

**BEHAVIOURAL AND
ELECTROPHYSIOLOGICAL ASPECTS OF
ERROR PROCESSING IN ALZHEIMER'S
DISEASE AND HEALTHY AGEING**

by

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Declaration

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Summary

Over the past one hundred and seventy years life expectancy has increased by as much as 3 months per year, reflecting the enormous medical and social advancements made by humankind. Concurrent to this we have seen exponential population growth, particularly of those whom we deem to be of advanced age. As a result, the global community will have to develop broad ranging strategies to deal with inevitable consequences of this expansion. For while increased life expectancy may be considered overwhelmingly positive, with it comes several challenges, particularly for those who find themselves advancing into their eighth, ninth and possibly tenth decade. Increased susceptibility to illness, injury and age-related disease such as Alzheimer's disease, Parkinson's disease, Osteoarthritis and CVD are but a few of the disadvantages of older age. Another inherent aspect of healthy, non-pathological ageing is a marked decline in cognitive ability across a distributed network of functions. One feature of this reduced cognitive capacity is a diminution in the ability to monitor and assess errors. While recent advances in the field of cognitive science, and in particular electrophysiology, have made it possible to delineate several aspects of error processing, relatively little is known regarding the precise impact of ageing upon the ability to appraise errors. By combining neuropsychological and electrophysiological methodologies this thesis aims to explore this phenomenon and add to the existing body of knowledge on age-related effects on error processing. This work also sought to examine, possibly for the first time, the process of 'online', real-time awareness of errors in those affected by Alzheimer's disease.

Chapter 1 begins by reviewing the literature that provides the theoretical basis for the work within this thesis. Following this Chapter 2 aims to explore age-related characteristics of error processing by comparing the performance of young and older adults on a newly developed error awareness dot task, the EADT. Electroencephalographic evidence pertaining to specific error associated neural signatures, namely the error positivity component (Pe) and the error related negativity (ERN), was recorded throughout testing. A multi-domain psychometric battery was also employed in order to assess current levels of cognitive function and to explore the possibility that performance on a laboratory based task would be reflected in everyday function. Data from this study seems to suggest that older adults are less aware but more accurate than younger individuals. This finding is influenced by the differing strategies engaged by the competing groups, which saw older individuals place an emphasis on accuracy and younger participants engage in uninhibited rapid responding. These strategies lead older and younger individuals to commit different types of error when engaged in the same task. This Chapter also provides further evidence to suggest there is identifiable attenuation of the Pe and ERN components in older adults when assessed for aware errors.

Chapter 3 sought to further this line of inquiry by including participants who had received a diagnosis of Alzheimer's type dementia along with our younger and older populations. Error related research in this patient group has been somewhat limited, and of that which does exist none has required participants to explicitly acknowledge errors in an 'online' manner. A

touchscreen version of the EADT was created for this study, the touchscreen error awareness task (TEAT). Convergent data from discrepancy measures on the Patient Competency Rating Scale and scores on the Montreal Cognitive Assessment (MoCA) was assessed in relation to performance on the TEAT. The findings from Chapter 3 suggest that the ability to generate high levels of sustained attention is somewhat preserved in AD patients, however, levels of online awareness are severely impacted by pathology. Lower levels of awareness are also reflected in lower scores on the MoCA.

In Chapter 4 of this thesis consideration was given to the potential impact that individual traits might have upon the ability to process errors and it's associated electroencephalography. Of particular interest was the potential role that underlying feelings of anxiety and depression, as measured by the Hospital Anxiety and Depression Scale, may have on performance. One's own self-concept and mindset regarding engagement in everyday activities was also considered. Specifically we assessed participants using Kuhl's Action Orientation Scale (ACS-90; Kuhl, 1990), which measures one's propensity to focus on current goals or engage in ruminative thinking. In line with our previous studies these factors were assessed for potential age-related difference. The evidence from this study suggests that the electrophysiological and behavioural correlates of erroneous behavior are indeed impacted by emotional factors, particularly anxiety. It is also possible that age related such aspects of emotional control mean that older adults are less susceptible to these effects. Chapter 4 contains the data for two concurrent experiments.

Finally Chapter 5 provides a discussion of the findings which have emerged and their impact on the current thinking in regard to the in the cognitive and electrophysiological substrates of error processing and awareness in healthy ageing and Alzheimer's disease. Chapter 5 also discusses the methodological issues associated with this body of work and contemplates path future research in this field might take.

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Chapter 1

Conceptual Background

1.1 Introduction

Over the past number of decades there has been an exponential increase in the global population of those aged sixty-five years and over. In Ireland alone this particular age cohort represents almost 15% of the population, and should this current trend continue it is expected that by the year 2050 roughly 30% of Irish citizens will fall into this category (Mamolo & Scherbov, 2009). Of course catch all terms such as old or 'elderly' are in and of themselves highly subjective as genetic, biological, ethnogerontological and social factors regularly serve to highlight the enormous heterogeneity of both the pathological and non-pathological cognitive aging process (Rowe & Kahn, 1997; Milne & Chryssanthopoulou, 2005; Bard, Ford, & Podell, 2007; Pedraza & Mungas, 2008; Habes, Janowitz, Erus, Toledo, et al., 2016). Despite this, much of what is discussed in terms of geriatric cognitive processing is framed, perhaps unintentionally, in a somewhat negative light. The overarching theme for much of this research seems to be the perceived degradation of functionality rather than attempt to describe a natural progressive process; analogous to the developmental changes which take place between infant cognition and early childhood.

With this in mind, the main aim of this thesis is to explore age related cognitive function in the domain of error processing. Within this framework we pay particular attention explicit awareness of errors. Studies have concluded that the ability to monitor and detect errors is reduced in older adults (Harty, O'Connell, Hester & Robertson, 2013), however there are similar reports to the contrary, suggesting that this domain is largely preserved. Some have even suggested that certain cognitive abilities such as sustained attention, which is vital to the monitoring process (Robertson, 2010), is in fact significantly increased in older individuals (Carriere, Cheyne, Solman & Smilek, 2010). This work also examines, we believe for the first time, the ability of those with a diagnosis of Alzheimer's type dementia to monitor and overtly signal errors in an 'online' manner. It is hoped that these findings will not only help to characterize alterations in neurological processing between healthy older adults and Alzheimer's patients, but that they might also inform our understanding of cognitive foundations of this process in early adulthood.

The disparity of opinions in the field suggests that we are still some distance from providing a clear model of this construct, and that the theme of this body of work is warranted.

1.2 The Healthy Ageing

There are a great many challenges which we face as we grow older. Even if we set aside the fact that ageing makes us susceptible to, and increases

the risk of, developing pathological disorders such as cardio-vascular disease (CVD;), osteoarthritis, Parkinson's Disease, fronto-temporal dementia (FTD;), Alzheimer's Disease (AD;), healthy older adults still experience significant cerebral, cognitive and overall physical changes. There are several non-pathological age-related neuro-biological changes such as decreased white and grey matter integrity (Hedden & Gabrieli, 2004; Peters, 2002; Raz, Lindberg, Rodrigue, et al., 2005), vasculature capability, cerebral metabolic rate, blood supply (Lu, Xu, Rodrigue & Kennedy et al., 2011, Raz et al., 2005) and significant dysregulation of neurotransmitter functionality (Backman, Nyberg, Lindenberger, Li & Farde, 2006). However, these effects do not occur in a uniform fashion; rather a largely heterogeneous process may see decrement in one domain lead to preservation or migration of function in another (Raz, 2000). What is of significance is that the prefrontal regions in particular seem to be effected by several of these structural and functional alterations, many of which lead to the cognitive changes observed in older individuals (Fjell, McEvoy, Holland, Dale & Walhovd, 2013)

Reductions for instance in white matter, have led some to describe the effects of these cerebral alterations as “disconnected ageing” (Bennett & Madden, 2014). What is proposed is that the global effect on cognitive function as a result decreased structural and functional connectivity contributes to overall cognitive decline. Therefore, the “disconnected brain” of older adults is unable to adequately support communication between brain regions responsible for rapid higher order cognitive functions. Executive function and speed of processing are particularly vulnerable to these effects and therefore it

is no surprise that many models of cognitive ageing focus on these domains (Bennett et al., 2014; Fjell, Sneve, Grydeland, et al., 2017).

With respect to the current thesis, the executive control of behavior is of particular interest as accurate task monitoring, processing of errors and compensatory actions are heavily reliant on several related, but dissociable, prefrontal functions (Garavan, Ross, Murphy, Roche, & Stein, 2002).

For instance, inhibition is a vital component in successful goal management as it helps us to avoid automaticity, where one might respond too quickly having not afforded adequate time to assess incoming stimuli and information (Shallice & Burgess, 1993). Behaviourally this can lead to what is commonly referred to as the ‘speed accuracy-trade off’, where rapid responses lead to an overall reduction in accuracy (Rabbitt, 1979). Again if we focus on the ageing process, younger people have been shown to be more likely to engage in this type of behavior, but what precisely causes this effect? Is it a conscious strategic decision on behalf of older individuals, cognizant of their own functional diminution, or is it perhaps as a slowing of responses due to reduced processing power of the increasingly disconnected brain of elderly adults. Others have however reported that older adults demonstrate an inhibitory deficit in certain domains. For instance previous research has suggested that there is an age-related decline at the conceptual level of the inhibitory processes on a Stroop task (West & Alain, 2000). In this instance it is possible that the complexity of the stimuli and inadequate processing speed may impede the process of inhibition. What may also be influential in this

process is the role played by endogenously generated sustained attention in dealing with incoming sensory information.

Vigilance or sustained attention has been defined as “the capacity to maintain aware responding to routine stimuli and responses while avoiding automaticity and in the absence of external challenge, difficult, novelty or emotional salience” (Robertson & Garavan, 2004). One might expect that this ability to sustain attention would be diminished in older adults; however there have been several reports to the contrary. Carriere and colleagues have demonstrated that older individuals have the endogenously generate higher levels of sustained attention when exogenous stimuli are unengaging (Carriere, et al., 2010). This may be buttressed by the suggestion that as we age we are less likely to engage in mind wandering, thus by avoiding task unrelated thoughts we compensate for age-related decrements in executive function (Christoff, Irving, Fox, Spreng & Andrews-Hanna, 2016; Maillet & Schacter, 2016).

It is interesting to note that the combined factors of inhibition and sustained attention have been reported as being responsible for two distinctive types of error. In a 2007 study Shalgi et al. found that when speeded responses were encouraged on a Go/No-Go task there was a decline in participant accuracy, while when participants were instructed to respond at stimulus offset errors decreased. They further suggested that unaware errors were more reflective of lapses in sustained attention, while the errors of which participants were aware occurred as a result of those in which they failed to

inhibit responding (Shalgi, O'Connell, Deouell & Robertson, 2007). By slowing down the process of responding task difficulty is thought to decrease, therefore the likelihood that attention will drift is increased, and participants will be less likely to notice their errors. On the other hand the elevated level of task difficulty due to the pressure of faster responding means that more errors committed, but the engaging nature of the task means that these errors are acknowledged.

O'Connell and colleagues also reported separable inhibitory and sustained neural mechanisms giving rise to errors on a Go/No-Go task (O'Connell, Dockree, Bellgrove, et al., 2009). In this instance stimuli on the Sustained Attention to Response Test (SART; Robertson, Manly, Andrade, Baddeley & Yiend, 1997) that were presented in a random fashion led to a greater number of errors being committed when compared to stimuli that were presented in a predictable. It is suggest that the random nature and unpredictability of stimuli increased demands on inhibitory control, while the predictable nature of fixed pattern stimuli elicit errors which reflect the attentional drift induced by the monotony of the task.

Returning again to the impact of ageing on prefrontal cortical regions, specifically the medial prefrontal cortex, is often activated during the process of internal assessment of emotional states of being (Johnson, Baxter, Wilder, Pipe, Heiserman & Prigatano 2002). There is also evidence to suggest that when one is engaged in the tasks which demand high levels of sustained attention in order to evaluate external stimuli and subsequent task

performance, adequate levels of activation in the right dorsolateral prefrontal cortex (rDLPFC) are required (Harty et al., 2013; Manly, Owen, McAvinue, Datta, et al., 2003). What this suggests is that the rDLPFC is of particular importance in the current study as both sustained attention and awareness of errors have been shown to be vital components of the ability to detect errors (Harty et al., 2014; Hester, Foxe, Molholm, Shpner, Garavan, et al., 2005).

1.3 On the Nature of Errors

Erroneous behavior in and of itself does not always yield negative outcomes; the proverbial spilt milk often proving less catastrophic than first feared. In fact, one might contend that from an early age errors bestow upon us enormous benefits, as we learn from previous mistakes then modify, adapt and regulate our behavior in order to execute proximal tasks and achieve distal goals (Ullsperger, Danielmeier & Joacham, 2014). Of course human error may also have dangerous and often fatal consequences, as is regularly witnessed in road traffic accidents. At other times what at first might seem like an innocuous mistake may have potentially devastating cumulative effects. Consider for instance the case of Dr Rolando R. Sanchez, the Tampa surgeon who mistakenly amputated the wrong leg of a patient in the spring of 1995 following a series of previously undetected administrative errors by nursing staff (Doctor Who Cut Off Wrong Leg Is Defended by Colleagues. *The New York Times* September 17th, 1997).

Of course when we speak of adaption, modification and eventual realignment of behavior we are assuming that the initial error has been detected, for this is an essential requirement of the monitoring process (Norman & Shallice, 1985). Corrective action is reliant upon accurate self-referential assessment of current actions, following which adjustments can be made in order that previous errors will not be repeated. Therefore whilst heeding Seneca's celebrated maxim '*Errare humanum est, sed in errore perseverare diabolicum...*' perhaps we could be so bold as to adapt it by suggesting that *to err is human, but to correct is divine*.

1.4 Age Related Differences in Error Processing

There have been several studies to suggest that older adults are more likely to engage in erroneous behaviour (Burke & Shafto, 2004; Gold, Powell, Xuan, Jicha & Smith, 2010; Harty et al., 2013; Young & Bunce, 2011). For instance Young and Bunce, amongst others, have reported on how older drivers are more susceptible to driving errors when there is an elevated mental workload (Groeger, 2000; Hole, 2007; Young et al., 2011). While a decline in visual capabilities play no small part in this phenomenon, more cognitive aspects such as attention and executive function have been highlighted as predictors of diminished driving ability (Adrian, 2009; Brouwer, Waterink, Van Wolffelaar & Rothengatter, 1991). Gold and colleagues have also suggested that the ability to redirect attentional is diminished in older adults, this time in a task switching paradigm, is negatively impacted and slowed by the ageing process, thus increasing erroneous behaviour (Gold et al., 2010). This process of overall cognitive disturbance suggests that advanced age is

associated with a decrease in the speed of processing and diminished ability to execute tasks for which there is a limited amount of time (Salthouse, 1996). Despite these several reports, little is known about the impact of ageing on the ability to consciously detect and signal errors.

Two relatively recent studies by Harty and colleagues (2013 & 2014) have shed new light on this process. In what was a new departure the first of these studies somewhat nullified the impact of task difficulty by including a 'staircase' method that altered both the stimulus and inter-stimulus interval, thus promoting equitable levels of accuracy between younger and older individuals. What this allowed for was an examination of awareness levels, as indexed by a motor-response, following commission errors. It was found that older adults had diminished awareness compared to younger individuals, and further that this correlated with inaccurate assessment of ones performance when engaged in activities of daily living. This finding materialized, as it emerged that diminished error awareness correlated with overestimation of ability on a discrepancy measure of real world activities.

In the second of these studies a direct link between the aforementioned rDLPFC and online awareness of errors was highlighted. Participant levels of awareness were shown to increase following the application of anodal transcranial direct current stimulation (tDCS) to the right, but not the left, DLPFC. This would seem to provide direct evidence to support previous report of a similar kind (Hester et al., 2005; Manly et al., 2003). It is particularly in light of the importance of this region in the generation of vigilant attention for

task monitoring (Robertson, 2010). These findings provide exciting new insights into awareness and also suggest that this capability may be open to remedial therapies.

There have also been reports of age related attention of underlying error associated event-related potentials (ERP'S), which will be discussed in the next section.

1.5 Electrophysiological Correlates of Error Processing

As researchers the ability to stand sentinel over the monitoring process in what one might term an 'online' fashion has allowed us to begin the process of constructing a comprehensive model of erroneous behavior. Multi-layered electrophysiological and neuro-imaging studies have concluded that the neural substrates of this ability to monitor performance reside in posterior mesial frontal cortex (pmFC) regions, from the anterior cingulate cortex (ACC) to the pre-supplementary motor area (pre-SMA) (Cohen & van Gaal, 2012; Di Pellegrino, Ciaramelli & Ladavas, 2007; Ridderinkhof, Ullsperger, Crone & Nieuwenhuis, 2004).

Scalp recorded electroencephalographic evidence in particular has provided us with an in depth understanding of the temporal dynamics of the underlying cortical responses related to failures of the monitoring process, commission errors. Particular attention has been paid to two distinct event related potential (ERP's), the error related negativity (ERN; Falkstein,

Hohnsbein, Hoorman & Blanke, 1990; Gehring Goss, Coles, Meyer & Donchin, 1993) and the error positivity component (Pe; Falkstein et al., 1991, 1995).

The ERN, sometimes termed the error negativity (Ne), is a fronto-central negative deflection which peaks between 50 and 100ms when aligned to an erroneous response. Electrical source localizations studies have suggested that the ERN originates in the posterior mesial frontal cortex (pmFC), and more specifically on the posterior fronto-medial wall of the anterior midcingulate cortex (amCC) (Gruendler, Ullsperger & Huster, 2011). Synchronous recording of EEG and functional magnetic resonance imaging (fMRI) has previously suggested that hemodynamic responses in the amCC were significantly correlated with the amplitude of the ERN (Debner, Ullsperger, Siegal, Fiehler, von Cramon & Engel, 2005). Interestingly, elicitation of the ERN is not thought to be related to, or dependent on, any particular sensory modality, being generated by visual, haptic and auditory stimuli (Ullsperger, Danielmeier & Jocham, 2014). The ERN has been interpreted as a correlate of early error detection (Falkstein et al., 1990, 2000) which is sensitive to response conflict (van Veen & Carter, 2002; Yeung et al., 2004) and changes outcome probability and reward expectation (Holroyd & Coles, 2002; Holroyd et al., 2004). Notably the amplitude of the ERN has been shown to be susceptible to manipulation, when high levels accuracy on a given task is monetarily rewarded (Gehring, Goss & Coles, 1993; Hajcak, Moser, Yeung & Simmons, 2005). As this thesis places an emphasis on awareness of errors, it is worthy noting that the ERN has been shown to occur regardless of whether an error is consciously detected or not (Ullsperger & Von Cramon, 2001; Wessel,

Danielmeir, Morton & Ullsperger, 2012). There have however been some reports to suggest that the amplitude of the ERN is positively affected by conscious detection of an error (Steinhauser & Yeung, 2010; Shalgi & Deouell, 2012, Navarro-Cebrian, Knight, Kayser, 2013).

Clinical studies have also shown the ERN to be affected in several population including obsessive-compulsive disorder (OCD; Matthews et al. 2012, Ruchow et al., 2005), generalized anxiety disorder (GAD; Weinberg et al, 2010) and schizophrenia (Bates, Kiehl, Laurens and Liddle, 2002; Morris, Yee & Nuechterlein, 2006). This is not however simply a case of high versus low amplitude between clinical and healthy populations. For instance, the amplitude of the ERN has been shown to fluctuate based on the level of anxiety reported by individuals Moser et al., 2013; Simons, 2010; Weinberg et al., 2012). In contrast to this, the Pe seems largely resistant to change even in the presence of pathology such as Parkinson's Disease even when the ERN is affected (Falkstein, Willemsen, Honsbein & Hielscher, 2005). This further suggests that even though the ERN and the Pe are both related to the error processing they reflect different aspects of this phenomenon (Overbeek, Nieuwenhuis & Ridderinkhof, 2005).

There have however been reports that the amplitude and latency of both these components are attenuated in patients with Alzheimer's type dementia (Ito & Kitagawa, 2005), with peak amplitude occurring between 30-50ms later and with peak amplitude being almost fifty percent lower than that of age-matched controls. Mathalon and colleagues on the other hand have

reported that the amplitude of the Pe, and therefore they suggest error awareness, is somewhat preserved in Alzheimer's patients, despite decrease amplitude of the ERN and lower levels of accuracy (Mathalon, Bennett, Askari & Gray et al., 2003).

Source localization studies have suggested that the parietal cortex and rostral ACC contribute to the generation of the classical Pe component. This positive slow waveform, which follows the ERN, peaks in centro-parietal regions between 300-500 ms following an error (Ullsperger et al., 2014). Whilst the Pe has been widely studied, the precise nature of this component is still not fully understood (Ridderinkhof et al., 2009). One particular difference between the Pe and its predecessor the ERN is that the Pe seems to occur following conscious detection of an error. Recent conceptualizations of the Pe have suggested that it represents the accumulation of evidence for, and emergence of, conscious perception of errors, with the peak amplitude reflecting the point at which awareness of an error emerges (Murphy, Robertson, Allen, Hester & O'Connell, 2012; Steinhauser & Yeung, 2010; Ullsperger, 2010). For the purposes of this thesis, the Pe will be regarded in this light, conscious awareness of an error as proposed by Falkstein (2004).

Importantly there is evidence to suggest that the amplitude of the ERN (Band & Kok, 2000; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000; Mathalon et al., 2003; Mathewson, Dywan, & Segalowitz, 2005) and the Pe (Band & Kok, 2000; Falkenstein et al., 2000; Leuthold & Sommer, 1999; Mathewson, Dywan & Segalowitz, 2005) are attenuated in healthy older

individuals when compared to younger participants. Using a standard flanker task Mathewson et al. (2005) found that older adults produced ERN and Pe components of lower amplitude compared to younger individuals. They also reported that older adults were more erroneous in task related behaviour.

1.6 Challenging Times: Alzheimer's Disease

A major component of this thesis is the inclusion of an Alzheimer's population. The reason for pursuing this line of inquiry is twofold. First we believe that the error processing ability of Alzheimer's patients is poorly understood and underreported in the current literature. To the best of our knowledge there have been no studies that examine the ability of AD participants to explicitly signal commission errors as they occur. By examining this phenomena it may be possible to disambiguate the cognitive decrement associated with underlying pathology from that of the healthy ageing process. Secondly, there is an urgent need to develop evermore-sensitive diagnostics tools which support the process of early diagnosis of Alzheimer's disease. It is quite possible that online awareness of errors may illuminate hitherto unreported pathological substrates of cognitive decline. Let us therefore consider the ongoing and exponential impact of Alzheimer's disease in modern society.

Concurrent to the global increase in life expectancy there has also been an unprecedented rise in the number of individuals being diagnosed with age associated disorders such Alzheimer's disease, is a neurodegenerative disorder which is purported to be responsible for between 60-80 % of all cases of

dementia. Current figures estimate that there are 55,000 people in Ireland living with dementia, with numbers projected to rise to 113,000 by 2036 (Fens, 2014), while in the United States it is thought that at least one in eight people (13% or 5.3 million people) over the age of sixty-five has received a diagnosis of Alzheimer's disease (Gooch, Pracht & Borenstein, 2017). This figure rises to roughly 14% for those aged seventy years and a staggering 45 to 50% of those aged eighty-five or over. To put these statistics in context, current estimates suggest that globally there will be upwards of 81.1 million dementia sufferers by the year 2040, with the number of patients projected to double every twenty years (Ferri, Prince, Brayne & Brodaty et.al, 2006).

In terms of our capability to respond to this problem, there are clearly a great many challenges to be faced. Considers that while deaths resulting from stroke, CHD, and prostate cancer have decreased by 23%, 14%, and 11% respectively between the years 2000 and 2013, during the same period AD related deaths in the United States have increased by as much as 71% (Alzheimer's Association Report, 2016).

Although clinical, surgical and pharmaceutical advances will no doubt have played an important role in both the decrease in fatalities caused by certain pathologies and the increased number of AD diagnoses, these figures nonetheless reveal the scale of the challenge faced by both the medical/care communities and society in general.

