AGE-RELATED CHANGES IN PREFRONTAL CORTEX FUNCTION: LINKS BETWEEN SLEEP EEG AND COGNITION

by

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Abstract

Healthy ageing has been found to be accompanied by changes in slow wave activity (SWA) and cognitive function. Furthermore, these changes have been seen predominantly in the prefrontal cortex (PFC) compared to other regions of the cortex. Current theories of cognitive ageing propose that this occurs due to a specified deterioration of neuronal substrates of the PFC, and as such, changes in SWA and cognitive function may decline at similar rates due to similar underlying aetiology.

The main aim of the current thesis was to explore age-related differences in electroencephalographic (EEG) SWA during the first NREM period and cognitive performance that relies on the integrity of the PFC: executive function and social cognition. The extent to which executive function (reliant on dorsolateral PFC areas) and social cognitive function (reliant on ventromedial PFC regions) show similar age-related deterioration was investigated in Study 1. Here, 16 young (22.2 years) and 16 older (71.5 years) adults were administered with a cognitive testing battery including executive function measures: Verbal Fluency (VF) and Tower of London (TOL); as well as measures of social cognition: Go/No-go, Emotional Prosody and Ekman 60 Faces. Not all measures of PFC function were affected to the same extent. The older group performed significantly worse on the TOL, but not on the VF test. Additionally, simple aspects of social cognition did not display differences between the groups, but the older group performed significantly worse than the young group on more complex aspects of recognition of emotion from facial expression (Ekman 60 Faces) and Emotional Prosody.

As most studies of cognitive ageing are cross-sectional and show large age-related changes, the remainder of this thesis focused on age-related changes using a longitudinal design over a relatively small ageing period (mean = 6.29 years). The average age of participants at baseline was 67.1 years and the average age at follow-up was 73.4 years. In Study 2, in a

sample of 11 participants, performance on executive function tests was measured (TOL, VF and Wisconsin Card Sorting Test: WCST). As found in the cross-sectional analyses reported in Study 1, the TOL task was found to be the most sensitive indicator of age-related changes, as this showed a decline with age; whereas, VF and WCST remained stable over time. Furthermore, in Study 3, localised SWA was recorded via EEG, and significant declines were found in low frequency delta (0.5 – 1 Hz), which was localised to the left frontal region.

While reductions in EEG-determined-SWA from the left frontal region and performance on tasks known to rely on left frontal region (i.e. TOL) were found at the 6.29 year follow-up, it is important to establish whether one can predict this decline from biomarkers at baseline. Previous analysis of this sample (Anderson & Horne, 2003) revealed low frequency delta in the left PFC (LPFC) to be a marker of left frontal cognitive function. As such, it was hypothesised that LPFC low frequency delta may best predict age-related changes in cognition associated with the LPFC. However, it was reported here that low frequency delta did not predict performance at follow-up on executive function measures. Furthermore, the relationship between EEG and performance as previously observed failed to persist at follow-up. Whether or not the relationship between low frequency delta and cognition originally observed by Anderson and Horne (2003) was coincidental or a functional one is inconclusive due to the homogeneity of the 'retained' group in follow-up analyses. Further exploration of the data hinted at individual differences (and possible 'protective' factors) in the extent to which localised EEG could predict localised cognitive function. Guided by literature, an explorative investigation into the plausibility of other biomarkers of prefrontal function (i.e. K-Complex density and spindle density) did not yield a particular link to cognition.

In summary, low frequency delta in the left frontal region and performance that relies on the integrity of the LPFC both show declines over a relatively short period of ageing (6.29 years). However, the ability to predict this decline based on these markers requires further work. Analysis of further

potential biomarkers for prefrontal function in healthy older people concludes that low frequency delta appears to be the most credible slow wave sleep EEG marker of PFC cognitive function in healthy ageing.

KEYWORDS: prefrontal cortex, ageing, sleep EEG, low frequency delta, cognitive function, sleep spindle, K–Complex, slow wave activity.

Dedication

This thesis is dedicated to Patrick Gifford: my partner and best friend. Thank you for your support.

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Abbreviations

ANOVA	Analysis of Variance
CBF	Cerebral Blood Flow
CCCF	Cattell & Cattell's Culture Fair Test
DLPFC	Dorsolateral Prefrontal Cortex
DSR	Delayed Serial Recall
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
ESS	Epworth Sleepiness Scale
fMRI	Functional Magnetic Resonance Imaging
IQ	Intelligence Quotient
KC	K-Complex
KSS	Karolinska Sleepiness Scale
LOPC	Left Occipital/Parietal Cortex
LORETA	Low Resolution Brain Electromagnetic Tomography
LPFC	Left Prefrontal Cortex
NREM	Non–Rapid Eye Movement
PET	Positron Emission Tomography
PFC	Prefrontal Cortex
PVT	Psychomotor Vigilance Test
rCBF	Regional Cerebral Blood Flow
REM	Rapid Eye Movement
ROPC	Right Occipital/Parietal Cortex
RPFC	Right Prefrontal Cortex
S1	Stage 1 (sleep)
S2	Stage 2 (sleep)
S3/4	Stage 3 and 4 (sleep)
SPECT	Single Photon Emission Computed Tomography
SWA	Slow Wave Activity
SWS	Slow Wave Sleep
TOH	Tower of Hanoi
TOL	Tower of London
TST	Total Sleep Time
U3A	University of the Third Age
VF	Verbal Fluency
VMPFC	Ventromedial Prefrontal Cortex
WASO	Wake After Sleep Onset

1 Introduction and Literature Overview

1.1 Aims

The overall aims of this thesis originate from a cognitive neuroscience perspective, in which there is an attempt to establish a link between cognition and biological substrates in a healthy older population. The observation that age-related degradation has been found in the brain, and to a greater extent in the prefrontal cortex (PFC) in comparison to other regions of the brain (Gerard & Weisberg, 1986; Haug et al., 1983; Terry, DeTeresa & Hansen, 1987), led to surge in research exploring the behavioural and cognitive manifestations of PFC ageing, and this interest persists to date.

A wealth of literature has accumulated indicating a dominant role of the PFC in executive function (e.g., Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001; Barceló & Knight, 2002; Glosser & Goodglass, 1990; Goldstein, Obrzut, John, Ledakis, & Armstrong, 2004; Milner, 1963; Monchi et al., 2001; Newman, Carpenter, Varma & Just, 2003; Owen, Downes, Sahakian, Polkey & Robbins, 1990; Peterson, van Miere, Fiez & Raichle, 1998; Ravnkilde, Videbech, Rosenberg, Gjedde, & Gade, 2002; Rezai et al., 1993). Furthermore, executive function has been found to be particularly vulnerable to cognitive ageing in healthy adults (e.g., Ardila, Ostrosky-Solis, Rosselli, & Gómez, 2000; Comptom, Bachman, Brand, & Avet, 1999; Davis & Klebe, 2001; Macpherson, Phillips, & Della Sala, 2002; Parkin & Walter, 1991; Robbins et al., 1998). Added to findings suggesting that age-related declines are found in slow wave activity (SWA) associated with the PFC (e.g., Carrier, Land, Buysse, Kupfer, & Monk, 2001; Dijk, Beersma, & Hoofdakker, 1989; Landolt, Dijk, Achermann, & Borbély, 1996), a picture has emerged that suggests that SWA originating in the PFC and cognitive function associated with it, share a common path of decline with age. Whether or not this shared path indicates a functional relationship or not,

remains equivocal, as few researchers have attempted to explore both SWA and cognitive function in the same individuals.

Anderson and Horne (2003) were the first to explore the link between PFC localised SWA and PFC associated cognitive function in the same individuals. In an attempt to establish a sleep electroencephalography (EEG) marker of 'healthy' cognitive ageing, they found a relationship between relative percentage of low frequency delta in the PFC and performance on PFC tests of executive function, in that greater power of low frequency delta was predictive of better performance. However, although the study involved the testing of an older cohort, the study was never intended to be one of ageing.

One of the main aims of the studies presented in this thesis is to bridge the gap between two dominant domains of PFC ageing research (sleep and cognition), by using a longitudinal observation of an older cohort. This is with the purpose of elucidating more about the relationship between SWA and cognition, and the way that this develops over time, as well as providing further evidence of a biomarker of cognitive decline (e.g., Anderson & Horne, 2003).

Another main aim of the thesis is to attempt to expand research in the area of cognitive ageing with PFC specificity. Observations of age-related declines in cognition associated with the PFC have typically been isolated to aspects of executive function. However, recent attention is now turning to social cognition since recent advances in social neuroscience show social abilities to also rely on the integrity of the PFC (e.g., Goldstein et al., 2007; Horn, Dolan, Elliott, Deakin, & Woodruff, 2003; Hornak et al., 1996; Mitchell, Elliott, Barry, Cruttenden, & Woodruff, 2003; Nakamura et al., 1999; Rubia et al., 2001; Wildgruber et al., 2005).

1.2 Slow Wave Sleep is for the Prefrontal Cortex

The focus of this thesis is the exploration of age-related changes in cognitive functions associated with the PFC, age-related changes in slow wave sleep (SWS) associated with the PFC and to ascertain a link between the two indices (a review of the relevant literature will be presented in sections, 1.3, 1.4 and 1.5, respectively). Before the question of whether sleep EEG can be established as a marker of cognitive decline can be investigated, literature around the assumption that 'SWS is for the PFC' will be reviewed.

1.2.1 Introducing the Prefrontal Cortex

The PFC, referred to as the 'organ of civilization' by Luria (1966), is considered to be the seat of cognition believed to be unique to the human being. The PFC has undergone the most considerable increase in fissures and convolutions (and therefore in surface area) in humans from non-human primates (Bok, 1959) in comparison the other regions of the neocortex. In evolutionary terms, this is proposed to support the advancement of higher order cognitive functions.

The PFC furthermore, is the most abundantly connected region of the cortex, receiving reciprocated afferent fibers from other regions of the neocortex; brainstem; hypothalamus; limbic system (amygdala and hippocampus); and thalamus (Fuster, 1999). Investigators have proposed a number of models to explain the functions of the PFC, largely based on patients with PFC injury. Levine, Stuss, and Milberg (1995) suggest that the PFC, in particular the dorsolateral PFC (DLPFC), is involved in 'executive' characteristics such as forming mental sets, sequencing behaviours and integrating behaviour. Others have suggested that the ventromedial PFC (VMPFC) on the other hand, is involved in motivation, drive, will (Stuss, Shallice, Alexander, & Picton, 1995), in selecting appropriate social behaviours and making social decisions (Damasio, 1994).

Attempts to differentiate regions of the PFC vary amongst researchers. Some dissect the PFC into two main regions based upon connectivity with the mediodorsal (MD) nucleus of the thalamus (Nauta, 1971). Magnocellular afferents projecting from the MD nucleus mainly terminate in the VMPFC, whereas parvocellular afferents are received by the DLPFC (Goldman-Rakic & Porrino, 1985). The most commonly utilised differentiation of region of interest comes from Brodmann areas. These loosely correspond to the types of neurons and connections that are characteristic of that region. However, there is some variation in the literature as to which Brodmann areas (BAs) constitute the DLPFC and VMPFC. The DLPFC is often ascribed to areas 8, 9, 44, 45, 46 and 47 (Muzur, Pace-Schott & Hobson, 2002); however, when considering the VMPFC, more controversy exists. According to Muzur et al. (2002), the VMPFC encapsulates BAs 11, 25, 24, 32 and 33; whereas Eslinger (1999) includes BAs 10, 11, 12, 13, 14 and 47. Figure 1.1 gives an approximate visual representation of Brodmann's map.

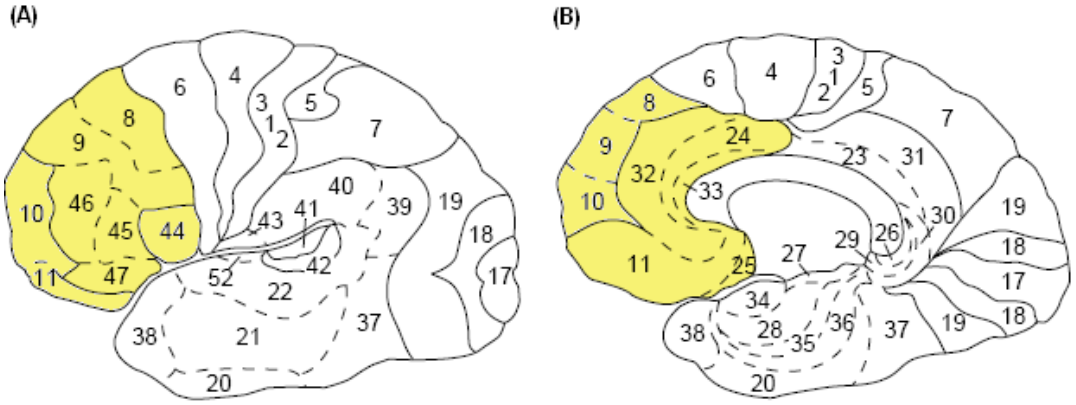

Figure 1.1: The Brodmann Classification of regions (shown in the left hemisphere) in (A) lateral view and (B) mid-sagittal view. Dorsolateral and ventromedial regions of the PFC are highlighted in yellow.

1.2.2 Effects of Disrupted Sleep on Cognition

The typical picture that has emerged over recent years is that the PFC is sensitive to changes in sleep, and particularly benefits from it. The effects of disrupted sleep on the function of the PFC have been demonstrated in paradigms in which tasks believed to be subserved by the PFC are selectively impaired as a result of sleep deprivation.

Much of what has been discovered about the structure of sleep has been gained from the use of the EEG first described by Hans Berger in 1929. The EEG is thought to be a measure of electrical fields recorded through the scalp, and has been found to be directly reflective of the activity of populations of neurons within the neocortex (Glenn, Hada, Roy, Deschênes & Steriade, 1982). The Rechtschaffen and Kales (1968) classification of sleep stages has been ubiquitously employed by researchers and clinicians in the identification of sleep stages via EEG. Their technique differentiates between five major sleep states. These are rapid eye movement (REM) sleep characterised by high frequency and low amplitude activity in the EEG, and non-REM (NREM) sleep stages 1 – 4, which correspond to the increasing depth of sleep. NREM sleep is composed of background activity over a broad range of frequencies, including slow waves and transient events such as spindles and K-Complexes (KCs); the former characterised by a progressively increasing, then gradually decreasing amplitude (waxing and waning) in the 12 – 14Hz range and the latter by a sharp surface negative component followed by a positive deflection.

Deficits as a result of sleep deprivation have been found in the performance of long, repetitive and monotonous tasks. Corcoran (1964) established, using a simple task in which participants were required to sort cards, that sleep loss (after 22hr and 46hr of continued wakefulness) elicited deficits in performance, particularly when practice was given. This was in concurrence with earlier findings in which the effects of one night's loss of sleep resulted in decrements on a reaction time test which worsened with increased exposure to the test (Wilkinson, 1961). It was believed that sleep deprivation had a particular negative impact on tasks where motivation was low, due to boredom (Webb & Levy, 1984). From this point of view, it might be that tests that are short and more cognitively challenging might elicit more motivation from individuals that are sleep deprived, and thus result in preserved functioning.

In contrast to this however, Harrison and Horne (1998) found that sleep deprivation (in excess of 34 hours) resulted in impaired ability to generate innovative responses in a semantic verbal fluency test, and decreased response inhibition when faced with the requirement to inhibit an obvious response on the Haylings test. The former test involved the generation of as many associated verbs as possible in response to a given noun. The Haylings test (Burgess & Shallice, 1996) involved the completion of a given sentence with either a word that was congruent or incongruent to the context of the sentence. Harrison and Horne argued that as these tests of executive function were associated with the PFC, that it demonstrated the detrimental effects of prolonged wakefulness on the integrity of PFC function. Evidence pertaining to the association between executive function and the PFC is reviewed in section 1.3.2.

Nillson et al. (2005) administered a battery of short tests to a group that had undergone 31-32hrs of sleep deprivation. One of the tests targeted executive function abilities: the Six Elements test (SET) and was deemed to be a measure of everyday planning and organisation (Burgess & Shallice, 1996). The other two were presumed to be non-PFC specific and involved measures of memory (involving components of both episodic and verbal working memory) and reaction time. Compared to a control group, the sleep deprived group performed significantly worse on the SET test, whilst the reaction time and memory test performance remained intact. One interpretation of these results in combination of those of Harrison and Horne (1998) would be that executive function associated with the PFC is selectively impaired by prolonged wakefulness. Furthermore, these effects might be present in the absence of deficits on tests that are non-PFC specific, particularly when these tests are not administered in a manner that promotes loss of motivation (e.g., such as repetition).

As to why waking PFC function is particularly vulnerable to the detrimental effects of sleep deprivation has been the cause of much speculation amongst researchers regarding the potential of a functional link between sleep and cognition. Horne (1992) hypothesises that sleep particularly

benefits cognition subserved by the PFC. Muzur et al. (2002) suggested that during SWS, the PFC is offered “passive respite” by undergoing deactivation to recover its cognitive functions (p. 475). This would explain why extended wakefulness would result in decrements in PFC associated functions.

1.2.3 Cortical Deactivation during Slow Wave Sleep

A dominant method utilised for identifying levels of cortical activation in waking and in sleeping is via the observation of levels of cerebral blood flow (CBF). CBF is a measure of blood supply in the brain and it is widely accepted that it is tightly linked to neuronal activity; increased CBF reflects increased synaptic activity. Via Positron Emission Tomography (PET) observations, increased synaptic activity has been found to cause an increase in glucose uptake and subsequent localised increases in blood flow (Fox, Raichle, Mintun & Dence, 1988). As distribution of neuronal activity is not homogenous across the cortex, and some areas demonstrate greater levels of activity than others, regional CBF (rCBF) has been utilised to reveal neuronal activation in specific brain regions under waking and sleep states.

Münch et al. (2004) provided evidence that suggested that delta is tied to previous waking. They observed that in baseline sleep, young adults had greater relative delta power in the range of 1.25 – 3.75 Hz in frontal regions in comparison to parietal regions, which the authors interpreted as increased requirement for SWA in frontal lobes after normal sleep. An augmentation of delta in this range was found in the recovery sleep received after 40 hours of sleep deprivation, the most substantial increase being in the frontal regions. These findings therefore indicate that the requirement of delta to support waking activity may be greater in the frontal lobes, which are particularly vulnerable to the effects of prolonged waking.

Clark et al. (1998) attempted to assess the relationship between delta during sleep and waking CBF as assessed by Single Photon Emission Computed Tomography (SPECT). Although largely flawed due to small sample sizes and failure to correct for substantial multiple comparisons, the findings

interestingly demonstrated that there were positive correlations between amount of SWA during sleep at night and waking CBF. Thus indicating that greater levels of delta may be required to support greater levels of cortical activity during the waking hours.

However, Maquet et al. (1997) criticised studies in which waking CBF is compared with SWS CBF; waking is associated with its own CBF, therefore potentially confounding the results. In their study they looked at the areas in which the greatest levels of depression were found during SWS. They reported negative correlations between rCBF using Positron Emission Tomography (PET) with the presence of stages 3/4 in the following regions: VMPFC (BAs 11, 24, 25); the precuneus and mediotemporal regions (BAs 7, 19, 28); subcortical structures (pons, mesencephalon, basal ganglia and basal forebrain/hypothalamus). Also concerned with the association between SWA and cortical deactivation, Hofle et al. (1997) observed the relationship between normalised rCBF (via PET) with absolute EEG in the transition from waking to SWS. Significant decreases in normalised rCBF as a function of delta (1.5 – 4.0 Hz) were found. Areas found to undergo the greatest levels of deactivation were the VMPFC (BA 11, 24, 32), as well as bilateral cerebellar hemispheres, midline base of pons and left temporalis muscle. The most significant decrease was found in the medial thalamus. Therefore, as rCBF decreased, delta activity increased concomitantly in these regions, indicating regions of deactivation.

Although using different techniques, the implication in both studies by Hofle et al. (1997) and Maquet et al. (1997) of the VMPFC undergoing the greatest cortical deactivation is consistent, as was the deactivation of subcortical regions. The deactivation of subcortical regions was suggested by authors of both studies to be due to the role of these structures in the thalamo-cortical[1] generation of delta. Maquet et al. speculated that due to the particular deactivation of the PFC during delta SWA, that functions

[1] This refers to the thalamo-cortical system, in which fibers irradiate between the thalamus and cortex.

associated with that region would be at greater vulnerability of sleep loss. The authors were however, at a loss as to why there were no significant levels of deactivation in the DLPFC. This would be expected when considering that executive functions associated with that area are vulnerable to the effects of sleep loss (e.g., Harrison & Horne 1998; Nillson et al., 2005). The authors of both suggested that this may have been due to a small sample size, and may have been found to be significant with greater statistical power.

In summary it was found that:

i) Daytime activity is tied to amount of delta during sleep (Clark et al., 1998; Münch et al. 2004).

ii) Cortical deactivation during SWS is not homogenous and is greater in some brain regions (particularly the VMPFC) than others (Hofle et al., 1997; Maquet et al., 1997).

The attenuation of neuronal activity with SWA appears to be greatest in the PFC, in comparison to other regions of the cortex. This is hypothesised to be in order to support daytime cognitive function, as it is associated with deactivation processes.

1.2.4 Plasticity during Slow Wave Sleep

Another perspective on the link between SWA and cognition is that rather than SWA having the function to provide "passive respite" (Muzur et al., 2005, p. 475) to the cortex, that it provides a more active, use-dependent function associated with synaptic plasticity. Plasticity refers to changes in synaptic connections such as weakening and strengthening (Hebb, 1949), and is crucial to support cognitive function, as it supports learning and the potential ability of brain structures to reorganise following damage (e.g., transference of function from one brain structure to another). According to Tononi and Cirelli (2003) enhanced SWA may reflect a cellular need for sleep; in that it is required to support synaptic plasticity. They stated that "…the homeostatic regulation of slow-wave activity is tied to the amount of

synaptic potentiation that has occurred during the previous wakefulness." (p. 144).

Kattler, Dijk and Borbély (1994) found that vibration of the right hand during waking caused enhanced inter-hemispheric asymmetry in the subsequent nights' sleep EEG of the contralateral hemisphere (specific to C_3-A_1); the right hand vibration caused increases predominantly in the delta frequency range (0.75 – 4.5 Hz) in the somatosensory cortex involved in right hand movement. This was interpreted as localised processes being activated during delta to support waking increases in activity (thus, increased synaptic potentiation). Also, a declarative learning task (paired-associates recall) compared to a non-learning control task caused a significant increase in spindle density (number of spindles per minute) in participants' EEG during subsequent stage 2 sleep in the first 90 minutes after sleep onset (Gais, Mölle, Helms, & Born, 2002). Furthermore, the largest increase was observed in the PFC. The authors offered support for the hypothesis posited by Kattler et al., that aspects of sleep provide a use-dependent function, supporting previous activity. However, an alternative interpretation of these results is that increases in SWA concomitant to increases in daytime activity, are due to metabolic fatigue as a by-product of enhanced synaptic potentiation. Establishing a functional relationship between synaptic plasticity and SWA is challenging, particularly as the processes involved in such can not be directly observed.

1.2.5 Summary

It has been argued that the PFC benefits from SWA, and is negatively affected by the disruption of it. This has been demonstrated in sleep deprivation paradigms (e.g., Harrison & Horne, 1998; Nillson et al., 2005). It is difficult to ascertain whether the functional significance of SWA is for synaptic plasticity enhancement, or whether it is due to restoration of function via passive respite. The mechanisms as to why SWA and cognition are associated are unclear; however the evidence for a link between the two domains is compelling, to the point as to suggest that SWA as a marker of

cognitive function is plausible. The remainder of the literature review is concerned with the observation of similar paths of decline with older age in cognitive function, and in SWA and associated components.

1.3 Age-Related Changes in Cognitive Function: A PFC Focus

1.3.1 Frontal Lobe Modifications

General changes in the brain have been found with increasing age. These have included rapid decreases in brain weight after 80 years of age (Ho, Roessmann, Straumfjord & Monroe, 1980), as well as a progressive loss of dendrites, and increase in neuronal swelling and cell death (Scheibel, Lindsay, Tomiyas & Scheibel, 1975).

The PFC in particular is thought to deteriorate earlier and to a greater extent than other brain regions (Haug et al*.,* 1983). Evidence for this has included a decrease in the number of large neurons as well as cortical thickness, to a greater extent in the PFC than in other regions of the cortex (Terry et al., 1987). Furthermore, demyelination of white matter has also been found in the subcortical PFC with ageing (Gerard & Weisberg, 1986). The extent to which these structural changes may manifest into cognitive changes are investigated in section 1.3.3.

1.3.2 The Role of the PFC in Executive Function and Social Cognition

Possibly the most famous instance of injury to the PFC and the effects on behaviour comes from the much cited case of Phineas Gage (Harlow, 1848). Gage was injured after a lead rod was driven through his frontal lobes in a railroad explosion, which appeared to result in no long-term ill effects at the time. However, it was later reported by Harlow (1868) that Gage had undergone a personal transformation in which he had begun to demonstrate socially undesirable behaviour that he had not done so prior to the incidence (e.g., using ‘profane’ language in front of fellow employees

and displaying inpatient and impulsive behaviour). According to his colleagues, he was “no longer Gage”.

The PFC has for a long time been considered as contributing to the identity of an individual. After it was observed in chimpanzees that aggression could be subdued after the severing of the PFC from other regions (e.g., Crawford, Fulton, Jacobsen & Wolf, 1948) ‘prefrontal lobotomies’ have been widely used to remedy psychiatric disorders including anxiety, insomnia and nervous tension (Freeman & Watts, 1937), as well as severe depression (Worchel & Lyerly, 1940). Not all were considered to be a success. For example, 7 of the patients ‘treated’ by Worchel and Lyerly were reported as becoming so hyperactive and excitable post-operation that they had to remain hospitalised or institutionalised.

These cases demonstrate instances of general changes in personality and social functioning, and indicate little about the underlying changes in cognition that may account for it. More recent brain injury studies have pinpointed more specific changes in higher cognitive function associated with the PFC. Standardised clinical assessment of PFC functions, have typically investigated executive function, which broadly refer to cognitive processes involved in planning, cognitive flexibility and rule acquisition (Stuss & Knight, 2002). These tests include the Wisconsin Card Sorting Test (WCST), Verbal Fluency (VF) and Tower of London (TOL). The validity of these tests has been established through the use of lesion studies, and more recently through the use of brain imaging techniques. More recent interest has also been generated, pertaining to the role of the PFC in social cognition. According to Amodio and Frith (2006), social cognition refers to “... knowledge about the self, perceptions of others and interpersonal motivations ...” (p. 268).

Executive Function –

The WCST is proposed to involve hypothesis generation, as well as aspects of working memory (Aron, Robbins & Poldrack, 2004) and was developed by Grant and Berg (1948) as a measure of PFC dysfunction. The test

generally requires sorting cards to categories: colour, number and shape. Sorting rules change throughout the task without prior notification to participants (although positive and negative feedback is given), therefore requiring reactive flexibility in cognition and behaviour in order to appropriately respond to the demands of a change in situation (Eslinger & Grattan, 1993). The VF task requires the participant to generate as many words that are related to another given word or letter as possible. There are two dominant versions of the task (phonemic and semantic). Phonemic VF, involves the generation of words that begin with a specified letter (e.g., “p”, to which one might respond “pencil”, “pear”, and so on...). Semantic VF involves the generation of words that belong to a semantic category (e.g., “apple” might prompt the generation of “peel”, “eat”, “bite”). The VF has been viewed as a measure of spontaneous flexibility, that is “... the ready flow of ideas and answers, often in response to a single question. Encompassing the notion of “fluency”... requires divergent thought and production.” (Eslinger & Grattan, 1993, p. 18). The Tower of London (TOL) is primarily a measure of non-verbal planning (Shallice, 1982), in which participants are presented with a tower with pegs of various sizes and beads of various colours. In this task, participants are required to solve a number of problems that involve moving the beads into a different formation in a specified number of moves.

Lesion studies have shown that the WCST is sensitive to PFC function. Milner (1963) found that performance on the WCST was impaired in patients with DLPFC lesions. The patients were more susceptible to stuck in set tendency: a series of all perseverative errors (perseverative errors are incurred due to failure to change category after negative feedback is received). In another study it was found that six patients presented with more perseverative errors on a computerised version of the task, in comparison to healthy controls (Barceló & Knight, 2002). Furthermore, in that study, all lesions were situated in the left hemisphere. To support the specificity of WCST sensitivity to the LPFC, Goldstein, Obrzut, John, Ledakis, and Armstrong (2004) found that patients with injury to the left frontal regions were more prone to making perseverative errors in

comparison to those with injury to the right frontal cortex, to other brain regions, or when compared to healthy controls. One interpretation of these findings is that integrity of the left but not the right PFC is necessary for functioning of the WCST. To this end, when Goldstein et al. (2004) compared all frontal patients to non-frontal patients or healthy controls there were no significant differences in perseverative errors incurred.

Monchi et al. (2001), decomposed the WSCT, and observed brain activation during different stages of the task. In comparison to a control task in which identical cards were matched, receiving feedback (both negative and positive) on a computerised version of the WCST resulted in increased activation in the bilateral mid-dorsolateral PFC (BAs, 9 and 46). Further increases in activation were seen specifically in response to negative feedback in the mid-ventromedial PFC (BAs, 47 and 12), caudate nucleus and mediodorsal thalamus. According to the authors, the difference in activation between the two stages of the task was due to the greater demands of receiving negative feedback; negative feedback signals a necessity to shift to a new response (avoidance of perseverative errors), whereas positive feedback requires monitoring the contents of working memory.

Patients with frontal lesions were found to demonstrate a deficit in the performance on both semantic and phonological versions of the VF task, in that they were unable to generate as many words as a healthy control group (Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001). It was additionally reported in that study that those with LPFC lesions demonstrated greater impairment on both versions of the task in comparison to those with right PFC (RPFC) lesions, indicating that the left hemisphere may be more relevant to successful performance on this task.

Brain imaging revealed that on a phonological version of VF, increased activation was found (via PET with $H_2{}^{15}O$) in the DLPFC (BAs 9, 44, 45); the VMPFC (BAs 11, 24, 25, 32, 47); the supplementary motor area (BA 6); temporal and parietal/occipital regions (BAs 7, 19, 21 and 38); and the

thalamus and cerebellum (Ravnkilde, Videbech, Rosenberg, Gjedde, & Gade, 2002). With the exception of BAs 32 and 47 (which were activated bilaterally), increases observed in the PFC were lateralised to the left hemisphere. In line with these findings, Peterson, van Miere, Fiez and Raichle (1998) observed that in response to the completion of a verb generation task associated with semantic processing, regions of significant increases in activation were: the left frontal regions; the anterior cingulate cortex (of the VMPFC); and right hemispheric cerebellum.

Owen, Downes, Sahakian , Polkey and Robbins (1990), observed deficits in performance on the TOL in patients with lesions isolated to the frontal lobes, in comparison to healthy controls. Although there were no differences between groups in ability to solve each problem, the frontal lobe patients were less efficient. They took significantly more moves to complete each problem, as well as having prolonged completion times. Furthermore, they found no lateralisation to the left or right hemisphere of functioning on the task. This was at odds with findings by Glosser and Goodglass (1990); they found that deficits on the TOL appeared to be more common after lesions to the LPFC, in comparison to the RPFC. Differences in implication of lateralisation might be explained by differences in lesion location or size, underlying aetiology, etc, however.

Imaging evidence (SPECT) in support of the bilateral involvement of the PFC in TOL performance, indicated that regions with significant increases in blood flow included the left and right mesial frontal cortex as well as some parietal regions (Rezai et al*.,* 1993). Using Functional Magnetic Resonance Imaging (fMRI), a more sensitive imaging technique, Newman, Carpenter, Varma and Just (2003) confirmed bilateral involvement during completion of the TOL. Regions of activation included the DLPFC (BAs 8, 9, 44, 45, 46), the VMPFC (BA 10), the superior parietal cortex (BAs 5 and 7) and inferior parietal cortex (BAs 39, 40). The authors speculated that the left and right DLPFC are involved in different capacities of TOL performance: the left involved in execution and the right more dominantly in planning.

Social Cognition –

Mentalising is the process of understanding that the actions of others' are driven by their knowledge of the world and not actually the state of that world (Amodio & Frith, 2006). This helps us to predict the behaviour of others. Human social communication can involve strong nonverbal elements such as facial and body gestures as well as prosodic cues in the voice (Nakamura et al., 1999). Prosody refers to the rhythmic and melodic intonation in speech, which contributes to the social and emotional meaning behind language. According to Carton, Kessler and Pape (1999), the ability to interpret emotional cues from tone of voice and facial expression is important in the self-reported success of relationships and is associated with self-reported lower levels of depression.

Recent research in the area of recognition of emotion has particularly focused on emotion in facial expression, such as those utilising a range of photographs as stimuli (commonly from the Ekman & Friesen series, 1976). It requires participants to label (from a choice of emotions) the emotion expressed in each photograph. Measures of emotional prosody have been developed in which participants are required to state the emotion of the speaker as recognised by prosody alone. This may be in the presence of congruent cues in the content of the sentence (e.g., "My dog had to be put down", spoken in sad prosody) or in the presence of cues that are incongruent (e.g., "My dog had to be put down" spoken in happy prosody). The latter may be more analogous to more complex forms of social function such as recognition of irony and sarcasm in others (what is spoken may not always concur with the intention of the speaker).

Inhibition is an important aspect of social cognition, as it requires ignoring irrelevant information and suppressing responses that are inappropriate (Aron et al., 2004). The Go/No-go paradigm is utilised as a measure of response inhibition. In that task, the participant is exposed to (usually visually) to continuously presented series of stimuli comprising of target 'Go' stimuli and distracter 'No-go' stimuli. Participants are instructed to respond (by pressing a button) to 'Go' stimuli' and to ignore 'No-go' stimuli. The task

yields a measure of inhibition, particularly as 'Go' and 'No-go' stimuli switch between trials so that what was once the target, becomes the stimulus to be ignored; thereby requiring the participant to inhibit a prepotent response. According to Amodio and Frith (2006), the Go/No-go paradigm is relevant to behavioural regulation in the context that actions must be monitored to ensure that they are consistent with intention. When 'No-go' stimuli is substituted with affective stimuli (e.g., words with emotive connotations such as 'elated' and sorrow'), processing these, compared with neutral stimuli (e.g. 'village' and 'enter') can be observed. It allows a measure of response inhibition in the context of emotional modulation.

Hornak et al. (1996) utilised a test involving recognition of emotion via facial expression, to measure ability of patients with frontal lobe injury to correctly identify a range of emotions. Participants were instructed to label faces, from the options of sad, angry, disgusted, frightened, surprised, happy or as neutral, as taken from the Ekman and Friesen (1976) series. Patients with lesions to the ventral frontal region correctly identified fewer emotions (using a composite score) than those that had lesions to other regions. In this vein, Nakamura et al. (1999) found that the explicit identification of emotion from facial expression (from the choice of calm, angry, happy and sad) compared to a colour discrimination task caused significant increases in activation (using PET $H_2{}^{15}O$) in the right inferior frontal cortex and left orbitofrontal cortex of the PFC, as well as the lateral occipital cortex of both hemispheres. Comparison of performance on the emotion identification test, to an alternative test in which participants had to rate attractiveness caused significant activations in the right inferior frontal cortex only. Therefore, there appears to be a strong association between PFC activity and specific identification of emotion in contrast to other visual discrimination paradigms.

Utilising a basic version of the Emotional Prosody paradigm, Hornak et al. (1996) found that patients with ventral frontal lesions, compared to patients with injury to other regions were found to exhibit deficits in the encoding of emotional intent reflected in vocal expression. Due to the level of functioning in the patients and the inherent complexity of recognition of intention of

speaker via emotional prosody in the absence of facial expression, stereotyped emotional vocalisations (rather than spoken sentences) were used in this study to express the emotions sad, angry, frightened, disgusted, puzzled, contented and neutral (e.g., sobbing to express the emotion sadness). Although, being a simplified aspect of social communication, it does indicate the role of the ventral frontal regions in recognition of emotion via vocal expression.

Mitchell, Elliott, Barry, Cruttenden and Woodruff (2003) using the blood oxygen-level dependent (BOLD) fMRI technique found that whether the emotional prosody of a speaker and the content of the sentence being spoken was congruent or incongruent implicated different brain structures. Sentence scenarios were either sad (e.g., “the dog had to be put down”) or happy (e.g., “she had won the lottery”); spoken in either a sad, happy or neutral prosody. When scenario and emotional prosody matched (congruent), compared to a resting state, there was increased activity in the right hemispheric DLPFC (BAs 44, 46), middle temporal gyrus (BA 21), inferior parietal lobule; as well as increased activation in the left hemispheric superior temporal gyrus (BA 22). When scenario and emotional prosody did not match (incongruent), compared to resting, there was increased activation in the bilateral medial temporal gyrus (BA 21) and postcentral gyrus (BA 2).

Results found by Mitchell et al. (2003) are unexpected as the incongruent stimuli resulted in less activity than congruent stimuli. Presumably recognition of incongruent stimuli would create greater cognitive demands. It would also be expected that due to the social relevance, that frontal regions would have been activated. One explanation is that in the paradigm the participants were instructed to listen passively, rather than attempt to identify emotion. Furthermore, when attending to incongruent stimuli participants were instructed to focus on content of the sentence spoken, whereas for congruent they were asked to focus on emotional prosody; therefore, precluding any clear interpretation of brain activation during identification of emotional prosody in the presence of incongruent cues.

Using an emotional prosody paradigm arguably more analogous to social interaction rather than passive exposure to stimuli, Wildgruber et al. (2005) instructed participants to explicitly identify the emotion expressed during presentation of stimuli whilst undergoing fMRI. Stimuli consisted of declarative sentences with a neutral content spoken in the prosody of happiness, anger, fear, sadness or disgust. Regions of marked activation included the DLPFC (BAs 9, 44, 45, 46, 47); the VMPFC (BAs 24, 32) extending to supplementary motor areas (BAs 4, 6); parietal regions (BAs 3, 7, 40), temporal regions (21, 22, 41, 42); the thalamus; and cerebellum. No differences were observed for specific emotions. However, this may have been due to the temporal resolution of imaging techniques being relatively poor and might not necessarily indicate that the encoding of all emotions activate the same regions.

The extent of involvement of the PFC has also been explored, in regards to the Go/No-go response inhibition paradigm. Horn, Dolan, Elliott, Deakin, and Woodruff (2003) found that by using BOLD fMRI, that when regional activation associated with ‘No-go’ distracter stimuli was compared to ‘Go’ target stimuli, significant increases were found in the DLPFC (BAs 8, 9, 45, 47), the VMPFC (BAs 10, 11), parietal/occipital regions (BAs 7, 18, 31, 38) and in the superior temporal gyrus (BAs 40). Increases were the most significant in the VMPFC. Rubia et al. (2001) using the Go/No-Go during fMRI, also found that there was increased activation primarily in PFC regions. These included the DLPFC (BAs 8, 9, 44, 45) and the VMPFC (BA 32) and extended to the supplementary motor area (BA 6), as well as parietal/occipital regions (BAs 7, 18, 19, 40). Miller and Cohen (2001) described the PFC involvement in inhibition of response as like a signalman at a railway junction, directing traffic towards different outcomes.

Interestingly, whether or not the ’No-go’ (distracter) stimuli was emotive in context (e.g., positive or negative words presented visually) had an effect on the activation of fronto–limbic as ascertained by fMRI (Goldstein et al., 2007). When the stimuli carried negative compared with neutral connotations, there was increased activation in the VMPFC (BAs 11, 25);

the DLPFC (BAs 9, 45, 46); and extensive activation in limbic and temporal structures (BAs 20, 22, 36, 37, 40–42, 46). When the stimuli carried with it positive compared to neutral connotations, the same PFC regions underwent increased activation as with negatively worded stimuli, along with the amygdala and supramarginal gyrus. The increased implication of the PFC when the stimuli is emotive might indicate even greater difficulty in response inhibition with compromised PFC function when the 'No-go' stimulus is emotive in comparison to neutral. According to the authors, this has relevance to behavioural regulation within the context of emotional processing.

Interestingly, executive function and social cognition appear to be dominantly associated with the PFC. Interestingly, executive function has been primarily associated with the DLFPC and social cognition with the VMPFC. Unfortunately, it is often difficult to ascertain the role of the orbitofrontal cortex (located in the VMPFC) in cognition using imaging techniques due to the air-tissue interface of the perinasal sinuses making it difficult to observe this region (Wildgruber et al., 2005). Therefore, activity in the VMPFC may be underreported in response to social cognition. Furthermore, empirical evidence suggests the right hemisphere might be more relevant to the encoding of emotional cues in others; whereas aspects of response inhibition and executive functions might be more dominantly associated with the left hemisphere.

1.3.3 Age-Related Changes in Executive Function and Social Cognition

Age-related changes have been observed on WSCT ability that have been reminiscent of the performance of individuals with frontal lobe pathology. For example, Parkin and Walter (1991) compared a group with a mean age of 33.9 years (*SD* = 6 years) and a mean age of 80 years (*SD* = 5.1 years) and reported that the older group accumulated a significantly greater number of perseverative errors and completed fewer categories than their younger counterparts. This was further supported by Macpherson, Phillips, and Della Sala (2002), who reported similar findings despite having a smaller age

difference between groups. The older group (mean age = 69.9 years, *SD* = 5.5 years), in comparison to a young group (mean age = 28.8 years, *SD* = 6 years) and middle aged group (mean age = 50.3 years, *SD* = 5.7 years) produced more perseverative errors, completed fewer categories, as well as demonstrated a greater failure to maintain a set. Comptom, Bachman, Brand and Avet (1999) found that in a sample of highly educated individuals aged 30 – 76 years of age there was a linear age-related decline on the WCST. This suggests that there is a gradual decline with increasing age, rather than a sudden 'drop–off' in later life that might be observed with cognitive ageing associated with pathology.

Significant age-related declines were found on both semantic and phonological VF, with those aged 66 – 85 years performing significantly worse (number of words generated) than the groups aged 16 – 30, 31 – 50 and 51 – 65 years (Ardila, Ostrosky-Solis, Rosselli & Gómez, 2000). Similar results were found when comparing a young (mean age = 33.9 years, *SD* = 6 years) and an older group (mean age = 80 years, *SD* = 5.1 years; Parkin and Walter, 1991). Henry and Phillips (2006) however, found that in young individuals (mean age = 22.3 years, *SD* = 6.54 years), compared to older individuals (mean age = 72 years, *SD* = 6.36 years), there were no significant difference on number of words produced in the semantic VF, whereas the older group performed significantly better on phonological VF. Therefore, although there is an implication of the PFC in VF, there appears to be some controversy in the literature as to the effects of ageing on this. This might be due to differences in measures such as whether the findings are based on phonological or semantic similarities. Furthermore, aspects such as education attainment impact greatly on performance of semantic and phonological versions of the task (Ardila et al., 2000), which may also contribute to the ambiguous age-related findings.

Age-related declines have also been found in the frontal lobe associated TOL test. Robbins et al. (1998) demonstrated age-related declines in performance on this measure in individuals aged between 21 – 79 years, that were found to be independent of 'global' cognitive ageing (as

ascertained by stability of fluid intelligence over time). Furthermore, longitudinal changes, after only a period of 6.5 years have been found on Tower of Hanoi performance (TOH; a test similar in concept to TOL) in a group aged 70 – 91 years at follow-up (mean = 81 years, *SD* = 6.6 years; Davis & Klebe, 2001). Thus, indicating the vulnerability of problem solving and planning ability to decrements over a relatively short ageing period.

Some researchers have suggested that whilst some aspects of cognition decline with age (i.e. executive function), increasing age is also associated with greater experience of decoding social cues and therefore, ageing should bring with it a development in social cognition (Magai, 2001). However, as many facets of social cognition have been associated with PFC function it would be plausible that these social abilities may be vulnerable to cognitive ageing. However, much research into the effects of ageing on social ability has focused on general social functioning (e.g., self reported social interest and interpersonal functioning) rather than exploration of the cognitive processes involved in social ability.

A particular area of interest has recently developed concerning the effects of ageing on the recognition of emotion in others via facial expressions. Calder et al. (2003) found significant differences between the recognition of emotion on the Ekman 60 Faces in an older group (58 – 70 years) compared to a younger group (18 – 30 years), with the older group recognising fewer fear and sadness emotions, but more accurately recognising disgust (from a choice of anger, happiness, fear, disgust, surprise, sadness). This was explored further by the researchers, with a greater number of age groups (17 – 30 years, 31 – 40 years, 41 – 50 years, 51 – 60 years and 61 – 70 years), in which significant declines were also found in fear and sadness as age increased. Phillips, MacClean, and Allen (2002) found that in adults aged 20 – 40 years (mean = 29.9 years, *SD* = 7.1 years) and 60 – 80 years (mean = 69.2 years, *SD* = 6.1 years) no overall effects of age were found on the recognition of emotion from facial expression on an Ekman and Friesen (1976) task. However there were significant differences on labelling anger and sadness. Unlike Calder et al.,

they failed to find a significant difference for the recognition of fear. The age groups consist of rather broad age bands in the study by Phillips et al., whereas those by Calder et al. were much more restricted; this might account for some variation between the studies.

Calder et al. (2003) posited that recognition of some emotions were more vulnerable to ageing effects than others, because they tap into different brain regions. Unfortunately, this is a contentious issue, regarding implicating different brain structures in the identification of specific emotions. Firstly, many studies observe 'composite' scores, rather than ability to recognise each emotion individually. Also, due to poor temporal resolution, brain imaging is not a reliable method to isolate brain activation during recognition of each emotion in succession. If there were to be a focus on specific emotions (e.g., brain imaging during recognition of surprise stimuli only), this would not create substantial cognitive demands, as the presentation of stimuli would not be in the context of the presentation of stimuli reflecting other emotions.

1.3.4 Summary

As previously stipulated, tasks that have been associated with the PFC have been found to undergo disproportionate age-changes. This is in support of the 'frontal lobe theory' of decline, in which the frontal lobes are predicted to age at a faster rate than other brain regions. Although there is a rationale for the exploration of social cognition changes with age, this area of research has been largely underrepresented in the literature. Given the importance of social function, and the possible real-life relevance there is a need for further exploration into this area of cognitive ageing. It is suspected that social cognition would undergo the same age-related declines previously observed in executive function measures. Furthermore, although the age effects on executive functions have been rather well established in the literature, there is a clear short-fall in repeated measures designs. This is surprising given the potential vulnerability of executive functions to cohort effects. Utilising a longitudinal design, with a large enough time period to

counteract any practice effects, might give a more realistic view of the effects of ageing.

