deficit specific to a sleep state, sparing the memory functions during waking has not yet been identified and reported in the clinical literature and thus remained to be justified.

E. Conclusion

The patients with deficient dream experience did suffer from memory problems. Almost all cases demonstrated various degrees of memory difficulties. This weakens the neurobehavioural approach and the findings generated by this method. This is indeed an unavoidable clinical constraint. On the other hand, several points should also be taken into account. Firstly, dream recall is not difficult in nature (Chapter Two). Secondly, profound memory deficits do not necessarily result in deficient dream recall and awareness (Chapter Three). Thirdly, the discrepancies between the patients with dream deficiency and the patient with preserved dream experience in their memory functions were not significant. Fourthly, information that is not accessible with one cue can be accessible using another cue. Therefore, although many neurological patients display memory disorders which are specific to a certain modality, they are still able to retrieve personal or dream experience via other channels or cues. Fifthly, all patients in the current study were not amnesic, and some of their "memory disorders" could be evidently attributed to other primary neuropsychological deficits. Finally, all patients included in the current study were diagnosed with infarctions, which provide the best specimens for neurobehavioural investigation amongst many types of neuropathologies. In most of the cases with deficient dream recall and awareness, the lesions were circumscribed to the deep

medial frontal regions, sparing the prefrontal convexity, the inferior parietal lobule, the diencephalic areas, and the medial temporal regions, that is, the neural substrates of memory. It is also generally accepted that there is no true amnesia in frontal patients. In view of these, memory failure does not constitute a convincing reason for defective dream experience.

Chapter Seven

A Neuropharmacological Study of Dreaming in Psychiatric Patients

A. Introduction

A.I. Dopamine Abnormality and Patients with Schizophrenia

Hypermetabolism in structures implicated in the dopamine pathways was revealed by an early PET study of individuals with schizophrenia (Resnick, Gur, & Alavi, 1988). Excessive occupancy of D2 receptors by dopamine in schizophrenia has been further confirmed by both stimulation (using D-amphetamine) (Abi-Dargham, et al., 1998; Breier, et al., 1997; Laruelle, et al., 1996) and depletion (Abi-Dargham, et al., 2000) paradigms combined with SPECT or PET imaging. In a more recent study, McGowan, Lawrence and Sales (2004) assessed presynaptic dopaminergic function in patients with schizophrenia by means of [¹-sup-8F]fluorodopa uptake and a PET scan. Increased [¹-sup-8F]fluorodopa uptake circumscribed to the ventral striatum was observed.

For the past few decades, some psychopharmacological studies which aimed to examine the dopamine receptor occupancy of antipsychotic medications in medicated and unmedicated schizophrenia have been documented (e.g., Abi-Dargham, et al., 1998, 2000; Bondy, 1984; Dolan, Fletcher, & Frith, 1995; Frankle, et al., 2004; Gattaz,

1983; Gefvert, Lindström, Waters, Waters, Carlsson, & Tedroff, 2003; Gruen, 1978; Gründer, Vernaleken, & Müller, 2003; Hedges, El-Mallkh, & Carvey, 1995; Johnstone, Crow, & Mashiter, 1977; McGowan, Lawrence, & Sales, 2004; Rotrosen, 1978; Rotstein, Mishra, & Singal, 1983; Sapru, Rao, & Channabasavanna, 1989; Segal, et al., 2004; Warner, Walker, & Cyril D'Souza, 2001). It was generally shown that various antipsychotic medications are effective in reducing dopamine activity and thus psychotic symptoms, albeit through different mechanisms.

One of these studies (Gefvert, et al., 2003) investigated ten medication-free patients with psychosis, nine patients treated with classical antipsychotics, and ten healthy volunteers by using L-[¹¹C] DOPA PET. It indicated that schizophrenia is associated with abnormal patterns of L-[¹¹C] DOPA utilization in corticostriatal systems, and that treatment with classical neuroleptics induces "normalization" of the abnormal patterns exhibited in untreated schizophrenia. However, the exact nature of the neurochemical changes as a result of the antipsychotic treatments has not been described clearly by the authors.

Abi-Dargham's group conducted a series of SPECT studies (Abi-Dargham, et al., 1998, 2000; Frankle, et al, 2004), which provided relatively clear information on the occupancy of striatal D2 receptors by antipsychotic medications. In one of their studies (Frankle, et al, 2004), 16 patients with schizophrenia taking either risperidone

(6 mg/day) or olanzapine (10 mg/day) underwent a SPECT scan following three weeks of treatment. At the time of the scan, each patient therefore had been taking the medication for three weeks. In addition, data from their previous study (Abi-Dargham, et al., 2000) were used to calculate the occupancy of striatal D2 receptors by antipsychotic medications that were required to reduce the occupancy of these receptors by endogenous dopamine to control values (occupancy of the D2 receptors by DA in healthy controls was 8.8% and in medication-free schizophrenic individuals was 15.8%). A significantly larger occupancy in schizophrenic patients treated with risperidone (69±8%) compared to olanzapine (55±11%) was noted, and both conditions in turn showed larger occupancy of striatal D2 receptors than unmedicated patients with schizophrenia. This study also demonstrated that the dosage of these medications reduces dopamine stimulation of D2 receptors to levels lower than those found in unmedicated healthy subjects. Their data further suggested that clinical efficacy of the medication treatment in schizophrenia requires that stimulation of D2 receptors by dopamine be reduced to a level lower than that observed in healthy subjects.

In contrast to most of the studies, Gründer, Vernaleken and Müller (2003) argued that the antipsychotic effect of neuroleptics are not only attributable to blockade of postsynaptic D2 receptors, but also arises in conjunction with delayed depolarization

block of presynaptic neurons and reduced dopamine synthesis capacity. They measured relative activity of DOPA decarboxylase in nine patients with schizophrenia before and after receiving haloperidol treatment. There was a 25% decrease in the magnitude of k-super(D)-sub-3 in both caudate and putamen following five weeks of haloperidol. In addition, reductions in the magnitudes of k-super(D)-sub-3 in cerebral cortex and thalamus were also observed. According to Gründer, Vernaleken and Müller (2003), these findings are consistent with the hypothesis that the antipsychotic effect of chronic neuroleptic treatment is associated with a decrease in dopamine synthesis, reflecting a depolarization block of presynaptic dopaminergic neurons.

A.II. Dreams of Patients with Schizophrenia

Clinicoanatomical studies have advanced the scientific understanding of dreams by suggesting that the critical component of the frontal region responsible for dreaming is the mesocortical-mesolimbic dopaminergic system, the neural substrate for exploratory and gratifying behaviours. Damage to the ventromesial frontal region (Solms, 1995, 1997, 2000b; Yu, 2001b), particularly to the ventral striatum including the head of the caudate nucleus and the nucleus accumbens (Yu, 2001b), leads to adynamia and simultaneously renders dreaming malfunctioned. If dreaming is, as revealed by the neuroanatomical analyses, modulated by the ventromesial frontal

region, which is associated with mesolimbic dopaminergic activity, then individuals who sustain the neurochemical roller coaster of dopaminergic hyperactivity and antagonism may, by definition, undergo abnormal dream patterns. Psychiatric patients with Parkinson's disease, and those suffering schizophrenia, a hypothetically reverse neurological condition, best fit this criterion.

An early study of a relatively large sample indicated that levodopa-treated subjects have a significantly higher dream recall frequency than healthy controls and drug-free subjects (Massetani, et al., 1986). Following comparable observations, dream abnormalities and alterations (i.e., excessive dreaming, unusually vivid dreams, nightmares, night terrors) that precede the occurrence of hallucinations in Parkinson's disease are now generally thought to be triggered by dopamine agonists such as levodopa and pramipexole (Comella, Tanner, & Ristanovic, 1993; Factor, Molho, Podskalny, & Brown, 1995; Nausieda, Weiner, Kaplan, Weber, & Klawans, 1982; Pal, Calne, Smii, & Fleming, 1999; Scharf, Moskowitz, Lupton, & Klawans, 1978; Thompson & Pierce, 1999; see Razmy & Shapiro, 2000, for a review).

In addition to intensified dreaming in response to dopamine agonists, further evidence for the dopaminergic basis of dreams has been provided by studies on schizophrenics (Chang, 1964; Dement, 1955; Desroches & Kaiman, 1963, 1964; Hadjez, et al., 2003; Julien, D'Agostino, & Balzamo, 1981; Gaillard & Moneme,

1977; Hartmann, 1966; Jus, et al, 1973a, 1973b; Karla, Natu, Deswal, & Agarwal, 2000; Kelly, 1998; Kramer, 2000; Kramer, & Roth, 1973; Kramer, Whitman, Baldridge, & Ornstein, 1970; Ornstein, Whitman, Kramer, & Aldridge, 1969; Scarone, Spoto, Penati, Canger, & Moja, 1976; Tandon, Greden, & Silk, 1988; Zarcone, 1988). Surprisingly, most of these studies did not consider the neuropharmacological mechanisms, given the context of the underlying neural pathology and dopamine antagonism of the treatment of schizophrenia.

Early reports of dream recall of schizophrenics following administration of dopamine antagonists include those of Gaillard and Moneme, 1977; Hartmann, 1966; Sacks, 1985, 1990, 1991; and Scarone, Spoto, Penati, Canger, and Moja, 1976. These are largely single-case studies and their findings are neither consistent nor instructive. Kramer, Whitman, Baldridge and Ornstein (1970) conducted an investigation into the dream content of 11 male paranoid schizophrenics who were treated with dopamine antagonists (i.e., chlorpromazine, trifluoperazine, perphenazine, or thioridazine). They discovered that the medication treatments resulted in the suppression of verbal productivity in describing dreams; a decline in dreams marked by aggressive social interaction; and a decline in emotions in dreams. Paradoxically, the frequency of dream recall did not change.

By contrast, in another study, involving 50 psychiatric patients (Karla, Natu,

Deswal, & Agarwal, 2000), dreams were suppressed in 78% of patients after the institution of medication. However, all patients in this study were on a treatment regime incorporating multiple psychoactive drugs, resulting in the authors being unable to identify the specific psychoactive drug responsible for dream suppression. According to the authors, the dream suppression could be broadly attributed to sedative-hypnotic drugs such as benzodiazepines, antidepressant drugs such as imipramine, clomipramine, and fluoxetine, as well as antipsychotic drugs like thioridazine and haloperidol.

On the basis of converging lines of evidence, it seems that the crucial component of the ventromesial frontal region responsible for deficiency of dream experience following anterior forebrain lesions lies in the mesocortical-mesolimbic dopamine system. Nevertheless, clinicoanatomical studies only provide an indirect test of the dopamine hypothesis of dreaming, insofar as certain cognitive deficits are pathognomonic of mesocortical-mesolimbic dopamine system lesions. Likewise, while considerable empirical works have focused on the dreams of patients with schizophrenia, few have considered the effects of specific neuropharmacological agents, and their results are not entirely consistent. Therefore, the current study attempted to examine the dopamine hypothesis by thoroughly investigating the dream experience and medication regime of patients with psychotic features.

B. Method

B.I. Design

In examining the dopamine hypothesis of dreaming, the present study investigated 55 psychiatric patients on dopamine antagonist therapies. All subjects received sleep and dream interviews, in which past and present sleep and dream experiences were recorded in detail. All patients' full medical and medication history were traced. The relevant professionals (including their psychiatrists, psychiatric nurses, social workers, etc.) were contacted in order to collect comprehensive information on their daily routines, behaviours, social interactions, and symptom manifestations. To ensure, as far as possible, that the obtained information was reliable, questions were repeated intermittently throughout interviews with different wordings, further questions and interviews were made for clarification, and patients' mental status and neuropsychological functions were examined. Each patient was followed up intermittently for three months. Patients who reported low frequency or deficiency of dream recall and awareness were followed up via daily morning interviews for the first two weeks after the initial dream interviews. Guidelines for facilitating dream recall (Dream Recall Instruction) were given. The neurochemical effects of the medication taken by the psychiatric patients with different frequencies of dream

experience were then compared and analyzed, together with the materials collected from the interviews and the relevant professionals.

