Parietal thalamocortical circuitry in global dream cessation

Mini-dissertation presented in partial fulfillment for the Degree

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by

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This thesis is dedicated to my father, Coenraad J Hattingh. Sorry you couldn't see this last one, Dad.

Abstract

Until relatively recently, the overarching agreement in the clinical literature was that total cessation of dreaming is related to posterior parietal lesions. Two recent case reports (Bischof and Bassetti, 2004; Poza and Martí-Massó, 2006), in which patients with medial occipital lesions demonstrated total cessation of dreaming, cast doubt on this clinic-anatomical correlation, and the neuropsychological theory of dreaming associated with it (Solms, 1997). In the current study, seven patients with medial occipital lesions (with posterior cerebral artery ischemic lesions) were recruited. Three patients had total dream cessation and four had intact dreaming (confirmed on REM awakening). Acute phase clinical neuroimaging was reviewed and the extent of the lesions in both groups was meticulously analysed by a neuroanatomist, who was blind to the dreaming status of each patient. The three patients with total cessation of dreaming all demonstrated posterior thalamic infarctions involving the pulvinar nucleus. All four of the patients with intact dreaming demonstrated medial temporo-occipital lesions, and none had thalamic lesions. Upon review of the source images of one of the two case studies with medial occipital damage and total dream cessation (Bischof and Bassetti, 2004), it was noted that the patient also demonstrated infarction of the pulvinar of the thalamus. The pulvinar of the thalamus has discrete thalamo-cortical connections to the parietal lobe, which it innervates. Disruption in the pulvinar of the thalamus can, therefore, reasonably be expected to result in parietal dysfunction. This study represents the largest case-report comparison in patients with REM-confirmed dream cessation with suitably circumscribed pathology. These findings cast doubt on claims of medial occipital mechanisms of dream cessation and suggest that posterior parietal circuitry remains involved.

Keywords: non-dreamers; cessation of dreaming; dream loss; neural correlates of dreaming; medial temporo-occipital lesions; posterior cerebral artery infarction

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1) Introduction

The classical method used by neuropsychological researchers has been to analyse how mental activity is affected by various focal brain lesions (Damasio, 1989). Dreaming is one aspect of mental activity that has captivated researchers since antiquity.

The neurobiological basis of dreaming, and of dream cessation following focal brain lesions in particular, has received significant attention in the neuropsychological literature (Charcot, 1883; Wilbrand, 1887; Pötzl, 1928; Nielsen, 1946; Critchley, 1953; Murri et al., 1984; Doricchi & Violani, 1992; Solms, 1997, 2000, 2011; Domhoff, 2001; Bischof & Bassetti, 2004; Domhoff & Christoff, 2013). Despite decades of research, there is still some uncertainty regarding the exact role played by the lateral and medial *posterior* regions of the brain in the dream process. The role of anterior structures seems less uncertain (Solms, 1997). Part of the difficulty in addressing these remaining uncertainties is the dearth of patients who have discrete lesions in the lateral and medial posterior regions of the brain, and who actually *report* cessation of dreaming as a symptom - a situation that is exacerbated by the fact that the loss of dreaming seems to recover rapidly with posterior lesions.

The aim of this mini-dissertation is to investigate individuals who have acute cerebrovascular occlusive disease (CVOD) in the vasculature that supplies the posterior areas of the brain and who present with global cessation of dreaming. Although they may be an extremely rare group of patients, the observations should shed important light on the uncertainties that still exist in trying to understand the role of the lateral and medial posterior regions of the brain in dream cessation.

1.1) Review of the literature

Charcot (1883) was the first to describe a patient who had impaired dreaming following an occipital lesion. The patient's dreams were described as lacking all visual imagery; however, other modal details of the dream were intact, such as dreaming in words. A *unimodal* cortical occipital lesion was inferred on the basis of this clinical picture, as there are few other areas in the cortex where such a visual-specific lesion could be located (Solms, 1997). Unfortunately, autopsy data for Charcot's case was lacking, which meant that the exact anatomical identification of the lesion was impossible.

Building upon Charcot's work, Wilbrand (1887) was the first author to describe a patient who suffered *global* cessation of dreaming following a lesion to the inferior parietal region. In contrast to Charcot's findings (and 11 other cases like his that had verified unimodal occipital lesions), clinicoanatomical research suggests that *global* cessation of dreaming occurs when there is *heteromodal* parietal cortex lesioning, specifically when it involves the inferior parietal lobule (Solms, 1997).

The concept of the Charcot-Wilbrand syndrome was established following the early case study reports of Charcot and Wilbrand (Charcot, 1883; Charcot, 1889; Wilbrand, 1887; Wilbrand, 1892). Pötzl (1928: 306) defined the syndrome as, "mind blindness with disturbance of optic imagination". The concept of the Charcot-Wilbrand syndrome is described by more recent authors as, "… the association of loss of the ability to conjure up visual images or memories and the loss of dreaming … indicating a lesion in an acute phase affecting the posterior regions" (Murri et al., 1984: 185). Loss of visual content (referred to as "irreminiscence" by Nielsen (1946)) was regarded as the core clinical deficit in most standard definitions of the syndrome. The complete cessation of dreaming was considered a secondary sequalae of the primary visual dream imagery deficit (Critchley, 1953).

In an exhaustive review of the literature available at the time, Solms (1997) reformulated the Charcot-Wilbrand syndrome into two variants, based on the body of evidence he reviewed and the large clinical series that he reported: isolated loss of visual dream imagery resulted from occipital (frequently bilateral) lesions (referred to as Charcot's variant); and global cessation of dreaming resulted from lesions in the inferior parietal lobule (Wilbrand's variant).

The distinction between these unimodal (occipital) and heteromodal (parietal) variants made by Solms (1997) was challenged when several functional neuro-imaging studies of dreaming sleep were published. These studies demonstrated glucose hypometabilisation and therefore deactivation of the heteromodal association cortex localized to the inferior parietal lobule during the Rapid Eye Movement (REM) stage of sleep (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1997). Thus, deactivation and not activation (as would be expected if Solms was correct (1997)) was observed in precisely the area that Solms had localised as being critical for the production of heteromodal dream imagery.[1]

To resolve this contradiction between Solms' (1997) clinical anatomical investigation and the functional neuro-imaging data available at the time, Yu and colleagues (2001) re-analysed the exhaustive body of literature that was reviewed by Solms (1997) and the 361 cases reported by Solms that contained precise anatomical data. This re-analysis included: all the case studies that were published before Solms published his 1997 study; all the available Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the case reports investigated by Solms, and the available functional neuro-imaging data published. Yu (2001) was able to identify the specific Brodmann's areas (BA) in most of these studies, comparing Brodmann's areas in relation to similar templates that Damasio and Damasio (1989) used. Yu (2001) was thus able to establish the degree of the involvement of the inferior parietal lobule, including the angular and supramarginal gyri (BA 39 and BA 40, respectively), in cases that included a complete loss of dreaming being reported.

[1] These early functional neuroimaging studies have since come into question.

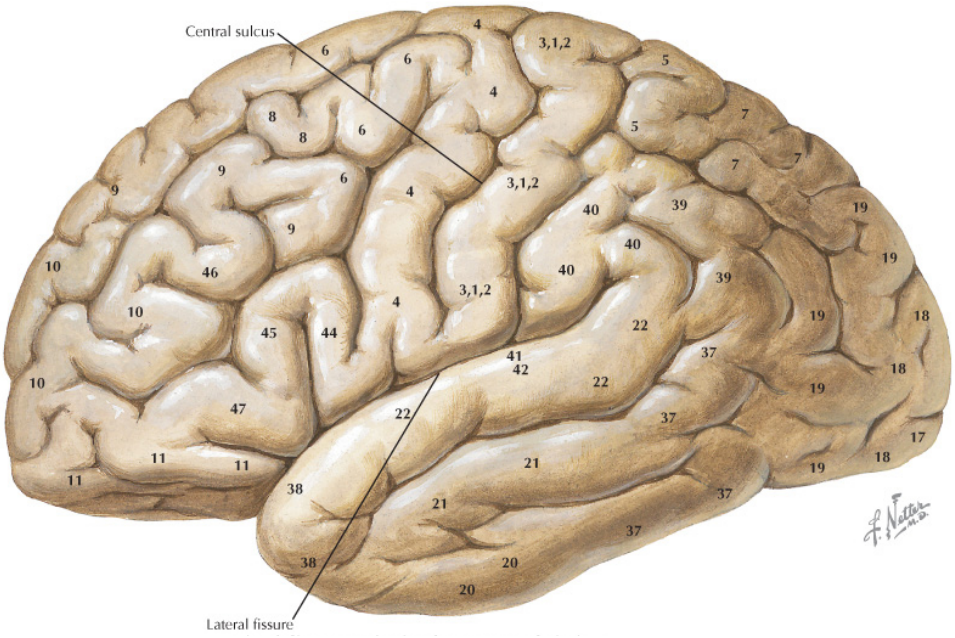

Figure 1: Left lateral convexity of the brain, demonstrating Brodmann's areas
Source: Netter (2009)

Yu (2001) found: that only one case had a lesion *circumscribed* to BA 40, out of the 61 cases in the literature before Solms' 1997 study; the most prevailing region involved in the various studies (16.4%) was the temporo-occipital region (BA 18, BA 19 and BA 37).[2] See Figure 1.2.

An investigation of Solms' (1997) original data found that 60% of cases had involvement of BA 40; however, the same frequency of lesion distribution was demonstrated in the superior temporal gyrus (BA 22). Specifically, within the group of 21 patients with discrete BA 40 lesions: 76% *demonstrated concurrent* lesions in BA 22; 48% demonstrated temporo-occipital lesions (BA 37); 38% demonstrated thalamic involvement; and 24% demonstrated occipital lesions (BA19). Yu (2001) concluded that 90.5% of Solms' (1997) cases with lesions involving BA 40 demonstrated *concurrent temporo-occipital and thalamic involvement.* This is perhaps not surprising, when considering that the middle cerebral artery feeds this entire territory.

[2] The previously reported cases were selected mainly for the investigation of visual agnosic phenomena and were therefore a distorted sample.

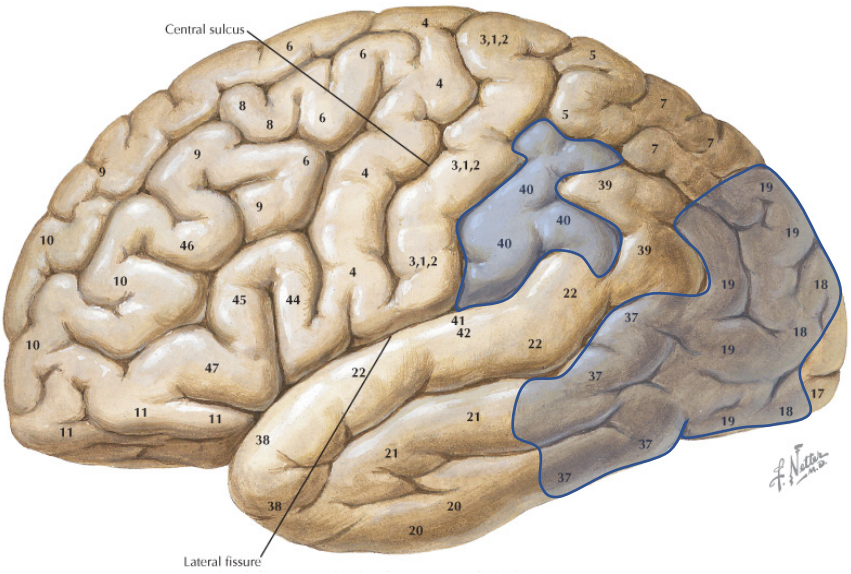

Figure 1.2: Illustration demonstrating the regions involved in the 61 cases published before Solms' 1997 study. BA 40 was involved in 1/61 cases, while BA 18, BA 19 and BA 37 were involved in 16.4% of cases.