1.4 Age-Related Changes in PFC SWS

1.4.1 Sleep Architecture

Structural changes in the PFC might underlie changes in sleep quality with age. Observations at the sleep EEG level have revealed declines with increasing age in the percentage of total sleep time spent in stage 4 sleep at night, when comparing an older group aged 65 – 96 years (mean age 77 years) to a young adult group aged 20 – 25 years (mean age 22.3 years; Feinberg, Koresko & Heller, 1967). Concurrent findings were found when comparing a young group aged 20 – 25 years (mean = 22.3 years) to an older group aged 57 – 64 years (mean = 62 years; Landolt & Borbély, 2001). Declines with increasing age have also been found in percentage of stage 3 and 4 (combined) between a young group (mean age = 21.4 years, *SD* = 2.5 years) and an older group (mean age = 75.5 years, *SD* = 6.3 years) by Crowley, Trinder, Kim, Carrington and Colrain (2002). Further to this, Bonnet and Arand (2007) found that percentage of combined 3/4 stage sleep presented with linear declines from 18 years to 60 years of age. Conversely, those studies demonstrating declines in amount of 3/4 and 4 (Bonnet & Arand, 2007; Crowley et al., 2002; Feinberg et al., 1967; Landolt & Borbély, 2001) found decreases in sleep efficiency (percentage of time spent asleep from sleep onset to sleep cessation) and increases in amount of stage 1 sleep, with advancing age. The results, interpreted together, might indicate that restorative aspects of sleep undergo decrements with age.

Much less clear is the change in stage 2 and 3 sleep (the latter when it is not combined with stage 4) in older age. With regards to percentage of stage 2 sleep with advancing age, decreases have been found (Landolt & Borbély, 2001), as well as no change at all (Crowley et al., 2002). This is surprising, given that the young groups utilised by both studies were similar

in age; but the mean age of the older group was more than a decade greater in the Crowley et al. study than in the Landolt and Borbély study. It cannot therefore be assumed that lack of decline, as found by Crowley et al., was due to a lack of ageing effect that would present itself later in life. Further observations of age-related differences in amount of stage 3 could not be found by Landolt and Borbély. This was contrary to findings by Feinberg et al. (1967). In their study, it was revealed that significant increases with age were found in amount of stage 3 sleep. This was explained by the authors as possibly being due to degradation of stage 4 sleep.

No difference has been found in percentage of REM sleep between the young and older groups observed by Bonnet and Arand (2007), and Landolt and Borbély (2001). However, Crowley et al. (2002) found less REM sleep in the older group, compared to the young adult group. The older sample in that study was later in life than the older groups reported by Bonnet and Arand (2007) and Landolt and Borbély (2001). This might account for the variation in the literature; REM may decline later on in the life.

In summary, there appears to be some disagreement in the literature pertaining to age-related changes in sleep structure. This may be due to differences in methods employed, such as in standardisation of sleep times, as well as differences in the age groups of participants. More precision might be obtained from studies investigating the changes in sleep at the level of EEG amplitude and frequencies, rather than time spent within any particular stage.

1.4.2 EEG Power Density

Researchers have come to agree that the method of scoring sleep states by grouping them into sleep stages is unnecessarily inflexible. As technology has developed, much can be gained from exploring sleep by observing individual frequency bands not necessarily confined to predefined sleep stages. Therefore sleep is now often studied outside of the parameters of

sleep stages and within specified frequency bands. The importance of this is demonstrated by the example that there have been two types of oscillations (< 1 Hz and 1 – 4 Hz) found to be prominent during stages 3 and 4 and that are reflective of differential neuronal activity (Amzica & Steriade, 1998).

Carrier et al. (2001) utilising power spectral analysis demonstrated age-related changes in delta and theta (1.25 – 8Hz), with declines from 20 – 60 years of age, as ascertained by a correlation technique. Furthermore, they found an association between increasing age and increases in higher frequency activity (18.25 – 32Hz). Delving into changes in deeper aspects of sleep, Dijk et al. (1989), found that young adults aged 20 – 28 years had greater power in the 0.75 – 4.5Hz delta range compared to a middle aged group 42 – 56 years. This pattern of results was mirrored by Landolt et al. (1996) in a later study in 0.45 – 4.5Hz delta; the young group was aged 20 – 26 years (mean = 22.4 years) and the older group aged 57 – 64 years (mean = 62 years). These findings indicate decrements with increasing age in SWA and augmentation in cortical activation during sleep.

Transient rhythms defining SWS, Spindles and KCs have been observed to undergo changes with age. Spindles were first described by Loomis, Harvey and Hobart (1939) as rhythmic oscillations lasting 0.5 – 3 seconds in the 12 – 14 Hz range; although later research has demonstrated that spindles can oscillate at a slower and faster frequency than this (e.g., 11 – 16 Hz; Crowley et al., 2002). KCs have been identified as having a well delineated negative component followed by a positive deflection. KCs have been found to be spontaneous or evoked; spontaneous ones not being known to be associated with an inducing factor and evoked ones are associated (in time) to a know sensory stimulus (Halász, 2005). Declines, hypothesised to be due to ageing effects have been found in spindle density (total number of spindles per minute), duration and amplitude (Crowley et al., 2002) when comparing a group in their 20s (mean = 21.4 years) to a group in their 70s (mean = 75.5 years) as ascertained by visual scoring. This was concurrent with earlier findings by Feinberg et al. (1967) who also found a decline in spindle density with increasing age, when comparing a young group aged

19 – 36 years (mean = 26.6 years) to older counterparts aged 65 – 96 years (mean = 77 years). Using power spectral analysis, Landolt et al. (1996) found greater power in the sigma frequency range of spindles in a young group aged 20 – 26 years (mean = 22.4 years) compared to an older group aged 57 – 64 years of age (mean = 62 years). This was specific to slower sigma (12.25 – 14 Hz) but not faster sigma (14.25 – 15 Hz), leading the authors to conclude that this slower sigma was more susceptible to ageing. Slower sigma, consequently shows an anterior dominance (Werth, Achermann & Borbély, 1997).

Age-related changes have also been found in KC density, in that younger adults (23.1 years) had greater occurrences than older individuals (75.6 years; Wauquier, 1993). This supported the findings of Kubicki, Scheuler, Jobert and Pastelak-Price (1989), who found a reduction in KCs in those aged above 50 years in comparison to those below 30 years. Colrain et al. (2010) found linear age declines in individuals aged 19-78 years in the amplitude of evoked KCs (N550). In that study it was found that greater than 50% of the variance was explained by age. Interestingly, these declines were steepest at frontal derivations, in comparison to central and parietal derivations.

In addition to the more established age-related changes in delta, there appears to also be a specific decline in KCs and spindles. According to Halász (2005), this could be due to an alteration of the mechanisms involved in thalamo-cortical regulation. Assuming that delta, KCs and spindles are involved in cortical deactivation during SWS, the consequences of these changes on the individual might be greater susceptibility to disturbance of sleep.

1.4.3 Topographic and Temporal Distribution

Sleep EEG power spectral density is not homogenous across all regions. The particular dominance of SWA in some regions may be indicative of an increased need for ‘restorative’ sleep in that region. A frontal lobe

predominance in the power of delta, 0.5 – 7 Hz (Borbély, 2001) and a dominance in power 1 – 2 Hz (Werth, Achermann & Borbély, 1997) in fronto-central regions was found in comparison to more posterior regions. Werth et al. furthermore, demonstrated a dominance in frontal derivations of low frequency spindles (11.5 – 11.75 Hz), and conversely a dominance of higher frequency spindles (peak 13.5) in occipital/parietal regions. Interestingly, Anderer et al. (2001) demonstrated, using low-resolution electromagnetic tomography (LORETA) a spindle source originating in the PFC (BAs 9 & 10), with a frequency below 13 Hz, and spindles originating in the parietal region (BA 7) with a frequency above 13 Hz. Brodmann areas 9 and 10 are connected to the dorsomedial thalamic nucleus, whereas Brodmann area 7 is strongly connected to the lateroposterior, laterodorsal and rostral intralaminar centrolateral thalamic nuclei. This may point towards different underlying mechanisms of those spindles that are localised to anterior regions and those that localised to posterior regions; as they are connected to different parts of the dorsal thalamus (where spindles are generated).

Topographic observations of KCs also revealed a frontal predominance. McCormick, Nielsen, Nicolas, Ptito and Montplaisir (1997) found that the majority of visually scored KCs during night-time sleep occurred in the frontal regions; KC density dissipated in an anterior-posterior gradient, in that the fewest were observed in the most posterior regions of the cortex. The amplitude of evoked KCs was also found to be maximal over frontal derivations, and this was found to persist across the lifespan (from 19-78 years; Colrain et al., 2010).

In addition, SWA does not remain constant over the duration of the night. Some aspects of SWS show a particular dominance in the first sleep period. This is interpreted as to be reflective of homeostatic responses to sleep pressure (Carrier et al., 2001). For example, delta and theta (1.25 – 8 Hz) activity has been found to be particularly dominant in the early stages of the night, and to attenuate as sleep pressure decreases in later phases of the night (Carrier et al., 2001). When the amount of wakefulness prior to sleep is particularly elongated, then this sleep pressure rises further. With this rise in

sleep pressure, concomitant increases in intensity in delta occur (0.75 – 4.5 Hz) in the early stages of the night (Achermann et al., 1993). Therefore, the assumption is that SWA (i.e. delta power) is reflective of sleep need.

The dominance of SWA in the early stages of the night may make it more susceptible to age-related changes. Feinberg et al. (1967) found that the amount of stage 4 in the first NREM period declined significantly from childhood (6 – 10 years, mean = 8.4 years) to young adulthood (19 – 36 years, mean = 26.6 years) as well as from young adulthood to older adulthood (65 – 96 years, mean = 77 years). In addition, the inverse temporal relationship between delta and spindle activity (attenuation of delta and augmentation of sigma over successive sleep periods) in a population aged 20 – 60 years was found to degrade with increasing age (Carrier et al., 2001). An increase in young participants (24.6 years, *SD* = 20.4 years) but not in older participants (71.9 years, *SD* = 3.7 years) was also found in spindle density as the night progressed (Guazzelli et al., 1986). Landolt and Borbély (2001) additionally observed a suppression of the increase in spindling as the night evolved in an older group (62 years, range = 57 – 64 years), in comparison to a younger group (22.3 years, range = 20 – 25 years). Furthermore, the inverse relationship between SWA and spindling was less pronounced in the older group. One interpretation of these studies, taken together is that there is a decrease in sleep pressure with increasing age. Alternatively, due to age-related changes in the underlying processes of sleep there may be an effect of age on sleep homeostasis mechanisms.

1.4.4 Summary

Age-related declines have been found in defining features of SWA (delta, KCs and spindles). A regional phenomenon of hyperfrontality of low frequency delta, and spindle and KC activity, has supported the notion that SWA may support a high recovery need of anterior regions. Additionally, the temporal progression of delta may also indicate a preference of SWA (and thus greater cortical deactivation), at the beginning of the night when sleep pressure is at it's greatest.

1.5 Sleep EEG: A Predictor of Cognitive Function

In previous sections, literature has been reviewed that has indicated that SWA is preferential for the PFC. Research has also pointed towards cognition and SWA as being vulnerable to changes with age, with particular specificity to the PFC. This section focuses on the plausibility of establishing a link between the two domains of ageing research that appear to have similar paths of decline.

The EEG for decades has been used to explore underlying functional brain changes associated with pathology, such as dementia. For example, during eyes closed, there was found to be a slowing of waking EEG in patients with mild-moderate Alzheimer's disease, in comparison to healthy controls, as evidenced by greater amounts of theta activity (4 – 7 Hz; van der Hiele et al., 2007). Furthermore, the authors found that greater relative power in the theta band, indicated poorer performance on memory and language tasks; and semantic verbal fluency. Other studies have found higher levels of theta and lower levels of beta, in the waking EEG of individuals with Alzheimer's disease to be predictive of subsequent decreased performance on the CAMCOG[2] (a battery of tests used to diagnose cognitive impairment associated with pathology; Claus et al., 1998), as well as the MMSE[3] (also a test of cognitive impairment; Princhep et al., 1994).

However, recent attention has also focused on the relationship between sleep EEG and cognitive function in healthy adults, as the similar paths of decline in the domains of cognition and SWA in healthy ageing have been noted. Furthermore, establishing a marker of cognitive function utilising sleep EEG encapsulates the benefits of using waking EEG, such as low-cost, portability, and low-invasiveness, but with the added benefit of reduced

[2] The cognitive section of the Cambridge Examination for Mental Disorders, which measures domains of orientation, language, memory, attention, praxis, calculation and perception.
[3] The Mini-Mental State Examination includes questions and problems pertaining to time and place of the test, repeating lists of words, basic motor skills, arithmetic, language use and comprehension.

artefact contamination as a result of movement. It additionally, may elucidate more about any functional relationship between sleep and cognition.

A slow oscillation (< 1 Hz) prominent during SWA has been found to be particularly important in the cortical deactivation processes of SWA. This novel oscillation was found *in vivo* in anesthetised cats (Steriade, Nuñez, & Amzica, 1993) and later in humans (Achermann & Borbély, 1997). Slow oscillations are hypothesised to be distinct from higher frequencies of delta as they are generated during SWS in the cortico-cortico networks and are capable of grouping other sleep oscillations (such as delta, which is produced in thalamo-cortico networks; Contreras, & Steriade, 1995). The cortical localisation of the slow oscillation, was demonstrated in cats in which generation persisted after thalamectomy[4] (Steriade, Contreras, Curro Dossi, and Nunez, 1993).

Interestingly, the depolarising-hyperpolarising cycle of a slow oscillation corresponds to the graphic shape in the EEG (Amzica & Steriade, 1998); hyperpolarisation of neurons corresponded to the surface negative EEG and depolarisation of neurons to the surface positive EEG (Amzica & Steriade, 1998; Contreras & Steriade, 1995). Contreras and Steriade (1995) proposed that the long hyperpolarisation of neurons reflected as a surface negative wave in the EEG, was a mechanism by which cells became synchronised. For example, cells are brought together via inhibition and the first to escape that inhibition may be the driver for the depolarisation phase. The long hyperpolarisation seen in the slow oscillation indicated removal of excitatory inputs, decreased synaptic efficacy, thus bringing about functional disconnection of cortical networks.

As the slow oscillation (<1 Hz; low frequency delta) was found to be generated in the cortex, and to be involved in cortical deactivation, this attracted interest as a potential marker of localised cortical function.

[4] Destruction of the thalamus.

Anderson and Horne (2003) observed sleep EEG localised to the PFC and its relationship to executive function (also associated with the PFC). They proposed that localised low frequency delta was reflective of the function of cognitive measures subserved by that same area. They found in healthy adults aged 61 – 75 years that low frequency delta (0.5 – 1 Hz) in the LPFC significantly correlated with the WCST (perseverative errors; r = -0.48), TOL (mean completion time; r = -0.60) and VF (number of verbs generated; r = 0.57). Delta in the RPFC correlated, close to significance, with WCST (r = -.36); significantly with TOL (r = -0.46); and significantly with VF (r = 0.50). Greater power of low frequency delta was predictive of better performance on the measures. In contrast, none of the tasks were found to correlate with low frequency delta originating in occipital/parietal derivations. As EEG and cognitive testing occurred a week apart, this is suggestive of both measures being an underlying 'trait' measure and not simply a case of poor sleep resulting in subsequent poor performance. These results confirm that cognition can be linked to SWA, and that this link can be localised; this has important implications concerning establishing a marker of 'healthy' cognitive ageing, of which to compare changes in EEG as a result of age-associated pathology (e.g. dementia). Furthermore, the stronger link with the left hemisphere concurs with previous data suggesting a greater association between executive function and the LPFC, compared to the RPFC (e.g., Glosser & Goodglass, 1990; Goldstein et al., 2004; Ravnkilde, et al., 2002; Rezai, et al., 1993).

Other rhythms that define SWA include spindles and KCs. Although interest has persisted for decades around the functional aspect of spindles and KCs, their role is still a relative mystery. Research suggests that KCs may facilitate delta production, perhaps in the capacity of playing a role in thalamo-cortical synchronisation. Evidence to support this came from the observation that there were significantly more KCs in the period of stage 2 sleep preceding a period of SWS, compared to that preceding REM sleep (De Gennaro, Ferrara, & Bertini, 2000a). Additionally, the authors found that linear increases in KC density were found in the transition from stage 2 to

SWS but not in the transition between stage 2 and REM. Therefore, KC density appears to increase until SWS is achieved.

Support for the potential role of KC activity in cortical deactivation was offered by Czisch et al. (2004). They observed visually scored KC density during stage 2 sleep combined with BOLD fMRI and found that in response to external auditory stimulation, there was an increase in number of KCs and subsequent delta, as well as concomitant reductions in BOLD signal; reductions are associated with decreases in CBF. The authors concluded that KC increases in stage 2, occurring as a result of external stimuli, indicate a process by which deactivation processes are triggered in order to avoid sleep disruption, i.e., SWA is promoted. The assumption by Amzica and Steriade (2002), is that it is the sharp onset of the KC that results in the wide synchronisation of rhythms at the cortical level.

Whilst low frequency delta and KCs have been suggested as being involved in driving depth of sleep, spindles are also believed to provide a sleep protective function. Triggered by hyperpolarisation of thalamo-cortical and cortical neurons (Steriade, Contreras et al., 1993), spindles may be involved in sleep maintenance. Consistent with this, it was found that the presence of external stimuli (single tone pips) hampered ability of participants to reach deeper levels of sleep; the time it took to reach the plateau of deep sleep was extended and sleep was generally lighter and more disrupted (Yamadori, 1971). In contrast, when participants were exposed to pips that were synchronised with spindle activity, the effects of stimulation on the sleep deepening pattern ceased. The authors posited that the spindles blocked incoming stimuli from reaching the cortex, and therefore, aiding in sleep maintenance. Interestingly, KCs were also found to be evoked when pips were delivered out of phase with spindles, but not when the pips were synchronised with spindles. This is compatible with the findings by Czisch et al. (2004); KCs may be produced as a driver of SWA, when spindles are not successful in suppressing stimuli from reaching the cortex.

Bódizs et al. (2005) found that general intelligence as ascertained by Raven's Progressive Matrices (Raven, Court, & Raven, 1976) positively correlated with fast spindle density in frontal regions (FP_2, F_4) in individuals 27 – 64 years of age. The authors suggested that general intelligence is reflected by the triggering of spindles during SWS. Guazzelli et al. (1986) however failed to find significant correlations between spindle density and performance on an extensive battery of tests administered to an older group aged 66.5 – 78.3 years. The authors suggested that the older group utilised had unusually high IQs (performance IQ = 121.7, *SD* = 9.25; verbal IQ = 121.7, *SD* = 9.25) which may have accounted for the findings. However, EEG recordings were taken from C_3-A_1 which corresponds to the cortex mid-way between the frontal and occipital/parietal region, and then correlated to general measures of cognition (some associated with the PFC and some not). It is suspected that more success would have been achieved in correlating SWA EEG components with cognitive function, if the EEG source and cognitive tasks were localised to the same cortical regions.

1.5.1 Summary

Although the inter-relationship between KCs, spindles and low frequency delta is not entirely clear, each appear to contribute to the maintenance of SWA and the associated inhibition of cortical activity achieved with sleep; making the case for the link between SWA associated phenomena and cognition plausible. Unfortunately the research in this area is limited. Those studies that do exist, do not take into account localisation of function. The only exception that could be found to this was the evidence of Anderson and Horne (2003; in the context of low frequency delta). Furthermore, no literature could be found pertaining to the exploration of longitudinal changes in both domains in the same individuals. This has the potential to reveal the nature of any functional links and the development over time. For example, if past EEG could predict future cognition, then it might implicate that changes in SWA precede changes in cognition.

1.6 Conclusion

Summary and Gaps in the Literature –

1. SWS particularly benefits the PFC. Research has indicated that this may be via cortical deactivation, or synaptic plasticity mechanisms. This however, remains unclear.
2. Cognitive function associated with the PFC such as executive function (e.g., WCST, TOL and VF) was found to undergo specific age-related declines. However, ageing research is limited in the context of social cognition. Also, despite abundant literature exploring age-related changes in executive function there was found to be a short-fall in longitudinal observations.
3. Low frequency delta, KCs and spindles have been shown to be vulnerable to age-related declines. However, studies exploring localised changes (e.g., to the PFC) are limited, as are longitudinal observations.
4. Anderson and Horne (2003) found a link between low frequency delta localised to the PFC and executive function in an older sample. However, these domains were not observed in the context of ageing (e.g. the authors did not utilise a longitudinal design).
5. Evidence suggests that SWA associated phenomena (i.e., KCs and spindles) are important in maintaining depth of sleep, and achieving cortical deactivation. However, few studies have attempted to link spindles and KCs, to cognition, even though there is a strong rationale to do so. Those that have, have not localised the EEG source to the region that would correspond to the cognitive tasks.

General Research Questions –

1. Are social cognitive function measures found to undergo the same age-related declines, as found in executive function?
2. Are longitudinal age-related declines found in executive function?
3. Are longitudinal age-related declines found in SWA and associated phenomena (e.g. amount of low frequency delta, spindles and KCs)?

Are these declines greater in the PFC, in comparison to others regions of the cortex?

4. Can the EEG–cognition link established by Anderson and Horne (2003) remain stable in follow-up analyses? Furthermore, can past (baseline) EEG predict future (follow-up) executive function?
5. Can PFC localised KC and spindle density predict executive function in an older sample?

General Hypotheses –

1. Age-related changes will be found in measures of social cognition due to the association of these with the PFC.
2. Longitudinal declines in executive function will be found in an older sample.
3. Longitudinal age-related declines will be found in SWA and associated phenomena; with a specificity to the PFC.
4. The link established by Anderson and Horne (2003) between low frequency delta and executive function will remain stable over time, and past low frequency delta with predict future (follow-up) executive function ability.
5. PFC localised KC and spindle density will predict executive function in an older sample.

Specific Hypotheses –

Ch 3: Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus

- An older group will be less successful in the correct identification of emotional stimuli via facial expression and emotional prosody, than a young group. These age-differences will be increased when stimuli are incongruent.
- Age differences will be found in response inhibition with an older group having greater difficulty in ignoring distracter stimuli. Furthermore, this difference will be more substantial when the stimuli are emotive in content, compared to neutral.

Ch 4: Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus

- Decrements in performance on executive function measures (WCST, TOL and VF) will be found in an older cohort over a period of 6.29 years.

Ch 5: Study 3: Age-Related Changes in PFC Sleep EEG

- Age-related declines will be found in low frequency, KC density, and spindle density. These declines will be more pronounced in EEG localised to the PFC.

Ch 6: Study 4: Links between Sleep EEG and Cognitive Function Revisited

- Past (baseline) low frequency delta localised to the LPFC will predict future (follow-up) performance of executive function measures in a healthy, older sample.
- The link between LPFC low frequency delta and executive function as ascertained by Anderson and Horne (2003) will be present in follow-up analyses.

Ch 7: Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective

- Spindle density and KC density localised to the PFC, will predict performance of executive function measures; whereas spindle density and KC density localised to other regions will not.
- LPFC KC density will be found to partially mediate the relationship found between LPFC low frequency delta and executive function; controlling for KC density will reduce the relationship between low frequency delta and executive function.

2 General Method

2.1 Participants

All participants were provided with monetary incentives for their contribution to the experiments, and all provided informed consent for cognitive testing and EEG measurements (Appendix 1). Ethical clearance was obtained for all studies, via the Loughborough University's Ethical Advisory Committee.

2.1.1 Participant Screening

All participants underwent screening for health and sleep problems that may have impacted upon healthy sleep or upon cognitive functioning. This included interviews, the Karolinska Sleepiness Scale (KSS), the Epworth Sleepiness Scale (ESS) and actigraphy.

Interview –

Volunteers were interviewed in their home to assess general health as well as sleep health (Appendix 2). The interview ascertained that participants had:

- A healthy Body Mass Index (BMI).
- No physical problems that might cause discomfort or difficulties during testing such as eyesight and hearing problems, as well as mobility restrictions.
- No emotional problems such as undue anxiety, stress or depression.
- No self-reported history of vascular disease, or were currently undergoing treatment for it, (vascular disease is particularly associated with declines in cognitive function in an ageing sample; Breteler, Claus, Grobbee & Hofman, 1994).

- Regular sleeping patterns: 8 hours sleep per night ± 1 hour, as well as infrequent napping and free from sleep related disorders or disturbances.
- Not recently undergone any medication or treatments that are known to impact on sleep or the central nervous system, in particular antidepressants such as selective serotonin reuptake inhibitors (SSRIs), which have been found to depress REM sleep.

Epworth Sleepiness Scale –

The ESS (Johns, 1991) was carried out at the same time as the interview (Appendix 2). The purpose of the ESS was to ensure that participants had a typical general level of daytime sleepiness independent of short-term variations in sleepiness. The ESS is designed to measure how likely someone is of falling asleep in different activities with low levels of stimulation. Scores obtained can be between 0 and 24, but levels of 2 – 10 are found to be typical of healthy sleepers. Anything above 10 may be indicative of sleep disorders such as narcolepsy or obstructive sleep apnoea. However, as noted by Johns (1991) there is a wide range of scores in typical sleepers, perhaps indicating that there may be individual differences in sleepiness levels in healthy people.

Karolinska Sleepiness Scale –

The KSS was completed in order to elicit more information about daytime sleepiness. The ESS is a measure of general sleepiness, whereas the KSS is more sensitive to variations in levels of sleepiness across the day, such as those in line with the normal circadian rhythm.

The KSS was developed by Åkerstedt and Gillberg (1990), in which participants were required to rate their level of sleepiness every waking hour for the duration of 3 days on a scale of 1 to 9, with 1 being the most alert (Appendix 3). Taken with information gathered from the ESS, this is a useful measurement to screen out any excessive daytime sleepiness as well as to test for normal circadian variation. This information was also utilised to

ascertain times of testing cognitive function in order to ensure maximal alertness in participants.

Actigraphy –

Actiwatches (Figure 2.1) were disseminated to volunteers at the same time as the KSS, and were completed alongside one another. Actiwatches were worn on the participants' dominant wrist during waking and sleeping for 3 days (removed only for bathing and exercise). The data obtained was transformed into an actigraph and visually examined for periods of activity and inactivity.

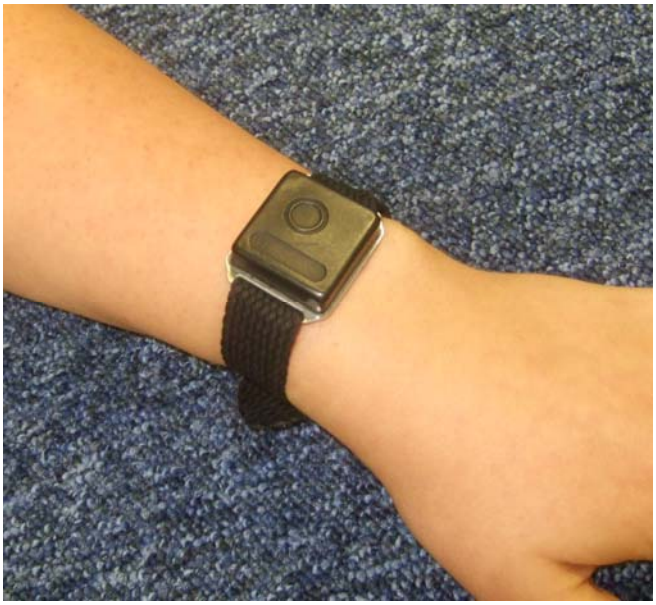

Figure 2.1: Light-weight Actiwatch worn on the dominant wrist of the wearer.

The assumption behind using actigraphy during the screening process is that long periods of inactivity on an actigraph are indicative of periods of sleep. Due to difficulties in interpreting lack of activity as sleep or due to another reason, participants were required to note down any periods in which the actiwatch was removed, as well as any periods in which they napped, etc.

The purpose of the actiwatch was to confirm that participants had regular sleeping habits. For example as demonstrated in Figure 2.2., the actigraph presents activity of a participant that was considered as having good sleep

habits. This was due to there being similar sleep and wake times over the 3 days, low levels of activity during the sleep period, and any periods of inactivity during the day were accounted for (e.g. due to exercise and bathing). Also, the participant is fairly consistent with obtaining sleep lasting approximately 8 hours ± 1 hour.

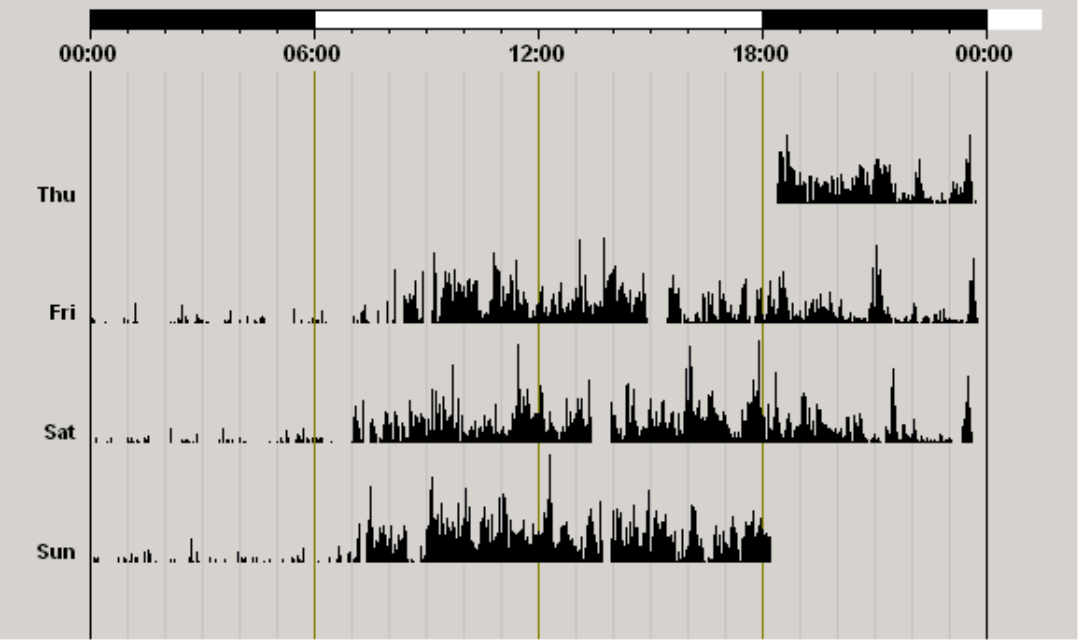

Figure 2.2: Actigraph showing levels of activity over a 3 day period for a male, aged 65 years. The recording began around 18:00 hrs on Thursday and ended at a similar time on Sunday.

2.1.2 Cross-Sectional Design Cohort

The participants detailed in this section appear in:

- Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus

Two groups were recruited for Study 1: a young group (n = 16) with a mean age of 22.25 years (SD = 2.35 years) and an older group (n = 16) with a mean age of 71.5 years (SD = 4.4 years). There was a 50:50 female to male ratio in each group. Participants in the young group were recruited from Loughborough University after responding to posters distributed around the campus. Older individuals were recruited from the University of Third Age (U3A), an organisation involved in the promotion of activities and education

in those retired in the community. This was done by contacting the chairperson of the organisation, who contacted members via a mailing list with the details of the study. Younger and older participants were matched as closely as was possible for past educational attainment.

During the selection process, 12 young and 5 older respondents were excluded from the study after the initial questionnaire phase. The reason for both young and older individuals not proceeding through the interview screening was unusual sleep habits. No individuals were excluded or 'dropped-out' during and after the actigraphy and KSS monitoring phase. All participants fulfilled the criteria as set out in section 2.2.1. The age and sex of all participants is presented in Table 2.1.

Table 2.1: The young group and older group sex and age at the time of testing.

Young Group			Older Group		
Ps	**Sex**	**Age**	**Ps**	**Sex**	**Age**
PW01	m	20	JH01	f	77
DS02	m	24	PM02	m	65
DW03	m	21	AM03	m	71
SB04	m	23	WB04	m	65
KB05	f	20	RT05	m	74
JK06	m	24	BM06	f	66
LU07	f	25	BW07	f	79
PB08	m	24	EA08	f	78
SE09	m	20	BF09	f	68
PT10	f	20	GK10	m	69
HJ11	f	20	WK11	f	69
SF12	f	20	IJ12	f	71
VH13	f	23	NB13	m	72
LM14	f	20	KJ14	m	73
KB15	f	26	JF15	m	75
VB16	m	26	CF16	f	72
Mean		**22.25**	**Mean**		**71.50**
SD		**2.35**	**SD**		**4.40**

2.1.3 Longitudinal Design Cohort

The participants detailed in this section appear in:

- Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus
- Study 3: Age-Related Changes in PFC Sleep EEG
- Study 4: Links between Sleep EEG and Cognitive Function Revisited
- Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective

An older group was utilised for the purpose of Studies 2 – 5. For all of these studies, baseline testing was conducted in 2000 on 24 participants (participants have appeared elsewhere; Anderson & Horne 2003[5]). For Studies 2 – 4, follow-up testing was additionally conducted in 2006 on the 11 participants that were retained (follow-up data was not required for Study 5). The sex and age of participants at baseline and follow-up is presented in table 2.2. At baseline there were 14 females and 10 males and at follow-up there were 6 females and 5 males. The mean time that lapsed between the two time points for those 11 participants retained for follow-up testing was 6.29 years (*SD* = 0.48 years). All participants fulfilled the screening criteria as set out in section 2.2.1.

Baseline recruitment –

All participants at baseline were recruited via the U3A by Anderson and Horne (2003) for the purpose of their research. The chairperson of the organisation was contacted initially, who then shared the information of the study with the organisation's members.

Follow-up recruitment –

To obtain follow-up testing, all 24 baseline participants were contacted initially by Anderson and Horne (2003), with details of the current research.

[5] At baseline (2000), Anderson and Horne (2003) recruited all 24 participants and obtained raw sleep EEG and cognitive function data in these individuals. This raw data was reprocessed, rescored and reanalysed for the purpose of the present thesis.

Replies were obtained from 15 individuals. Twelve expressed interest in the research, 1 individual declined but did not offer a reason why, 1 individual no longer lived in the area and 1 was in a care home and unable to take part. One individual dropped out after the interview stage, citing changes in personal circumstances as a reason. The remaining 11 respondents were retained after interview, actigraphy and KSS screening.

Table 2.2: Participants sex and age at baseline (2000) and follow-up (2006) testing.

		Age	
Ps	**Sex**	**Baseline**	**Follow-up**
BC01	f	64.00	-
RR02	f	67.08	-
AT03	m	61.67	68.58
EM04	m	68.00	-
SS05	m	68.67	-
IK06	m	66.33	-
TK07	f	64.92	71.17
BF08	m	64.50	70.83
YF09	f	63.33	69.92
JC10	f	67.17	73.75
JY11	f	66.67	73.42
JT12	f	68.25	-
BP13	f	70.17	-
RW14	m	68.58	74.67
OC15	m	62.00	-
RD16	m	71.58	77.25
RL17	m	69.42	-
LL18	f	66.17	-
GM19	m	70.25	76.25
MM20	f	67.33	72.67
EP21	f	72.17	78.80
DF22	f	74.00	-
ES23	f	75.33	-
MF24	f	71.17	-
Mean		**67.87**	**73.39**
SD		**3.54**	**3.18**

- Where data is missing, participants were not retained for follow-up testing.

Data Source Acknowledgement–

All sleep EEG and cognitive testing raw data collected at baseline from the Longitudinal Design Cohort was done so by Anderson and Horne (2003; data collected 2000). All of this raw data was rescored and reanalysed for

the purpose of the present thesis. This was done primarily for reliability purposes, so that baseline data was processed and scored by the same experimenter as at follow-up.

2.2 Cognitive Testing

All participants underwent cognitive testing. The combination of tests administered varied from study to study, and as such, cognitive test batteries are detailed further in each individual experimental chapter.

All cognitive testing took place at the Sleep Research Centre at Loughborough University. All participants were required to obtain their 'typical' night's sleep during the night preceding testing and this was confirmed by actigraphy. Participants were additionally required to refrain from consuming caffeinated or alcoholic beverages on the evening prior to testing and on the day of testing. No more than 90 minutes of cognitive testing was conducted during a given testing session and short breaks were taken between tasks in order to prevent fatigue and boredom. Order of administration of tests was counterbalanced for each testing procedure.

Time of Testing –
If sleep EEG recordings were required from participants (as was the case for Studies 3 – 5), then it was ensured that cognitive function testing occurred at least 7 days prior to, or after EEG recordings. This was in order that cognitive testing did not influence sleep EEG and vice versa.

As previously noted (section 2.2.1), participants completed the KSS (Åkerstedt & Gillberg, 1990) in order to screen for excessive daytime sleepiness, and to ascertain normal circadian rhythm. The KSS is a measure of variation in levels of sleepiness across the day and therefore important in identifying a time of day suitable for cognitive testing of all groups.

Cross-Sectional Design Cohort

KSS scores (reported hourly, over the period of a day and averaged across 3 days) for the young and older groups of the Cross-Sectional Design Cohort, are presented in Figure 2.3. These appear to be demonstrative of typical levels of alertness in-line with the circadian rhythm. However, there appears to be marked differences between KSS scores of the young group and older group at particular times of the day, such as after waking, with older participants experiencing greater alertness. This appears to converge at 13:00 hrs and the differences remain relatively marginal until bedtime. Due to the possibility of differences in daytime sleepiness affecting daytime cognitive functioning, all participants were tested between the hours of 18:00 and 20:00, which was at a time of day in which mean KSS scores were similar for both groups. This is also a time in which participants were relatively alert (an average score of 1 being the most alert and 9 being the least alert).

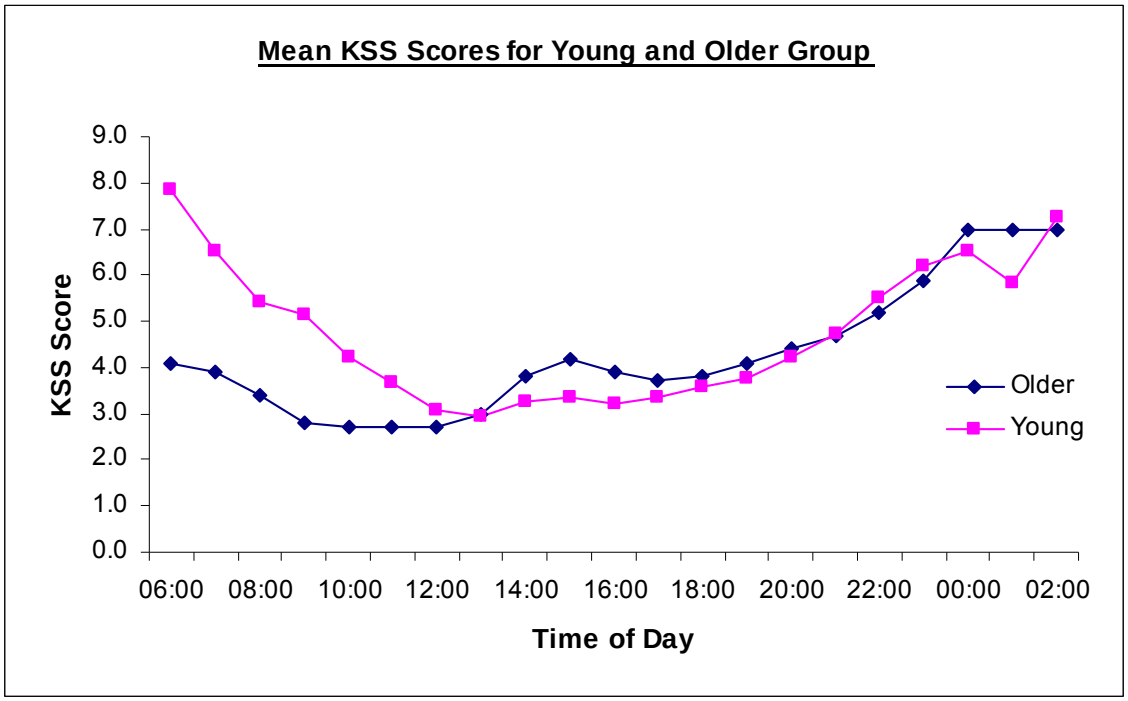

Figure 2.3: KSS scores over the course of the day for the young (*n* = 16) and older group (*n* = 16).

Longitudinal Design Cohort

All participants in the Longitudinal Design Cohort were required to undergo cognitive testing at baseline and follow-up. The scores were reported hourly over the period of a day and averaged across 3 days (Figure 2.4). At both time points, it appears as though levels of daytime alertness were in-line with the natural circadian rhythm and there was little change in this over time. Participants at baseline and follow-up were tested between 10:00 and 12:00 hrs. As can be seen in Figure 2.4, this was at a time where alertness levels were high, as well as mean KSS scores being relatively matched for both time points.

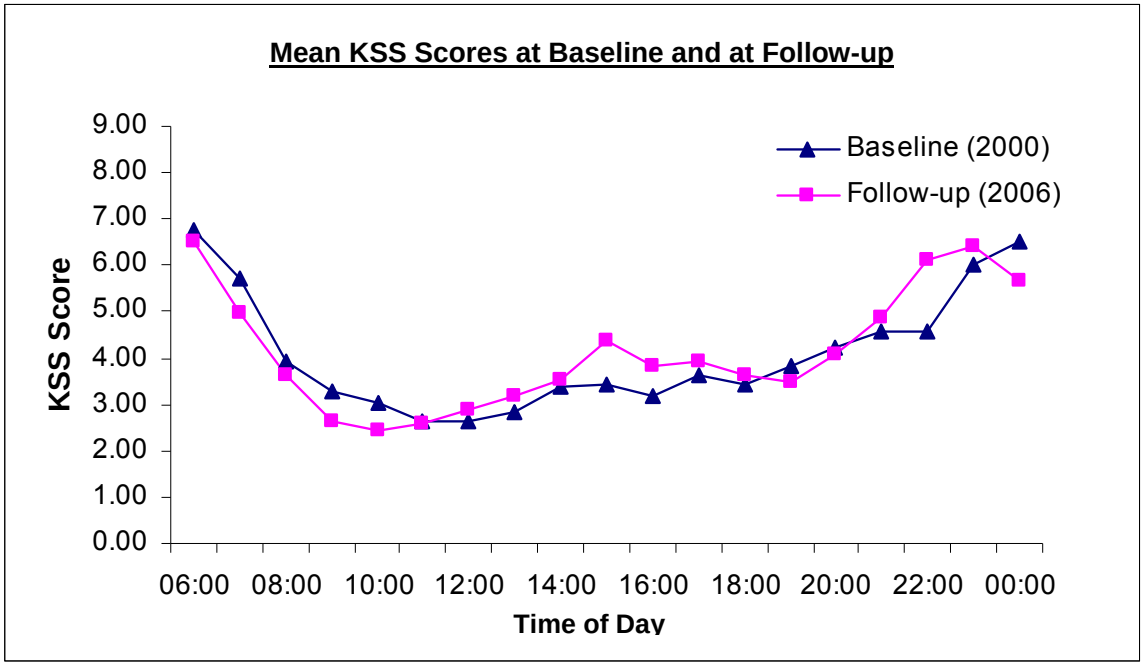

Figure 2.4: Mean KSS scores over the course of the day at baseline (2000; *n* = 24) and at follow-up (2006; *n* = 11).

2.2.1 Social Cognition Test Battery

Tests selected in this section are associated with social cognition and have previously been implicated in PFC function.

Ekman 60 Faces –

The Ekman 60 Faces test requires the ability to recognise emotion from facial expression. The VMPFC in particular has been associated with the ability to identify emotion from facial expression (Hornak et al., 1996;

Nakamura et al., 1999). The Ekman 60 Faces test utilises a range of photographs from the Ekman and Friesen (1976) bank of pictures of facial affect which are well validated and the most commonly reported measure of recognition of facial affect.

Black and white photographs of facial expressions depicting an emotion (fear, sadness, surprise, happiness, anger and disgust) were presented to participants in random order on a computer screen. Each expression was posed by ten models, which included six females and 4 males, so that a total of 60 faces was presented to each participant. An example of a stimulus is presented in Figure 2.5.

Figure 2.5: Example of a stimulus presented during the Ekman 60 Faces task.

Below the photographs were six labels of the six emotions, and participants were required to make a choice (using a computer mouse) as to which label most accurately described the emotion expressed in the photograph. Participants were given as long as they needed to make their selection and were given no feedback on their responses. The participants, in order to familiarise themselves with the procedure, completed a practice trial in the

presence of the experimenter using stimuli independent from the main task. For the main task, the stimuli were automatically presented and participants were left alone in a dimly lit, quiet room to complete the task. The measure of interest was number of correctly identified facial expressions for each of the emotions as well as a composite total score.

Measure: Total number of correct responses (for each emotion and a composite total).
Task Completion Time: Approximately 5 minutes

Emotional Prosody –

The Emotional Prosody task involves the ability to identify emotion in others on the basis of prosody alone. Ability to discriminate emotion via tone of voice has previously been dominantly associated with the DLPFC and VMPFC (Hornak et al., 1996; Mitchell et al., 2003; Wildgruber et al. 2005).

Stimuli

A large bank of sentences was created which described scenarios typically associated with six emotions: sadness, happiness, fear, surprise, anger and neutral. Examples of sentences conveying each emotion are presented below:

- Sadness: “My dog had to be put down”
- Happiness: “I just won the lottery”
- Fear: “I don’t like walking there alone”
- Surprise: “You just startled me!”
- Anger: “I can’t stop shouting!”
- Neutral: “Today is Wednesday”

All sentences were of a similar length and consistent in style, and were surveyed on 10 individuals. Only those sentences that had 100% agreement as to emotional content were selected for the next stage. During the next stage, the sentences were audio recorded by two actors, one male and one female (one of each sex in order to reduce sex-associated biases). Actors were instructed to speak each sentence in all of the 6 emotions, therefore a

bank of spoken sentences was created. This further bank of stimuli was surveyed, but this time for intended emotional prosody conveyed by the actor. This was judged by a panel of 4 and those stimuli in which there was a majority agreement of emotional prosody were deemed appropriate for use in the main study.

Congruent Condition

Those stimuli in which sentence content matched emotional intonation of the actor were used in this condition. This condition included 24 stimuli in total: 4 of each emotional intonation (sadness, happiness, fear, surprise, anger and neutral). Each emotion had an equal representation from both actors. The measure of interest was the number of correctly identified emotions, as identified by tone of voice in the presence of complementary congruent cues (sentence content).

Incongruent Condition

Those stimuli in which sentence content and emotional intonation did not match were used in this condition. This condition included 60 stimuli in total. Table 2.3 visually demonstrates the representation of emotions in this condition. For example, there were 10 sentences spoken with sad intonation, all of which were incongruent to sentence content (e.g., 2 of the sentence contents conveyed happiness, 2 fear, 2 surprise, 2 anger and 2 neutral). The measure of interest was the number of correctly labelled emotions expressed by the actors by intonation alone, in the presence of incongruent (conflicting) cues.

Table 2.3: Number of stimuli representing each emotion for the incongruent condition.