B.II. Subjects

Fifty-five patients with psychiatric disorders participated in the current study. They were drawn from mental health centres and residential services for mental illness in Hong Kong. Forty-eight of them suffered from schizophrenia, and the rest subjects with psychotic features were diagnosed with bipolar disorder (Case No. 4, 5, and 13), delusional disorder (Case No. 26), dysmorphophobia (Case No. 19), mild-grade mental disability with affective features (Case No. 12), and obsessive-compulsive behavior with borderline behavioral problems and a history of cough mixture abuse (Case No. 23).

All patients had been receiving dopamine antagonists as neuropharmacological treatment. Patients whose medication regimes had been changed within six months were removed from the current analysis. In other words, all patients included in the current series had been receiving a stable dose of dopamine antagonistic agents for the past six months and were receiving the same medication regimes during the further three-month investigation period. This sample comprised 30 (54.5%) male and 25 (45.5%) female patients. Mean age was 40.7 years (S.D. = 9.19; range = 21-59).

While the study intended to approach every potential psychiatric patient, participants were selected based on some necessary criteria, including for instance their willingness, mental status and medication treatment (i.e., receiving primarily dopamine antagonists), etc.

B.III. Procedure

In the first interview, information about sleep and dream experience (e.g., frequency of dream awareness, recurrent dreams or nightmares, etc.) was obtained, and patients' neuropsychological status was examined. Most information was reconfirmed by different investigators (the author and employed research assistants) in subsequent interviews.

After the first interview, all patients were followed up by means of intermittent morning interviews for three months. The dream recall instruction was provided (in the initial interview) to the patients to increase their ability to remember their dream experience (see Chapter Two). If the patients reported no dream recall, it was distinguished carefully whether the patients did not have any dream experience/awareness or they had dreamed but had forgotten the dream content. For those patients reported low frequency or deficiency of dream experience, their sleep and dream experience were monitored *daily* for two weeks and after that they were

followed up weekly for the rest of the three-month investigation period.

Each patient was at least interviewed by two separate investigators (the author and at least one trained interviewer). The trained interviewers (employed research assistants) were blind to the hypotheses of the current study. Consistency of the dream and sleep findings collected by the different interviewers was checked by the end of the investigation.

In addition to the dream interviews, all patients' full medical and medication history were traced. The relevant professionals were contacted in order to collect comprehensive information on their daily routines, behaviours, social interactions, and symptom manifestations. The patients' sleep and dream experiences were then compared and analyzed, taking into account the neuropharmacological effects of the medication regimes and other collected clinical information.

B.IV. Materials

B.IV.1. Survey on Previous Dream Experience

Similar to the protocol used in the previous studies of non-patient subjects (Chapter Two) and neurological patients (Chapter Three to Six), the patients' dream experience was clarified carefully in the initial interviews (Appendix A). These questions broadly included subjects' general concept about dreams, frequency of dream experience,

common themes of their dreams, and multiple dreams in a single night, etc. To reiterate, the interviewers tried to obtain a frequency of awareness of dream experience by using questions such as "How often did you dream in the past six months (including both the dreams you remember clearly and the dreams that you do not remember their contents)?"

The average dream recall frequency documented by several studies is two to three times per week (e.g., Görtelmeyer, 1986; Schredl, 2000a, 2000b, 2002a, 2003; Schredl, Ciric, Gotz, & Wittmann, 2003; Stepansky et al., 1998; Webb & Kersy, 1967; Zadra & Nielsen, 1999). Combining the existing findings (including the results reported in Chapter Two), *awareness* of dream experience once per week for a significant period (i.e., six months) can be adopted as a relatively reliable cutoff score for defining low frequency of dream awareness. In addition to general dream experience, the subjects were required to report the latest dream that they could remember, primarily adopting the Most Recent Dream Report (Domhoff, 1996) (Appendix G).

B.IV.2. Dream Diary

All subjects were required to provide any dreams that they could remember each morning throughout the three month follow-up. The Most Recent Dream Report

(Domhoff, 1996) was adopted as guidance for the subjects to report their dreams (Appendix H).

B.IV.3. Dream Recall Instruction

Guidelines were provided to the subjects for aiding their dream recall (see Chapter Two and Appendix C, for details).

B.IV.4. Receptor Tables

Psychotropic medications block different neuroreceptors with various potencies. Therefore, each psychoactive agent has its own pattern of blocking effects on a variety of receptors. The current neuropharmacological analyses adopted primarily Seeman's (1993) Receptor Tables which include a collection of 12,000 drug dissociation constants for 28 G protein-coupled receptors (GPCRs) families and subfamilies extracted from the literature. Seeman's Receptor Tables have thus far been the most comprehensive collection of data for the blocking effects of psychotropic medications on neuroreceptors.

B.V. Research Ethics

Ethical approvals from relevant bodies were obtained. Ethical considerations are

provided in Appendix K.

C. Neuropharmacological Analyses

More than half of the psychiatric patients in the current series were regularly aware of their dream experience. Awareness of dreams for these patients ranged from at least once a week up to every night for the past six months (Table 7.1). Almost 30% of the patients dreamed nightly. At least half of these psychiatric subjects with nightly dream experience engaged in habitual awareness of multiple dreams in a single night. On the other hand, a considerable number of the psychiatric subjects (36.4%) had experienced a marked low frequency of dream experience (including both recall and awareness less than once a week or a month). Furthermore, five (9.1%) psychiatric patients reported no dream experience for years. Less than 10% of the psychiatric subjects had difficulty quantifying their dream experience, reflecting an irregularity of dream awareness. At least 25.5% of all 55 patients had experienced consecutive, recurrent nightmares.

The proportion of the psychiatric subjects who had dream awareness frequency less than once a month was high, but the number of this group did not seem to be significantly higher than those of the other four groups (chi-square (4) = 11.09, p = 0.026), especially when the "uncertain/irregular" group was removed (chi-square (3)

= 6.16, p = 0.10). Nonetheless, this distribution pattern was obviously different from that of the normal population (see Chapter Two, Table 2.1, for comparison).

The frequency of dream awareness of the patients was confirmed in the follow-up interviews during the three-month investigation period. The use of the dream recall instruction did not seem to have a significant effect on increasing the frequency of dream awareness in the psychiatric sample on the whole. That is, most patients remained in the same groups except the five "uncertain" cases. The five patients who were initially unable to quantify their dream experience could provide relatively regular dream reports (ranged from two to four times per week) during the follow ups. Throughout the three-month investigation, the 15 patients who had dream awareness frequency less than once a month provided a total of six reports of dream experience which were vague and had no available dream content, even with the aid of the dream recall instruction. No or no more than one dream could be triggered in each case.

Table 7.1 Dream Awareness Frequency of Psychiatric Patients

Dream Experience	Schizophrenia	Other Disorders	Total
Less than 1/month	13 (27.1%)	2	15 (27.3%)
Less than 1/week	4 (8.3%)	1	5 (9.1%)
1-6/week	13 (27.1%)	1	14 (25.5%)
Nightly	13 (27.1%)	3	16 (29%)
Uncertain/Irregular	5 (10.4%)	0	5 (9.1%)
Total	48 (100%)	7	55 (100%)

Not all subjects experienced a deficiency of dream experience, although they were all receiving dopamine antagonists. The medication regimes of the five different dream frequency groups are provided in Table 7.4-7.8. A total of 14 dopamine antagonists were noted in the medication regimes of the psychiatric patients. While all neuroleptics block dopamine receptors, each neuroleptic has its own pattern of blocking effects on a variety of dopamine and non-dopamine receptors. The psychiatric subjects in the current sample received five potent neuroleptics which have relatively strong preferential blockage of D2-type receptors: sulpiride, stelazine, thioridazine, risperidone, and haloperidol (Appendix L). Amongst the five potent antipsychotics, sulpiride and stelazine have the strongest preferential blockage of D2 receptors, relatively devoid of the effects on other neuroreceptors. Sulpiride is highly selective and acts primarily as a dopamine D2 antagonist (Appendix M). Sulpiride blocks mainly D2 and D4 receptors (but with much stronger effects on D2 receptors), and its antagonist potency is relatively strong for D2 as compared with the other

antipsychotics. By contrast, chlorpromazine, clozapine and quetiapine were three less potent agents as a specific D2 antagonist.

There was a propensity that compared to the patients treated with nonselective D2 antagonists, the patients who received highly potent and D2-selective antagonists were more likely to have low frequency or deficiency of dream experience (Table 7.2). For instance, 36.8% of the patients treated with highly D2-selective antagonists were aware of their dream experience less than once a month, whereas 36% of the patients treated with nonselective D2 antagonists were nightly dreamers.

The numbers of the psychiatric patients who utilized the five highly dopamine D2-selective antagonists, together with their frequencies of dream experience, are summarized in Table 7.3. For the patients whose frequency of dream awareness was less than once a month, four received sulpiride and three were treated with haloperidol. Further details of the neurochemical effects of the dopamine antagonists and other psychoactive drugs taken by the psychiatric patients in each dream frequency group are provided in the following passage.

Table 7.2 Dream Awareness Frequency between Psychiatric Patients on Highly Selective D2 Antagonists and Psychiatric Patients on Nonselective D2 Antagonists

Dream Experience	Highly Selective D2 Antagonist Users	Nonselective D2 Antagonist Users	Total
Less than 1/month	11 (36.8%)	4 (16%)	15 (27.3%)
Less than 1/week	4 (13.3%)	1 (4%)	5 (9.1%)
1-6/week	7 (23.3%)	7 (28%)	14 (25.5%)
Nightly	7 (23.3%)	9 (36%)	16 (29%)
Uncertain/Irregular	1 (3.3%)	4 (16%)	5 (9.1%)
Total	30 (100%)	25 (100%)	55 (100%)

Table 7.3 Dream Awareness Frequency of Psychiatric Patients on Highly Selective D2 Antagonists

Dream Experience	sulpiride	stelazine	thioridazine	risperidone	haloperidol	Total
Less than 1/month	4	4	0	2	3	13
Less than 1/week	1	1	0	1	1	4
1-6/week	4	1	0	1	1	7
Nightly	2	3	1	0	2	8
Uncertain/Irregular	0	0	1	0	0	1
Total	11	9	2	4	7	33

Note. The frequencies are not exclusive.

Of the five subjects who had dream recall and awareness less than once a week, four received the aforementioned potent neuroleptics which have strong selective blocking effects on D2 receptors. Four patients concurrently took benzhexol, an anticholinergic agent, for managing the side effects of neuroleptics (Table 7.4). Case No. 20's prescription comprised three different dopamine antagonists (i.e., sulpiride, chlorpromazine, and modecate) and one serotonin (5-HT) agonist (citalopram),

excluding any agents with direct effects on cholinergic transmission.

Ten (66.7%) of the 15 patients presenting with dream experience less than once a month consumed purely antipsychotic medication, without taking other classes of psychotropics (e.g., antidepressants, anticonvulsants, hypnotics, etc.) (Case No. 6, 14, 15, 29, 35, 38, 40, 51, 52, & 62) (Table 7.5). Almost all patients in this group were treated with the strong D2-selective antagonists. Eight patients were either sulpiride or stelazine users. Benzhexol was used by 10 subjects.