Internationally the cost of caring for our aging population places a significant burden on our health services, with a report by the recently established World Dementia Council estimating that the cost of caring for individuals with AD is expected to rise to \$1 billion annually by the year 2030 (Gillings, WDC Annual Report, 2014). In an attempt to break this deadlock, or at least halt the current negative trajectory, the diagnostic domain may provide the best hope for arresting current trends in onset, progression and fatality rates associated with AD. Early diagnosis and treatment may also go some way toward alleviating the enormous societal pressures associated with, what some have termed, the “Alzheimer’s pandemic” (Carrillo, 2013; Hake & Scherer, 2000; Holtzman, 2010).

Despite a wealth of research and almost daily newspaper reports which suggests both potential causes and cures, the majority of current research would suggest that a potential ‘cure’ for AD seems ever more distant. With this in mind, current thinking points towards early diagnosis and successful management of the disease as offering the best outcomes for patients, families and health care workers (Thies & Bleiler, 2011). Early diagnosis allows not only for the implementation of pharmaceutical interventions, which delay the need for full time care (Geldmacher, Provenzano, McRae, Mastey & Ieni, 2003), but it also enables patients and carers to be actively involved in the construction of a plan for their own future, whereby they put in place strategies aimed at slowing the inevitable cognitive and physical decline associated with the disease. Perhaps more importantly it also allows individuals, where possible, to remain living independently in their own home,

a key factor which has been shown to influence and potentially slow the progress of the condition.

It should also be mentioned that clinical benefits aside, in economic terms early diagnosis significantly decreases the cost of care not only to the exchequer but also to patients and families (Weimer & Sager, 2009). This point is worth mentioning as outside of the emotional difficulties associated with caring for a loved one (Starkstein, 2014), the stress involved with practical issues such as finance can often place a heavy burden on both patients and their families (Shim, Landerman & Davis, 2011).

1.7 Alzheimer's Disease, Awareness and Errors

The term *anosognosia* was first used by Babinski (1914) to describe patients with left-sided paralysis due to right hemisphere cerebral damage. What was curious about these patients is that they seemed to be completely unaware of their paralysis, paying little or no attention to their impairment. In more recent years reports of this phenomenon have been reported in several other clinical populations including schizophrenia (David, Bedford, Wiffen & Gileen, 2012, Alzheimer's Disease (McGlynn & Schacter, 1989; Starkstein, Vázquez, Migliorelli et al., 1995), TBI (O'Keefe, Dockree, Moloney, Carton & Robertson, 2007) and substance abuse (Hestor, Nestor & Garavan, 2009). Despite a large body of literature on the topic, the term anosognosia is rather poorly defined and has been associated with denial, of deficit, impaired self-awareness of deficit and lack of insight (Kasznik & Edmonds, 2010). In general

terms, and for the purposes of this thesis, it may be described as the ability of an individual to “appraise aspects of their own current situation, performance, or functioning”, (Roberts, Clare & Woods, 2009).

Alzheimer’s disease is a largely age-related neurological illness and is responsible for between 60-80% of dementia diagnoses. It is characterized by severe atrophy and neuronal loss, neuritic plaques and neurofibrillary tangles which across several cortical regions. These include frontal, mediotemporal, posterior temporal and parietal sites (Braak & Braak, 1991; Dekosky & Scheff, 1990). Severe atrophication of the hippocampal formation has also been regularly recorded with one study suggesting an 8% reduction over a two-year period (Fox, Warrington, Freeborough, et al., 1996).

As a result of this neurobiological degradation common symptoms of Alzheimer’s include progressive memory loss and significant deterioration of overall cognition (Baddeley, Della Sala, Logie & Spinnler, 1986; Berardi, Parasuraman & Haxby, 2005; Wang & Wang, 2006). While memory impairment is particularly impeded, there are also both attention and executive function deficits associate with AD, the symptoms of which tend to increase as the illness progresses (Kaszniak et al., 2010; Kaszniak, Wilson, Fox & Stebbins, 1986; Michon, Deweer, Pilon, Agid & Dubois, 1994; Collette, Van der Linden & Salmon, 1999). This often means that patients have trouble in relatively simple tasks requiring attention, inhibition and planning (Kirova, Bays & Lagalwar, 2015). Some have even suggested that executive dysfunction, including attentional processes, are possibly the earliest sign of developing pathology (Albert et al., 2001; Perry et al., 2000).

It is difficult to accurately suggest the prevalence of anosognosia in AD as there are a great many methodologies employed in its assessment (Clare, 2004). Further to this, it is difficult to precisely describe the behavioural and cognitive impact of impaired insight because the methods of measurement are not standardised and the construct is poorly defined (Horning, Melrose & Sultzer, 2014). It is however commonly reported (anywhere between 20-80%, according to different reports (Starkstein, 2014)) and more importantly has been shown to negatively impact the diagnostic process and compliance with treatment. It also increases the risk of injury to the patient and increases caregiver burden (Cosentino & Stern, 2005, Pachana & Petriwskyj, 2006; Seltzer, 1997; Starkstein, Jorge, Mizahi, Adrian & Robinson, 2007). Paradoxically, patients with relatively intact insight, those who are aware of their condition, are often rated as being more depressed, anxious and apathetic (Horning et al., 2014; Kashiwa, Kitabayashi, Narumoto et al., 2005).

Patient-informant discrepancy measures are perhaps a regular method of assessing impaired insight in clinical studies. Following early discrepancy reports in AD (Reisberg, Gordon, McCarthy, et al., 1985) there have been a multitude of studies which report over estimation of ability by AD patients for activities of daily living, self-care and grooming, and of course memory (Kaszniak, 2010, Salmon, Perani, Collette, et al., 2008, Clare & Wilson, 2006). There has been a suggestion that level of discrepancy increases in line with the progression of illness in AD when measure over a period of 12-20 months (Derousen  et al, 1999, Vasterling, Seltzer & Watrous, 1997). However, Linda

Clare and Wilson reported only a minor, non-significant, change in discrepancy reports over a period of one year. This is particularly interesting as patient scores on the mini-mental state exam (MMSE; Folstein et al., 1975) decreased over the same period suggest a disparity between cognitive symptoms and levels of insight (Clare et al., 2006). Also, changes in discrepancy scores were observed in both patients and informants. Several other studies have reported findings similar to those of Clare and Wilson (e.g. DeBettignies, Mahurin, & Pirozzola, 1990; Kotler-Cope & Camp, 1995). Starkstein (2014) has previously described how anxiety, perceived burden and depression can impact on the accuracy with which carers assess ability on ADL's, often underestimating the competence of the patient.

Evidence from neuroimaging techniques is also characterized by inconsistency. However, the vast majority of studies have highlighted right frontal abnormalities as playing an important role in the phenomenon of anosognosia, particularly in superior dorsolateral frontal and lateral frontal regions (Starkstein & Power, 2010). For instance in an fMRI study Ries and colleagues reported a significant negative correlation between discrepancy scores on the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm, 2004) and activation of medial prefrontal and posterior cingulate regions (Ries, Jabbar, Schmitz, et al., 2007). Cortical activation in this case was measured while participants viewed a word stream, containing adjectives such as calm, obnoxious, creative, sharp, and had to decide whether these words accurately described their personality. Starkstein and colleagues (1995), using a single-photon emission computed tomographic scans, have also

suggested that impaired insight in AD may be more linked to dysfunction of the dysfunction of the right inferior and dorsal regions rather than to diminished cognitive function.

It is important to highlight the role of right hemispheric regions in anosognosia in light of our previous assertion that the rDLPFC is also of vital importance to many of those cognitive functions required for task maintenance and error processing. What this perhaps suggests is that those with AD who overestimate their ability on a discrepancy measure will also show diminished ability to negotiate a task reliant on sustained attention and error assessment. It will further require them to inhibit responses, placing further pressure on executive network. There have until now been no examination of explicit error awareness / signaling in an AD population. While we previously discussed electrophysiological reports of Pe elicitation in AD participants, these patients did not have to signal their errors.

1.8 Structure of Thesis

Having considered the evidence from both the healthy ageing literature and pathological aspects of insight in Alzheimer's Disease, this thesis aims to add a novel perspective into the domain of error processing. Chapter 2 is an assessment of age related differences in both the behavioural and electrophysiological aspects of performance on a newly developed Go-No task. While Chapter 3 is an extension of this line of enquiry, there is also an exploration of the ability of those with a diagnosis of Alzheimer's type dementia to explicitly signal their errors. Chapter 4 describes the impact that individual traits such as anxiety and depression may have on the process of

error monitoring. In Chapter 5 we present a general analysis of these finding and discuss methodological issue and potential lines of inquiry for future research.

Chapter 2

Older Adults are Less Aware but More Accurate than Younger Individuals

2.1 Introduction

At the outset of the previous chapter we discussed the exceptional challenges faced as a result of the exponential population expansion of those whom society deem to be elderly and therefore in a state of both mental and physical decline (e.g. *World report on ageing and health*; WHO, 2015). Concurrent to this population growth there has been an increase in the number of research hours dedicated to geriatric neurological function, though understandably these often address pathological domains such as Alzheimer's disease (AD), Parkinson's disease (PD), cerebrovascular accident (CVA) and cardiovascular disease (CVD). In more recent times there has been a concerted effort to further elucidate on the cognitive and physiological effects of aging in healthy populations. However, much of what is discussed in terms of geriatric cognitive processing is framed, perhaps unintentionally, in a somewhat negative light. Several studies have in fact shown that the 'aging' brain is capable of remarkable compensatory and adaptive function, where previously dedicated systems and structures are recruited to cope with progressive cerebral changes (Cabeza, Anderson, Locantore & McIntosh, 2002; Park & Lorenz, 2009). The current chapter will seek to avoid the prevailing narrative

as it examines the phenomenon of error processing in older adults. It will explore potential age-related differences in the cognitive, electrophysiological and behavioral aspects of error processing with a specific focus on error awareness.

Erroneous behaviour is a common feature of human activity. Though there may unfavourable short-term consequences, errors can quite often provide long-term benefits as they teach us to modify our behaviour and inform us on our ability to carry out certain tasks. An essential part of corrective action is awareness of ones errors, for if I am unaware I cannot evaluate and modify my behavior, at least consciously. It would thus seem to follow that compromised self-awareness or insight, will lead to compromised error processing (Robertson; 2014, Harty, 2013).

Impaired self awareness as a result of one's illness, often termed anosognosia (Babinski, 1914; McGlynn & Schacter, 1989; Prigatano 2010), is a common phenomena associated with many clinical conditions and has been implicated in negative outcomes for several clinical populations including, Alzheimer's disease (Starkstein et al., 1995), frontotemporal dementia (O'Keeffe, Murray, Coen, Dockree, Bellgrove, Garavan, Lynch & Robertson; 2007a), traumatic brain injury (O'Keeffe, Dockree, Moloney, Carton & Robertson, 2007), hemiplegia (Bottini, Paulesu, Gandola, Pia, Invernizzi & Berti, 2010) and Schizophrenia (David, Bedford, Wiffen & Gilleen, 2012). Importantly, in light of our current study, there is also a growing body of evidence to suggest that a diminution of awareness and diminished ability to monitor performance

is characteristic of the healthy aging process (Burke & Shafto, 2004; Gold, Powell, Xuan, Jicha & Smith, 2010; Harty, et al., 2013; Young & Bunce, 2011). However many would dispute the impact of this perceived degradation, claiming it to be somewhat overstated (Clare, Whitaker & Neilis, 2010; Rabbitt, 2002; Verhaeghen, 2011).

High levels of vigilance and insight are required in order to successfully perform even the most basic of our daily activities (Harty et al., 2013, Robertson, 2010; Robertson, Manly & Andrade et al., 1997). Awareness in goal directed behavior, perhaps unsurprisingly, has been shown to rely heavily upon vigilance and sustained attention (Corbetta & Shulman, 2002; Hoerold et al., 2008; O’Keeffe et al., 2007; Robertson, 2010) Of equal importance is our ability to accumulate sufficient evidence in order to make a decision as to whether an error has been committed (Steinhauser & Yeung, 2012; Steinhauser & Yeung, 2010). There does however seem to be a lack of consensus in the literature regarding age related effects on attention (Gold et al., 2010), For instance, it has been reported that older individuals are less likely to engage in mind wandering or daydreaming, which in turn helps them to compensate for age related decrement in executive function by avoiding task unrelated thoughts (Christoff et al., 2016; Maillet et al., 1998). Others suggest that older individuals regularly outperform younger counterparts in their ability to sustain their attention in the absence of any meaningful exogenous stimulation (Carriere et al., 2010).

In recent times much has been done to expound upon both the behavioural and neurophysiological structures and systems which enable us to monitor and successfully maintain adequate performance levels (for a review see Ullsperger, 2014), and as is often the case, the most fruitful method for studying this construct has been when we encounter what one might term a performance monitoring systems failure. Though behavioural markers such as the speed accuracy trade off, post error slowing and improved performance following an error (Laming, 1979) have provided us with identifiable signatures associated with erroneous behaviour, the enormous strides made using electrophysiological measures such as fMRI, EEG and electrodermal activity (EDA) have allowed us to gain an in depth understanding of what occurs not only pre and post error commission, but also at the very moment that the aforementioned systems failure occurs (Murphy et al., 2012; O'Connell et al., 2009).

As was mentioned in Chapter 1, electroencephalographic evidence on the nature of error detection has consistently identified two event related potentials (ERP's), the error related negativity (ERN; Falkstein, 1990) and the error positivity component (Pe; Falkstein, 1991) as key neural signatures of erroneous behavior. Originating in the medial prefrontal cortex, and more specifically the anterior midcingulate cortex (aMCC), the ERN is a fronto-centrally located waveform which deflects and negatively peaks 20-100ms following an erroneous response. It seems to be evoked regardless of whether an error is consciously detected or not (Ullsperger & Von Cramon, 2001; Wessel, Danielmeir, Morton & Ullsperger, 2012). The parietal and rostral

anterior cingulate cortex (rACC) generated Pe is a positive waveform which peaks in centro-parietal regions 300-500ms following an error, thus far it has only been recorded in participants who have consciously perceived their errors (Endrass, Franke & Kathmann, 2005; O'Connell, Dockree, Bellgrove, Turin, Ward, Foxe & Robertson, 2007; Murphy, Robertson, Allen, Hester & O'Connell, 2012, Ullsperger, 2014). Whilst the ERN is potentially a preconscious marker that arises as a result of response conflict (Yeung et al, 2004), the precise nature and neural substrates of the Pe remain less clear (Shalgi et al., 2009; Ullsperger, 2014). Recent evidence by Murphy and colleagues has suggested that the Pe reflects a rapid internal decision making process whereby the build up rate, latency and amplitudinal peak of the Pe reflect and track evidence accumulation and the emergence of awareness following a commission error (Murphy et al., 2012). There have also been several studies which suggest that the amplitude of both the ERN (Band & Kok, 2000; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000; Mathalon et al., 2003; Mathewson, Dywan, & Segalowitz, 2005) and the Pe (Band & Kok, 2000; Falkenstein et al., 2000; Leuthold & Sommer, 1999; Mathewson et al., 2005) are attenuated in older individuals when compared to younger participants.

Functional imaging studies have also played a key role in identifying several important cortical regions which are implicated in active self-awareness, with the right dorsolateral prefrontal cortex (rDLPFC) considered to be of particular significance (Manly et al., 2003; Rosen, Alcantar, Rothlind, Sturm, Kramer, Weiner & Miller, 2010). Evidence for this link has also been found in several clinical populations including Alzheimer's disease and

attention deficit/hyperactivity disorder (Starkstein, 1995; O'Connell et al., 2009). Within our own laboratory Harty and colleagues have successfully highlighted this relationship by demonstrating that the application of anodal transcranial direct current stimulation (tDCS) over the right, but not the left, dlPFC in a healthy population of older individuals produces a significant increase in levels of error awareness (Harty, 2014). As the effects were seen in the right dlPFC only, one could interpret these results as supportive of the 'Hemispheric Asymmetry Reduction in Older Adults' (HAROLD; Cabeza, 2002) model which suggests that age-related neurofunctional changes are characterized by a significant reduction in the functional lateralization in the prefrontal cortex. What the HAROLD essentially posits is that prefrontal activity during cognitive performance is somewhat less lateralised in older adults. Cabeza suggests that this phenomenon is largely compensatory in nature and is likely to be task dependent. For a more in depth review of HAROLD and other models, including the Compensation-related utilisation of neural circuits hypothesis (CRUNCH; Reuter-Lorenz & Cappell, 2008) see Berlingeri, Danelli, Bottini, Sberna & Paulesu (2013).

Importantly, what Harty's work also suggests is that though older individuals regularly display compromised awareness in laboratory tasks, one's ability to monitor their own performance is a dynamic process which may benefit from intervention.

In the present study we aim to further elucidate on these previous findings by assessing levels of error awareness/insight using a modified

version of Hester et al's error awareness task (EAT; Hester, Foxe, Molholm, Shapner & Garavan, 2005) and a series of psychometric measures. The error awareness dot task, EADT, is a Go No-Go task which requires participants to acknowledge commission errors as they occur. It was decided to create a novel version of the EAT primarily to reduce the level of task difficulty. Hester's original task, though not overly complicated, requires participants to retain and act upon several operational rules; including the avoidance of repeated stimuli and incongruent stroop stimuli while also requiring participants to acknowledge errors (see **Figure 2.1**). Though this in and of itself is not particularly problematic, stimuli which require additional cognitive resources (in this case word recognition and processing) may unduly impact on the variable being recorded, specifically the ERN and Pe components. It was felt that by adapting and simplifying the stimuli presented we could still reliably capture the underlying cortical and behavioural phenomena associated error processing.

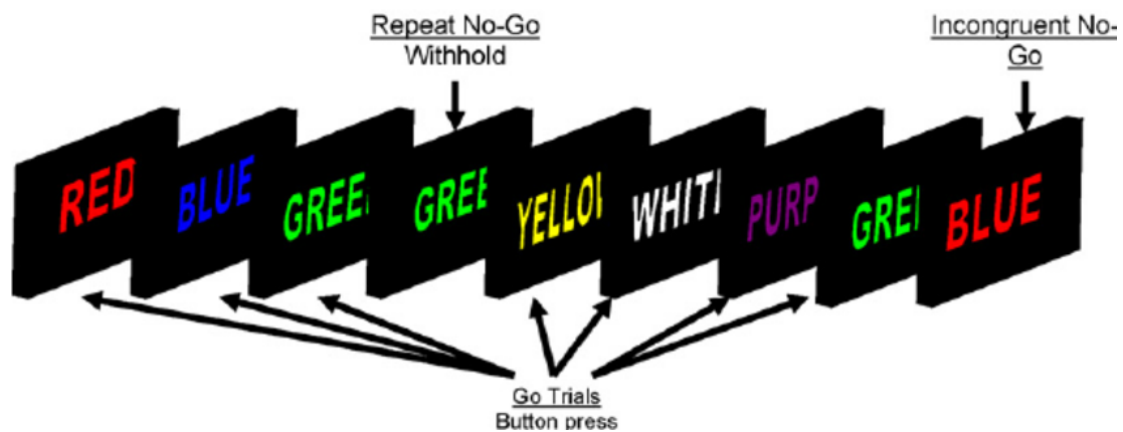


Figure 2.1 Error-awareness task (EAT; Hester et al., 2005). The EAT presents a serial stream of single color words in congruent fonts. Participants respond to each of the words with a single 'Go trial' button press, and withhold this response if the same word was presented on two consecutive trials (Repeat No-go) or if the word and font of the word did not match (Stroop No-go). To indicate 'error awareness' participants press the go-trial button twice following any commission errors.

The inclusion of the Cognitive Failures Questionnaire discrepancy measure will allow us to assess a potential relationship between online error awareness and diminished insight in daily functioning (CFQ; Broadbent, Cooper, Fitzgerald and Parkes, 1982). While such a relationship has suggested (Jenkinson, Edelstyn, Drakeford, & Ellis, 2009; Larson & Perlstein, 2009) and previous research by Harty and colleagues (2013) has empirically demonstrated a link between these two factors, further evidence is required to identify the robustness of this hypothesis. In line with previous research we predict that older adults will display lower levels of error awareness when compared to their younger counterparts, but in doing so we aim to uncover

and examine previously unidentified factors which contribute to this phenomenon.

2.2 Materials & Methods

Participants

Fifty-eight participants volunteered to take part in the study. Older participants were recruited via the Trinity College Institute of Neuroscience (TCIN) participant panel, while younger participants were drawn from the student body of the School of Psychology, Trinity College Dublin. A number of older participants ($n=5$) were excluded from the final analysis due to their inability to complete the EADT. Exclusion was due to the fact that these participants could not complete the training process for the task, where individuals are required to exhibit a relevant level of test proficiency, this includes demonstrating that they understood and could execute the error correction response 'ECR'. Subsequently, shortly after the testing session it emerged that two participants had in fact been diagnosed with MCI. A final sample of 53 participants; 29 young (19 female) and 24 older (15 female) were included in the final analysis. The younger participants had a mean age of 24.14 years ($SD = 5.4$), whilst the older participants had a mean age of 70.67 years ($SD = 4.9$). All participants reported no history of psychiatric illness, head injury or photosensitive epilepsy, had normal-to-corrected vision and no history of color-blindness, with 1 left-handed (1 older male). Older participants on the TCIN participant panel are screened for motor issues or pharmacological prescriptions which may impact on their ability to engage in

research of this kind. There were no reports of attentional issues, such as attention deficit disorder (ADD) or attention deficit hyperactivity disorder (ADHD) amongst our younger participants. All participants were asked to refrain from consuming caffeine products for twelve hours prior to testing. Written informed consent was provided before testing began, and all procedures were approved by the Trinity College Dublin ethics committee and in accordance with the Declaration of Helsinki.

Psychometric battery /Background Measures

Prior to EEG recording all participants completed a series of standardized psychometric tests aimed at assessing cognitive function at the time of testing. Measures included were the Mini Mental State Exam (MMSE; Folstein, Folstein & McHugh, 1975), the Clock Drawing Task (CDT;), the National Adult Reading Test (NART; Nelson, 1982; Nelson & Wilson, 1991), Cognitive Failures Questionnaire (CFQ; Broadbent et al., 1982) and the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983).

Error Awareness Dot Task (EADT), Parameters and Procedure

As part of our protocol we developed the Error Awareness Dot Task (EADT); a novel variant of Hester and colleagues Error Awareness Task (EAT; Hester et al., 2005, 2012). The EADT employs a Go/No-Go paradigm that requires participants to signal errors of commission via a motor response (see **Figure 2.2**). Participants view a series of randomized, differently coloured, on screen dots. As soon as each dot appears participants are required to

acknowledge its appearance by performing a left click on a computer mouse, there are however two conditions under which participants are required to withhold responding: (i) if the colour of the dot is blue – *colour condition* (ii) if the colour of the dot is identical to the colour which preceded it – *repeat condition*. If a participant does commit an error of commission they are required to acknowledge it by making a second speeded mouse click, this time using the right side of the mouse; the error correction response (ECR). Participants are asked to perform this task as quickly as possible whilst also being reminded that accuracy is of equal importance.