		Intonation of Actor					
		Sadness	Happiness	Fear	Surprise	Anger	Neutral
Sentence Content	Sadness	*	2	2	2	2	2
	Happiness	2	*	2	2	2	2
	Fear	2	2	*	2	2	2
	Surprise	2	2	2	*	2	2
	Anger	2	2	2	2	*	2
	Neutral	2	2	2	2	2	*

*Sentences are not used in this condition in which intonation of actor and emotional content are congruent.

Procedure

Stimuli from both congruent and incongruent conditions were combined and presented in random order via an audio recording. Early piloting revealed that if all congruent stimuli were presented in the same block, separate from the incongruent stimuli, participants quickly learned to ignore emotional intonation and to focus on the contextual information of the sentence. As the purpose of the task was to measure recognition of emotional prosody it was important to randomise the stimuli to avoid this.

Participants were informed that they would hear an audio recording of a series of sentences spoken to them by a male or female and that they had to decide from the possible choices (sadness, happiness, fear, anger, surprise and neutral) the emotional intention of the speaker, from the tone of voice alone. Participants were asked to make responses verbally, in a loud clear voice, and to respond with “don’t know” to any that they were unsure of. It was made clear that ‘neutral’ referred to lack of emotional intonation, rather than being a ‘don’t know’ option. Participants were given a visual cue (a piece of card with the emotion labels presented on it) throughout the duration of the task and the task was audio recorded and later analysed. The experimenter was present during a practice trial which included 3 stimuli not used in the main task. Participants were left alone to complete the main task in a sound-proofed room. Each stimulus presentation varied in duration (depending upon emotional intonation and sentence length) but the inter-stimulus interval was kept constant at 3 seconds.

The congruent condition was believed to be less cognitively challenging than the incongruent condition due to contextual cues being given, whereas, the incongruent condition included contrasting cues which made it more difficult. The measure of interest was number of correctly identified stimuli.

Measure: Total number of correct responses (for each emotion and a composite total).
Task Completion Time: 16 minutes.

Simple Go/No-go –
Response inhibition has been previously associated with the DLPFC and the VMPFC (Horn et al., 2003; Rubia et al., 2001). Here, a simple Go/No-go paradigm was utilised. This required a motor response to a 'Go' (target) stimulus and the inhibition of response to a 'No-go' (distracter) stimulus.

In this version of the test half of the participants were instructed that the large X shape was the 'Go' (target), therefore small X shapes were to be ignored for the duration of all trials; the other half were instructed to respond to the small X shape as the 'Go' (target), therefore large X shapes were to be ignored for the duration. There was a 50:50 representation of the two sizes of X shapes in the task.

Stimuli was randomised within blocks of 36 (18 large X shapes and 18 small X shapes in each block) until 9 blocks were created. The first block formed a practice trial (36 stimuli) and the remaining eight blocks formed the main task trial (288 stimuli).

The task was automated and presented on a computer screen using the software Superlab Pro, on a black background. Participants made responses using the 'G' key on the keyboard. Each trial began with the automated instructions on the screen "Please press 'G' when you are ready to begin". This was centrally presented on the screen in grey (Arial Baltic, point 50). Pressing 'G' initiated the trial presentation which began with decreasing numbers of centrally located grey asterisks (from 5 to 1; Arial

Baltic, point 50) and lasted for 250 milliseconds each. After the presentation of the asterisks, the target and distracter stimuli began to be presented in random order. Participants were instructed to rest their finger gently above 'G' and to press down in response to any target stimuli. An example of the order of stimulus presentation at the beginning of a trial is presented in Figure 2.6.

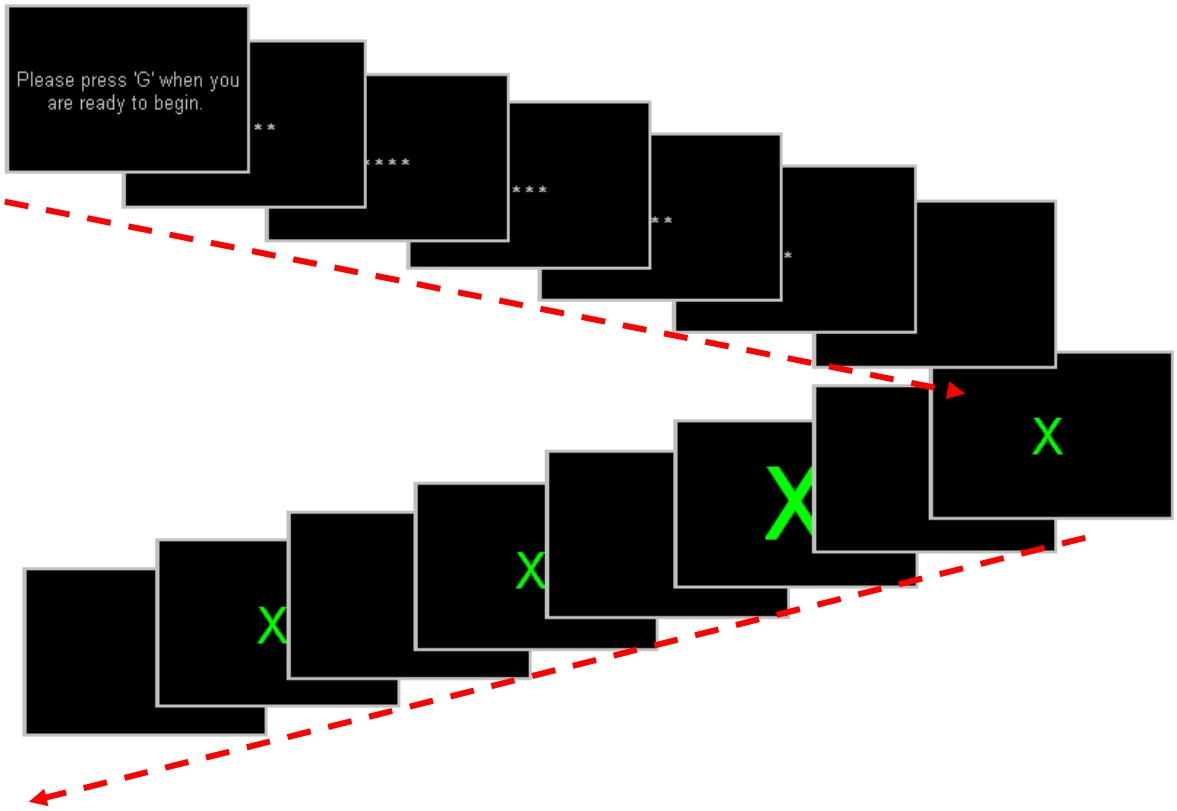

Figure 2.6: Example of the sequence of stimulus presentation at the beginning of a trial in the Simple Go/No-go task. Decreasing numbers of asterisks signify the beginning of a trial and each stimulus shape is punctuated by an inter-stimulus interval.

Stimulus presentation lasted for 250 milliseconds with an inter-stimulus interval of 750 milliseconds. Therefore participants had a window of 1 second to respond to a stimulus. Large X shapes were centrally presented in green (Arial Baltic, point 200) and the small X shapes were centrally presented in green (Arial Baltic, point 80). The experimenter was present for the duration of the practice trial to ensure participants understood the procedure and could clearly and easily differentiate between the 'Go' and

'No-go' stimuli. Participants were left alone in a quiet, dimly lit room for the main task.

The measure of interest was 'No-go' hit rate, as this was reflective of ability to inhibit a habitual response. In order to assist with interpretation of the results, 'Go' hit rates were noted, as were average response times for 'No-go' and 'Go' stimuli. Hit rate for 'Go' stimuli gave a measure of accuracy in which to compare 'No-go' hit rate; optimal performance on this task would result in a 0% 'No-go', and 100% 'Go' hit rate. Low responses to both types of stimuli would raise suspicion of participants having difficulty with making a response, or difficulty in grasping the task concept.

Measure: 'No-go' (distracter) hit rate.
Task Completion Time: 6 minutes.

Affect Go/No-go –

This was adapted from the methods used by Murphy, Smith, Cowen, Robbins and Sahakian (2002). Instead of using happy and sad words as alternating target 'Go' and distracter 'No-go' stimuli, in the present task, emotive (sad or happy) and neutral words were used as alternating 'Go' and 'No-go' stimuli. The purpose of the task was to measure response inhibition with a focus on whether emotional content has an influence on hit rates of 'Go' or 'No-go' stimuli. Emotive 'No-go' stimuli was found to cause greater cortical activation of DLPFC and VMPFC regions than neutral 'No-go' stimuli (Goldstein et al., 2007). Therefore, it was assumed to require greater PFC processing than the Simple Go/No-Go task.

Stimuli

Stimuli consisted of either words with emotive connotations (positive: happy and negative: sad) or those that were neutral. A thesaurus was used to find words that were synonyms of happy and sad. The final list was surveyed on 3 judges who were asked to rate which words were sad, happy and neutral. Only words that were agreed upon by all 3 judges were used for the final word selection process. These words were then sorted into word length

(from 5 – 9 letter words), so that at the end of the selection process, sad and happy words were matched for word length, which in turn were matched to neutral words.

In the main task there were 18 neutral type words and 18 emotive type words (9 sad, 9 happy; see Appendix 4 for the full word list). Selected words were randomised into blocks of 36, until 9 blocks were created, the first being the practice trial. Subsequent blocks were presented two at a time (2 blocks making up 1 trial), with the target 'Go' alternating between emotive and neutral words. Each block contained 50% emotive and 50% neutral words.

There were two versions of the task which were counterbalanced between participants. This is presented in visual form in Figure 2.7. In the first version, the practice trial was an emotive target 'Go' trial, followed by a neutral 'Go' trial, and so on. In the second version, the practice trial was a neutral 'Go' trial, followed by an emotive 'Go' trial and so on.

The task was automated on a computer screen using the software Superlab Pro and responses were made using a keyboard. At the beginning of each trial participants were presented with instructions as to the whether the 'Go' stimuli would be emotive or neutral words. These instructions were presented on the computer screen for 10 seconds on a black background in orange lettering (Arial, point 35). After the instructions, the presentation of a decreasing number of asterisks, from 5 to 1 (Arial, grey, 35 point: lasting for 250 milliseconds each) prepared the participant for the presentation of stimuli. Stimulus words were presented in the centre of the screen in green capitalised lettering (Arial, 45 point). Stimulus presentation lasted for the duration of 300 milliseconds with an inter-stimulus of 900 milliseconds before the next stimuli. Therefore, participants were given a window of 1200 milliseconds to respond to each stimulus, although they were instructed to respond to stimuli as quickly as they could.

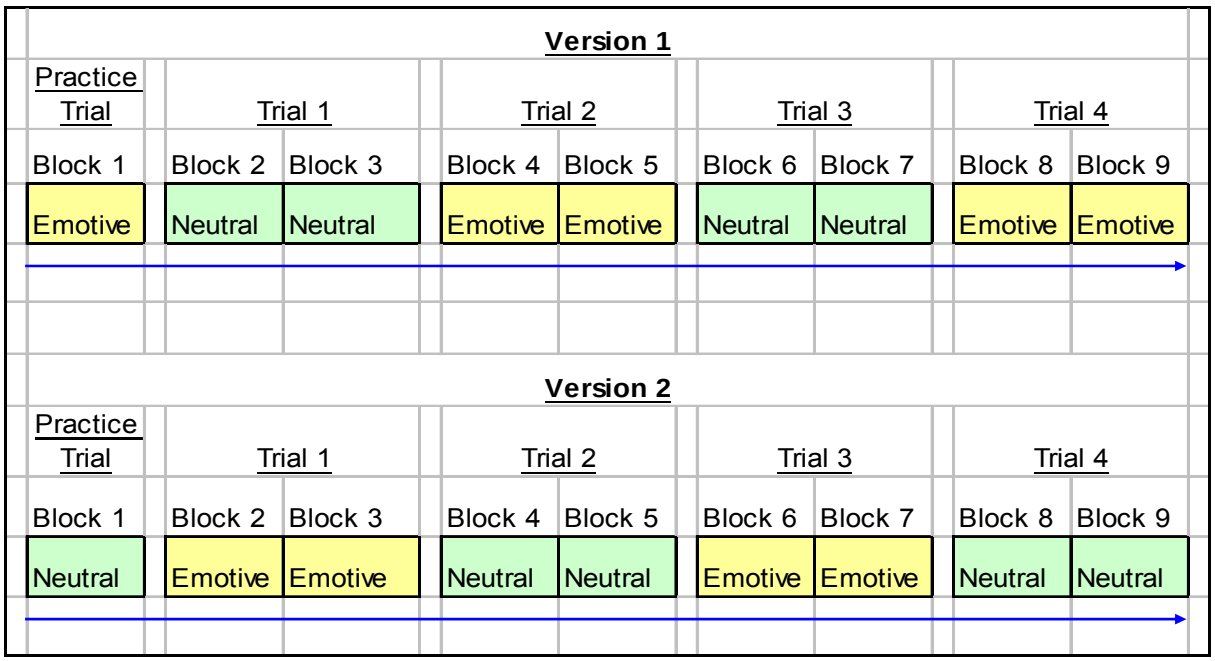

Figure 2.7: Order in which blocks were administered in the Affect Go/No-go, in version 1 and version 2. In each trial, either emotive or neutral words were specified as 'Go' targets.

For the duration of the trial, participants were reminded by a prompt at the top of the screen (e.g., "Target = Emotive"), as to the 'Go' of that trial in order to reduce confusion. This was centrally presented in grey lettering (Arial, 15 point). An example of the order of presentation of stimuli at the beginning of a trial is presented in Figure 2.8.

Procedure

Participants were instructed to rest their finger gently above 'G' on the keyboard for the duration of the task and to press down on it in response to a 'Go' (target) and instructed to ignore the 'No-go' (distracter) stimuli. The experimenter was present during the practice trial, and participants were encouraged to repeat the practice trial as many times as they required until they felt confident with the procedure and were familiar with all words presented. It was important that lack of understanding of word meanings did not interfere with the purpose of the task. For the duration of the main task, participants were left alone in a quiet and dimly-lit room.

The measure of interest was neutral 'No-go' and emotive 'No-go' hit rate, as this was reflective of ability to inhibit a habitual response (therefore the PFC-

specific component of the task). In addition, to assist with interpretation of the results, 'Go' hit rates were noted as a measure of accuracy, as were average response times for 'No-go' (neutral Vs emotive) and average response times for 'Go' (neutral Vs emotive) stimuli.

Measure: 'No-go' hit rate.
Task Completion Time: 9 minutes.

2.2.2 Executive Function Test Battery

The executive function test battery was chosen based on previously discussed literature suggesting a dominant role of the PFC in the performance of them (see section 1.3.2).

Wisconsin Card Sorting Test –
The WCST is a relatively well-established method of assessing PFC function (Grant & Berg, 1948). WCST performance has been implicated via lesion studies (Barceló & Knight, 2002; Goldstein et al., 2004; Milner, 1963) and brain imaging studies (Monchi et al., 2001) in PFC function, with a specificity for the left hemisphere (Barceló & Knight, 2002; Goldstein et al., 2004).

The 64 card version of the task was administered to participants and scored via the standardised procedure outlined in the manual (Heaton, 1981), which is the most common method used (Rhodes, 2004). The task was completed on a one-to-one basis, with the experimenter providing positive and negative feedback. Participants were presented with 4 stimulus cards which remained constant throughout the duration of the task (see Figure 2.9). Participants were instructed to sort the 64 cards which contained between one and four of the same shape (either triangle, star, cross or circle), all of which were the same colour (blue, green, red or yellow). Cards potentially could be sorted by colour, shape or number of shapes presented

Figure 2.8: An example of the sequence of stimulus presentation at the beginning of a trial on the Affect Go/No-go. Decreasing numbers of asterisks signify the beginning of a trial and each stimulus word is punctuated by an inter-stimulus interval

on the card. The first sorting category was colour. Participants were given no information as to sorting rule but were instructed to sort the cards into categories using the stimulus cards.

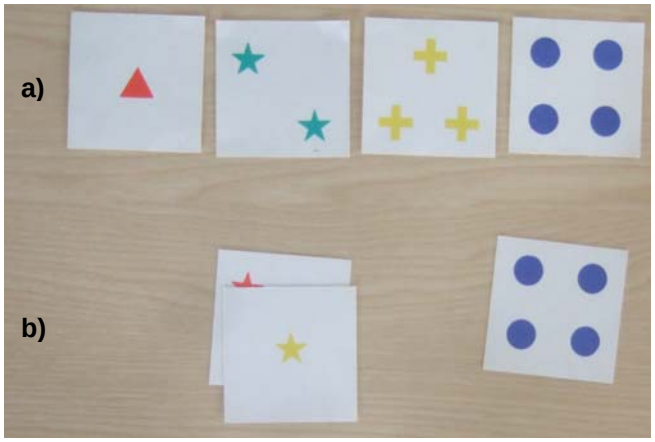

Figure 2.9: Cards used in the WCST: a) stimulus cards, b) examples of where cards might be sorted to.

The only information provided was positive "that's correct" and negative "that's incorrect" feedback. When ten correct responses were made in a row, the sorting category changed to shape, and then after another 10 correct responses, the rule changed to number for another 10 correct responses.

The task came to an end when all 64 cards were placed, or after three categories had been completed: whichever came first. The measure of interest obtained from the task was number of perseverative errors, which are believed to reflect cognitive flexibility. Furthermore, perseverative errors have been implicated as a measure of PFC function (Barceló & Knight, 2002; Goldstein et al., 2004; Milner, 1963).

Measure: Mean number of perseverative errors.
Task Completion Time: Approx 15 minutes

Verbal Fluency –

The VF test requires the production of verbal responses to a verbal cue and requires flexible responses that are contextually sensitive. It also has a relatively heaving memory loading (Henry & Craword, 2004). This task was

found to be particularly vulnerable to left frontal injury (Baldo et al., 2001; Peterson et al., 1998; Ravnkilde et al., 2002).

Participants were presented with a verbal prompt which was a noun (e.g., apple) and were instructed to produce out loud as many verbs that were related to that noun as possible for the duration of one minute (for example, 'peel', 'eat', 'bite'). The stimulus nouns consisted of four objects ('pencil', 'shirt', 'cake' and 'fish'), a concept ('game') and a place ('cinema'), and were given the opportunity to familiarise themselves with the procedure using the stimulus noun 'Apple'. Participants were presented with the stimuli on one-to-one basis with the experimenter.

The task was audio recorded and later scored by two independent scorers. Any ambiguous responses were discussed by both scorers and dealt with accordingly. Responses were scored as incorrect if they were a repetition of a previously mentioned verb given in response to the same stimulus noun, if they were not a verb or if they were not unambiguously related to the stimulus noun. The majority of incorrect responses given were in the form of repetition. However, these were not included in analyses, as there was a tendency for there to be a low rate of error production in all groups observed.

Due to findings in the literature of effects of educational attainment on VF (Ardila et al., 2000), this factor was considered when utilising the measure. Ardila et al. found that education accounted for 26.3% of the variance between scores, when observing performance in individuals aged 17 – 84 years, with 0 – 24 years in education. Ardila et al. furthermore suggested that the educational effects on cognitive function are not linear. For example there may be a large difference between 0 and 3 years of education but there is likely to be little between 12 and 15 years of education. The greatest significance is reportedly at the lower end of educational attainment. Interestingly, Bolla, Lindgren, Bonaccorsy, and Bleecker (1990) found that in a population aged 40 – 89 years, that education did not account for any variance in VF performance beyond that that could be attributed to verbal

intelligence. Due to the potential effects of education on the VF task, individuals with less than 12 years in education were removed from analyses. This is outlined further in sections to follow.

Measure: Mean number of verbs generated
Task Completion Time: Approximately 10 minutes

Tower of London –

The TOL is commonly used as a tool to measure PFC function and involves non-verbal planning (Shallice, 1982). Although it appears to be well established as a measure of PFC function (Glosser & Goodglass, 1990; Newman et al., 2003; Owen et al., 1990; Rezai et al., 1993), some controversy exists as to whether this is predominant to the left (Glosser & Goodglass, 1990) hemisphere or whether it is bilaterally implicated (Newman et al., 2003; Owen et al., 1990; Rezai et al., 1993).

For the TOL, participants were presented with a wooden apparatus of a tower with 3 wooden pegs of various lengths, and 3 coloured beads (1 red, 1 green and 1 blue). Participants were presented with problems on a one-to-one basis and instructed to solve the problem by moving one bead at a time, with only one bead in their hand at any one time and instructed that no more than three beads were allowed on the first peg, two on the second peg and no more than one on the third peg. Coloured beads were to be moved from an initial standard configuration which stayed constant throughout the task to match a target configuration. Before each problem was presented, the instructions given by the experimenter included only the number of the problem (e.g., “problem one…”) and the number of moves required to complete it (e.g., “…can be solved in two moves”). An example of a problem is presented in Figure 2.10. All twelve configurations of the problems can be found in Appendix 5. Twelve problems were presented to participants on stimulus cards (one problem to one card), systematically increasing in number of moves allowed from 2 to 5 as well as in difficulty. Problems were presented in the same order to all participants. A practice problem was

completed (using none of the problems from the main task) in order to familiarise participants with the procedure.

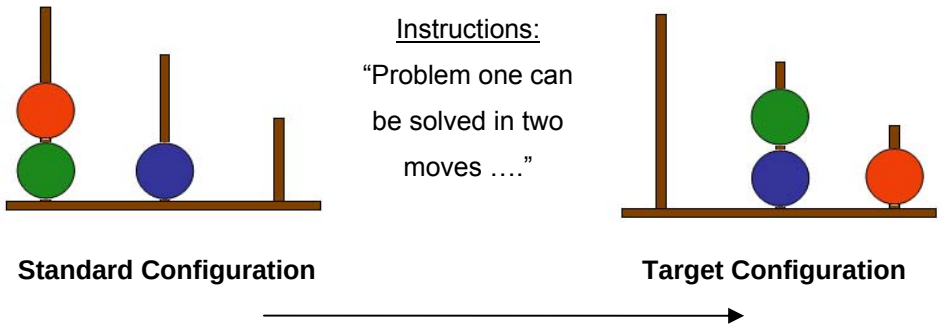

Figure 2.10: An example of a TOL problem.

Participants were instructed that they were allowed to pass on any problems they felt they could not complete and that they had no more than three attempts to solve each problem. When a participant identified that they had made an error, the stop-watch was paused, and the participant instructed to move the apparatus back to the standard configuration. At this point, the stop-watch recommenced. All problems were completed by all participants tested.

Data was collected using an audio recorder and later analysed using the computer software Cool Edit Pro: Version 2, which meant that the task could be digitally timed for greater accuracy. The measure used was mean total time (planning time and execution time combined).

Measure: Mean completion time.
Task Completion Time: Approximately 15 minutes.

Delayed Serial Recall –

A Delayed Serial Recall task (DSR; adapted from that used by Chein & Fiez, 2001) was used to ascertain verbal working memory function. Verbal working memory, has previously been dominantly linked to the PFC as well

as the supplementary motor and premotor, and cerebellar regions (Chein & Fiez, 2001; D'Esposito & Postle, 1999; D'Esposito, Postle & Rypma, 2000).

Stimuli

Stimuli were presented to participants on a computer screen with automated instructions using Microsoft PowerPoint. Stimulus words used were phonologically and semantically dissimilar, of one syllable, 4 – 7 letters long and with a written frequency of > 30 (Francis & Kucera, 1982). These were presented in white, Arial (size 40) font on a black background.

Procedure

Participants were administered with 8 consecutive trials each consisting of one presentation of a list of 5 words (different words were used in each trial). At the beginning of each trial, participants were required to focus on a fixation point in the centre of the screen (*). After 20 seconds the list of 5 words was presented, each word for 1 second with an inter-stimulus interval of 600 milliseconds. Participants were then presented with a rehearsal prompt (……), in which they were given 20 seconds to covertly rehearse the previous list of words presented to them. A recall prompt (####) lasting 4 seconds and accompanied by an audible tone, signified the requirement to recall out loud and as clearly as possible all words previously seen and in the same order as presented. Any word that participants were unable to recall was to be replaced with the word 'skip'. Visual representation of one of the trials is presented in Figure 2.11.

Participants were given an opportunity to familiarise themselves with the procedure with a practice word list. Participants were left alone to complete the task in a dimly lit and quiet room. Responses were recorded onto an audio recorder and later analysed. Participants were not given any feedback as to correct and incorrect answers.

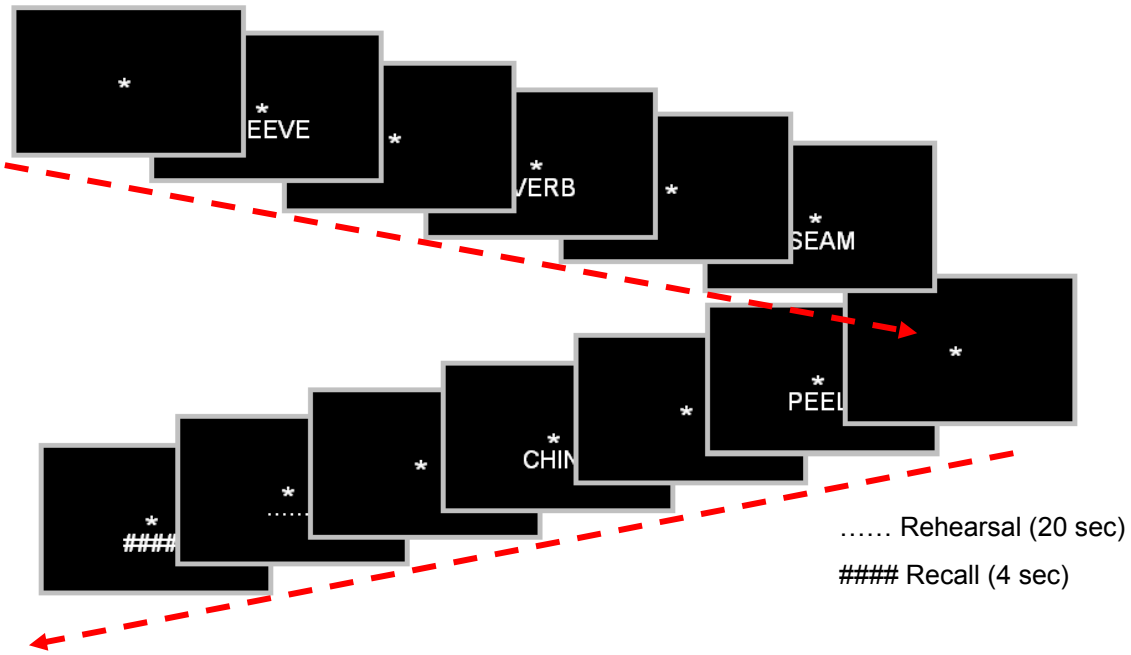

Figure 2.11: Sequence of stimulus presentation during a trial in the DSR task. Each sequence began with a fixation point (an asterisk) lasting for 20 seconds. All fixation points signifying an inter-stimulus interval lasted for 600 ms.

The measure used in this task, was number of correctly recalled words. Any words that were correctly recalled but in an incorrect order were scored as incorrect.

Measure: Total number of correctly recalled words.
Task Completion Time: 8.5 minutes.

2.2.3 Control Test Battery

Measures described here are used as control tasks, as they were not found to be strongly implicated in PFC ability.

Psychomotor Vigilance Test –
Simple reaction time was measured using the Psychomotor Vigilance Test (PVT; Dinges & Kribbs, 1991). Salthouse (1993, 1996) suggests that cognitive ageing occurs due to changes in processing speed with advancing age that then impact upon complex functions such as those associated with

the PFC. In order to investigate this further, simple reaction times were obtained.

This task was run on DOS on an IBM PC. Participants were presented with a millisecond counter in the centre of the computer screen. The aim of the task was to respond by pressing a button as fast as possible, whenever numbers appeared in the counter. Stimuli were set to appear in random intervals (between 2 and 12 seconds) for the duration of 10 minutes. Mean reaction time was the measure used. Any reaction times of more than 500ms were deemed to be lapses and were therefore removed. In order to familiarise themselves with the procedure, participants were allowed a one-minute practice opportunity before the test commenced.

During the main task, participants were left alone in a quiet, dimly lit room, with the purpose of reducing distractions. Although the presentation of all other cognitive tests was counterbalanced, this task was presented last due to the monotonous nature of it and the importance of keeping motivation high during the testing procedure.

Measurement: Mean reaction time.
Duration: 10 minutes.

Fluid Intelligence –

Fluid intelligence was assessed using the Cattell and Cattell Culture Fair test (CCCF; Cattell, 1963). Fluid intelligence refers to novel problem solving ability and reasoning, independent of acquired previous knowledge (Cattell, 1971). This was used as a screening measure, to ensure that participants did not differ significantly on IQ, which has been suggested as being an aspect of individual difference (Cattell, 1971). In addition, this was chosen as a control measure for global functioning. Empirically, fluid intelligence has been found to be a predictor of performance on a wide range of tests, indicating that it has a high level of general intelligence, or “g” loading (Carroll, 1993).

The CCCF was chosen as a measure of IQ, due to the limited effects on it caused by educational attainment, verbal fluency and cultural climate. These are factors that are important to consider, when comparing groups of different ages. The CCCF has been tested extensively for reliability and validity (e.g., construct validity; the test correlates with other measures of general intelligence).

The tests (forms A and B on scale 3) were administered and scored via the standardised procedures as outlined in the manual, with imposed time constraints. Tests were completed on a one-to-one basis, with the experimenter being present to provide instructions, but leaving the participant alone during the completion of problems.

The test consists of four subtests (*series, classification, matrices*, and *conditions*). These are visually presented in Figure 2.12. The *series* subtest requires participants to ascertain from choices given (a – f), the next figure in the sequence. The *classification* subtest involves problems in which participants are asked to decide which two of the choices (a – e) are the odd ones out. The *matrices* subtest involves choosing from (a – f), an appropriate figure to complete the matrix shown (e.g., which shape completes the design?). Finally, the fourth subtest *conditions,* requires participants to decide in which of the choices (a – f) could a dot be placed so that it duplicates the conditions in the example given.

Measurement: Intelligence Quotient (IQ).
Duration: 15 minutes per form.

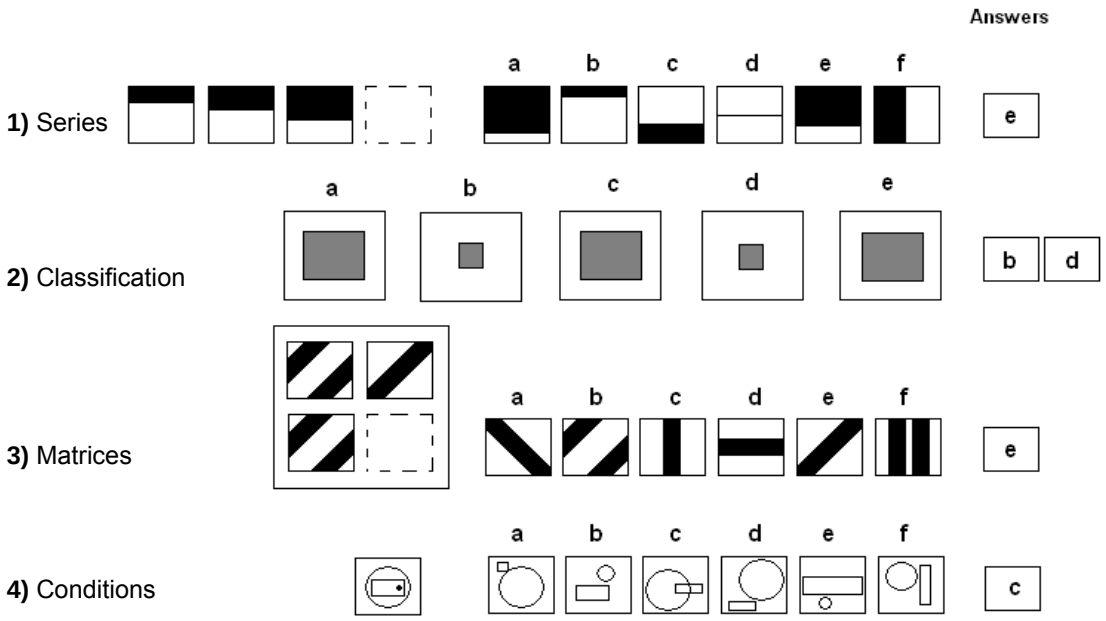

Figure 2.12: An example of a problem from each of the 4 subtests in the CCCF (Scale 3); 1) Series, 2) Classification, 3) Matrices and 4) Conditions.

2.3 Sleep Electroencephalography (EEG)

Sleep EEG recordings were obtained from participants for the purpose of Studies 3 – 5. These were carried out in the homes of participants using ambulatory recordings[6]. Home recordings were believed to be preferential to laboratory testing in order to emulate as far as possible an individual's typical nights' sleep.

Electrode placement took place 2-3 hours before participants' typical bedtime. The procedure took no longer than 1.5 hours to complete, and afterwards participants were able to go about their normal bedtime routine.

Participants were instructed to refrain from the consumption of caffeinated or alcoholic beverages for the 24 hours leading up to the night of EEG recording. In addition, participants were instructed to try to obtain their 'typical' nights sleep as far as possible.

[6] Embla™ system, Flaga HF. Medical devices, Iceland.

2.3.1 EEG Recording

EEG was recorded using an ambulatory recording device. Silver chloride cup electrodes were placed according to the International 10-20 system at sites: FP_1/F_3, FP_2/F_4 O_1/P_3 and O_2/P_4, (see Figure 2.13). Each electrode pair corresponded to a particular region of the cortex:

FP_1/F_3 → Left Prefrontal Cortex (LPFC)
FP_2/F_4 → Right Prefrontal Cortex (RPFC)
O_1/P_3 → Left Occipital/Parietal Cortex (LOPC)
O_2/P_4 → Right Occipital/Parietal Cortex (ROPC)

A ground electrode was placed on the forehead and electrode impedances were maintained below 5 kΩ. In order to aid in the identification of sleep states, bipolar submental electromyogram (EMG; electrical currents of muscles below the chin) as well as bilateral electro-oculogram (EOG; electrical currents of muscles around eyes) were recorded as suggested by Rechtschaffen and Kales (1968). In addition, C_3-A_1 EEGs were taken (corresponding to central regions of the right hemisphere) for sleep staging purposes.

Two nights EEG recording was obtained for each participant, the first as an adaptation night and the second was used for analysis. Research has found first night effects in older participants, particularly in sleep architecture (Crowley et al., 2002), therefore data obtained during the first night was discarded.

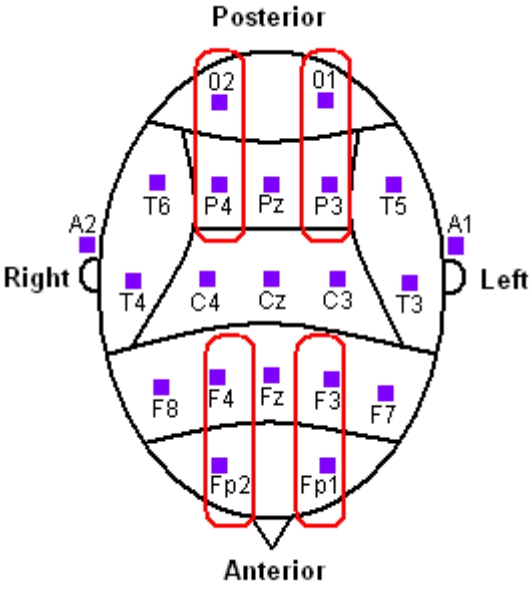

Figure 2.13: Regions of interest corresponded to electrode placements on derivations FP_1/F_3, FP_2/F_4, O_1/P_3, and O_2/P_4, which are outlined in red. The figure demonstrates all possible sites of electrode placements according to the 10-20 system.

2.3.2 Spectral Analysis

Spectral analysis was utilised for the identification of low frequency delta in derivations FP_1/F_3, FP_2/F_4, O_1/P_3 and O_2/P_4. Raw EEG was band-pass filtered, for frequencies:

1) 0.5 – 1 Hz
2) 1 – 1.5 Hz
3) 1.5 – 2 Hz
4) 2 – 2.5 Hz
5) 2.5 – 3 Hz
6) 3 – 3.5 Hz
7) 3.5 – 4 Hz
8) 4 – 4.5 Hz

The EEG signal was sampled at 100 Hz and filters set at 45 Hz to filter any extraneous signal caused by electrical equipment in the vicinity. EEG was spectrally analysed in 30 second epochs; the frequency band of interest was low frequency delta, 0.5 – 1 Hz, due to findings of recent literature (Anderson & Horne, 2003) of links with localised cognitive function. This band was observed as a percentage, relative to the other 7 delta frequency bands. Therefore, the parameter of interest was the proportion of delta,

oscillating at 0.5 – 1 Hz, in comparison to higher frequencies of delta. Delta less than 0.5 Hz was not analysed, due to the potential of contamination due to eye movements, which are usually < 0.3 Hz. All raw EEG was checked for artefacts. These were removed from each frequency band, across all four derivations, within 30 second epochs; epochs either side were averaged in order to compensate for the removed epoch.

Delta EEG was observed in the first NREM period only. This was due to the beginning of the night being less interrupted (therefore the potential for fewer artefacts), as well as the NREM at the beginning of the night containing the most intense low frequency delta concentration. For example, Achermann and Borbély (1997) discovered that slow oscillations peaked in the first two NREM periods of the night and that there were no significant differences between the first and second NREM period.

Measurement: Percentage of 0.5 – 1 Hz delta relative to 1 – 4.5 Hz during the first NREM period.

2.3.3 Visual Scoring

Sleep architecture parameters were visually scored using Somnologica software (version 2.0) at C_3-A_1. Due to visual scoring of sleep parameters being fallible to experimenter effects, this was attempted to be counteracted by recordings being coded so that the scorer was blind to the identity of the participant, and the year of recording in the repeated measures comparisons. In order to ensure reliability between the scoring of the baseline and follow-up recordings, all recordings were scored by the same person.

Sleep architecture -

Sleep stages and sleep continuity were visually scored via the Rechtschaffen and Kales (1968) standardised technique. Derivation C_3-A_1 was used for this, as suggested by Rechtschaffen and Kales but checked

against prefrontal and occipital/parietal recordings (FP_1/F_3, FP_2/F_4 O_1/P_3 and O_2/P_4) for any anomalies. Parameters scored were:

- Sleep period time (SPT: total time between sleep onset and sleep cessation).
- Sleep efficiency (percentage of time spent asleep between sleep onset and waking).
- Total sleep time (TST: total time during SPT spent asleep).
- Waking after sleep onset (WASO: total time during SPT spent awake).
- Stage 1
- Stage 2
- Stages 3 and 4 combined [7]
- Rapid eye movement (REM) sleep.

Sleep spindles –

Spindles were identified on all four derivations (FP_1/F_3, FP_2/F_4, O_1/P_3, and O_2/P_4). These were scored visually, as opposed to spectrally, as spectral analysis does not differentiate between the frequency of spindling and background sigma EEG (for example, it does not take into account the graphic shape of spindles).

According to Rechtschaffen and Kales (1968), spindles should only be scored if the duration is more than 0.5 seconds and oscillating at 12 – 14 Hz. However, most studies of age-related declines in spindle occurrence take into account changes in the morphology of these during the ageing process. For example, Guazzelli et al. (1986) identified spindles in 11.5 – 14.5 Hz range and Crowley et al. (2002) identified spindles in the 11 – 16 Hz range, in older participants. Taking into account literature suggesting age-related changes in spindle characteristics, criteria as asserted by

[7] Stages 3 and 4 were combined due to lack of stage 4 in many of the older participants.

Rechtschaffen and Kales (1968) were relaxed to include lower frequencies of spindle activity. The criteria were that spindles had to:

a) Be longer than 0.5 seconds in duration.
b) Oscillate at 11 – 16 Hz.
c) Clearly stand out from the background EEG.

Spindles were identified in the first two NREM periods of stage 2 sleep that descended into stage 3/4. Stage 2 was deemed more appropriate (compared to stage 3/4) for the visual identification of spindles, due to the graphic shape being difficult to identify in the SWA prevalent in stage 3/4. Also, sleep at the beginning of the night tends to be less prone to artefact interference, in comparison to cycles at the end of the night.

Measurement: Spindle density (number of spindles per minute) of stage 2 sleep in the first 2 NREM periods.

K-Complexes –

KCs were visually scored at four derivations: FP_1/F_3, FP_2/F_4, O_1/P_3, and O_2/P_4. Although it is more labour intensive, the method of visually scoring was chosen over that of spectral analysis because automatic techniques are able to identify phenomena on the basis of frequency and amplitude but cannot pick out the KC graphic shape from background EEG. According to Rechtschaffen and Kales (1968), KCs should last no longer than 0.5 seconds and show a well delineated negative sharp wave followed by a positive component. The criteria for KCs were that they had to:

a) Last no longer than 0.5 seconds in duration.
b) Clearly stand out from the background EEG.

KCs were taken from the first 2 NREM periods of stage 2 sleep that descended into stage 3/4. The reason for stage 2 being observed and not other sleep stages is that KCs are particularly prominent during this period and although they also occur during stage 3/4, it is difficult to distinguish

them from background SWA. In addition, literature has suggested an important role of KCs in the stage 2 descending into stage 3/4 sleep, in SWA facilitation (De Gennaro et al., 2000a).

Measurement: KC density (number of KCs per minute) of stage 2 sleep in the first 2 NREM periods.

2.4 Data Analysis

A mixture of designs was used to analyse data, depending upon the study; therefore this is discussed separately for each individual study. Accepted level of significant was set at the conventional $p < 0.05$ for Study 1. However, with the presentation of cross-correlation matrices, the accepted level of significance was set at a more stringent $p < 0.01$ to reduce for the likelihood of a type I error. Furthermore, due to the large number of analyses utilising the same cohort in the remainder of the studies, significance was accepted at the more stringent $p < 0.01$.

Outliers –
Outliers were identified on the basis that:

1. The 5% trimmed mean differed considerably from the original mean.
2. They were found to be more than 2 standard deviations from the group mean.
3. A box-plot or scatter–plot demonstrated that they were exerting an influence over the distribution of values.

If extreme values were identified using these criteria, results with and without the suspected outlier was presented for reference purposes: the latter within a footnote. This is as suggested by Kruskal (1960). However, if the outlier was found to affect the results substantially, they were removed to avoid data distortion. However, in this case justification for removal is offered in the relevant sections.

Effect Sizes –

Effect sizes were reported, in order to inform about the magnitude of effect. Eta squared (η^2) values were calculated to reflect effect sizes when parametric techniques were employed (with the exception of those that explore correlation). This represents the amount of variance of the dependent variable that can be explained by the independent variable. Cohen (1988) suggested guidelines to interpret the size of an effect utilising η^2. Cohen proposed that 0.01 indicated a small effect, 0.06 a medium effect and 0.14 a large effect. Measures of degree of association (*r*) were utilised to suggest effect sizes for non-parametric tests. As with correlation coefficients, 0.10 indicates a small effect, 0.30 a medium, and 0.50 a large effect size (Cohen, 1988).

2.5 Summary Table

Table 2.4 summarises the usage of cognitive function and sleep EEG methods in the individual studies reported in this thesis.

Table 2.4: A summary of the inclusion of tests of cognitive function and sleep EEG methods in individual chapters.

	Social Cognition				Executive Function				Control Tests	
	Ekman 60 Faces	Emotional Prosody	Simple Go/No-Go	Affect Go/No-Go	Wisconsin Card Sorting Test (WCST)	Verbal Fluency (VF)	Tower of London (TOL)	Delayed Serial Recall (DSR)	Fluid Intelligence (IQ)	Psycho-motor Vigilance Test (PVT)
Ch 3: Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus	✓	✓	✓	✓	✗	✓	✓	✗	✓	✓
Ch 4: Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus	✗	✗	✗	✗	✓	✓	✓	✗	✓	✓
Ch 5: Study 3: Age-Related Changes in PFC Sleep EEG	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗
Ch 6: Study 4: Links between Sleep EEG and Cognitive Function Revisited.	✗	✗	✗	✗	✓	✓	✓	✓	✓	✓
Ch 7: Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective	✗	✗	✗	✗	✓	✓	✓	✗	✓	✓

		Visual Scoring		
	Spectral Analysis	Sleep Architecture	Sleep Spindles	K-Complexes
Ch 3: Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus	✗	✗	✗	✗
Ch 4: Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus	✗	✗	✗	✗
Ch 5: Study 3: Age-Related Changes in PFC Sleep EEG	✓	✓	✓	✓
Ch 6: Study 4: Links between Sleep EEG and Cognitive Function Revisited.	✓	✗	✗	✗
Ch 7: Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective	✓	✗	✓	✓

3 Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus

3.1 Introduction

Age-related changes in the brain have been found to occur to a greater extent in the PFC, in comparison to other regions (Gerard & Weisberg, 1986; Haug et al., 1983; Terry, et al., 1987). Furthermore, particular higher cognitive processes such as executive function, have been reliably found to be reliant on PFC integrity (e.g., Baldo et al., 2001; Barceló & Knight, 2002; Glosser & Goodglass, 1990; Goldstein et al., 2004; Milner, 1963; Monchi et al., 2001; Newman et al., 2003; Owen, et al., 1990; Peterson et al., 1998; Ravnkilde et al., 2002; Rezai et al., 1993).

Aspects of social cognition are also believed to be subserved by regions of the PFC, such as the VMPFC. Functions implicated include response inhibition (Horn et al., 2003; Rubia et al., 2001), particularly when stimuli is emotive (Goldstein et al., 2007); recognition of emotion in others via facial expression (Hornak, et al., 1996; Nakamura et al., 1999); and via emotional prosody (Hornak, et al., 1996; Mitchell et al., 2003; Wildgruber et al., 2005).

Age-related declines have been shown in the recognition of emotion via facial expression. Although Calder et al. (2003) found age-related deficits in the recognition of sadness and fear (whilst no declines were seen in disgust, anger, happiness and surprise), Phillips et al. (2002) reported that sadness and anger were selectively affected with advancing age, leaving the recognition of disgust, fear, happiness and surprise intact. Differences in the recognition of specific emotions within groups may be accounted for by the likelihood that the recognition of each emotion taps into diverse brain regions, as posited by Calder et al. On the other hand, contrasting findings between studies may be explained by difference in age groups. In the study conducted by Phillips et al., comparisons were made between broad age-

bands (20 – 40 and 60 – 80 years). It is argued that if the age-band within a group is too wide, it will reduce the sensitivity of the test to detect age differences between groups. The age-bands were more restricted in the research by Calder et al. (18 – 30 and 58 – 70 years) but deficits might not present themselves in the other emotions until later in life. Therefore, there is an arguable need for further exploration into age-associated changes in the recognition of emotion via facial expression between groups that have relatively restricted age-bands, and utilising an older group, that are later in life than has been previously utilised.