Four subjects without dream recall and awareness for a month or more took one dopamine antagonist exclusively without using benzhexol or any other medications (Case No. 14, 38, 52, & 62). Case No. 38 used olanzapine exclusively, which is however a less selective agent and has wide potent blocking effects on D3, D4, M1 (muscarinic cholinergic receptor) as well as 5-HT2 receptors (Appendix L). Case No. 14 and 52 used stelazine, and Case No. 62 used sulpiride. As mentioned, sulpiride and stelazine have strong preferential blockage of D2 receptors.

Table 7.4 Medication Regimes of Psychiatric Patients with Dream Experience Less than 1/Week (N = 5)

Case No.	Gender/ Age	Classification	Recent Treatment
5	Female 40	Bipolar Disorder	- Haloperidol 1.5-3mg/N - Lithium Carbonate 750mg/OM & N - Valproate Sodium 800mg/N - Zopiclone 7.5mg/N - Benzhexol 2mg/BD

9	Female 39	Schizophrenia	- Chlorpromazine 175mg/N - Propranolol 10mg/N - Benzhexol 2mg/N
20	Male 42	Schizophrenia	- Sulpiride 500mg/N - Chlorpromazine 200mg/N - Depot Modecate 100mg Q4W - Citalopram 40mg/OM & 20mg/N
27	Male 30	Schizophrenia	- Risperidone 3mt/BD - Depot Fluanxol 50mg - Valium 2mg/OM & 4mg/N - Benzhexol 4mg/BD
53	Female 38	Schizophrenia	- Stelazine 2mg/N - Zopiclone 3.75mg/N - Benzhexol 2mg/BD - Multivitamin 1tab/day

Table 7.5 Medication Regimes of Psychiatric Patients with Dream Experience Less than 1/Month (N = 15)

Case No.	**Gender/ Age**	**Classification**	**Recent Treatment**
4	Male 49	Bipolar Disorder	- Sulpiride 200mg/OM & 400mg/N - Depot Clopixol 500mg/IMI - Lithium Carbonate 500mg/OM & 750mg/N - Gabapentin 600mg/OM&N - Valproate Sodium 800mg/BD - Benzhexol 2mg/BD
6	Female 40	Schizophrenia	- Clozapine 175mg/N - Benzhexol 2mg/N
14	Female 35	Schizophrenia	- Stelazine 2mg/N
15	Male 55	Schizophrenia	- Stelazine 10mg/BD - Depot Haldol 100mg Q4W - Benzhexol 2mg/BD
18	Male 54	Schizophrenia	- Sulpiride 200mg/BD - Haloperidol 20mg/N - Depot - Mianserin 30mg/N - Flurazepam 15 mg/N

			- Zopiclone 7.5mg/N - Orphenadrine 100mg/OM - Panadol 250mg/QIDprn - Doxazosin 4mg/OM - Esomeprazole 7.5mg/N - Sennatoside B 15mg/N - Metamucil/TDS - Lactulose Liquid/BD
22	Male 37	Schizophrenia	- Clonazepam 0.25mg/BD - Depot - Benzhexol 2mg/BD
23	Male 31	OCB	- Haloperidol 6.5mg/N - Clomipramine HCl 225mg/5pm - Depot Modecate 75mg Q4W - Valproate Sodium CR 600mg/N - Propranolol 10mg/TDS - Benzhexol 4mg/TDS
29	Male 54	Schizophrenia	- Stelazine 10mg/N - Depot Fluanxol 20mg - Benzhexol 4mg/OM
35	Female 38	Schizophrenia	- Clozapine 250mg/N - Benzexol 4mg/N
36	Female 21	Schizophrenia & OCD	- Risperidone 1mg/D&N - Prozac 20mg/D - Benzhexol 2mg/D&N
38	Female 25	Schizophrenia	- Olanzapine 10mg/N
40	Male 45	Schizophrenia	- Risperidone 4mg/D & N - Benzhexol 4mg/TDS
51	Male 38	Schizophrenia	- Sulpiride 400mg OM & 800mg/N - Benzhexol 4mg/BD
52	Female 43	Schizophrenia	- Stelazine 6mg/N
62	Female 37	Schizophrenia	- Sulpiride 500mg/D&N

The prescriptions of all 16 subjects who experienced nightly dream awareness are summarized in Table 7.6. Nine (56.3%) of the 16 patients' treatment prescriptions

were principally dopaminergic antagonists (Case No. 12, 16, 17, 21, 25, 28, 34, 55, & 56). More than half of the patients used the dopamine antagonists, which are less selective to the D2 receptors. Four subjects (Case No. 12, 16, 34, & 55) used dopamine antagonists without concomitant anticholinergic agents, and Case No. 12 was the only subject who took a single medication. Chlorpromazine, which was the most common antipsychotic utilized by the frequent dreamers, is relatively nonselective as an antagonist (Appendix L). Two subjects (Case No. 24 & 26) used sulpiride. Both received high doses of medications. Six of the 13 subjects diagnosed with schizophrenia with nightly dream awareness consumed antidepressants and/or sedatives.

The prescriptions of the subjects who had dream experience one to six times a week are provided in Table 7.7. There were six cases receiving potent dopamine antagonist treatment relatively devoid of other neuromodulatory agents (Case No. 1, 13, 37, 47, 49, & 54). Case No. 1 was in an active phase of schizophrenia, exhibiting all positive symptoms as well as confusion between dream content and delusional thoughts, despite the antipsychotic medication treatment. Case No. 13 had been taking a relatively low dose of sulpiride since two years prior, when she was diagnosed with bipolar disorder. She noticed that after taking sulpiride, she dreamed less frequently. She previously dreamed nightly, but since taking sulpiride, she had dream awareness

one to two times a week. Hallucinations and delusions were evident in Case No. 37 and 41, and Case No. 47 demonstrated all three primary positive symptoms (i.e., hallucinations, delusions, and disorganized speech), despite pharmacological treatment. Case No. 48 had been diagnosed with schizophrenia one year ago. Case No. 49 was treated with chlorpromazine, which is as mentioned a nonselective agent. Case No. 54 sustained delusions of grandeur and deterioration of self-care, with an onset three years prior. He was a sulpiride user and had dream awareness once a week. The medication prescriptions of the subjects in the category of uncertain dream experience are available in Table 7.8.

Table 7.6 Medication Regimes of Psychiatric Patients with Dream Experience Nightly (N = 16)

Case No.	Gender/ Age	Classification	Recent Treatment
7	Female 28	Schizophrenia & Borderline Intelligence	- Haloperidol 6.5mg/N - Depot Haldol 50mg - Prozac 30 mg/N - Benzhexol 2mg/OM & Noon
11	Female 45	Schizophrenia	- Stelazine 35mg/N - Valium 2mg/N - Benzhexol 4mg/TDS
12	Female 43	Mild Grade MD with Affective Features	- Chlorpromazine 150mg/N
16	Male 53	Schizophrenia	- Stelazine 10mg/N - Depot Clopixol 400mg Q4W
17	Male 50	Schizophrenia	- Depot Fluanxol 20mg - Congentin 2mg IMI Q4W
19	Male 41	Dysmorphophobia	- Haloperidol 3mg/N

			- Paroxetine 20mg/QD - Benzhexol 2mg/N
21	Male 41	Schizophrenia	- Chlorpromazine 75mg/N - Depot Fluanxol 40mg Q5W - Benzhexol 2mg/BD
24	Male 38	Schizophrenia	- Sulpiride 200mg /OM & N - Chlorpromazine 500mg/N - Depot - Prozac 20mg/OM - Propranolol 10mg/TDS - Benzhexol 2mg/TDS
25	Male 33	Schizophrenia	- Clozapine 50mg/OM & 200mg/N - Benzhexol 2mg/OM
26	Male 52	Delusional Disorder	- Sulpiride 400mg/N - Depot Clopixol 200mg 1ml Q4W - Valium 4mg/BD - Senokot 15mg/N - Propranolol 20mg/TDS - Benzhexol 2mg/TDS
28	Male 47	Schizophrenia	- Pimozide 8mg/OM - Depot Modecate 100mg 1ml Q4K - Benzhexol 2mg/BD
34	Female 33	Schizophrenia	- Quetiapine 700mg/N - Valproate Sodium 1000mg/N
42	Female 39	Schizophrenia	- Stelazine 5mg/D, 15mg/N - Zopiclone 7.5mg/N - Mirtazapine 45mg/N - Valproate Sodium CR 500mg/N - Benzhexol HCl 2mg/D&N
55	Female 27	Schizophrenia	- Flupenthixol 2mg/N - Chlorpromazine 50mg/N - Propranolol 10mg/BD - Multivitamin 1tab, 2times/D
56	Male 56	Schizophrenia	- Pimozide - Thioridazine - Benzhexol
58	Male 42	Schizophrenia	- Antipsychotics (details unavailable)

Note. Details unavailable: Patient did not want the details to be published.

Table 7.7 Medication Regimes of Psychiatric Patients with Dream Experience 1-6/Week (N = 14)

Case No.	Gender/ Age	Classification	Recent Treatment
1	Male 26	Schizophrenia	- Clozapine 325mg/N - Propranolol 20mg/OM
3	Male 58	Schizophrenia	- Sulpiride 200mg/OM & 400mg/N - Depot Clopixol 300mg IMI Q4W - Lithium Carbonate 250mg/TDS - Orphenadrine 100mg/BD - Benzhexol 2mg/TDS
8	Female 41	Schizophrenia	- Quetiapine 500mg/N - Clonazepam 2mg/N - Valporate Sodium 600mg/N - Zopiclone 7.5mg/N - Benzhexol 2mg/BD
13	Female 31	Bipolar Disorder	- Sulpiride 200mg/N - Valporate Sodium 800mg/N
30	Male 50	Schizophrenia	- Risperidone 2mg/OM & 3.5mg/N - Propranolol 20mg/BD - Benzhexol 2mg/OM
31	Male 49	Schizophrenia	- Haloperidol 8mg/N - Depot - Propranolol 10mg/TDS - Benzhexol 2mg/BD
37	Female 51	Schizophrenia	- Clozapine 25mg/D & 50mg/N
41	Male 24	Schizophrenia	- Sulpiride 400mg/D & 600/N - Benzhexol 2mg/D & N
47	Female 34	Schizophrenia	- Olanzapine 10mg/N
48	Male 28	Schizophrenia	- Stelazine 20mg/N - Benzhexol 4mg/N
49	Male 36	Schizophrenia	- Chlorpromazine 150mg/N
54	Male 38	Schizophrenia	- Sulpiride 550mg/N
59	Female 59	Schizophrenia	- Antipsychotics (details unavailable)

61	Female 39	Schizophrenia	- Antipsychotics (details unavailable)

Note. Details unavailable: Patient did not want the details to be published.

Table 7.8 Medication Regimes of Psychiatric Patients with Uncertain Dream Frequency (N = 5)

Case No.	Gender/ Age	Classification	Recent Treatment
33	Female 47	Schizophrenia	- Olanzapine 30mg/N - Clonazepam 1mg/N - Valproate Sodium 1600mg/N
39	Male 33	Schizophrenia	- Perphenazine 8mg/N & 10mg/N - Lithium Carbonate 250mg/N & 500mg/N - Benzhexol 2mg/D&N
50	Male 45	Schizophrenia	- Quetiapine 200mg/OM & 550mg/N - Clonazepam 1.5mg/N - Piriton 8mg/N
57	Female 42	Schizophrenia	- Antipsychotics (details unavailable)
60	Female 39	Schizophrenia	- Thioridazine 150mg/N - Propranolol 10mg/D&N - Benzhexol 2mg/TDS

Note. Details unavailable: Patient did not want the details to be published.