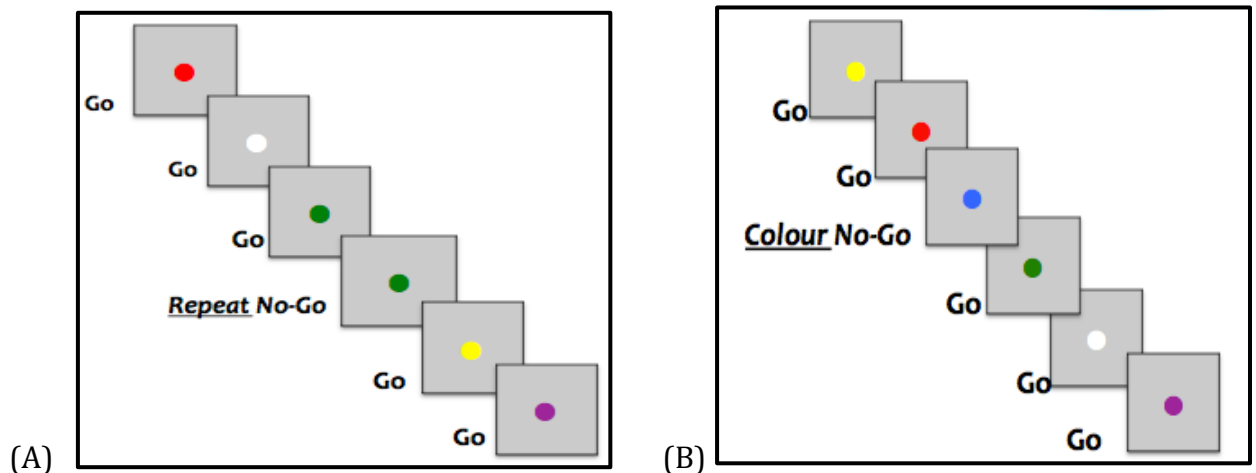


Figure 2.2 The Error Awareness Dot Task (EADT) is a Go/No-Go task which requires participants to make a speeded response via a button press as soon as a coloured dot appears on screen. However, participants must withhold responding when the colour that appears is a repeat of the previous colour **(A)** and for all instances of the colour blue **(B)**. Should participants fail to withhold they are required to acknowledge their error via a second button press, the error correction response (ECR).

In order to minimize the risk of participant variability as a result of task difficulty becoming a potential confounding factor the EADT uses an adaptive 'staircase' method similar to that successfully employed by Harty et al. (2013, 2014). Participant performance is continuously assessed throughout each block by evaluating the accuracy of their responses after each set of 40 trials. If participants achieve accuracy levels of between 50 and 60% the stimulus duration remains at 750ms, the starting duration for all participants. However, should accuracy levels drop below 50% the stimulus duration increases by 250ms to 1000ms, conversely should participants achieve accuracy levels >60% a 250ms decrease in stimulus duration is imposed, meaning that for at least the next 40 trial stimulus duration will be set at 500ms. This accuracy assessment and time adjustment continues every 40 trials. The inter-stimulus interval (ISI) remains stable at 750ms throughout testing. Each task block consists of 200 trials, one hundred and seventy-six of which are Go trials and twenty-four are No-Go (8 colour condition No-Go's and 16 repeat condition No-Go's). Participants completed eight blocks of the task with each lasting approximately 6 minutes.

Prior to testing participants engaged in a practice block in which they were required to display an understanding of the task parameters by successfully negotiating three consecutive No-Go trials, this could include an error of commission followed by an appropriate awareness press. Once participants had achieved this result they were deemed capable of engaging in the full-length version of the task.

All visual stimuli were presented on a gray background and participants were instructed to align their focus with a white fixation cross which remained on screen and was positioned under the centrally located task stimuli. A 55-cm LCD monitor with a 120-Hz frame rate was used to display all task stimuli. The EADT was developed using **Presentation®** software developed by Neurobehavioural Systems.

The Mini Mental State Exam

The Mini-mental state exam (MMSE; Folstein, Folstein & Hugh, 1975) is perhaps one of the most widely used cognitive tests when assessing elderly patients both in a laboratory and a clinical setting (see **Appendix A**).

Though it has been criticized by many as lacking the ability to access for instance executive function, it is quite often the only cognitive measure which at risk patients will encounter prior to engagement with a clinical team. MMSE scores have been consistently shown to correlate with elements of cognitive dysfunction and as a result it is often used in clinical settings as a first response tool in the assessment of suspected dementia.

CFQ

The CFQ is a well-established measure of attentional control in everyday life. It is a 25-item scale which focuses on performance of activities of daily living (ADL's) such as one's ability to sustain attention whilst reading, locating items in a supermarket, forgetting people's names, forgetting appointments and failing to recognize signposts on the road (see **Appendix B**).

Importantly it records one's ability to recognize a decrement in carrying out these tasks. The CFQ utilizes a discrepancy scoring method whereby a significant other, relative or carer, completes the same questionnaire in relation to the participants behavior with the recorded differential in score acting as a proxy measure of the participants level of insight into their own performance of ADL's. Though there has been much criticism of discrepancy measures in the past, scores on the CFQ have consistently been shown to correlate to indices of attention (Harty et al., 2013; Manly, Robertson, Galloway & Hawkins, 1999; Robertson et al., 1997).

Clock Drawing Test (CDT)

Regarded by many as the gold standard in psychometric cognitive assessment the clock drawing task was originally used as a measure of attention in hemi-neglect patients. It is an easy to administer 'bedside' test regularly employed in the assessment of cognitive dysfunction and dementia severity/progression, stroke, traumatic brain injury and Parkinson's disease. Its virtues as a diagnostic measure have been widely extolled throughout the literature with various authors reporting scores of 85% for both validity and reliability (Pinto & Peters, 2009; Schulman, 2000). One of the many benefits of the CDT is that it is multi-dimensional, in that it examines elements of executive function through organization and planning, visuospatial awareness, language skills, abstraction and numerical ability (Kirby, Denihan & Bruce et al., 2001). Also, as it taps into such a wide array of cognitive skills it has been

suggested that a high level of integrative cortical function is required for successful completion of the CDT (Thomann, Toro & Dos Santos et al., 2008). Whilst the vast majority of research carried out using the CDT is in the clinical sphere there is a growing body of literature that employs it as a normative tool. As is the case with most psychometric measures there are of course certain limitations, and in the case of the CDT these are often associated with patient levels of education, literacy and linguistic ability (see Pinto & Peters, 2009). Participants were required to draw an analogue clock face and set the time to ten past eleven. The St. Vincents University Hospital, Dublin five point scoring system was used to evaluate performance where;

- 1 point is awarded for the clock circle.
- 1 point is awarded for all the numbers being in the correct order.
- 1 point is awarded for the numbers being in the correct spatial position.
- 1 point is awarded for inserting two hands of the clock.
- 1 point is awarded for the correct time

Participants who achieve a score of ≥ 4 are considered to be within the normal range.

HADS

Much like the CDT the HADS (Zigmond & Snaith, 1983) is a widely used test aimed at measuring anxiety, depression and overall emotional distress (Johnston, Pollard & Hennessey, 2000). Again it is a quick and easy to administer measure and whilst it may not provide an in depth insight into the

psychological well being of a participant it is nonetheless capable of identifying anxiety and depression related symptoms at the time of testing.

NART

The NART is a widely used psychometric tool for the assessment of preclinical intelligence (IQ) in clinical populations. Participants are required to read and pronounce a list of fifty. An Estimated Full Scale IQ score is then calculated as $-127.7 - 0.826 \times \text{NART error score}$.

Electroencephalography Acquisition and Statistical Analysis

The ActiveTwo System (BioSemi) was used to record all EEG data. 64 scalp electrodes were applied using the recognized 10-20 placement system and before being digitized to 512 Hz. 2 EOG electrodes were placed at the outer cantus of each eye and a further 2 were positioned above and below the left eye. 2 electrodes were placed at the left and right mastoid area. Continuous EEG data were re-referenced offline to the average reference, high-pass filtered to 0.5Hz, low-pass filtered up to 95Hz and notch-filtered at 50Hz. Noisy EEG channels were interpolated using spherical spline interpolation. All data was processed using EEGLAB formulated scripts designed to read BDF files in MATLAB_R2014b. In order to facilitate our analysis on relevant ERP's it was decided to time-lock our analysis to participant correct go responses, error commission responses and the error correction responses (ECR's). The build up rate, latency and peak amplitude for the ERN and Pe was calculated for each individual participant. Following a detailed analysis of grand average

topographies it was decided to calculate the ERN at the FCz electrode where an epoch of 1200ms was extracted, this constituted a period 400ms prior to and 800ms post the erroneous responses on each no-go target. The ERN was defined as the peak negative amplitude 30-120ms following an erroneous response; it remained error response locked in all subsequent analysis. The same epoch was extracted for the purpose of Pe analysis, however it was derived from the Pz electrode, this was again based upon previous models and an analysis of grand average topographies. The error aligned Pe in this instance was defined as the time at which the peak positive amplitude occurs within a 300-500ms period following an erroneous response. The 'awareness' aligned Pe was measured at the moment in which a participant signals that an error has been committed and is locked to the ECR. The extracted epoch for this particular ERP was 600ms prior to the ECR and 200ms post the awareness press. The error-aligned was defined as the time at which the peak positive amplitude occurred during the period 300ms prior and 200ms post the ECR. The error aligned build up rate of the Pe was calculated by measuring the slope of this waveform 75-200 milliseconds post error commission, whilst the awareness aligned Pe constituted the slope 375-225 prior to participant ECR.

All subsequent statistical analysis was performed using IBM SPSS Statistics Version 22. Participant awareness levels for the EADT were calculated as the percentage of no-go errors which each participant successfully signaled. Participant accuracy was calculated as the percentage of no-go targets that a participant correctly withheld on. All neuropsychological tests and EADT data was analysed using one-way ANOVA's and

bivariate/partial correlations. Post-hoc analysis was conducted by filtering groups as required and performing Bonferroni adjusted paired and independent sample t-tests.

2.3 Results

A summary of the demographic data for both groups is listed in **Tables 2.1** and **2.2**. Participants did not significantly differ with regard to the number of years they had spent in formal education, NART full scale IQ, HADS, HADS depression, HADS anxiety or performance on the CDT (all $p > .11$). Interestingly both groups reported similar levels of cognitive disturbance on the CFQ, with neither the participant, relative or discrepancy scores reaching significantly different levels (all $p > .63$). Younger participants did however score significantly higher than their older counterparts on the MMSE ($F(1,48) = 4.85, p = .032$).

Table 2.1 Demographics and Psychometric Data. Older and Younger participants differed only in MMSE scores. The Mean $\pm$ SD is reported for each group.

	YA (n=29)	OA (n=24)
Mean Age	24.14 $\pm$ 5.4	70.67 $\pm$ 4.94
Age Range	18 – 34	65 – 80
Sex	19 F, 10 M	15 F, 9 M
Handedness	27 right, 2 left	24 right
Years of education	16.96 $\pm$ 2.35	15.71 $\pm$ 2.97

These results suggest that participants were matched on several key factors and whilst a small, yet significant, difference was observed between groups on MMSE scores, older participants still remain well within the accepted range for healthy cognition. This difference likely represents expected age related cognitive effects. It is perhaps more significant that all older participants successfully completed the CDT, a measure considered by many to be far more sensitive when identifying clinically relevant cognitive impairment.

Table 2.2 Psychometric Data. Older and Younger participants differed only in MMSE scores The Mean $\pm$ SD is reported for each group.

	YA (n=29)	OA (n=24)
NART	114 $\pm$ 3.68	116.27 $\pm$ 5.18
MMSE*	29.44 $\pm$ 0.7	28.73 $\pm$ 1.52
Clock Drawing Test	4.92 $\pm$ 0.28	4.79 $\pm$ 0.42
CFQ Participant rating	35.79 $\pm$ 10.59	36.12 $\pm$ 12.15
CFQ Informant rating	29.25 $\pm$ 14.48	26.38 $\pm$ 10.70
CFQ Discrepancy	7.47 $\pm$ 13.89	8.33 $\pm$ 12.01
HADS	9.54 $\pm$ 6.09	8.69 $\pm$ 4.81
<i>Anxiety</i>	6.77 $\pm$ 3.70	6.18 $\pm$ 3.25
<i>Depression</i>	2.77 $\pm$ 2.86	3.06 $\pm$ 2.63

*** p<.001; ** p<.01; * p<.05. Indicates a main effect of group.

Performance on the EADT

Both older and younger performance related results for the EADT are summarized in **Table 2.3**. Older participants achieved higher levels of accuracy; withholding on No-Go trials at a significantly more successful rate compared to younger participants ($F(1,50) = 6.59, p < .05$). Younger participants on the other hand were significantly more aware of their commission errors ($F(1,50) = 14.37, p < .001$) (see also **Figure 2.2**). In order to assess the possibility that this main effect of group was perhaps related to participant accuracy, we performed a bivariate correlation where it was found that overall levels of awareness were not significantly correlated with accuracy in either the old ($p = .97$) or younger group ($p = .956$). Following this an analysis of covariance was conducted, controlling for levels of accuracy within each group, from which we determined that awareness was still significantly higher in younger participants ($F(2,49) = 12.88, p = .001$).

Table 2.3. Group accuracy, levels of error awareness mean commission error reaction times, stimulus duration times and error signaling response.

	YA	OA
Accuracy (%)*	61.41 ± 12.65	69.59 ± 12.69
Error Awareness (%)***	92.41 ± 6.35	82.16 ± 12.70
Mean Go trial RT (ms)***	299.16 ± 56.66	407.88 ± 56.51
Mean Error RT (ms)**	311.6 ± 71.94	400.47 ± 122.03
Mean Error RT (Aware Errs; ms)***	297.91 ± 42.36	378.98 ± 59.32
Mean Error RT (Unaware Errs; ms)	449.02 ± 246.09	554.36 ± 237.19
Mean ECR RT (ms)**	129 ± 87.82	200.09 ± 101.90
Stimulus Duration (ms)	643.16 ± 76.75	621.50 ± 73.10

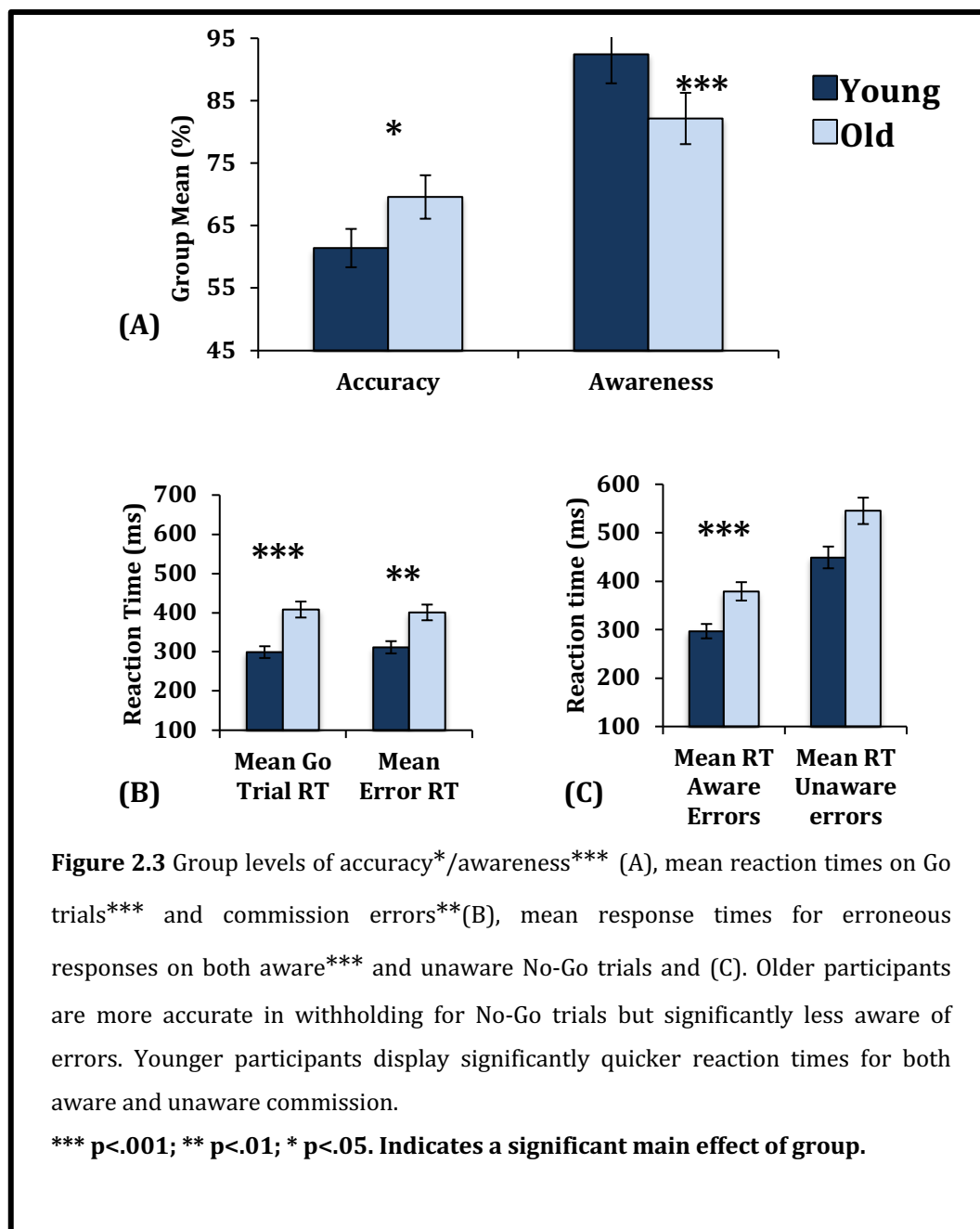
*** $p < .001$; ** $p < .01$; * $p < .05$. Indicates a main effect of group

Response times for *Go* targets on the EADT were significantly faster for younger participants ($F(1,51) = 48.46, p < .001$). This trend continued across all response types with older participant RT's for error responses, whether aware or unaware, significantly slower than the younger group ($F(1,50) = 10.76, p = .002$.) A main effect of group was also observed in relation to the average time it took participants to acknowledge their errors (ECR) with younger participants again responding at a faster rate ($F(1,50) = 7.11, p = .01$).

In order to further investigate mean RT's on errors a mixed factorial ANOVA was conducted. The between-subject factor was Group (young, old) and the within-subject factor was Awareness response (Aware, unaware). There was a main effect of Group ($F(1,46) = 5.79, p < .05$) indicating that the older participants were slower in RT, irrespective of the type of awareness response. In addition, there was a main effect of the awareness response showing that all participants were slower on unaware errors ($F(1,46) = 18.52, p < .001$).

It was also found that participant response times for go trial were correlated with RT's on unaware errors in younger ($r(29) = .76, p < .001$) and older participants ($r(23) = .59, p = .003$). A similar relationship between RT's for go trials and aware errors did not materialize (all $p > .77$).

Upon further analysis we found that in the older group overall levels of error awareness were lower in those who took longer to signal errors which they were aware of ($r(23) = -.45, p = .033$), this was not the case in younger participants ($p = .6$).



Whilst older participants did indeed display slower reaction times it would seem that this was not the result of increased stimulus duration providing a longer window in which to make a decision. In fact older participants were on average exposed to the stimuli for a shorter, though not significantly so, period of time.

Electrophysiological Data and ERP Analysis

The grand average waveforms and spatial topographies for the error aligned ERN component of aware errors is displayed in **Fig 2.3**. There was a main effect of group with younger participants displaying a significantly higher amplitude than their older counterparts ($F(1,49) = 4.43, p = .041$), however older adults had similar peak latency with no main effect of group being recorded ($p = .272$).

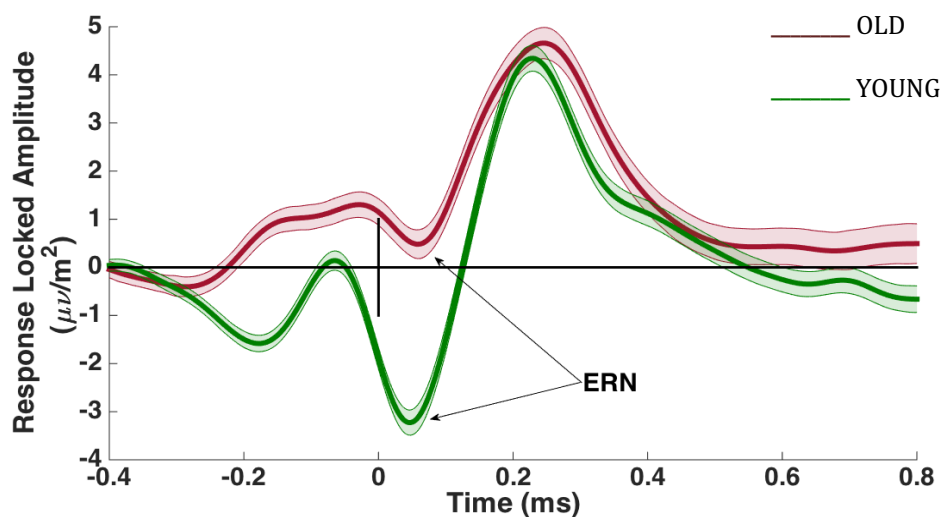


Figure 2.4 Error Related Negativity (ERN). Waveforms are for aware errors and are locked to participant erroneous responses at FCz. Younger participants exhibit a significantly greater negative amplitude deflection than older participants* in the immediate aftermath of aware errors (0-100ms). Topographies represent a window that is 0-100ms post the erroneous response. *** $p < .001$; ** $p < .01$; * $p < .05$.

The grand averages and spatial topographies for the Pe, when both error and awareness aligned, are displayed in **Figure 2.5** and **Figure 2.6**. In

terms of error positivity there was a main effect of group on Pe amplitude when participant responses were aligned with the commission error ($F(1,49) = 17.51, p < .001$). However, a more pronounced relationship was identified when the Pe was aligned to the point at which participants signal their awareness. When evaluated at this juncture the younger group exhibited significantly higher Pe peak amplitude compared to the older group ($F(1,49) = 14.4, p < .001$).

When responses were error aligned there was a main effect of group on the build up rate of the Pe component ($F(1,47) = 4.16, p < .05$). This was matched by a more substantial main effect of group when participant responses were aligned to the awareness press ($F(1,48) = 9.05, p < .005$) suggesting that the Pe is more closely linked to the awareness response than the commission error and that regardless of alignment younger participants have much higher build up rate than older participants.

As with the ERN, no main effect of group for Pe latency was identified when either response locked ($p = .79$) or awareness locked ($p = .6$).

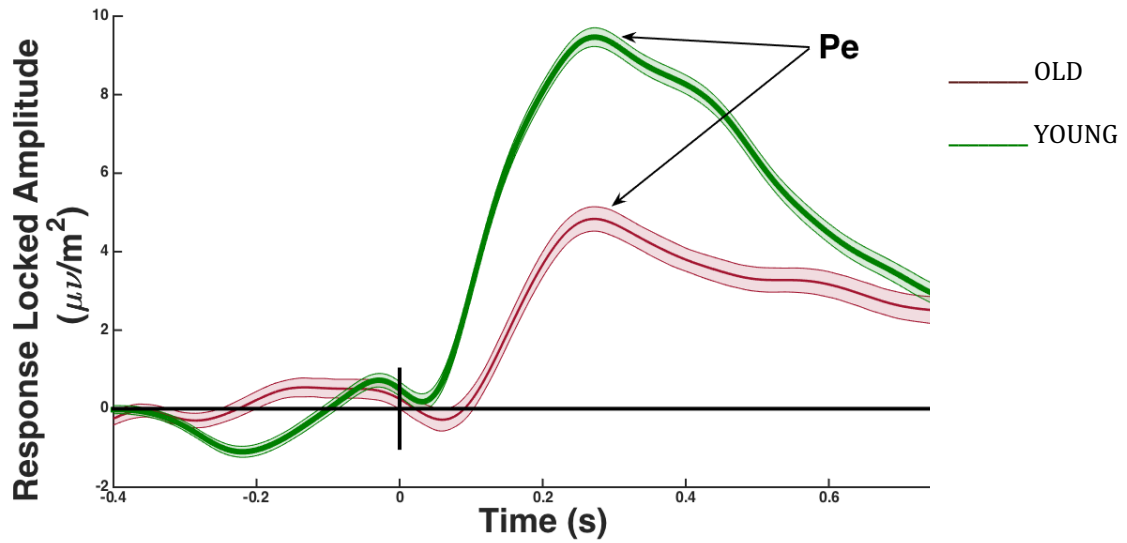


Figure 2.5 Error aligned *Error Positivity component (Pe)*. Younger participants recorded significantly higher Pe amplitude than the older group*** although Pe latency did not differ significantly between groups. A significantly steeper build-up rate of the Pe was identified in younger participants. *** $p < .001$; ** $p < .01$; * $p < .05$.