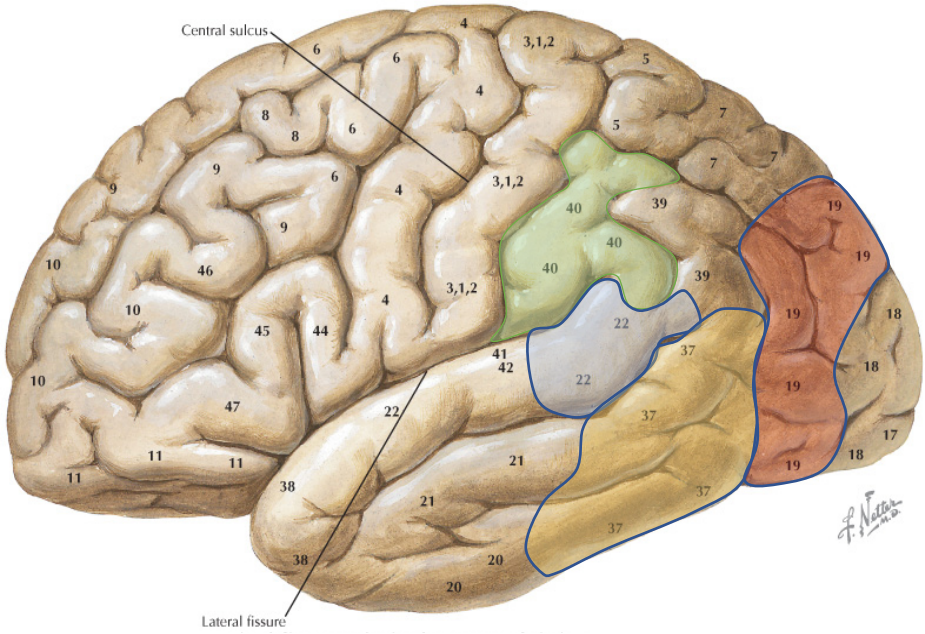

Figure 1.3: Illustration demonstrating the regions involved in Solms' 1997 study. In patients with lesions in BA 40: 76% *had concurrent* lesions in BA 22; 48% demonstrated lesions involving the occipto-temporal junction (BA 37); 38% presented with lesions involving the thalamus (not shown here); and a further 24% demonstrated lesions involving the occipital lobe (BA 19).

Since the functional neuro-imaging studies demonstrated consistent deactivation of BA 39 and BA 40, but no changes in BA19, 22, and 37, Yu (2001) suggested that the dream cessation in Solms' investigation is attributable to lesions in the temporo-occipital region, rather than to parietal lesions. In short, Yu (2001) suggested that the temporo-occipital region is involved in the dreaming process. The disparity between Solms' findings and the findings within the functional neuro-imaging literature had thus been reconciled. The critical lesion for global cessation of dreaming did not appear to be in the

inferior parietal lobule, but rather a few centimeters further backwards, in the *lateral* temporo-occipital cortex.

The new consensus in the literature regarding cerebral localization of global dream cessation was short lived. In 2004, Bischof and Bassetti (2004) published a case report of a 73-year-old female patient who was right-handed and presented with total cessation of dreaming after an ischaemic infarction involving the posterior cerebral artery vascular territory. MRI localised the lesion to bilateral *medial* occipital lobes, with involvement of the right lingual gyrus. However, the authors mentioned this only in passing: the patient also demonstrated a focal infarct in the posterolateral aspect of the pulvinar nucleus of the thalamus, and extending laterally to involve the thalamocortical projections from the pulvinar.

Bischof and Bassetti's (2004) patient therefore presented with global cessation of dreaming, as Wilbrand (1887) had first described it, following involvement of the *medial* occipital lobe, and extending into the temporo-occipital region (*unimodal* visual association area). This region was specifically implicated by Solms (1997), which was associated with the unimodal Charcot variant (as opposed to the global Wilbrand variant) of the Charcot-Wilbrand syndrome; however, Bischof and Bassetti (2004) reported global cessation of dreaming. They concluded that bilateral medial occipital involvement might represent the minimum lesion burden required to produce the Charcot-Wilbrand syndrome *as a whole*.

The MRI of Bischof and Basetti's patient demonstrated involvement of BA 37 (medially), BA 17, BA 18 and BA 19. This specific lesion distribution was consistent with the bilateral *medial* temporo-occipital lesions that Solms (1997) associated with unimodal loss of visual dream-imagery. Bischof and Basetti's findings are, however, discordant with Solms (1997) and Yu's (2001) findings, which demonstrated that the *posterolateral* cortical regions is the area that was consistently associated with complete cessation of dreaming. However, Bischof and Bassetti's (2004) case report stood as one of global cessation of dreaming following medial temporo-occipital infarction. Once again, Solms' (1997) redefinition of the Charcot-Wilbrand syndrome into occipital and parietal variants was called into question.

Bischof and Bassetti's (2004) case undermines Solms' view that complete dream cessation and non-visual dreaming are "independent entities from both the clinical and anatomical points of view" (1997, p.91). Bischof and Bassetti's findings challenge Solms' imputation of: unimodal dream deficits to lesions involving unimodal association cortex; and heteromodal cessation of dreaming following lesions involving heteromodal association cortex.

In 2006, Poza and Martí-Massó published a case report of a 24-year-old man who presented with global dream cessation due to a left-sided temporo-occipital haemorrhage, which originated from an

underlying arteriovenous malformation (AVM). The authors posited that a unilateral left temporo-occipital lesion was sufficient to cause complete dream cessation. Vascular malformations on their own, and certainly in the case of haemorrhages, cause large haemodynamic fluctuations within the brain parenchyma (Love et al., 2008). Exact localisation therefore becomes difficult and uncertain. The case by Poza and Martí-Massó (2006) is therefore of less relevance to the current study; however, it did add to the controversy and uncertainty of the status of the lateral and medial posterior cortical regions at the time.

1.2) Aims of the current study

The lack of consensus in the literature is due to a paucity of observed cases, as only two sleep-laboratory confirmed non-dreaming cases with (supposedly) focal medial occipital lesions currently exist in the modern neuropsychological literature (Bischof and Bassetti, 2004; Poza and Martí-Massó, 2006). The aims of the current study are, therefore, to:

- investigate individuals who have discrete acute-phase damage to the *medial* posterior regions of the brain;
- and to then determine: 1) the status of their dreaming, i.e. intact vs loss of visual dream imagery vs global cessation of dreaming; 2) how this relates to the anatomical distribution of the lesion.

2) Methods

2.1) Posterior cerebral artery territory infarction

The posterior cerebral artery (PCA) supplies the posterior medial parietal region, the inferior temporal region and the occipital region of the brain, as well as sub-cortical structures such as the hippocampus and thalamus (Standring, 2016). Cerebrovascular occlusive disease (CVOD) is one of the most common causes of mortality and morbidity in the world (World Health Organisation, 2016) and results in significant clinical impairment. Although finding patients who have PCA infarcts, is not, in itself, challenging, due to the incidence of CVOD, finding patients who have suffered infarcts within the medial occipital lobes, and who actually *report* dream cessation as a symptom, is extremely challenging. This is because most CVOD include large arterial territorial regions that involve both the occipital and inferior temporal regions. Additionally, noting dream cessation as a symptom within a larger over-arching neurological deficit is equally rare, due to the subtlety of dream cessation as an entirely subjective symptom. Additionally, these patients typically experience rapid recovery, which makes finding them in time to study their deficits equally challenging. The clinical cohort consists of patients who have sustained acute PCA infarcts, which significantly increases the likelihood of medial occipital involvement.

2.2) Participants

Participants were recruited from referrals by neurological specialists within the Cape Town area of the Western Cape. The standard neurological examination of patients with acute PCA infarction included specific questions regarding dreaming. Patients were only recruited if it was suspected that they had experienced dream cessation following a PCA infarction. A total of ten patients were referred. Exclusion criteria included: the involvement of other vascular territories outside the posterior cerebral artery territory; the absence of acute PCA infarction, even if chronic PCA infarction was present; or co-occurring neuropathology, such as space occupying lesions and any acute or chronic medications that could result in a functional impact on sleep.

Three potential participants were excluded, due to concurrent involvement of regions of the brain outside the posterior cerebral artery territory. The other seven patients had sustained thrombotic arterial occlusion involving *only* the posterior cerebral artery vascular territory. In order to confirm dream cessation, these seven participants underwent Rapid Eye Movement (REM) awakenings and two morning interviews. The presence or absence of dreams (as reported during two consecutive REM sleep

awakenings and two morning interviews following nights spent in a sleep laboratory) were used to divide the participants into two groups: dreamers and non-dreamers.

2.3) Sample size

The sample size of this study was: n = 3 non-dreamers; and n = 4 dreamers. Factors limiting the inclusion of more participants included: (1) the extremely low incidence of individuals who have circumscribed posterior cerebral artery territory occlusion without previous cerebrovascular incidents and total dream cessation that was REM confirmed; (2) that patients with this clinical presentation experience rapid recovery, which makes them difficult to study; and (3) the stringent inclusion criteria that were used to keep confounding factors to a minimum. Despite the limited size of this sample, it is the largest sample of its kind in the literature on this topic to date.

2.4) Measures

2.4.1) Dream cessation

The presence or absence of dreaming following infarction was initially assessed by the neurological specialist overseeing the clinical management of the patient. The patients' subjective reports of dream cessation or unaffected dreaming were confirmed by semi-spontaneous nocturnal REM sleep awakenings. These occurred during the first of two nights in the sleep laboratory. They were conducted by a sleep laboratory technician at the Gatesville Medical Centre or Tygerberg Hospital.

Polysomnographic recordings were used to identify REM sleep in real-time by a registered sleep technologist. Participants were woken 10 minutes into the second REM period, and 15 minutes into the third REM period, or were interviewed after spontaneous awakening during REM sleep. Additionally, all participants were interviewed the morning after each night spent in the sleep laboratory. These morning interviews consisted of brief questions regarding: (a) whether the participant could remember any dreams other than those reported to the researcher during the REM sleep awakenings; (b) the quality of their sleep during the preceding night. Participants were also asked to report their episodic recall of the entire night, from arrival at the laboratory through the awakenings, etc., to determine whether the lack of dream recall was specific or part of a larger amnesic picture.

The polysomnographic recordings were performed with a portable Alice © 5 Respironics polygraphic amplifier (Cape Sleep Centre, Gatesville Medical Centre, Cape Town). The American Association of

Sleep Medicine's (AASM) recommended recording montage was utilised in this study, including: (a) an electroencephalogram (EEG: 4 leads, 2 channels); (b) an electrooculogram (EOG: 2 channels); (c) a sub-mental electromyogram (EMG: chin and leg); and (4) chest and abdominal strain gauges, a snore microphone, positional marking, and finger pulse oximetry. Sleep stages were visually scored for 30-second epochs by a certified polysomnographic technologist; these were based on AASM standard criteria (Hirshkowitz & Sharafkhaneh, 2009).

2.4.2) Neuro-imaging

All neuro-imaging data were obtained from the respective medical centres' picture archiving and communication system (PACS). Where possible, the diffusion weighted images (DWI) taken during the acute stage and the early sub-acute stage were utilised to identify lesions, as the DWI is the most sensitive sequence for cytotoxic changes associated with ischemia. Where DWI sequences were not available, the fluid-attenuated inversion recovery (FLAIR) sequences were used to identify ischemic changes. Only one participant had a CT brain scan and no MRI.

2.4.3) Lesion analysis

The lesion analysis was performed by a lecturer in neuroanatomy who specialises in clinical neuro-imaging. All lesions were traced using MRICron software (NeuroDebian Inc. 2008) on the ch2.nii template brain (Holmes, 1998), using an Intuos5 pen and tablet. Each volume of interest was traced in the axial plane and then saved. Because all the lesion mapping was done on the ch2.nii template, the lesions were automatically encoded into standard MNI space. Throughout the tracing procedure, the expert neuro-anatomist was blind to the status of the subject (i.e. dreamer or non-dreamer). It was only after the lesion analysis that the status of each participant was revealed. Lesion overlays for each group (i.e. dreamers and non-dreamers) was created by MicroGL and Mango software packages.

2.5) Data Analysis

Lesion overlay maps of the dreamers and non-dreamers were compared side by side, so as to identify structures involved exclusively in the non-dreamer group. Due to the small sample size, statistical instruments were of limited use.

2.6) Ethical Considerations

The current research fulfilled the ethical guidelines for research with human subjects, as specified by Health Professions Council of South Africa and the Institutional Review Board of the University of Cape Town. Ethical clearance was obtained through the Department of Psychology and Faculty of Health Science's Research Ethics Committees of the University of Cape Town. Institutional consent was obtained from the Cape Sleep Centre, the Gatesville Medical Centre and the Department of Neurology at Groote Schuur Hospital. Individual informed consent was obtained in writing from each participant before any data collection was done.