D. Discussion

D.I. Neuromodulatory Correlates of Dreaming

A number of the subjects receiving dopaminergic antagonists experienced significantly lower frequency of dream experience than the average documented by previous normative studies (e.g., Görtelmeyer, 1986; Schredl, 2000a, 2000b, 2002a, 2003; Schredl, Ciric, Gotz, & Wittmann, 2003; Stepansky et al., 1998; Webb & Kersy, 1967; Zadra & Nielsen, 1999) and the dream recall study of neurologically and

psychiatrically healthy subjects reported in Chapter Two. Some patients even sustained deficiency of dream recall and awareness for years. Their frequency of dream experience was confirmed in the subsequent follow-up investigation, with the aid of the dream recall instruction.

Although most neuroleptics block both dopamine D1- and D2- families, as well as other neuroreceptors in various degrees, all effective antipsychotic drugs block D2 type receptors. Some exemplars of antipsychotics such as sulpiride, stelazine, and haloperidol, which were frequently prescribed amongst the patients with low frequency of dream experience and were used exclusively by a few patients, are highly selective to D2 receptors. No obvious D1 receptor occupancy was induced by these neuromodulators. On the other hand, sulpiride appears to lack effects on acetylcholine, serotonin, norepinephrine, histamine, or gamma-aminobutyric acid (GABA) receptors. The relatively low incidence of extrapyramidal and other adverse effects observed with sulpiride have indeed been attributed to its highly specific D2 blocking activity (Asghari, et al. 1994; Chio, et al., 1994; Farde & Nordstrom, 1992; Hidaka, et al., 1996; Hurley, Stubbs, Jenner, & Marsden, 1996; Merchant, et al., 1996; Newman-Tancredi, Audinot, Chaput, & Millan, 1997). It is worth noting that D2 receptors are distributed both pre- and postsynaptically on neurons in the ventral striatum and nucleus accumbens. It is believed that these regions and the mesolimbic

dopaminergic systems are the primary sites for antipsychotic effects (Breggin, 1980; Hurley, Stubbs, Jenner, & Marsden, 1996; Panksepp, 1985; Role & Kelly, 1991).

In psychiatric practice, benzhexol (trihexyphenidyl/Artane®), which is one of the centrally acting cholinergic and specifically muscarinic M1 antagonists used for treatment of Parkinsonian disorders and drug-induced extrapyramidal movement disorders (i.e., the side effects of antipsychotics), is almost invariably prescribed together with antipsychotics. This is certainly a clinical constraint of conducting human neuropharmacological research in naturalistic settings. Benzhexol was commonly included in the prescriptions of the current sample. This centrally active anticholinergic drug blocks excitatory cholinergic pathways in the basal ganglia, and is *expected* to restore the dopamine/acetylcholine balance disrupted by neuroleptic drugs, thus treating extrapyramidal side effects. However, anticholinergic agents do not necessarily potentiate dopaminergic restoration in the ventral striatum, counteracting the dopaminergic antagonism induced by antipsychotics. There is evidence that neuroleptic-induced dopamine levels in the nucleus accumbens are not affected by muscarinic antagonism (Gray & Connick, 1998). Benzhexol may even suppress dopamine release in the mesolimbic areas (Shimosato, Watanabe, & Kitayama, 2001; Shimosato, Nagao, Watanabe, & Kitayama, 2003). Evidence also shows that benzhexol treatment is unable to counteract the imbalance in prepropeptide

messenger RNA expression produced by a unilateral striatal dopaminergic denervation, and even amplifies this effect (Mavridis, Rogard, & Besson, 1995). These observations challenge the concept that the striatum is the site of action of antimuscarinic drugs.

Antidepressants such as fluoxetine, clomipramine, and mianserin were used by some nightly dream patients in the current series. These drugs preferentially inhibit the reuptake of serotonin into brain synaptosomes and platelets, and have either no or very low affinity for a series of receptors including D2 receptors (see Seeman, 1993).

In view of the overall evidence, it appears that the neurological effect of attenuation of dream experience is associated with D2 receptor blockade. Nevertheless, the present neurochemical findings were only partially consistent with the dopamine hypothesis. The neuroleptic treatment, by directly modulating D2-type receptors in the mesolimbic areas, only suppresses dream recall and awareness in some cases. It can even be argued that perhaps the present neuropharmacological analyses cast a doubt on the dopamine hypothesis. A considerable number of patients on dopamine antagonistic therapies reported regular frequency of dream experience. Some of them received potent dopamine D2 antagonists. Not every patient on dopamine antagonist treatment experienced a cessation, or even a deficiency, of dream recall and awareness. The differences in the blocking effects of the dopamine

antagonist consumption between the patients presented with different frequencies of dream experience were not substantial, albeit perceptible.

D.II. "Clean" Experiment?

It should be made clear that the present neuorpharmacological study only intended to provide a preliminary view of the dream experience of patients receiving dopamine antagonist treatments. This is a tentative investigation rather than an attempt to validate the dopamine hypothesis. Even though some patients on dopamine antagonists continued to dream quite often, and not every patient experienced a cessation of dream recall and awareness, this is nevertheless not entirely unexpected. First, psychotic symptoms do not necessarily entail irreversible structural lesions, but instead only reflect soft signs of frontal impairment or neurochemical deregulation.

Second, the psychopharmacological mechanisms are far from simple. For instance, the neuropharmacological effects of sulpiride are indeed dose-dependent. A lower dose of sulpiride can produce an opposite effect that potentiates, instead of suppresses, dopamine agonistic actions (Cabib, Castellano, Cestari, Filibeck, & Puglisi-Allegra, 1991; Smith, Neill, & Costall, 1997; Tang, Noda, & Nabeshima, 1997; Zarrindast, Sattari-Naeini, & Motamedi, 1992). Still, a combination of drugs can produce interaction effects. However, it is obvious that a complex interaction of

multiple neurotransmitter systems can produce psychotic symptoms (Hobson, 2001; Vollenweider, 1998) including for instance, glutamatergic (Coyle, 1996; Olney, Newcomer, & Faber, 1999) and serotonergic (Aghajanian & Marek, 2000; Bantick, Deakin, & Grasby, 2001) neurotransmission, substances also implicated in the sleep and dreaming cycle. For instance, some patients who had been studied but were not included in the current analyses reported changes in their dream experience immediately after receiving some other psychotropic medications like mood stabilizer.

Third, there are perhaps essential differences in clinical features between patients with different dream experiences. For instance, some of the schizophrenic patients with nightly dream experience showed evident depressive symptoms, and consumed antidepressants and/or sedatives (for their sleep disturbances). Note that increased dreaming sleep is associated with depression (Rush et al., 1997; Shelton, Hollon, Purdon, & Loosen, 1991; Thase & Howland, 1995) as well as sleep disturbance (Levin, 1994; Schredl, Bozzer, & Morlock, 1997; Schredl & Engelhardt, 2001; Starker, 1985). In the same vein, each patient with weekly dream awareness in the current series presented with idiosyncratic clinical pictures in terms of the severity, onset, and duration of their psychiatric symptoms. A contrast between dream recall during the acute phase and those during the remission phase in schizophrenics has been documented (Julien, D'Agostino, & Balzamo, 1981). Individuals in different

phases of the developmental course of psychosis vary in their psychotic symptoms and cognitive functions, which are perhaps associated with the underlying neural mechanisms.

Furthermore, there are some ethical issues that should be considered when conducting neuropharmacological investigation. For instance, it is potentially unethical to delay or withdraw medication treatment for research purposes. Accordingly, all drugs and neuropharmacological experiment that impact on dreaming are confounded by multiple factors which are extremely difficult to be "partialled out" authentically. In other words, there is perhaps virtually no "clean" human neuropharmacological experiment in a naturalistic environment. When inspecting seriously the literature, it can be found that such confounding factors are commonly ignored among the previous human neuropharmacological studies and experiments. To partial out or control all the confounding factors statistically, a very large sample is required. Considering also the ethical and clinical constraints, longitudinal or qualitative case research which takes the important factors into account may provide valuable findings for approaching the dopamine hypothesis of dreaming.

Despite all enumerated limitations and confounding factors, the present study highlighted three findings. First, some exemplars of antipsychotics such as sulpiride, stelazine, and haloperidol, which were used *exclusively* by a few patients with

significantly low frequency of dream experience, are highly selective to D2 receptors. Second, almost all patients with significantly low frequency of dream experience utilized the potent D2-selective antagonists. Third, there was a tendency that the patients treated with potent D2-selective antagonists were more likely than the patients treated with nonselective D2 antagonists to sustain low frequency or deficiency of dream experience.

It is perhaps also worth adding that while some patients showed relatively regular dream awareness, most of them only provided the main themes of their dreams, even with the aid of the dream recall instruction. The descriptions of their dreams were brief (i.e., several sentences), fragmented and far less complete than those provided by the normal subjects (i.e., detailed story-like description). This appeared to echo the early findings (Kramer, Whitman, Baldridge, & Ornstein, 1970). However, the reason for this is unclear and this observation can be attributable to many factors (e.g., attention problems, speech impoverishment, reluctant to give details of dreams, vague dream recall, decrease in vividness of dreaming, etc.).

Although recent evidence provided by animal experiments suggests that dopamine may play a role in arousal (e.g., Bubser, Fadel, Jackson, Meador-Woodruff, Deqiang, & Deutch, 2005; Kume, Kume, Sang, Hirsh, & Jackson, 2005; Ongini, Bo, & Dionisotti, 1992; Ouyang, Hellman, Abel, & Thomas, 2004; Staedt, Wassmuth, &

Stoppe, 1996), the location of the dopaminergic neurons that may regulate arousal remains unclear. It is sometimes assumed that the dopaminergic neurons in the ventral tegmental area that project to the prefrontal cortex and striatum may regulate the state of arousal; however, the firing of these dopaminergic neurons does not correlate with overall levels of behavioural wakefulness. The observation that the firing rate of dopaminergic neurons is regular and monotonous across different behavioural states (wakefulness, NREM and REM sleep) raised a controversy about the possible role played by central dopamine as the "seeking system" in dreaming. Interestingly, Lu, Jhou and Saper's (2006) recent study identified wake-active dopaminergic neurons in the ventral periaqueductal gray matter. They also showed that these wake-active dopaminergic cells have extensive reciprocal connections with the sleep-wake regulatory system. They suggested that the ventral periaqueductal gray matter dopaminergic cells may provide the long-sought ascending dopaminergic waking influence.

Chapter Eight

Summary

By using the human lesion method, Solms (1997) asserted that the occurrence of dreaming is actively generated by the forebrain, but not necessarily by the pons, in view of the clinicoanatomical evidence that cessation of dream experience is associated with lesions in the inferior parietal lobule and in the bifrontal white matter. In contrast to the classical REM-pons hypothesis, Solms (1995, 1997, 1999) proposed an alternative model which is more forebrain based. In this neuropsychological model, frontal dopaminergic mesolimbic reward circuits produce an instigating impetus for dreaming when activated by arousing stimuli. Only if the initial stimulus is sufficiently intense or persistent to activate the motivational mechanisms of the brain, does the dream process proper begin. The functioning of the motivational systems of the brain is normally channelled towards goal-directed action but access to the motor systems is blocked during sleep. As a result, the process of activation takes a regressive pathway from the higher parts of the perceptual systems to the lower parts.

The findings of modern researchers with respect to the brain mechanisms of dreaming are for the most part consistent among different neurological methods, though a couple of uncertainties surrounding the brain mechanisms remained without being properly answered. One of the disagreements concerns the roles of the pons and

the ventromesial frontal region pathway in the functional architecture of dreaming, which also underpins the underlying discrepancy between the classical REM-pons hypothesis and the latest forebrain models. By conducting clinicoanatomical and neuropharmacological analyses, this dissertation attempted to resolve some controversies in the field with respect to the brain mechanisms of dreaming.