Whilst a recent interest has developed in the area of recognition of emotion via facial expression, over the life-span, the area of cognitive ageing relating to social cognition is somewhat limited. This may be due to lack of age-appropriate measures; most tasks that currently exist in the area of social cognition have been constructed for the observation of cognitive development in children or adolescents. Therefore, usage of these measures in the context of cognitive ageing may be misleading. For example, Macpherson, Phillips, and Della Sala (2002) found a lack of age-related differences in a faux pas recognition task between age groups: 20 – 38, 40 – 59 and 61 – 80 years. However, closer inspection of the results illustrated notable ceiling effects, that may have masked any ageing effects.

Lack of availability of age-appropriate measures meant that for the purpose of the research in Study 1, it was important to develop measures of social cognition suitable for testing adults that have high levels of cognitive functioning. This was done whilst retaining a well established, validated, and extensively used measure (Ekman 60 Faces). The construction of the following tests: Simple Go/No-go, as a measure of response inhibition; Affect Go/No-go, as a measure of response inhibition with an emotive component; and Emotional Prosody test, as a measure of recognition of emotion in others via prosody; was guided primarily by lesion and imaging studies that have converged on the implication of these tasks in PFC integrity (see section 1.3.2).

3.1.1 Main Aims and Hypotheses

The main aim of the study reported in the present chapter is to expand recent developments in the area of cognitive ageing, with a focus on social cognition. It is suspected that as other functions (e.g., executive function) associated with the PFC undergo age-related declines, that social cognition will follow a similar course. It was hypothesised that:

i) An older group will be less successful in the correct identification of emotional stimuli via facial expression and emotional prosody, than a young group. These age-differences will be increased when stimuli are incongruent.

ii) Age differences will be found in response inhibition with an older group having greater difficulty in ignoring distracter stimuli. Furthermore, this difference will be more substantial when the stimulus is emotive in content, compared to neutral.

3.2 Method

3.2.1 Participant Characteristics

All participants in Study 1 were taken from the Cross-Sectional Design Cohort described in the *General Method* (section 2.1.2). Participant characteristics are presented in Table 3.1. The young group (n = 16) had a mean age of 22.25 years (SD = 2.35 years) and the older group (n = 16) a mean age of 71.5 years (SD = 4.4 years). There was a 50:50 female to male ratio in each group.

Table 3.1: Younger group (*n* = 16) and older group (*n* = 16) participant characteristics.

Young Group					Older Group				
Ps	**Sex**	**Age**	**ESS**	**TIB (hrs)**	**Ps**	**Sex**	**Age**	**ESS**	**TIB (hrs)**
PW01	m	20	3	9.50	JH01	f	77	6	8.50
DS02	m	24	2	9.00	PM02	m	65	9	8.50
DW03	m	21	4	8.00	AM03	m	71	6	8.00
SB04	m	23	6	7.00	WB04	m	65	1	8.50
KB05	f	20	3	10.00	RT05	m	74	4	8.25
JK06	m	24	0	8.50	BM06	f	66	6	9.00
LU07	f	25	6	7.75	BW07	f	79	5	9.00
PB08	m	24	6	7.00	EA08	f	78	8	8.75
SE09	m	20	1	8.50	BF09	f	68	6	8.50
PT10	f	20	4	8.75	GK10	m	69	8	7.50
HJ11	f	20	6	9.00	WK11	f	69	1	8.50
SF12	f	20	5	8.00	IJ12	f	71	8	8.00
VH13	f	23	1	9.00	NB13	m	72	8	7.00
LM14	f	20	2	9.00	KJ14	m	73	3	8.00
KB15	f	26	8	8.00	JF15	m	75	5	8.50
VB16	m	26	1	8.00	CF16	f	72	7	9.25
Mean		**22.25**	**3.63**	**8.44**	**Mean**		**71.50**	**5.69**	**8.36**
SD		**2.35**	**2.36**	**0.83**	**SD**		**4.40**	**2.44**	**0.57**
Male Mean		**22.75**	**2.88**	**8.19**	**Male Mean**		**70.50**	**5.50**	**8.03**
Male SD		**2.19**	**2.30**	**0.88**	**Male SD**		**3.85**	**2.78**	**0.54**
Female Mean		**21.75**	**4.38**	**8.69**	**Female Mean**		**72.50**	**5.88**	**8.69**
Female SD		**2.55**	**2.33**	**0.74**	**Female SD**		**4.93**	**2.23**	**0.40**

General Daytime Sleepiness and Time in Bed –

Due to the scope of the thesis being that of PFC function and links between cognition and sleep EEG, basic parameters of sleep were noted in both groups. Along with sex and age, Epworth Sleepiness Scale (ESS) scores and time in bed (TIB) are displayed in Table 3.1.

As can observed in Table 3.1 there was no substantial difference between the mean TIB for the young group and the older group. Although there are slight differences between males and females within each group, this is fairly balanced between groups, with females in both sleeping for longer on average. On the other hand, the older group seemed to report more general daytime sleepiness via ESS than the young group, although all scores are acceptable within the parameters set out by Johns (1991). Males and

females are fairly matched for ESS within the older group, but males tended to report more daytime alertness than the females in the young group.

3.2.2 Cognitive Test Battery

Cognitive tests were administered via the standardised procedures as set out in the Chapter 2 (*General Method:* see section 2.2). Cognitive testing involved measures of social cognition that have been implicated in PFC function:

Social Cognition Tests –

- Ekman 60 Faces
- Emotional Prosody
- Simple Go/No-go
- Affect Go/No-go

Due to the utilisation of tests of social cognition being relatively novel in the context of cognitive ageing, executive function measures were also administered in order for comparisons to be made between more established tests of PFC function.

Executive Function Tests –

- Verbal Fluency (VF)
- Tower of London (TOL)

A fluid intelligence (IQ) test was administered in order to explore potential non-PFC specific differences between the young and the older groups. The PVT reaction time test was administered to the older group only, in order to explore potential 'global slowing'.

Control Tests –

- Fluid Intelligence (IQ).
- Psychomotor Vigilance Test (PVT).

3.2.3 Data Analysis

All data met the assumptions for parametric data, therefore mixed ANOVAs were utilised (with Greenhouse-Geisser corrections where appropriate), with independent samples t-tests to explore group differences. Pearson product-moment correlation coefficient was utilised to explore the relationship between cognitive function measures. Effect sizes were reported in order to inform of magnitude of effect; these were eta squared (η^2), for independent samples t-tests, and ANOVAs; and for Pearsons correlation, *r* denotes the effect size.

Significance was accepted at the conventional $p < 0.05$ level. With regards to correlation matrices, in order to correct for multiple analyses, significance was accepted at the more stringent $p < 0.01$. All hypotheses were one-tailed (unless otherwise noted). This was due to guidance in the literature regarding the expected direction of differences.

Equal variance was assumed between the groups, unless otherwise denoted in the footnotes. Furthermore, no outliers were identified on the basis of criteria set out in *General Methods* (*Outliers:* section 2.4).

3.3 Results

3.3.1 Differences in Social Cognition

Ekman 60 Faces –

The young and older groups were compared on recognition of emotion on Ekman 60 Faces Task. Correct recognition rates of all emotions were submitted to a 3 way mixed ANOVA with Greenhouse-Geisser corrections due to violation of the assumption of sphericity. Factors of interest included: emotion (within subjects: happiness, surprise, disgust, anger, sadness and fear), age group (between subjects), and sex (between subjects).

A significant effect was found for emotion [$F(3.62, 101.24) = 19.64$, $p < 0.0005$, $\eta^2 = 0.38$]. There was not a main effect for age group ($p = 0.13$), although the effect size was moderate ($\eta^2 = 0.07$); nor was there a main effect for sex, although it was found to approach significance [$F(1, 28) = 3.48$, $p = 0.07$, $\eta^2 = 0.09$]. A significant interaction was found between emotion and age [$F(3.62, 101.24) = 2.65$, $p < 0.05$, $\eta^2 = 0.05$]. All other interactions (emotion*sex, age*sex and emotion*age*sex) were not significant ($p > 0.19$) and effect sizes were small ($\eta^2 < 0.05$).

In order to compare age groups on the recognition of specific emotions, each emotion was analysed separately using independent samples t-tests with bonferroni alpha adjustments (0.05/6 = 0.0083). The older group recognised significantly fewer fear stimuli, than did the young group [$t(30) = 2.55$, $p < 0.0083$, $\eta^2 = 0.18$]. However there were no significant differences on any other emotion ($p > 0.32$)[8] and effect sizes were small ($\eta^2 < 0.03$). As can be observed in Figure 3.1, young and older groups followed similar gradients with regards to number of correctly recognised stimuli for each emotion (e.g., both find happiness the easiest and fear the most difficult).

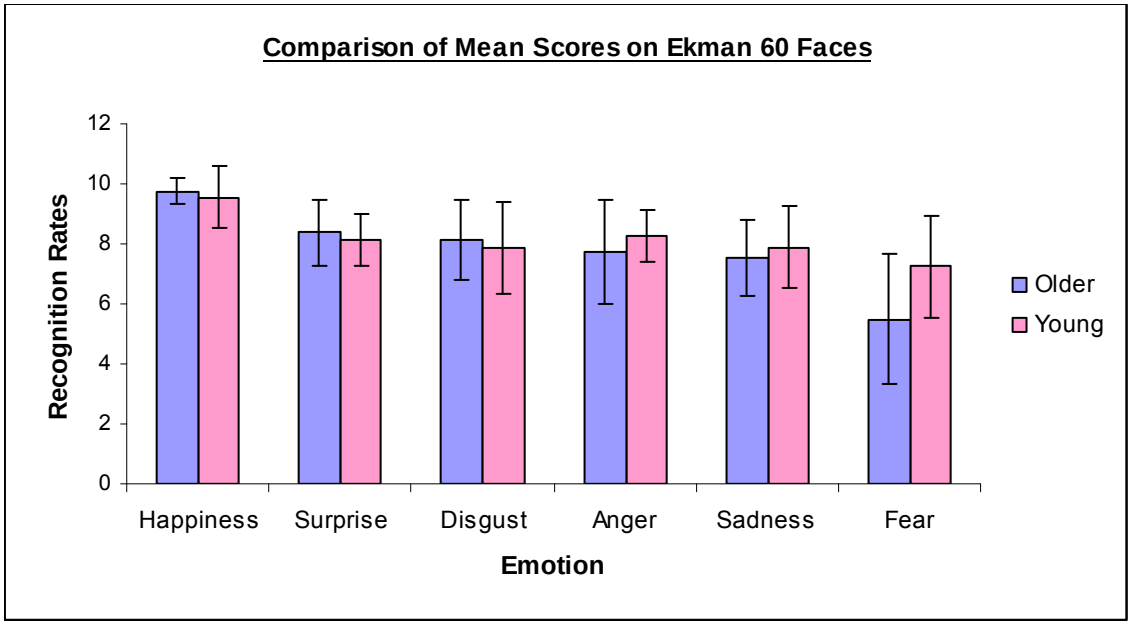

Figure 3.1: Comparison of recognition of emotion via facial expression in the young (*n* = 16) and older group (*n* = 16). Vertical lines represent standard deviations.

[8] Equal variance was not assumed for group comparison on the emotion anger.

Emotional Prosody –

Mean correct recognition rates on the Emotional Prosody task were submitted to a 3 way mixed ANOVA with Greenhouse-Geisser corrections. Factors of interest were emotion (within subjects: sadness, fear, happiness, anger, surprise and neutral), age group (between subjects) and sex (between subjects). Means and standard deviations for each emotion are presented in Figure 3.2.

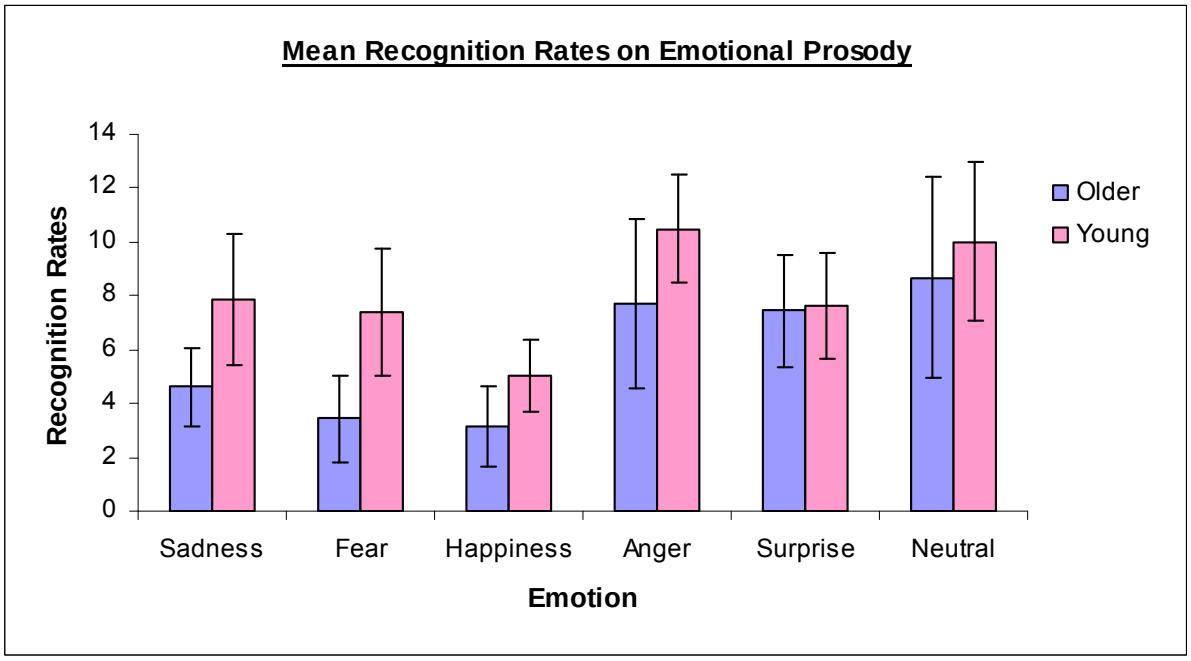

Figure 3.2: Mean recognition rates on the Emotional Prosody task for the young (*n* = 16) and older groups (*n* = 16). Vertical lines depict standard deviations.

A significant main effect was observed for emotion [$F(3.29, 92.16) = 31.81$, $p < 0.0005$, $\eta^2 = 0.47$] and age group [$F(1, 28) = 27.46$, $p < 0.0005$, $\eta^2 = 0.46$]; but a main effect was not found for sex [$F(1, 28) = 3.90$, $p = 0.06$, $\eta^2 = 0.07$], although it approached significance. A significant interaction was found between emotion and age group [$F(3.29, 92.16) = 3.44$, $p < 0.05$, $\eta^2 = 0.11$]. All other interactions (emotion*sex, age*sex, and emotion*age*sex) were not significant ($p > 0.07$) and effect sizes were small ($\eta^2 < 0.05$).

Further independent samples t-tests were performed to compare age groups on specific emotions. Bonferroni adjustments were applied to take into account all 14 t-tests pertaining to the Emotional Prosody measure (0.05/14 = 0.0036). Results indicated that older participants demonstrated

significantly worse recognition of sadness [$t(30) = 4.57$, $p < 0.0036$, $\eta^2 = 0.41$], fear [$t(30) = 5.49$, $p < 0.0036$, $\eta^2 = 0.50$], happiness [$t(30) = 3.85$, $p < 0.0036$, $\eta^2 = 0.33$], and anger[9] [$t(25.37) = 3.01$, $p < 0.0036$, $\eta^2 = 0.23$]. However, no significant difference was found on the recognition of surprise or neutral ($p > 0.14$), and effect sizes were small ($\eta^2 < 0.04$).

Due to the nature of the task, incongruent and congruent sentences were presented together in a random order. Therefore it is difficult to know which variable affects the emotion being presented the most. Total percentage of correct responses of congruent sentences and incongruent sentences (composite of all 6 emotions) was compared; this is presented in Figure 3.3. These were submitted to a 3 way ANOVA, exploring type of stimuli (within subjects: congruent and incongruent), sex (between subjects) and age (between subjects). The assumption of sphericity was not violated.

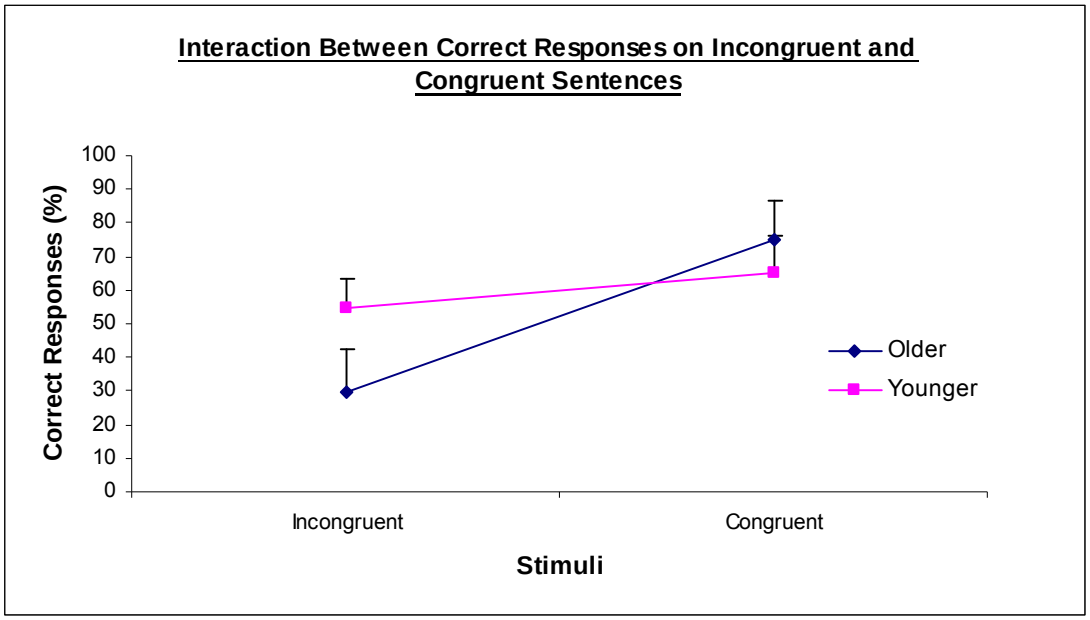

Figure 3.3: Percentages of incongruent and congruent Emotional Prosody stimuli correctly recognised by the older (*n* = 16) and the young (*n* = 16) groups. Vertical lines demonstrate standard deviations.

There was a significant main effect for type of stimuli [$F(1, 28) = 155.46$ $p < 0.0005$, $\eta^2 = 0.63$], for group [$F(1, 28) = 6.10$, $p < 0.05$, $\eta^2 = 0.16$], but no significant effect for sex [$F(1, 28) = 4.18$, $p = 0.05$, $\eta^2 = 0.09$], although this

[9] Equal variance not assumed.

was close to significance. A significant interaction between age group and type of stimuli was found [$F(1, 28) = 60.33$, $p < 0.0005$, $\eta^2 = 0.24$], whereas all other interactions (stimuli*sex, sex*age and stimuli*sex*age) were not significant ($p > 0.08$) and effect sizes were small ($\eta^2 < 0.006$).

According to Figure 3.3, there appears to be a cross-over in which the older group achieve a greater number of correct responses in comparison to the young group if the stimuli are congruent, but the young group achieve a greater number of correct responses than the older group if the stimuli are incongruent. This was explored further with independent samples t-tests. The older group recognised significantly fewer incongruent stimuli than the young group [$t(30) = 6.43$, $p < 0.0036$, $\eta^2 = 0.58$] and there was a difference in the recognition of congruent stimuli, with the older group recognising more congruent stimuli than the young group, and this approached significance [$t(30) = -2.42$, $p = 0.02$, $\eta^2 = 0.16$].

With the removal of the congruent stimuli, independent samples t-tests indicated that older participants demonstrated significantly worse recognition of sadness [$t(30) = 5.17$, $p < 0.0036$, $\eta^2 = 0.47$], happiness [$t(30) = 9.03$, $p < 0.0036$, $\eta^2 = 0.73$], anger[10] [$t(24.79) = 3.98$, $p < 0.0036$, $\eta^2 = 0.35$] and fear[11] [$t(20.39) = 6.49$, $p < 0.0036$, $\eta^2 = 0.58$] emotions. The older group recognised fewer neutral[12] stimuli than the young group, although it was not found to reach statistical significance [$t(24.44) = 3.98$, $p = 0.047$, $\eta^2 = 0.09$]. There was no significant difference for the recognition of surprise ($p = 0.14$) and the effect size was minimal ($\eta^2 = 0.04$). These results concur with those found before the removal of congruent stimuli. However, all effect sizes were larger with the removal of congruent, as would be expected from the results, suggesting that the older participants recognised fewer incongruent but more congruent stimuli.

[10] Equal variance not assumed.
[11] Equal variance not assumed.
[12] Equal variance not assumed.

Therefore, significant age-related differences were observed on some (sadness, happiness, fear and anger) but not other emotions (surprise and neutral). Furthermore, this appeared to show specificity for incongruent stimuli. The younger group demonstrated better performance on incongruent measures, whereas older participants demonstrated better performance on congruent measures.

Go/No-go –

The Go/No-go test was presented in two levels of difficulty, as outlined in Chapter 2 (*General Method:* see section 2.2.1). One level was a Simple Go/No-go and the other was the Affect Go/No-go. Both levels of the task were analysed separately due to the differences in parameters such as length of presentation of stimuli. A mixed between-within groups ANOVA was used in the analysis of both versions of the Go/No-go task. Bonferroni adjustments were applied to take into account all 12 independent samples t-tests pertaining to both versions of the task (0.05/12 = 0.0042).

Simple Go/No-go

Hit rates of 'Go' (target) and 'No-go' (distracter) data were submitted to a 3 way mixed ANOVA. The assumption of sphericity was not violated. Means and standard deviations for hit rates of 'Go' and 'No-go' stimuli are presented in Figure 3.4. Factors of interest were stimulus type (within subjects: 'Go' and 'No-go'), age group (between subjects) and sex (between subjects).

There was a significant main effect for stimulus type [$F(1, 28) = 7397.37$, $p < 0.0005$, $\eta^2 = 0.99$], and for age group [$F(1, 28) = 10.47$, $p = < 0.0005$, $\eta^2 = 0.27$]; but no main effect was found for sex ($p = 0.68$) and the effect size was small ($\eta^2 = 0.005$). A significant interaction was found between stimulus type and group [$F(1, 28) = 21.26$, $p < 0.0005$, $\eta^2 = 0.20$]. No other interactions (stimulus*sex, sex*age, and stimulus*sex*age) were significant ($p > 0.74$) and effect sizes were small ($\eta^2 < 0.04$).

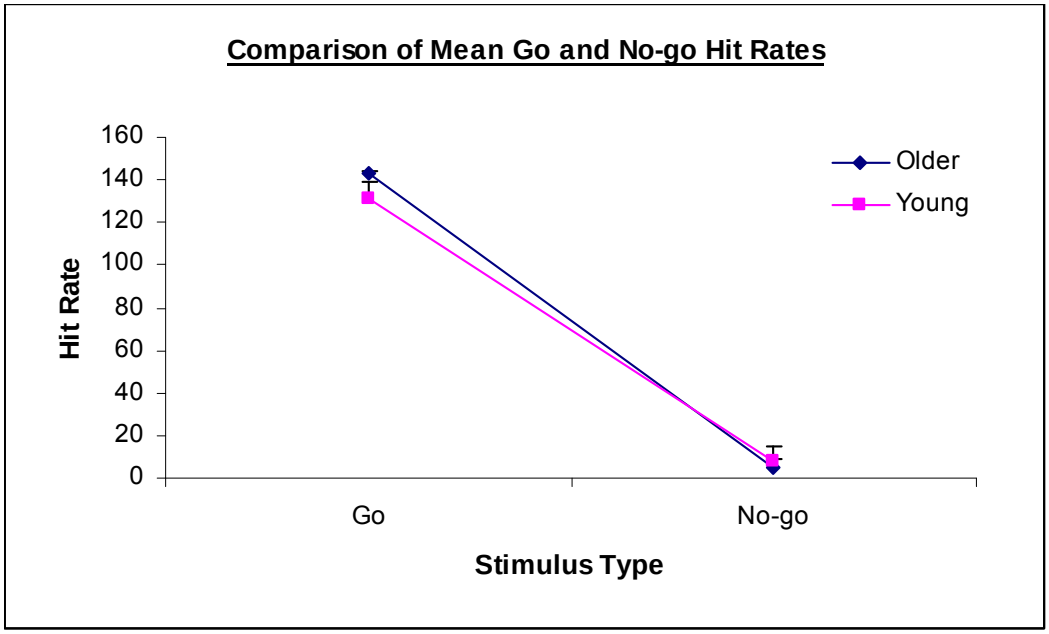

Figure 3.4: Hit rates of the older (*n* = 16) and young (*n* = 16) groups in response to 'Go' (target) and 'No-go' (distracter) stimuli. Vertical lines demonstrate standard deviations.

To explore the age group main effect further, all stimulus types were analysed separately using independent samples t-tests. The older group responded to significantly more 'Go'[13] stimuli than the young group [$t(15.83) = -5.74$, $p < 0.0042$, $\eta^2 = 0.52$], though there was no significant difference in response to 'No-go'[14] stimuli ($p = 0.18$), and the effect size was moderate ($\eta^2 = 0.06$).

Further 2-tailed t-tests revealed that the older group took significantly longer to respond to 'Go'[15] stimuli than the young group [$t(22.57) = -5.42$, $p < 0.0042$, $\eta^2 = 0.50$] and took longer to respond to 'No-go' stimuli, although this did not reach significance [$t(30) = -2.49$, $p = 0.02$, $\eta^2 = 0.17$]. This is presented in Figure 3.5.

Therefore, there were no age-related differences on number of 'No-go' responses, although there was greater accuracy of hitting 'Go' targets in the older group in comparison to the young group. However, the older group took longer to respond to 'Go' stimuli.

[13] Equal variance not assumed.
[14] Equal variance not assumed.
[15] Equal variance not assumed.

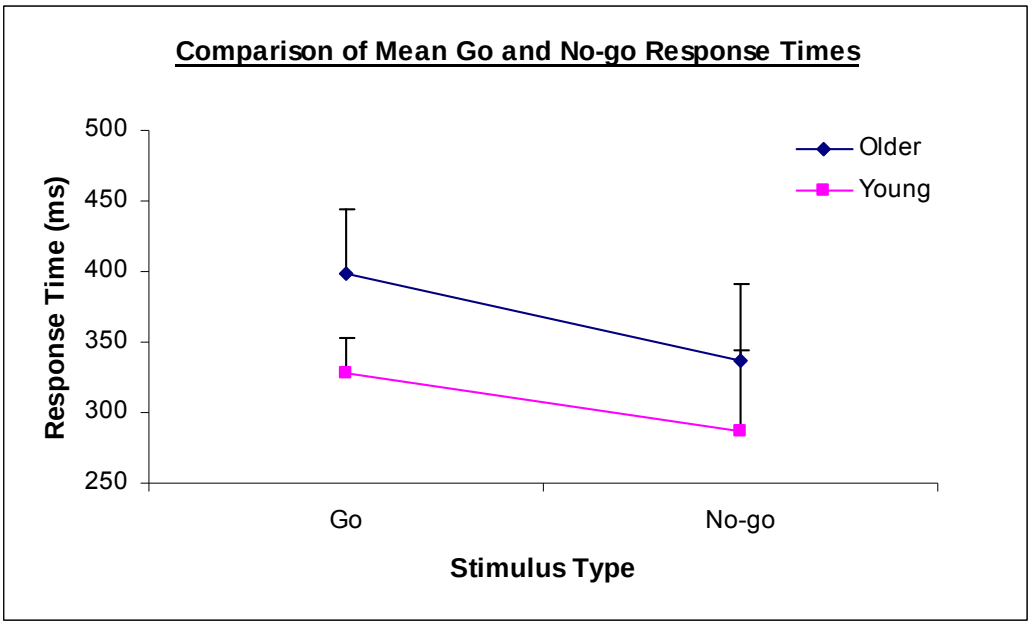

Figure 3.5: Response times of the older (*n* = 16) and young (*n* = 16) groups, for 'Go' (target) and 'No-go' (distracter) stimuli. Vertical lines depict standard deviations.

Affect Go/No-go

Hit rates of target 'Go' stimuli and distracter 'No-go' stimuli were submitted to a 3 way mixed ANOVA, with Greenhouse-Geisser corrections. Target stimuli consisted of words with both neutral and emotive connotations (e.g., Neutral 'Go' and Affect 'Go'), as were distracter stimuli (e.g., Neutral 'No-go', and Affect 'No-go'). Means and standard deviations of hit rates are presented in Figure 3.6. Factors of interest were stimulus type (within subjects), age group (between subjects) and sex (between subjects).

A significant main effect was found for stimulus type [$F(1.73, 48.43) = 1617.99$, $p < 0.0005$, $\eta^2 = 0.34$]; for age group [$F(1, 28) = 4.089$, $p < 0.05$, $\eta^2 = 0.12$]; but not for sex ($p = 0.82$), and the effect size was small ($\eta^2 = 0.002$). All interactions (stimulus*age, stimulus*sex, age*sex, and stimulus*sex*age) were not significant and effect sizes were small ($\eta^2 < 0.04$).

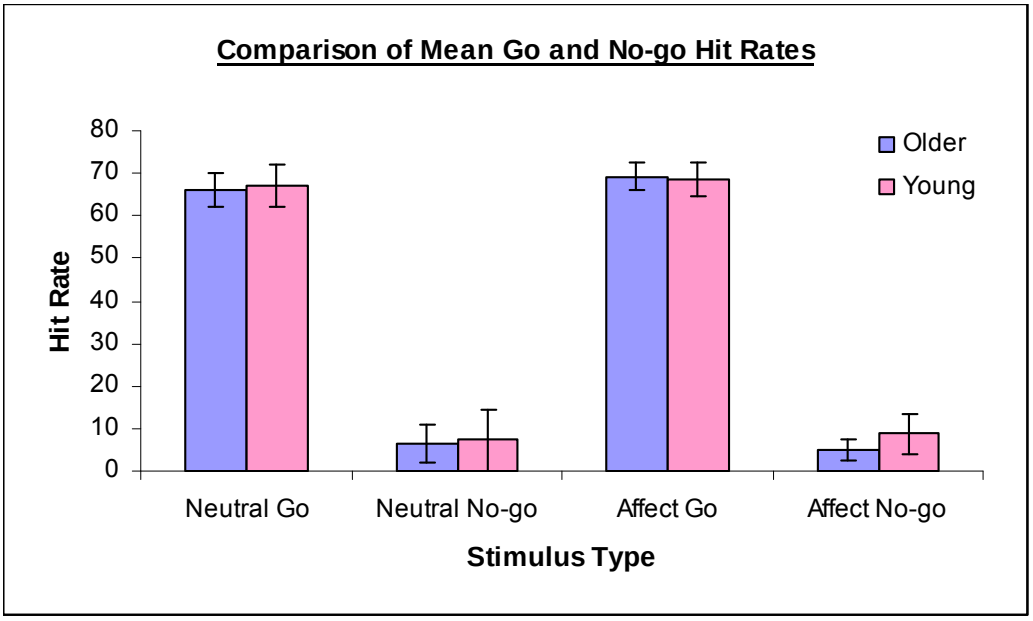

Figure 3.6: Hit rates of the older (*n* = 16) and young (*n* = 16) groups, for neutral and affect target 'Go' stimuli; and neutral and affect distracter 'No-go' stimuli. Standard deviations are presented using vertical lines.

Independent samples t-tests were performed on hit rates to investigate this further. The older group responded to fewer affect 'No-go'[16] stimuli, in comparison to the young group, and this approached significance [$t(22.32) = 2.75$, $p = 0.01$, $\eta^2 = 0.20$]. There were not any significant differences on any other hit rate measures ($p > 0.56$) and effect sizes were small ($\eta^2 < 0.01$).

Additionally, 2-tailed independent samples t-tests were performed on neutral 'Go' and 'No-go' response times, as well as on affect 'Go' and 'No-go' response times; this is presented in Figure 3.7. The older group took significantly longer than the young group to respond to neutral 'Go' stimuli [$t(30) = -7.48$, $p < 0.0042$, $\eta^2 < 0.65$], neutral 'No-go' stimuli [$t(30) = -4.48$, $p < 0.0042$, $\eta^2 < 0.40$], as well as affect 'No-go'[17] stimuli [$t(18.53) = -5.93$, $p < 0.0005$, $\eta^2 < 0.54$]. However, the slower response time in the older group for affect 'Go'[18] stimuli did not achieve significance ($p = 0.25$) and the effect size was small ($\eta^2 = 0.04$).\

[16] Equal variance not assumed.
[17] Equal variance not assumed.
[18] Equal variance not assumed.

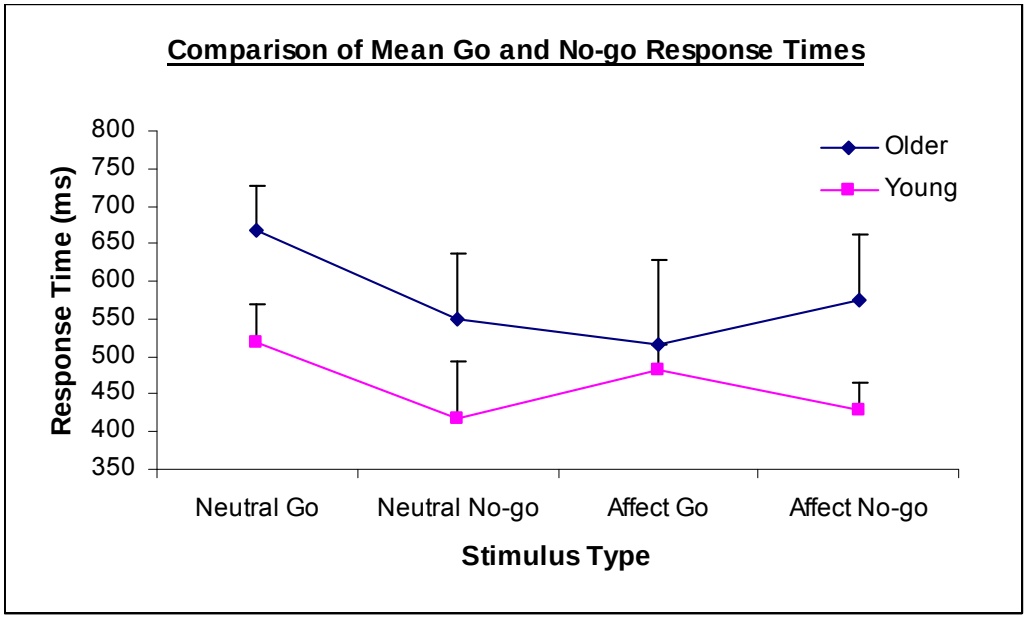

Figure 3.7: Response times of the older (*n* = 16) and young (*n* = 16) groups, for neutral and affect target stimuli 'Go' and neutral and affect distracter stimuli 'No-go'. Standard deviations are depicted by vertical lines.

3.3.2 Differences in Executive Function

Although age-related differences have been seen on executive function measures previously, for the purpose of comparison to the less well established PFC cognitive function measures, the difference between young and older groups on executive functions were measured. Differences in mean number of verbs generated on the VF and on mean completion time on the TOL task are presented in Figure 3.8 and Figure 3.9, respectively.

The older group generated more verbs on the VF test, although this was not significant ($p = 0.11$), and the effect size was moderate ($\eta^2 = 0.08$). This was based on n =11, due to controlling for educational attainment (see *General Methods;* section 2.2.2). An independent samples t–test revealed that there were significant differences between the young and older groups on mean completion time on TOL [$t(30) = 2.37$, $p < 0.02$, $\eta^2 = 0.16$]. Therefore, age-related differences were demonstrated on TOL with the young group performing better than the older group. However, no significant differences were observed for VF performance.

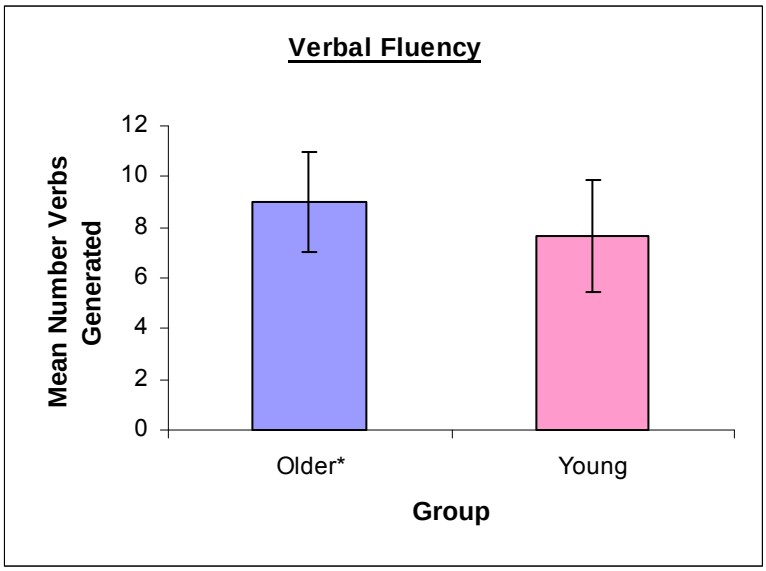

Figure 3.8: Differences between the young and older groups (*n* = 11) on mean number of verbs generated on VF.
*Based on *n* = 11, due to controlling for educational level (see section 2.2.2).

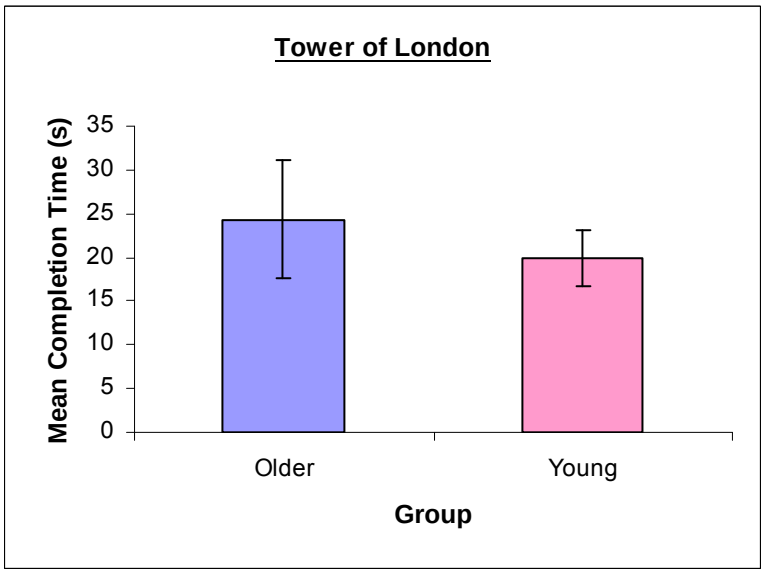

Figure 3.9: Differences between the young (*n* = 16) and older (*n* = 16) groups on mean completion time on the TOL, in seconds (s). Vertical lines depict standard deviations.

3.3.3 Executive Function Vs Social Cognition

It is important to observe how executive function and social cognition interact in an older sample. Social cognition is relatively novel in the context of ageing research, although the literature has strongly implicated the PFC in the performance of them. These are presented in the correlation matrix in Table 3.2 (this also includes control tests, which will be addressed in later

sections 3.3.4 and 3.3.5). Significance was accepted at the more stringent < 0.01, in order to reduce the likelihood of obtaining a type I error.

As can be noted, the Ekman 60 Faces correlates the most consistently with other measures proposed to be frontally associated. With the exception of Go/No-go measures, all relationships with executive function and social cognition demonstrate an association in which successful performance on the Ekman 60 Faces predicts successful performance on the other measure. The correlation between Ekman 60 Faces and percentage incongruent on Emotional Prosody, as well as with VF approached significance (< 0.05) with large effect sizes (r > 0.56). Medium but non-significant associations were found between the Ekman 60 Faces and percentage congruent on Emotional Prosody (r = 0.34, n = 16, p = 0.20), as well as between Ekman 60 Faces and mean completion time on TOL (r = -0.37, n = 16, p = 0.16).

Other non-significant relationships with medium-large effect sizes were found in which successful performance on one measure predicted successful performance on another. These were between total score on Emotional Prosody and neutral 'No-go' hit rate (r = -0.44, n = 16, p = 0.09), between total score on Emotional Prosody and number of verbs generated on the VF task (r = -0.38, n = 11, p = 0.26), and between percentage incongruent on Emotional Prosody and neutral 'No-go' hit rate (r = 0.44, n = 11, p = 0.18). Other associations were found between percentage congruent on Emotional Prosody and affect 'No-go' hit rate (r = -0.36, n = 16, p = 0.17), and between affect 'No-go' hit rate and 'No-go' hit rate on the Simple Go/No-go (r = -0.43, n = 16, p = 0.09).

A medium relationship was also found between the executive function measures, in which successful performance on VF predicted successful performance on TOL. This however, was not statistically significant (r = -0.31, n = 11, p = 0.36).

Relationships between all other executive function and social cognition measures were not significant (p = 0.28). Furthermore, all of these effect sizes were small-medium (r < 0.29).

3.3.4 Influence of IQ

IQ has been argued to be an important indicator of levels of global cognitive function. An independent samples t-test was conducted to compare IQ between the young group (mean = 120.5, *SD* = 7.03) and the older group (mean = 105.88, *SD* = 13.50). The younger group had a significantly higher IQ score than the older group [t(22.59) = 3.84, p < 0.005, η^2 = 0.40].

In order to ascertain whether there is a possibility of IQ influencing aspects of social cognition, the relationship of it to social cognition measures was observed. Results are presented in the correlation matrix in Table 3.2. As can be seen, there appears to be an association of IQ with the percentage of congruent stimuli recognition on Emotional Prosody, and this approached significance [r = 0.54, n = 16, p = 0.03]. There is also a non-significant relationship between IQ and 'No-go' hit rates on the Simple Go/No-go task [r = 0.35, n = 16, p = 0.18], although it is not in the direction that would suggest that successful performance on one would predict successful performance on the other task. Associations between IQ and all other measures were non-significant (p > 0.43), with small effect sizes (r < 0.21).

Although there was found to be a significant difference in the IQ scores of the young and older groups, there appears to be no significant associations between IQ and any social cognition measures. Therefore, it is unlikely that global changes in cognition can account for changes in social cognition to any great extent.

Table 3.2: Correlation matrix of the relationship between social cognition (Ekman 60 faces, Emotional Prosody and Go/No-go), executive function (TOL and VF) and control (IQ and PVT reaction time) tests.

			Ekman 60 Total	Emotional Prosody			Go/No-go (Hit rates)						
				Total	% Incong	% Cong	Simple No-go	Neutral No-go	Affect No-go	IQ	PVT	TOL	VF^
	Ekman 60 Total	Pearson's *r*		0.60*	0.56*	0.34	0.01	-0.05	-0.03	0.12	0.36	-0.37	0.66*
	(n=16)	Sig.	–	0.01	0.03	0.20	0.98	0.85	0.91	0.66	0.61	0.16	0.03
Emotional Prosody	**Total**	Pearson's *r*			0.95**	0.50*	0.15	-0.44	-0.10	0.21	0.05	-0.25	0.38
	(n=16)	Sig.	–	–	0.00	0.05	0.58	0.09	0.71	0.44	0.85	0.35	0.26
	% Incongruent	Pearson's *r*				0.20	0.23	-0.39	0.02	0.04	0.07	-0.21	0.44
	(n=16)	Sig.	–	–	–	0.46	0.40	0.13	0.95	0.88	0.79	0.43	0.18
	% Congruent	Pearson's *r*					-0.16	-0.29	-0.36	0.54*	-0.03	-0.18	-0.09
	(n=16)	Sig.	–	–	–	–	0.56	0.28	0.17	0.03	0.90	0.50	0.79
Go/No-go (Hit Rates)	**Simple No-go**	Pearson's *r*						-0.02	0.43	0.35	-0.15	0.19	-0.01
	(n=16)	Sig.	–	–	–	–	–	0.95	0.09	0.18	0.58	0.48	0.97
	Neutral No-go	Pearson's *r*							0.29	-0.21	-0.05	0.20	0.05
	(n=16)	Sig.	–	–	–	–	–	–	0.28	0.43	0.85	0.47	0.89
	Affect No-go	Pearson's *r*								0.15	-0.18	0.03	0.05
	(n=16)	Sig.	–	–	–	–	–	–	–	0.58	0.50	0.91	0.89
	IQ	Pearson's *r*									0.15	0.05	-0.10
	(n=16)	Sig.	–	–	–	–	–	–	–	–	0.50	0.86	0.77
	PVT	Pearson's *r*										-0.26	0.13
	(n=16)	Sig.	–	–	–	–	–	–	–	–	–	0.32	0.64
	TOL	Pearson's *r*											-0.31
	(n=16)	Sig.	–	–	–	–	–	–	–	–	–	–	0.36
	VF^	Pearson's *r*											
	(n=11)	Sig.	–	–	–	–	–	–	–	–	–	–	–

^VF is based on *n* = 11, due to individuals with < 12 years in education being removed (see section 2.2.2).

* Significant at < 0.05

** Significant at < 0.01

3.3.5 Influence of Reaction Time

According to Salthouse (1996) age-related cognitive declines occur due to slowing of reaction time. Therefore, to ensure that age group differences in social cognition are not due to slowing of reaction time, relationships between social cognition tasks and reaction time (PVT) were observed. These are presented in Table 3.2. It might be expected that if global slowing was present in the older group that there would be a relationship between these tasks. The strongest association was between RT and Ekman 60 Faces performance, although this was not in a logical direction, or significant [r = 0.30, n = 16, p = 0.61]. All other relationships were non-significant (p > 0.50), with small effect sizes (r < 0.26).

3.4 Discussion

3.4.1 Recognition of Emotion

It was expected that age-related differences would be found on recognition of emotion with an older group recognising fewer stimuli via facial expression and prosody, than their younger counterparts. Mixed results were found in the present chapter pertaining to cross-sectional changes in emotion recognition. On the Ekman 60 Faces task, only fear was found to present with significant age-related differences. No differences were observed in the recognition of anger, sadness, happiness, disgust and surprise. The age differences revealed in the recognition of fear concur with previous findings (Calder et al., 2003). Calder et al. however, additionally found a decline in recognition of anger, although to a lesser extent. This was not found to be the case in Study 1.

Literature has suggested that happiness appears to be the least ambiguous of emotions to recognise via facial expression (Gosselin, Kirouac & Dorê, 1995); the most difficult, in comparison to other emotions has been found to

be fear (Kirouac & Dorê, 1983). These are in agreement with the results of the present chapter, but only in the older group. It might therefore be argued, that the most difficult emotions to recognise are those subject to age-related declines, as fear was found to be the only emotion subject to group differences. However, it is important to note, that the older group found sadness the second most difficult emotion to recognise, yet the difference in mean scores was comparatively small. Unfortunately, it is difficult to interpret the results in terms of differential PFC loading of each emotion, due to lack of attempts in the literature to establish associated brain regions of each isolated emotion via brain imaging techniques.