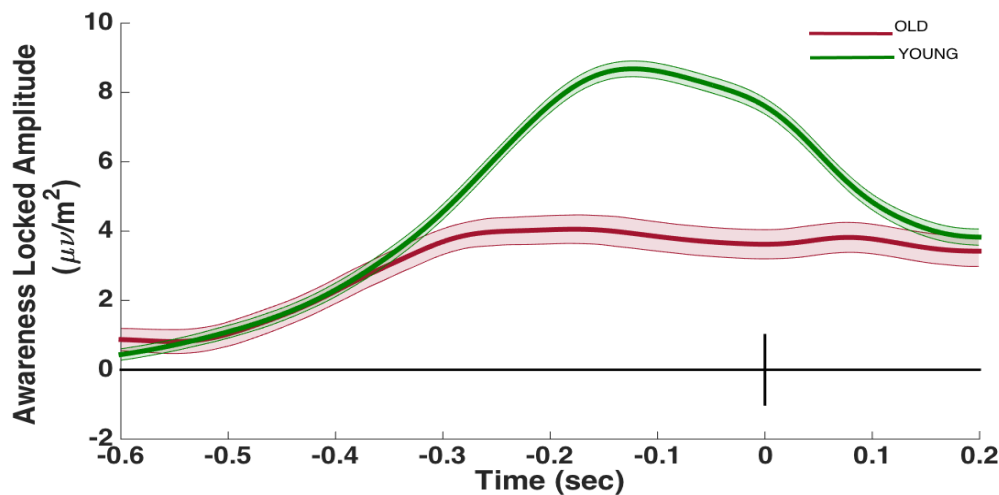


Figure 2.6 Awareness aligned *Pe*. Younger participants recorded significantly higher Pe amplitude than the older group*** although Pe latency did not differ significantly between groups. The Pe was aligned to the centro-parietal Pz electrode in both groups and topographies represent - 100 – 0ms prior to the error awareness response. A significantly steeper build-up rate of the Pe was found in younger participants*. *** $p < .001$; ** $p < .01$; * $p < .05$.

The EADT & ERN/Pe Amplitude, Latency and Build-Up Rate

Overall levels of error awareness on the EADT did not correlate with the awareness or response aligned amplitude, build-up rate or latency of the Pe in either group (all $p > .18$). Nor did participant accuracy on the EADT correlate with the amplitude, build-up rate or latency of the awareness and error aligned Pe component (all $p > .14$).

The peak amplitude and latency of the awareness aligned Pe did not correlate with mean reaction times for aware errors for older and younger participants (all $p > .57$). Nor did we see a significant relationship between awareness aligned Pe amplitude and the time it took participants to signal their awareness (ECR) following an error in both the young ($p = .864$) and older group ($p = .569$).

In younger participants a slower build-up rate ($r(29) = .43, p = .02$) and later latency ($r(29) = .46, p = .01$) of the error aligned Pe was significantly correlated with slower initial response times for aware errors. This was not the case for older participants (all $p > .56$). No other significant correlations were identified regarding any aspects the Pe component, whether awareness or response aligned, and the aware error response times or ECR response time for both groups (all $p > .189$).

Whilst a larger awareness locked Pe peak amplitude was significantly correlated with an increased build-rate of the Pe in younger participants ($r(28)$

= .765, $p < .0001$) a similar relationship was not discovered in the older group ($p = .501$).

Higher levels of awareness were associated with increased amplitude ($r(21) = .51, p = .02$) and earlier elicitation ($r(21) = .7, p = .002$) of the ERN in the older but not the younger group (all $p > .55$).

Psychometric measures, Error Awareness and Electrophysiology

Lower levels of error awareness in our older group were significantly correlated with lower participant scores on the MMSE ($r(22) = .532, p = .01$); the only measure which at the outset produced significantly different values. Older participant performance on the MMSE was also significantly correlated with the latency of the awareness aligned Pe ($r(22) = .45, p = .041$).

No other correlations arose between the awareness/accuracy scores on the EADT and psychometric or electrophysiological measures in the older group (all $p > .08$).

In younger participants awareness and accuracy did not correlate with any of the recorded variables from our psychometric battery (all $p > .14$) or electrophysiological measures (all $p > .13$).

Discussion

Much has been done over the past number of years to elucidate on the structures underlying error awareness (Ullsperger, 2014). In more recent times our own laboratory has sought to further this knowledge by examining potential differences not only in clinical populations but also between older and younger adults. By doing so we have gained an insight into the profound cognitive changes which occur over the lifespan (e.g. see Harty et al, 2013). The principle aim of this chapter is not only to underscore these recent findings but also to attempt to evaluate some of the age-related characteristics of error processing and awareness. We sought to do this by comparing the behavioural and electrophysiological data for competing age groups on a range of established measures and our newly developed Go/No-Go task, the EADT. The current data seems to suggest that when engaging in a task such as the EADT, error awareness is diminished in older individuals while accuracy is largely preserved due to elevated levels of sustained attention. While lower levels of awareness on the EADT were related lower scores on the MMSE in older individuals they were not however related to participant insight regarding daily cognitive functionality.

Upon analysis we found that older participants demonstrated significantly lower levels of error awareness on the EADT when compared to younger individuals. Older adults did however display significantly higher levels of task related accuracy, despite the inclusion of an adaptive 'staircase' design aimed at equating performance between high and low scoring individuals. It is possible however that the unintentional consequence of this

potential design flaw may have, somewhat serendipitously, illuminated the age-related strategic tendencies of our participants.

As a result of increased levels of accuracy, older adults have in fact a shorter exposure to on screen stimuli and it thus follows that they have less time in which to make a decision as to whether a target is *Go* or *No-Go*. Faced with this shorter stimulus exposure task difficulty increases, engendering a heightened sense of vigilance which concomitantly leads to higher levels of endogenously generated sustained attention (Manly, 2003; O'Connell 2007). As was mentioned previously older adults have in the past been shown to achieve this self-generated attentive state more successfully than their younger peers (Carriere et al., 2010). Task strategy on the EADT for older individuals is then characterized by their making full use of the time for which all stimuli are presented, often responding just prior to stimulus offset, allowing maximum possible time for stimulus processing. This conservative approach coupled with increased task related vigilance leads to significantly fewer errors being committed but more falling under the radar of awareness (Forstman, Tittgemeyer, Wagenmakers et al., 2011; Shalgi et al., 2007; Starns & Ratcliff, 2010; Rabbitt, 1979). When a commission error does occur, it most likely the result of a lapse in sustained attention (Bunce, 2001; Davies & Davies, 1975; McAvinue et al., 2012; Mouloua & Parasuraman, 1995). We are of course currently unable at this to generalize this hypothesis to the execution of activities of daily living or other everyday behaviours, but it is perhaps not unreasonable to see how the strategy describe above might translate to for instance driving a car.

If we extend this hypothesis to our electrophysiological findings, the attenuation of the build-up rate and amplitude of the Pe in older adults may not solely be caused by the diminished processing ability of the ageing brain (Deary, Johnson & Starr, 2010). As the Pe component is thought to reflect the process of evidence accumulation and decision-making (Murphy et al., 2012; Steinhauser et al., 2014), one could therefore surmise that resulting from the temporal dynamics of their task engagement, older participants have less evidence with which to base their decisions upon. Potentially, it is at this juncture that reduced processing power and disengagement of the rDLPFC impedes the ability accurately appraise the evidence that is available. These factors combined promote decisions based on lower criterion, which are reflected in the reduced build-up rate and amplitude of the Pe, and decreased levels of awareness (Band et al. 2000; Leuthold et al., 1999; Mathewson et al., 2005).

Younger participants on the other hand, exposed to stimuli for a longer period of time, meaning depressed levels of task difficulty and ensuing lower levels endogenously generated sustained attention (O'Connell, 2009). They then embark upon a path of automaticity where habituated responses are executed immediately following, and at times prior to, the onset of a target. The increased number of errors in this case possibly resulting from failures to inhibit responses to No-Go trials. There is then an extended window in which younger individuals can assess evidence, supported by superior processing power and higher decision criterion, the net result of which is awareness of

errors at an almost ceiling levels. These factors combined suggest that temporal and behavioural elements may augment the significantly higher amplitude and build-up rate of the Pe. It is worth mentioning that this proposition is not an entirely new concept. Steinhauser and Yeung (2012) have previously demonstrated that manipulations of the speed-accuracy-trade off influence the build-up rate of the Pe.

It is of course important to stress that these potential phenomena are at present specific to the execution of the EADT and while it may possible to hypothesise how they might manifest in everyday behaviour, this would require a great deal of further research.

Several characteristics of the current study echo previous findings by Shalgi and colleagues (Shalgi et al, 2007). They demonstrated that an emphasis on speeded responding reduces accuracy levels and leads to a concomitant increase in the number of aware errors, similar to that of the younger participants in the current study. They also found that when participants were instructed to delay responding, accuracy levels increased whilst levels of error awareness decreased. As a result of their findings they suggest that there are perhaps two distinctive types of error; the sustained attention error which is representative of a true lapse in sustained attention which occurs when speed is discouraged, and the inhibitory error which represents a failure to inhibit one's response as a result of a speeded response. O'Connell and colleagues went on to report similar findings (O'Connell, Dockree et al., 2009). These two types of error are clearly identifiable in the current data.

What this evidence seems to suggest therefore is that older and younger adults commit different kinds of errors whilst engaged in the same task. It further suggests that this is driven by underlying cognitive, electrophysiological and behavioral mechanisms associated with the aging process. These failures or lapses in response inhibition and sustained attention, two critical but separable factors of executive function, give rise to two unique kinds of error in healthy populations. Therefore, it is possible that up until now much of what has been reported in the literature regarding age related error processing, particularly when comparing older and younger counterparts, has described two dissociable processes.

This is not to suggest that diminished awareness in older adults is entirely due to strategic factors. What it does perhaps indicate is that the oft-reported diminution of cognitive function, may arise as a result of the fusion of suboptimal cortical function and compensatory behavioural mechanisms.

Electrophysiological differences in the ERN support previous evidence which reported an attenuation of the ERN in older adults (Mathalon et al., 2003; Mathewson, Dywan, & Segalowitz, 2005) The slower build up rate and lower amplitude of both the ERN may in this case be reflective of the weakening processing ability in age related cognition (Deary, Johnson & Starr, 2010).

Though several others have suggested a relationship between everyday measures of insight and online awareness (Harty et al, 2013; Hoerold et al.,

2008; Jenkinson et al, 2009; Larson et al., 2009) a significant relationship between electrophysiological and psychometric measures did not emerge. Interestingly, a significant relationship between diminished error awareness and lower scores on the MMSE did materialise. Impoverished online error awareness may indeed be an underlying symptom of age-related cognitive abnormality and as such its addition to the existing diagnostic battery may help to illuminate previously undetected markers of dysfunction.

In conclusion, our current findings seem to suggest that older adults use alternative strategies and executive subsystems to complete a computerized Go/No-Go task, similar to the 'two types of error' model proposed by O'Connell et al. (2009) and Shalgi and colleagues (2007). The current data also supports the hypothesis that older individuals exhibit poorer levels of error awareness, at least in a laboratory setting. It is possible however, that this is in part a by-product of an age-related compensatory shift in neurological function and strategic choices by older individuals which place an emphasis on accuracy. Age-related attenuation of ERP's such as the ERN and the Pe may also be impacted by this cognitive strategy, rather than simply being the result of degraded cortical processing power (Mathewson et al., 2005). Of course it would be naïve to suggest that cognitive function remains at optimal levels throughout the entire life span, however the level to which this shift in function truly impacts on ones ability to carry out activities of daily living is debatable and perhaps overstated (Clare et al., 2010). Our finding that scores on the MMSE are reflected in older adult levels of awareness on the EADT are suggestive of this point. There are also potential methodological ramifications

to these findings. Future research in this field may need to recognize that as we examine age-related cognitive phenomena, specifically error processing, older and younger adults may employ two distinctive and dissociable executive functions.

Chapter 3

Alzheimer's Patients have Diminished Error Awareness but Preserved Accuracy.

3.1 Introduction

Alzheimer's disease (AD) is a largely age related neurodegenerative disorder which is characterized by progressive memory loss and deterioration of comprehensive cognition (Baddeley, Della Sala, Logie & Spinnler, 1986; Berardi, Parasuraman & Haxby, 2005; Wang & Wang, 2006). Whilst memory dysfunction is perhaps the most notable characteristic of Alzheimer's, individuals regularly display an inability to carry out a multitude of activities which rely upon both the executive and attentional networks (Baddeley et al., 2001; Bondi, Salmon & Kaszniak, 2009). Anosognosia, or lack of awareness, has long been reported as a clinical feature of Alzheimer's type dementia (Gustafson & Nilsson, 1982; Sevush & Leve, 1993; Starkstein, 2014) and is often seen in the early stages of pathology (Green, Goldstein, Sirockman & Green, 1993). A relationship between anosognosic symptoms of AD and dysregulated executive function has been previously reported (e.g. Michon et al., 1994). Difficulties in executive processing mean that when asked to engage in tasks that require control over primarily frontal functions such as planning, inhibition and attention, patients often perform well below the levels we have come to expect following the natural diminution of cognitive processing associated with healthy ageing (Baddeley, Bressi, Della & Sala et al., 1991;

Kirova et al., 2015). Such is the importance of these distributed frontal deficits, it has been posited that dysregulated executive and attentional function are potentially the earliest signifiers of possible underlying pathology (Albert et al. 2001; Perry et al. 2000). Diminished awareness may also engender a range of obstacles for individuals with an Alzheimer's diagnosis. For instance, it has been shown to impede early diagnosis and hinder compliance with treatment strategies (Cosentino et al., 2005), increase the risk of injury to patients (Pachana et al., 2006; Starkstein, Jorge, Mizrahi, Adrian & Robinson, 2007) and elevate the real and perceived level of caregiver burden (Seltzer, 1997). In terms of daily function anosognosia can be further characterized by "the underestimation of limitations in activities of daily living...and a tendency to adopt dangerous behaviours" (Spalletta, Girardi, Caltagirone & Orfei 2012). Also quite interesting is the finding that mildly affected AD patients regularly seem to overestimate their ability on ADL's while still possessing an understanding of the memory problems associated with their illness. This apparent lack of insight therefore cannot be explained by simply suggesting that they cannot remember that they have a deficit (Kasznick et al, 2010). This current chapter aims to further explore the multifaceted phenomenon of awareness in an Alzheimer's affected population. In particular we are interested in the ability of those with an AD diagnosis to report performance related errors on a cognitive task.

For the purpose of the current study awareness is defined as "the accuracy with which individuals appraise aspects of their own current

situation, performance, or functioning”, and may be used interchangeably with the terms anosognosia and insight (Roberts, Clare & Woods, 2009).

While several reports have highlighted either a decrease or preservation in one’s ability to appraise and monitor task related performance as we age (Harty et al, 2013; Staub et al., 2013), there is scarcity of data on the error processing ability associated with AD. Electrophysiological evidence has variously suggested slower but intact processing and detection of errors (Ito & Kitagawa, 2005), or in some cases lower levels of accuracy and preserved awareness (Mathalon et al, 2003). In both of these studies awareness was assumed by the presence of the Pe component, however, no conscious, overt signaling of an error was required of the participants. In the first case the ERN and the Pe were both found to be attenuated in AD participants, whilst in the second study Alzheimer’s patients recorded a significantly lower ERN amplitude but a similar Pe to that of the control group.

Previous research in an ageing population conducted by Harty and colleagues (2013) has demonstrated that awareness of one’s ability to carry out activities of daily living (ADL’s) was mirrored by a decrement in awareness for errors committed on the error awareness task (EAT; Hester et al., 2005). As successful management of ADL’s is often a significant difficulty faced by AD patients, it is possible to hypothesize that they may also struggle to complete a task requiring high levels of vigilance, sustained attention and active error signaling. In support of this assertion are previous reports of a decline accuracy related to the severity of symptoms in AD patients (e.g. Agnew & Morris, 1998).

Given the well-documented volumetric reduction, decrease in gray matter, hypo-metabolism and neuro-degeneration in the prefrontal cortex associated with AD, and this particular regions significant role in awareness related behaviors (Hardwood, Sultzer, Feil, Monserratt, Freedman & Mandelkern, 2005; Harty et al., 2014), further evidence is provided to suggest that self-referential performance will be compromised in AD patients. Indeed it is quiet possible that the neurophysiological deficits associated with AD would seem to suggest impaired awareness is an inevitable consequence of the illness (Raz, Gunning & Head et al., 1997; Salat, Kaye & Janowsky, 2001).

Perhaps unsurprisingly impaired awareness in Alzheimer's disease is quite broad ranging and has been shown to impact upon several cognitive functions including memory, language, social cognition and executive functions (Morris & Mograbi, 2012). It has been suggested that impaired online error detection in AD is a result of compromised metamemory strategies, a failure of monitoring and control processes (Consentino et al., 2007; Souchay, 2007). In this case, immediate error monitoring is highly dependent on the iconic and working memory systems retaining sufficient information for error evaluation to occur. The complicated nature of anosognosia in AD is further highlighted by the fact when engaged in tasks which require online self-referential judgments, the less aware a patient is of his or her overall level of cognitive deficit the greater the discrepancy between their judgment of actual performance and self-perceived performance (Hannesdottir & Morris, 2007).

Whilst there seems to be a general consensus in the literature, pointing towards severely reduced awareness in AD patients, not all agree. In particular, Professor Linda Clare and her colleagues have consistently argued that levels of awareness and the cognitive abilities of AD patients' have been continuously underestimated (e.g., Clare, Whitaker, Nelis, Martyr, Markova, Roth & Morris, 2013; Clare, 2003). Clare has suggested that not enough consideration is given to both psychological and social factors such as anxiety or a patient's environmental circumstances when assessing levels of awareness (Clare et al., 2012a, 2012b). There are several factors which contribute to this lack of unanimity, not least the enormous methodological and theoretical inconsistencies which permeate the literature on awareness. For instance, depending on which study you read the prevalence of anosognosia in Alzheimer's patients can be up to 80% (Sevush & Leve, 1993) or as little as 15% (Reed, Jagust & Coulter, 1993) of the population. Others suggest that underlying emotional and depressive symptoms associated with the disease may confound prevailing theories of anosognosia (Smith, Henderson, McCleary, et al., 2000).

Current Study

Our current research is largely of an exploratory nature as, to the best of our knowledge; no other studies have examined online error awareness in an Alzheimer's population. By requiring our participants to explicitly acknowledge their errors of commission, we hope to add to the current understanding of awareness decrements in AD. In order to do so we have

developed a touchscreen error awareness task (TEAT), which is a simplified mobile version of the EADT. Successful completion of the TEAT not only requires intact error processing but also high levels of vigilance and sustained attention, both of which are prerequisites for optimum awareness in goal directed behavior (Corbetta & Shulman, 2002; Robertson, 2010). Previously we reported that older and younger individuals engage different strategies in response to this type of task, suggestive of a ‘two types of error’ model (O’Connell et al., 2009, Shalgi et al., 2007). As older adults seem to rely more upon the sustained attention network it will be interesting to observe the extent to which this phenomenon traverses healthy aging to AD cognitive function.

In line with previous findings, particularly those of Harty et al. (2013) on who’s model the current protocol is largely based, we expect to find diminished levels of awareness in AD participants when compared to younger and older adults. We further hypothesize that levels of awareness and accuracy will be associated with psychometric discrepancy measures of function in ADL’s and social functioning. We will also assess whether performance on the Montreal Cognitive Assessment (MoCA), widely used in the early stages of the diagnostic process, is associated with diminished levels of error awareness and accuracy on the TEAT.

Patient-caregiver discrepancy measures are regularly used in the assessment of anosognosia. In this method patient and caregiver ratings regarding levels of performance on ADL’s and emotional function are

compared and the level of discrepancy is considered indicative of the level of impairment. Though this method has been criticized, mainly due to concerns relating to the influence factors such as stress, depression and burden might have on caregiver ratings (Starkstein, 2014), we felt it was important to include a measure of this type in order to evaluate our task alongside established methodological practices in this area of study.

3.2 Materials & Methods

Participants

Seventy-two participants were recruited for our experiment: 31 Alzheimer's affected patients (22 female, 9 male), 21 older adults (OA) (12 female, 9 male) and 23 younger adults (YA) (X female, X male). Older participants and Alzheimer's patients were aged between 55 and 78 years of age while younger patients were 18 to 30 years old. Older participants were recruited via the Trinity College Institute of Neuroscience participant panel, whilst the younger participants were recruited from the undergraduate student body of Trinity College Dublin. All AD volunteers were recruited through the memory clinic at the Mercer's Institute for Successful Ageing (MISA), St James Hospital, Dublin, Ireland. Testing of AD participants took place at the Mercer Institute, older and younger participants completed the test protocol in Trinity College Institute of Neuroscience. AD patients were diagnosed in accordance with the NINCDS-ADRDA criteria for AD (McKhann et al. 1984). Five patients (3 female, 2 male) with a mean age of 73.6 (SD 4.51) years, MoCA score of 16.4 (SD 2.07) at the time of testing and MMSE score of 24.8 (SD 1.3) at time of diagnosis, were unable to complete the training protocol

for the TEAT. These participants were excluded from the final analysis. Those patients who did complete the entire protocol had a mean MoCA score of 16.62 (3.85) at the time of testing; in line with current normative data which suggests a mean score of 16.2 (4.8) for an individual with AD. The mean MMSE score at the time of diagnosis was 24.92 (1.67) which would fall within the 'mild' category. AD patients were accompanied on the day of testing by a close family member or carer in order assist with issues surrounding consent. They were also required to complete the relative/carer section of the Patient Competency Rating Scale. All participants had normal to corrected vision, no incidence of colour blindness, no history of neurological/psychiatric illness or photosensitivity to flickering light. Written informed consent was provided before testing began and all procedures were approved by the St James's Hospital / Tallaght Research Ethics Committee.

Awareness Measures and Psychometric Assessment

Touchscreen Error Awareness Task (TEAT)

The TEAT is a modified version of the EADT Go/No-go task, developed specifically for the current experiment. Participants were required to complete three blocks each lasting 6.5 minutes. Participants are exposed to 200 differently coloured 'dot' targets, 25 of which are 'No-Go' and 175 are 'Go'. No-Go targets are those in which the colour presented is a repeat of the previous colour (e.g. green follows green). Initial stimulus display time is 750ms. However, depending on the response time of the participant the stimulus display time either lengthens or shortens. If a participants responds within the first time quarter of the stimulus duration is decreased by 25 ms on the next

trial. Should participants respond within the final quarter of the stimulus presentation a further 25 ms is added to the stimulus duration. Stimulus display time changes on each subsequent trial depending on participant response times. The maximum stimulus time that can be reached is 1500ms and the minimum is 750ms. The aim of this manipulation is to self-pace the task. If participants are responding quickly they most likely find the task relatively easy and therefore task difficulty is increased. On the other hand, those participants who respond later in the trial may require extra time in which to make a decision and so are afforded extra time. In addition to this participants are required to adapt to the demands of the task by manipulating the speed of their responses to achieve the optimum outcomes. The inter-stimulus interval (ISI) remains stable at 750ms through out testing. Participants are not made aware of this manipulation. In the event of a commission error, participants were required to engage an error correction response (ECR) by touch a grey coloured button located at the bottom of the screen. The TEAT was presented on an ASUS ZenPad 8" Tablet.

Prior to the commencement of the task participants were asked to complete a practice block where they were required to make three successive correct withholds. Participants were also required to simulate an error correction response. AD patients in particular were required to give a verbal description of the task and its rules. Prior to the beginning of each block all participants were asked to restate the parameters of the task. AD participants were informed that in addition to pressing the onscreen ECR button they may also, if they so wish, acknowledge their awareness of a commission error by

using a verbal signal. The attendant researcher recorded both ECR responses and verbal indications of error awareness.