To reiterate, the dissertation aims to:

1. assess the usefulness of subjective dream reports as a neuropsyhological tool to differentiate between normal population and neurologically-compromised patients;

2. expand previous knowledge about the relationship between dream deficiency and the precise location of brain lesions, using high resolution brain imaging techniques now available;

3. investigate the correlation between dreaming and alterations in the central dopaminergic system in a population of psychiatric patients treated with different medications affecting this neurochemical system.

A. A Response to Controversy I (Memory Problems)

Solms's (1997) conclusions were principally based on bedside observation rather than

systematic investigation. Similarly, most of the previous clinicoanatomical studies on dreaming were not systematic. It is worth noting that the dream recall method adopted by the current study is different from Solms's approach. Solms directly asked patients whether or not they still dreamed; and if he received a negative answer he asked supplementary questions to ensure that the patients believed they had truly stopped dreaming as opposed to other possibilities. Thereafter Solms sought to establish a temporal association between the subjective cessation of dreaming and the objective onset of neuropathology. The potential methodological flaw is that cessation of dream experience is a secondary effect of memory failure, rather than a direct consequence of neurological insults. There are two specific arguments within the memory controversy: first, dream recall is difficult per se, even in normal people, and second, stroke patients' memory is poor. Both factors can lead to a failure in reporting dream experience.

A.I. Dream Recall is Not Difficult

In considering the first argument, Chapter Two reviewed the pervious studies of dream recall frequency in normal populations. Frequency of dream recall has been investigated extensively in western countries, and dream recall in general does not seem to be difficult, at least in western people. However, most of the previous studies

focused on dream recall frequency instead of frequency of awareness of dream experience. It is unclear whether the dream recall frequency that was expected to be measured included also the dream experience that the subjects were aware of but could not remember clearly (dream content). Moreover, for measuring dream recall frequency, some of the previous studies adopted a Likert-like scale which is relatively imprecise (e.g., very frequently, frequently, occasionally, rarely, and never).

Therefore, the study of normal subjects with blind procedures was carried out to further clarify and confirm whether or not memory of dream experience is poor in nature. The study consisted of two parts. The first part was a general survey, and the second part was a between-subject experiment. One hundred and seventy Chinese subjects were interviewed for their general dream experience, and their frequencies of awareness of dream experience (i.e., dream experience with or without recalled dream contents) were classified. A considerable number of subjects were aware of their dream experience every night, and 80% of the subjects were aware of their dream experience at least once a week.

The second purpose of the study is to develop relatively systematic, nonintrusive procedures for investigating and facilitating dream recall. Based upon the three comparatively reliable factors and principles associated with dream recall frequency (focusing on emotions, visualization, and reinstating a "sleep" state) revealed by the

literature evidence, the dream recall instruction was developed, and its efficacy was examined. The study explored the issue by using the between-subject experimental method. This was the second part of the study. The 170 subjects were randomly allocated to one of two groups. The 100 subjects in the experimental group received instruction on dream recall techniques (Dream Recall Instruction), whereas the 70 subjects in the control group did not receive any guidelines for facilitating dream recall. The experimental group was significantly more likely to recall dream experience than the control group. The dream recall instruction and daily recording method were shown to be effective in triggering dream recall from neurologically and psychiatrically healthy individuals. The dream recall frequency was high. Eighty-nine percent of the experimental subjects could provide their dream experience within three nights, with the aid of the dream recall instruction.

Although the dream recall instruction potentially involves some "suggestive" elements, the entire design of the dream recall instruction resembles the cognitive interview technique which is based upon psychological principles of remembering and retrieving information from memory and has been proved to be effective. Likewise, in order to reduce demand characteristics and increase the accuracy of the collected data, the most recent dream report form was used and all the interviews were carried out by the investigators who were blind to the hypotheses of the current

study.

Both the survey and experimental methods revealed a high frequency of dream awareness. The findings did not suggest that dream recall and retrieval of dream content are difficult. Therefore, memory of dream experience is not necessarily poor.

A.II. Memory Loss is Not Equal to Loss of Dream Experience

In diagnosing cessation of dreaming, Solms (1997) asked directly patients whether they continued to dream or had ceased dreaming since the onset of their neurological illness. Associating cessation of dream experience with posterior brain lesions is particularly alarming because the important neural substrates of memory are situated in the posterior brain. The study of patients with posterior brain lesions was therefore conducted to examine whether or not memory dysfunction necessarily results in loss of dream recall and awareness (Chapter Three).

To clarify the memory and anatomical issues, the study included eight patients who had posterior brain lesions as a consequence of recent cerebrovascular insults. Patients who could not provide clear pre-stroke dream experience or whose neuropathologies were not suitable for neurobehavioural investigation were excluded. Their sleep and dream experiences before and after stroke were compared. Different from most of the previous neuroanatomical studies, the current study investigated

patients' sleep and dream experience and memory and other neuropsychological functions systematically on a daily basis from initial hospital admission to discharge. Each case was interviewed by at least two separate investigators. Moreover, the dream recall instruction which had been proved to be effective in retrieving dream experience was provided to the patients to increase, as far as possible, their ability to remember their dreams.

No patients reported premorbid absence of dream experience (including both dream recall and awareness). The premorbid frequency of dream awareness ranged from three times per week to nightly. Almost all patients in the study presented with some degree of memory difficulty, and included visual, verbal, and short- and long-term memory spectrums. Nevertheless, seven out of the eight cases presenting with posterior lesions experienced no evident alteration in their dream experience since their strokes and were able to report their dream experience in detail during hospitalization. There seems to be an essential dissociation between memory disorders and alterations in dream experience.

In any event, this phenomenon is in agreement with the clinical neuropsychological understanding of memory disorders. While memory disorders are widespread amongst neurological patients, severe amnesia and episodic memory deficits as a result of stroke are indeed rare. Mostly, only *bilateral* lesions

circumscribed to the medial temporal lobe (Steinvorth, Levine, & Corkin, 2005), and in particular to the hippocampal region (Bayley & Squire, 2003) can result in axial amnesia. Therefore, lesions to the posterior brain or even to the hippocampus do not necessarily result in episodic memory deficits.

Considering the clinical evidence that memory is affected by many neuropathologies, it is perhaps unsurprising to find that most patients who have ceased dreaming also experience memory deficits. Yet, patients who have memory deficits but a preserved ability to dream provide equally important evidence for the dissociation between the two syndromes. Cessation of dream recall or awareness does not appear to be a secondary symptom of memory dysfunction. Even patients who suffer from profound memory deficits due to strokes are able to report their dream experiences. Therefore, although stroke patients' memory is poor, impaired memory by no means provides a sufficient explanation for a total lack of awareness of dream experiences.

A.III. Further Investigation into the Memory Controversy

Chapter Three and Five demonstrated that the same procedures could regularly elicit dream experience from one group of patients with similar posterior brain lesions, but not from the other group of patients with comparable ventromesial frontal region

lesions. Chapter Six investigated the memory abilities of patients with deficient dream recall and awareness on the one hand and patients with preserved dream experience on the other, by using the two widely-adopted measures for visuospatial and audioverbal memory. In addition to the visuospatial and audioverbal memory functions, the patients were assessed for amnesic features. Differences in memory capacities between the two groups of patients were at the heart of the question.

Thirty-two neurological patients were included in the analyses. The patients with preserved dream experience scored higher than the patient with deficient dream experience in the visuospatial memory functions. Nevertheless, the discrepancies in the visuospatial memory functions between the two groups did not hold statistical significance. Moreover, there were no significant differences between the two groups in the audioverbal memory functions. The comparison analyses of the patients with ventromesial frontal region lesions and the patients with posterior brain lesions generated very similar results. All these findings support the early assertion (Doricchi & Violani, 1992; Solms, 1997) that deficient dream experience does not seem to be the result of memory failure, even though it may be related to visuospatial and constructive deficits.

Although the patients with deficient dream awareness (or ventromesial frontal region lesions) performed worse than the patients with preserved dream experience

(or posterior brain lesions) in the ROCF short- and long-term visual recall trials, they also obtained lower scores in the ROCF copy trial. Therefore, the poor performances of the patients in the ROCF recall trials were more related to the deficits in organization and strategic planning than to memory dysfunction per se. Moreover, although many neurological patients sustain profound memory disorders which are always specific to a certain modality, they are still able to retrieve personal or dream experience via other channels or cues.

In contrast to the material specific memory disorders, axial or true amnesia which is associated with bilateral medial temporal lobe lesions debilitates one's memorizing ability pervasively and non-specifically, leading to amnesia for ongoing events. None of the patients were diagnosed as axial amnesia. Only two cases suffered infarctions involving the posterior cerebral arteries, and dream experience was preserved in both cases. Considering also that elaborative confabulation does not provide a convincing explanation to the absence of dream recall and that there is no true amnesia in frontal patients, memory failure does not seem to constitute the raison d'être for the occurrence of defective dream recall and awareness.

As summarized above, neurologically healthy individuals are consistently aware of their dream experiences. In stark contrast, some neurological patients who share analogous specific brain lesions consistently exhibit a cessation of dream experiences.

Not only do they lack the ability to recall their dreams, they also sustain complete unawareness of dream experiences since their neurological insult. Accordingly, subjective dream reports appear to constitute a useful neuropsychological tool to differentiate between normal population and neurologically-impaired patients.

B. A Response to Controversy II (Precision of Anatomical Localization)

The power of the clinicoanatomical method is limited by the choice of pathological specimen and the lesion's size (Damasio & Damasio, 1989). With a few exceptions, tumour material is unsuitable. Infarctions provide good specimens for neuroanatomical and neuropsychological study investigating the correlations between behavioural dysfunctions and sites of brain destruction, because they entail actual destruction of brain parenchyma. Lacunar infarct is the best fit for human lesion studies of all types of neuropathology.

In practically most of the neuropathological insults, the precise anatomical definition of lesions is problematic. None of the cases in Solms's clinical series were good specimens for neurobehavioral establishment because most of them were either diffuse or tumour cases. Both conditions render neuroanatomical analysis difficult and imprecise.

Chapter Five reconsidered the association between alternations in dream

experience and lesions to the ventromesial frontal region by investigating patients diagnosed with infarctions. Moreover, the study tried to identify the precise neural structures that are implicated in the generation of dreaming within the "ventromesial frontal region".

A total of 21 neurological patients sustained medial frontal lobe lesions as a consequence of recent cerebrovascular insults were included in the study. The majority of the cases were diagnosed with lacunar infarct. Their lesions were charted and coded more strictly and precisely. No patients reported premorbid absence of dream experience (including both dream recall and awareness). The pre-stroke frequency of dream awareness of all patients was three times per week or more. Of the 21 cases with lesions to the medial frontal lobes, 17 experienced a deficiency of dream experience since CVA.

In most of these cases the lesions were circumscribed to the deep medial frontal regions, sparing the prefrontal convexity, the inferior parietal lobule, the diencephalic areas, and the medial temporal regions (i.e., the neural substrates of memory). These findings were established using the best specimens of the human lesion method, and were consistent with the results drawn from the previous studies using the non-infarct samples (Solms, 1997; Yu, 2001b, 2003).

In contrast with Solms's proposition that cessation of dream experience is

associated with bilateral ventromesial frontal region lesions, the current findings suggested that both unilateral and bilateral lesions can result in deficient dream experience. Moreover, the present study indicated that the head of the caudate nucleus in the ventromesial frontal region appeared to be a particularly crucial component of the neural network of dreaming. Lesions to the head of the caudate nucleus were common amongst the patients with dream deficiency. Considering that the head of the caudate nucleus is one of the most important constituents of the motivational and instinctual system of the brain, the significant role of this neural structure in dreaming encourages further systematic investigation of motivational determinants in dreaming processes.