Lack of statistical differences between groups in all emotions, with the exception of fear may have been due to ceiling effects, in particular in regards to happiness which was the easiest emotion to identify. This may prevent the clear interpretation of the effects of ageing on recognition of this emotion. This issue has arisen in earlier studies of emotion recognition (Calder et al., 2003; Phillips et al., 2002). The results however, importantly point towards some deficit in emotion recognition via facial expression with age, at least on more challenging aspects of emotion recognition. It also points towards the need for future development in this area to create facial recognition tests more suitable for testing high functioning adults.

Another explanation of the aforementioned results is that fear was particularly affected due to its association with the amygdala. For example, the amygdala is activated during the recognition of fear but not of other emotions, as indicated via PET (Morris et al., 1996) and via fMRI (Breiter et al., 1996) studies. Therefore, the differences in emotion detection may be due to the important role of the amygdala, in fear recognition, that may instead be affected with advancing age. However, recent research has indicated that the role of the amygdala in recognition of emotion may be limited to the initial response to emotional stimuli, e.g., prior to conscious encoding of social information. This is supported by Critchley et al. (2000), in an investigation of brain activity (using fMRI) during the explicit (labelling of emotion) and implicit (identification of gender) processing of facial

expressions conveying the emotions of angry, happy and neutral. Significantly greater activity was found in the amydala–hippocampal region during implicit rather than explicit processing of emotional stimuli; thus, indicating that the amygdala may be involved in early representations of external stimuli, as opposed to explicit identification, as was the focus of Study 1 in the present thesis.

On the emotional prosody task, age effects were found to be specific to incongruent stimuli and included age associated declines in the recognition of sadness, fear, happiness and anger. No significant differences were found on surprise and neutral recognition, although the younger group correctly labelled more stimuli. In contrast to recognition of emotion via facial expression, in the literature, happiness has been shown to be the most difficult to recognise via prosody, followed by fear, sadness, neutral and then anger (the emotion of surprise was not observed; Scherer, 2003). This is in agreement to results reported for Study 1, in which the young group followed this gradient of accuracy rates; the older group followed this pattern except for the recognition of neutral and anger. Although happiness was the most difficult emotion to recognise, it did not demonstrate the largest effect size, fear did (both before and after removal of congruent stimuli), indicating that difficulty alone could not account for ageing effects. Also, although the recognition of fear has been implicated in amygdala function in facial expression, this has not found to be the case with recognition of emotion from voice. Research has found that the intact amygdala is not critical for the recognition of emotion in this domain (Adolphs & Tranel, 1999) and fMRI did not detect activity in the amygdala during explicit identification of this emotion in an emotional prosody task (Wildgruber et al., 2005).

The large effect sizes seen between age groups on the Emotional Prosody task, in contrast to the Ekman 60 Faces task, might be due to the added focus on encoding prosody in the presence of incongruent cues; this is demonstrated by the finding that the older group had greater difficulty in the recognition of composite incongruent stimuli but better recognition of congruent stimuli. In the context of irony, assessing emotional prosody in

the presence of conflicting cues places upon the individual much greater social cognitive demands than merely the encoding of emotion, as it also involves encoding of intentions, as well as beliefs (Shamay-Tsoory, et al., 2005). Ability to understand ironic utterances, has been found to be impaired in those with PFC lesions (Shamay-Tsoory, Tomer, & Aharon-Peretz, 2002), and to a greater extent in those with VMPFC damage, in the right hemisphere, compared to other regions of the PFC (Shamay-Tsoory et al., 2005). In addition, understanding of sarcastic utterances correlated with recognition of emotional prosody in the latter of these studies. The enhanced recognition of congruent stimuli in the older group in Study 1, may point towards a greater dependency on using other cues (i.e., sentence content), rather than tone alone, to process emotion in others.

3.4.2 Response Inhibition

It was hypothesised that the older group would have greater difficulty ignoring distracter stimuli on the Go/No-go paradigm than the young group, and that this difficulty would be more pronounced with 'No-go' stimuli that had emotive connotations. The results were unexpected, but tended to be consistent, in that the older group performed comparably to the young group, in regards to ability to ignore 'No-go' stimuli on both the Simple Go/No-go and Affect Go/No-go paradigms. However, this was at the expense of response times, which were longer in the older group.

There are some deviations from this pattern of results. Most notable, is for the Simple Go/No-go, in which the older group responded to more target 'Go' stimuli than the young group, indicating better accuracy. This is not consistent with the findings of the Affect Go/No-go, in which 'Go' hit rate was not significantly different between groups. One explanation of this is that in the Simple Go/No-go measure, the older group were able to perform more accurately due to the extra time spent assessing the greater potential for accuracy; this may have been curtailed in the Affect Go/No-go version, due to the greater cognitive demands imposed by it.

The lack of ageing effects on 'No-go' responses was surprising, given that the Go/No-go paradigm has been shown to yield a heavy PFC loading (e.g. Horn et al., 2003; Rubia et al., 2001). Furthermore, low levels of correlation between PVT measured reaction time and Go/No-go measures indicate that slower response times in the older group may have been intentional, and not owing to deficits in reaction time speed. Rabbitt (1988) explained that older adults have a tendency to make very few fast responses on performance measures, and furthermore, that if they make mistakes they respond by slowing down; younger adults on the other hand shrug off mistakes relatively quickly.

3.4.3 Executive Functions

Significant differences between the young and older group were found for mean completion time on the TOL, indicating that the young group required less time to complete problems involving a strong non-verbal planning component. This is in agreement with current literature (Davis & Klebe, 2001; Robbins et al., 1998). However, no significant difference was found between the young and older groups on VF performance, although previous literature has suggested that this is vulnerable to age-related decrements (Ardila et al., 2000; Parkin and Walter, 1991).

One explanation for the variation in ageing effects could be that the TOL is more sensitive to age-effects than the VF; individuals might undergo age-related declines at a younger age with regards to TOL performance in comparison to VF performance. Indeed, those studies implicating age-related declines in VF made comparisons with comparatively older individuals than utilised in Study 1 (mean = 71.5 years, *SD* = 4.4). For example, the oldest group in the cross-sectional comparison made by Ardila et al. (2000) was 66–85 years of age; whereas the oldest group in the study by Parkin and Walter (1991) had a mean age of 80 years (*SD* = 5.1 years). In contrast, Henry and Phillips (2006) found no significant deficits on semantic VF in an older group with a mean age of 72 years (*SD* = 6.36 years), which is similar in age to that used in Study 1. It is also suspected

that performance on the VF task is more susceptible to factors such as cohort effects. Evidence has demonstrated that VF performance may be influenced by past educational attainment (e.g., Ardila et al., 2000). Although this was controlled for in Study 1, it is unknown the extent to which other cohort factors could present an influence. The older participants may have had a better overall grasp of VF than the young group, therefore masking any age differences that might have occurred; this however, is entirely speculative.

3.4.4 Control Measures

There was a difference in fluid intelligence IQ scores between the young and older groups, with the young group having a higher mean IQ. This is unlikely to have affected the cognitive measures to a substantial extent as none of the 'PFC measures' showed a significant association with the task. The strongest association was with percentage of correctly recognised congruent stimuli on the Emotional Prosody task (r = 0.54). However, it is suspected that these stimuli are less frontally-specific, than incongruent stimuli. Consistent with this, is the finding that ageing effects on this task are amplified with the removal of congruent stimuli.

Lack of association was also found between 'PFC measures' and PVT reaction time in the older group. According to Salthouse (1996), slowing in reaction time can account for deficits in PFC measures with increasing age. This would therefore be a concern when considering tasks with time constraints or with measures of which performance is associated with response time (e.g., TOL and Go/No–go paradigms). The implication that the tests of PFC cognition are independent of 'global measures' is important in retaining the assumption that declines seen in PFC associated tasks are not due to general 'global' changes.

3.5 Conclusion

- Ekman 60 Faces: The older group recognised significantly fewer fear stimuli. No significant differences were found on the recognition of happiness, surprise, disgust, anger and sadness.

- Emotional Prosody: The older group recognised significantly fewer sadness, fear, happiness, and anger stimuli. These effects were amplified when stimuli was incongruent. No significant differences were found on the recognition of surprise and neutral.

- Simple Go/No-go: There were no differences in the hit rate of distracter 'No-go' stimuli, although the older group were significantly more accurate in their hit rate in response to target 'Go' stimuli. The older group furthermore took longer to respond to target 'Go' and 'No-go' stimuli, compared to the young group.

- Affect Go/No-go: When stimuli had neutral or affective connotations there were no differences between groups in the hit rate of distracter 'No-go' or target 'Go' stimuli. With the exception of affect target 'Go' stimuli, the older group took significantly longer to respond to all types of stimuli.

- Significant differences were found in performance of the TOL, with the older group taking significantly longer to complete problems than the young group. Age differences were however, absent on the VF.

- Measures of social cognition were found to be independent of 'global' changes in cognition (fluid intelligence IQ and PVT reaction time).

It was revealed that age-related declines may not be specific to cognition already well-represented in the literature such as executive function, and that other higher functions previously associated with the PFC are also

vulnerable to age-related decrements. It also suggests the importance of continued ageing research, to explore many facets of cognition, as not all tests are affected uniformly with age. Some are more sensitive than others. Furthermore, age-differences in social cognition were unlikely to be due to overall ‘global’ changes in cognition.

4 Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus

4.1 Introduction

As demonstrated in Study 1, age-related differences were evident in aspects of cognition associated with the PFC when comparing a high functioning young group with a mean age of 22.25 years (*SD* = 2.35 years) and a high functioning older group with a mean age of 71.5 years (*SD* = 4.40 years). Regarding the Go/No-go paradigm, significantly greater response times were required by the older group to maintain the same level of response inhibition found in the young group (ability to ignore distracter 'No-go' stimuli). The older group also recognised fewer emotions via facial expression (specific to fear, but not anger, sadness, disgust, surprise and happiness) and via prosody (specific to fear, anger, sadness and happiness, but not surprise and neutral). Also found in Study 1, was an age-difference in the performance of TOL; although performance of VF remained intact. This was despite literature indicating the contrary, that increasing age is associated with decrements in VF ability (e.g., Ardila, et al., 2000; Parkin & Walter, 1991). Cross-sectional data in the literature also supports age-related declines in WCST (Comptom, et al., 1999; Macpherson, et al., 2002; Parkin & Walter., 1991) and on the TOL task (Robbins et al.,1998).

Although executive function is often observed in the context of cognitive ageing, limitations exist that arise from using a cross-sectional method, such as an inflation of genuine PFC function differences due to cohort effects and individual differences. Surprisingly, there is a general lack of observation of the effects of longitudinal age-related changes in executive function in the literature. One study has elicited changes on the Tower of Hanoi (TOH) in a sample aged 70 – 91 years (mean = 81 years, *SD* = 6.6 years), after a period of 6.6 years (Davis & Klebe, 2001). However, this was limited to number of excess moves and unusually, no difference was found between

the older group and that of a younger group (mean = 32.4 years, *SD* = 8.4 years) using the same technique. Moreover, Goel and Grafman (1995), query the role of the TOH in planning. Although it has been employed as a more challenging alternative to TOL, the majority of studies of frontal lobe function have utilised Shallice's (1982) TOL (often mistakenly used interchangeably with the TOH). Therefore, there is a need for the investigation of ageing changes in executive function with a repeated measures design.

4.1.1 Main Aims and Hypotheses

The main aim of Study 2 is to explore age-related changes in aspects of executive function (WCST, TOL and VF) with a repeated measures design (over a period of 6.29 years). Age differences have been well established between young and older groups, however, changes may be observed longitudinally in a relatively shorter ageing period. It is hypothesised that:

i) Decrements in performance on executive function measures (WCST, TOL and VF) will be found in an older cohort over a period of 6.29 years.

4.2 Method

4.2.1 Participant Characteristics

Participants in Study 2 were taken from the Longitudinal Design Cohort described in the *General Method* (section 2.1.3). Due to the repeated measures design used, only baseline (2000) and follow-up (2006) data for the 11 individuals retained at follow-up are reported in this chapter. Participant characteristics are presented in Table 4.1. Rows in Table 4.1 that are shaded offer a visual representation of those participants for which baseline data was collected, but follow-up data was not. Those participants are excluded from Study 2.

Table 4.1: Baseline (2000) and follow-up (2006) participant characteristics. Shaded rows depict participants not utilised in Study 2. Means and standard deviations are presented separately for those participants that were retained at follow-up and included in the present study.

		Age		ESS		TIB(hrs)	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**	**2000**	**2006**
BC01	f	64.00	-	3	-	8.00	-
RR02	f	67.08	-	6	-	8.00	-
AT03	m	61.67	68.58	6	9	8.00	9.00
EM04	m	68.00	-	9	-	9.00	-
SS05	m	68.67	-	5	-	8.00	-
IK06	m	66.33	-	3	-	8.00	-
TK07	f	64.92	71.17	8	6	8.00	9.00
BF08	m	64.50	70.83	4	7	8.00	7.00
YF09	f	63.33	69.92	4	7	8.00	7.00
JC10	f	67.17	73.75	3	2	8.00	8.00
JY11	f	66.67	73.42	1	0	8.00	8.00
JT12	f	68.25	-	5	-	8.50	-
BP13	f	70.17	-	1	-	9.00	-
RW14	m	68.58	74.67	3	7	8.00	7.00
OC15	m	62.00	-	5	-	8.00	-
RD16	m	71.58	77.25	6	8	8.00	8.50
RL17	m	69.42	-	5	-	8.00	-
LL18	f	66.17	-	3	-	8.00	-
GM19	m	70.25	76.25	2	3	8.00	9.00
MM20	f	67.33	72.67	8	1	8.00	9.00
EP21	f	72.17	78.80	6	4	8.50	9.00
DF22	f	74.00	-	0	-	8.00	-
ES23	f	75.33	-	2	-	8.00	-
MF24	f	71.17	-	9	-	8.50	-
Mean		**67.87**	**73.39**	**4.46**	**4.91**	**8.15**	**8.23**
SD		**3.54**	**3.18**	**2.50**	**3.05**	**0.31**	**0.88**
Retained Mean		**67.11**	**73.39**	**4.64**	**4.91**	**8.05**	**8.23**
Retained SD		**3.37**	**3.18**	**2.34**	**3.05**	**0.15**	**0.88**

- Data not obtained

The mean age of the group (*n* = 11) at baseline was 67.11 years (*SD* = 3.37 years) and at follow-up was 73.39 years (*SD* = 3.18 years). The mean lapse in time between baseline and follow-up testing was 6.29 years (*SD* = 0.48 years). There were 6 females and 5 males in the group.

Daytime Sleepiness and Time in Bed –

As can be observed from Table 4.1, there was little change in ESS scores and TIB from baseline to follow-up. There was a slight increase in self-

reported daytime sleepiness as ascertained by ESS from baseline (mean = 4.64, *SD* = 2.34) to follow-up (mean = 4.91, *SD* = 3.05). There was also a small increase in TIB from baseline (mean = 8.05hr, *SD* = 0.15hr) to follow-up (mean = 8.23hr, *SD* = 0.88). However, all participants were found to satisfy the screening criteria as set out in section 2.1.1 at both time points.

4.2.2 Cognitive Test Battery

Cognitive tests were administered as set out in the Chapter 2 (*General Method;* see section 2.2). Testing at baseline and follow-up involved tasks that have been implicated in PFC function:

Executive Function Tests –

- Wisconsin Card Sorting Task (WCST)
- Verbal Fluency (VF)
- Tower of London (TOL)

Further control testing was administered in order to explore potential 'global'/non-PFC specific changes over time:

Control Tests –

- Psychomotor Vigilance Test (PVT)
- Fluid Intelligence (IQ)

4.2.3 Data Analysis

Due to small sample sizes and lack of normal distribution in many of the data sets reported in this chapter, most analyses involving comparison of means between baseline and follow-up utilised the non-parametric Wilcoxon signed ranks test. Where data was found to meet the assumptions of parametric data, paired samples t-tests were utilised. To explore levels of inter-relation between executive function measures, Pearson correlations were employed, with the Spearman rank correlation as a non-parametric alternative, utilised where appropriate.

Effect sizes were reported as *r* for non-parametric tests and eta squared (η^2) for parametric equivalents. Hypotheses were one-tailed guided by cross-sectional literature with the level of significance set at $p < 0.01$ (see section 2.4). Outlying data was identified on the basis of criteria set out in *General Methods* (see section 2.4). BF08 was identified as an outlier in the present study; this is outlined in sections to follow.

4.3 Results

4.3.1 Changes in Executive Function

Participants were tested at baseline and at follow-up on executive function measures (WSCT, TOL and VF), shown by a wealth of literature as being implicated in PFC function. Means and standard deviations for WCST are presented in Figure 4.1, for VF in Figure 4.2, and for TOL in Figure 4.3.

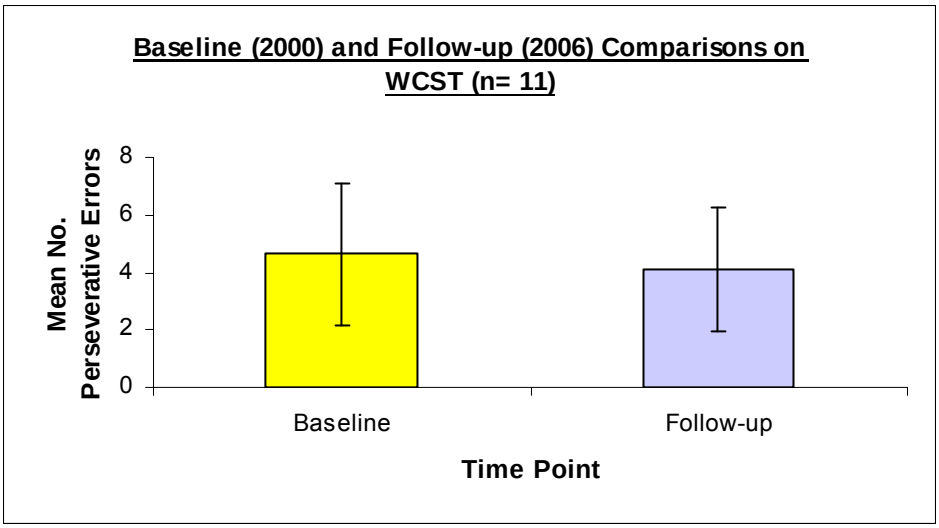

Figure 4.1: Change over time in performance on WCST at baseline (2000) and at follow-up (2006). Vertical lines depict the standard deviations.

Comparisons were made between baseline and follow-up performance on executive function tasks. No significant difference was found on WCST, as ascertained using Wilcoxon signed rank test [$Z = -0.42$, $p = 0.34$, $r = 0.13$]. Using a paired samples t-test, no significant difference was found on VF [$t(6) = 0.76$, $p = 0.24$, $\eta^2 = 0.09$].

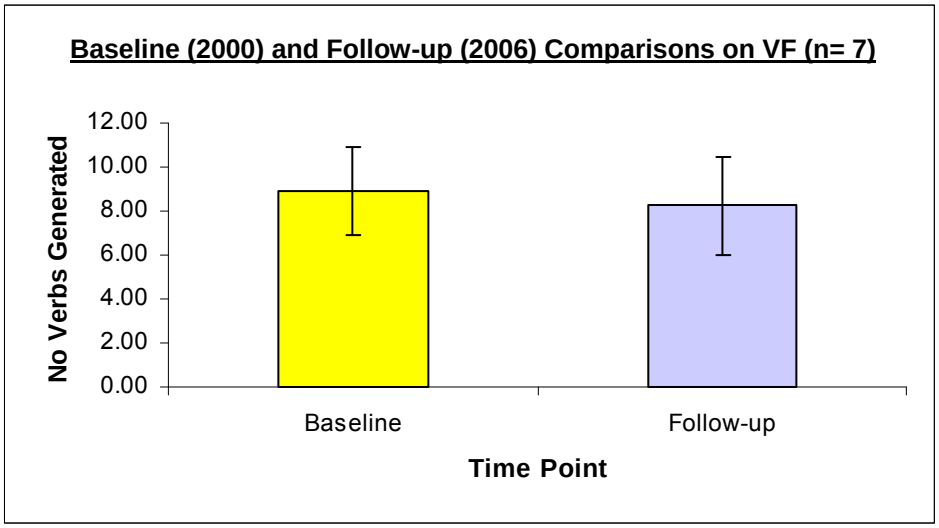

Figure 4.2: Change over time on performance on VF at baseline (2000) and at follow-up (2006). Vertical lines depict the standard deviations. VF is based on *n* = 7, due to controlling for educational attainment.

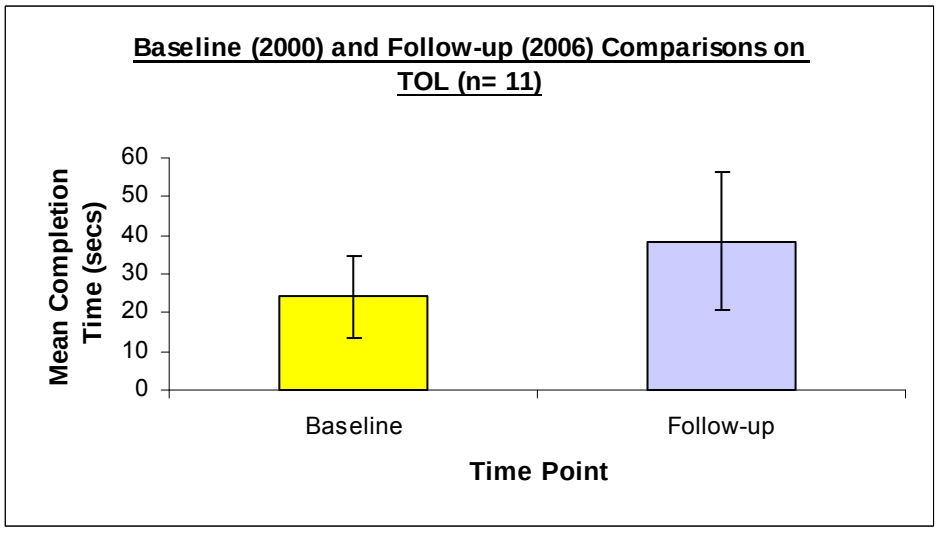

Figure 4.3: Change over time on performance on TOL at baseline (2000) and at follow-up (2006). Vertical lines depict the standard deviations.

Preliminary scatter-plot examinations indicated that participant BF08 was an outlier for the TOL. Box-plot analyses indicated that this was only so for the baseline value. A box-plot (Figure 4.4) supports the likelihood of participant BF08 as being an outlier, as does the finding that this individual is more than 2 standard deviations from the group mean. Therefore, in order that the data not be distorted, this value was removed from all subsequent analyses. Using a paired samples t-test, significant declines were found on TOL performance [$t(9) = -3.21$, $p < 0.01$, $\eta^2 = 0.53$].

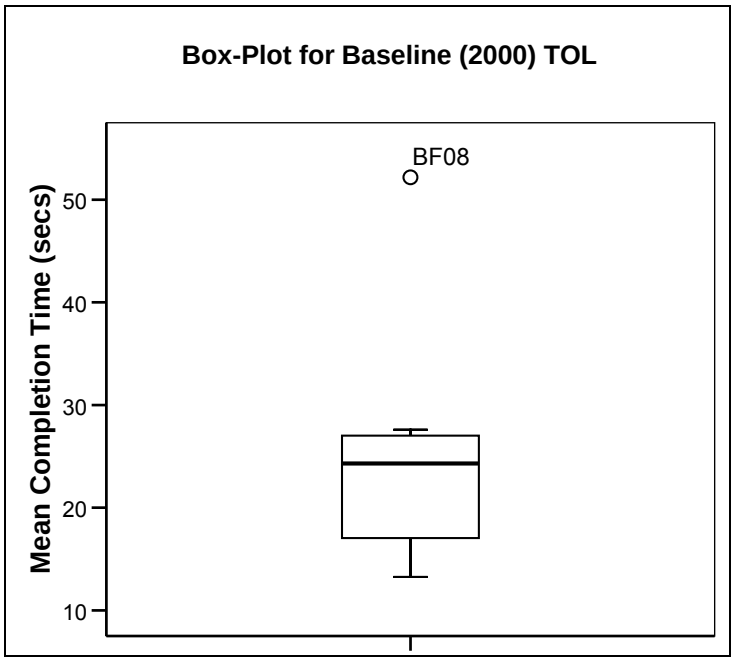

Figure 4.4: Box Plot of mean completion time of TOL at baseline (2000).

Control Tests –

PVT reaction time and fluid intelligence (IQ) were measured as a means of comparison to the executive function tasks, as literature suggests these tasks to be less reliant on PFC integrity and thus act as a global measure. As such, any differences between baseline and follow-up measurements may be indicative of general global declines in cognition in the cohort. The means and standard deviations of PVT reaction time and fluid intelligence IQ data for baseline and follow-up measurements are presented in Table 4.2.

Table 4.2: Mean and standard deviation of control tests at baseline (2000) and at follow-up (2006)

		PVT		IQ	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**
AT03	m	302.83	303.74	114	94
TK07	f	284.1	299.37	104	96
BF08	m	338.6	381.95	91	81
YF09	f	322.8	341.13	96	100
JC10	f	356.99	335.13	98	94
JY11	f	284.8	294.4	80	96
RW14	m	294.1	302.57	93	88
RD16	m	302.83	301.24	103	117
GM19	m	287.65	295.42	117	140
MM20	f	340.96	286.25	88	106
EP21	f	395.72	338.88	88	88
Mean		**319.22**	**316.37**	**97.45**	**100.00**
SD		**35.67**	**29.10**	**11.30**	**16.36**

Using a paired samples t-test, no significant difference between baseline and follow-up was found over time with regards to IQ [$t(10) = -0.62$, $p = 0.55$, $\eta^2 = 0.04$]. In addition, as ascertained using the Wilcoxon signed ranks test, no significant differences were found on PVT reaction time [$Z = -0.18$, $p = 0.86$, $r = 0.05$].

4.3.2 Relationship between Executive Functions

A correlation matrix was created in order to ascertain the degree of relationship between executive function measures in the group at follow-up (Table 4.3). In all cases (with the exception of PVT reaction time data, where Spearman rank correlation was used) Pearson correlation coefficients were obtained.

Table 4.3: Cross-correlation matrix of follow-up executive function measures (WCST, TOL and VF) and control measures (IQ and PVT). Based on *n* = 11.

	WCST	TOL*	VF**	PVT	IQ
WCST	–	0.31	-0.55	-0.25	-0.22
TOL	–		-0.11	-0.41	-0.32
VF	–	–	–	-0.13	-0.04
RT	–	–	–	–	-0.63
IQ	–	–	–	–	–

*TOL based on *n* = 10

**VF based on *n* = 7 due to educational attainment; see section 2.2.2.

None of the parameters were found to significantly correlate, although WCST and VF demonstrated an association in which a low number of perseverative errors on the WCST predicted greater number of verbs generated on the VF, although this was not significant [r = -0.55, n = 7, p = 0.10]. A lack of significant association was found between executive function measures, despite literature suggesting their common role in PFC function.

4.4 Discussion

It was hypothesised that over a comparatively small period of time (6.29 years) that declines would be found in performance of executive function measures in a healthy older group (aged 73.39 years at follow-up). In the literature, cross-sectional declines in performance, with advancing age have been reported on the TOL (Robbins et al., 1998), VF (Ardila et al., 2000; Parkin & Walter, 1991) and WCST (Comptom, et al., 1999; Macpherson, et al., 2002; Parkin & Walter., 1991). This was partially supported in Study 2. Significant declines were observed in performance of TOL, with the group taking significantly longer at follow-up to solve problems, in comparison to at baseline. Although the group generated fewer verbs at follow-up on the VF measure, this was not significant. Conversely there was some improvement on WCST over time, although this was also not significant. In addition to this no significant declines were found between baseline and follow-up for the control tests (fluid intelligence IQ and PVT reaction time), suggesting stability in more general measures of cognition.

The longitudinal study conducted by Davis and Klebe (2001) concurs with results in the present chapter. They found longitudinal age-related declines in Tower of Hanoi (TOH; a test similar in concept to TOL) performance over a period of 6.6 years in a group that was older at follow-up than in the present study (mean age = 81 years, SD = 6.6 years) and of similar sample size (n = 12). Therefore the present study indicates that over a similar time frame, but in a younger sample than that observed by Davis and Klebe

(2001), there was a significant decline in performance on non-verbal planning performance.

Few studies have attempted to observe age-related changes in executive function by utilising a longitudinal design. One of the benefits of doing so is greater control over variability between groups. However, although longitudinal studies can account for a greater control over aspects of variability, it is more prone to an underestimation of group differences. Lack of a significant change over time was found in VF and WCST, even though current literature has reported declines using a cross-sectional method. It is plausible that VF and WCST are more prone to the problems associated with repeated measures designs than the TOL.

There would inevitably be a loss of novelty in the presentation of the executive function tasks at follow-up. This brings in the potential of problems such as practice effects, decreasing the difficulty of the tasks, perhaps in turn decreasing the frontal-loading of the tasks. According to Rabbitt (1977), when a task is novel, the executive control functions of the tasks are at their highest. This has been demonstrated in performance on the TOL, in that signal intensity increased with difficulty of problem in the DLPFC (Newman et al., 2003). If performance became easier due to practice effects, frontal loading would consequently decrease.

Loss of novelty is perhaps more problematic for WCST, than it is for the other tasks, as this is strongly based on hypothesis generation, and once the premise of the task is identified, the task decreases in difficulty dramatically. This is supported by findings that practice effects have been found in middle aged males on the WCST after 12 months (Basso, Bornstein & Lang, 1999), which may account for the lack of change in number of perseverative errors on WCST from baseline to follow-up in Study 2. According to those authors, during the completion of tasks at baseline, participants tend to eventually learn that set shifting occurs and that this may have been recalled at follow-up. It is not known whether this would

translate into practice effects over the period of 6.29 years so this interpretation of the results remains speculative.

Another interpretation of the variability between measures to longitudinal changes with age is that they vary in sensitivity to detect age associated changes. This is supported by findings of Study 1, in which significant cross-sectional age differences were observed in TOL but not VF performance (WCST was not observed). Given that the older group was of a similarly high functioning level, cognitively speaking, it could be concluded that the VF task may not be as sensitive to ageing effects as others (i.e. TOL). Interestingly, as previously noted for the interpretation of results of Study 1 (see section 3.4), one suggestion for no age-related differences in VF was potential cohort effects between the young and older group which may have masked any declines in VF. However, the results from the present chapter utilising a repeated measures design, help to dispel this.

Although imaging studies have implicated PFC regions as being dominantly associated in completion of the WCST (Monchi et al., 2001), VF (Peterson et al.,1998; Ravnkilde et al., 2002) and TOL (Newman et al., 2003; Rezai et al*.,* 1993), cross-correlation levels were not significant. The relationships were: strong for WCST and VF (r = -0.55), moderate for TOL and WCST (r = 0.31), and weak for TOL and VF (r = 0.11). Low levels of correlation between measures proposed to dominantly tap into the PFC have consistently been found in the literature to be low to moderate in strength (r < 0.40; Miyake et al., 2000). This might be explained in some part by the highly integrative nature of the PFC (it is abundantly connected to other brain regions). It is acknowledged that not all executive function measures will implicate the PFC in isolation, but involve a range of other brain structures. This might not only account for low inter-relation between 'PFC measures', but may account for the sensitivity of executive function tasks to detect age-related changes.

An alternative viewpoint of the selective vulnerability of the TOL is due to its involvement in functions not necessarily encapsulated by executive

functions. The susceptibility of the TOL to greater age-related declines than the other tasks may be due to the heavy memory loading involved in the task, which is known to be vulnerable to the ageing process (Gilhooly, Wynn, Phillips, Logie, & Della Sala, 2002). However, nondeclarative memory (memory involved in skill acquisition), is not impaired to a substantial extent with age (Light, Singh & Capps, 1986) and so memory loading may be a small contributory factor at best.

It might also be argued that the selective decline on the TOL was due to time constraints. For example, Salthouse (1993) suggested that slowing of reaction time may be responsible for age-related declines in cognition. Although participants were not given time restrictions to complete the task, the measure of interest was mean completion time. It is therefore reassuring that no significant declines were found in the same individuals on PVT reaction time, making it unlikely that TOL scores were influenced a great deal by unintentional slowing of reaction time.

4.5 Conclusion

- Age-related increases were found from baseline to follow-up in mean completion time of TOL task (executive function), indicating a decrement in performance in this measure over a period of 6.29 years.

- No difference over time was found for number of verbs generated on the VF task and number of perseverative errors incurred on the WCST.

- Performance on non-PFC specific tasks (fluid intelligence IQ and PVT reaction time) remained stable over time.

- Cross-correlation of executive functions associated with the PFC was not significant.

Only significant age-related declines were found over a period of 6.29 years in TOL performance. Lack of decline in WCST and VF may have been due to greater vulnerability to practice effects. However, due to the concurrence of the results to those found in the cross-sectional findings of Study 1, it is concluded that measures of executive function may differ in sensitivity to detect age-associated changes in healthy older adults. Stability on 'global' measures may indicate intact general cognitive abilities in the presence of specific age-associated changes in TOL performance.

5 Study 3: Age-Related Changes in PFC Sleep EEG

5.1 Introduction

It is well established in the literature that sleep changes with age. It becomes more fragmented, there are more awakenings and there is greater difficulty in maintaining sleep stages (Phillips & Ancoli-Israel, 2001). At the EEG level, there appears to be decreases in the lower frequencies (Carrier, et al., 2001; Dijk, et al., 1989; Landolt et al., 1996) and increases in higher frequencies (Carrier, et al., 2001) perhaps indicating greater cortical activation during sleep with age. Furthermore, there are also declines in spindle (Crowley et al., 2002; Feinberg et al., 1967; Landolt et al., 1996) and KC parameters with increasing age (Colrain et al., 2010; Kubicki, et al., 1989; Wauquier, 1993).

Changes in SWA, spindles and KCs with advancing age, coincidentally, or not, appear to mirror changes in the underlying structures of the brain (Gerard & Weisberg, 1986; Haug et al., 1983; Terry, et al., 1987). Furthermore, there is the implication that these SWA changes are associated with cognitive ageing associated with PFC; a link between SWA and cognitive function was observed by Anderson & Horne (2003) in an older sample, specifically localised to the LPFC. Whether this is by virtue of a functional link via synaptic plasticity (Kattler, et al., 1994; Gais et al., 2002), due to cortical deactivation (Hofle et al., 1997 & Maquet et al., 1997), or due to mere commonality of ageing of the PFC (Gerard & Weisberg, 1986; Haug et al., 1983; Terry, et al., 1987) is inconclusive. There does however appear to be a particular vulnerability of SWA decrements with increasing age, and this may have implications for cognitive function.

Research into age-related changes in sleep with age is largely limited by the tendency of studies to not take into consideration topographic distribution, in

that there appears to be a bias to report measurements taken from central derivations. This is disappointing considering that mechanisms involved in SWA activity originating in anterior regions are different from SWA originating in posterior regions. For example, spindle activity in frontal and parietal regions can occur simultaneously, but have a dominance in different spindle frequencies (Anderer et al., 2001; Werth et al., 1997). As such, this points towards the importance of the focus on localisation of EEG.

Another limitation of existing research into the effects of ageing on SWA and associated components is that there is a lack of longitudinal comparisons. Repeated measures observations, as opposed to the frequently made cross-sectional comparisons may be of particular importance, as significant sex differences have been noted in young (21.4 years, *SD* = 2.4 years) but not in older individuals (75.5 years, *SD* = 6.3 years; Crowley et al., 2002) with regards to specific SWA components. One explanation for this may have been that there is an effect of reproductive hormones on EEG. For example, Brunner et al. (1994) found that sigma varied with levels of reproductive hormones. This therefore has wider implications for ageing research, when comparing young adults, (especially in the context of spindle activity) and older, postmenopausal adults, as results may become distorted.

5.1.1 Main Aims and Hypotheses

The present chapter aims to elucidate more about the development of aspects of sleep over a period of 6.29 years in an older sample, with a particular focus on the PFC. It is hypothesised that:

i) Age-related declines will be found in low frequency delta, KC density, and spindle density. These declines will be more pronounced in EEG localised to the PFC.

5.2 Method

5.2.1 Participant Characteristics

This study includes sleep EEG data obtained from the Longitudinal Design Cohort outlined in the *General Method* (section 2.1.3). Due to the repeated measures design used, only baseline (2000) and follow-up (2006) data for the 11 individuals retained at follow-up are reported in this chapter. Participant characteristics are presented in Table 5.1. Rows in Table 5.1 that are shaded represent those participants for which baseline data was collected but follow-up data was not. Those participants are therefore excluded from the present chapter.

The mean age of the group (*n* = 11) at baseline was 67.11 years (*SD* = 3.37 years) and at follow-up was 73.39 years (*SD* = 3.18 years). The mean lapse in time between baseline and follow-up testing was 6.29 years (*SD* = 0.48 years). There were 6 females and 5 males in the group.

Daytime Sleepiness and Time in Bed –
As can be seen in Table 5.1 there were no substantial changes in ESS scores and TIB from baseline to follow-up. There was a slight increase in self-reported daytime sleepiness as ascertained by ESS from baseline (mean = 4.64, *SD* = 2.34) to follow-up (mean = 4.9, *SD* = 3.05). There was also a small increase in TIB from baseline (mean = 8.05hr, *SD* = 0.15hr) to follow-up (mean = 8.23hr, *SD* = 0.88hr). However, all participants were found to satisfy the screening criteria as set out in section 2.1.1 at baseline and at follow-up.

Table 5.1: Baseline (2000) and follow-up (2006) participant characteristics. Shaded rows depict participants not utilised in Study 3.

		Age		ESS		TIB(hrs)	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**	**2000**	**2006**
BC01	f	64.00	-	3	-	8.00	-
RR02	f	67.08	-	6	-	8.00	-
AT03	m	61.67	68.58	6	9	8.00	9.00
EM04	m	68.00	-	9	-	9.00	-
SS05	m	68.67	-	5	-	8.00	-
IK06	m	66.33	-	3	-	8.00	-
TK07	f	64.92	71.17	8	6	8.00	9.00
BF08	m	64.50	70.83	4	7	8.00	7.00
YF09	f	63.33	69.92	4	7	8.00	7.00
JC10	f	67.17	73.75	3	2	8.00	8.00
JY11	f	66.67	73.42	1	0	8.00	8.00
JT12	f	68.25	-	5	-	8.50	-
BP13	f	70.17	-	1	-	9.00	-
RW14	m	68.58	74.67	3	7	8.00	7.00
OC15	m	62.00	-	5	-	8.00	-
RD16	m	71.58	77.25	6	8	8.00	8.50
RL17	m	69.42	-	5	-	8.00	-
LL18	f	66.17	-	3	-	8.00	-
GM19	m	70.25	76.25	2	3	8.00	9.00
MM20	f	67.33	72.67	8	1	8.00	9.00
EP21	f	72.17	78.80	6	4	8.50	9.00
DF22	f	74.00	-	0	-	8.00	-
ES23	f	75.33	-	2	-	8.00	-
MF24	f	71.17	-	9	-	8.50	-
Mean		**67.87**	**73.39**	**4.46**	**4.91**	**8.15**	**8.23**
SD		**3.54**	**3.18**	**2.50**	**3.05**	**0.31**	**0.88**
Retained Mean		**67.11**	**73.39**	**4.64**	**4.91**	**8.05**	**8.23**
Retained SD		**3.37**	**3.18**	**2.34**	**3.05**	**0.15**	**0.88**

- Data not obtained.

5.2.2 Sleep EEG Recording

All participants, at baseline and follow-up underwent sleep EEG recordings as described in detail in Chapter 2 (*General Method:* see section 2.3). In Study 3 quantification of EEG included:

- Spectral analysis of low frequency delta corresponding to LPFC, RPFC, LOPC and ROPC.
- Visual scoring of spindle and KC density corresponding to LPFC, RPFC, LOPC and ROPC

These methods were used in order to explore any age-related changes in low frequency delta, and spindle and KC density (including any specificity to the PFC), as well as any changes in regional dominance.

- Visual scoring of sleep architecture.

This was to explore localised low frequency delta, and spindle and KC density in the context of possible global changes in sleep architecture.

5.2.3 Data Analysis

Due to a small sample sizes and lack of normal distribution in many of the data sets reported in this chapter, most analyses involving comparison of means between baseline and follow-up utilised the non-parametric Wilcoxon signed ranks test. Where data was found to meet the assumptions of parametric data, paired samples t-tests were utilised. Effect sizes were reported as *r* for non-parametric tests and eta squared (η^2) for parametric equivalents.

Hypotheses were one-tailed (unless otherwise reported) guided by cross-sectional literature with the level of significance set at $p < 0.01$ for comparison of means analyses (see section 2.4).

Outlying data was identified on the basis of criteria set out in *General Methods* (see section 2.4). BF08 was identified as an outlier in Study 3, for baseline low frequency delta; this is detailed further in sections to follow.

5.3 Results

5.3.1 Changes in Sleep Architecture

Changes in sleep parameters were explored from baseline (2000) to follow-up (2006): the means and standard deviations of these, as determined via overnight sleep EEG recordings are presented in Table 5.2. Parameters include total sleep time (TST), waking after sleep onset (WASO), sleep period time (SPT) and sleep efficiency. Percentages of total sleep time in each of the sleep stages were taken from visually scored sleep EEG: stage 1 (S1), stage 2 (S2) and rapid eye movement sleep (REM). Due to the scarcity of stage 4 in the sample, stage 3 and stage 4 were combined (S3/S4).

Sleep Continuity –

Changes over time in TST, WASO, SPT and sleep efficiency were explored using the Wilcoxon signed ranks test. No significant differences were found for TST ($p = 0.72$), for SPT ($p = 0.66$), or for sleep efficiency ($p = 0.66$). No significant difference was found for WASO ($p = 0.51$) either. Furthermore, all effect sizes ($r < 0.20$) were small.

Table 5.2: Sleep parameters at baseline (2000) and at follow-up (2006; *n* = 11). There were no significant differences between baseline and follow-up for sleep continuity factors, despite there being a slight reduction in sleep quality at follow-up.

	Baseline (2000)		Follow-up (2006)	
	Mean	SD	Mean	SD
Sleep Continuity				
TST (mins)	342.36	42.40	321.86	60.11
WASO (mins)	102.68	46.95	120.91	60.67
SPT (mins)	445.05	46.72	442.77	46.49
Sleep Efficiency (%)	77.26	9.01	72.88	12.68
% of Total Sleep Time				
S1	14.34	4.74	14.87	3.19
S2	51.47	7.38	54.53	12.46
S3/S4	10.01	6.79	8.28	5.29
REM	24.18	3.87	22.32	8.21

Percentage of Total Sleep Time –

Time spent in each of the sleep stages (S1, S2, S3/4 and REM), was expressed as a percentage of TST. The percentage of time spent in each sleep stage was compared from baseline to follow-up. Mean changes in percentages of sleep stages are presented in Table 5.2.

Using a two-tailed paired samples t-test, due to an uncertainty in the literature, significant changes were not found in percentage of S1 from baseline to follow-up ($p = 0.76$). Using Wilcoxon signed ranks test, changes were also not significant in percentage of S2 from baseline to follow-up ($p = 0.42$), in percentage of S3/S4 ($p = 0.21$), or in percentage of REM ($p = 0.37$). Effect size was small in magnitude for S1 ($\eta^2 = 0.01$) and effect sizes for all other sleep stages were small to moderate ($r < 0.34$). As can be observed in Figure 5.1, sleep at both time points was found to be dominated by S2 sleep, with the smallest representation being that of S3/S4.

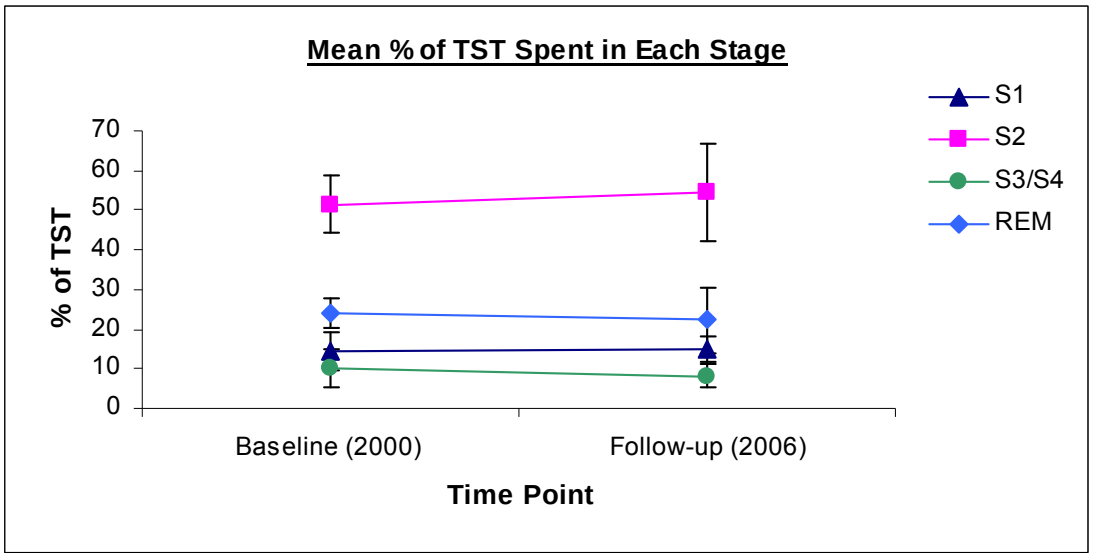

Figure 5.1: Mean percentages of S1, S2, S3/S4 and REM at baseline (2000) and follow-up (2006). Points represent mean values and vertical lines represent standard deviations.

5.3.2 Changes in Frontal Sleep EEG

Some aspects of sleep have been found to be particularly vulnerable to age-related changes, as demonstrated in previous cross-sectional studies. These changes appear to be particularly relevant to aspects of low frequency delta, and spindle and KC density. These aspects of sleep, in the context of age-related changes were observed using a repeated measures design in the present section.

Low Frequency Delta –

Delta 0.5 – 4.5 Hz was spectrally analysed and split into bands of 0.5 Hz intervals (e.g., 0.5 – 1, 1 – 1.5 Hz, and so on). Each band was expressed as a relative percentage of total power. A summary of these percentages are represented in Figure 5.2. It is apparent that there is a dominance of the lowest bands (particularly 0.5 – 1 Hz and 1 – 1.5 Hz delta), across all four regions at baseline and at follow-up. Change over time was explored further in the 0.5 – 1 Hz delta range due to the previous links having been found between this and executive function (Anderson & Horne, 2003). Further to this, relative delta (0.5 – 1 Hz) in the four regions is presented in Figure 5.3.