Psychometric Battery /Background Measures

Upon completion of the TEAT task participants were required to complete a short psychometric battery aimed at assessing their current state of cognitive function and their perceived competency in their ability to carry out ADL's. This consisted of the Montreal Cognitive Assessment (MoCA; Nasreddine, Phillips, Bédirian, et al., 2005), the Clock Drawing Test (CDT) and the Patient Competency Rating Scale (PCRS; Prigatano, 1986).

Montreal Cognitive Assessment (MoCA)

Developed by Ziad and colleagues over several years, the MoCA has become one of the most widely used psychometric tools in the diagnosis of MCI, Alzheimer's Disease and other dementias. Its greatest value lies perhaps in the fact that it provides a comprehensive overview of a patient's current global cognitive function at a given moment in time. Amongst the many cognitive abilities it examines are executive function, visuospatial ability, attention, memory and abstract thought (see **Appendix C**). Although primarily employed in MCI and dementia screening it has also been used to assess cognitive function in those with Multiple Sclerosis, Huntington disease and TBI (Dagenias, Rouleau & Demers et al., 2005, Gluhm, Goldstein & Broen et al., 2013, De Guise, Alturki & LeBlanc et al. 2014). The MoCA takes between 10 and 15 minutes to administer and has been validated for 55-85 year olds.

Clock Drawing Test (CDT)

See Chapter 2.2 for a complete description of the CDT. The same protocol was followed in the current experiment.

Patient Competency Rating Scale (PCRS)

The PCRS is a self-report scale that aims to assess levels of insight and self-awareness. It is a 30-item list which focuses variously on an individuals perceived proficiency in domains such as cognitive ability, ADL's (including those of a physical nature) and social functioning; both behavioral and emotional. It is administered to participants who respond based on their belief in their own ability in relation each domain. Questions are scored on a five point Likert-scale ranging from 1: '*Can't do*' to 5: '*Can do with ease*' (see **Appendix D**). Informants; in this case a spouse or relative, then complete the questionnaire and patient insight is calculated as a measure of the discrepancy in scoring.

Though several methods of scoring have been suggested, we have decided to use that employed by Fleming and colleagues (1996) as it is reported to be the most sensitive to the intricacies of the items being measured (Kolakowsky-Hayner, Wright & Bellon; 2012). This mean that scores can range from 30-150, with higher scores indicating greater competency. It is also possible for scoring purposes to further fractionate the PCRS into various domains of patient proficiency, such as social functioning and patient ability on ADL's and self-care.

Originally developed to assess these phenomena in TBI patients it has since been used in a variety of disciplines in the assessment of multiple sclerosis (Sherman, Ryan, Hanks, Rapport, et al., 2007), stroke (Alexander & Wilz; 2010), cancerous brain tumors (Ownsworth, Henderson, Chamber & Shum, 2009) and importantly AD and other dementias (Shanly, 2014; Seltzer, Vasterling & Yoder et al., 1997).

PCRS Social Subscale.

Seltzer and colleagues isolated several features of the PCRS which they felt were representative of a patient's, in this case Alzheimer's disease, ability to function in a social environment (Seltzer et al., 1997)(see **Appendix D**). The Social Subscale of the PCRS concentrated on issues such as emotional control, the perceived appropriateness of one's behavior and participation in group activities. It requires the researcher to extract fourteen questions from the original 30 item PCRS. The same scoring procedures are then followed in order to calculate the level of discrepancy between the patient and their relative/carer. Scores on the Social subscale range from 14-70.

Statistical Analysis

Participant level of awareness on the TEAT was calculated as the percentage of no-go errors which the participant successfully signaled. Participant accuracy was calculated as the percentage of no-go targets that a participant correctly withheld on. All neuropsychological tests and TEAT data was analysed using one-way ANOVA's and bivariate/partial correlations. Post-

hoc analysis was conducted by filtering groups as required and performing Bonferroni adjusted paired and independent sample t-tests. All analysis was carried out using IBM SPSS Statistics Version 22.

3.3 Results

Provided below in **Table 3.1** is a summary of the demographics for our participating groups. Participants did not significantly differ with regard to their age ($p = .08$), the number of years they had spent in formal education ($p = 0.58$) and were equally balanced in terms of Gender.

Table 3.1 Demographics. The Mean $\pm$ SD is reported for each group.

	YA (n=23)	OA (n=23)	AD (n=23)
Age	21.55 $\pm$ 1.59	66.07 $\pm$ 4.84	71 $\pm$ 6.81
Gender (m/f)	12/11	11/11	13/13
Years of education	16.74 $\pm$ 1.29	16.19 $\pm$ 2.80	16.96 $\pm$ 3.07

Performance on the TEAT

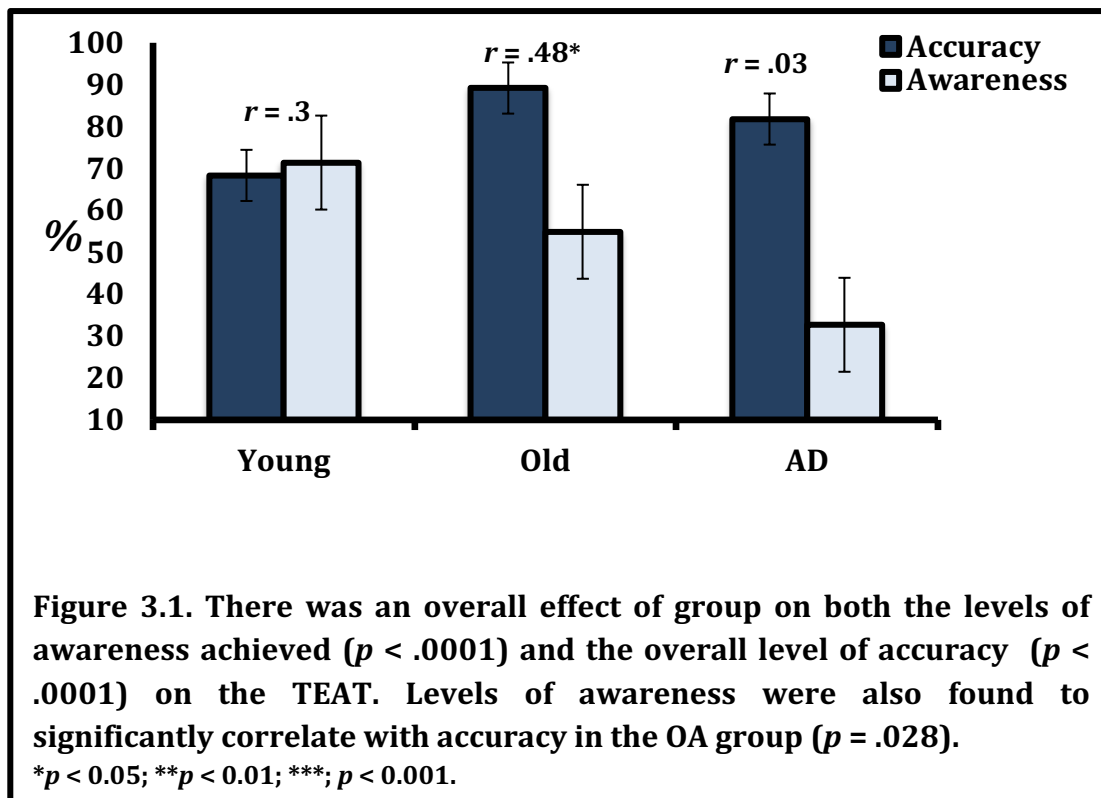
Listed in **Table 3.2** is the performance related data for the TEAT. Participant awareness, accuracy and the mean stimulus duration times (the length of time individual target stimuli remain on-screen) are listed. There was a main effect of group in relation to participant levels of awareness following an error of commission ($F(2,67) = 9.74, p < .0001$). Post-hoc analysis revealed that the AD group but were less aware of the errors they had committed compared to the younger adults than ($t(47) = -4.941, p < .0001$). Older adults

were also significantly more aware of errors than their AD counterparts ($t(45) = -2.456, p = 0.018$). Younger adults did not differ significantly from the OA group ($p = .13$).

A significant main effect of group was identified for degree of accuracy in performing the TEAT ($F(2,67) = 10.54, p < .0001$). However, whilst a post-hoc analysis indicated that the AD and OA groups did not differ in how accurate they were ($p = .081$), both the AD ($t(47) = 2.997, p = .004$) and the OA group ($t(42) = -4.256, p < .0001$) were more accurate when compared to younger participants ($M = 68.35, SD = 17.59$).

Despite the inclusion of a staircase method to account for task difficulty, as a precaution we decided to perform a one-way ANCOVA which controlled for participant accuracy levels. The main effect of group on levels of awareness remained statistically significant ($F(2,67) = 12.83, p < .001$). Interestingly post-hoc analysis revealed that when accuracy is controlled for younger adults are significantly more aware than both the AD group ($p < .0001$) and OA group ($p = .031$), however, older adult levels awareness do not exceed those of their AD counterparts ($p = .11$).

A bivariate correlation suggested that the overall level of error awareness significantly correlated with accuracy in the OA group ($r(21) = .48, p = .028$), but not the YA group ($p = .167$) or the AD group ($p = .89$). See **Fig.3.1**.



When examining group differences in stimulus exposure times, the dynamics of which change in accordance with participant accuracy and awareness, we found a main effect of group on the average time participants were exposed to on-screen stimuli ($F(2,67) = 70.77, p < .0001$) (see **Table 3.2**). All of our groups recorded significantly different exposure times. Younger participants were exposed to on-screen stimuli for a significantly shorter period than both the AD ($t(47) = 11.383, p < .0001$) and the OA ($t(42) = -5.921, p < .0001$) groups while AD patients viewed stimuli for a significantly longer period than the older adult group ($t(45) = 5.795, p < .0001$).

Table 3.2 Accuracy, Error Awareness and Stimulus displays times on the TEAT. There was a main effect of group on all aspects of performance

	YA	OA	AD
Accuracy	68.35% ± 17.59	89.2% ± 14.61	81.8% ± 13.77***
Awareness	71.41% ± 29	54.9% ± 39	32.7% ± 27.92***
Display Time (ms)	1034 ± 100.1	1191 ± 72.8	1313 ± 70.95***

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Montreal Cognitive Assessment (MoCA)

Detailed below in **Table 3.3** are the mean scores for our participating groups on the MoCA. Also listed are the composite scores for the Visuospatial / Executive Function and Attention elements of the test. Selected individual subsections are reported. There was a main effect of group on the MoCA attention scores ($F(2,67) = 13.41, p < .0001$). Post-hoc analysis also revealed that healthy older adults performed at a significantly lower level than the YA group ($t(42) = 2.85, p < .05$) but at a higher level than the AD group ($t(45) = -3.27, p = .002$) on the Attention component. AD adults also performed significantly worse than the YA group ($t(47) = -4.32, p < .0001$)

There was also a main effect of group for performance on VSP/ EF components of the MoCA ($F(2,67) = 57.39, p = .000$). Younger people performed better on the EF_VSP element when compared to AD patients ($t(47) = -9.91, p = .000$) and older individuals ($t(42) = 2.95, p < .005$). The AD group also performed significantly worse than healthy older participants ($t(45) = -6.51, p < .0001$)

Clock Drawing Task (CDT)

Mean scores for the Clock Drawing Test (CDT) have been included at the bottom of **Table 3.3**. There was a main of group for mean CDT scores ($F(2, 67)=26.41, p < .0001$). Post-hoc analysis revealed that the AD group scored significantly lower than both the YA group ($p < .0001$) and the OA group ($p < .0001$). Older and younger participant scores did not differ significantly in completing the CDT ($p = 1.0$).

Table 3.3 Details of selected MoCA component scores and overall MoCA score and their relationship to awareness levels on the TEAT. Included are participant means for the Clock Drawing Test.

	YA	OA	AD
MoCA	28.26 ± 1.39	28.05 ± 1.68	16.62 ± 3.85*
VSP / EF	4.87 ± 0.34	4.33 ± 0.8	2.42 ± 1.14**
Attention	5.91 ± 0.29	5.67 ± 0.8	4.27 ± 1.73*
Trails / Cube	1.91 ± 0.29	1.55 ± 0.61	0.19 ± 0.4
M Clock	3 ± 0.21	2.81 ± 0.4	2 ± 0.75
Digit Span	1.91 ± 0.29**	1.9 ± 0.45	1.65 ± 0.56
Letter A	1 ± 0.00	1 ± 0.00	0.77 ± 0.43
Serial 7	2.52 ± 0.51	2.7 ± 0.66	2.04 ± 1.18*
Sentence Rep	1.96 ± 0.21	1.95 ± 0.22	1.27 ± 0.78
Delayed Recall	3.47 ± 1.38	3.9 ± 1.21	0.19 ± 0.49
CDT	4.96 ± 0.21	4.71 ± 0.46	3.35 ± 1.29

Correlations indicate a relationship with participant levels of error awareness.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Error Awareness and Standardised Neuropsychological Test

AD participant level of error awareness on the TEAT was significantly correlated with their overall MoCA score ($r(26) = -.39, p < .05$), while OA ($p = .08$) and YA ($p = .95$) MoCA scores did not significantly correlate with awareness (see **Table 3.3**).

AD scores on the attention subset of the MoCA significantly correlated with awareness ($r(26) = .411, p = .037$), but not in the healthy older group ($p = .41$) or the younger adults ($p = .47$)

The Serial 7 subtraction component was also correlated with level of awareness ($r(26) = .43, p < .05$) in our Alzheimer's affected group, but not the OA ($p = .232$) or YA ($p = .315$) groups.

A significant correlation emerged between younger adult performance on the Digit span/repetition section of the MoCA and their overall level of error awareness ($r(23) = .60, p = .002$) but not in the OA ($p = .45$) or AD group ($p = .50$)

No other correlations were identified with regard to MoCA subsections and awareness levels; Trail completion (AD ($p = .78$), OA ($p = .95$), YA ($p = .48$), Clock section (AD ($p = .42$), OA ($p = .95$), YA ($p = .45$) or the Letter A signaling (AD ($p = .38$), as all OA and YA participants attained maximum scores for the Letter A section Pearson's r value was not computed.

Younger participant scores on the Sentence repetition section did however come close to reaching significance ($r(23) = .411, p = .051$), but not in the OA ($p = .16$) or AD ($p = .73$) groups. Similarly healthy older participant performance on the Delayed word recall task was close to significance ($r(20) = .43, p = .058$), but not in the AD group ($p = .6$) or YA ($p = .47$) group.

Accuracy and the MoCA

Levels of accuracy achieved by AD patients were also significantly correlated with their performance on the Visuospatial/Executive Function subsection of the MoCA ($r(26) = .51, p < .01$), but not in the OA ($p = .85$) or YA ($p = .38$) participants.

AD participant scores on the Attention subset of the MoCA were also significantly correlated with accuracy ($r(26) = .43, p = .028$), a result not found in the OA ($p = .59$) nor the YA group ($p = .31$).

Awareness of Everyday Competency

There was a main effect of group on discrepancy levels as recorded by the PCRS ($F(2, 67) = 17.14, p < .0001$), with both the YA ($t(46) = .438, p < .0001$) group and the healthy older group ($t(46) = 4.625, p < .0001$) recording significantly different scores from the AD group but not from each other ($p = .46$). See **Table 3.4** for details of mean group scores for participants and relatives on the PCRS and the Social Subscale of the PCRS.

On the social subscale of the PCRS there was also a main effect of group ($F(2, 67) = 11.19, p < .0001$). AD participants recorded significantly different scores from the YA group ($t(46) = 4.04, p < .0001$) and the older group ($t(46) = 4.064, p < .0001$), but again older and younger participants did not differ in the level of discrepancy ($p = .58$). Suggesting that AD patients over-reported their competency on both aspects of the PCRS when compared to significant-other reports.

Table 3.4 Group scores on the PCRS and the Social subscale. Included are means for participants, their significant others and the level of discrepancy. Only AD participants significantly differed from their carers overall PCRS score.

	Participant (Mean, SD)	Relative (Mean, SD)	Discrepancy (Mean, SD)
<u>PCRS</u>			
YA	130.00 ± 15.28	132.57 ± 13.58	-3.38 ± 19.69
OA	136.00 ± 7.18	136.94 ± 10.25	0.67 ± 8.98
AD	133.48 ± 9.39	107.71 ± 19.48	25.83 ± 19.76***
<u>Social PCRS</u>			
YA	57 ± 8.79	58.43 ± 8.61	-1.86 ± 12.73
OA	59.89 ± 5.05	60.56 ± 6.19	-0.07 ± 6.17
AD	61.4 ± 7.76	51.21 ± 9.94	12.17 ± 10.55

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

PCRS Discrepancy Scores

Participant scores on the PCRS did not significantly differ from those of their relative counterparts for both the OA ($p = .997$) and YA ($p = .389$) groups,

nor did they differ on the PCRS Social Subscale (YA ($p = .465$), OA ($p = .866$)). There was a significant difference in levels of competency on the PCRS as reported by AD patients when compared to their carers evaluation of their ability ($t(25) = 6.40, p < .001$), a result not identified in the Social Subscale ($p = .339$).

Online TEAT levels of awareness were not significantly correlated with the discrepancy scores on the neither PCRS (AD ($p = .168$), OA ($p = .75$), YA ($p = .51$)), nor the Social Subscale of the PCRS (AD ($p = .21$), OA ($p = .47$), YA ($p = .68$)).

There was no significant correlation between how accurate participants were in their performance on the TEAT and discrepancy scores on the PCRS (AD ($p = .981$), OA ($p = .739$), YA ($p = .66$)), or the Social subscale of the PCRS (AD ($p = .59$), OA ($p = .94$), YA ($p = .32$)).

Partial correlations controlling for group revealed an overall significant relationship between overall MoCA score and levels of discrepancy on the PCRS ($r(67) = -.467, p \leq .001$) and the Social subscale ($r(67) = -.424, p \leq .001$). Within group analysis found that there was no significant relationship between overall MoCA scores and the discrepancy measures for the PCRS and MoCA in either the YA ($p = .125$), OA ($p = .56$) or AD ($p = .172$) groups. The same was true of the Social Subscale of the PCRS and MoCA scores in YA ($p = .106$), OA ($p = .308$) and the AD ($p = .161$) groups. There was however a negative correlation between PCRS discrepancy scores for the AD group and the

Memory Delayed Recall subsection of the MoCA ($r(26) = -.46, p < .05$), but not the YA ($p = .33$) or the OA group ($p = .94$).

Education was not significantly correlated with awareness levels in the AD group ($p = .27$), but was for both the YA ($r(23) = 0.42, p < .05$) and OA groups ($r(21) = .55, p < .05$).

AD Patient MMSE Scores

As MMSE scores for AD patients, recorded at their time of diagnosis, were available to us it was decided to investigate whether or not they correlated with levels of error awareness on the TEAT. MMSE scores at time of diagnosis were significantly correlated with awareness ($r(26) = .55, p < .005$), but not accuracy ($p = .47$). See **Figure 3.2**.

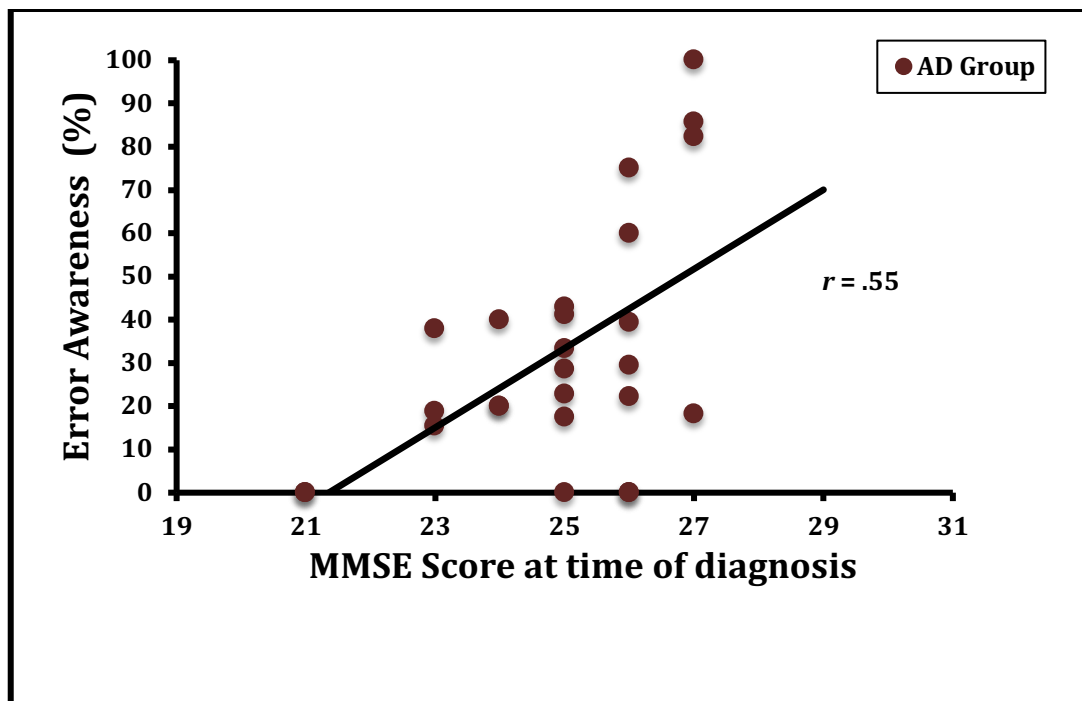


Figure 3.2 Alzheimer patient MMSE scores recorded at the time of their diagnosis were significantly correlated with levels of Awareness ($r(26) = .55, p < .005$)

3.4 Discussion

Reports regarding the prevalence and severity of anosognosic symptoms in Alzheimer's disease provoke many differing opinions amongst the research community (Clare et al., 2003; Ownsworth, Clare & Morris, 2006; Starkstein, 2014). In this chapter we sought to add to the current understanding of patient insight by examining 'online' awareness through observation of participant error related behaviour. We did so using a newly developed touchscreen error awareness task, the TEAT, which required participants to demonstrate active insight by signaling erroneous behavior. An attempt was also made to examine whether online error awareness levels would display a relationship to standardized psychometric measures such as the MoCA and the PCRS. Consistent with our hypothesis, the current data suggests that AD participants are significantly less aware of their commission errors on a relatively simple laboratory based cognitive task compared to a sample of older and younger adults. Lower levels of awareness on the TEAT were also correlated with lower overall score on the MoCA test in the patient group. We further observed that Alzheimer's patients seemed to demonstrate preserved sustained attention ability, as indexed by their high accuracy levels on the TEAT, though. Online error awareness was not however correlated with discrepancy measure scores on the PCRS related to ADL's and social functioning.

As predicted, AD affected individuals were significantly less aware of their errors than both older and younger adults, with patients acknowledging less than half of their errors (32%). In many ways it is quite difficult to

speculate as to precisely why this might be the case, primarily because the levels of accuracy achieved by our patients group far exceeded our expectations (82%), and so relatively few errors committed by AD participants. It would however be unwise to overstate our results by suggesting that these high levels of accuracy are representative of everyday levels of cognitive function in those with a diagnosis of AD. It is more accurate to consider this finding purely in terms of performance on a straightforward laboratory task where participants dedicate significant cognitive resources without distraction. Our findings do however contradict previous reports of lower accuracy and preserved awareness in AD (Agnew et al., 1998; Ito et al., 2005; Mathalon et al., 2003), again highlighting the vastly differing results which pervade the literature. This is due perhaps in no small part to the varying levels of difficulty associated with laboratory based cognitive testing. We are confident however that the inclusion of an overt ECR, whether verbal or motor, provides the first clear measure of conscious error signaling in AD.

There are several potential underlying causes which may have given rise to our current findings. It is quite possible that the aforementioned cerebral changes, such as increased frontal atrophy and hypometabolism, are contributory factors to the diminished levels of awareness displayed by the patient group. The trajectory of diminution in awareness; from young to old to AD, suggest that pathological changes to frontal cortical regions, such as the DLPFC, might precipitate a decline in error awareness beyond what we expect as a result of the natural ageing process. Previous evidence highlighting the significant role played by the rDLPFC in awareness would seem to support this

hypothesis (Harty et al., 2013 & 2014). Also, Hardwood and colleagues (2005) suggestion that hypometabolism in the right lateral and superior dorsolateral frontal regions correlates with disrupted insight provides further evidence for this line of enquiry. Though in the absence of relevant neuroimaging data this remains purely speculative.