C. A Response to Controversy III (REM-Pons Hypothesis)

The classical REM-pons hypothesis was questioned by Solms's research (1997, 2000b) which demonstrated that "large" pontine lesions do not lead to a cessation of dreaming. Solms has not, however, been able to show that precise lesions to the target pontine nuclei (in the pontomesencephalic tegmentum and pontine peduncule), whose activity have been proved associated with REM sleep are compatible with preserved dreaming. Likewise, Pace-Schott, Solms, Blagrove and Harnad (2003) argued that further human lesion studies are required in order to prove that, as Solms (1997,

2000b) argued, the pons is not a crucial neural substrate for dream generation.

Neuroanatomically, the brainstem tegmentum contains distinct nuclei. The reticular formation which includes the pontine reticular nuclei, raphe nuclei and locus coeruleus, the crucial neural substrate of consciousness, runs through the dorsal part of the brainstem in the paramedian tegmental zone, from the medulla to the midbrain.

Chapter Four presented three neurological case examples of various brainstem lesions to illustrate the paradox and difficulties in carrying out pontine lesion studies. The first case experienced alterations in dream experience after the ventral pontine lesions. The ventral aspect is, however, not a critical area according to the REM-pons hypothesis. Lesions to the critical region, the medial dorsal aspect of the pons, were instead noted in the second and third cases. The second patient was, nevertheless, clearly orientated with no apparent symptoms of changes in dream experience and consciousness, and therefore the targeted system can be considered as functionally intact. In the third case, "cessation" of dream experience may be due to a collapsed sleep-wake cycle (dyssomnias).

The brainstem tegmentum, in particular the ascending reticular activating system, plays a unique role in mediating the levels of consciousness and REM-NREM oscillation, and in Hobson's dreaming model. In addition, damage to the pontine tegmentum is known to cause comas, the most radical disturbance of general

consciousness (and even loss of life). Any kind of dream report or investigation from this kind of patient with full pontine tegmental lesion is ipso facto almost impossible even if they "survive".

The paradox is that a patient with a completely damaged tegmentum or with lesions to the critical nuclei should accordingly be unable to answer any question (i.e., comatose) or cannot be properly studied (e.g., dyssomnias), while a patient who does not suffer from the symptoms of coma (e.g., the second case) is considered atypical, or deemed to have a lesion that is so insignificant that the compromised region more or less continues to function. Therefore, investigating dreams of patients with ponto-tegmental lesions is clinically impractical in that such precise lesions which lead to REM cessation in particular, should, by definition, also result in severe disturbance of consciousness. Nevertheless, from the functional point of view, the pons is undoubtedly essential for dream formation as it provides the basic energy for all consciousness and cognitive activities.

D. A Response to Controversy IV (Posterior Cortex and Dream Formation)

Most PET studies revealed that the inferior parietal cortex, including the supramarginal gyrus, deactivates during REM sleep, whereas Solms (1997, 1999) claimed that the lesion circumscribed to this specific part of brain, to which he

attributed the important functions of dream formation, leads to the loss of dreaming. Chapter Three clarified if lesions to the posterior brain and in particular the inferior parietal lobule necessarily lead to alterations in dream experience.

The study indicated that unilateral lesions to the supramarginal gyrus and its adjacent areas, including the sensorimotor cortices, the angular gyrus, Wernicke's area, and the insula, do not necessarily alter dream experience. The reason for this may lie in the anatomical characteristic that there are multiple pathways for connecting the motivational systems and the imagery representation systems.

The current findings cast a doubt on notion that the inferior parietal cortex is an essential component in dream formation. A comparison study of bilateral and unilateral posterior lesions (in particular involving the inferior parietal lobules on both sides) may further identify the necessary components in the neural pathway of dream formation.

E. A Response to Controversy V (Dopamine Theory)

Solms (2000a, 2000b) argued that the crucial component of the ventromesial frontal region responsible for cessation of dream experience following anterior forebrain lesions lies in the mesocortical-mesolimbic dopamine system. Nevertheless, clinicoanatomical studies only provide an indirect test of the dopamine hypothesis of

dreaming. If dreaming is modulated by the mesolimbic dopaminergic activity, then individuals who sustain the neurochemical roller coaster of dopaminergic hyperactivity and antagonism may undergo abnormal dream patterns. Psychiatric patients with schizophrenia best fit this criterion. While considerable empirical works have focused on the dreams of patients with schizophrenia, few have considered the effects of specific neuropharmacological agents, and their results are not entirely consistent. Therefore, Chapter Seven attempted to examine the dopamine hypothesis by thoroughly investigating the dream experience and medication regime of patients with psychotic features.

Fifty-five psychiatric patients with psychotic features were investigated. All patients had been receiving a stable dose of dopamine antagonists as neuropharmacological treatment for six months and during the further three-month investigation period. All subjects received sleep and dream interviews, in which past and present sleep and dream experiences were recorded in detail. After the first interview, all patients were followed up for three months. The dream recall instruction was provided to the patients to increase their ability to remember their dream experience. Each patient was investigated by at least one trained interviewer who was blind to the hypotheses of the study.

On the whole, a considerable number of the psychotic subjects receiving

dopaminergic antagonists experienced significantly lower frequency of dream experience than the average documented by the previous normative studies and the dream recall study of neurologically and psychiatrically healthy subjects reported in Chapter Two. Over 30% of the psychiatric subjects experienced a marked low frequency of dream recall and awareness. Some patients even sustained cessation of dream recall and awareness for years. However, on the other hand, more than half of the psychiatric patients in the clinical series were regularly aware of their dream experience. Awareness of dreams for these patients ranged from at least once a week up to every night for the past six months. Their frequency of dream awareness was confirmed in the subsequent follow-up investigation, with the aid of the dream recall instruction.

The neuroleptic treatment, by directly modulating D2-type receptors in the mesolimbic areas, only suppressed dream recall and awareness in some cases. The differences in the dopamine antagonist consumption between the patients with different frequencies of dream experience were not clear-cut. Therefore, the present neurochemical findings were only partially consistent with the dopamine theory of dreaming. It can even be argued that the present neurochemical findings cast doubt on the dopamine hypothesis.

The present neuorpharmacological study provided a preliminary review of the

dream experience of patients receiving dopamine antagonist treatments. Furthermore, the study underscored the circumstance that conducting human neuropharmacological research in naturalistic or clinical settings is confounded by a number of factors. To partial out or control all the confounding factors statistically, a very large sample is required.

F. Conclusion

The previous clinicoanatomical studies were mostly based on bedside observation rather than systematic investigation. In the series of clinicoanatomical studies presented in this dissertation, the cognitive status of each subject was examined more systematically from the neuropsychological viewpoint. The alterations in dream experience associated with lesions in various brain sites (previously determined using bedside methods of evaluation) were documented and measured more systematically, using standardized methods. Neurologically-compromised subjects were interviewed rigorously to clarify the details of their dream changes and other neuropsychological parameters.

Little doubt is placed on the functional significance of the pons in any neural architecture of mentation, considering that the whole brain symbiotically depends for its existence upon an energy system in the brainstem that precedes and supports it. Being the basic neural scaffolding which provides nonspecific arousal, cortical activation and tone for building up more complex and specific cognitive processes, lesions to the pons can characteristically result in a change in the level of consciousness, ranging from sleepiness to coma and even fatality. Parvizi and Damasio's theory of consciousness (2003) goes further to suggest that core consciousness, the simplest form of consciousness modulated largely by the pons, is

regarded as another level of biological processing aimed at ensuring the homeostatic balance of a living organism.

The contemporary neuroscience is no longer inclined to the belief that any single part of the brain is responsible or sufficient for any mental process. Instead, only on the basis of the specific combination of neural substrates, can progress be made on the understanding of such sophisticated functional properties of the mental process. The forebrain lesion sites producing deficient dream recall and awareness are localized in the basal forebrain including, in particular, the head of the caudate nucleus and the ventromesial quadrant of the frontal white matter. The role of the inferior parietal lobule or the posterior regions is by contrast less robust or unique in the neural architecture of dreaming. This is at least partly due to the functional neuroanatomy that several pathways are available for bridging the anterior motivational-emotional system and the posterior representation apparatus in dream formation. These include, as shown by the aggregated evidence (Yu, 2001a), the temporo-occpital junction and the thamalus. Functional imaging research, using the PET technique (Braun, et al., 1997, 1998; Maquet, et al., 1990, 1996; Nofzinger, Mintun, Wiseman, Kupfer, & Moore, 1997, see also Yu, 2001a, 2001b, 2003, for review), has confirmed that these forebrain structures are selectively hyperactivated during dreaming. Other forebrain structures implicated in dreaming by the lesion method (structures which, when

damaged, produce distinctive qualitative changes in dream experience, see Solms 1997) are also selectively implicated in the PET imaging research.

Although it is difficult, if not impossible, to conduct a "clean" study of psychiatric patients, the present neuropharmacological analyses did not find a strong support to, and even cast a doubt on, the dopamine hypothesis of dreaming in that a substantial proportion of the psychiatric patients continue to have dream experience despite the dopamine antagonist treatments.

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Appendix A: Survey on Previous Dream Experience

1. Can you tell me what a dream is?
2. How often do you recall your dreams for the past six months (before your stroke)?
3. Some people know that they have dreamed at night even though they cannot remember the details of their dreams when they are awake. Do you ever think that you have dreamed even though you cannot remember any dreams in the morning?
4. People often forget the content of their dreams. However, on waking, they may know whether they have dreamed or not. How often did you dream in the past six months (before your stroke) (including both the dreams you remember clearly and the dreams whose contents you do not remember)? (Options were given if the participants could not tell spontaneously: "nightly", "1-6 times/week", "less than 1/week", "less than 1/month", and "uncertain").

Try to further explore and foster subjects' interest in their dream and sleep experience through the following prompting questions:

5. Do you ever have multiple dreams in a single night?
6. Do you ever know during a dream that you are dreaming?
7. Do you ever have dreams that are so nice you want to go back into them? Can you ever really go back into them?
8. Can you ever make your dreams do what you want them to do?
9. Do you have any memories of incidents or events that feel like they could have happened to you but you know must have been dreams? Give example.
10. Do you have any memories of incidents that you know actually happened to you but they have a kind of dream-like quality to them? Give example.
11. Do you have any memories that when you think back you simply do not know whether they are of events that really happened or they are dreams? Give example.
12. Do you have any memories that when you think back you simply do not know whether they are fantasies or dreams? Give example.
13. If you could chose, do you want to dream? Why?
14. If you could chose, what would you want to dream?
15. Do you have more good dreams, more bad dreams, or the same amount? Please give an example of a bad and a good dream you have had.
16. Do you have recurrent nightmares (nightmares for several consecutive nights)? If so, are they exactly the same or just similar? Please give an example.

Appendix B: Dream Diary (For Neurologically and Psychiatrically Healthy Subjects)

Did you dream last night?

If yes:
We would like you to write down the dream. But first please tell us the date this dream occurred: _____. Then tell us what time of day you think you recalled it: _____. Then tell us where you were when you recalled it: _____.

Please describe the dream exactly and as fully as you remember it. Your report should contain, whenever possible: a description of the setting of the dream, whether it was familiar to you or not; a description of the people, their age, sex, and relationship to you; and any animals that appeared in the dream. If possible, describe your feelings during the dream and whether it was pleasant or unpleasant. Be sure to tell exactly what happened during the dream to you and the other characters. Continue your report on the other side and on additional sheets if necessary.
(Domhoff, 1996)

1. Did you *really see* anything in your dream?
2. Did you *really hear* anything in your dream?
3. Did you *speak* in your dream?
4. Did someone *speak to* you in your dream?
5. Did you *experience* anything in or on your body in your dream?
6. Did your body *move* in your dream?
7. Did you *smell* anything in your dream?