3) Results

The demographic characteristics of the cohort are discussed in this chapter. Thereafter, the results are presented for each case, grouped under non-dreamers and dreamers.

3.1) Demographics

A total of seven patients were included in the analysis. Three participants were identified as non-dreamers and four participants as dreamers. The mean age of the participants in the non-dreamers group was 60-years-old, and the group consisted only of women. Mean chronicity (number of weeks between onset of stroke and the sleep lab assessment) was 85 weeks. The mean age for the participants in the dreamers group was 56-years-old, and the group consisted of three men and two women. Mean chronicity was 57 weeks.

3.2) Neuro-imaging

There is notable heterogeneity in the neuro-imaging of all seven patients. Most patients had a Magnetic Resonance Imaging (MRI) scan done at the time of presentation at the Emergency Department; however, one patient had a Computed Tomography scan done at the time of presentation. For all patients who had undergone MRI, diffusion weighted imaging was available to corroborate areas of abnormal signal with diffusion restriction, which is done to confirm that the abnormal area is indeed affected by cytotoxic change. The imaging parameters also varied in terms of the slice thickness and resolution of the imaging. The most representative image of the pathology is demonstrated in the results below. Where the pathology is demonstrable across several slices, these are also included; however, this was not possible for all patients due to thick slices, which are typical of emergency brain imaging protocols used to reduce time in the scanner and time between onset and diagnosis.

3.2.1) Non-Dreamers

Case 1

This patient is a right-handed woman, who was 61-years-old at the time of presentation to the Emergency Department, which occurred on 25 February 2006. The patient presented with acute onset visual field loss, headache, vertigo and meningism. On examination, the patient was delirious.

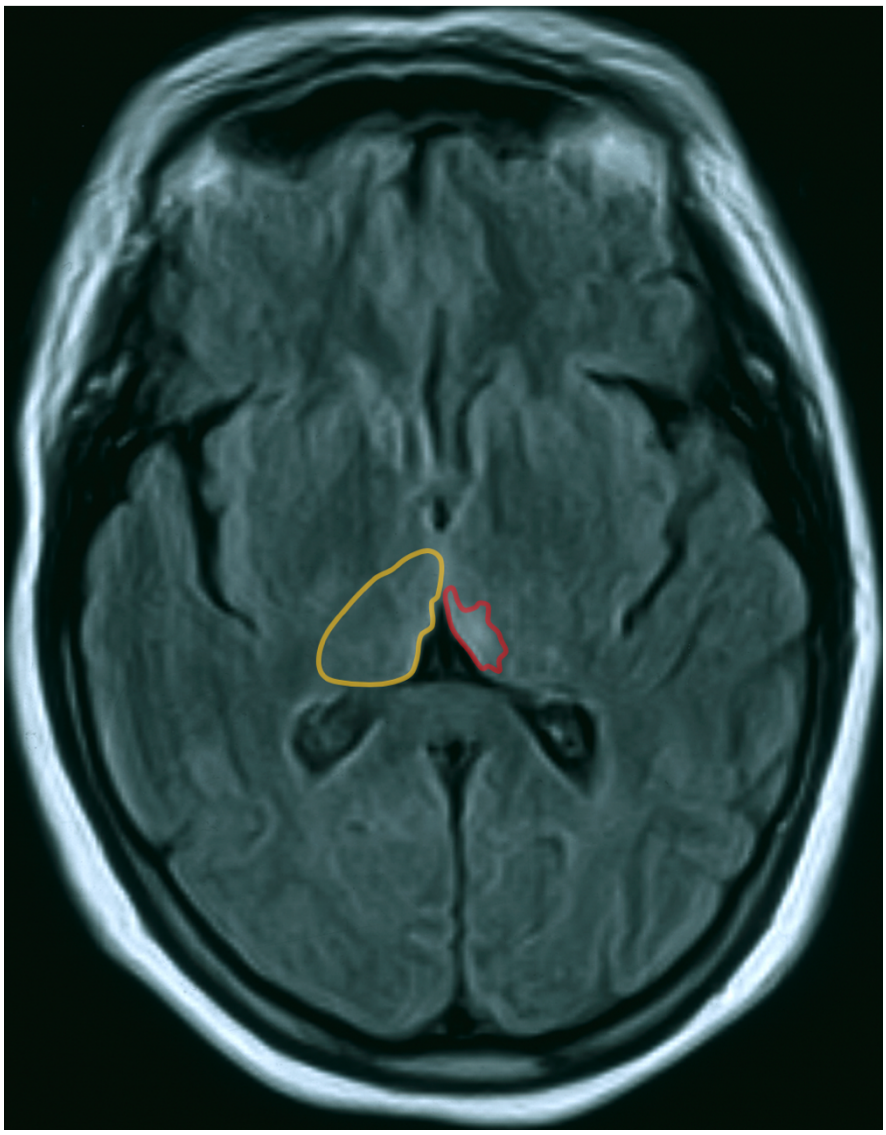

Image 4.1: Case 1 - FLAIR in the axial section at the level of the basal ganglia. Normal thalamic outline demonstrated (yellow); lesion represented by a focal area of high signal involving the postero-medial aspect of the thalamus demonstrated (red).

Acute stage neuro-imaging with MRI demonstrated the following for Case 1:

- Increased T2-weighted (T2W)/ fluid attenuated inversion recovery (FLAIR) signal and associated diffusion restriction involving the left postero-medial thalamus, with specific involvement of the pulvinar nucleus of the thalamus (Image 4.1).
- Increased T2/FLAIR signal involving the right hippocampal formation and amygdala, with evidence of cytotoxic change (Image 4.2).
- High T2/FLAIR signal involving bilateral medial occipital cortex (BA 17, 18) (Image 4.3).
- High T2/FLAIR signal involving the right parahippocampal gyrus medially (BA 26, 27, 28) (Image 4.2).

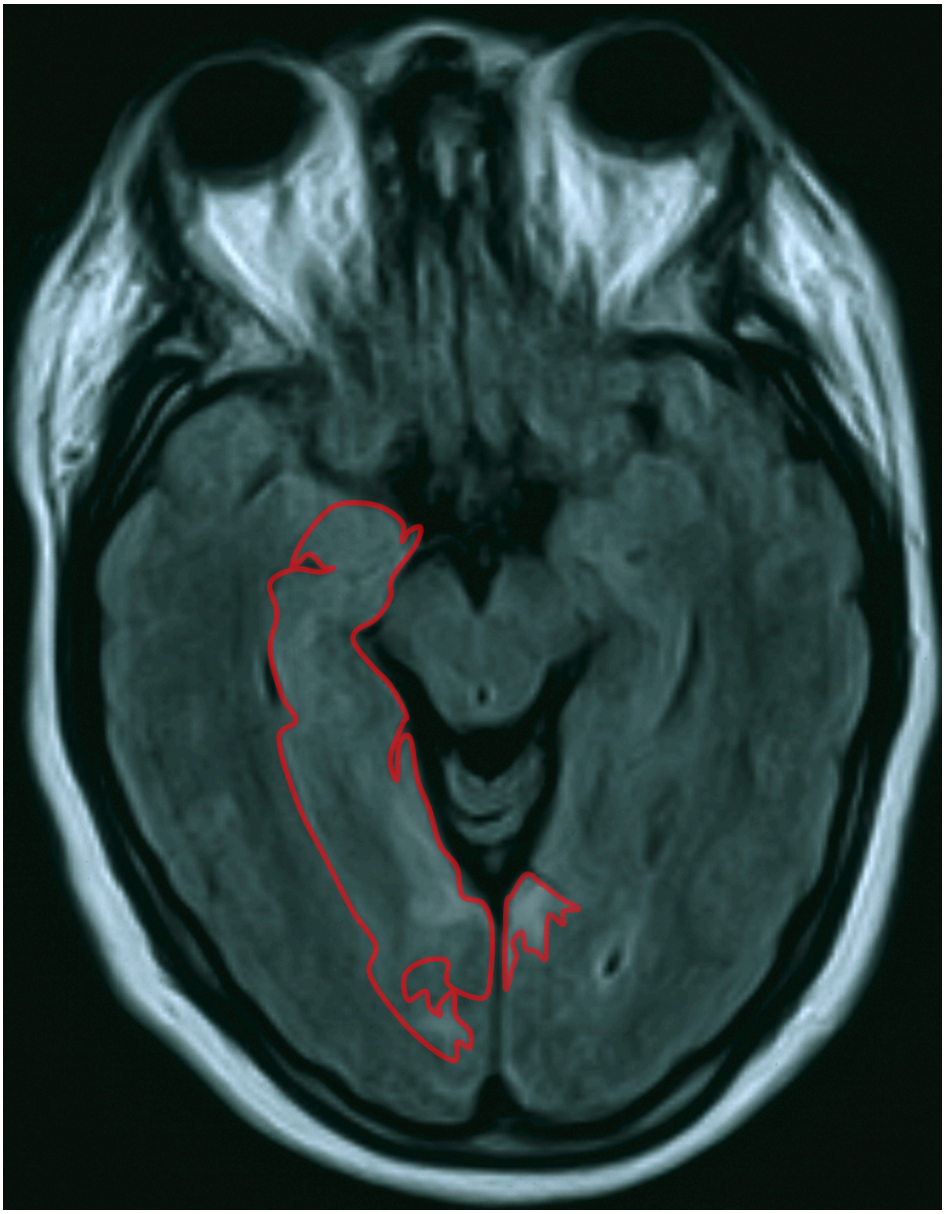

Image 4.2: Case 1 - FLAIR in the axial section at the level of the midbrain. Evidence of high signal involving the right hippocampal formation, adjacent parahippocampal gyrus, amygdala and bilateral medial occipital cortex is demonstrated (red).

The patient reported total dream cessation since her stroke. The total cessation of dreaming was consistent over multiple clinical interviews. The patient reported regular dreaming before the incident, particularly when she was stressed, however since the incident, she fails to dream even during periods of significant stress. Global cessation of dreaming could therefore be attributed to the stroke, for an approximate duration of 4-years-and-5-months.

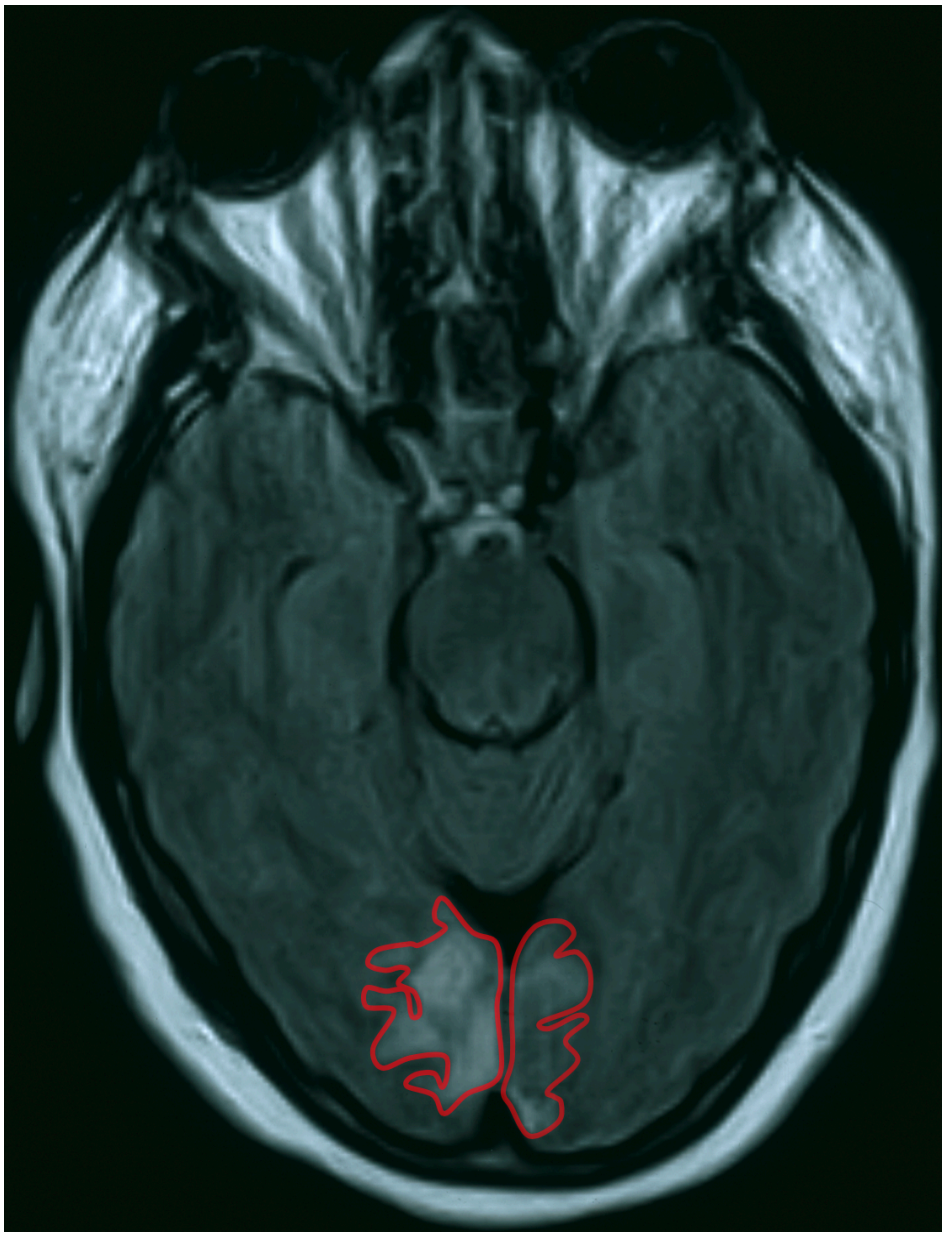

Image 4.3: Case 1 - FLAIR in the axial section at the level of the pontomesencephalic junction. Bilateral medial occipital high signal is demonstrated (red).