Unraveling the significance of lower awareness levels in AD participants is further exacerbated by our current lack of evidence linking this phenomenon to specific ADL or social functioning type behaviours. In light of our finding that AD participants were significantly less aware of their errors and were the only group to record significantly overestimate their ability on ADL's, as evidence by the discrepancy measures on the PCRS, it would not be unreasonable to expect that a relationship between these factors might exist. It is also possible that patient insight regarding ADL's and awareness of errors on a cognitive task are dissociable abilities. Both may index diminished ability, but perhaps for entirely different reasons. As mentioned at the outset the level of patient dysfunction on ADL's can often be under or over reported (Starkstein, 2014) and if so, any potential relationship to error awareness may have failed to materialize. It was however interesting that patients and carers did not report significantly different ratings on the social functioning subsection of the PCRS. We cannot rule out the possibility that our particular cohort of patients were simply highly functional in this regard or that their carer underreported on socio-emotional difficulties.

Levels of awareness and accuracy on the TEAT were also correlated with overall score on the MoCA in the AD group, once again demonstrating the value of this measure as a diagnostic tool, and suggestive of a potential role for the error awareness paradigm in clinical assessment. When we further analysed the constituent parts of the MoCA, the visuospatial/executive function and attention subsections of the test were also found to correlate with levels of error awareness. This of course seems to contradict our earlier assertion that attention is relatively preserved, yet accuracy and awareness on the TEAT were not correlated in our AD group. We would therefore suggest that the nature of the attentional resources required of participants on the MoCA and those on the TEAT are not entirely comparable. For instance, consider that the Serial 7 task of the MoCA was the only one of three attention related tasks which correlated with lower levels of awareness. This task, originally conceived by Hayman in 1942, requires participants to perform a series of mental arithmetic calculations; subtracting the number 7 from 100 and then subtracting 7 from the answer obtained (Hayman, 1942). While we are confident that accuracy on the TEAT, a simple laboratory based task, relates to sustained attention, the Serial 7 certainly requires participants to engage a greater range of metacognitive abilities. It is quite possible therefore that any potential link between poor performance on the Serial 7 and limited error awareness is not based solely on a disruption to the attentional network, though further investigation is necessary to expand on this possibility.

At this point it is important to point out that a significant number of correlations were run whilst no correction for multiple comparisons was made.

This of course means that, due to low statistical power, conclusions drawn from our results are done so tentatively. Despite this clear methodological limitation and the problem it poses when interpreting our results, we believe enough evidence has been provided to warrant further study.

Previously in Chapter 2 we demonstrated that older adults were more accurate in their performance when compared to younger individuals. We suggested that this was as a result of an increased ability to endogenously generate significant levels of sustained attention in the absence of any meaningful exogenous stimulation. Our current data would seem to suggest that this potentially age related cognitive characteristic is somewhat preserved in Alzheimer's patients. At least in the execution of a simple laboratory based task. AD participants were found to achieve accuracy levels not only comparable to that of healthy older adults, but they also significantly outperformed their younger counterparts. As was previously suggested in relation to older individuals, it is possible that AD patients engage in conservative strategies which place an importance on maintenance of task-orientated goals. The self-paced nature of our task means that they experience significantly longer stimulus display times, a result of slower reaction times, and in the process do not succumb to the inaccurate speeded responses we have come to associate with younger adults. It seems that the self-generated drive to respond accurately and stay on task compensates for potential executive dysfunction, such as response inhibition. Again, these findings seem to contradict previous reports of an increased level of inaccuracy in AD (Agnew et al., 1998).

In essence, this suggests that two types of errors, encompassing failures of inhibition and lapses of sustained attention (e.g. Shalgi et al., 2007), are potentially evident in the error processing behavior of AD affected individuals. Inherent in this suggestion is that the speed accuracy trade off which benefits AD and older participants in achieving high rates of accuracy, also means that inevitable lapses in sustained attention will lead to a significantly higher number of errors falling under the radar, particularly in the AD group. While this is suggestive of a somewhat preserved sustained attention network, we acknowledge that it is specific to the task employed in our experiment and further research is necessary to support this claim. It is further possible that while attention of this kind may be preserved, it does not offset the diminished capacity for awareness in AD participants, increased levels of which may be due to pathological deterioration of the rDLPFC.

As an aside, there is another possible contributory factor to accuracy levels in AD participants. Intact awareness of illness/memory related difficulties (Kaszniak et al., 2010) might motivate patients to afford themselves extra cognitive resources in order to successfully complete the task. In a sense, this demonstrates a level of insight regarding their personal cognitive ability, though it must be said this runs contrary to the overestimation of ability demonstrated on the PCRS. Alternatively, as a result of higher motivationally driven effort being deployed to achieve maximum accuracy, resources suffer higher than normal depletion. This leads to an internal neglect of the awareness process, thus we witness what might be termed a dual task trade off, where both speed and awareness are neglected in favour of accuracy. Again

it is important to acknowledge that this finding is specific to the current task and that in order to fully explore any associated hypotheses a great deal of further research would be required.

It would of course be remiss not to mention that five AD participants were unable to complete the TEAT task. The main difficulty reported by these participants was an inability to consider dual task parameters at the same time, withholding on go targets and signaling errors. The remaining participant, aware of personal cognitive difficulties, chose not to undergo the training protocol. What this further highlights is the enormous heterogeneity present in the AD symptomology.

In conclusion our current data seem to suggest that levels of online error awareness are significantly lower in those affected by Alzheimer's type dementia. We believe that this deficit results from a confluence of factors including, pathological structural and functional changes in the prefrontal cortex. This contravenes previous findings which had claimed preserved awareness in AD participants (e.g. Mathalon et al.2003). Deficient error awareness was also reflected in scores achieved on two widely used screening tools, the MoCA and the MMSE. As the need for evermore-sensitive diagnostic measures increases, the potential to investigate error awareness as a potential marker of early cognitive dysfunction is an exciting prospect (Albert et al. 2001). We have reported how AD patients achieve levels of accuracy comparable to healthy older adults and greater than that of younger individuals, and so, diminished ability to adequately signal online errors may

distinguish age related decline from pathological deficits. Analysis of our data also seems to suggest, in line with our previous findings, that errors committed by AD participants are overwhelmingly the result of lapses in sustained attention. Impaired awareness of illness can seriously impact on the lives of both patients and their carers (Seltzer, 1997; Starkstein, 2014). It is possible that the online deficits highlighted in this chapter may present significant challenges to AD patients, not only in successfully executing tasks but also in their ability to adapt and modify their behavior. Lack of awareness on a rather simple laboratory based cognitive task may be reflected in a series of activities such as driving and food preparation, the kind of activities which many in the early stages of the illness rely upon to prolong their independence. By harnessing the potential high levels of vigilance patients are capable of, it may be possible to improve an individuals ability to complete ADL's to a higher standard by focusing on procedural rather than global aspects of an activity. This might in turn help to reduce the number of overall errors committed and thus decrease the reliance on an already overburdened frontal system. This is the first study to report on AD patients' ability to explicitly signal their online errors; therefore the prospects for future research are boundless. The incorporation of electrophysiological and imaging techniques have the potential to dramatically increase our understanding of the pathologically affected error processing network. Acquiring this knowledge may assist in the development of cognitive strategies which aid and improve the daily functioning of those affected by Alzheimer's disease.

Chapter 4

The Impact of Anxiety, Depression and Action-Orientation on Error Processing

4.1 Introduction

Erroneous behavior in humans can set a whole host of autonomic nervous system reactions in motion. These may include enhanced pupil-dilation, fluctuations in electro-dermal activity and deceleration of heart rate (Harsay, Spaan, Wijnen & Ridderinkhof, 2012; O'Connell & Bellgrove et al., 2009). Biochemical reactions such as those involving cortisol and dopamine might also impact behavior immediately preceding or following a misjudged action (Tops, Boksem, & Wester et al., 2006; Holyrod & Coles, 2002). Throughout our previous chapters we have seen how event-related potentials, specifically the error-related negativity (ERN; Gehring, Coles, Meyer, & Donchin, 1990; Falkstein et al., 1990) and error-positivity (Pe; Falkenstein et al., 1991, 1995) can reliably trace underlying cortical activity over the time course of an isolated error (Murphy et al., 2012; Nieuwenhuis et al., 2001; Ullsperger et al., 2014). However, what we are perhaps less informed upon is the effect that individual traits, be it mindset or one's personal approach to engaging in everyday activities, have on error related behavior in healthy populations.

This chapter aims to address some of these issues by examining whether or not anxiety, depression and ‘action orientation’ impact upon error processing and its related electrophysiology. We also consider the effect these traits may have on one’s ability to successfully complete established cognitive screening tools such as the Montreal Cognitive Assessment (MoCA; Nasreddine, Phillips, & Bédirian et al., 2005).

The elicitation of the ERN and Pe components in laboratory based cognitive tasks are often characterized as solely representative of cognitive processes; e.g. decision-making, evidence accumulation (Pe) or conflict monitoring (Murphy et al., 2012, Yeung et al., 2004). There is however evidence that the ERN is perhaps open to manipulation, as studies have shown significant increases in its amplitude when participants are offered monetary incentives (Gehring et al., 1993; Gehring & Willoughby, 2002; Hajcak et al., 2005). Inherent in this finding is the possibility that the ERN is reflective of more than purely cognitive events (Pailing & Segalowitz, 2004). In the case of these particular studies one could argue that in an attempt maximize accuracy for monetary gain, participants assign increased cognitive resources to the task at hand.

Several studies have demonstrated that the amplitude of the ERN may fluctuate based on an individual’s level of anxiety (Moser, Moran, Schroder, Donnellan & Yeung, 2013; Simons, 2010; Weinberg et al., 2012). It has also been shown in certain circumstances to be affected in those diagnosed with

obsessive-compulsive disorder (OCD; Matthews et al. 2012) and generalized anxiety disorder (GAD; Weinberg et al, 2010).

With error processing being considered as both a monitoring and adaptive behaviour, the increased amplitude of the ERN in anxious individuals is thought by some to signal a propensity towards hyper-vigilance and hyper-arousal elicited by a persistent perception of threat (Aarts & Pourtois, 2010; Olvet & Hajcak, 2008). On the other hand, Moser and colleagues have instead suggested that apprehensive anxiety, characterized by rumination and worry, is more closely associated with the differential amplitude changes witnessed in the ERN (Moser et al., 2013).

In contrast to the ERN, the Pe component seems to be largely unaffected by individual differences. For instance Holmes & Pizzagalli found a significantly higher ERN amplitude in healthy participants compared to those with major depressive disorder, while no difference in the Pe was reported (Holmes & Pizzagalli, 2008). Other reports of this kind, this time in a child population, looked at a range of measures such as social sensitivity and positive adaptation and found them to contribute to a larger ERN amplitude, but again identified no significant alterations in the Pe component (Santesso, Segalowitz, Schmidt, 2005).

A range of studies have demonstrated that hypoactivation of the anterior cingulate cortex (ACC) and the lateral prefrontal cortex, two regions closely linked with eliciting the ERN and error processing in general (Brazdil,

Roman, Daniel & Rektor, 2005; Gehring, Goss & Coles et al., 1993; Ridderinkhof et al., 2004), is associated with a decreased tendency to correct errors in participants diagnosed with OCD (Ruchow et al., 2005) or schizophrenia (Morris et al., 2006). Sonia Bishop and colleagues also found that those with higher levels of anxiety levels exhibited decreased rostral ACC activity (Bishop, 2007; Bishop, Duncan, Brett & Lawerence, 2004). In addition Bishop's investigations found that in a task containing 'threat related distractors' higher level anxious individuals had decreased activation of the dorsolateral prefrontal cortex (DLPFC), an area not only associated with cognitive control but also importantly for our current experimental programme, awareness (Harty et al., 2013). Interestingly, previous research has shown that lower levels of anxiety are associated with higher levels of error awareness (O'Keefe et al., 2007), which when considered along with DLPFC findings is suggestive of a potential relationship involving a triumvirate of emotion (anxiety), awareness and cortical function (the ACC and the DLPFC) in successful error monitoring.

Further roles for the ACC have been suggested in a host of cognitive domains (Vassena, Holyrod & Alexander, 2017), including the detection and evaluation of behaviourally relevant events (Khamassi, Enel, Dominey & Procyk, 2013), prediction of effort required for task completion (Chong, Apps, Giehl, et al., 2017) and even animal models of pain perception (Fuchs, Peng, Boyette-Davis & Uhelski, 2014). If we consider also that the ACC has also been implicated in reward prediction (Silvetti, Seurinck & Verguts, 2013), it is

perhaps not all that surprising that we witness evaluative driven changes in the ERN component (Gehring et al., 1993).

There has been a long held belief that the vast majority of human behavior is goal-orientated (e.g. Ajzen, 1985; Heider, 1958). An essential part of this process is the ability to adapt behaviour, which at times may mean that to disengage from a current goal is more advantageous, particularly when the desirable outcome becomes unattainable (van Randenborgh & Hüffmeier et al., 2010).

Over several decades German psychologist Julius Kuhl has developed his theory of action control and behaviour (Kuhl, 1984). An intrinsic idea in this model is that some individuals are 'action orientated'; in that they have the ability to exert a great deal of control over current behavior and reduce the impact of real, perceived or potential negative outcomes. Alternatively, one might be considered to be more 'state orientated', prone to rumination, find it difficult to proceed following unwelcome outcomes, and have difficulty attending to tasks, even those they view positively (Kuhl, 1990). In Kuhl's structure this leaves certain individuals in a state of 'functional helplessness', as they are unable to adequately exert control over their behavior. Rumination in this sense can be considered a maladaptive cognitive style (Opdebeeck, Nelis, Quinn & Clare, 2015), whilst in terms of emotional control it is "repetitive and passive thinking about ones symptoms ...possible causes and consequences" (Nolen-Hoeksema, 1991).

Though we do not have direct evidence linking these specific constructs to existing error processing paradigms, it would not be unreasonable to hypothesize that performance on an error awareness task might be effected by ones action orientation and possible propensity towards ruminative thoughts. This assertion is also based on findings from a diverse body of work that details the powerful impact human emotions and beliefs on a range of cognitive and behavioural phenomena.

For instance the mindset of an individual, the mental attitude that determines how people will interpret and then respond to situations, interacts and affects various personal phenomena such change in IQ (Blackwell et al., 2007) and physical fitness (Plischke & Kohls, 2009). Rather than being entirely stable, people are capable of holding different mindsets about various different personal qualities (Elliot, Dweck & Yeager, 2017; Dweck et al., 1995). Though mindset is defined in different terms to that of action orientation, because both constructs reflect dynamic individual approaches and beliefs on a range of personal behaviours and abilities, we believe both are relevant to our current investigation.

Interestingly we also have evidence that belief systems can impact performance at the electrophysiological level. For instance, Mangels and colleagues reported that upon being presented with feedback, in this case the correct answer to an incorrectly answered general knowledge question, students recorded significantly different waveform amplitudes based on their mindset and individual approach to learning (Mangels, Butterfield, Lamb, Good

& Dweck, 2006). When provided with the correct answer students with an 'incremental' approach; those who view learning as a long-term process, recorded significantly higher amplitudes (anterior frontal P3) than students who had an 'entity' approach; individuals who seem to be more concerned simply with whether or not they are correct or incorrect. What this research suggests is that incremental learners are not unduly concerned with immediate validation and therefore value feedback (the correct answer), they then seem to dedicate more cognitive resources to processing this new incoming information. Entity learners on the other hand tend to switch off once they have learned whether or not their initial response was correct. Again, in light of these findings it would not be unreasonable to expect that internally driven cognitive tendencies might impact our underlying error processing ability and behaviours.

Psychometric testing is utilized in a variety of clinical and non-clinical setting. For instance, the Mini Mental State Exam (MMSE; Folstein et al., 1983) and the MoCA will often be employed as first response diagnostic tools when examining cases of suspected dementia. However, suboptimal performance on a range of cognitive measures has been associated with both anxiety and depression (Beaudreau & O'Hara, 2008; Crocco, Castro, & Loewenstein, 2010). For instance, Del Brutto and colleagues found that depression and anxiety were associated with poorer performance on the MoCA in an aged rural population (Del Brutto, Mera, Del Brutto, Maestre, et al., 2015). Similarly a recent study suggested that when assessing attendees at a memory clinic, depressive symptoms negatively impacted on MoCA performance (Blair & Coleman et al.,

2016). This point is of particular interest as clinicians are often required to evaluate the level to which symptoms, of depression for example, impact on and contribute to impaired cognition (Steffens, 2008).

Current Research

Much of cognitive research was founded upon and influenced by a post-war desire to understand how human beings behave in stressful situations. For example, Norman Mackworth's clock task was largely inspired by a desire to explore how soldiers performed radar duty during World War II (Mackworth, 1948). Continuing this tradition we believe that potential stress inducing individual traits such as anxiety and depression (as measured by the HADS) may impact performance on the EADT and the TEAT. We further assert that an individuals self-reported beliefs regarding failures in everyday activities and ability to persevere with exogenously engaging and unengaging tasks (as measured by the ACS-90), will impact on said measures.

An intrinsic part of our research has included the development a new digital measure that we believe has the potential to support existing psychometric protocols. Throughout our previous experiments we have compared performance indicators such as awareness and accuracy on the EADT and the TEAT to a range of psychometric tests and so, in the interest of continuity, we have included the MoCA test in the current research design. We also felt that the inclusion of both our newly developed measures would

provide us with an opportunity to assess the impact of individual traits in a range of situations and also in completing a range of tasks. In this case, the potentially more formal setting of an electroencephalographic laboratory where the task, the EADT, is carried out on a desktop PC and the informal environs of an open testing room using a touchscreen tablet task, the TEAT. It should however be noted that it is not the intention of this experiment to compare the tasks. Another benefit of using both tasks is that we can begin to formulate normative scores for these novel tests.

In keeping with the theme of our previous research we examined potential age-related differences with regard to action orientation, anxiety and depression allowing for the possibility that how we experience or respond to these traits and emotions may indeed change as part of the ageing process. All potential age-related determinants of error processing were analysed. We examined these potential relationships in two distinct groups, healthy older adults (65 years +) and healthy younger individuals (18 – 35 years old).

Two experiments were carried out to assess our hypotheses; the details for each will be detailed below as **Phase 1** and **Phase 2** of the project. In carrying out this project we will attempt to highlight the impact that individual traits will have on performance. We hypothesize that elevated levels of anxiety or depression may negatively impact on one's ability to successfully generate the required levels of sustained attention to complete an error awareness task. We also hypothesize that one's action orientation and propensity toward rumination will impact on performance factors. For example, it is perhaps

possible that those who exhibit a predisposition towards rumination might respond to errors at a slower rate than those whom we consider more 'action' orientated. Participants who are highly anxious might record more errors as they fall victim to lapses in sustained attention. Alternatively anxious individuals may in fact be shown to be hyper vigilant and therefore record higher accuracy levels than their less anxious counterparts. The findings of both phases of our research will be jointly discussed at the end of the current chapter.

4.2 Materials & Methods

4.2.1 Participants Phase 1 & Phase 2

Forty-one participants, 21 young adults (16 female, 5 male) and 20 older adults (12 female, 8 male), were recruited for **Phase 1 (P1)** of the programme while forty-three were recruited for **Phase 2 (P2)** of the project, 23 young adults (11 female, 12 male) and 21 older adults (12 female, 9 male). **P1's** younger participants had a mean age of 25.19 years ($SD = 5.65$), (range; 18-34) whilst the older participants had a mean age of 71.56 years ($SD = 5.40$) (range; 65-80). Participants in the **P1** group were assigned to the PC version of our error awareness task, the EADT. **P2's** YA group had a mean age of 21.91 years ($SD = 2.35$) whilst the OA group had a mean age of 67.62 years ($SD = 4.64$). Participants in **P2** completed the mobile version of the task, the TEAT. Younger participants were recruited from the student population of Trinity College Dublin. The majority of older volunteers were recruited from a preexisting participant list used by researchers at Trinity College Institute of

Neuroscience; the remaining participants were recruited through word of mouth (family and friends of the research team). All volunteers reported that they had normal-to-corrected vision and there were no cases of color-blindness. Participants did not report a history of psychiatric illness, traumatic injury or photosensitive epilepsy. All older participants were right handed while there was one left-handed younger female participant in the **P1** YA group. Participants were asked to refrain from consuming caffeine products for at least twelve hours prior to testing. Written informed consent was provided before the testing protocol began. All measures were approved by the Trinity College Dublin ethics committee and in accordance with the Declaration of Helsinki.

4.3 Materials & Methods Phase 1

Psychometric Measures

Prior to electrophysiological measures participants completed the Action Control Scale (ACS-90; Kuhl, 1990), the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983) and the Montreal Cognitive Assessment (MoCA;)

Action Control Scale – 90

The **ACS-90** is an English language version of the HAKEMP-90 (Kuhl, 1990). It is a thirty-six-point scale which may be divided into three further subscales each containing twelve dual choice questions. Each question describes a particular situation and asks participants to select either answer **A**

or **B**, each answer will be indicative of whether they would likely be 'Action' or 'State' orientated in the situation described. Further, as the questions relate to specific types of situations, we are able to record how participants might behave in perceived **Failure** related situations, **Decision** related situations or in a **Performance** related event.

The 'action orientation subsequent to failure vs. preoccupation (AOF)' section examines a participant's propensity to proceed or ruminate following unwelcome outcomes. In this section participants will be asked questions such as:

Q4: When I've worked for weeks on one project and then everything goes completely wrong:

(A) *It takes me a long time to get over it.*

(B) *It bothers me for a while, but then I don't think about it anymore.*

or

Q16: When I've bought a lot of stuff at a store and realize when I get home that I paid too much - but I can't get my money back:

(A) *I can't concentrate on anything else.*

(B) *I easily forget about it.*

In both of these questions should a participant respond by answering (B), they would be considered to be more 'action' orientated rather than ruminative or preoccupied with past outcomes.

The 'prospective and decision-related action orientation vs. hesitation (AOD)' section looks at the likelihood that an individual is likely to procrastinate or engage in a task which they are required to carry out. For instance they might be asked:

Q11: When I have to solve a difficult problem:

(A) *I usually get on it right away.*

(B) *I have trouble sorting out things in my head so that I can get down to working on the problem.*

or

Q26: When I have to carry out an important but unpleasant task:

(A) *I do it and get it over with.*

(B) *It can take a while before I can bring myself to do it.*

In this instance the participant who answers (A) for both questions will be considered more 'action' orientated, while participants who answer (B) could be deemed to be more likely to procrastinate, finding it difficult to engage in tasks which they find uninteresting, unpleasant or perhaps unrewarding.

In the 'action orientation during performance of activities vs. volatility (AOP)' portion of the questionnaire participants are asked to report on their ability to remain focused and engaged with activities which they enjoy. For example this might be whether or not they are capable of reading the entirety of an interesting newspaper article they are interested in or if they are more

likely to stop prior to the end of the piece. This particular aspect of action orientation is probed by asking questions such as:

Q24: When I am busy working on an interesting project:

(A) *I need to take frequent breaks and work on other projects.*

(B) *I can keep working on the same project for a long time.*

or

Q27: When I am having an interesting conversation with someone at a party:

(A) *I can talk to him or her the entire evening.*

(B) *I prefer to go do something else after a while.*

In the situations described above a participant who answers (A) to **Q24** and (B) to **Q27** may find it difficult to sustain interest in a task or activity even though they perceive it to be engaging and perhaps stimulating.

The **HADS** and the **MoCA** have been previously described in **Chapters 2** and **3** respectively.

The error awareness dot task (**EADT**) was used in Phase 1 of our study. This task has been previously described in **Chapter 2**. Participants completed 8 blocks of the EADT during which time electrophysiological data was recorded.