If no:
Do you think that you did dream last night even though you no longer remember any dream details this morning?
(1) I did not have any dreams;
(2) I had dreamed but had forgotten the dream content;
(3) I did not remember whether I had dreamed or not.

Appendix C: Dream Recall Instruction

Here are some tips for remembering your dreams better:

When falling asleep:

1. Tell yourself: "I want to remember my dreams, and I will remember them".

When waking:

2. Try to keep your sleeping posture and lie still while you go over your dream.
3. Start by concentrating on the first feeling or emotion you have just as you wake up from a dreaming sleep (e.g., cheerful, sad, exciting, peaceful, etc.).
4. Dwell on the main themes of your dream (event, people, environment, time, etc.).*
5. Dwell on the specific vignettes and details of your dream (including what you see, hear, smell, speak, do, feel with your body, etc.).*
6. Think about what you are feeling in each specific vignette (e.g., cheerful, sad, exciting, peaceful, etc.).
7. Fill in the provided dream report form immediately after leaving your bed.

* If you cannot remember any main themes or story, it is fine. Just try to feel your feelings and emotions in your dream and, at the same time, remember any images or fragments that come to you. When you remember a single portion, concentrate on it for a while, fix the image in your mind, and then try to generate another image or fragment by concentrating on your feelings and emotions until no more images come up. Then repeat all the images and translate them into words.

Appendix D: Pathophysiological Classification of Stroke

A pathophysiological classification of stroke is shown as follows. This divides stroke into its two main subtypes of cerebral haemorrhage and cerebral ischaemia, and subdivides each of these. The division of ischaemic stroke is based on the trial of ORG 10172 in acute stroke treatment (TOAST) classification (Adams, et al., 1993).

Ischaemic stroke
- Large artery
- Cardioembolic
- Lacunar
- Other determined aetiology
- Undetermined aetiology
- Multiple possible aetiologies

Cerebral haemorrhage
- Primary subarachnoid haemorrhage
- Primary intracerebral haemorrhage

Definitions

Large artery stroke: Occlusion or stenosis (>50%) in large extracranial or intracranial cerebral artery, with ischaemia in that arterial territory.

Cardioembolic stroke: One or more of the following conditions: Mechanical prosthetic heart valve, atrial fibrillation, myocardial infarction within last 2 months, dilated cardiomyopathy/congestive heart failure at stroke onset, endocarditis, sick sinus syndrome, atrial myxoma, left ventricular thrombus.

Lacunar stroke: Lacunar syndrome (pure motor stroke, pure sensory stroke, ataxic hemiparesis, clumsy hand dysarthia) with either no lesion on brain imaging or a deep infarct (</= 1.5 cm diameter) in a location consistent with the clinical syndrome.

Appendix E: Damasio and Damasio's Lesion Method in Humans

The standard procedure for analysis of CT and MR images proffered by Damasio and Damasio (1989) is as follows:

1. In the case of CT, determine the angle of incidence in which tomographic cuts were obtained on the basis of a pilot scan and of the relative position of anatomical, cerebral and bone landmarks.
2. In the case of MR, make the same determination on the basis of a midsagittal pilot cut. MR images do not show bone landmarks but their resolution is such that actual anatomical structures, for example, sulci, gyri, and visually recognizable gray matter structures, can be clearly identified.
3. Choose the set of best-fitting templates on the basis of the above determination.
4. Chart the lesion on the templates, at every level at which it occurs, using an X/Y plotting approach.
5. Superimpose over the template an appropriate "in-register" transparency that contains anatomical cells representing neural "areas of interest" in both grey and white matter structures (Each of those cells is limited by a linear boundary and has a letter and number code on the basis of which it can be anatomically identified).
6. Assign the area of damage charted in the template to the cells that encompass the abnormal images.
7. Estimate the amount of involvement within target cells (Coded as 0 when less than 25% involvement of the total area is noted. 1 if the involvement is between 25% and 75% and 2 if more than 75% of the total area is damaged). This step can be achieved by using a transparent square grid, count the number of units involved by the lesion at each level, and calculate the percentage in relation to the total number of units encompassed by each area of interest (which is the sum of units occupied by the region at each template level).
8. Determine the vascular territory in which the lesion occurred, using the appropriate vascular transparency.
9. Fill in the results of the previous analysis as a hard-copy visual record and a computerized record, keyed to the codes mentioned.

Appendix F: Solms's Protocol for Dream Alterations

Patients were asked whether or not their dreams had changed *since the onset of their neurological illness*, and, if so, they were asked to describe in their own words the manner in which they had changed. Thereafter the patients were asked a series of questions about specific aspects of their dreams. The questions were asked according to the following basic plan, which was adapted in consideration of each patient's individual circumstances. The requirement of flexibility when assessing the subjective experience of a seriously ill neurological population is obvious, especially in view of the fact that it was desirable to study a wide cross-section of cases.

1. Patients were asked how they were sleeping at night, and whether or not their sleep had been affected by their illness. Responses were classified under four headings: (a) Sleep was considered to be better since the onset of illness, (b) sleep was considered to have been disrupted since the illness, (c) sleep was considered to be unaffected, or (d) patients were unsure as to whether or not there had been any change in the quality of sleep.
2. Patients were asked whether or not they still dreamed at night. If the response was negative, the patient was carefully questioned to determine whether or not this had also been the case prior to the onset of the illness. All patients who claimed that they never dreamed premorbidly, were closely questioned in this regard (e.g., they seldom dreamed or they never remembered their dreams). Subsequent changes from a patient's personal baseline were then determined. Patients were classified under three headings, namely, (a) those who continued to dream, (b) those in whom all dreaming had ceased, and (c) those who were unsure as to whether or not they were still dreaming.
3. Patients were asked about their ability to recall dreams. Many who had initially claimed that they had stopped dreaming corrected their observations at this point to state that although they were aware that they still experienced dreams, they could no longer remember them in the morning. In all cases of alleged cessation of dreaming this distinction was carefully explored. Here patients were classified in terms of (a) better, (b) worse, or (c) unchanged morning dream-recall, or they were classified as (d) unsure if there was no definite response.
4. The difficult matter of narrative complexity of dreaming was then addressed. Patients were asked whether or not their dreams seemed simpler, more straightforward, or more banal than usual, whether or not they were more bizarre, incredible, or convoluted, and whether or not they appeared to be derived more or less directly from real daytime experiences than they used to be. A great deal of

clarification and discussion of responses was necessary before patients could be classified with confidence. The four headings used for classification of dreams were, (a) more simple, straightforward, banal, and mundane than before; (b) less simple, straightforward, banal, and mundane than before (i.e., more bizarre, incredible, convoluted, and strange); (c) dreams that were unchanged in these respects; and (d) unsure responses.

5. The emotional intensity of dreams was difficult to assess. The literature is devoid of any report of a patient who actually reported decreased narrative (or symbolic) complexity and emotional intensity of their own dreams. In every instance it was the investigator who characterized the patient's dreams in such terms. Patients were asked whether or not they themselves felt that their dreams were (a) more pleasant or (b) more unpleasant than before, as opposed to being (c) unchanged from the affective point of view. Patients were unable to provide unequivocal answers to these questions were classified as (d) unsure about this point. A subset of patients specifically complained of recurring nightmares at this stage in the interview. This symptom was classified separately (see item 6).
6. Patients were asked about the (a) presence versus (b) absence of recurring nightmares. Care was taken to ascertain whether or not recurring nightmares were also present premorbidly.
7. Next, patients were asked whether or not the frequency of their dreaming had changed since the onset of their illness; that is, they were asked whether they dreamed more or less often than they used to. Responses were classified under four headings: (a) more frequent dreams, (b) less frequent dreams, (c) unchanged frequency of dreams, and (d) unsure.
8. Patients were then asked whether or not there had been any change in the visual imagery of their dreams. In this respect, patients were classified according to whether visual dream-imagery was (a) absent or (b) present. Any qualitative variations in imagery were recorded descriptively. Discussion of the quality of dream-imagery led naturally to the next category (item 9).
9. Patients were questioned about the vivacity of their dream-imagery. Patients were therefore classified in accordance with their responses as having (a) more or (b) less vivid (or real) dream-imagery, (c) as having dreams of unchanged vivacity (or reality), or (d) as being unsure about this aspect of their dreams.
10. Actual inability to distinguish between dreams and reality is not the same as increased vivacity or reality of dream-imagery. Cases reporting this distinctive symptom were classified separately, in terms of (a) presence versus (b) absence of dream-reality confusion.
11. Continuity or duration of dreams (which was also related in the literature to

increased vivacity of dreaming) was then explored. Patients were asked whether or not their dreams tended to be unusually long or to display unusual continuity over a single night, or, alternatively, whether or not they seemed uncharacteristically short and clipped. Responses were classified under four headings: (a) longer, (b) shorter, (c) unchanged or (d) unsure.

12. An assessment of recency versus remoteness of mnemic material in dreams was extremely difficult to obtain. Cases of individuals who clearly recognized (a) more recent mnemic material in their dreams than before, or who recognized (b) more remote material than before, or (c) who felt sure that their dreams were unchanged in this respect, or (d) who felt unsure, were classified as such.
13. Finally, patients were asked whether they had noticed any other changes in their dreams that had not yet been discussed. At this point patients also clarified previous responses.

Summary of Dream Classification

Category	Excesses	Deficits	Normality	
Sleep	Better	Worse	Unchanged	Unsure
Dreams	-	Absent	Present	Unsure
Dream-Recall	Better	Worse	Unchanged	Unsure
Narrative Complexity	Increased	Decreased	Unchanged	Unsure
Emotional Intensity	More Pleasant	More Unpleasant	Unchanged	Unsure
Recurring Nightmares	Present	-	Absent	Unsure
Dream Frequency	Increased	Decreased	Unchanged	Unsure
Visual Imagery	-	Absent	Present	Unsure
Dream Vivacity	Increased	Decreased	Unchanged	Unsure
Reality Confusion	Present	-	Absent	Unsure
Dream Duration	Increased	Decreased	Unchanged	Unsure
Mnemic Material	Recent	Remote	Unchanged	Unsure
Miscellaneous	-	-	-	-

(Solms, 1997)

Appendix G: Most Recent Dream Report Form (For Neurological and Psychiatric Patients)

We would like you to tell us the last dream you remember having, whether it was last night, last month, or last year. But first please tell us the date this dream occurred: _____. Then tell us what time of day you think you recalled it: _____. Then tell us where you were when you recalled it: _____.

Please describe the dream exactly and as fully as you remember it. Your report should contain, whenever possible: a description of the setting of the dream, whether it was familiar to you or not; a description of the people, their age, sex, and relationship to you; and any animals that appeared in the dream. If possible, describe your feelings during the dream and whether it was pleasant or unpleasant. Be sure to tell exactly what happened during the dream to you and the other characters.
(Domhoff, 1996)

1. Did you *really see* anything in your dream?
2. Did you *really hear* anything in your dream?
3. Did you *speak* in your dream?
4. Did someone *speak to* you in your dream?
5. Did you *experience* anything in or on your body in your dream?
6. Did your body *move* normally in your dream? (specifically referring to the patient's motor problem)
7. Did you *smell* anything in your dream?
8. I know that you are currently suffering from.... Is that problem the same in your dreams, or is it worse or better? Please describe.... (for neurological patients only)

Appendix H: Dream Diary (For Neurological and Psychiatric Patients)

Did you dream last night?