The patient's global dream cessation was confirmed in the sleep laboratory by conducting nocturnal REM sleep interviews from unprompted awakening occurrences during the first and second REM periods. During both interviews, the patient reported that she had not been dreaming or experiencing any thoughts or mentation.

Case 2

This patient is a right-handed woman, who was 62-years-old at the time of presentation to the Emergency Department, which occurred on 2 July 2011. The patient presented with sub-acute delirium and visual impairment.

Neuro-imaging with MRI at the time of presentation demonstrated the following for Case 2:

- Increased T2W/ FLAIR signal and associated diffusion restriction involving the right postero-lateral thalamus with involvement of the pulvinar nucleus of the thalamus (Image 4.4).

- Increased T2/FLAIR signal involving bilateral medial occipital cortex (BA 17, 18) (Image 4.5).

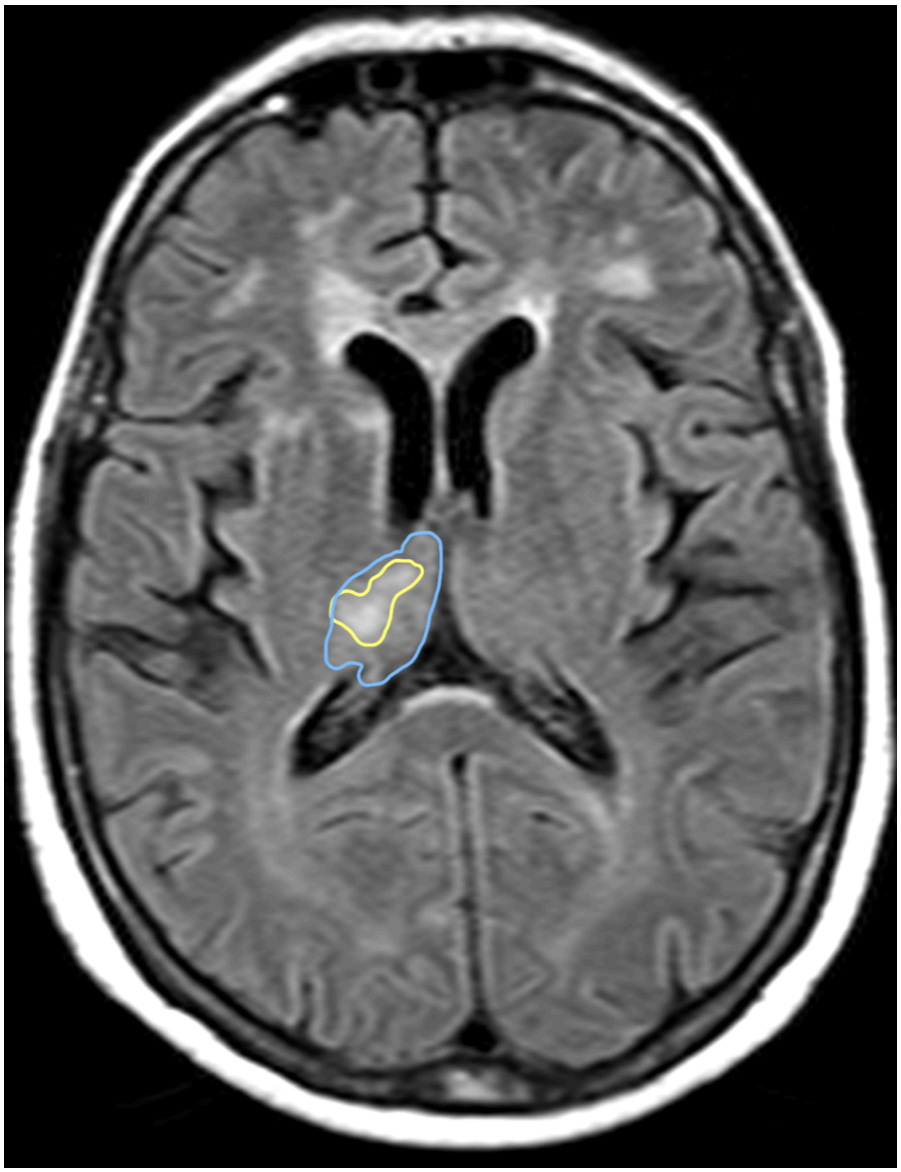

Image 4.4: Case 2 - FLAIR in the axial plane at the level of the thalamus and planum temporale. The blue outline demonstrates a normal thalamic boundary. The yellow outline demonstrates the right thalamic infarct, which corresponds with restricted diffusion.

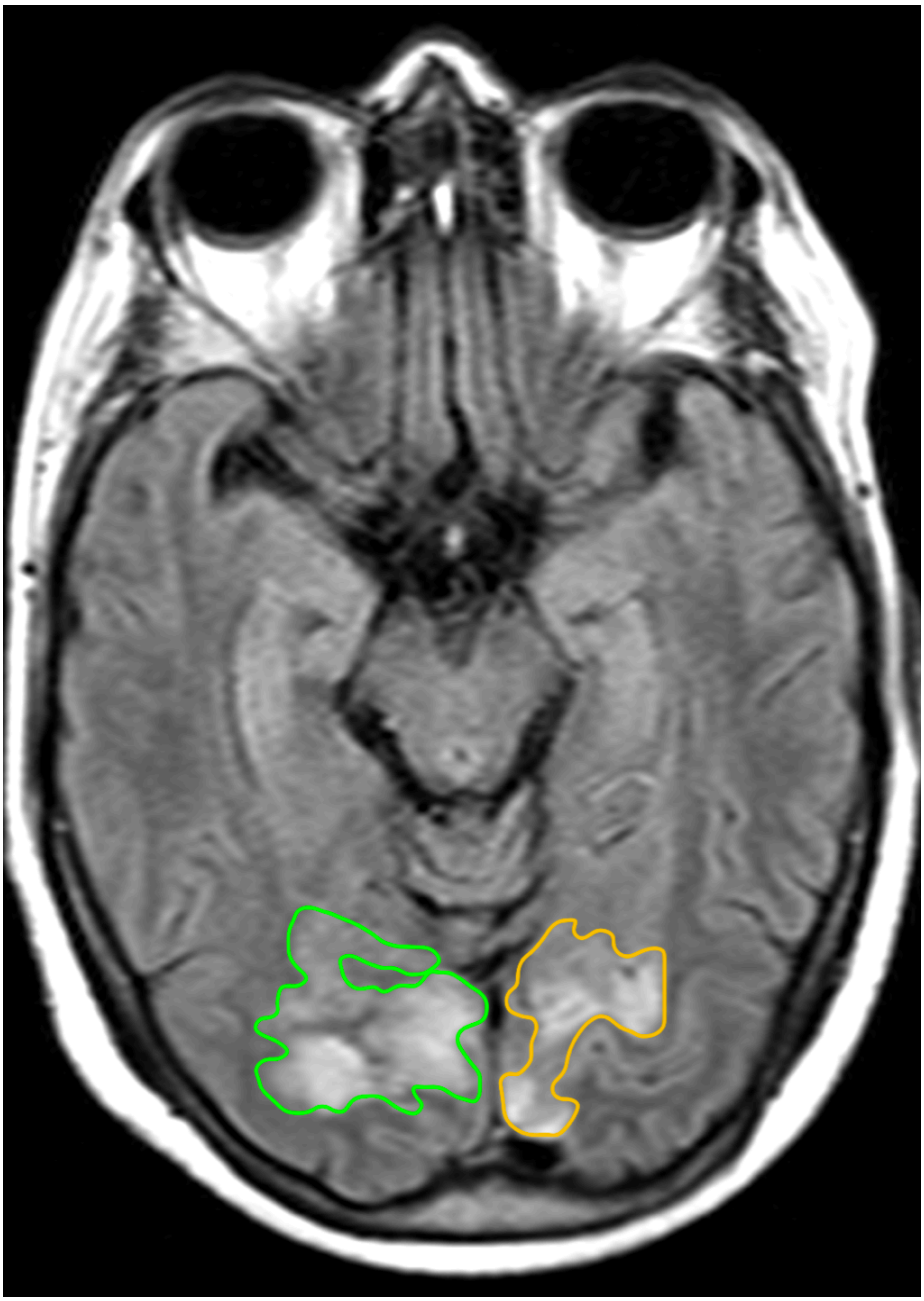

Image 4.5: Case 2 - FLAIR in the axial plane at the level of the mid-brain and superior colliculus. The green and orange outline demonstrate the postero-medial occipital areas of ischemic infarction. These lesions demonstrated corresponding diffusion restriction.

This patient reported an inability to remember any dreams since her stroke. This presentation remained constant over two clinical interviews, which occurred at two months and three months after the stroke. She noted that prior to the incident she had dreamt frequently, suggesting that complete cessation of dreaming had occurred as a result of the stroke.

This was confirmed in the sleep laboratory. Nocturnal REM sleep interviews could not be performed on the first night in the sleep laboratory, as the patient did not enter REM sleep on that night. However,

lack of dream recall in the morning and with unprompted awakening episodes during the first and second night in the sleep laboratory suggested that she was, in fact, not dreaming. In addition, a third sleep study night was specifically designed to confirm the lack of dreaming. Whilst normal REM was achieved on the third night, no positive dream reports were obtained.

Case 3

This patient is a right-handed 56-year-old woman who presented to the Emergency Department with sudden onset right-side upper-limb weakness and right-side homonymous hemianopia, vertigo and sensori-neural hearing loss.

The MRI brain scan demonstrated right-side postero-medial thalamic infarction with specific involvement of the pulvinar nucleus of the thalamus (Image 4.6) and involvement of the medial geniculate nucleus (Image 4.7). The images show no evidence of medial occipital involvement. The patient reported that she could not remember having dreamt since her stroke. This was verified by REM sleep awakenings in the sleep lab. However, the patient only entered one convincing period of REM sleep during the first night, so only one awakening occurrence could be performed. Other evidence that she had lost the ability to dream came from the two morning interviews performed. No dreams were reported during any of the three interviews.