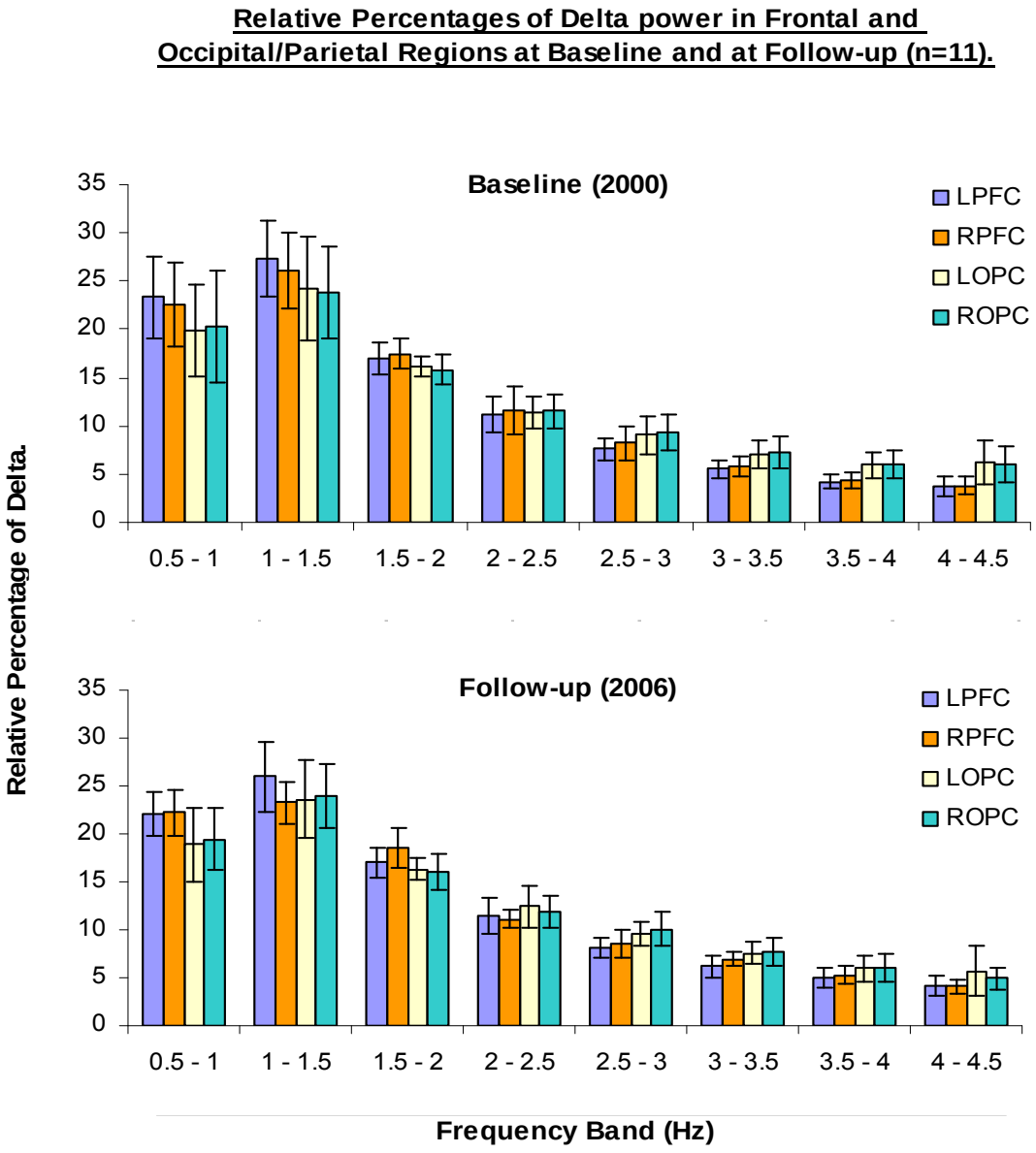

Figure 5.2: Relative percentages of power in each of the bands 0.5 – 1 Hz, 1 – 1.5 Hz, 1.5 – 2 Hz, 2 – 2.5 Hz, 2.5 – 3 Hz, 3 – 3.5 – Hz, 3.5 – 4 Hz and 4 – 4.5 Hz, across all derivations (LPFC, RPFC, LOPC and ROPC). This is presented for baseline (2000) and at follow-up (2006) measurements. Vertical lines depict standard deviations.
*LPFC is based on *n* = 10 at baseline due to removal of outlying value for BF08.

Change in Low Frequency Delta (< 1Hz)

A Wilcoxon signed ranks test was utilised to explore differences in low frequency delta power from baseline to follow-up. There were no changes over time in percentage of 0.5 – 1 Hz delta in the LPFC, RPFC, LOPC or ROPC ($p > 0.06$). However, although effect sizes were small for delta in the

right hemisphere (RPFC and ROPC; $r < 0.24$), they were moderate to large in the left hemisphere (LPFC and LOPC; $r > 0.40$).

Participant BF08 was found to be more than 2 standard deviations from the group mean for the LPFC at baseline. Therefore, this was treated as a potential outlier as it was found to demonstrate a large influence on the overall distribution. With the removal of participant BF08, the change in low frequency delta power (< 1Hz) became significant [$Z = -2.19$, $p < 0.01$, $r = 0.69$]. A box-plot in Figure 5.4, also supports that participant BF08 is likely to exert a substantial influence on the overall distribution of values. Therefore, this value was removed from subsequent analyses in order to avoid data distortion.

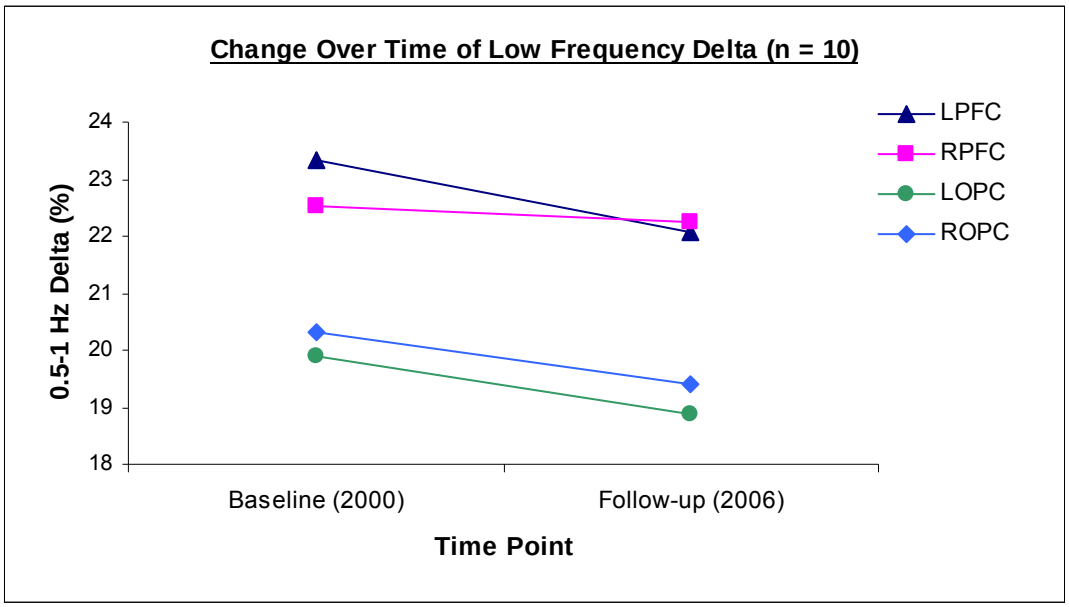

Figure 5.3: Relative percentages of power in the 0.5 – 1 Hz band across all derivations (LPFC, RPFC, LOPC and ROPC). This is presented for baseline (2000) and at follow-up (2006) recordings.
Based on $n = 10$ at baseline due to removal of outlying value for BF08.

Although participant RW14 also appears to be a possible outlier from observations of the box-plot, this value was not found to be more than 2 standard deviations from the group mean (contrary to participant BF08). As a check on this, the additional removal of participant RW14 (as well as participant BF08) did not cause a substantial change in effect size [$Z = -$

1.96, p = 0.05, r = 0.65]. On this basis, participant RW14 is believed to be a genuine score, whereas participant BF08 a probable outlier for removal.

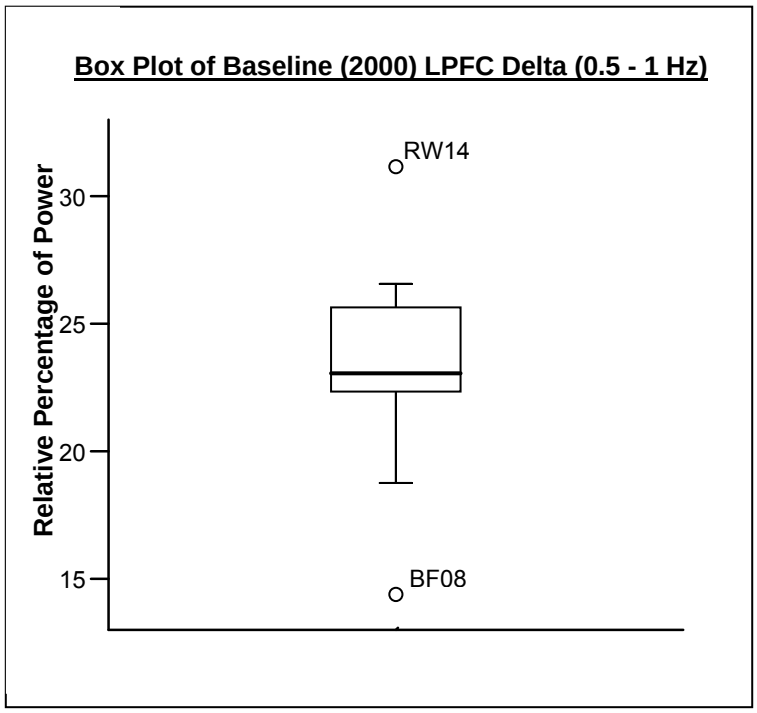

Figure 5.4: Box Plot of relative percentages of power in the 0.5 – 1 Hz band in LPFC at baseline (2000).

Regional Dominance

Regional dominance may be an important indicator of requirement of low frequency delta for particular brain regions. To explore whether frontal dominance changes with age, LPFC and RPFC data were combined to obtain a frontal composite relative percentage, and LOPC and ROPC to obtain an occipital/parietal composite relative percentage. This data is presented in Table 5.3.

Differences between frontal and occipital/parietal delta power were analysed using Wilcoxon signed ranks test, at baseline and at follow-up. The difference between percentage of power 0.5 – 1 Hz was greater in the frontal region, in comparison to occipital/parietal region, and this approached significance [Z = -1.98, p = 0.02, r = 0.62]. At follow-up, percentage of power was also greater in frontal derivations, and again this was found to approach significance [Z = -2.05, p = 0.02, r = 0.65]. The

frontal dominance of delta power (frontal – occipital/parietal) was not significantly different between baseline and follow-up [Z = -0.46, p = 0.64, r = 0.14].

Table 5.3: EEG regional dominance at baseline (2000) and at follow-up (2006; *n* = 11), with comparisons made between mean percentage of power in 0.5 – 1 Hz delta band, spindle density and KC density in frontal (composite LPFC and RPFC) and occipital/parietal (composite ROPC and LOPC) regions.

	Frontal		Occipital/Parietal	
	Mean	**SD**	**Mean**	**SD**
Baseline (2000)				
0.5-1 Hz delta	23.80	3.17	20.19	5.55
Spindle density	2.89	1.92	1.92	1.63
KC Density	1.79	0.53	1.34	0.58
Follow-up (2006)				
0.5-1 Hz delta	22.29	2.22	18.82	3.45
Spindle density	2.77	1.84	1.71	1.50
KC Density	1.42	0.50	1.40	0.80

*0.5 – 1 Hz delta based on *n* = 10, due to BF08 being an outlying value for the LPFC.

Spindle Density-

Changes in spindle density were of interest due to prior findings suggesting its link to SWA. Spindles (11 – 16 Hz) occurring during stage 2 were visually scored across the four regions: LPFC, RPFC, LOPC and ROPC. Total number of spindles was divided by number of minutes in the first two stage 2 periods, leading into SWS. Spindle densities across the four regions are presented in Figure 5.5.

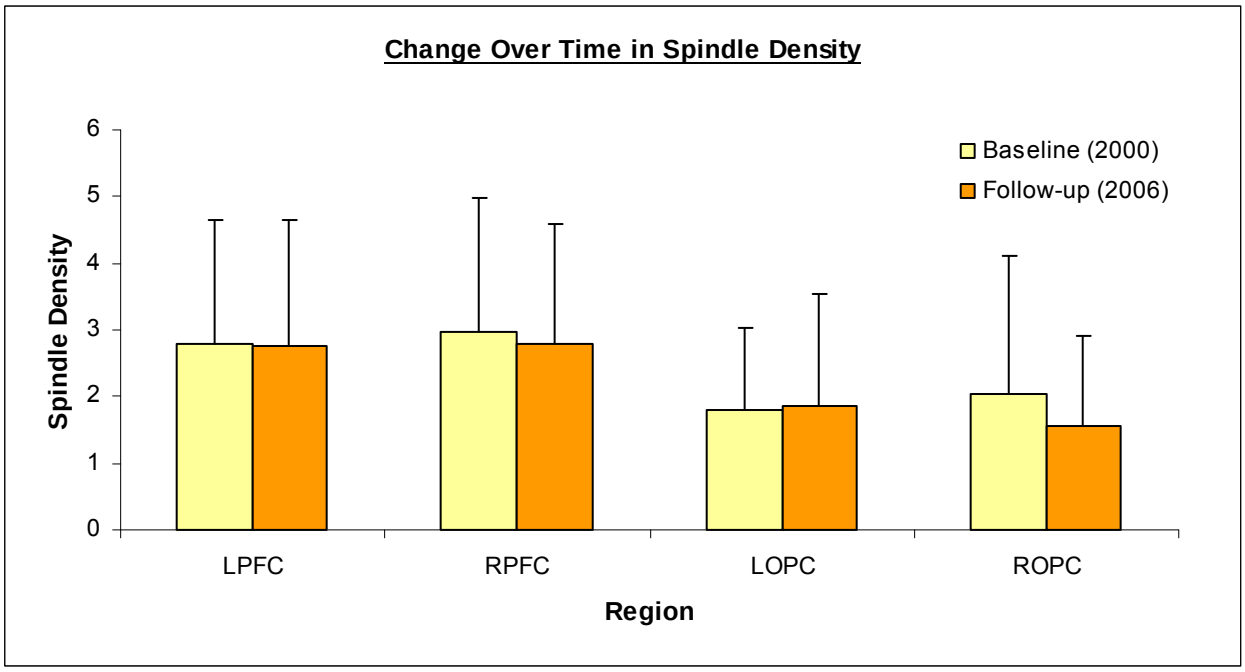

Figure 5.5: Baseline (2000) and follow-up (2006) spindle densities in the LPFC, RPFC, LOPC and ROPC. Vertical lines represent standard deviations. Based on *n* = 11.

Change in Spindle Density

Wilcoxon signed rank tests ascertained that there were no significant differences from baseline to follow-up in spindle density in the LPFC, RPFC, LOPC, or in the ROPC ($p > 0.37$). Furthermore, all effect sizes were small to moderate ($r < 0.27$). Therefore it does not appear as though spindle density has changed substantially from baseline to follow-up in any of the 4 regions.

Regional Dominance

As presented in Table 5.3, spindle density is greater in frontal regions (composite LPFC and RPFC), in comparison to occipital/parietal regions (composite LOPC and ROPC). Wilcoxon signed ranks confirmed that spindle density was significantly greater in the frontal region, in comparison to the occipital/parietal region at baseline [$Z = -2.76$, $p < 0.01$, $r = 0.83$]. Furthermore, this frontal dominance was also significant at follow-up [$Z = -2.60$, $p < 0.01$, $r = 0.79$]. The frontal dominance of spindle density (frontal – occipital/parietal) was not significantly different between baseline and follow-up [$Z = -0.36$, $p = 0.42$, $r = 0.11$].

K-Complex Density-

KCs occurring during stage 2 were visually scored across the four regions: LPFC, RPFC, LOPC and ROPC. Total number of KCs was divided by number of minutes in the first two stage 2 periods leading into SWS. KC densities in all 4 regions are presented in Figure 5.6.

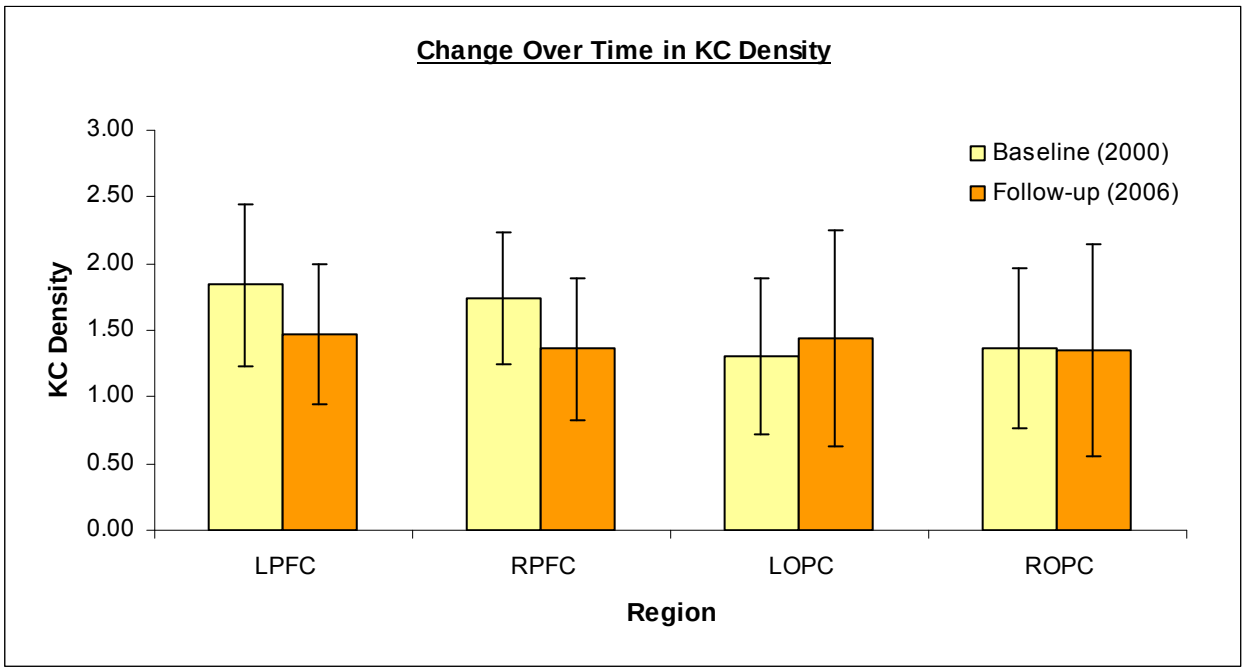

Figure 5.6: Baseline (2000) and follow-up (2006) KC densities in the LPFC, RPFC, LOPC and ROPC. Vertical lines represent standard deviations.

Change in K-Complex Density

There appears to be a decline in KC density from baseline to follow-up in the LPFC and RPFC. However, Wilcoxon signed rank tests revealed that this decline was not significant for LPFC, RPFC, LOPC, or ROPC ($p > 0.11$). Furthermore, effect sizes were deemed to be small ($r < 0.18$).

Regional Dominance

As presented in Table 5.3, KC density is slightly greater in frontal regions (composite LPFC and RPFC), in comparison to occipital/parietal regions (composite LOPC and ROPC). A Wilcoxon signed ranks test demonstrated that the regional difference in KC density at baseline was not significant and there were no significant differences at follow-up ($p > 0.14$). Furthermore,

effect sizes were small (r < 0.16). The frontal dominance of KC density (frontal – occipital/parietal) was not significantly different between baseline and follow-up [Z = -1.25, p = 0.21, r = 0.37].

5.4 Discussion

It was hypothesised that significant declines would be found in SWA and associated components, and that this would be greater in the PFC in comparison to occipital/parietal regions, utilising a longitudinal analysis technique over 6.29 years in an older sample (aged 73.39 years, *SD* = 3.18 years at follow-up). However, results were mixed. No declines were observed in all of the four investigated derivations corresponding to LPFC, RPFC, LOPC and ROPC, in KC density and spindle density. Declines were found in low frequency delta (0.5 – 1Hz) over 6.29 years, but this was significant only in the LPFC. Therefore, the LPFC appears to be the region most sensitive to the effects of ageing in low frequency delta power.

Other findings included stability in sleep continuity (TST, WASO, SPT, sleep efficiency), as well as percentage of S1, S2, S3/S4 and REM sleep. These measurements were taken on central derivations, in order to ascertain any general changes in sleep. The results therefore, indicated stability in general sleep structure over a period of 6.29 years. This also indicates that no substantial changes in sleep habits had occurred between testing time points.

Although much literature pertaining to age-related changes has been contradictory, the literature has consistently demonstrated age-related changes in deeper sleep states. Declines in relative percentages of S4 have been found (Feinberg et al., 1967; Landolt & Borbely, 2001), as well as in S3/S4 sleep (Bonnet & Arand, 2007; Crowley et al., 2002). However, 6.29 years is a relatively short ageing period, and therefore unlikely to result in gross changes at the sleep structure level.

A particular dominance of low frequency delta and spindle density was found in the frontal regions in comparison to the posterior regions at both time points, as expected (although this dominance approached significance in the former), indicating that a frontal necessity was still present in the older sample. This was not found to be the case for KC density at both time points, and this remained stable over time. The findings were contrary to those found by Landolt and Borbély (2001). Their results indicated that although a frontal dominance was found in young males aged 20-25 years (mean = 22.3 years) in spindle and delta activity, that this was absent in the older males aged 57-64 years (mean = 62 years). The authors suggested that dominance decreases with age due to a reduction in PFC recovery requirement or due to modifications of underlying mechanisms. This however, was not supported in the Study 3, utilising an older group with a mean age of 73.39 years at follow-up. Previous research has suggested that delta activity, spindle activity (Hofle et al., 1997), as well as KC activity (Czisch et al., 2004), is associated with decreased cortical activation. Therefore, a particular regional dominance in these aspects of sleep in a given region potentially signifies a greater necessity for greater cortical deactivation is still relevant in the older adult group in the present study.

An unfortunate limitation of Study 3, originates from the longitudinal design. There was a failure to reach statistical significance in the comparison of SWA from baseline to follow-up (except in change over time in low frequency delta in the LPFC). The lack of statistical finding is suspected to be due partly to limited group size (due to drop-out rates), and also may be due to the time period between baseline and follow-up analyses being too small to detect a significant difference. Unfortunately, the latter cannot be extended without the prospect of the sample size reducing even further.

Age-related changes may have also been diminished due to carryover effects. For example, although EEG is relatively non-invasive it can cause small levels of anxiety in individuals not used to the procedure that may impact the amount of sleep they obtain, particularly S3/S4. In the follow-up measurements, individuals may have become less sensitive to sleeping with

the EEG equipment and exhibit less sleep interfering anxiety than they may have had at baseline. However, habituation nights at baseline and follow-up, would have remedied this to some extent.

A lack of significant difference in spindle density between time points might be due to the frequency range observed in Study 3. Spindle density was identified on the basis of the frequency range of 11 – 16 Hz. Previous literature has suggested that there should be a definition of fast and slower spindles due to the possibility that slower spindles (11.5 – 11.75 Hz) originating in the frontal derivations may have different underlying mechanisms than faster spindles (peak = 13.5) which originate in the occipital/parietal regions (e.g., Anderer et al., 2001). A pilot study was carried out on data reported in Study 3 in which there was to be a differentiation made between slow and fast spindles. However, slow spindles were either scarce, or not present in all participants. This was surprising given that the literature suggests a predominance of the slow oscillating spindles, particularly in frontal regions (Anderer et al., 2001).

Reasons that might account for this are that:

1. Spindles have a tendency to oscillate faster in S2, in comparison to S3 (Dijk et al., 1993). In Study 3, only S2 spindle density was observed due to the difficulty in distinguishing between the spindle graphic shape and background slow delta activity.
2. Spindles oscillate faster at the beginning and end of the night (Himanen et al., 2002). In Study 3, the EEG activity at the beginning of the night was observed. This is because sleep pressure is much stronger in the early stages of the night. It is also the most undisturbed part of the night with regards to external stimuli causing artefact contamination of the EEG.
3. In NREM sleep (including S2), faster spindles were more easily identified from background activity than slower ones, potentially creating a bias towards faster spindle identification. This may be particularly so in older participants, in which spindle graphic shape is often atypical.

If slow spindles are typically reflective of underlying mechanisms of the frontal lobes, then the results presented in Study 3 may not have been a true expression of PFC spindle activity.

However, it is argued that the limitations of the method are outweighed by the benefits. Cross-sectional studies may give an over-inflation of group differences, due to factors including individual differences and cohort effects. It may be that the results of Study 3 reveal more of a realistic picture of the rate of change of sleep in later life; the rate of change may not be as sharp as cross-sectional studies would suggest. The large inter-individual variability, as demonstrated by large standard deviations, found on sleep parameters (particularly KC and spindle density in Study 3) highlight the importance of using a repeated measures design, rather than cross-sectional observation of age-related changes in sleep.

5.5 Conclusion

- Age-related changes were not observed in sleep architecture.

- Significant declines were found in low frequency delta (0.5 – 1hz) in the LPFC region only. Delta power (0.5 – 1Hz) in the RPFC, LOPC or ROPC showed no significant change over time. Spindle density and KC density in all observed derivations remained stable over time.

- Low frequency delta (0.5 – 1Hz) and spindle density demonstrated a similar frontal-occipital/parietal gradient of dominance which remained stable over time (although this only approached significance for low frequency delta). No frontal dominance was found for KC density, which remained stable from baseline to follow-up.

The specificity of declines to the LPFC, is in agreement with the assumption that the PFC is more vulnerable to age-related declines than other regions.

The dominance of low frequency delta and spindle density EEG in the PFC, may highlight greater cortical deactivation in these areas, which did not change with age.

6 Study 4: Links between Sleep EEG and Cognitive Function Revisited

6.1 Introduction

The 'frontal lobe theory' of age-related declines has been well established in the literature: functions (such as executive function) associated with the frontal lobes, are particularly vulnerable to 'healthy' cognitive ageing (e.g., Ardila et al., 2000; Comptom et al., 1999; Davis & Klebe, 2001; Macpherson et al., 2002; Parkin & Walter, 1991; Robbins et al., 1998). Decrements in SWA, suggesting greater cortical activity during sleep have been observed with advancing age (Carrier, et al., 2001; Dijk, et al., 1989; Landolt et al., 1996). In Study 3, PFC delta (specific to the left hemisphere) was found to undergo longitudinal age-related changes, and cognition associated with the PFC (i.e. TOL) in Study 2 was observed as undergoing concurrent declines with age.

Although ageing appears to selectively impair PFC cognition and SWA; the reason for a similar trajectory of decline is equivocal. Explanations have emerged that might account for this:

i. Changes with age in PFC SWS (e.g., due to underlying morphological changes in the PFC), could consequently result in decrements in cognitive ability, as cortical deactivation would be interrupted. EEG has been shown to reflect underlying neuronal activity (e.g., Amzica & Steriade, 1998).
ii. An increase in sleep disturbance (e.g., due to unrelated factors such as increased prevalence of disease with age) could result in compromised cognitive ability; declines in sleep quality with progressing age have been seen (e.g. Bonnet & Arand, 2007; Crowley et al., 2002). The PFC may be more vulnerable because it undergoes the greatest cortical deactivation with SWA (e.g. Hofle et al., 1997; Maquet et al., 1997).

iii. The changes seen in PFC morphology with age affect both localised SWA and cognitive function associated with that same area, and the relationship is non-functional and coincidental.

The first two points prescribe to the assumption that 'SWS is for the cortex' and as such, would suggest a functional link.

Although not a study of ageing, Anderson and Horne (2003) demonstrated that PFC localised low frequency delta predicted executive function ability in an older adult cohort, with stronger links found in the LPFC than the RPFC. Whether both ageing domains share a functional link is unknown as both have not been explored in the same individuals using a longitudinal method.

A longitudinal study of SWA and executive function developments with age would help to elucidate further the nature of the link. If baseline EEG was found to significantly relate to follow-up cognitive function, then it might indicate a functional relationship, as well as implicate sleep EEG as a potential predictive marker of cognitive decline. Furthermore, follow-up analyses on the cohort utilised by Anderson and Horne (2003) allows an investigation into the test-retest reliability of low frequency delta as a clinical marker.

6.1.1 Main Aims and Hypotheses

Anderson and Horne (2003) established a link between PFC low frequency delta and executive function in healthy older individuals. The focus of the present study was to ascertain whether this link would persist with increasing age. It was hypothesised that:

i) Past (baseline) low frequency delta localised to the LPFC will predict future (follow-up) performance of executive function measures in a healthy, older sample; greater EEG power will be associated with better performance.

ii) The link between LPFC low frequency delta and executive function as ascertained by Anderson and Horne (2003) will be

present in follow-up analyses; greater EEG power will be associated with better performance.

Study 4 is split into two main parts. Part I is concerned with addressing the main aims and hypotheses, and Part II is concerned with observing potential cohort effects, arising from the longitudinal design.

6.2 Method I

6.2.1 Participant Characteristics

Study 4: Part I includes participants obtained from the Longitudinal Design Cohort outlined in the *General Method* (section 2.1.3). The aims of Part I are as follows:

- To observe whether baseline PFC low frequency delta can predict future (follow-up) performance on executive function measures.
- To observe the stability of the low frequency delta-executive function link observed by Anderson and Horne (2003).

Due to the longitudinal nature of the research outlined in Part I, only baseline (2000) and follow-up (2006) data for the 11 individuals retained at follow-up are reported. Participant characteristics are presented in Table 6.1. Rows in Table 6.1 that are shaded represent those participants that are excluded from Study 4: Part I, due to follow-up data not being available.

Table 6.1: Baseline (2000) and follow-up (2006) participant characteristics for Study 4: Part I. Shaded rows depict participants not utilised in Study 4: Part I.

		Age		ESS		TIB(hrs)	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**	**2000**	**2006**
BC01	f	64.00	-	3	-	8.00	-
RR02	f	67.08	-	6	-	8.00	-
AT03	m	61.67	68.58	6	9	8.00	9.00
EM04	m	68.00	-	9	-	9.00	-
SS05	m	68.67	-	5	-	8.00	-
IK06	m	66.33	-	3	-	8.00	-
TK07	f	64.92	71.17	8	6	8.00	9.00
BF08	m	64.50	70.83	4	7	8.00	7.00
YF09	f	63.33	69.92	4	7	8.00	7.00
JC10	f	67.17	73.75	3	2	8.00	8.00
JY11	f	66.67	73.42	1	0	8.00	8.00
JT12	f	68.25	-	5	-	8.50	-
BP13	f	70.17	-	1	-	9.00	-
RW14	m	68.58	74.67	3	7	8.00	7.00
OC15	m	62.00	-	5	-	8.00	-
RD16	m	71.58	77.25	6	8	8.00	8.50
RL17	m	69.42	-	5	-	8.00	-
LL18	f	66.17	-	3	-	8.00	-
GM19	m	70.25	76.25	2	3	8.00	9.00
MM20	f	67.33	72.67	8	1	8.00	9.00
EP21	f	72.17	78.80	6	4	8.50	9.00
DF22	f	74.00	-	0	-	8.00	-
ES23	f	75.33	-	2	-	8.00	-
MF24	f	71.17	-	9	-	8.50	-
Mean		**67.87**	**73.39**	**4.46**	**4.91**	**8.15**	**8.23**
SD		**3.54**	**3.18**	**2.50**	**3.05**	**0.31**	**0.88**
Retained Mean		**67.11**	**73.39**	**4.64**	**4.91**	**8.05**	**8.23**
Retained SD		**3.37**	**3.18**	**2.34**	**3.05**	**0.15**	**0.88**

- Data not obtained.

As can be seen in Table 6.1, the mean age of the group (n = 11) at baseline was 67.11 years (SD = 3.37 years) and at follow-up was 73.39 years (SD = 3.18 years). The mean lapse in time between baseline and follow-up testing was 6.29 years (SD = 0.48 years). There were 6 females and 5 males in the group.

Daytime Sleepiness and Time in Bed –

EES scores and TIB did not change significantly from baseline to follow-up. Only slight increases in both were observed. These are presented in Table

6.1. However, all participants were found to satisfy the screening criteria as set out in section 2.1.1 at baseline and at follow-up.

6.2.2 Cognitive Testing

Cognitive tests were administered via the standardised procedures as set out in the Chapter 2 (*General Method:* see section 2.2). For the purpose of Part I tests found to be dominantly associated with the PFC were administered during follow-up testing. These were:

Executive Function Tests –

- Wisconsin Card Sorting Task (WCST)
- Verbal Fluency (VF)
- Tower of London (TOL)
- Delayed Serial Recall (DSR)

For purposes of comparison, control tests were administered at follow-up that have been found to be measures of 'global'/non-PFC specific cognitive function:

Control Tests –

- Psychomotor Vigilance Test (PVT)
- Fluid Intelligence (IQ)

6.2.3 Sleep EEG Recording

All participants, at baseline and at follow-up underwent sleep EEG recordings as described in detail in Chapter 2 (*General Method;* see section 2.3). In Part I quantification of EEG included:

- Spectral analysis of low frequency delta corresponding to the LPFC.

6.2.4 Data Analysis

Analyses reported in Part I were based on correlation methods, using Pearson correlation, or the non-parametric version; Spearman rank order correlations. Effect sizes were reported as *r.* Hypotheses were one-tailed (unless otherwise reported) guided by the observations of Anderson and Horne (2003) with the level of significance set at $p < 0.01$ level of acceptance (see section 2.4).

Outlying data was identified on the basis of criteria set out in *General Methods* (see section 2.4). As participant BF08 had been previously identified as an outlier for baseline LPFC 0.5 – 1 Hz delta in Study 3 (see section 5.3.2), associated values were removed from subsequent analyses involving baseline data to avoid data distortion.

6.3 Results I

The focus of Study 4 was to assess whether one can predict age-related change in frontal lobe ability using a known biomarker of frontal performance: low frequency delta (< 1Hz). Also observed was the stability of the interrelationship between these two indices, as found by Anderson and Horne (2003) previously.

6.3.1 EEG as a Predictor of Executive Function

Anderson and Horne (2003) ascertained a link between LPFC low frequency delta (< 1Hz) and executive function. An exploration was carried out to discover the extent to which baseline EEG (< 1Hz) isolated to the LPFC could be a marker for future (follow-up) executive function. Unless otherwise noted, all relationships were observed utilising Pearson's product moment correlations.

Means and standard deviations of executive function measures are summarised in Table 6.2. These include WCST, TOL and VF, as well as Delayed Serial Recall (DSR). Also presented are means and standard deviations of control measures.

Table 6.2: Follow-up Executive Function measures (WCST, TOL, VF and DSR) and control measures (IQ and PVT).

Ps	Sex	WCST	TOL	VF	DSR	PVT	IQ
AT03	m	2	21.91	10.8	20	303.74	94
TK07	f	4	32.37	10.6	24	299.37	96
BF08	m	3	70.00	9	22	381.95	81
YF09	f	2	34.21	7.4	24	341.13	100
JC10	f	7	21.15	*	21	335.13	94
JY11	f	8	58.57	*	18	294.40	96
RW14	m	2	49.75	*	28	302.57	88
RD16	m	4	28.67	*	30	301.24	117
GM19	m	2	17.34	7.8	19	295.42	140
MM20	f	5	59.84	7.8	12	286.25	106
EP21	f	6	29.06	4.2	12	338.88	88
Mean		**4.09**	**38.44**	**8.23**	**20.91**	**316.37**	**100.00**
SD		**2.17**	**18.01**	**2.24**	**5.70**	**29.10**	**16.36**

*VF based on n = 7 due to education attainment adjustments: see section 2.2.2.

Wisconsin Card Sorting Task Vs Prior Delta EEG–

The relationship between baseline 0.5 – 1 Hz delta in the LPFC and number of perseverative errors on the WCST at follow-up was explored. As demonstrated in Figure 6.1, no significant relationship was observed between the two [r = 0.05, n = 10, p = 0.89].

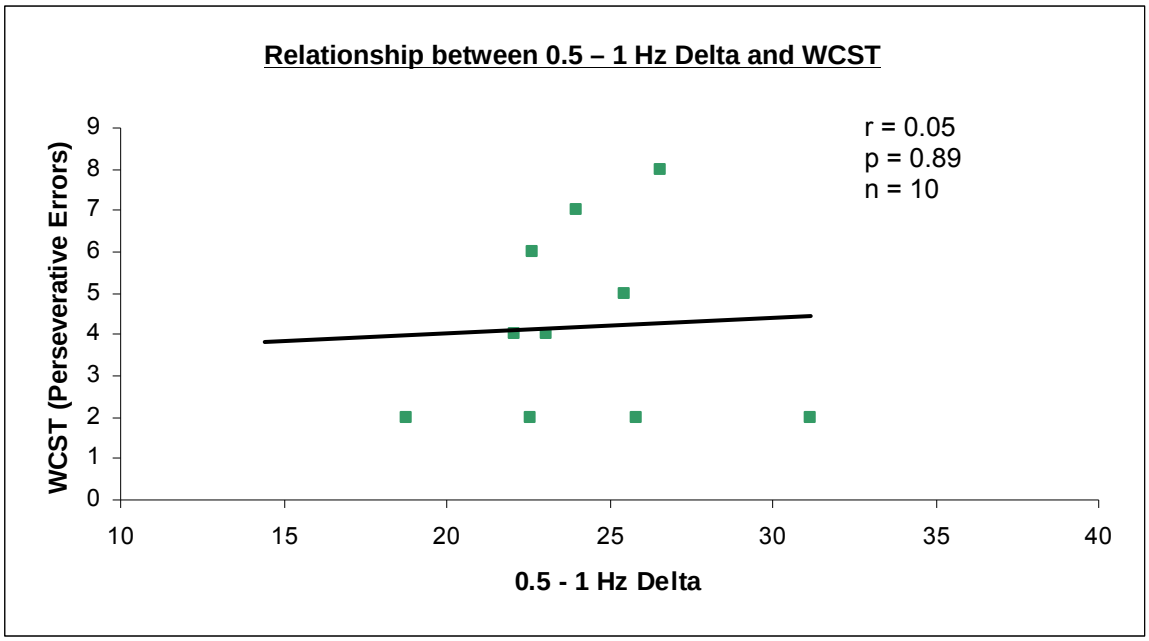

Figure 6.1: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC at baseline (2000) and perseverative errors on the WCST, at follow-up (2006).

Verbal Fluency Vs Prior Delta EEG –

Due to literature suggesting that VF may be influenced by previous educational attainment, correlations were based on individuals who had continued education or professional training past secondary school. The relationship between baseline 0.5 – 1 Hz delta in the LPFC and follow-up VF is presented in Figure 6.2. No significant relationship was observed [r = 0.31, n = 6, p = 0.19].

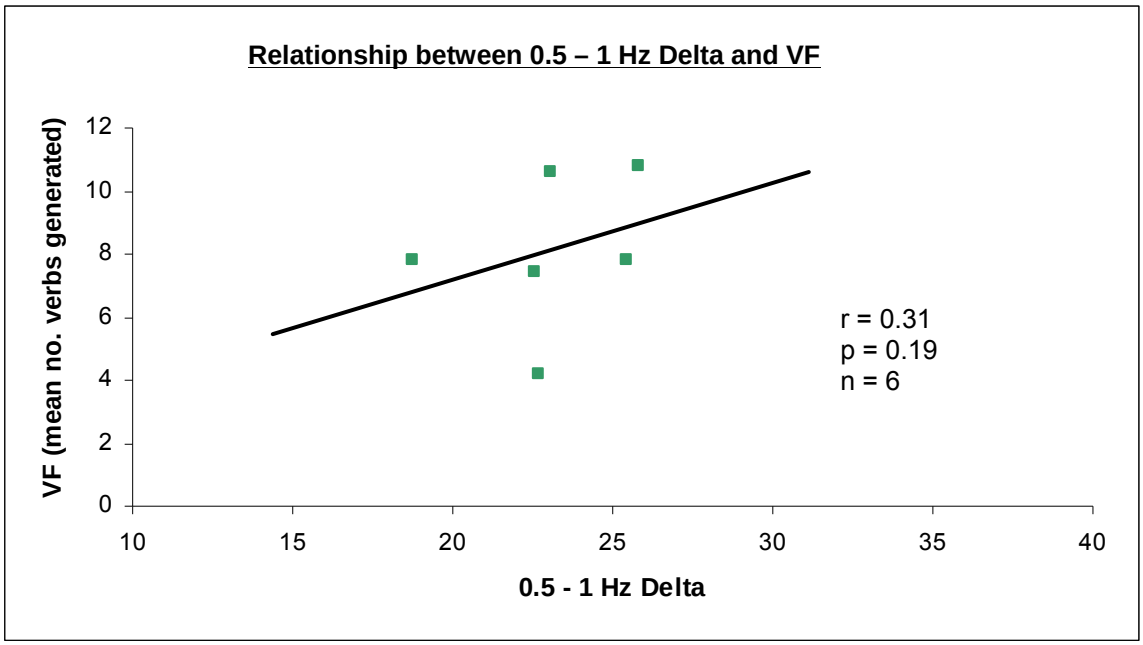

Figure 6.2: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC at baseline (2000) and number of verbs generated in VF at follow-up (2006).

Tower of London Vs Prior Delta EEG –

The relationship between baseline low frequency delta (0.5 – 1 Hz) in the LPFC and mean completion time on the TOL at follow-up was explored. A scatter-plot of this is presented in Figure 6.3. No significant relationship was observed here either [r = 0.64, n = 10, p = 0.05], although the association approached significance; this is in an unexpected direction though, with greater amounts of delta at baseline predicting decrements in performance on TOL at follow-up.

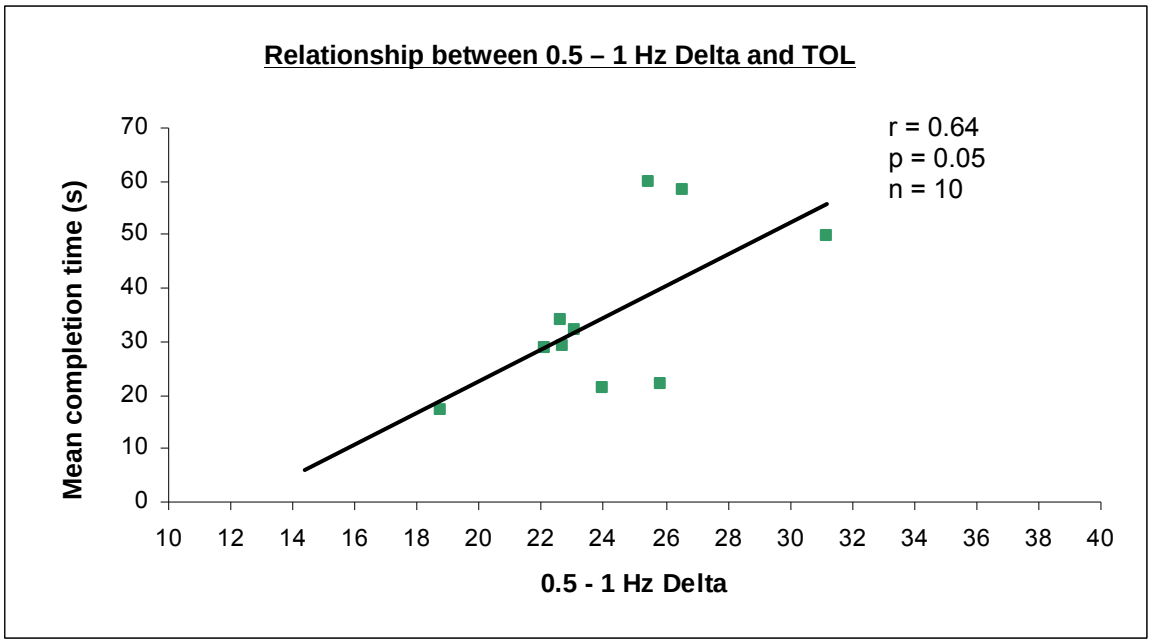

Figure 6.3: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LFPC at baseline (2000) and mean completion time (s) on the TOL, at follow-up (2006).

Delayed Serial Recall Vs Prior Delta EEG –

A scatter–plot exploring the relationship between baseline low frequency delta in the LPFC and number of nouns recalled on the DSR at follow-up are presented in Figure 6.4. No significant relationship was observed [r = 0.15, n = 10, p = 0.34].

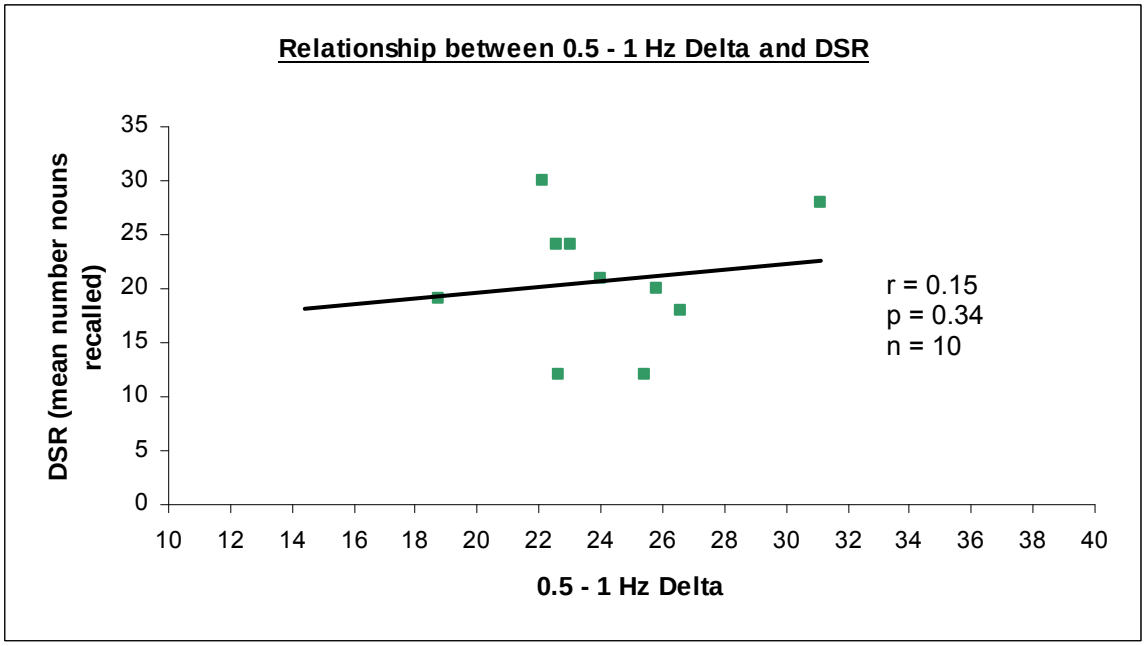

Figure 6.4: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC at baseline (2000) and mean number nouns recalled on DSR, at follow-up (2006).