Electroencephalography (EEG) Acquisition and Statistical Analysis

The ActiveTwo System (BioSemi) was used to record all EEG data. 64 scalp electrodes were applied using the recognized 10-20 placement system and before being digitized to 512 Hz. Continuous EEG data were re-referenced offline to the average reference, high-pass filtered to 0.5Hz, low-pass filtered up to 95Hz and notch-filtered at 50Hz. All Subsequent EEG procedures were carried out using precisely the same protocol as that employed in **Chapter 2**. Participant awareness and accuracy was calculated in line with our previous chapters.

As part of our analysis a series of one-way ANOVA's, in which group was controlled for, were completed. Bonferroni adjusted independent and paired t-tests were also utilized to assess within group measures. Bivariate and partial correlations were conducted to assess all potential relationships. Statistical analysis for all these measures was performed using IBM SPSS Statistics Version 22.

4.4 Results Phase 1

Listed below in **Table 4.1** are demographic details for both younger and older participants. Our groups did not significantly differ in the number of years that they had spent in formal education ($p = .37$).

Table 4.1 Contain the mean and standard deviation related to group demographics of P1.

	YA	OA
Age	25.19 $\pm$ 5.65	71.4 $\pm$ 5.29
Gender	16 Female, 5 Male	12 Female, 8 Male
Education	16.9 $\pm$ 2.56	16 $\pm$ 3.46

Behavioural Analysis: The EADT

Contained in **Table 4.2** are the behavioural related results detailing accuracy and awareness on the EADT. A one-way ANOVA found that the YA group was significantly more aware of their errors of commission when compared to the OA group ($F(1,40) = 13.02, p < .001$). A main effect of group also suggested that older people were significantly more accurate than their younger counterparts in correctly withholding on NO-GO trials ($F(1,40) = 4.074, p = .05$).

Table 4.2 Group means for older and young adult groups on the EADT.

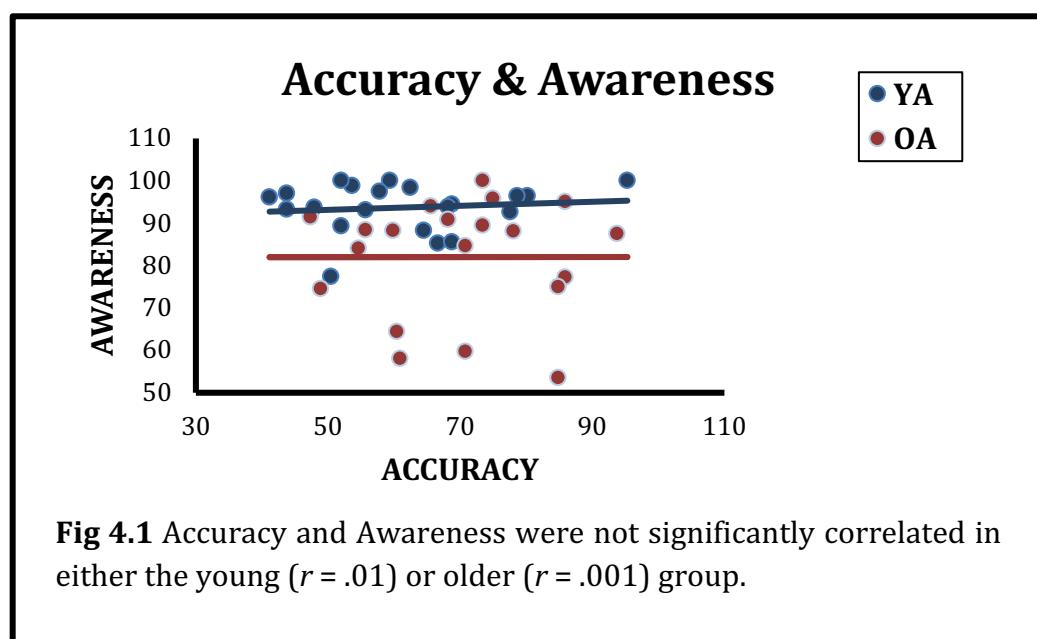
Older adults were more accurate but less aware than younger adults

Mean and standard deviation reported unless otherwise stated.

	YA	OA
Awareness (%)	93.7 ± 5.78	82 ± 13.63***
Accuracy (%)	61.38 ± 13.97	67 ± 13.22*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ suggest a main effect of group.

To assess whether or not this difference in awareness was associated with difficulties completing the task an ANCOVA was performed, which controlled for levels of accuracy within each group. From this analysis we determined that awareness was still significantly higher in younger participants ($F(2,41) = 10.8$, $p = .002$). Indeed this suggestion was further supported by our finding that levels of awareness did not interact significantly or depend on levels of accuracy in either the OA group ($p = .997$) or their younger counterparts ($p = .756$), (see **Fig 4.1**).



Group Reaction Times on the EADT

A multivariate analysis of variance, which looked at overall error reaction times, and both aware and unaware errors, found that RT's for YA adults were significantly faster across all categories ($F(1,40) = 8.03, p < .001$), (see **Table 4.3**). Younger people were also significantly faster when responding to correct Go targets ($F(1,38) = 27.95, p < .001$). There was a main effect of group in the time it took participants to acknowledge an error had occurred via the error correction response (ECR) ($F(1, 40) = 4.34, p < .05$), with younger participants again responding at a faster rate. However, groups did not significantly differ in reaction times associated with unaware errors ($p = .052$).

Table 4.3 Mean reaction times (RT'S) for Go trials, No-Go errors and error correction response times on the EADT.

	YA	OA
RT Go-Trials (ms)	302.58 ± 63.38	396.4 ± 58.6***
Error RT (ms)	306.98 ± 64.12	394.3 ± 118.07**
Aware Error RT (ms)	305.07 ± 43.1	379.99 ± 63.77***
Unaware Error RT (ms)	401.81 ± 230.1	577.05 ± 293.68
ECR (ms)	128.1 ± 69.66	183.64 ± 99.19*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a main effect of group.

Older adults responded significantly slower on error trials of which they were unaware when compared to those that they were aware of ($t(17) = 2.96, p$

< 0.01) whereas younger people did not differ significantly in the time which they took to respond to both aware and unaware errors ($p = 0.1$). Neither the YA group ($p = .244$) nor the OA group ($p = .92$) differed in how quickly they responded on correct go trials when compared to overall error times. Older individuals did record slower reaction times on unaware errors compared to the time it took to respond on correct go trials ($t(18) = -2.63, p = .017$), while younger participants did not ($p = .08$). Correct go trials and aware error trial reaction times did not significantly differ in either the OA ($p = .224$) or YA ($p = .78$) group.

Relationship between Awareness & Accuracy and EADT RT's

Awareness was found to significantly correlate with reaction times on Go trials ($r(20) = -.491; p = 0.03$) and reaction times on aware errors ($r(19) = -.448; p = 0.48$) for older adults. Accuracy was significantly correlated with RT's on Aware errors in the YA ($r(19) = .785; p < 0.0001$) and OA ($r(20) = .668; p = 0.001$) groups. Accuracy was also correlated with overall error RT's for YA's ($r(21) = .659; p = .002$) but not older adults ($p = .051$). Levels of accuracy were correlated with the ECR in OA's ($r(20) = -.459; p = .042$) but not YA's ($p = .652$).

Behavioural Analysis: The ACS & the HADS

Listed below in **Table 4.4** are the group means and standard deviations for the ACS-90 and the HADS psychometric measures. A main effect of group was detected between younger and older participants for performance-related action orientation vs. volatility (AOP) ($F(1,40) = 4.12, p = .05$), the section of

the ACS-90 which might be considered most related to sustained attention. However, no other significant differences were identified on either overall ACS-90 scores or any of its subscales (all $p > .09$).

Groups did not significantly differ on the overall HADS score ($p = .81$) or the Anxiety and Depression subscales (all $p > .41$). Young adults who had a lower overall Action Control Scale score were however more likely to score higher for Anxiety ($r(20) = -.74, p < .001$), Depression ($r(20) = -.85, p < .001$) and both combined (HADS; ($r(20) = -.84, p < .001$)). This was not evident in our older group, though there did seem to be an emerging relationship between ACS-90 score and Depression ($p = .051$).

Table 4.4 Phase 1 group means and standard deviation on the ACS and the HADS. OA and YA groups differed on the AOP section of the ACS ($p = .05$).

	YA (n= 21)	OA (n = 20)
ACS-90	20.85 ± 5.77	24.27 ± 5.44
AOP	8.20 ± 1.99	9.40 ± 1.3*
AOF	6.4 ± 2.62	6.8 ± 3.43
AOD	6.25 ± 2.26	8.07 ± 3.45
HADS	9.38 ± 5.94	8.93 ± 4.88
Anxiety	6.76 ± 3.78	5.73 ± 3.41
Depression	2.62 ± 2.64	3.2 ± 2.6

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant main effect of group. AOP - action orientation during performance of activities vs. volatility; AOF - action orientation subsequent to failure vs. preoccupation; AOD - prospective and decision-related action orientation vs. hesitation.

Electrophysiology

Surprisingly, our participants did not differ significantly with regard to the peak amplitude of the ERN ($p = .07$) when the component was aligned with the original error response. Neither was there a significant difference in the latency at which the peak amplitude occurs ($p = .41$). See **Fig. 4.2**.

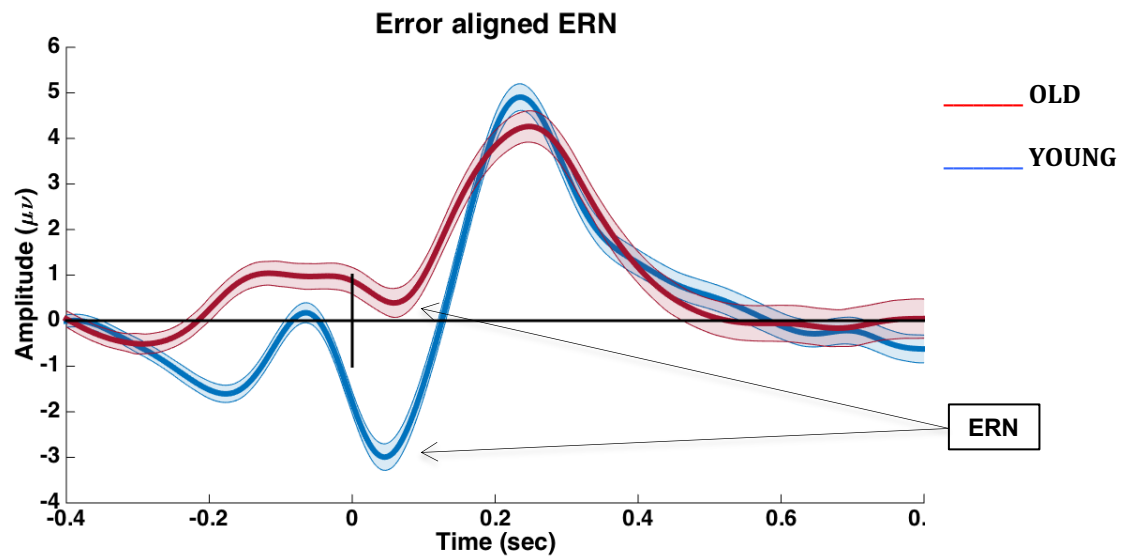


Fig 4.2 Shows the error-aligned ERN component. There were no statistically significant differences between groups for the ERN component.

There was a main effect of group for the peak amplitude of the Pe component when aligned to both the awareness press ($F(1, 40) = 19.22, p < .001$) and the initial error response ($F(1, 40) = 15.98, p < .001$), with younger participants recording significantly higher amplitudes (See **Figure 4.3** and **Figure 4.4**). There was also a significant difference in the build up rate of the aware-locked Pe component ($F(1, 40) = 10.18, p < .005$) with younger respondents exhibiting an increased build-up to peak amplitude when compared to older individuals.

There was no significant difference between our groups in the build-up rate of the Pe component when it was aligned to the erroneous response ($p = .052$). It is worth noting at this point that awareness aligned Pe values are considered to be more closely associated with the point at which peak evidence accumulation has occurred. The latency at which the Pe occurred, whether aligned to awareness ($p = .55$) or error response ($p = .89$) did not significantly differ between groups.

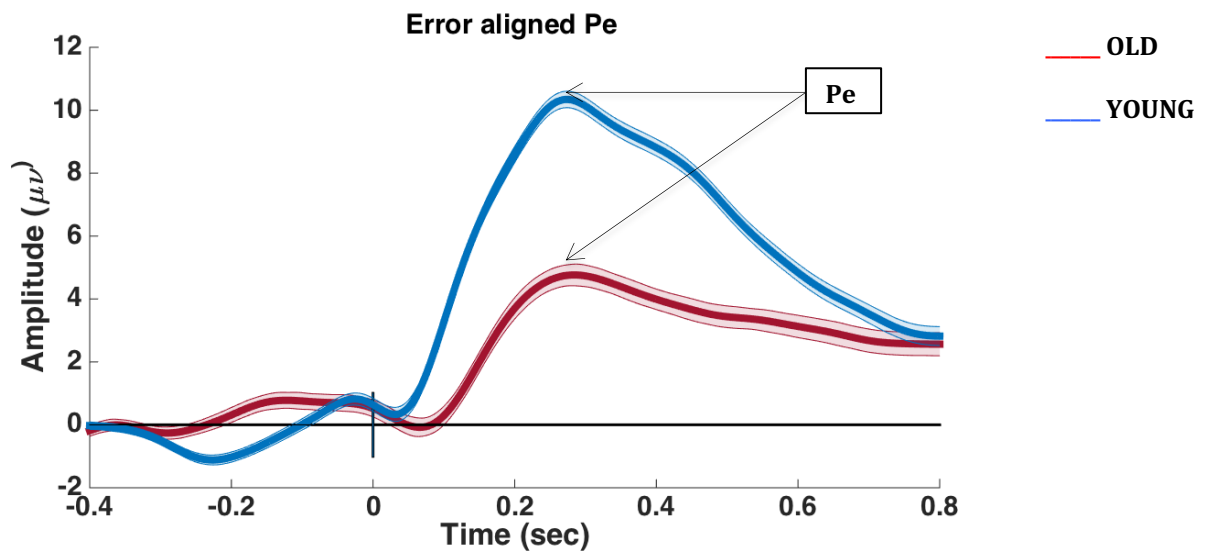


Fig 4.3 Shows the error aligned Pe. There was a significant difference in the amplitude of the error aligned Pe ($p < .001$), but not the build-up rate ($p = .052$),

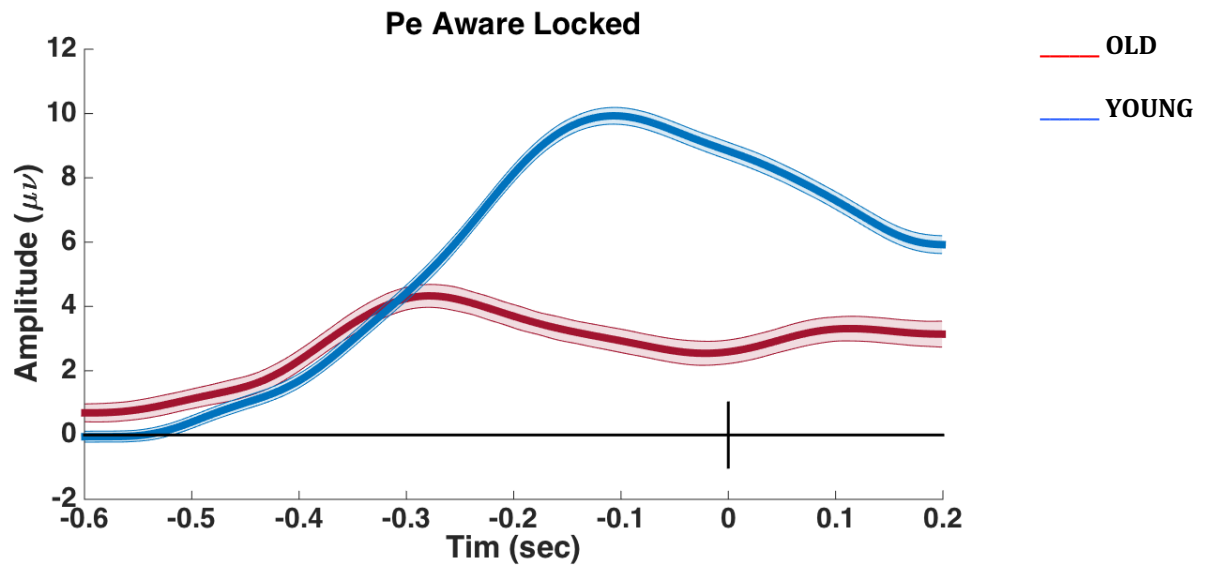


Fig 4.4 Shows the aware aligned Pe. Groups differed significantly with regard to both the amplitude ($p < .001$) and build-up rate ($p < .005$) of the awareness aligned Pe.

Electrophysiology & Psychometric Measures

The Pe component and the ACS-90

A significant correlation between overall ACS-90 scores and the peak amplitude of the Pe was identified in younger adults when it was aligned to the erroneous response ($r(20) = -.461$; $p = .041$) but not in the OA group ($p = .95$). This relationship was not evident when responses were aligned to the awareness locked Pe amplitude, in the YA group ($p = 0.6$) or the OA group ($p = .58$). See **Table 4.5** for details.

We also found that within our YA group the awareness-aligned amplitude ($r(20) = -.532$; $p = .016$) and build-up rate ($r(20) = -.46$; $p = .041$) of the Pe were significantly correlated with the failure-related action orientation

(AOF) subscale, but not in our OA group (amplitude ($p = .63$), build-up rate ($p = .61$)). The AOD subscale was also significantly correlated with the peak error-aligned amplitude of the Pe in the young ($r(20) = -.462$; $p = .04$) but again not in the old group ($p = .87$). The build-up rate of the awareness-locked Pe was significantly correlated with performance related action (AOP) for our older participants ($r(19) = .572$; $p = .041$) but not our younger group ($p = .69$).

Table 4.5 Details correlations between scores on the ACS and error and awareness aligned responses for the Pe. (Relevant Pearson's r -value listed)

		Pe Amplitude <i>Aware aligned</i>	Pe Build-up rate <i>aware aligned</i>	Pe Amplitude <i>Error aligned</i>	Pe Build-up rate <i>error aligned</i>
Young Adults	ACS-90	-.42	-.36	-.461*	-.303
	AOD	-.402	-.373	-.462*	-.322
	AOP	.055	.094	-.106	-.038
	AOF	-.532*	-.46*	-.437	-.295
Older Adults	ACS-90	-.169	.238	.018	.334
	AOD	-.368	.026	-.05	.383
	AOP	-.036	.572*	.379	.18
	AOF	.148	.156	-.07	.072

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant main effect of group. AOP - action orientation during performance of activities vs. volatility; AOF - action orientation subsequent to failure vs. preoccupation; AOD - prospective and decision-related action orientation vs. hesitation.

The Pe component & the HADS

Higher scores on the HADS in our younger adults ($r(20) = .508$; $p = 0.02$) but not older adults ($p = .37$) were significantly correlated with an increased build-up rate of the Pe when error-aligned (see **Figure 4.6** for details). Isolated anxiety scores on the HADS in the YA group were also significantly correlated with increased build-up rate of the error-aligned Pe for younger individuals ($r(20) = .566$; $p = 0.009$) but not in the OA group ($p = .27$). Depression did not correlate with the build-up rate of the Pe in either the young ($p = .154$) or the older ($p = .82$) group.

Table 4.6 Gives details of correlations (Pearson's r value listed) between the HADS and the Pe component.

		Pe Amplitude <i>Aware aligned</i>	Pe Build-up rate <i>aware aligned</i>	Pe Amplitude <i>Error aligned</i>	Pe Build-up rate <i>error aligned</i>
Young Adults	HADS	.229	.129	.135	.508*
	Anxiety	.303	.174	.079	.566*
	Depression	.081	.044	.190	.331
Older Adults	HADS	.129	.159	.023	-.259
	Anxiety	.028	.331	.093	-.317
	Depression	.210	-.141	-.081	-.068

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant correlation.

Relationship Between the ERN, ACS-90 and the HADS

Our analysis found that neither the amplitude nor latency of the ERN was significantly correlated with any aspects of the ACS-90 (all $p > .07$) or the HADS (all $p > .09$).

The EADT, Psychometric Measures & Electrophysiology

Awareness /Accuracy & the ACS-90

There were no significant correlations between awareness levels and scores on the ACS or its subscales for both the younger and older adults (all $p > .07$). This was also found to be the case for accuracy levels in both groups as participant ability to correctly withhold on no-go targets did not significantly correlate with their overall ACS score, their AOP, AOF and AOD scores (all $p > .16$).

Awareness /Accuracy & the HADS

Levels of error awareness on the EADT did not correlate with scores on the HADS, or its depression and anxiety subsections, for either the YA or OA group (all $p > .57$). HADS scores, including anxiety and depression levels, for both the younger and older groups did not correlate with levels of accuracy achieved on the EADT (all $p > .08$).

Awareness / Accuracy & Electrophysiology

The ERN

A bivariate analysis found that the amplitude of the ERN in older participants ($r(17) = -.507, p = .038$) was significantly correlated with the

levels of error awareness but not for younger participants ($p = .928$). Further analysis found that the latency of the ERN was not significantly correlated with awareness in both participating groups (all $p > .45$).

Levels of accuracy on the EADT were not significantly correlated with either the amplitude or the latency of the ERN (all $p > .23$).

Awareness / Accuracy and the Pe component

Younger and older levels of error awareness on the EADT were not significantly correlated with the response locked Pe amplitude, latency or build-up rate (all $p > .18$). When we examined for potential relationships between participant error awareness and the awareness aligned Pe component, again we did not find significant correlations with regard to amplitude, latency or build-up rate (all $p > .19$).

Group levels of accuracy did not interact to a significant level with the error aligned Pe component for amplitude latency or build-up rate (all $p > .16$). We also found that the awareness aligned Pe again in both younger and older adults did not significantly correlate with accuracy levels on the EADT for amplitude, latency and build-up rate (all $p > .19$).

4.5 Materials and Methods Phase 2

Psychometric measures

Again participants completed the **ACS-90** (described in **P1**), the **HADS**, and the **MoCA** (see **Chapters 2** and **3** respectively for a full description).

The TEAT

Participants completed three blocks of the TEAT. As described in **Chapter 3**, each block contains 25 'No-Go' repeat target and 175 'Go' targets. Should participants fail to withhold on No-Go target they were required to engage an error correction response (ECR) via a second touch response at the bottom of the screen. See **Chapter 3** for a full description.

Statistical Analysis

Analysis of our P2 data utilised the same methods as those employed in P1. Statistical analysis for all measures was performed using IBM SPSS Statistics Version 22.

4.6 Results Phase 2

Demographic data for the YA and OA groups who took part in phase 2 (P2) of our project are contained in **Table 4.6**. Older participants and younger adults did not differ significantly in the amount of time they had spent in formal education ($p = .402$).

Listed in **Table 4.7** are the demographics for participants who took part in P2 of the programme. Means $\pm$ standard deviations are reported.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

	YA (n=21)	OA (n = 21)
Age	21.91 $\pm$ 2.35	67.62 $\pm$ 4.64
Gender	12Female, 11 Male	12 Female, 9 Male
Education	16.74 $\pm$ 2.56	16.19 $\pm$ 2.8

OA and YA group performance on the TEAT

A one-way ANOVA suggested that levels of awareness did not significantly differ between younger and older groups ($p = .130$). Older participants were however significantly more accurate than their younger counterparts ($F(1, 42) = 18.17, p < .001$). See **Table 4.7** for further details.