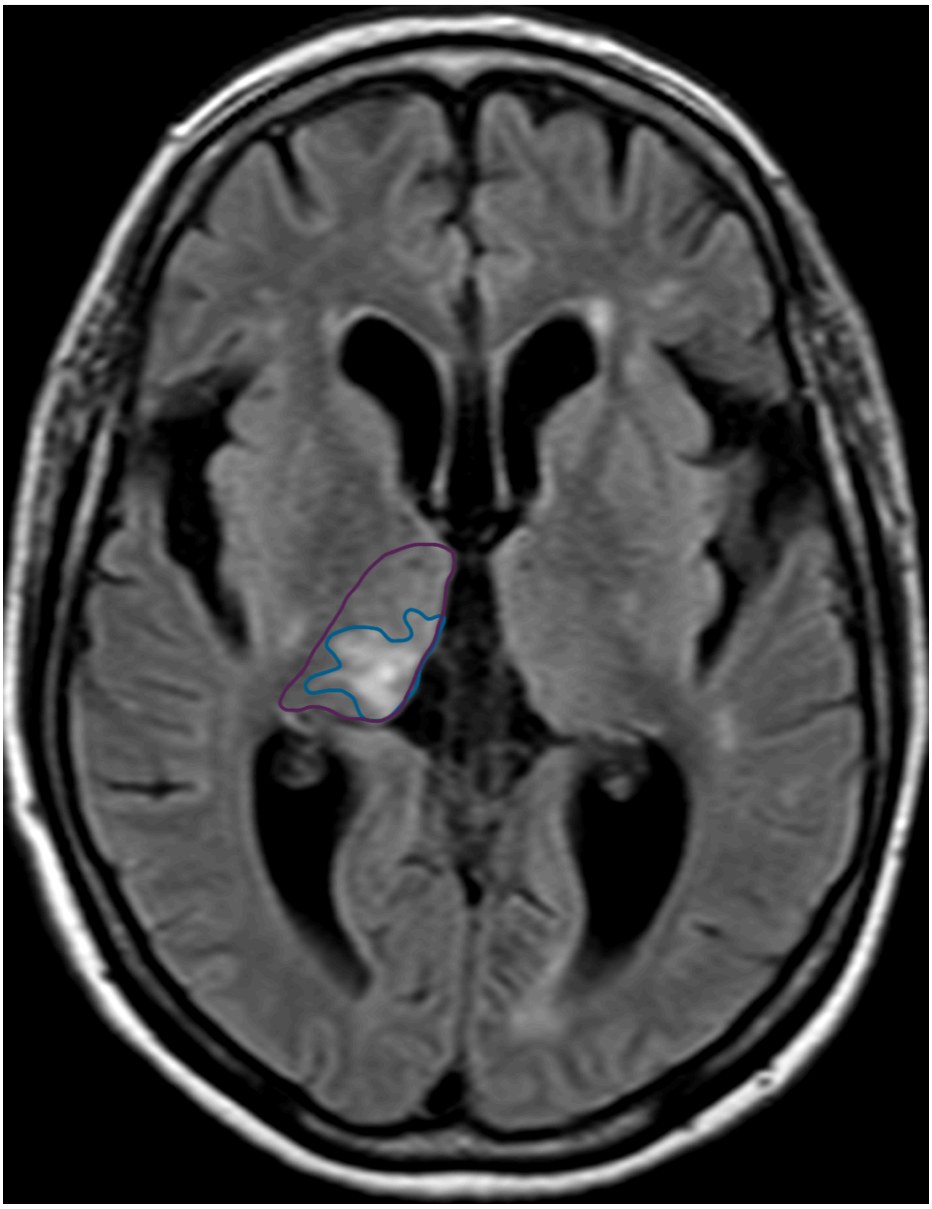

Image 4.6: Case 3 - FLAIR in the axial plane at the level of the internal capsule. High signal is seen involving the postero-medial thalamus (blue outline), which demonstrated corresponding diffusion restriction. The purple outline represents normal thalamic boundary.

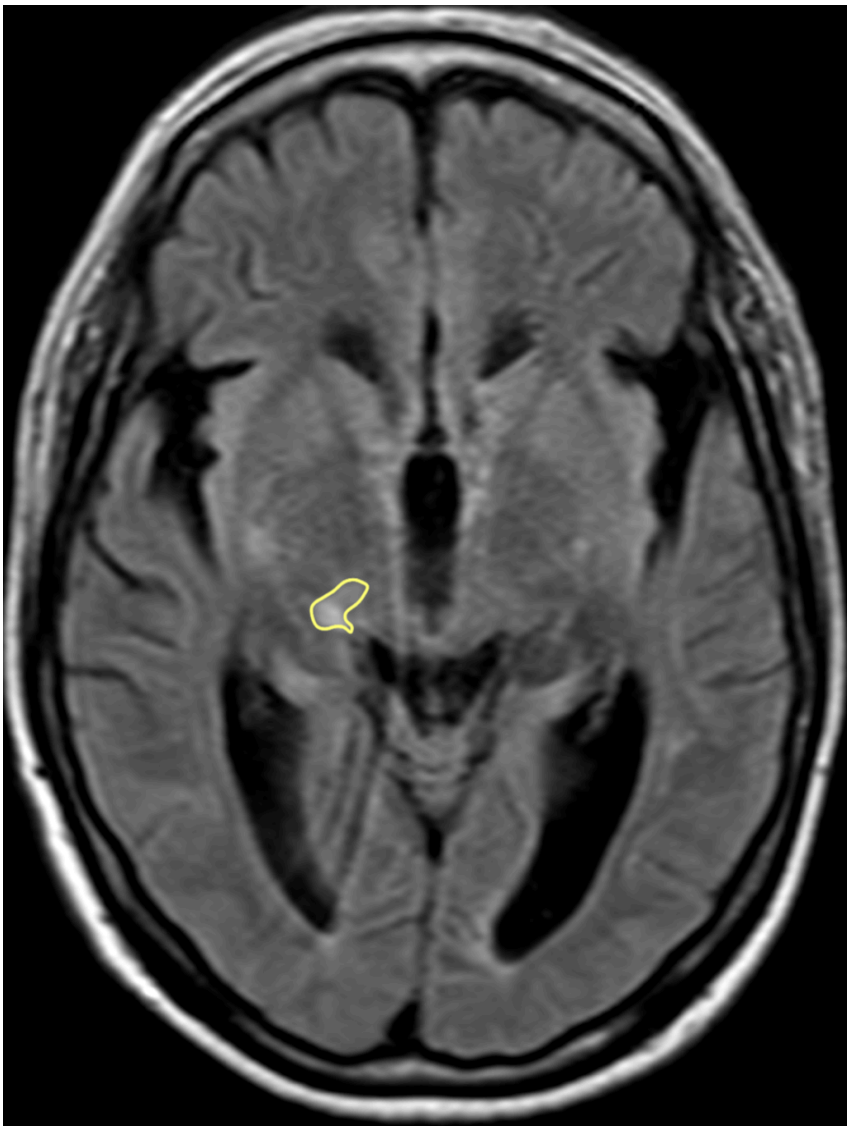

Image 4.7: Case 3 - FLAIR in the axial plane at the level of the midbrain-diencephalic junction. The yellow outline demonstrates inferior extension of the thalamic infarction involving the medial geniculate nucleus, which correlates clinically to the patient's ipsilateral sensori-neural hearing loss.

3.2.2) Dreamers

Case 4

This patient is a 41-year-old right-handed woman, who presented to the Emergency Department with diplopia, sudden onset migraine and vertigo. The MRI brain scan demonstrated a unilateral right-side area of restricted diffusion involving the entire hippocampal formation (Image 4.8). No thalamic (Image 4.9) or other arears of infarct are noted on the MRI.

This patient reported that she was a frequent dreamer, but was unsure if the infarct had affected her ability to dream. Three nocturnal REM sleep interviews were performed during the first night in the sleep laboratory - one from a spontaneous awakening occurrence during the second REM period, as well as after waking the patient during the second and third REM periods. From these awakenings, two positive dream reports were obtained. (See images 4.8 – 4.9.)

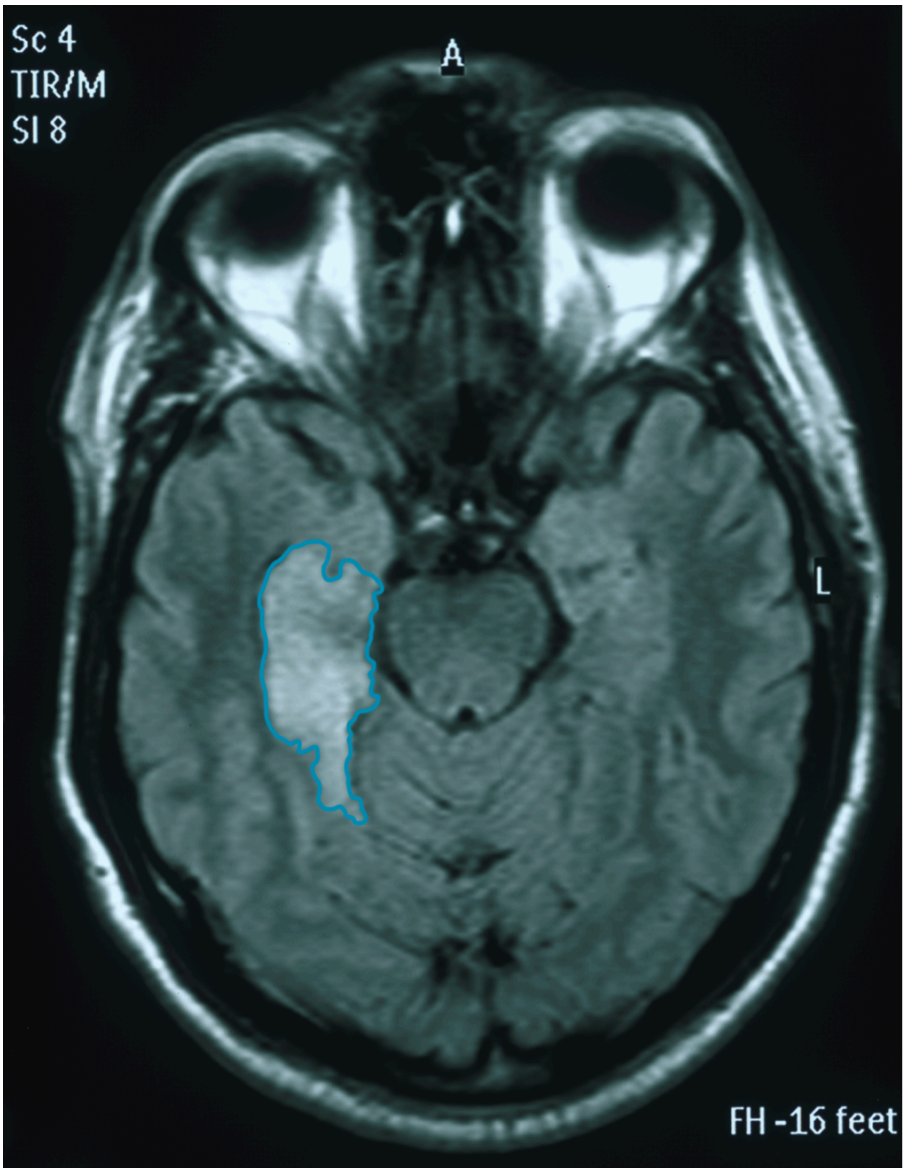

Image 4.8: Case 4 - FLAIR in the axial plane at the level of the pontomesencephalic junction, demonstrating a circumscribed area of high signal involving the right hippocampal formation. The area of high signal demonstrated corresponding diffusion restriction.

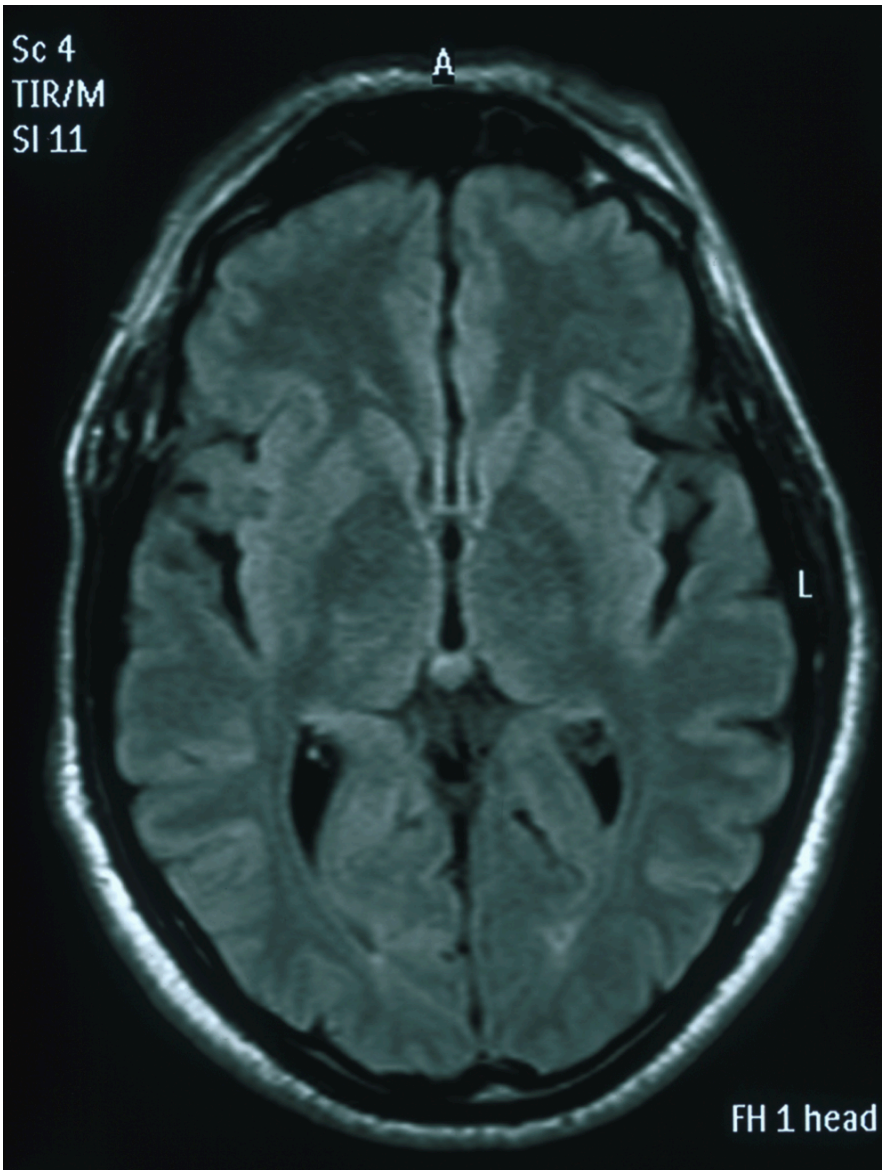

Image 4.9: Case 4 - FLAIR in the axial plane at the level of the pineal gland, demonstrating no evidence of signal abnormality in the thalami.