Performance Vigilance Task Vs Prior Delta EEG –

The relationship between baseline low frequency delta in the LPFC and PVT reaction time at follow-up was explored using Spearman's rank order correlation. A scatter-plot of this is presented in Figure 6.5. No significant association was observed [r = -0.19, n = 10, p = 0.60].

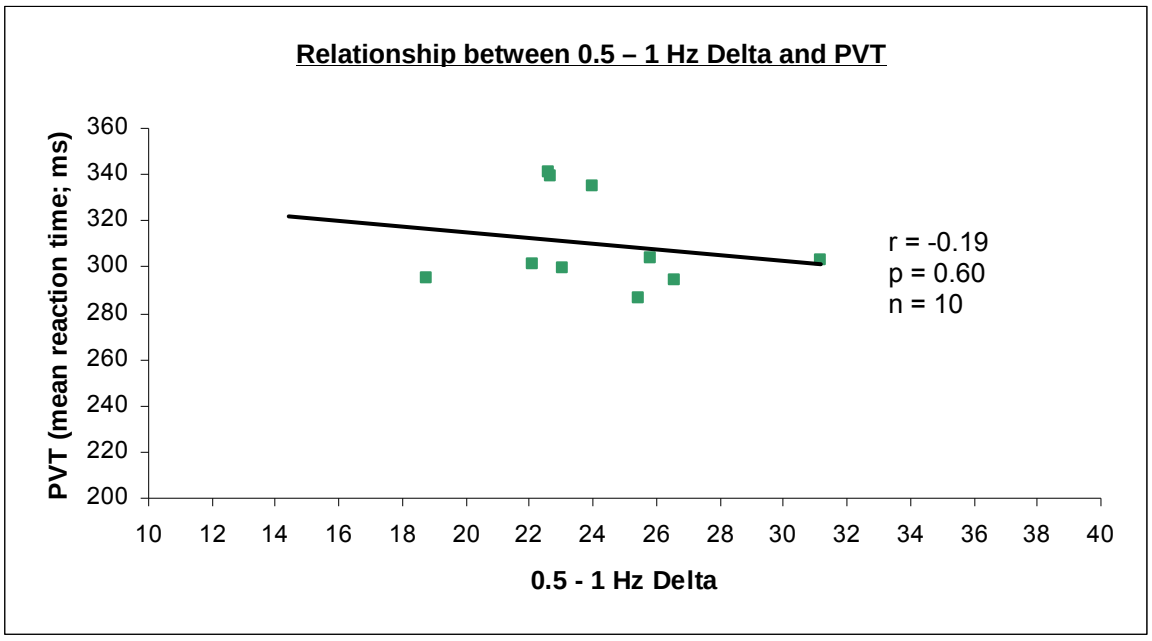

Figure 6.5: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC at baseline (2000) and mean reaction time on PVT, at follow-up (2006).

Fluid Intelligence Vs Prior Delta EEG –

The relationship between baseline low frequency delta (0.5 – 1 Hz) in the LPFC and fluid intelligence IQ at follow-up was explored. This is presented in Figure 6.6. A relationship was observed, that approached significance [r = -0.68, n = 10, p = 0.02]. This relationship was unexpected, firstly due to the lack of specificity of fluid intelligence to the PFC, and also because it suggests that greater percentages of low frequency delta are associated with lower IQ scores.

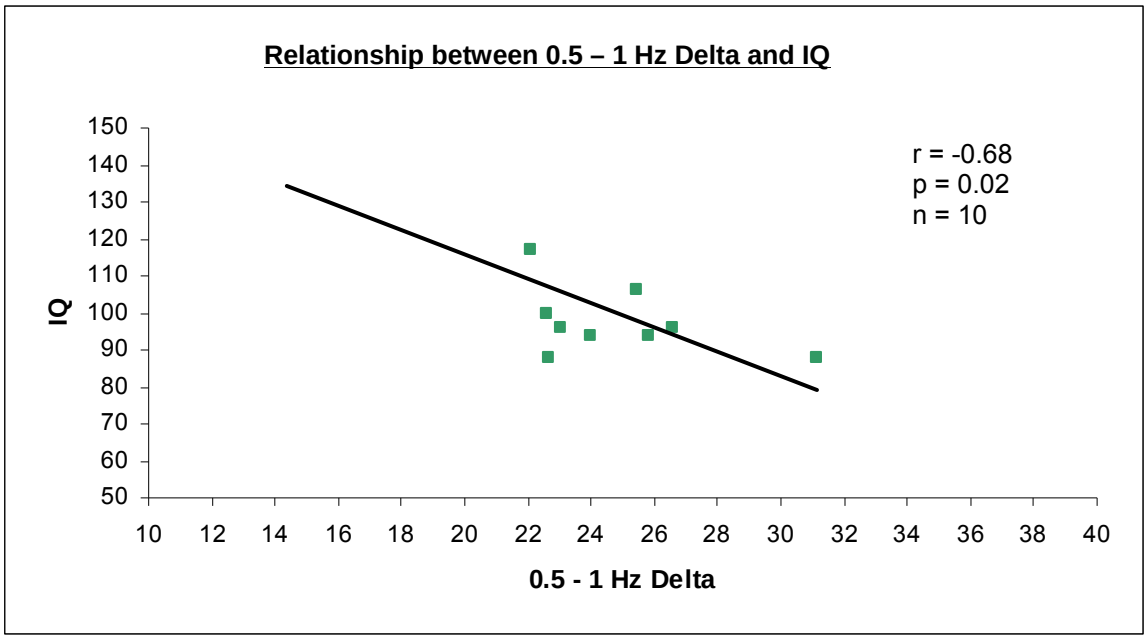

Figure 6.6: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC and fluid intelligence IQ at follow-up (2006).

6.3.2 EEG and Executive Function Relationship Stability

Another aim of Study 4: Part I was to ascertain the stability of the link found by Anderson and Horne (2003). Here, the relationship between follow-up low frequency delta in the LPFC and follow-up performance on executive function measures was explored. Again, 0.5 – 1 Hz was observed in the LPFC. Executive function and control measures were previously presented in Table 6.2. Unless otherwise noted, all relationships were observed utilising Pearson's product moment correlations.

Executive Function Vs < 1Hz EEG Activity –

At follow-up, 0.5 – 1 Hz delta in the LPFC was not found to significantly correlate with number of perseverative errors on the WCST. [r = -0.26, n = 11, p = 0.23], with mean completion time on the TOL, [r = -0.26, n = 11, p = 0.22], with number of verbs generated on the VF [r = 0.23, n = 7, p = 0.31], or number of nouns generated on the DSR [r = 0.06, n = 11, p = 0.42]. Therefore indicating that low frequency delta was not a predictor of performance on executive function measures.

Control Tests Vs < 1Hz EEG Activity –

As ascertained by Spearman's rank order correlation, no relationship was demonstrated between low frequency delta and PVT reaction time [r = -0.03, n = 11, p = 0.94]. Also, no significant relationship was noted between fluid intelligence IQ and low frequency (0.5 – 1 Hz) delta in the LPFC [r = -0.29, n = 11, p = 0.38].

6.4 Method II

6.4.1 Participant Characteristics

Study 4: Part II includes participants from the Longitudinal Design Cohort outlined in section 2.1.3. As outlined in that section, participants have been utilised in research reported elsewhere (Anderson & Horne, 2003) in which a low frequency delta – executive function link was established. In Study 4: Part I it was expected that this link would persist in the same cohort 6.29 years later. However, no significant links were observed. Due to the unexpected results found, analyses were completed in Part II in order to explore further whether the results obtained are likely to be genuine age-related changes or sampling issues. To do this, comparisons were made using baseline data only, between those individuals retained for follow-up testing (referred to as the 'retained' group from this point forward) and those that were not retained (referred to as the 'non-retained' group from this point forward). Columns in Table 6.3 that are shaded represent that follow-up data was not required for Study 4: Part II.

Table 6.3: Participant characteristics for Study 4 Part II. Shaded columns depict that follow-up data was not utilised.

		Age		ESS		TIB(hrs)	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**	**2000**	**2006**
BC01	f	64.00	-	3	-	8.00	-
RR02	f	67.08	-	6	-	8.00	-
*AT03	m	61.67	68.58	6	9	8.00	9.00
EM04	m	68.00	-	9	-	9.00	-
SS05	m	68.67	-	5	-	8.00	-
IK06	m	66.33	-	3	-	8.00	-
*TK07	f	64.92	71.17	8	6	8.00	9.00
*BF08	m	64.50	70.83	4	7	8.00	7.00
*YF09	f	63.33	69.92	4	7	8.00	7.00
*JC10	f	67.17	73.75	3	2	8.00	8.00
*JY11	f	66.67	73.42	1	0	8.00	8.00
JT12	f	68.25	-	5	-	8.50	-
BP13	f	70.17	-	1	-	9.00	-
*RW14	m	68.58	74.67	3	7	8.00	7.00
OC15	m	62.00	-	5	-	8.00	-
*RD16	m	71.58	77.25	6	8	8.00	8.50
RL17	m	69.42	-	5	-	8.00	-
LL18	f	66.17	-	3	-	8.00	-
*GM19	m	70.25	76.25	2	3	8.00	9.00
*MM20	f	67.33	72.67	8	1	8.00	9.00
*EP21	f	72.17	78.80	6	4	8.50	9.00
DF22	f	74.00	-	0	-	8.00	-
ES23	f	75.33	-	2	-	8.00	-
MF24	f	71.17	-	9	-	8.50	-
Mean		**67.87**	**73.39**	**4.46**	**4.91**	**8.15**	**8.23**
SD		**3.54**	**3.18**	**2.50**	**3.05**	**0.31**	**0.88**
Retained Mean		**67.11**	**73.39**	**4.64**	**4.91**	**8.05**	**8.23**
Retained SD		**3.37**	**3.18**	**2.34**	**3.05**	**0.15**	**0.88**
Non-Retained Mean		**68.51**	**-**	**4.31**	**-**	**8.23**	**-**
Non-Retained SD		**3.68**	**-**	**2.72**	**-**	**0.39**	**-**

- Data not obtained.
* Those participants retained for follow-up analyses ('retained' group).

The mean age of the 'retained' group (*n* = 11) was 67.11 years (*SD* = 3.37 years) and the mean age of the 'non-retained' group (*n* = 13) was 68.51 years (*SD* = 3.68 years). In the 'retained' group there were 6 females and 5 males and in the 'non-retained' group there were 8 females and 6 males.

Daytime Sleepiness and Time in Bed –

Self-reported sleepiness via ESS was slightly higher in the 'retained' group (mean = 4.64, *SD* = 2.34) compared with the 'non-retained' group (mean =

4.31, *SD* = 2.72). On the other hand, TIB was slightly higher in the 'retained' group (mean = 8.05hr, *SD* = 0.15hr) compared to the 'non-retained group' (mean = 8.23hr; *SD* = 0.39hr). However, these differences were marginal, and all participants met general health and sleep criteria set out in the *General Method* (section 2.1.1).

6.4.2 Cognitive Testing

Cognitive tests were administered via the standardised procedures as set out in the Chapter 2 (*General Method:* see section 2.2). Tests found to be dominantly associated with the PFC, were utilised. These were:

Executive Function Tests –

- Wisconsin Card Sorting Task (WCST)
- Verbal Fluency (VF)
- Tower of London (TOL)

For purposes of comparison, control tests were administered at baseline that have been found to be measures of 'global'/non-PFC specific cognitive function:

Control Tests –

- Psychomotor Vigilance Test (PVT)
- Fluid Intelligence (IQ)

6.4.3 Sleep EEG Recording

All participants, at baseline underwent sleep EEG recordings as described in detail in Chapter 2 (*General Method:* see section 2.3). In Part II quantification of EEG included:

- Spectral analysis of low frequency delta corresponding to the LPFC.

6.4.4 Data Analysis

Analyses based on correlation methods, utilised Pearson product-moment coefficient, or the non-parametric version: Spearman rank order correlations. Comparisons between group means were investigated using independent samples t-tests, or the non-parametric equivalent, Mann Whitney U test. Effect sizes were reported, in order to inform of magnitude of effect. These were eta squared (η^2), for independent t-tests, and as *r* for non-parametric and correlation methods.

Hypotheses were one-tailed (unless otherwise reported) guided by the observations of Anderson and Horne (2003) with the level of significance set at the $p < 0.01$ level of acceptance (see section 2.4). Equal variance was assumed between groups.

Outlying data was identified on the basis of criteria set out in *General Methods* (see section 2.4). As participant BF08 had been previously identified as an outlier for baseline TOL for Study 2 (see section 4.3.1) and baseline LPFC 0.5 – 1 Hz delta in Study 3 (see section 5.3.2), associated values were removed from subsequent analyses to avoid data distortion.

6.5 Results II

6.5.1 Sampling Issues: Relationship between Executive Function and Low Frequency Delta (Retained Vs Non-Retained) –

Wisconsin Card Sorting Task (WCST) –

Low frequency delta (0.5 – 1 Hz) in the LPFC was compared to number of perseverative errors on the WCST at baseline. A scatter-plot of this is presented in Figure 6.7. Data was split into those that were retained for follow-up analyses and those that were not (the non-retained group) to explore differences in correlation between the two samples.

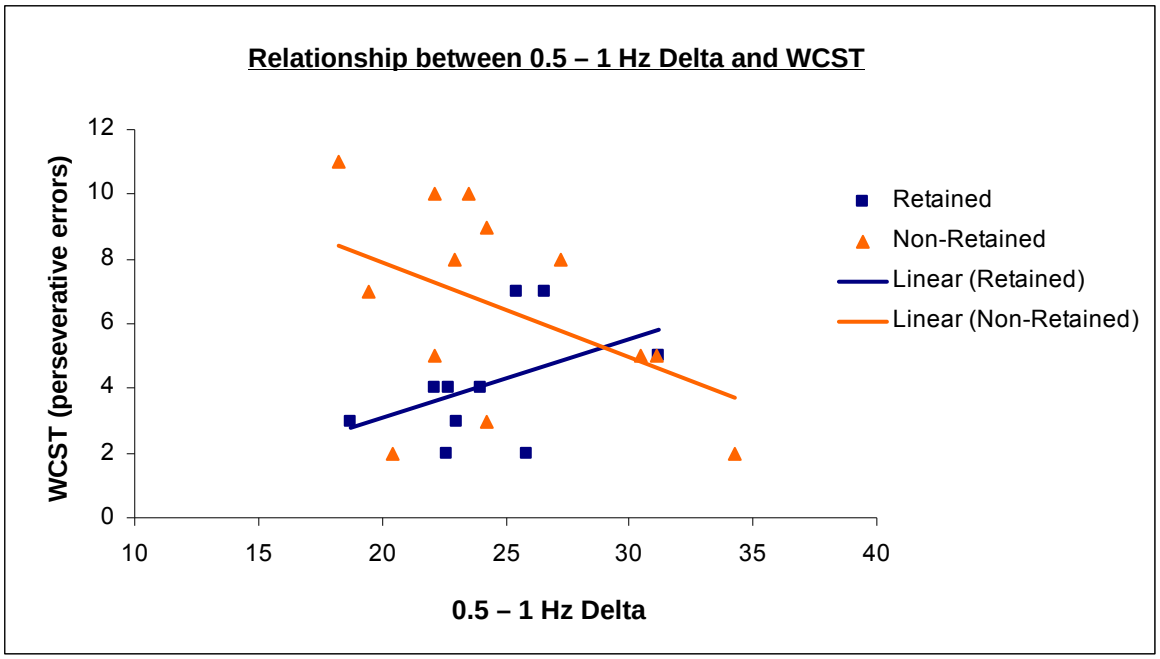

Figure 6.7: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC and perseverative errors on the WCST, at baseline (2000), with separate trendlines for retained and non-retained groups.

Non-Retained Group

For the non-retained group at baseline, the relationship between low frequency delta in the LPFC and number of perseverative errors, was negatively correlated as expected, in that the greater the percentage of delta, the better the performance [r = -0.46, n = 13, p = 0.06]. Although just below the acceptable level of significance, the relationship strength was moderate to large.

Retained Group

For the retained group, the relationship between low frequency delta in the LPFC and number of perseverative errors, was unexpectedly positively correlated [r = 0.46, n = 10, p = 0.19], although it did not reach significance.

- There appears to be a difference in the relationship between low frequency delta and WCST between the two groups, with the non-retained group demonstrating a negative correlation (approaching significance) between the two variables, and a non-significant positive correlation between the variables for the retained group.

Verbal Fluency (VF) –

Low frequency delta (0.5 – 1 Hz) in the LPFC was also compared to number of verbs generated on the VF task. A scatter-plot of this is presented in Figure 6.8. Trendlines are shown for those that were retained at follow-up and for those that were not ('non-retained' group).

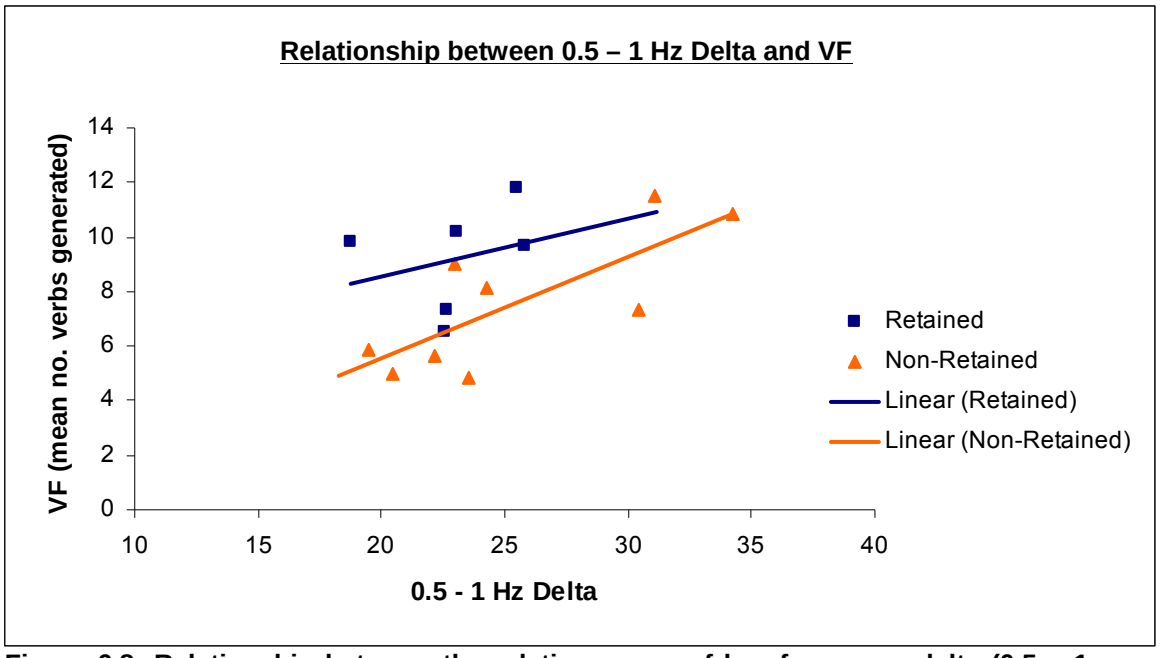

Figure 6.8: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC and number of verbs generated on the VF at baseline (2000), with separate trendlines for retained and non-retained groups.

Non-Retained Group

A positive correlation was found between low frequency delta and number of verbs generated on the VF task [$r = 0.77$, $n = 6$, $p < 0.01$]. This relationship was strong, and statistically significant, as would be expected from previous literature.

Retained Group

A positive correlation was also found between low frequency delta and number of verbs generated. This was not found to be statistically significant [$r = 0.28$, $n = 6$, $p = 0.29$].

- A significant relationship was found between low frequency delta in the LPFC and number of verbs generated, in that greater percentage of delta was associated with better performance on the VF task, for the non-retained group. A significant relationship was absent in the retained group.

Tower of London (TOL) –

Low frequency delta (0.5 – 1 Hz) in the LPFC was also compared to mean completion time on the TOL at baseline. A scatter-plot of this is presented in Figure 6.8. Trendlines are shown for those that were retained at follow-up and for those that were not ('non-retained' group).

Non-Retained Group

For the group not retained for follow-up analyses, as expected, there was a significant negative correlation between low frequency delta and mean completion time [$r = -0.73$, $n = 13$, $p < 0.01$].

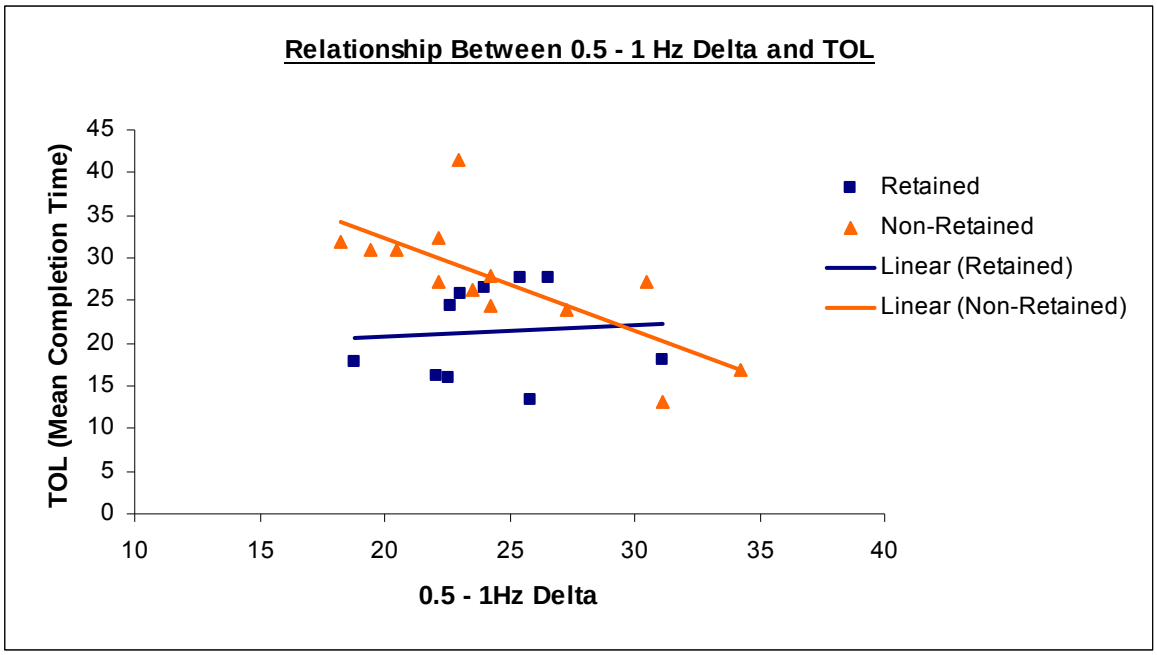

Figure 6.8: Relationship between the relative power of low frequency delta (0.5 – 1 Hz) in the LPFC and mean completion time (s) on the TOL, at baseline (2000), with separate trendlines for retained and non-retained groups.

Retained Group

For the retained group, no significant correlation was demonstrated at baseline between low frequency delta and mean completion time [r = 0.08, n = 10, p = 0.83].

- For the non-retained group, as expected, percentage of low frequency delta predicted performance on the TOL, in that greater percentage of delta was associated with better performance on the TOL. However, this relationship was absent in the retained group.

Control Tests –

As a control measure, low frequency delta (0.5 – 1 Hz) in the LPFC was compared to mean PVT reaction time and fluid intelligence IQ. Again, data was split between those that were retained and those that were not retained for follow-up analyses.

Non-Retained Group

No significant relationship was found in the non-retained group [r = 0.12, n = 13, p = 0.70] between PVT reaction time and low frequency delta in the

LPFC. As would be expected, no relationship was demonstrated between low frequency delta and fluid intelligence (IQ) either [r = -0.19, n = 11, p = 0.57].

Retained Group

Utilising Spearman's rank order correlation, no significant relationship was demonstrated between PVT reaction time and LPFC low frequency delta [r = -0.13, n = 10, p = 0.72] in the retained group. Furthermore, no significant relationship was found between low frequency delta and fluid intelligence in the retained group [r = -0.48, n = 10, p = 0.16].

Executive Function –

Means and standard deviations of executive function and control measures are presented in Table 6.4. Two-tailed (due to lack of guidance pertaining to direction of group difference in the literature) independent samples t-tests were utilised unless otherwise reported.

Table 6.4. Baseline (2000) executive function measures (WCST, TOL and WCST) and control measures (IQ and PVT), separated into those that were retained for follow-up analyses and those that were not.

Ps	Sex	WCST	TOL	VF*	PVT	IQ
Retained (n= 11)						
AT03	m	2	13.26	9.67	302.83	114
TK07	f	3	25.79	10.17	284.10	104
BF08	m	10	52.18	7.00	338.60	91
YF09	f	2	15.84	6.50	322.80	96
JC10	f	4	26.45	-	356.99	98
JY11	f	7	27.60	-	284.80	80
RW14	m	5	17.94	-	294.10	93
RD16	m	4	16.20	-	302.83	103
GM19	m	3	17.90	9.83	287.65	117
MM20	f	7	27.59	11.83	340.96	88
EP21	f	4	24.31	7.33	395.72	88
Mean		**4.64**	**24.10**	**8.90**	**319.22**	**97.45**
SD		**2.46**	**10.70**	**1.98**	**35.67**	**11.30**
Non-retained (n= 13)						
BC01	f	5	13.23	11.50	361.21	119
RR02	f	8	41.58	9.00	319.10	**
EM04	m	2	16.81	10.83	340.60	81
SS05	m	7	30.94	5.83	309.40	126
IK06	m	3	24.26	8.17	346.50	81
JT12	f	10	27.30	-	425.60	**
BP13	f	11	31.93	-	323.20	101
OC15	m	5	27.15	7.33	351.40	104
RL17	m	2	31.00	5.00	329.04	109
LL18	f	8	23.86	-	283.41	76
DF22	f	9	27.92	-	325.22	100
ES23	f	10	26.17	4.83	342.43	98
MF24	f	5	32.25	5.67	326.58	70
Mean		**6.54**	**27.26**	**7.57**	**337.21**	**96.82**
SD		**3.10**	**7.12**	**2.48**	**33.20**	**17.96**

*VF is based on a reduced sample size due to controlling for educational attainment (see section 2.2.2.
** data loss.
BF08 was found to be an outlier for TOL (see section 4.3.1) and so not included in the subsequent analyses.

WCST

The non-retained group incurred more perseverative errors than the retained group. This difference however, was not significant (p = 0.12) although the effect size was moderate–large (η^2 = 0.11).

Verbal Fluency

Mean number of verbs generated on VF was compared between the retained and the non-retained group. The retained group generated more verbs, in comparison to the non-retained group. However, this difference was not significant (p = 0.23), although the effect size was moderate (η^2 = 0.09).

TOL

The difference between the retained group and non-retained group at baseline on mean completion time was found to approach significance [$t(21) = -2.19$, p = 0.04, η^2 = 0.16], with the retained group exhibiting better performance on this measure.

Control Tests

There was no significant difference between groups on reaction time on the PVT, as ascertained using the non-parametric Mann-Whitney test (p = 0.16), with a small–medium effect size (r = 0.29). These results suggest that there doesn't appear to be a difference in the more 'global' reaction time measure between those that were retained and those that were not. Furthermore, the retained and non-retained groups were compared on fluid intelligence (IQ). No significant differences were found in the IQ of both groups (p = 0.92), and the effect size was small (η^2 = 0.05).

6.6 Discussion

PFC low frequency delta (< 1Hz) dominantly association with the PFC did not predict executive function 6.29 years later, as was hypothesised. Furthermore, although low frequency delta was found to be associated with cognition in healthy, older individuals (Anderson & Horne, 2003), this link was not apparent in follow-up analyses, as expected, in a subset of the original cohort.

It was plausible that baseline delta would predict follow-up performance, particularly as LPFC delta declines were found in Study 3 and also TOL declines were found in the same individuals in Study 2 after a period of only 6.29 years (Study 2). Although declines were not seen in the VF and WCST, it was suspected that changes in delta might precede changes in executive function, given that SWS has been proposed to support PFC function (see section 1.2).

Surprisingly, the delta-executive function link present in the study by Anderson and Horne (2003) had dissipated at follow-up in Part I. One conclusion might be that this is an ageing effect. In order to support or refute this, further exploration was carried out into potential sampling issues, in Part II. Further scrutiny of the results revealed that the retained group at follow-up may not have been reflective of the original cohort. It was found that at baseline, the non-retained group demonstrated strong relationships between LPFC low frequency delta and executive function measures; this was significant for TOL and VF, and approached significance for WCST. Conversely, these associations were absent at baseline in the retained group. Therefore, indicating that the link found by Anderson and Horne is not relevant to all healthy older individuals, and that the lack of link was unlikely to be due to ageing effects.

An important consideration in longitudinal designs is the possibility that the retained participants are not necessarily representative of the original baseline cohort. Rabbitt, Diggle, Holland and McInnes (2004) pointed out that less able participants tend to drop out of ageing studies earlier than others. An exploration into differences between those that were retained and those that were not retained, on executive function measures did not elicit any significant differences in the performance of the groups in Part II. However, effect sizes were moderate to large, with the retained group performing better than the non-retained group on all measures. Furthermore, the differences on the TOL was close to significance (p = 0.04). The retained group at baseline were an average of 5.97 seconds faster on the TOL, generated an average of 1.33 more words on the VF task

and had an average of 1.9 fewer perseverative errors on the WCST, in comparison to the non-retained group. Therefore, the retained group appear to moderately out–perform at baseline those that were not retained, particularly on TOL, which has been found to be the most sensitive of the executive function measures to ageing effects (i.e., Study 1 and Study 2).

These results might be explained by the implications of recent research in the area of 'successful ageing'. One major finding is that there appears to be a loss of localisation of function with ageing, particularly in high functioning older people. Localisation of function may be lost with age, perhaps due to compensatory mechanisms, e.g., transfer of function from compromised brain regions, to other healthier regions. This phenomenon has been reported in young healthy adults deprived of sleep (Drummond et al., 2000), following 35 hours of sleep loss, in which parietal lobe activation increased as a compensatory mechanism for a prevailing PFC. The extent to which this may occur in healthy ageing is unknown.

Furthermore, inability to lose this localisation of function may be detrimental to functioning. For example, language recovery in aphasic left hemispheric stroke patients was found to be more successful in those with greater bilateral brain activation (Cao, Vikingstad, George, Johnson, & Welch 1999). In addition, it has been observed that those older individuals that were the 'poorer' performers of tasks associated with the frontal lobes, showed brain activation of that more akin to that of a much younger group, whereas older individuals who were better performers, recruited other areas (Cabeza et al., 2002).

The retained group of the present chapter, although presented age-related declines in TOL performance in Study 2, performed better on the TOL at baseline than did the non-retained group; the latter incidentally showed greater cohesion between localised EEG and cognition. However, this does not exclude other extraneous factors that may influence the ability to continue participation (e.g., busy lives, illness, disinterest, etc). As data was not obtained from those who did not respond to the invitation to participate

at follow–up, we are unable to assess, beyond speculation, on reasons for non-participation.

Insufficient sample sizes in the retained group (*n* = 10) may explain lack of association between low frequency delta and executive function. This is unlikely to fully account for the findings though, as significant and strong relationships between low frequency delta and executive function measures were observed in only a marginally larger sample size for the non-retained group at baseline (*n* = 13). In addition, the relationships followed consistent and logical trends (e.g., increases in performance predicted increases in EEG power), which were not evident in the retained group.

6.7 Conclusion

- Baseline LPFC low frequency delta did not predict follow-up performance on executive function measures.

- The relationship between low frequency delta in the LPFC and executive functions reported by Anderson and Horne (2003) was no longer present in a sub-sample of the same cohort when re-assessed 6.29 years later.

- Lack of stability in the EEG-cognition link over 6.29 years was suspected to be due to cohort effects, rather than an ageing effect or due to a small sample size. This was because in the retained group (*n* = 10) at baseline, the EEG-cognition link was absent whereas it was evident for the non-retained group (*n* = 13).

Anderson and Horne (2003) established localised low frequency delta as a marker of executive function in an older group. Here, the novel approach of observing this link longitudinally was undertaken. Although stability of the marker at follow-up was not ascertained, nor baseline EEG as a predictor of future cognitive function, interesting results emerged indicating that the

biomarker observed by Anderson and Horne (2003) may not be relevant to all healthy, older individuals; individual differences may exist.

7 Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective

7.1 Introduction

Following on from Study 4, the purpose of Study 5 was to further address the question of whether localised EEG is a feasible marker of localised cognitive function. Aspects of SWA, namely relative percentage of power of low frequency delta has been associated with executive function performance in a health older group (Anderson and Horne, 2003); although stability of this marker over time could not be established in Study 4, nor could low frequency delta predict follow-up executive function performance.

Along with changes in executive function being found with advancing age (e.g., Ardila et al., 2000; Comptom et al., 1999; Davis & Klebe, 2001; Macpherson et al., 2002; Parkin & Walter, 1991; Robbins et al., 1998), selective changes with age have been found in SWA associated components. Kubicki et al (1989) reported declines with age in KC density, and Wauquier et al (1993) declines in KC amplitude; whilst selective declines have also been observed in spindle density (Feinberg et al., 1967), as well as amplitude and duration (Crowley et al., 2002; Feinberg et al., 1967).

Few studies have attempted to observe the link between localised EEG and cognition, together in the same individuals even though there is a rationale for this. Therefore the research presented in the present chapter is novel and exploratory. If the link observed between low frequency delta and cognitive function (Anderson & Horne, 2003) was due to the level of cortical deactivation concomitant to SWA (e.g., Hofle et al., 1997; Maquet et al., 1997) and associated benefits for cortical function, it would be suspected that spindle and KC activity would be associated with cognition also. Previous research has indicated that KCs and spindles are important in

driving SWA activity (e.g., De Gennaro, 2000a; Yamadori, 1971). Therefore, decrements with age, might have implications for the extent to which cortical deactivation mechanisms are able to take place during SWA.

The potential link between spindle density and cognitive function with age has been noted by Guazzelli et al. (1986), who suggested that older people whose spindle characteristics resemble that of young people are more likely to have preserved cognitive function and brain anatomy. Whilst Guazzelli et al. (1986) did not find a link between spindle density and cognition, they did not observe localised EEG and localised cognition. In Study 5, there will be an attempt to examine a potential link between KC and spindle density EEG localised to frontal channels (LPFC and RPFC), and cognition previously associated with these areas.

Whilst the relationship between localised PFC low frequency delta and PFC associated cognition is plausible, the literature suggests the important role of spindles and KC density in the production of low frequency delta. As such, it is important to explore this further, to see whether KCs and spindles share a common trajectory to cognitive ageing of the PFC. It would also be important to explore whether the relationship found between low frequency delta and cognition (Anderson & Horne, 2003), is mediated by KC density in the preceding stage 2, as has been implied in recent literature (De Gennaro et al., 2000a). This may be the process by which KC density is found to influence cognition.

7.1.1 Main Aims and Hypotheses

The aim of Study 5 is to ascertain whether a link between KC/spindle density and executive function is present in a healthy older group. Furthermore, due to the implication of KC density in the generation of delta (De Gennaro et al., 2000a), an interesting perspective would be to ascertain whether KC density partially mediates the relationship between low frequency delta and executive function (if KC density is controlled for, will

the relationship between low frequency delta and executive function weaken?). It was hypothesised that:

i) Spindle and KC density localised to the PFC, will predict performance of executive function measures, whereas spindle and KC density localised to other regions will not.

ii) LPFC KC density will be found to partially mediate the relationship found between LPFC low frequency delta and executive function: controlling for KC density will reduce the relationship between low frequency delta and executive function.

7.2 Method

This chapter explores the relationship between spindle and KC density, and cognitive functions associated with the PFC in a cohort of older individuals. This follows on from Study 4, which explored the relationship between low frequency delta and cognitive function.

7.2.1 Participant Characteristics

All participants in Study 5 were taken from the Longitudinal Design Cohort outlined in section 2.1.3. Participant characteristics are presented in Table 7.1. Although both baseline and follow-up data was obtained, the latter was not required for Study 5. The shaded rows in Table 7.1 depict this. The group utilised in the Study 5 (n = 24) had a mean age of 67.87 years (SD = 3.54 years). There were 14 females and 10 males.

Table 7.1: Participant characteristics for Study 5. Shaded rows depict that follow-up data was not utilised in Study 5.

		Age		ESS		TIB(hrs)	
Ps	**Sex**	**2000**	**2006**	**2000**	**2006**	**2000**	**2006**
BC01	f	64.00	-	3	-	8.00	-
RR02	f	67.08	-	6	-	8.00	-
AT03	m	61.67	68.58	6	9	8.00	9.00
EM04	m	68.00	-	9	-	9.00	-
SS05	m	68.67	-	5	-	8.00	-
IK06	m	66.33	-	3	-	8.00	-
TK07	f	64.92	71.17	8	6	8.00	9.00
BF08	m	64.50	70.83	4	7	8.00	7.00
YF09	f	63.33	69.92	4	7	8.00	7.00
JC10	f	67.17	73.75	3	2	8.00	8.00
JY11	f	66.67	73.42	1	0	8.00	8.00
JT12	f	68.25	-	5	-	8.50	-
BP13	f	70.17	-	1	-	9.00	-
RW14	m	68.58	74.67	3	7	8.00	7.00
OC15	m	62.00	-	5	-	8.00	-
RD16	m	71.58	77.25	6	8	8.00	8.50
RL17	m	69.42	-	5	-	8.00	-
LL18	f	66.17	-	3	-	8.00	-
GM19	m	70.25	76.25	2	3	8.00	9.00
MM20	f	67.33	72.67	8	1	8.00	9.00
EP21	f	72.17	78.80	6	4	8.50	9.00
DF22	f	74.00	-	0	-	8.00	-
ES23	f	75.33	-	2	-	8.00	-
MF24	f	71.17	-	9	-	8.50	-
Mean		**67.87**	**73.39**	**4.46**	**4.91**	**8.15**	**8.23**
SD		**3.54**	**3.18**	**2.50**	**3.05**	**0.31**	**0.88**

- Data not obtained.

Daytime Sleepiness and Time in Bed –

ESS scores (mean = 4.46, *SD* = 2.50) and TIB (mean = 8.15hr, *SD* = 0.31) for all participants fulfilled the criteria, as set out in section 2.1.1.

7.2.2 Cognitive Testing

Cognitive tests were administered via the standardised procedures as set out in the Chapter 2 (*General Method;* see section 2.2). Tests found to be dominantly associated with the PFC, were utilised. These were:

Executive Function Tests –

- Wisconsin Card Sorting Task (WCST)
- Verbal Fluency (VF)
- Tower of London (TOL)

For purposes of comparison, control tests were administered that have been found to be measures of 'global'/non-PFC specific cognitive function:

Control Tests –

- Psychomotor Vigilance Test (PVT)
- Fluid Intelligence (IQ)

7.2.3 Sleep EEG Recording

All participants underwent sleep EEG recordings as described in detail in Chapter 2 (*General Method:* see section 2.3). In Study 5, quantification of EEG included:

- Visual scoring of spindle and KC density corresponding to LPFC, RPFC, LOPC and ROPC.

This method was utilised in order to explore any relationship between PFC associated cognitive function and PFC localised spindle and KC density.

- Spectral analysis of low frequency delta corresponding to LPFC, RPFC, LOPC and ROPC.

Low frequency delta was utilised for the purpose of exploring the potential facilitating role of KCs in the relationship between low frequency delta and PFC cognitive function.

7.2.4 Data Analysis

Analyses were based on correlation methods, using Pearson product-moment coefficient, or the non-parametric version: Spearman rank order correlation. Group differences were observed utilising paired samples t-tests, or the non-parametric alternative (Wilcoxon signed ranks). Effect sizes were reported as *r.* Hypotheses were one-tailed (unless otherwise reported) guided by the observations of Anderson and Horne (2003) with the level of significance set at $p < 0.01$ level of acceptance (see section 2.4).

Outlying data was identified on the basis of criteria set out in *General Methods* (see section 2.4). As participant BF08 had been previously identified as an outlier for baseline LPFC 0.5 – 1 Hz delta in Study 3 (see section 5.3.2), associated values were removed from subsequent analyses to avoid data distortion.

After scrutinising scatter-plots, consistent extreme values were found for participants OC15 and MM20 for spindle density. EMO4 and GM19 were also found to be extreme values for VF, but only when correlated to KC

density localised to the LPFC and RPFC. However, these were not identified as being outliers on the criteria set out in *General Methods* (see section 2.4). For that reason, interpretations of data are based on results with the inclusion of all values. For comparison purposes, the results with extreme values removed are presented in footnotes, as suggested by Kruskal (1960).

7.3 Results

7.3.1 Regional Dominance

Spindle and KC density was calculated, for the first two stage 2 periods leading into SWS in frontal derivations (composite LPFC and RPFC) and occipital/parietal derivations (composite LOPC and ROPC) in all 24 participants. Number of spindles and KCs identified during these stage 2 periods was divided by the total duration (per minute). Spindle and KC density for composite frontal and occipital/parietal regions is presented in Figure 7.1 and Figure 7.2, respectively.

A one-tailed Wilcoxon signed ranks revealed that there was a difference between spindle density in the frontal and occipital/parietal regions, with there being a predominance in frontal regions and this approached significance [Z = -3.03, p = 0.03, r = 0.62][19]. A frontal predominance was found to be significant for KC density, using a paired samples t–test [t(23) = 2.58, p < 0.01, η2 = 0.22].

[19] Z = –2.68, p < 0.01, with the removal of participants 15 and 20.

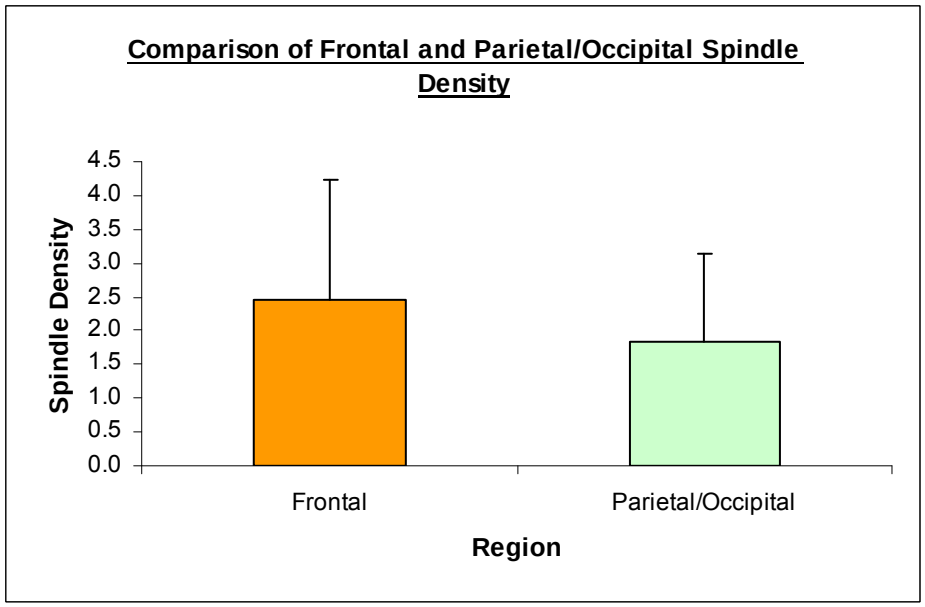

Figure 7.1: Spindle density in frontal (composite LPFC and RPFC) and parietal/occipital regions (composite LOPC and ROPC). Vertical lines represent standard deviations.

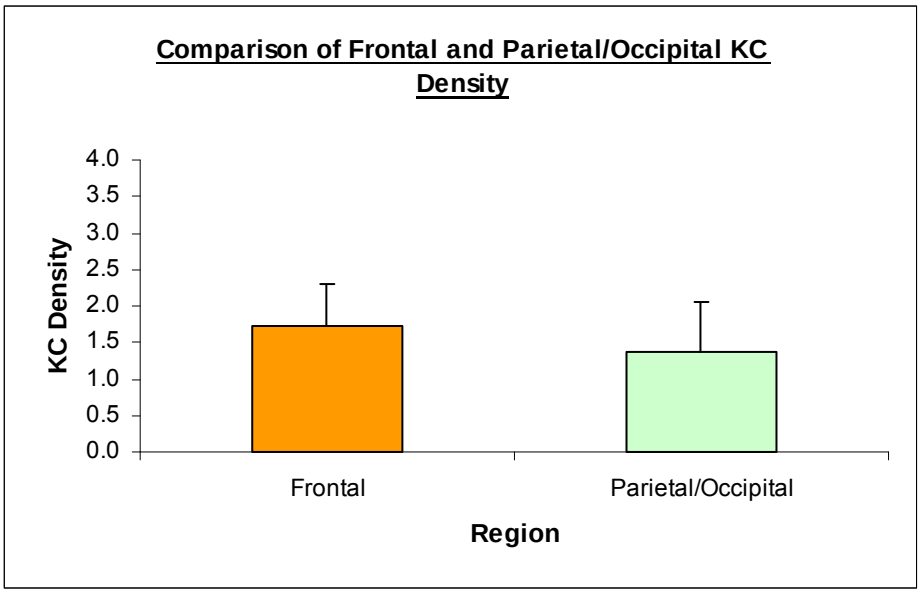

Figure 7.2: KC density in frontal (composite LPFC and RPFC) and parietal/occipital regions (composite LOPC and ROPC). Vertical lines represent standard deviations.

7.3.2 Relationship with Executive Function

Anderson and Horne (2003; data collected in 2000), found that daytime performance on the WCST, TOL and VF was selectively correlated to low frequency delta (0.5 – 1 Hz) in the PFC, in comparison to the parietal/occipital lobes: this was more pronounced in the LPFC. Analyses were conducted with a focus on spindle and KC density. As the

observations made in Study 5 were exploratory in nature, relationship with all four derivations was observed. Executive function measures are summarised in Table 7.2, which included WCST, TOL and VF, which have been previously associated with the PFC. Control measures were also included (PVT reaction time and fluid intelligence IQ).

Table 7.2: Executive Function measures (WCST, TOL, VF) and control measures (PVT and IQ).

Ps	Sex	WCST	TOL	VF*	PVT	IQ
BC01	f	5	13.23	11.50	361.21	119
RR02	f	8	41.58	9.00	319.10	**
AT03	m	2	13.26	9.67	302.83	114
EM04	m	2	16.81	10.83	340.60	81
SS05	m	7	30.94	5.83	309.40	126
IK06	m	3	24.26	8.17	346.50	81
TK07	f	3	25.79	10.17	284.10	104
BF08	m	10	52.18	7.00	338.60	91
YF09	f	2	15.84	6.50	322.80	96
JC10	f	4	26.45	-	356.99	98
JY11	f	7	27.60	-	284.80	80
JT12	f	10	27.30	-	425.60	**
BP13	f	11	31.93	-	323.20	101
RW14	m	5	17.94	-	294.10	93
OC15	m	5	27.15	7.33	351.40	104
RD16	m	4	16.20	-	302.83	103
RL17	m	2	31.00	5.00	329.04	109
LL18	f	8	23.86	-	283.41	76
GM19	m	3	17.90	9.83	287.65	117
MM20	f	7	27.59	11.83	340.96	88
EP21	f	4	24.31	7.33	395.72	88
DF22	f	9	27.92	-	325.22	100
ES23	f	10	26.17	4.83	342.43	98
MF24	f	5	32.25	5.67	326.58	70
Mean		**5.67**	**25.81**	**8.16**	**328.96**	**97.14**
SD		**2.93**	**8.88**	**2.31**	**34.82**	**14.65**

*Based on *n* = 16, due to educational attainment adjustments (see section 2.2.2).
**Data loss.