If yes:
Please describe the dream exactly and as fully as you remember it. Your report should contain, whenever possible: a description of the setting of the dream, whether it was familiar to you or not; a description of the people, their age, sex, and relationship to you; and any animals that appeared in the dream. If possible, describe your feelings during the dream and whether it was pleasant or unpleasant. Be sure to tell exactly what happened during the dream to you and the other characters.
(Domhoff, 1996)

1. Did you *really see* anything in your dream?
2. Did you *really hear* anything in your dream?
3. Did you *speak* in your dream?
4. Did someone *speak to* you in your dream?
5. Did you *experience* anything in or on your body in your dream?
6. Did your body *move* normally in your dream? (specifically referring to the patient's motor problem)
7. Did you *smell* anything in your dream?
8. I know that you are currently suffering from.... Is that problem the same in your dreams, or is it worse or better? Please describe.... (for neurological patients only)

If no:
Do you think that you did dream last night even though you no longer remember any dream details this morning?
(1) I did not have any dreams;
(2) I had dreamed but had forgotten the dream content;
(3) I did not remember whether I had dreamed or not.

Appendix I: Sleep Quality Assessment

1. Date:
2. Roughly what time did you start to sleep last night?
3. About how long did it take you to fall asleep?
4. About how many times did you awaken during the night?
5. For each awakening, about how long were you awake?

a. 1st
b. 2nd
c. 3rd
d. 4th
e. 5th
f. 6th
g. 7th

6. What time did you finally wake up this morning?
7. Approximately how many hours did you sleep last night?
8. Rate the quality of last night's sleep:

0: Poor
10: Excellent

0	1	2	3	4	5	6	7	8	9	10

9. Did you feel sleepy or have sleep attack during the day yesterday?
10. Did you nap during the day yesterday?
11. Did you have trouble concentrating during the day yesterday?

(Jacobs, 1998)

Appendix J: Neuropsychological Battery

The neuropsychological battery used in this research was composed of three primary parts, measuring the executive functions, visual memory and verbal memory, respectively. These assessments were above and beyond the screening of general cognitive performance. The three spectrums of neuropsychological functions which were associated with the anatomical areas of interest were selected on the grounds that assessing these functions could help: 1) establishing a diagnostic consistency between anatomical pathology and clinical observation 2); resolving the methodological controversy of cessation of dream experience as a secondary result of a memory deficit; and 3) understanding the functional network and mechanisms of dreaming (e.g., Are executive functions necessary for dream formation?).

Global Cognitive Functioning

The Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975) was used as a screening test that provided an objective global index of cognitive functioning. The index ranges from an extremely impaired score of 0 to a perfect score of 30. Five areas of cognitive functions are assessed: (1) orientation, (2) registration (short-term memory), (3) attention and calculation, (4) language, and (5) construction. Each discrete subtask completed correctly earns 1 point toward a maximum possible score of 30. The cutting score is 23/24; that is, scores of 23 and below indicate organicity, whereas scores of 24 and above suggest normal cognitive functions. Anthony, LeRexche, Niaz, Van Korff and Folstein (1982) evaluated the validity of the 23/24 MMSE cut score in detecting dementia and delirium in ninety-seven patients from a general medical ward. From a practical perspective, it is impressive that the MMSE cut score of 23/24 correctly identified 87% of the patients diagnosed as impaired (dementia or delirium) and 82% of the patients diagnosed as not impaired.

Executive Functions

Various definitions of executive function have been proposed, although these often overlap considerably (see Eslinger, 1996, for review). Executive functions are higher functions that integrate other more basic components - such as perception, attention and memory - and have been conceptualized as a collection of processes that guide, direct, and manage cognitive, emotional, and behavioural functions, especially during active, novel, and problem solving periods (Gioia, Isquith, Guy, & Kenworrythy, 2000). Executive functions are those mechanisms by which performance is optimized in situations requiring the simultaneous operation of a number of different cognitive processes (Baddeley, 1986). Therefore, intact executive functioning involves

flexibility of thought and action (Welsch, Pennington, & Groisser, 1991), and involves maintaining an appropriate set in order to achieve a future goal (Luria, 1973).

According to the conceptions above, executive functions necessitate a wide range of sub-functions: set shifting, hypothesis generation, problem solving, concept formation, abstract reasoning, strategic planning, organization, goal setting, fluency, working memory, inhibition, self-monitoring, initiative, self-control, impulse control, mental flexibility, attentional control, anticipation, estimation, organized search, behavioural regulation, common sense and creativity. Tests in the present research study were chosen based upon their capacity to measure distinct subcategories of executive functions. These included semantic fluency/category naming (animals and fruits) (Morris, et al., 1989; Spreen & Strauss, 1991), stroop color-word test (Lee & Chan, 2000), digit span (WAIS-III; Wechsler, 1997a), matrix reasoning (WAIS-III; Wechsler, 1997a), Go/No-Go test (Christensen, 1979), motor sequence test (Christensen, 1979; Luria, 1966), tapping rhythm test (MacQuarrie, 1953), and repeated pattern drawing test (Christensen, 1979; Luria, 1966).

The stroop color-word test, for instance, is a measure of selective attention (Lowe & Mitterer, 1982), the ability to shift from one perceptual set to another as test requirements change, and finally the ability to inhibit responses. It provides insight into the ability to concentrate and resist distraction (Lezak, 1995). The stroop procedure requires the individual to inhibit a prepotent well-learnt verbal response when faced with novel requirements. Other executive functions like cognitive flexibility and mental set shifting in response to environmental stimuli also affect stroop performance.

As a second example, the semantic fluency test examines ability to produce words in response to a category cue. This verbal fluency test involves speeded lexical production, promotes automatic lexical access, and reflects efficient lexical organization (Dunn, Gomes, & Sebastian, 1996). Two components of verbal fluency tests are: 1) the linguistic component associated with left cerebral hemisphere function (Milner, 1975; Tow, 1955), and 2) the ideational component associated with frontal lobe function (Janowksy, Shimamura, Kritchevsky, & Squire, 1989). There is also a working memory component since the subject must retrieve new words while remembering previously retrieved words to avoid perseverative errors (Watson, Balota, & Sergent-Marshall, 2001). The ability to self-monitor, initiate, and shift also impacts on performance on such tasks (Mahone, Cirino, & Cutting, 2002).

Visual Memory

Details are provided in Chapter Six.

Verbal Memory

Details are provided in Chapter Six.

Supplementary Tests

The above were the core tests used in the protocol. Depending on each individual case, other neuropsychological tests, such as Babcock Story Telling Test (Babcock, 1930; Babcock & Levy, 1940), Benton Visual Retention Test (BVRT; Benton, 1974), Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983), Object Hidden Test (Strub & Black, 1988; Terman & Merrill, 1973), Wechsler Adult Intelligence Scale Third Edition (WAIS-III; Wechsler, 1997a), and Wisconsin Card Sorting Test (WCST; Berg, 1948; Grant & Berg, 1948), were carried out in their entirety or in part in order to capture unique nature of different neuropathologies.

Appendix K: Ethical Considerations

Data was collected primarily from the neurological department of the Groote Schuur Hospital in South Africa and the mental health centres and residential services for mentally ill in Hong Kong. Ethical approval from the Groote Schuur (Health Sciences) Ethical committee was obtained. Ethical issues were discussed with the mental health centres and residential services, and the research was approved. The research procedures were also adapted to the Code of Professional Conduct of The Hong Kong Psychological Society. Relevant professionals were consulted for the suitability of each neurological/psychiatric patient to participate in the research.

An introduction was given before the initial interview and assessment including a description of the intended questions and testing, the purposes and process of the research, and a statement as to when, where and how the results might be released. The participants were ensured that any sensitive information (including their names) they provide would be treated as confidential. For certain data which might lead to identification of the participants, participants' permissions were obtained. It was emphasized that they had the right to choose whether or not answer any questions (especially for those potentially sensitive questions like sexual life or illness). They also had the right to cease or withdraw from the research at any stage. The intention was to give the participants sufficient information to make a reasonable decision. The participants were invited for raising questions and discussing after briefing. Informed consent was obtained from the participants (and/or next of kin for the schizophrenic and neurological patients) before the initial interview began.

The researchers paid a close attention to the participants' spontaneity, alertness and motivation during the interviews and neuropsychological testing. The researchers stopped proceeding whenever the participants became fatigue or unmotivated. As far as possible, the researchers tried to avoid causing any discomfort and distress to the participants. At the end of each interview, feedback about the outcomes of the neuropsychological assessment and sleep and dream interviews was provided to the participants. The participants' contribution to the understanding of the neural mechanisms of dreaming and sleep was stressed. In order to maximize their benefits from the interviews, caring and positive regards were shown, and relevant information with regard to the problems they facing such as sleep disturbance, nightmares and neurological diseases in addition to the detailed analysis based on the assessment was given.

Appendix L: Effects of Antipsychotics on Neurotransmitters and Receptors

Antipsychotics	blockade D_1	blockade D_2	blockade D_3	blockade D_4	blockade M_1	blockade α_1	blockade α_2	blockade 5-HT_1	blockade 5-HT_2	DA reuptake
Chlorpromazine	3+	3+	4+	4+	3+	4+	2+	+	4+	+
Clozapine	3+	2+	2+	4+	3+	3+	3+	2+	4+	+-
Depot Clopixol	5+	5+	?	4+	2+	4+	2+	+	4+	2+
Depot Fluanxol	4+	4+	4+	?	+	3+	2+	+-	3+	2+
Depot Haldol	3+	5+	4+	5+	+	3+	+	+	3+	+
Depot Modecate	3+	5+	5+	4+	+	3+	+	+	4+	+
Flupenthixol	4+	4+	4+	?	+	3+	2+	+-	3+	2+
Haloperidol	3+	5+	4+	5+	+	3+	+	+	3+	+
Olanzapine	3+	3+	4+	4+	4+	3+	2+	+	4+	?
Pimozide	2+	4+	4+	3+	+	3+	2+	+-	3+	2+
Quetiapine	+	2+	2+	-	+	4+	3+	2+	3+	?
Risperidone	3+	5+	2+	5+	+-	4+	4+	2+	5+	+
Stelazine	3+	5+	?	3+	+	3+	+	+	4+	?
Thioridazine	?	5+	4+	3+	?	?	+	?	2+	?

Note. The ratio of K_i values between various neurotransmitters/ receptors determines the pharmacological profile for any one drug.

Key: K_i (nM) > 100,000 = -; 10,000-100,000 = +-; 1,000-10,000 = +; 100-1,000 = 2+; 10-100 = 3+; 1-10 = 4+; 0.1-1 = 5+

$1/K_i$ < 0.001 = -; 0.001-0.01 = +-; 0.1-1 = 2+; 1-10 = 3+; 10-100 = 4+; 100-1,000 = 5+

Adapted from Seeman P. (1993). Receptor Tables, Vol.2: Drug dissociation constants for neuroreceptors and transporters. Toronto: SZ Research.

Appendix M: Relative Blockade Effects of Antipsychotics on D_2 and D_4 Receptors

Receptors	Relative Blockade Effects of Antipsychotics
D_2	fluphenazine (Ki = 0.6nM) > haloperidol (0.7nM) > *sulpiride (1.8nM)* > chlorpromazine (28nM) > clozapine (78nM) (George, Watanabe, Di Paolo, Falardeau, Labrie, & Seeman, 1985)
D_4	haloperidol (2nM) > risperidone (3nM) > olanzapine (27nM) > chlorpromazine (10nM) > clozapine (22-83nM) > *sulpiride (830 nM)*

Source: Asghari, et al. 1994; Chio, Drong, Riley, Gill, Slighton, & Huff, 1994; Hidaka, Tada, Matsumoto, Ohmori, Maeno, & Yamaguchi, 1996; Merchant, et al., 1996; Newman-Tancredi, Audinot, Chaput, & Millan, 1997