Case 5

This patient is a 60-year-old right-handed woman, who presented to the Emergency Department with a one-month history of worsening chronic headache and acute onset of visual disturbance in the form of light flashes in the right upper quadrant of her visual field. The MRI brain scan demonstrated left-side high signal, with corresponding diffusion restriction involving the medial occipital lobe (Image 4.10) and extending superiorly to involve the medial parietal lobe (Image 4.11). There is associated involvement of the ipsilateral tail of the hippocampus and the lateral aspect of the splenium of the corpus callosum (Image 4.11).

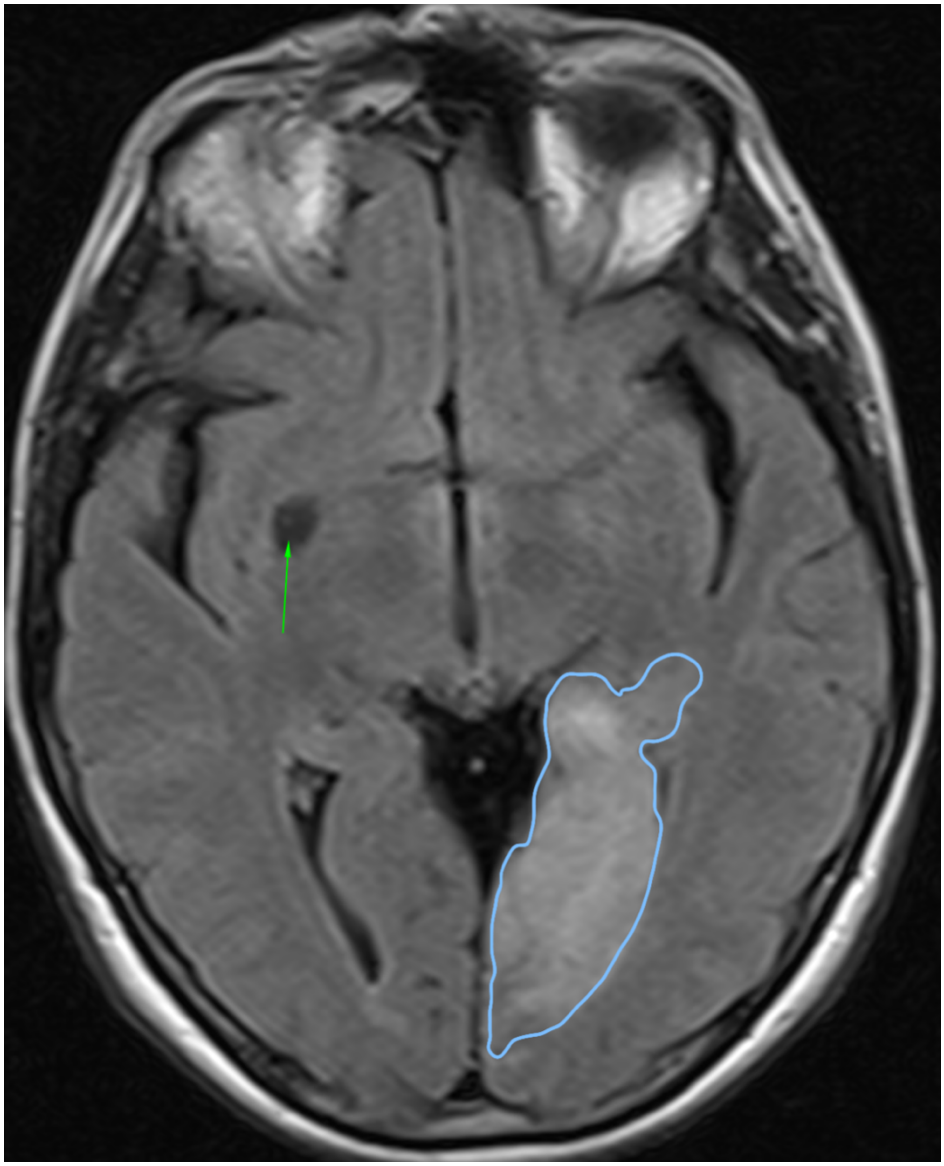

Image 4.10: Case 5 - FLAIR in the axial plane at the level of the mid-brain-diencephalic junction, demonstrating a large circumscribed left-side area of high signal involving the postero-medial occipital lobe and the tail of the hippocampus anteriorly (blue outline). An incidental finding of enlarged perivascular space is noted on the right (arrow). The perivascular space is distinguished from a chronic lacunar infarct, as there is no rim of high signal surrounding the cyst to suggest gliotic scarring.

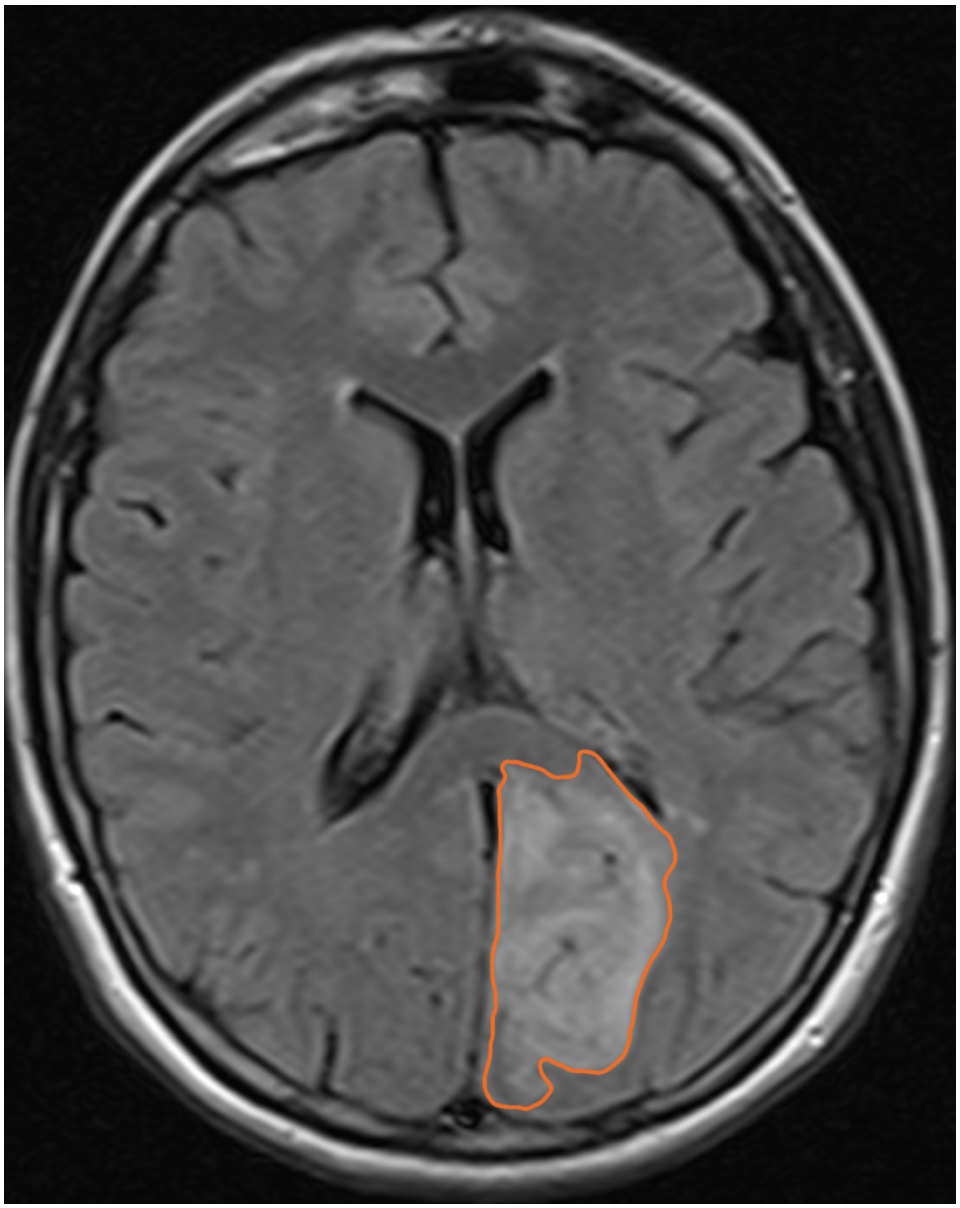

Image 4.11: Case 5 - FLAIR at the level of the splenium and genu of the corpus callosum demonstrates a large circumscribed area of high signal involving the medial parietal lobe, as well as the lateral aspect of the splenium (forceps major) (orange outline).

Case 6

This patient is a 60-year-old right-handed man, who presented to the Emergency Department with severe acute onset headache. The CT brain scan done at the time demonstrated a circumscribed area of low density involving the left medial occipital lobe and extending superiorly to involve the ipsilateral medial parietal lobe. The patient reported that he dreamt regularly before his stroke. He was uncertain as to the effect the stroke may have had on his dreams. Nocturnal REM sleep interviews were performed in the sleep laboratory during the first night, during the second and third REM periods. A positive dream report was elicited from the second awakening. In addition, in the morning, the patient reported that he could remember dreaming a few times during the night. (See Image 4.12.)