The relationship between spindle density and executive function was explored using the Spearman rank order correlation and the relationship between KC density and executive function using Pearson's product-moment coefficient. The coefficients for the former are presented in Table 7.3 and the latter in Table 7.4.

As can be observed in Table 7.3, medium effect sizes were found between spindle density in the RPFC and VF [r = 0.37, n = 16, p = 0.16], between

RPFC spindle density and WCST [r = -0.33, n = 24, p = 0.12], and between LOPC spindle density and VF [r = 0.36, n = 16, p = 0.17]. Although relationships were in the direction as expected, they were not significant. All other associations between spindle density (localised to the LPFC, RPFC, LOPC and ROPC) and performance measures (executive function measures and control tests) were non-significant (p > 0.18) with small effect sizes (r < 0.28).

Table 7.3: Correlation coefficients of the relationship between spindle density and performance measures (executive function and control tests).

			TOL (n = 24)	WCST (n = 24)	VF (n = 16)	PVT (n = 24)	IQ (n = 22)	
Spindle Density	LPFC (n = 24)	*Spearman's r*	-0.07	-0.22	0.25	0.13	0.09	
		Sig.	0.76	0.30	0.35	0.54	0.70	a)
	RPFC (n = 24)	*Spearman's r*	-0.17	-0.33	0.37	0.14	0.10	
		Sig.	0.42	0.12	0.16	0.52	0.66	b)
	LOPC (n = 24)	*Spearman's r*	0.22	0.12	0.36	0.00	0.10	
		Sig.	0.31	0.58	0.17	1.00	0.66	c)
	ROPC (n = 24)	*Spearman's r*	0.28	0.20	0.24	0.19	0.06	
		Sig.	0.18	0.34	0.60	0.37	0.80	d)
	LPFC (n = 22)	*Spearman's r*	-0.23	-0.30	0.13	0.02	0.12	
		Sig.	0.31	0.18	0.66	0.94	0.63	e)
	RPFC (n = 22)	*Spearman's r*	-0.30	-0.42	0.29	0.03	0.13	
		Sig.	0.18	0.05	0.32	0.91	0.58	f)
	LOPC (n = 22)	*Spearman's r*	0.14	0.09	0.28	-0.13	0.14	
		Sig.	0.56	0.70	0.34	0.56	0.56	g)
	ROPC (n = 22)	*Spearman's r*	0.20	0.19	0.12	0.09	0.09	
		Sig.	0.39	0.41	0.68	0.68	0.72	h)

Rows a-d) include coefficients without removal of outliers.
Rows e-h) include coefficients with the removal of participants OC15 and MM20 (extreme values for spindle density: all derivations).
VF is based on n = 16, due to controlling for educational attainment; see section 2.2.2.
IQ is based on n = 22, due to data loss.

As can be observed from Table 7.4, a relationship approaching significance was found between KC density localised to the LPFC and VF [r = 0.52, n = 16, p = 0.02]. A scatter-plot of this relationship is presented in Figure 7.3. Greater KC density in the LPFC appears to predict greater performance on the measure (number of verbs generated). All other associations between KC density (localised to the LPFC, RPFC, LOPC and ROPC) and performance measures (executive function and control tests) were not significant (p = 0.15), with small to moderate effect sizes (r = -0.22), although the relationships between LPFC KC density and executive function were in the direction as hypothesised.

Table 7.4: Correlation coefficients of the relationship between KC density and performance measures (executive function and control tests).

			TOL (n = 24)	WCST (n = 24)	VF (n = 16)	PVT (n = 24)	IQ (n = 22)
KC Density	LPFC (n = 24)	*Pearson's r*	-0.18	-0.22	0.52	0.18	-0.03
		Sig.	0.21	0.15	0.02	0.20	0.45
	RPFC (n = 24)	*Pearson's r*	-0.29	-0.22	0.24	0.17	0.15
		Sig.	0.09	0.15	0.18	0.22	0.25
	LOPC (n = 24)	*Pearson's r*	-0.22	0.05	0.16	-0.02	0.20
		Sig.	0.15	0.40	0.28	0.47	0.19
	ROPC (n = 24)	*Pearson's r*	-0.14	0.03	0.16	-0.01	0.17
		Sig.	0.25	0.45	0.27	0.49	0.22

Scatter-Plots revealed participants EM04 and GM19 as extreme values when VF was compared to LPFC/RPFC[20].
VF is based on *n* = 16, due to controlling for educational attainment; see section 2.2.2.
IQ is based on *n* = 22, due to data loss.

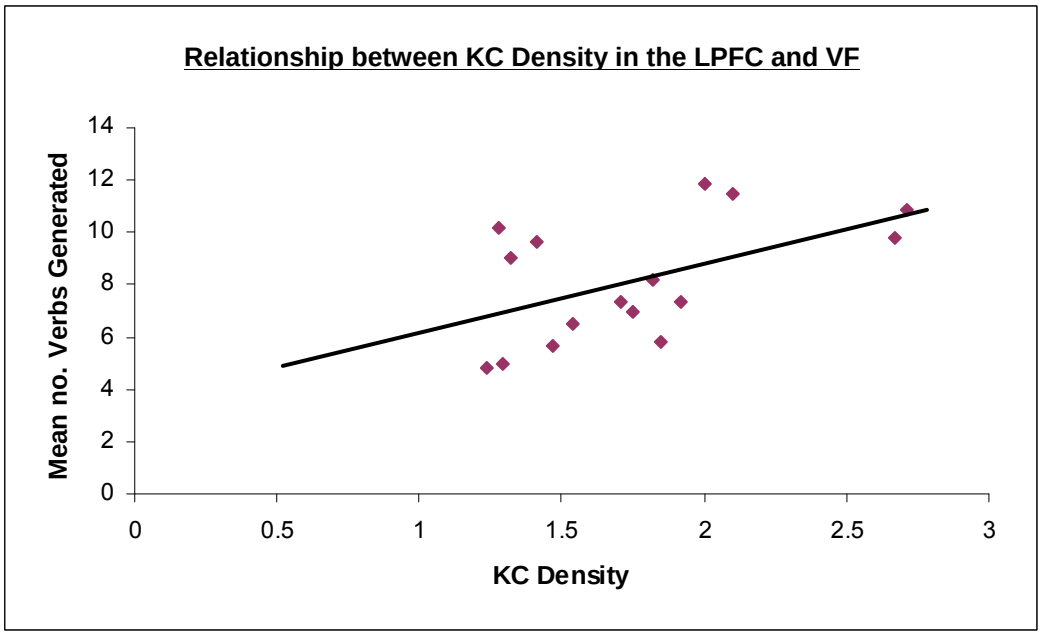

Figure 7.3: The relationship between KC density in the LPFC and mean number of verbs generated on the VF task.

Facilitation of Low frequency Delta –

Anderson and Horne (2003) demonstrated a link between LPFC low frequency delta (0.5 – 1 Hz) and executive function. To explore whether the small associations observed between KC density and executive function in the present study were due to a facilitating role of KC activity in the production of low frequency delta (e.g., as posited by De Gennaro et al., 2000a) partial correlations were conducted (Pearson product-moment

[20] *r*= 0.42, *n*= 14, *p* = 0.07 when outliers removed (VF and LPFC); *r*= –0.03, *n*= 14, *p* = 0.46 when outliers removed (VF and RPFC).

coefficient) exploring the relationship between low frequency delta localised to the LPFC and executive function, whilst controlling for LPFC KC density [21]. For example, does KC partially mediate the relationship between low frequency delta and executive function?

The association between relative percentage of power of low frequency delta in the LPFC (mean = 24.04, *SD* = 4.54) and executive function was explored. There was a positive but non-significant relationship between low frequency delta in the LPFC and WCST [r = -0.31, n = 24, p = 0.07]. Controlling for KC density reduced this relationship to a small degree [r = -0.28, n = 24, p = 0.10]. A stronger relationship was found between LPFC low frequency delta and TOL [r = -0.58, n = 24, $p < 0.005$]. This relationship reduced slightly but remained significant, after controlling for KC density [r = -0.57, n = 24, $p < 0.005$]. The relationship between low frequency delta and VF [r = 0.50, n = 16, $p < 0.03$] was slightly reduced [r = 0.49, n = 16, p = 0.03].

The results suggest that the relationship previously observed between low frequency delta in the LFPC and frontally associated executive function measures is not mediated to a substantial degree by KC density.

7.4 Discussion

KC density, nor spindle density localised to all observed regions (LPFC, RPFC, LOPC, ROPC) reliably predicted performance on executive function measures. This was contrary to the hypothesis, as a link was expected to be found between executive function and KC/spindle density in the PFC.

Lack of significant relationships between KC/spindle density and executive function was surprising given that a dominance was found in the frontal regions in comparison to the parietal/occipital regions in these associated

[21] These results varied slightly to those reported in the Anderson and Horne (2003) paper due to differences between scorers.

SWA phenomena (although the anterior dominance found in spindle density did not reach significance). This has important implications for the potential necessity of these aspects of SWA in the frontal lobes in cortical deactivation processes (Hofle et al., 1997; Czisch et al., 2004).

Small-medium effect sizes were found between KC/spindle density and executive function. However, these associations were not strong enough to infer a reciprocal relationship between the two indices. The strongest relationship was observed between VF and KC density in the LPFC. However, this must be interpreted with caution due to the large number of statistical analyses carried out. However, the consistency in these small associations could imply that there is some indirect link. Furthermore, although there has been an indication that KCs are a facilitating factor in SWA (De Gennaro et al., 2000a) these were not found to mediate the relationship between low frequency delta and executive function to any great extent, in Study 5.

It was surprising that KC and spindle density was not found to be a marker of localised cognitive ability, as the strength of relationship between LPFC low frequency delta and executive function was strong and significant in the same cohort (Anderson & Horne, 2003). One perspective might be that they reflect more general thalamo-cortical processes involved in sleep homeostasis, rather than that of localised function (as posited by Crowley et al., 2002), whereas low frequency delta may be more reflective of localised processes within the neocortex. This is supported by observations in the anesthetised cat of slow oscillations (that are thought to be akin to low frequency delta in the human), being generated by the cortex itself; they were present after the removal of the thalamus (Steriade, Nuñez et al., 1993).

Lack of significant correlation between spindles and performance on executive function measures may have been due to the spindle inclusion criteria being too stringent. For example, Feinberg et al. (1967) have found spindling in older adults (65-96 years; mean = 77.7 years) as slow as 8 Hz,

which in the present study was overlooked, as the frequency range included was 11 – 16 Hz. Furthermore, although visual scoring is thought to be the most appropriate method of scoring spindle as well as KC density, the atypical morphology of spindles and KCs with increasing age poses a greater challenge with regards to accurate identification. Therefore, there may have been a failure to detect all spindles and KCs.

7.5 Conclusion

- A frontal dominance was found in KC and spindle density (although the latter was found to approach significance).

- No significant relationships were found between KC and spindle density (in the LPFC, RPFC, LOPC and ROPC), and executive function.

- The relationship established between low frequency delta and executive function was not found to be significantly mediated by KC density.

In conclusion, although a dominance was found in KC and spindle density in anterior regions, these localised phenomena were not reliably implicated in executive function ability. KC and spindle density are not more effective in predicting frontal cognitive function than low frequency delta in an older sample.

8 General Discussion

8.1 Overview

The overall theme of this thesis was underpinned by the assumption that:

> *The PFC undergoes selective age-related declines, and that functions associated with it (i.e. cognitive function and SWA) follow a similar trajectory of decline due to localisation of function.*

Age-related changes have been noted in aspects of cognitive function associated with the PFC and SWA localised to the PFC (see sections 1.3 and 1.4), dominantly utilising cross-sectional techniques. Although appearing to undergo similar declines with age, few studies have attempted to link the two domains in the same individuals, although doing so could be potentially rewarding in revealing more about the role of SWA in cognitive function and in establishing SWA as a clinical marker of cognitive ageing. Furthermore, little is know about the effects of ageing on cognition associated with the PFC beyond executive function. The following research questions were addressed in the present thesis:

1. Are social cognitive function measures found to undergo the same age-related declines, as found in executive function?
2. Are longitudinal age-related declines found in executive function?
3. Are longitudinal age-related declines found in SWA and associated phenomena? Are these greater in the PFC, in comparison to other regions of the cortex?
4. Can the link established by Anderson and Horne (2003) remain stable in follow-up analyses? Furthermore, can past (baseline) EEG predict future (follow-up) executive function?
5. Can PFC localised KC and spindle density predict executive function in an older sample?

Table 8.1 outlines hypotheses pertaining to each study contributing to this thesis, as well as main findings.

Table 8.1: Main hypotheses and findings for Study 1, 2, 3, 4, & 5.

	Hypotheses	**Main Findings**
Ch 3: Study 1: Cross-Sectional Age-Related Changes in Cognitive Function: A PFC Focus	An older group will be less successful in the correct identification of emotional stimuli via facial expression and emotional prosody, than a young group. These age differences will be more substantial when the stimuli are incongruent.	Ekman 60 Faces: The older group recognised significantly fewer fear stimuli. No significant differences were found on the recognition of happiness, surprise, disgust, anger and sadness.
		Emotional Prosody: The older group recognised significantly fewer sadness, fear, happiness, and anger stimuli. These effects were amplified when stimuli was incongruent. No significant differences were found on the recognition of surprise and neutral.
	Age differences will be found in response inhibition with an older group having greater difficulty in ignoring distracter stimuli. Furthermore, this difference will be more substantial when the stimuli are emotive in content, compared to neutral.	Simple Go/No-go: There were no differences in the hit rate of distracter 'No-go' stimuli, although the older group were significantly more accurate in their hit rate in response to target 'Go' stimuli. The older group furthermore took longer to respond to target 'Go' and distracter 'No-go' stimuli, compared to the young group.
		Affect Go/No-go: When stimuli had neutral or emotive connotations there were no differences between groups in the hit rate of distracter 'No-go' or target 'Go' stimuli. With the exception of affect target 'Go' stimuli, the older group took significantly longer to respond to all types of stimuli.

	Hypotheses	Main Findings
Ch 4: Study 2: Longitudinal Age-Related Changes in Cognitive Function: A PFC Focus	Decrements in performance on executive function measures (WCST, TOL and VF) will be found in an older cohort over a period of 6.29 years.	Age-related increases were found from baseline to follow-up in mean completion time of TOL task, indicating a decrement in performance in this measure over a period of 6.29 years.
		No difference over time was found for number of verbs generated on the VF task and number of perseverative errors incurred on the WCST.
		Performance on non-PFC specific tasks (fluid intelligence IQ and PVT reaction time) remained stable over time.
Ch 5: Study 3: Age-Related Changes in PFC Sleep EEG	Age-related declines will be found in low frequency delta, KC density, and spindle density. These declines will be more pronounced in EEG localised to the PFC.	Significant declines were found in low frequency delta (0.5 – 1hz) in the LPFC region. Delta power (0.5 – 1Hz) in the RPFC, LOPC or ROPC showed no significant change over time. Spindle density and KC density in all observed derivations remained stable over time.
		Low frequency delta (0.5 – 1Hz) and spindle density demonstrated a similar frontal-occipital/parietal gradient of dominance which remained stable over time (although this only approached significance for low frequency delta). No frontal dominance was found for KC density, which remained stable from baseline to follow-up.

	Hypotheses	Main Findings
Ch 6: Study 4: Links between Sleep EEG and Cognitive Function Revisited	Past (baseline) low frequency delta localised to the LPFC will predict future (follow-up) performance of executive function measures in a healthy, older sample.	Baseline low frequency delta did not predict follow-up performance on PFC executive function measures.
	The link between LPFC low frequency delta and executive function as ascertained by Anderson and Horne (2003) will be present in follow-up analyses.	The relationship between low frequency delta in the LPFC and executive functions reported by Anderson and Horne (2003) was no longer present in a sub-sample of the same cohort when re-assessed 6.29 years later.
		Lack of stability in the EEG-cognition link over 6.29 years was suspected to be due to cohort effects, rather than an ageing effect or due to a small sample size. This was because in the retained group at baseline, the EEG-cognition link was absent whereas it was evident for the non-retained group.
Ch 7: Study 5: Links between Sleep EEG and Cognitive Function: A New Perspective	Spindle density and KC density localised to the PFC, will predict performance of executive function measures.	No significant relationships were found between KC density/ spindle density (in the LPFC, RPFC, LOPC and ROPC) and executive function.
	LPFC KC density will be found to partially mediate the relationship found between LPFC low frequency delta and executive function.	The relationship established between low frequency delta and executive function was not found to be significantly mediated by KC density.

8.2 Interpretation of Findings

As can be seen from Table 8.1, age-related differences were found in aspects of social cognition in Study 1. Results were mixed however, in that some emotions revealed age-differences, whereas other didn't (this was true for identification of emotion from facial expression, as well as from prosody). This high-lighted that due to various emotions potentially tapping into different brain regions, that in the context of cognitive ageing, each emotion should be analysed separately, rather than composite scores. Also revealed were the challenges of observing response inhibition in young compared to older counterparts; as both of the Go/No-go paradigms (despite the implication of these measures in PFC function) revealed no age differences. This was potentially due to differences in intentional response times between groups, and speculated differences in motivation (Rabbitt, 1988).

One of the main strengths of the thesis comes from the combination of cross-sectional and longitudinal observations. The differences in executive functions between the young group (mean age 22.25 years) compared to the older group (mean age 71.5 years) of Study 1 paralleled that of the changes in executive function in an older group from baseline (mean age 67.11 years) to follow-up (mean age 73.39 years) in Study 2. For example, the studies indicated that the TOL was the only measure to undergo age-related changes, and that VF remained intact (Study 2 additionally observed stability in WCST). Therefore, the studies were able to counteract weakness in the respective techniques. This however wasn't the purpose of the cross-sectional observation of executive function; the purpose was to cross-correlate novel measures of social cognition (e.g., Emotional Prosody and Go/No-go) with more established measures of frontal lobe function (e.g., TOL and VF). However, the results of Study 1 and Study 2 revealed differences in sensitivity of these measures when detecting cognitive ageing.

Results of Study 3, demonstrated that, pertaining to low frequency delta, the left hemisphere was more vulnerable to declines with age, longitudinally (although the LPFC was the only derivation in which this change was significant). This was in the presence of stability in sleep architecture (e.g., percentages of stage 1, stage 2, stage 3/4 and REM). These results would appear to be supportive of the view that 'SWA is for the cortex', considering that executive functions (i.e. TOL) have also been found to undergo age-related changes in the same individuals (Study 2), and that executive functions have been implicated in the PFC, particularly in the left hemisphere (e.g., Glosser & Goodglass, 1990; Goldstein et al., 2004; Ravnkilde, et al., 2002; Rezai, et al., 1993).

However, links between low frequency delta and executive function could not be established in Study 4, Part I; baseline low frequency delta power did not predict follow-up executive function, nor did the delta–executive function link seen by Anderson and Horne (2003) persist at follow-up. Furthermore, results from Study 4, Part II indicated that the link between the two indices was not present at baseline when considering just those individuals retained. This raises the question of why the results that were found did not concur with those of Anderson and Horne (2003)? Data collection and processing techniques were standardised in the present thesis to the ones employed by Anderson and Horne. It could be argued that subtle differences are present in older adults that might account for the degree in which localised EEG is predictive of cognitive function. Some suggest that localisation of function diminishes with age in some individuals and that successful cognition ageing is reliant on this change (Cabeza et al., 2002). Therefore, the extent to which low frequency delta and executive function measures link could be predictive of successful ageing. Unfortunately, this was beyond the scope of the present thesis; however, results from Study 4, Part II were suggestive that the sub-group which demonstrated consistent links between LPFC low frequency delta and executive function were less successful in executive function ability, in comparison to the other group that did not present this link.

An exploration into the potential of spindle and KC density being utilised as markers of cognitive decline failed to yield consistent associations (across frontal and occipital/parietal regions) with executive function. Therefore, indicating that low frequency delta is more relevant as a mirror to cognitive function. It was suggested that KC and spindle activity may be more reflective of general thalamo-cortical processes (e.g , Crowley et al., 2002) rather than localised cortical function; whereas low frequency delta has been indicated as being generated by the cortex itself (Steriade, Nuñez et al., 1993), and may be more reflective of localised function.

8.3 Experimental design

The opportunity to observe longitudinal changes in EEG and cognitive function in a healthy older sample is a rarity, and adds to it many benefits largely to do with minimisation of variation between groups and control of important influencing factors such as education, cohort effects and socioeconomic status. However, the main limitations of the studies reported in this thesis arise from this design. Using a repeated measures design meant that there may have been an overrepresentation of the highest performing older people at follow-up. Hedden and Gabrieli, (2004) suggested that this would be especially true for studies placing high demands on participants, such as attending testing sessions at a university. This however, may not be relevant to the studies reported in this thesis as initial stages of recruitment were carried out in the homes of participants, and the option of home-testing for cognitive measures was considered as being an option for those individuals with difficulty attending the university (although this was not found to be the case for any individuals retained at follow-up). However, it is acknowledged here, that due to the homogeneity of the older groups reported in this thesis, that the extent of generalisability is limited to high functioning, ‘healthy’ older adults.

Ultimately, the group at follow-up would have been likely to become more homogenised than the original cohort as observed by Anderson and Horne

(2003). Indeed, differences in the extent to which low frequency delta could be used as a marker of cognitive decline were different in the retained participants than in the non-retained participants (both at baseline) in Study 4, Part II, despite similarities in sample sizes. This unfortunately did not permit any interpretation of the test-retest reliability of the findings of Anderson and Horne (2003), which was one of the aims of this thesis.

Another contentious issue regarding the longitudinal method employed in Study 2, Study 3, and Study 4, is the question of whether lack of statistical significance was due to: i) insufficient sample size, ii) too short a period of time between baseline and follow-up testing to detect an ageing effect, or iii) a genuine lack of effect. The cross-sectional findings of Study 1 regarding ageing effects on executive function appear to allay some of the concerns regarding the small sample size of Study 2, as results concurred regarding TOL and VF. Furthermore, the results of Study 4, Part II revealed that consistently significant and strong relationships could be found in a small sample size (e.g., in the 'non-retained' group) between low frequency delta and executive function. Furthermore, the small effect sizes, both at baseline and follow-up in the retained group, indicate that it was likely that the null hypothesis was correctly accepted (as a large effect size might have indicated that greater power was required to achieve significance).

Although there appeared to be enough power to detect differences between low frequency delta from baseline to follow-up, the lack of significant changes in KC density and spindle density is a concern (Study 3). Age-related changes have been established in spindle (Crowley et al., 2002; Guazzelli et al. 1986) and KC parameters with increasing age (Kubicki et al., 1989; Wauquier, 1993). The small sample size (although again, effect sizes were small), preclude any clear interpretation of the results. Unfortunately, an increase in sample size to establish this was not an option given the longitudinal design. However, the results in themselves are interesting enough to justify a larger scale future investigation.

8.4 Tests of Cognitive Function

One of the main assumptions of the present thesis was that executive function and social cognition tests were indicators of PFC function. Therefore, stringent control and standardisation of task administration was crucial. All tests were consequently kept short, with easy to follow instructions and minimal practice required. This was vital, in order to maintain the novelty of the tasks (thus, ensuring maximal PFC orientation; e.g., Rabbitt, 1977). This in addition, meant that motivation was maintained throughout the testing procedure. Although little practice was given, no participants reported difficulty with understanding the premise of any of the tasks.

It was considered that there may have been differences between the young and older group in difficulties associated with completing the tasks. One main concern was differences in computer usage. Older adults report less computer usage than younger adults (Czaja et al., 2006). Where possible, the use of computers in task administration was avoided. For example, physical versions of the TOL (modelled out of wood) and WCST (set of cards) were utilised, even though computerised versions of the tests are becoming commonplace. This was unavoidable for some tests, such as PVT, Go/No-go and Ekman 60 Faces. In these instances, execution of the task was kept as simple as possible (e.g., a single button press response), in order to minimise any group differences caused by experience of computer usage.

Another issue to consider was the extent to which 'PFC measures' were subject to contamination. It is acknowledged here, that no one executive function or social cognition measure is subserved entirely by the PFC; all inevitably operate on other cognitive processes involving other brain structures. This was confirmed by a general lack of strong association between the measures in Study 1 and Study 2. This is mirrored in the literature, in which executive functions tend to exhibit small to moderate relationships to one another (usually $r = 0.40$ or less; Miyake et al., 2000).

However, although there was a general lack of cohesion between PFC measures (Study 1 and Study 2); this does not necessitate that they are not reliable markers of PFC function. Anderson and Horne (2003) demonstrated relationships between PFC SWA and all executive function tests utilised (TOL, WCST and VF).

One of the strengths of the research reported in this thesis is that tasks that were selected were done so based on rigorous evidence implicating the PFC in these tasks. Patient lesion studies have been found to be important in predicting the effects of compromised PFC function on specified cognitive tasks, whereas imaging studies can locate regional activity present during the completion of these same cognitive tasks. The use of both types of evidence has been crucial in balancing out the weaknesses inherent in lesion and in imaging studies. General problems encountered with lesion studies include lesions being uncommonly isolated to the region of interest alone, borders of lesions on MRI and CT scans not always being clearly defined, as well as lesions as a result of different aetiology being difficult to compare. Furthermore, damage is often followed by the reorganisation of brain structures (plasticity), making inferences regarding the underlying structure of a given function more complicated. Imaging techniques go some way in alleviating these shortfalls, given that the participants' brains are 'healthy' and lesion free. On the other hand, imaging techniques cannot infer causality, merely correlation. This is something that lesion studies can address to an extent. In summary, imaging studies can indicate associated brain activation and lesion studies can indicate if that same area was indispensable to the associated functions. Both types of study are therefore complementary in attributing a given function to isolated regions of the brain.

In addition, there is often no discrimination made between different methods. For example the TOL and TOH are often used interchangeably as the same measures, although both are believed to be involved in different functions (Goel & Grafman, 1995). This means that many 'PFC measures' may not in actuality be extensively associated with the PFC. In the present

thesis, only the most validated and reported measures were utilised where possible, so that comparisons to the literature could be made more reliably.

IQ fluid intelligence and PVT reaction time measurements were utilised as control tests. IQ and reaction time have not been found to encompass a PFC specificity. Therefore, lack of age-related changes on these measures, yet declines on executive function measures prop up the 'frontal lobe theory' of age-related decline. This was found to be the case in Study 2. However, age differences were observed when comparing a young and older group with regards to IQ, in that the older group had a lower mean IQ (Study 1). It is suspected that these differences were not genuine indicators that global changes had occurred in the older group though, as generational intelligence gains are to be expected to some extent (e.g., Colom, Lluis-Font, & Andrés-Pueyo, 2005) and a concurrent mean IQ was observed in a similar age group (Study 2) in which 'global' age declines were not observed longitudinally.

8.5 Sleep EEG

In order to minimise contamination of EEG data with artefacts (e.g., that caused by muscle movement) low frequency delta, and spindle and KC density were taken from the beginning of the night. The first NREM period has been found to possess the greatest intensity of SWA (Achermann & Borbély, 1997; Carrier et al., 2001) which was found to attenuate as sleep pressure diminished (with the progression of the night). Therefore, the beginning of the night is less prone to disruption, and assumed to be less susceptible to artefact contamination. Low frequency delta was taken from the entirety of the first NREM period. However, spindles and KCs were identified only in stage 2 leading into SWA. This was due to the difficulty in scoring both in the presence of high amplitude delta activity. This may have limitations, considering the role of KC and spindle density in SWA, as measurements during stage 3/4 would have presumably been a more direct reflection of depth of sleep. However, this would not have been plausible.

Spindles and KCs were scored visually. Visual scoring is unusual in current practice, as there has become an increasing reliance on automatic methods. However, although more time consuming, visual scoring was believed to be a more appropriate technique as it is imperative to observe the graphical shape in the scoring of KCs and spindles. It is argued that spectral analysis techniques do not make a distinction between phasic activity and background activity Himanen et al. (2002), further confirming the choice to rely on more rigorous scoring techniques.

8.6 Conclusion and Future Direction

Cognitive ageing is still an area of research undergoing great expansion. Declines in cognition, with healthy ageing, predominantly associated with the PFC have been found to stretch to aspects of cognition beyond executive function. The research reported in this thesis confirmed that significant declines in non-verbal planning (TOL), can be seen in a relatively short time frame (6.29 years) in older age. Furthermore, although social ability, or wisdom is stereotypically thought to improve with age, recognition of emotion in others may undergo some decline with increasing age, with particular difficulties arising in identifying emotion in tone of voice in the presence of conflicting (incongruent) cues. Expansion in this area is important in understanding the way in which the brain changes with 'healthy' ageing, particularly the PFC. It would also be crucial to ascertain 'healthy' cognitive ageing, as a baseline of which to compare changes associated with pathology that is prevalent in the later years (e.g., dementia). This is particularly relevant to a society that is fast becoming an 'ageing population'.

Although an area of research very much still in its infancy, establishing links between sleep EEG and cognition has far-reaching implications. These are not only in elucidating more around the functions of sleep, which despite decades of research is still a relative mystery, but in developing a marker of cognitive decline that may have clinical relevance. There is a current over-reliance on brain imaging techniques to ascertain changes associated with

cognitive decline, and a limited range of neuropsychological and cognitive testing procedures. Both of which are time-consuming; the former financially expensive and invasive (this is something that is particularly problematic when considering older individuals that may have mobility issues, or other restrictions etc.). On the other hand, EEG is relatively low in cost, portable, non-invasive, with almost instantaneous temporal resolution. Research that has been conducted observing the relationship between localised EEG and cognition predominantly associated with the same area (Anderson & Horne, 2003), with the purpose of identifying possible markers of PFC decline, have lead the way in important novel research into cognitive ageing. Although the present thesis was not able to provide clear evidence of the stability of this biomarker, the results indicated the potential for individual differences in the extent to which the link between SWA and cognition can be established. This warrants further investigation utilising a larger scale longitudinal method, in which exploration of other factors can be taken into account, e.g., level of cognitive ability, and the extension into other PFC measures such as social cognition. An interesting perspective would be to combine EEG and brain imaging techniques. Using brain imaging during waking hours would be an important aspect of the investigation in order to ascertain areas of brain recruitment during completion of executive function and social cognition measures, as such research sparsely utilises older age groups; bearing in mind, that recent research has indicated that areas of recruitment may change with age due to compensatory mechanisms at work (e.g., Cabeza et al., 2002).

In summary, SWA localised to the PFC and associated cognition share a common age-associated decline. EEG (particularly low frequency delta) can predict cognition to a certain extent, as found in Study 4: Part II. However, individual factors should be taken into consideration. Nevertheless, studies presented in this thesis, through observations of sleep EEG and cognitive function support the specificity of declines in PFC function due to healthy ageing.

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Appendices

Appendix 1

CONSENT/CONFIDENTIALITY

C.E.Webb@lboro.ac.uk

Consent of Participant to be included in Research Trial:

I……

Consent to taking part in a series of cognitive tests, within the sleep research laboratory and to be video recorded and audio recorded during testing, when necessary. An explanation of the nature and purpose of the procedure has been given to me

by……

I understand that I may withdraw from the experiment at any time, and that I am under no obligation to give reasons for such withdrawal. Upon withdrawal, I understand that I may request any data already collected to be discarded from the study.

I understand that any information about myself that I have given will be treated as confidential by the experimenter.

Signed: ……
Date: ……
Signature of Experimenter: ……

CONSENT/CONFIDENTIALITY

C.E.Webb@lboro.ac.uk

Consent of Subject to be included in Research Trial:

I……

Consent to taking part in an Electroencephalography (EEG) measurement. An explanation of the nature and purpose of the procedure has been given to me

by……

I understand that I may withdraw from the procedure at any time, and that I am under no obligation to give reasons for such withdrawal. Upon withdrawal, I understand that I may request any data already collected to be discarded from the study.

I understand that any information about myself that I have given will be treated as confidential by the experimenter.

Signed: ……

Date: ……

Signature of Experimenter: ……

Appendix 2

Sleep Questionnaire

STRICTEST CONFIDENCE

INTRODUCTION

I would like to ask you some questions regarding your sleeping habits and lifestyle. This is merely to find out about different types of people and their sleeping patterns. All the information you give is in the strictest confidence.

Date ……..
Name……..

Sex: ……
Weight and Height: ……..
Age/DoB: ……

Address
……..
……
……...

Phone No: ……

Occupation/ Past Occupation: ……..……..……

GENERAL QUESTIONS

I will begin with some general questions and then move onto your health and sleeping habits.

Where relevant: Please circle the number that lies next to the statement that you most strongly describes you. For example for question 1, if your answer is 'Don't know' then circle the '0' next to it.

1) One hears of people who feel 'best in the morning' or 'best in the evening'. Which of these types do you think you are?

Definitely a Morning Type	1
More 'morning' than 'evening'	2
Neither	3
More 'evening' than 'morning'	4
Definitely an Evening Type	5
Don't know	0

2) Do you consider yourself to be a “nervous” person?

Yes	1
Sometimes	2
No	3
Don’t Know	0

3) Do you consider yourself to be a “worrier”?

Yes	1
Sometimes	2
No	3
Don’t Know	0

4) Do you consider yourself to be a “stressed” person?

Yes	1
Sometimes	2
No	3
Don’t Know	0

5) Have any events you can think of caused you particular concern or anxiety?

Yes	1
No	3
Don’t Know	0

…..If yes, was this event….

More than 2 years ago	1
More than 3 months ago	2
Less than 3 months ago	3
Current Situation	4
Don’t Know	0

6) Do you eat regular meals?

Yes	1
Sometimes	2
No	3
Don’t Know	0

7) Do you regularly take exercise?

Yes	1
Sometimes	2
No	3
Don’t Know	0

8) How many cups of tea/coffee do you usually drink in a day?

None	1
1-2	2
3-4	3
5-6	4
Over 6	5
Don't Know	0

HEALTH QUESTIONS

10) In general would you say your health is:

Excellent	1
Very Good	2
Good	3
Fair	4
Poor	5
Don't Know	0

11) Compared to a year ago, how would you rate your health in general now?

Much better than a year ago	1
Somewhat better than a year ago	2
About the same	3
Somewhat worse than a year ago	4
Much worse than a year ago	5
Don't Know	0

12) The following questions are about activities that you might do during a typical day. Does your health limit any of these activities?

No, not limited at all = 1 **Yes, limited a little = 2**
Yes, limited a lot = 3 **Don't know = 4**

Vigorous activities	……..
Moderate activities	……..
Lifting/carrying	……..
Climbing stairs	……..
Bending/Kneeling	……..
Walking + 1 mile	……..
Walking ½ mile	……..
Walking 100yds	……..

13) During the past 8 weeks, have you had any problems with work or other daily activities as a result of your physical health?

Yes	1
No	3
Don't Know	0

14) During the past 8 weeks, have you had any problems with work or other daily activities as a result of your emotional health?

Yes	1
No	3
Don't Know	0

15) During the past 8 weeks, have you had any physical or health problems that have interfered with your normal social activities?

Yes	1
No	3
Don't Know	0

16) Have you ever experienced any of the following medical conditions, and if so when?

No = 1 **Yes in the past = 2**
Yes, sometimes = 3 **Yes, at present = 4**
Don't know = 0

(a)	Asthma	.....
(b)	Hay fever	..……
(c)	Eczema	.....
(d)	Allergies	.....
(e)	Thyroid Problems	.....
(f)	Undue anxiety	.....
(g)	Sleepwalking	.....
(h)	Loud snoring	.....
(I)	Nightmares	.....
(j)	Bruxism	..…..
(k)	Difficulty reading or writing	.....
(l)	Arthritis/Rheumatism	.....
(m)	Depression	.....
(n)	Heart problems	.....
(o)	Stomach problems	.....
(p)	Waking up with a jolt	.....
(q)	Waking up excessively early	.....
(r)	Difficulty falling asleep	.....
(s)	Stress/anxiety at home/work	.....
(t)	Epilepsy	.....
(u)	Migraine	.....
(v)	Colour blindness	.....
(w)	Hearing Problems	…….

17) Do you worry about your health?

Yes	1
Sometimes	2
No	3
Don't Know	0

….. If yes, in what way? ……
…….

18) Do you regularly take pills or medicines from the chemist or by prescription?

Yes	1
No	3
Don't Know	0

…..If so can you tell me what they are?
……..
……
……
……

SLEEP QUESTIONS

19) How much do you enjoy sleep?

Very much	1
Moderately	2
Not Much	3
Not at All	4
Don't Know	0

20) What time do you normally go to bed? ……

21) What time do you normally get up? ……

22) How long does it normally take you to fall asleep?

0-5 minutes	1
5-10 Minutes	2
10-20 Minutes	3
20-30 Minutes	4
Over 30 Minutes	5
Don't know	0

23) Do you ever miss a night's sleep or have much less sleep than usual?

No	1
Yes, sometimes	2
Yes, regularly	3
Don't know	0

….. If yes, can you tell me what is the reason for this?

……..
……
……
……

24) How would you describe your level of wakefulness in the hour before you go to bed?

Very Alert	1
Fairly Alert	2
Neither Sleepy nor Alert	3
Sleepy but not fighting sleep	4
Very sleepy, effort to stay awake.	5
Don't know	0

25) Have you any special technique or habit that you use to give yourself a good night's sleep?

Yes	1
No	3
Don't Know	0

…… If yes, can you describe this to me?

……..
……
…

26) How much does your quality of sleep vary from one night to the next?

Very much	1
Moderately	2
Slightly	3
Not at All	4
Don't Know	0

27) How often do you lie awake worrying at night?

Every night	1
Several nights/week	2
Several times/month	3
Once a month or less	4
Never	5
Don't know	0

28) How many times do you wake , on average, a night?

Never	1
Hardly Ever	2
Once or Twice	3
Never	5
Don't know	0

….. If you wake up: How long does it take you to get back to sleep again?

Less than 10 minutes	1
10 – 30 Minutes	2
30 – 60 Minutes	3
Over 60 Minutes	4
Don't know	0

….. What usually causes you to wake up?

Awake spontaneously	1
Nerves, tension, worry	2
Need to go to the toilet	3
Shortness of breath/coughing	4
Pain in the chest	5
Pain in the stomach	6
Pain in the legs	7
Twitching/Kicking of legs	
Noise	8
Dreams or nightmares	9
Don't know	0
Other	10

29) How easy do you find getting up on the morning?

Very easy	1
Fairly Easy	2
Okay	3
Fairly Difficult	4
Very Difficult	5
Don't know	0

30) How refreshed do you feel after waking?

Very refreshed	1
Refreshed	2
Neither refreshed nor tired	3
Tired	4
Very Tired	5
Don't know	0

31) How would you describe your general level of wakefulness 15 minutes after getting up in the morning?

Very Alert	1
Fairly Alert	2
Neither Sleepy nor Alert	3
Sleepy but not fighting sleep	4
Very sleepy, effort to stay awake.	5
Don't know	0

32) Do you ever have difficulty staying awake during the day?

Yes every day	1
Yes, several times a week	2
Yes, several times a month	3
Yes, once a month	4
Never	5
Don't know	0

…… If yes:

At about what time does this sleepiness usually start?

8-9am	1
9-10am	2
10-11am	3
11-12am	4
12-1pm	5
1-2pm	6
2-3pm	7
3-4pm	8
4-5pm	9
5-6pm	10
6-7pm	11
7-8pm	12
Don't know	0

…… How long does this sleepiness usually last for?

5-10 minutes	1
10-20 minutes	2
20-30 minutes	3
30-60 minutes	4
Over 60 minutes	5
Don't know	0

33) Is there usually a good reason for this sleepiness?

Yes	1
No	3
Don't Know	0

…… If yes, can you explain the reason to me?
……
……..……..……..……
……..……..……..……
……..……..……
……

34) Do you ever nap during the day?

Yes	1
No	3
Don't Know	0

…. If yes, how often on average?

Every Day	1
2-3 Times per week	2
Once per week	3
Once per month	0
Don't know	

35) Do you ever experience 'poor sleep'?

Yes	1
Sometimes	2
No	3
Don't know	0

…. If yes, what constitutes this 'poor sleep' Circle as many as applicable.

I moved a lot during the night	1
I took a long time to fall asleep	2
My dreams made me anxious	3
I had an headache on waking	4
I woke up a great deal	5
I had many dreams	6
I felt dizzy on waking	7
I was aware of thinking all night	8
I felt tired when I awoke	9
Parts of me ached when I awoke	10
I slept shorter than usual	11
Don't know	0
Other (Code & Write)	12

36) Which is most important in deciding if you had a poor night's sleep?…….....
.....

37) If you had a poor nights sleep, does it affect:

How you feel	1
How you perform	2
Both of these	3
Neither of these	4
Don't know	0

38) If you had a poor night's sleep, when do you feel the consequences?

The next day	1
The day after	2
Both of these days	3
Neither of these days	4
Never	5
Don't know	0

39) **Epworth Sleepiness Scale**: The Epworth Sleepiness Scale is a measure of how likely you are to fall asleep in the following situations. This is in reference to your life in recent times. If there are some activities you have not done in recent times then try to predict how they would have affected you. Next to each activity, please enter the number corresponding to the following rating guide

0 = Would *never* doze
1 = *Slight* chance of dosing
2 = *Moderate* chance of dozing
3 = *High* chance of dozing

Situation	**Chance of dozing**
Sitting and reading	_____
Watching T.V.	_____
Sitting inactive in a public place (e.g., theatre/meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____
	Score:

THE END: THANK YOU!

Appendix 3

Karolinska Sleepiness Scale

Confidential

This scale shows how sleepy you feel at a given time during the day. Please rate your feeling of sleepiness every hour that you are awake for 3 days using the scale below. Please write in what time you went to sleep and what time you awoke.

The Karolinska Sleepiness Scale (Åkerstedt & Gillberg, 1990)

1. Extremely Alert
2. Very Alert
3. Alert
4. Rather Alert
5. Neither Alert nor sleepy
6. Some signs of Sleepiness
7. Sleepy, but no effort to keep awake
8. Sleepy, some effort to keep awake
9. Very Sleepy, great effort to keep awake, fighting sleep

Day 1:		*Day 2:*		*Day 3:*	
Time	**KSS**	**Time**	**KSS**	**Time**	**KSS**
06:00		06:00		06:00	
07:00		07:00		07:00	
08:00		08:00		08:00	
09:00		09:00		09:00	
10:00		10:00		10:00	
11:00		11:00		11:00	
12:00		12:00		12:00	
13:00		13:00		13:00	
14:00		14:00		14:00	
15:00		15:00		15:00	
16:00		16:00		16:00	
17:00		17:00		17:00	
18:00		18:00		18:00	
19:00		19:00		19:00	
20:00		20:00		20:00	
21:00		21:00		21:00	
22:00		22:00		22:00	
23:00		23:00		23:00	
00:00		00:00		00:00	
01:00		01:00		01:00	
02:00		02:00		02:00	
03:00		03:00		03:00	
04:00		04:00		04:00	
05:00		05:00		05:00	

Any queries please contact Clare Webb; C.E.Webb@lboro.ac.uk, +44 (0)1509 228154

Appendix 4

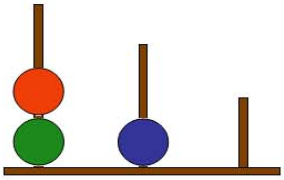
Affect Go/No-go Stimuli Words

Word Length	Word Type			
	Sad	Happy	Neutral (1)	Neutral (2)
5	upset	jolly	think	nature
6	sorrow	elated	remark	enter
7	despair	delight	village	example
7	weeping	gleeful	compose	outline
8	mournful	ecstatic	property	operator
8	bereaved	cheerful	continue	quantity
8	dejected	blissful	question	industry
9	depressed	hilarious	universal	meanwhile
9	miserable	overjoyed	framework	frequency

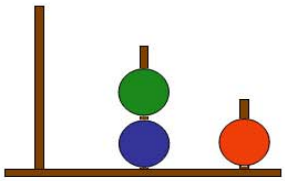
Appendix 5

Tower of London configurations of problems:

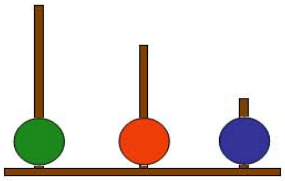
Standard Configuration



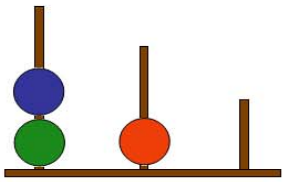
Problem 1:
2 Moves



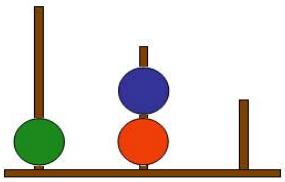
Problem 2:
2 Moves



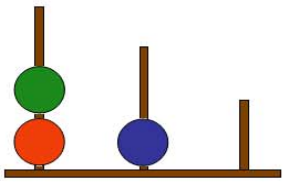
Problem 3:
3 Moves



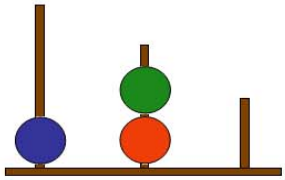
Problem 4:
3 Moves:



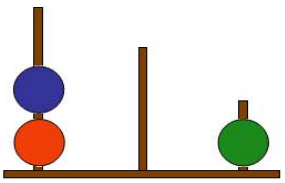
Problem 5:
4 Moves



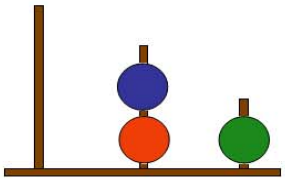
Problem 6:
4 Moves:



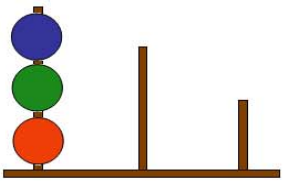
Problem 7:
4 Moves



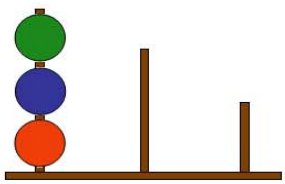
Problem 8:
4 Moves



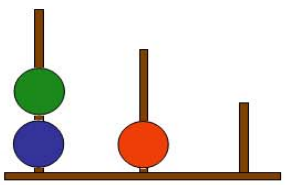
Problem 9:
5 Moves



Problem 10:
5 Moves



Problem 11:
5 Moves



Problem 12:
5 Moves