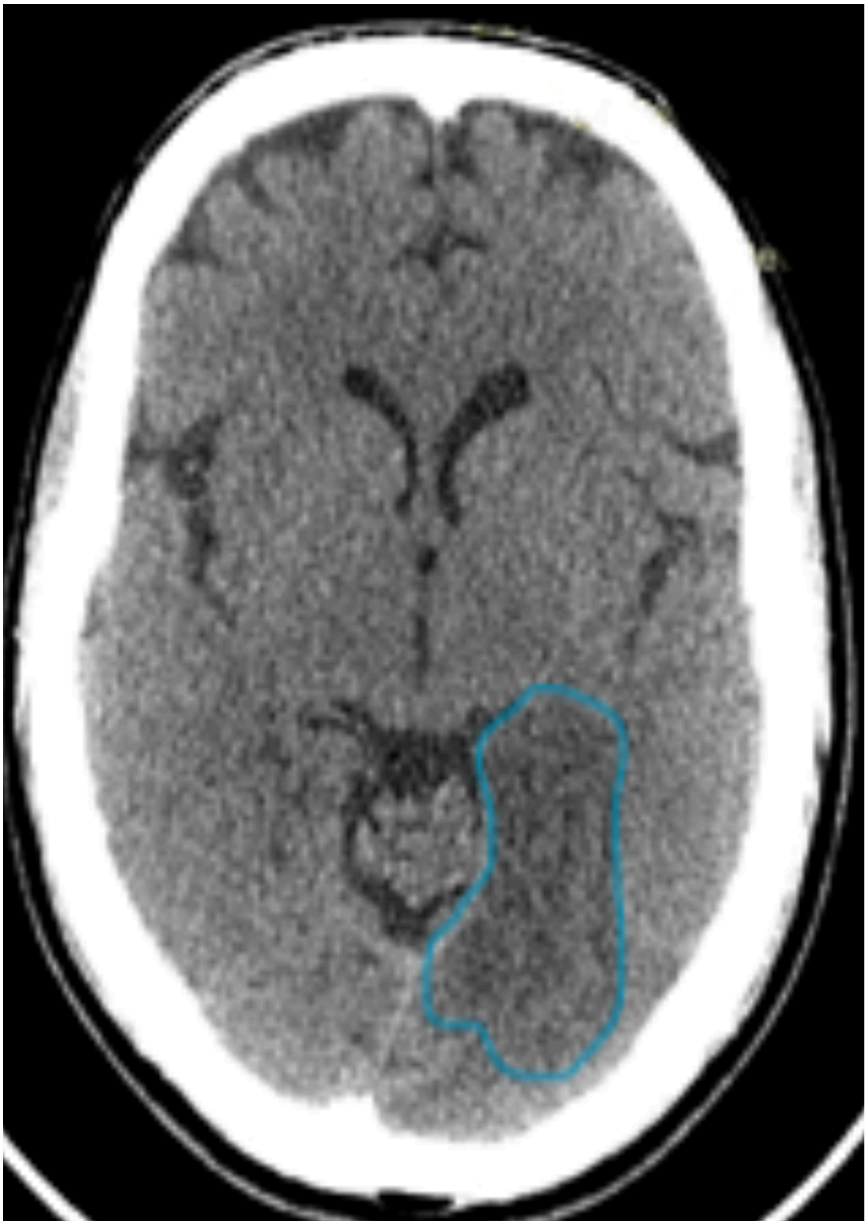

Image 4.12: Case 6 - CT brain scan with brain window demonstrates a circumscribed area of low density (blue outline) involving the postero-medial occipital lobe. The low resolution of the image was due to the nature of the image record, which was in the form of physical films that were printed and scanned in for purposes of illustration in this report.

Case 7

This patient is a 55-year-old right-handed gentleman who presented to the Emergency Department after sudden collapse and with associated signs of increased intracranial pressure, such as nausea, vomiting and severe occipital headache. The MRI brain scan demonstrates an area of circumscribed high signal involving the posterior temporo-occipital border zone, with evidence of haemorrhagic transformation (Image 4.13).

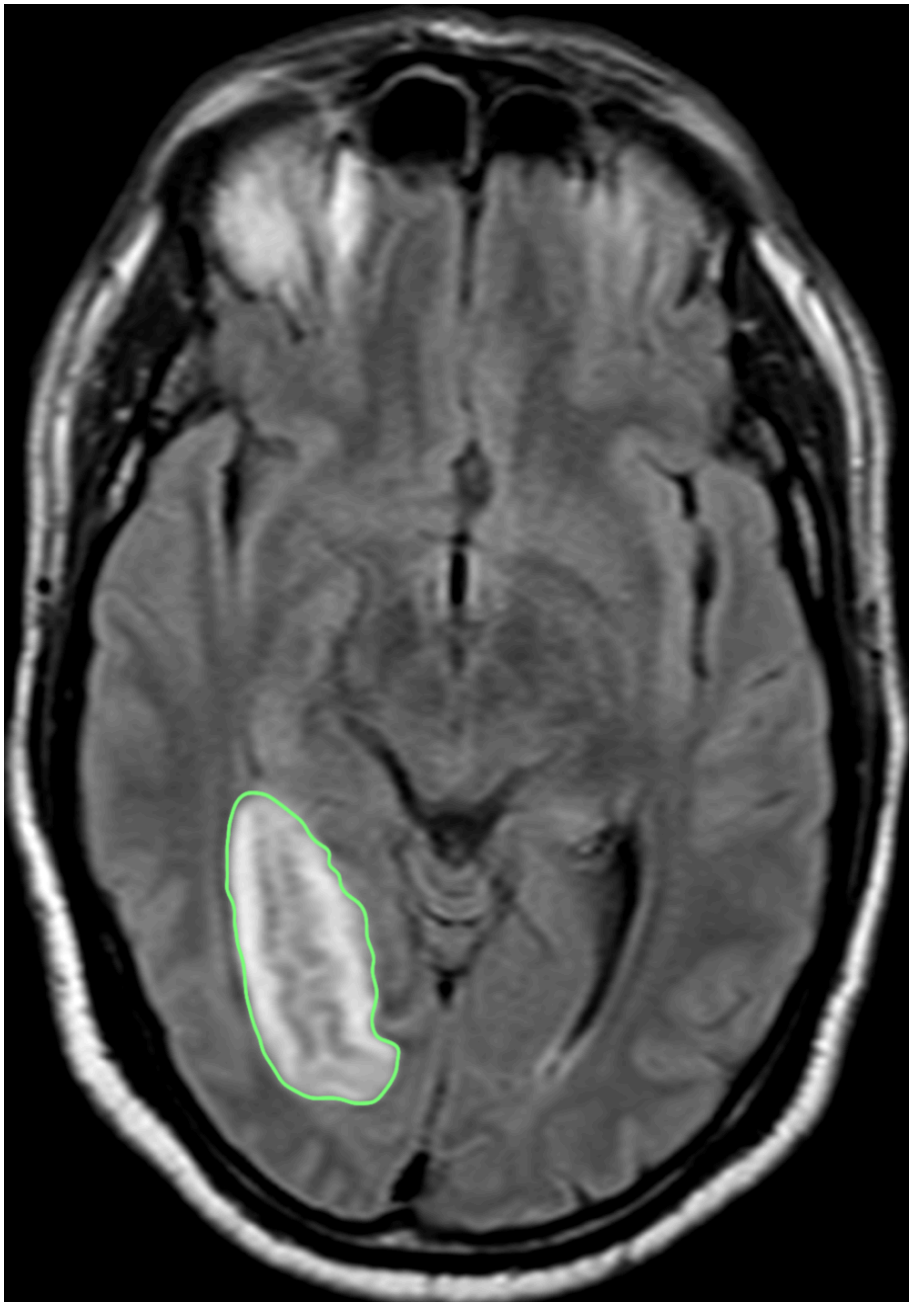

Image 4.13: Case 7 - FLAIR at the level of the midbrain-diencephalic junction, demonstrating a circumscribed area of high signal involving the temporo-occipital junction (green outline). There is associated low signal within the lesion, which suggests haemorrhagic transformation.

The patient reported that he did not know if his stroke had affected his ability to dream. There were two awakening occurrences in the sleep lab during the second and third periods of REM sleep and one positive dream report was obtained from these awakening occurrences. During the morning interview, although he did not report any other dreams, he was able to further clarify the dream that he had reported during the second awakening.

At a clinical interview, one month after the sleep lab assessment, he reported that he had been dreaming; however, he could not give specific details about any one dream at that time.

3.2.3) Summary of neuroimaging findings

All patients had suffered posterior cerebral artery thrombotic occlusion and presented to the Emergency Department for acute stage imaging. Except for one patient, all imaging done in the "dreaming" group had an MRI with associated diffusion weighted imaging to confirm cytotoxic change in the areas of abnormal signal seen on FLAIR sequences. Restricted diffusion attributes the area of abnormal signal seen on other sequences to true cytotoxic swelling that occurs in infarcted brain regions and distinguishes abnormal signal from chronic gliotic scarring.

All three of the patients in the non-dreaming cohort demonstrated infarction involving the posterior thalamic regions, and specifically involving the pulvinar nucleus of the thalamus. More specifically, Case 1 demonstrated FLAIR high signal involving the left postero-medial thalamus, specifically involving the pulvinar nucleus of the thalamus with associated restricted diffusion. Case 2 demonstrated FLAIR high signal in the right postero-lateral thalamus and specifically involving the pulvinar nucleus of the thalamus with associated restricted diffusion. Case 3 demonstrated right-sided postero-medial thalamic FLAIR high signal with specific involvement of the pulvinar nucleus of the thalamus and involvement of the medial geniculate nucleus with associated restricted diffusion.

None of the patients in the dreaming cohort demonstrated any form of thalamic involvement. Case 4 demonstrated a unilateral right-sided area of FLAIR high signal localized to the hippocampal formation. Case 5 demonstrated left-sided FLAIR high signal involving the medial occipital lobe and extending superiorly to involve the medial parietal lobe, with corresponding diffusion restriction. There is associated involvement of the ipsilateral tail of the hippocampus and the lateral aspect of the splenium of the corpus callosum. Case 6 was a CT scan that demonstrated a circumscribed area of low density involving the left medial occipital lobe, extending superiorly to involve the ipsilateral medial parietal lobe. The final dreaming patient, Case 7, demonstrated an area of circumscribed high FLAIR signal involving the posterior temporo-occipital border zone, with evidence of haemorrhagic transformation.

4) Discussion

The role of the posterior cortical regions in dream cessation is unclear, as contradicting data exists in the current neuro-imaging literature. Currently, there are only two reported cases of total dream cessation following vascular lesions involving the posterior cerebral artery vascular territory alone (Bischof and Bassetti, 2004; Poza and Martí-Massó, 2006). The current study includes modern neuro-imaging data of three patients with posterior cerebral vascular territory thrombotic infarctions with confirmed semi-spontaneous nocturnal REM sleep awakening occurrences with non-dreaming status, which were compared to four patients who also had posterior cerebral artery infarctions, but whose dreaming status was confirmed as being intact. The current study is the only one of its kind that compares a cohort of laboratory-confirmed non-dreaming patients with a cohort of dreaming patients with focal lesions confined to the PCA territory.

Thus, this mini dissertation sought to investigate how the neuroanatomical distribution of brain damage following focal posterior cerebral artery infarction differed in a cohort of three patients with total dream cessation compared to four patients with intact dreaming. The discussion is organized as follows: 1) summary of the methodological approach used in the current study; 2) potential limitations of the study; 3) relating current findings to previous research; 4) interpretation of current findings; 5) future directions; 6) concluding remarks.

4.1) Summary of the methodological approach

Clinical neuro-imaging data was reviewed by a neuroanatomist to compare three patients with dream cessation to four patients with intact dreaming. The reviewer was blinded during the neuro-imaging review, with regard to which cohort the patient belonged to. The neuroanatomical distribution of the lesions was meticulously documented with the highest level of neuro-anatomical detail possible. The distribution of the lesions in each group was then compared.

4.2) Hypothesis and results

The principle hypothesis here was to confirm that focal medial occipital lesions can result in total dream cessation, as proposed by Bischof and Bassetti (2004) and Poza and Martí-Massó (2006) in their case studies. The findings of the current study indicate that all three patients in the non-dreaming cohort had posterior thalamic involvement. Two patients in the non-dreaming cohort had medial occipital involvement. All three dreaming participants had medial occipital involvement, except one patient who had circumscribed medial temporal involvement. None of the dreaming patients had any thalamic

involvement. Therefore, the hypothesis that the medial occipital lesions alone are involved in dream cessation cannot be confirmed, as: the non-dreaming patients all had circumscribed thalamic involvement and one had no medial occipital involvement; the dreaming patients also demonstrated an extensive pattern of medial occipital and temporal involvement.

4.3) Limitations

General limitations

The principle limitation of this study is the small sample size of the non-dreaming group. An attempt was made to address the predicted rarity of the experimental group – participants with heteromodal cessation of dreaming due to PCA territory infarction – by recruiting patients from two large and busy medical institutions in Cape Town, South Africa. However, PCA territory infarctions are rare, when compared to middle cerebral artery territory (MCA) infarctions, and they account for only nine percent of all strokes (Bogousslavsky, Van Melle & Regli, 1988). In addition, heteromodal cessation of dreaming as a result of non-hemorrhagic PCA strokes has been shown to be exceptionally rare, with just two cases reported previously in the worldwide literature (Bischof & Bassetti, 2004; Wilbrand, 1887). A further limitation of this study is a direct consequence of the first limitation, i.e. no meaningful statistical analysis could be carried out, as a result of the small sample sizes.

Limitations in neuro-imaging

There is notable heterogeneity in the neuro-imaging across patients. Most patients had an MRI scan at the time of presentation at the Emergency Department. However, one patient had a CT scan at the time of presentation. For all patients who had undergone an MRI scan, diffusion weighted imaging was available to corroborate areas of abnormal signal with diffusion. The imaging parameters also varied in terms of the slice thickness and resolution of the imaging. Therefore, more subtle neuroanatomical detail was not visible with the current in plane resolution. Unfortunately, emergency stroke neuro-imaging protocols require fast scan times and therefore thick slices that inherently reduce the resolution of the imaging.

4.4) Relating current findings to previous research

Wilbrand (1887) reported bilateral temporo-occipital damage circumscribed to the unimodal association cortex in his original case of Fräulein G. The validity of Wilbrand's observations come into question because he did not report whether he sectioned the rest of the brain during his postmortem

examination, to look for other co-morbid lesions in the posterior vascular territories. It is therefore unknown if Wilbrand investigated the parietal lobes, deep parietal white matter or the thalamus. Following Solms' 1997 reformulation of the Charcot-Wilbrand syndrome, several functional neuroimaging studies at the time consistently reported deactivation of the heteromodal association cortex of the inferior parietal lobule, during REM sleep (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1997). In his exhaustive reanalysis of existing literature, Yu (2001) identified mainly lateral temporo-occipital cortex involvement as being critical in dream cessation.

Bischof and Bassetti (2004) reported a case of a 73-year-old woman, who had suffered total cessation of dreaming following a posterior cerebral artery infarction that involved bilateral medial occipital lobes. Bischof and Bassetti (2004) discuss their findings regarding the medial occipital lobe at length in their case report. The medial occipital distribution of the infarcted area in their patient corresponds to two of the patients in the current study, who have reported total cessation of dreaming. However, upon reviewing the source images of Bischof and Bassetti (2004) (Image 5.1), there is evidence of large right-side thalamic infarct involving the posterolateral aspect of the thalamus. This finding is not adequately discussed in Bischof and Bassetti's case study. The thalamic involvement corresponds perfectly with the posterior thalamic involvement in all three of the current study's non-dreaming patients. None of the dreaming patients demonstrated any involvement of the thalamus.

The only other case of pure posterior cerebral artery infarction in the literature, and therefore of medial occipital involvement in total cessation of dreaming, comes from a case report by Poza and Martí-Massó (2006). This relates to a 24-year-old man, who experienced total cessation of dreaming following a unilateral left temporo-occipital hematoma from a cerebral arteriovenous malformation (AVM). Source images of the patient in the case study were not available for evaluation, however, localization of brain dysfunction in AVMs is problematic. Non-haemorrhagic AVMs are known to cause chronic hypoperfusion and low-grade ischaemia in adjacent brain tissue, and haemorrhage causes potentially catastrophic perfusion alterations in adjacent tissue (Lo, E., 1993; Lee, B., et al. 2009). Therefore, circumscribed brain dysfunction cannot be convincingly concluded from a patient with a haemorrhagic AVM.

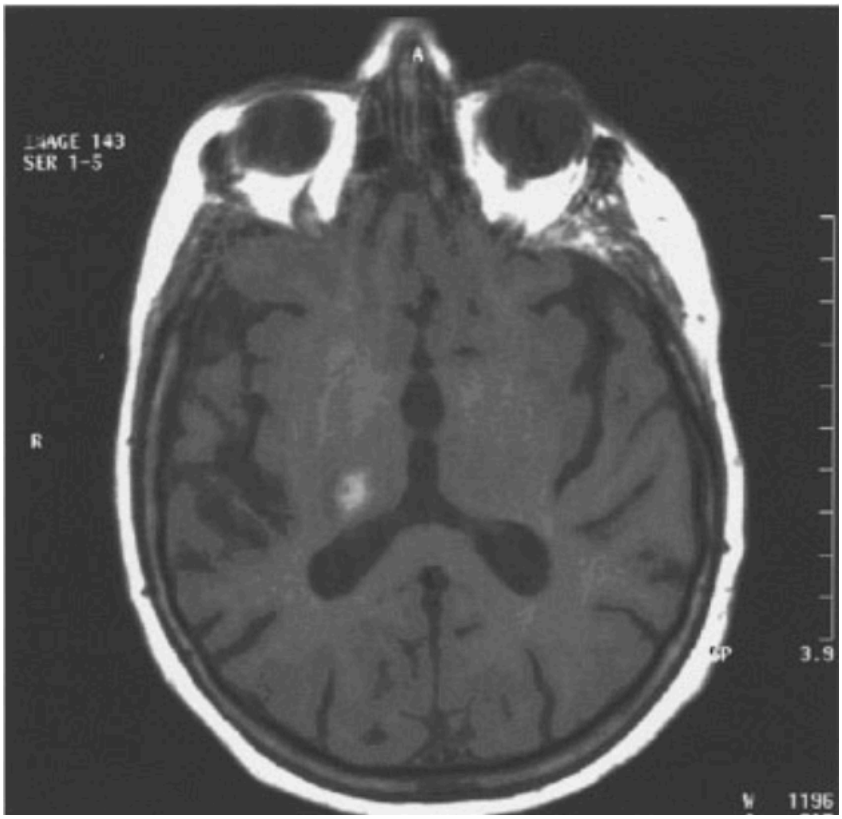

Image 5.1: MRI brain (FLAIR in the axial plane) of Bischof and Bassetti's (2004) case, at the level of the thalami, demonstrating discrete left-sided posterior thalamic infarct.

4.5) Interpretation of current findings

The existing literature does not convincingly implicate circumscribed areas of the medial occipital lobes in dream cessation. In fact, the study done by Bischof and Bassetti (2004) appears to corroborate the findings in the current study, where all patients with dream cessation had thalamic involvement, whereas all patients in the dreaming group had circumscribed medial temporo-occipital damage. If temporo-occipital regions are intimately associated with dream cessation, then the current findings of intact dreaming in patients with lesions in exactly these regions raises concern about the accuracy of these conclusions. Bischof and Bassetti's (2004) case demonstrated posterior thalamic involvement, which was the single common brain region in all three non-dreamers in the current study. Thalamic involvement was absent in all four dreaming participants. The only other recent case study is that of Martí-Massó (2006). It describes a case of a haemorrhagic AVM, which cannot convincingly be used as evidence for focal damage, due to inherent haemo-dynamic perfusion alterations that occur when an AVM bleeds. Therefore, thalamic involvement cannot be excluded in this case.

The regional thalamic involvement is interesting in itself. In all cases of dream cessation, including Bischof and Bassetti's (2004) case, the posterior region of the thalamus was involved. The posterior region of the thalamus is comprised of the pulvinar (Standring, 2016), which is strongly connected with the parietal lobe, which it modulates (Arcaro, et al. 2015) (Figure 5.1).

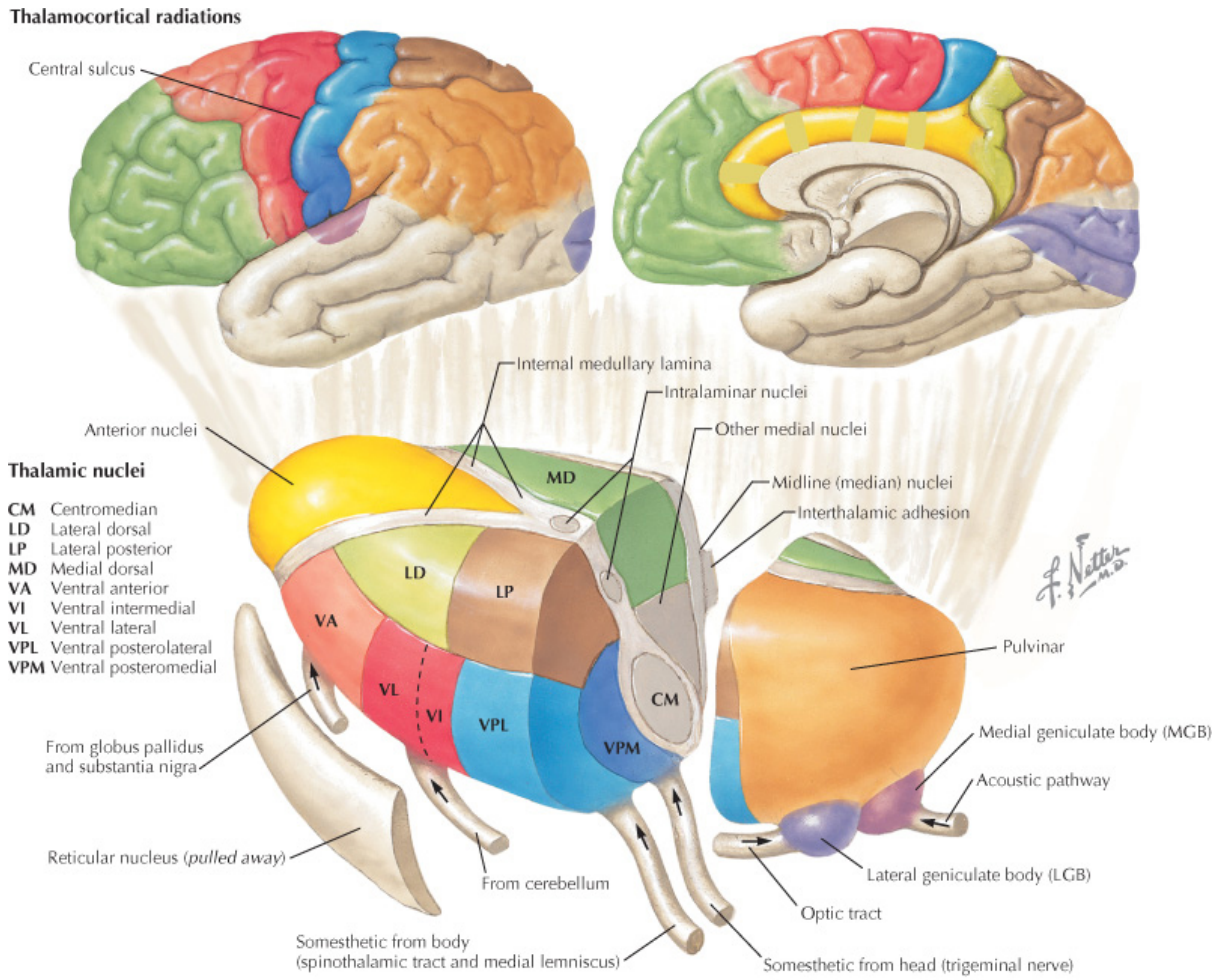

Figure 5.1: Illustration of the thalamocortical radiations. The pulvinar of the thalamus is demonstrated here in orange. The associated cortical innervation of the parietal lobe is demonstrated in corresponding orange.

Parietal cortical dysfunction has previously been attributed to involvement of the pulvinar of the thalamus, as in the case report by De Gobbie Porto et al. (2012), where a patient demonstrated alexia and agraphia, which is classically associated with left angular gyrus (cortical) lesions; but the patient had a circumscribed thalamic haemorrhage (sub-cortical) involving the left pulvinar of the thalamus (De Gobbi Porto et al., 2012).

Solms' (1997) assertion that parietal mechanisms are related to total dream cessation (Wilbrand's variant) - and therefore the distinction between unimodal (occipital) and heteromodal (parietal) variants of the Charcot-Wilbrand syndrome - still stands, therefore, as thalamic pulvinar dysfunction is likely related to distal parietal dysfunction, due to the pulvinar's innervation of the inferior parietal lobe.

4.6) Future directions

The case study published by Bischof and Bassetti (2004) and the current case comparison, are currently the best evidence available of possible parietal mechanisms in total dream cessation, in an exceedingly rare clinical population. It is, therefore, difficult to make definitive deductions concerning the posterior cortical locus of dream cessation. Continued observation of posterior cerebral pathology should take place to determine whether there is evidence of global cessation of dreaming with *focal* medial occipital pathology.

Solms' 1997 findings remain the best evidence for parietal (or at least posterior *convexity*) cessation of dreaming. Using a similar methodology as was used here, cases of circumscribed middle cerebral artery (MCA) infarction should now be observed, in order to clarify the fundamental contribution of the lateral posterior convexity in dreaming.

4.7) Concluding remarks

The current study describes the largest cohort of patients with REM-confirmed global cessation of dreaming after posterior cerebral artery ischaemic infarction, and it is the only comparison of patients with the same implicated vascular territory, who have confirmed intact versus lost dreaming. Solms' 1997 findings of parietal mechanisms underlying total cessation of dreaming stand, as current evidence suggests parietal circuitry (pulvinar parietal thalamocortical projections), and therefore dysfunction related to total dream cessation, as opposed to unimodal medial occipital cortical regions.

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