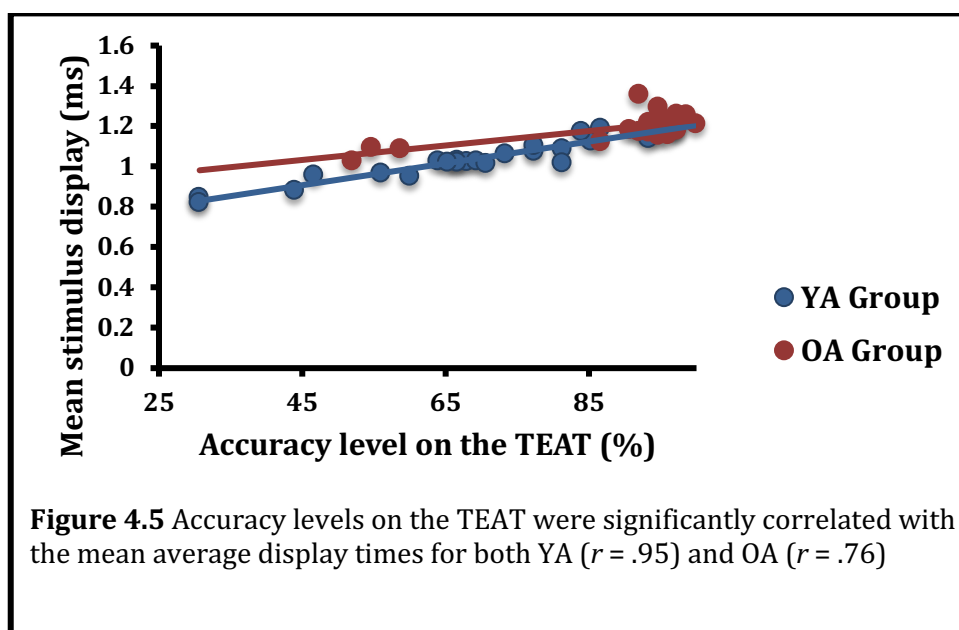
Participant accuracy levels were not found to be significantly correlated with awareness levels in our older participants ($p = 0.24$), this was also the case in our YA group ($p = .167$). See **Table 4.8** for levels of accuracy and awareness.

Table 4.8 Performance related means on the TEAT. Group differed in terms of accuracy and stimulus display time but not levels of awareness.

	YA	OA
Awareness (%)	73.39 ± 29.7	57.08 ± 40*
Accuracy (%)	67.05 ± 17.50	80.83 ± 21.46***
Stimulus display time (ms)	1028.9 ± 99.59	1171.8 ± 97.7***

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant main effect of group.

Younger participants were also found to be exposed to on-screen stimuli for a significantly shorter period of time than their older counterparts ($F(1, 42) = 35.06, p < .001$). As the TEAT is a self-paced task levels of accuracy and the mean average display time were found to significantly correlate in both the YA ($r(23) = .95, p = .000$) and OA ($r(21) = .759, p = .000$) groups. See **Fig 4.5**.



ACS-90 & HADS and performance on the TEAT

Listed below in **Table 4.9** are group means and standard deviations for the Action Control Scale (ACS) and the Hospital Anxiety and Depression Scale (HADS). As each measure can be further fractionated we have also reported scores for the AOD, AOP and AOF sections of the ACS and the Anxiety and Depression subcomponent scores for the HADS.

ACS-90

There was a main effect of group in overall ACS score ($F(1,41) = 4.73, p = .036$) and our groups also differed significantly on the AOD ($F(1,41) = 5.53, p = .024$) component of the ACS, but not the AOP ($p = .369$) or the AOF ($p = .184$).

Levels of error awareness in both the younger and older groups on the TEAT task were not significantly correlated with ACS score or with the AOF, AOD and AOP subsections (all $p > .09$).

Participant Accuracy was significantly correlated with AOF scores in the YA group ($r(23) = .457; p = 0.03$) but not the OA group ($p = .69$). However, accuracy levels on the TEAT did not significantly correlate with any other section of ACS measure (all $p > .09$).

Table 4.9 Psychometric means for YA and OA groups on the ACS and HADS, including subscales for both measures. Participants differed in terms of overall ACS, overall HADS scores, AOD and the Anxiety subsections.

	YA (n= 23)	OA (n = 21)
ACS	19.36 ± 7.27	23.65 ± 5.22*
AOP	7.59 ± 2.92	8.35 ± 2.43
AOF	5.59 ± 3.33	7.1 ± 3.91
AOD	6.18 ± 2.86	8.2 ± 2.69*
HADS	11.59 ± 7.6	6.95 ± 4.46*
Anxiety	7.82 ± 4.38	5 ± 3.05*
Depression	3.77 ± 3.69	1.95 ± 2.09

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant main effect of group. AOP - action orientation during performance of activities vs. volatility; AOF - action orientation subsequent to failure vs. preoccupation; AOD - prospective and decision-related action orientation vs. hesitation.

HADS

Younger individuals reported significantly higher scores on the HADS ($F(1,41) = 5.886, p = .02$) and also significantly higher levels of Anxiety ($F(1,41) = 5.937, p = .019$). Our groups did not differ significantly in reported levels of Depression ($p = .055$). See **Table 4.8** for further details of means and standard deviations.

Levels of awareness on the TEAT did not correlate with overall HADS scores (YA ($p = .44$), OA ($p = .72$)), Anxiety scores (YA ($p = .81$), OA ($p = .40$)) or reported levels of Depression (YA ($p = .19$), OA ($p = .64$)).

Several significant relationships were identified within our younger cohort as we found that YA participant's levels of accuracy decreased as reported levels of Depression ($r(23) = -.679$; $p = 0.001$), Anxiety ($r(23) = -.445$; $p = 0.038$) and overall HADS score ($r(23) = -.586$; $p = 0.004$) increased. Unlike our younger individuals the OA group Anxiety, Depression and overall HADS (all $p > .37$) scores did not significantly correlate with their ability to correctly withhold on TEAT no-go trials. See **Figure 4.6**.

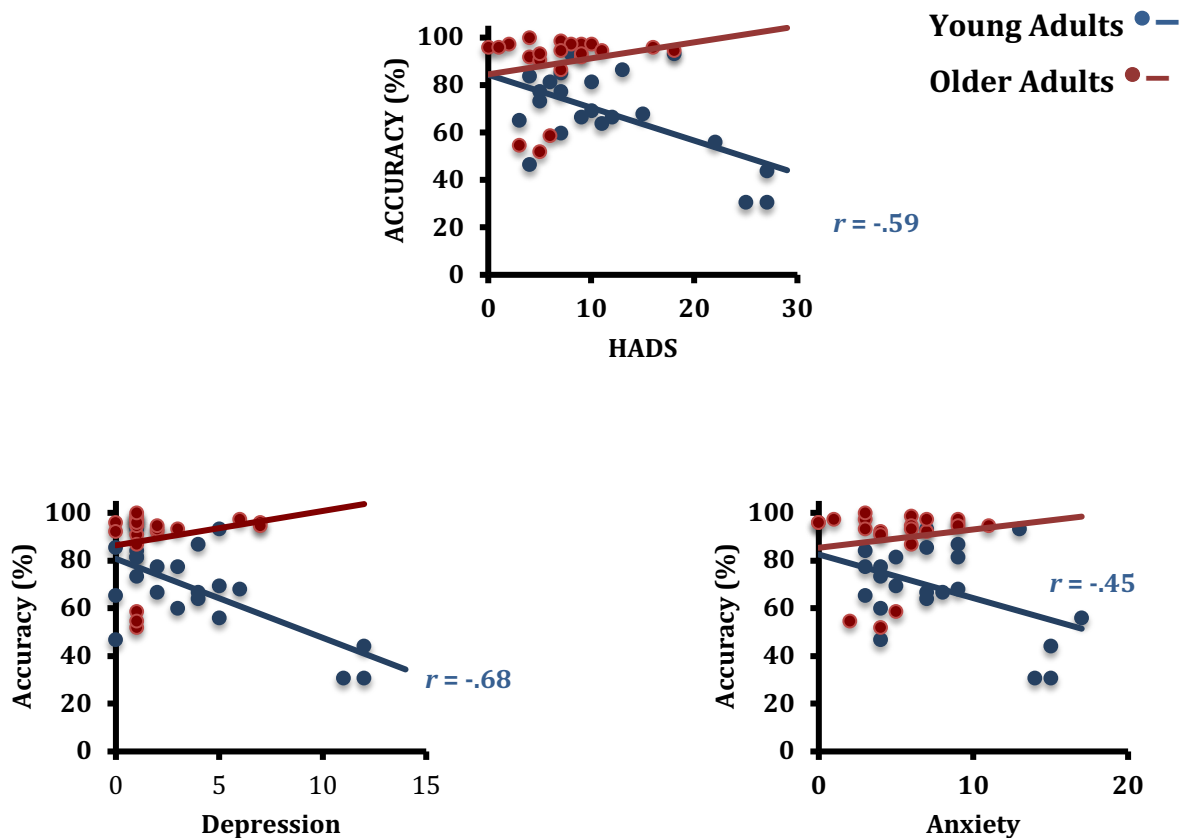


Figure 4.6 Correlations between Scores on the HADS and its subscales of Depression & Anxiety with participant levels of accuracy on the TEAT. Our findings show that the more anxious or depressed younger adults are the less accurate their performance is on a measure requiring high levels of sustained attention.

The MoCA

There was a main effect of group in relation to the clock drawing task section of the MoCA ($F(1, 42) = 5.166, p = .028$) with all younger participants ($M = 3, SD = .00$) achieving the maximum score, while the OA group ($M = 2.81, SD = .40$) recorded significantly lower scores. This aside, groups did not

significantly differ on the overall MoCA ($p = .51$), the Attention subscale ($p = .17$) or the Serial 7 subtraction task ($p = .32$).

MoCA scores and their relationship to the ACS

Overall MoCA score did not correlate with the ACS in either the younger or older group. Nor did it correlate with the AOP, AOD or AOF aspects of the ACS (all $p > .17$).

The MoCA attention subscale was significantly correlated with overall ACS score in the younger group ($r(22) = .55, p = .008$), with higher MoCA scores achieved by those who reported higher levels of action orientation. This was not the case in our older group ($p = .977$). Attention scores were also correlated with AOP in the YA group ($r(22) = .453, p = .034$) and the OA group ($r(20) = .518, p = .019$), while AOD was significantly correlated with attention in our YA participants ($r(22) = .587, p = .004$) but not the OA group ($p = .97$). See **Table 4.9** for full details.

Lower scores on the Serial 7 subtraction task of the MoCA was significantly correlated with the lower scores on the AOF subsection of the ACS for younger individuals ($r(22) = .461, p = .031$) but not for the older group ($p = .61$). No other significant correlations were found between the Serial 7 and either the AOP or AOD sections (all $p > .07$). While increased scores on the Serial 7 did not correlate with higher ACS scores, values were suggestive of an

emergent significant trend ($r(22) = .423, p = .05$) in younger individuals but not older participants ($p = .74$).

Bivariate analysis of the clock section of the MoCA and the ACS did not produce a significant correlation in the older group ($p = .57$). Neither were scores on the AOP, AOD and AOF significantly correlated with MoCA clock scores (all $p > .29$). As all younger participants achieved a maximum score on the clock task Pearson's r was not calculated.

Table 4.10 Correlations between MoCA scores, selected subscales of the MoCA and group means on the HADS and the ACS. Pearson's *r*-values reported.

		MoCA	MoCA <i>Attention</i>	MoCA <i>Serial 7</i>	MoCA <i>Clock</i>
Young Adults	ACS	-.088	.551**	.423	-.380
	AOP	.055	.453*	.143	-.504
	AOD	-.228	.587**	.391	-.405
	AOF	-.046	.3	.461*	-.04
	HADS	.429*	-.401	-.545**	.1
	Anxiety	.49*	-.309	-.51*	.06
	Depression	.301	-.459*	-.517*	.135
Older Adults	ACS	-.054	.007	-.08	-.133
	AOP	.372	.518*	.215	.021
	AOD	-.174	.01	-.052	-.248
	AOF	-.184	-.254	-.126	-.02
	HADS	-.285	-.216	.023	.023
	Anxiety	-.307	-.268	.041	.041
	Depression	-.16	-.07	-.006	-.011

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Indicates a significant main effect of group. AOP - action orientation during performance of activities vs. volatility; AOF - action orientation subsequent to failure vs. preoccupation; AOD - prospective and decision-related action orientation vs. hesitation.

MoCA scores relationship to recorded levels of Anxiety and Depression on the HADS questionnaire

A bivariate analysis found that lower overall MoCA score was significantly correlated with higher overall HADS score in the younger group ($r(22) = .429, p = .046$), but not in the older group ($p = .21$). Further analysis found that higher anxiety was also significantly correlated with lower MoCA scores in younger adults ($r(22) = .49, p = .02$) but not older adults ($p = .18$). Depression did not significantly correlate with overall MoCA score (all $p > .17$).

When we examined the Attention subscale of the MoCA we found lower attentional ability to be significantly correlated with higher levels of depression in our younger group ($r(22) = -.459, p = .032$) but not our older group ($p = .76$). However, attention did not significantly correlate with Anxiety or combined HADS score (all $p > .07$).

When analyzing the Serial 7 subtraction task and its potential relationship to HADS scores we found that the lower S7 score was significantly correlated with higher anxiety ($r(22) = -.51, p = .015$), depression ($r(22) = -.517, p = .014$) and combined HADS score ($r(22) = -.545, p = .009$) for younger participants. In older participants however Anxiety, Depression and combined HADS did not correlate with the S7 task (all $p > .86$).

Older participant reported levels of Anxiety, Depression and combined HADS score did not significantly correlate with the Clock section of the MoCA

(all $p > .86$). Again, as all YA individuals scored maximally on the MoCA Clock task calculating Pearson's r -value was not calculated.

The MoCA and Awareness on the TEAT

Overall score on the MoCA did not significantly correlate with either awareness or accuracy on the TEAT in the OA or YA groups (all $p > .08$). Indeed it was found that awareness and accuracy on the TEAT did not correlate with any aspects of the MoCA (all $p > .051$)

4.7 Discussion

Our understanding of the electrophysiological and cognitive processes that characterize error processing has grown exponentially over the past number of decades (Ullsperger et al., 2014). Recent attempts have also been made to add to this body of knowledge by incorporating affective individual traits such as anxiety and depression into the field (e.g. Aarts et al., 2010). Clinical studies involving TBI, OCD and ADHD affected populations have further helped to broaden the foundation upon which we conceptualize erroneous behavior (Weinberg et al., 2010). Within this chapter we sought to examine the potential role played by factors such as anxiety, depression and action orientation in completing an error awareness task and a commonly used cognitive screening tool, the MMSE. In our analysis we examined behavioural and electrophysiological responses to errors of commission. In line with Chapter 2 potential age related differences in the aforementioned constructs were analysed. Upon completion of analysis several interesting and potentially novel findings emerged. Of particular note was the finding that the build-up rate and amplitude of the Pe component were found to interact with several factors contained within the ACS-90.

As mentioned at the outset, the amplitude of the Pe has regularly been shown to be resistant to change (Holmes & Pizzagalli, 2008), however we believe we have uncovered evidence to suggest that significant changes in amplitude can be linked to the action orientation of younger individuals. Specifically, we assert that the more action orientated one is the larger the amplitude of the Pe when it is aligned to the original commission error.

Furthermore we have evidence to suggest that the build-up rate of the Pe component, linked to the process of evidence accumulation, is altered in older individuals based on whether or not they have difficulty in maintaining focus during goal orientated tasks.

As is often the case, there are several potential reasons as to why some of these findings have emerged. For instance, in terms of the build-up rate of the Pe it seems that the more action orientated an individual is following an error, the more efficient the process of arriving at a decision that an error has occurred becomes. These individuals seem to avoid overly analytical and ruminative thoughts following an error in favour of returning to the task at hand. Similarly the ability of older individuals to focus on a given task whilst excluding potential distractors, as indexed by the AOP section of ACS-90, again means that increased resources are made available for the purpose of making a decision. Though this may seem to advocate for increased levels of action-orientation, this strategy may not necessarily be the most profitable in cognitive terms. There is a distinct possibility that those who are overly eager to advance may fail to adapt and pursue high-risk strategies which make them prone to repeating past unsuccessful actions. The 'best' orientation, mindset or belief may simply be the one that objectively benefits the individual in any given situation.

Also, in what we believe to be a further novel finding, we suggest that the build rate of the Pe is increased in younger individuals with high levels of anxiety and depression. An increased build-up rate may reflect the

aforementioned hyper-vigilance and impending threat perception of anxious individuals (Aarts et al, 2010). This would seem to lay the foundation for a highly accurate, though perhaps stressful, performance. However, what we find is that a higher level of anxiety in younger adults actually coincides with lower accuracy. Unfortunately, as it is quick 'bedside' measure the HADS does not afford us the ability to distinguish between anxiety related symptomology in our participants. This may be further confounded by the fact that depression in the YA group was also correlated with accuracy. What we can state however is that even though increased anxiety has been linked with hypoactivation in the ACC and DLPC (Bishop et al., 2004), these regions are dissociable from the medial prefrontal cortex /anterior midcingulate cortex, the potential source of the Pe, and therefore perhaps we should not anticipate similar patterns of activation.

Anxiety and depression in younger individuals were also linked with lower overall score on the MoCA. Depression, anxiety, and action orientation were implicated in lower scores attained for the attention and Serial 7 subsections of the MoCA for both groups. This again seems to echo previous findings which show that emotional processing and executive control affect performance on cognitive tasks (Del Brutto et al., 2014, O'Keefe et al., 2007). Let us consider for a moment the Serial 7 aspect of the MoCA, (Hayman, 1942).

In theory, younger people with intrusive levels of anxiety and insufficient levels of action orientation may feel unduly stressed when completing a task which they would be expected to complete quite easily. One

might speculate that following an answer on the S7 an anxious individual, uncertain as to whether or not their response was correct, might engage in ruminative thinking which might diminish their ability to answer correctly on the next trial. Increased anxiety and ruminative thinking have been shown to affect attentional processes (Del Brutto et al., 2015), and thus the ability to successfully complete a task becomes even more difficult. These factors combined leave the excessively anxious young adult prone not only to the effect of the speed accuracy trade off, but also to an increased risk of errors due to lapses in sustained attention. On an electrophysiological level, this may be demonstrated by the increased build-up rate of the Pe in overly anxious young adults. Under self-perceived pressure, anxious participants may overly emphasize rapid decision-making, rather than accurate evidence accumulation. Whether the increased build up of the Pe represents improved or impeded performance would then depend on the level of anxiety experienced by the individual.

It is also reasonable to suggest that attention scores on the MoCA, in both younger and older individuals, are influenced by their self-reported ability regarding task and goal maintenance (AOP). Diminished performance on this section of the MoCA by healthy younger adults is unlikely to be the result of pathologically related cognitive deficits; therefore this may reflect ineffective cognitive strategies. These strategies may also be unduly influenced by individual traits such as anxiety. Such individuals may be more prone to attentional drift, or less equipped to endogenously generate the required levels of sustained attention. What is interesting is that these participants seem to

have an awareness of this functional difficulty, expressed through their rating on the ACS-90.

As was previously mentioned we also examined potential age related differences in our groups. In general our data identified similar characteristics to our previous studies, the main finding of which is that older people are more accurate but less aware on the error awareness task. Phase 2 of our study however did seem to contradict this finding, as we found younger and older individuals were not significantly different for awareness. It is quite possible that this may be largely due to the extremely high level of variance within our older sample ($M = 57.08\%$, $SD = 40$).

It was interesting to note that individual traits such as anxiety seemed be more influential in younger participants than the older group. Potentially, this is as a result of elderly individuals exerting increased emotional control and elevated levels of sustained attention. This suggests that a confluence of emotional control and increased ability to generate sustained attention might offset the negative impact of underlying anxiety and depression. This is not to suggest that clinical levels of anxiety and depression would not impact older adult performance.

A more interesting possibility is that older individual are actually less awareness of their negative symptoms. As our measures of anxiety and depression are self reported there is also the possibility that older individuals are underreporting or overestimating (Harty et al., 2013). Of particular interest

would be to examine if this underreporting was as a result of diminished insight into one's emotional state. Earlier we noted how increased anxiety might be related to hypoactivation in the DLPFC and ACC (Bishop et al., 2007). There has also been evidence to suggest that cortical function in these regions is attenuated in older adults. If this is indeed the case, then compromised DLPFC function and thus decreased insight, may account for underreporting of anxious symptoms. The inclusion of a reliable discrepancy measure of anxiety in further research might illuminate this possibility.

Interestingly, outside of a correlation with the amplitude of the ERN in the OA group, levels of error awareness on the EADT and the TEAT were not related to the several emotional and cognitive factors.

In conclusion our data suggests that the electrophysiological and behavioural correlates of erroneous behavior are impacted by anxiety, depression and action orientation. This is evidenced by the effect these factors have on performance of an error awareness task and a well-established cognitive screening tool. We also tentatively suggest that age related changes in emotional and cognitive processing alter error processing over the lifespan. Our findings are supportive of a growing body of evidence which suggests that anxiety in particular may impinge upon or, at least influence, error related research (Moser et al., 2013). For instance we have provided evidence contrary to previous findings that the both the build-up rate and the amplitude of the Pe component are influenced by individual traits (e.g. Santesso et al., 2005). The significance of these findings we believe is manifold. Emotional control it

would seem has the ability to both enhance and hinder performance on complex cognitive tasks. On the one hand anxiety may induce a heightened sense of vigilance leading to improved performance, however, should these feelings cross a certain threshold an individual may be inclined towards stress reducing strategies rather than ones which geared toward optimal task performance. There is also the possibility that complex processes involved in completing laboratory based cognitive tasks may potentially be responsible for creating the undue levels of stress in participants. This is essentially a methodological which should be a consideration at the design stage of future research. Finally, we would suggest that serious consideration should be given to the effects of anxiety and depression on cognitive ability in clinical settings (Blair et al., 2016). Cognitive and emotional dysfunction are often inextricably linked and by evaluating both concurrently at the earliest point, the diagnostic process will be greatly enhanced.

Chapter 5

Discussion

5.1 Summary of Findings

Over the past number of decades we have witnessed a global increase in human life expectancy which has ignited a flurry of research into the multifaceted domain of ageing. Perhaps loudest amongst the many voices within the research community are those who highlight the cognitive, cortical and physical diminution of function in older adults, with compromised executive function being particularly affected. Of particular interest has been the possible deleterious effect of ageing on our ability to monitor, appraise and accurately report on our own behavior. We have already recounted how imprecise knowledge of illness in clinical populations can impact on early diagnosis, responsiveness to treatment, proneness to injury and increased caregiver burden (Kaszniak et al., 2010, Starkstein, 2014). There has been also been a limited amount of evidence to suggest that this ability is diminished as part of the natural healthy aging process (Bruce, Coyne, & Botwinick, 1982; Harty et al., 2013; Harty et al., 2014; Graham, Kunik, Doody, & Snow, 2005; Rabbitt, 1990; Suchy, Kraybill, Frnachow, 2011), while there have also been findings to the contrary (Clare, Whitaker, & Nelis, 2010; Lovelace & Marsh, 1985; Rabbitt, 2002). Similarly there have been reports to suggest that levels of vigilance and sustained attention are attenuated in older adults, in part as a

result of hypoactivation of the rDLPFC (Manly et al., 2003), which combined may result in lower levels of awareness.

Again however there are dissenting voices, who claim that older individuals actually possess a greater ability than younger individuals to endogenously generate heightened attentional states even in the absence of any meaningful exogenous stimulation (Carriere et al., 2010). In light of these many competing theories it is often difficult to precisely characterize which areas of cognitive dysfunction are solely age related and those that are associated with underlying pathology, individual traits or task related phenomena. This latter issue, which includes elements such as speed of processing, task difficulty and the speed accuracy trade off, may play a more important role than many might wish to believe. Due to the enormous heterogeneity of the ageing process, we believe that by examining function across several populations we may be able to unravel and isolate certain age related characteristics of error awareness. By focusing on younger adults, older adults and those with a diagnosis of Alzheimer's disease we have employed strategy in which we believe each participating group has the ability to delineate the error processing signatures specific to their own cohort and those of competing groups.

In Chapter 2 of this thesis we examined the error processing ability of younger and older adults on the newly developed error awareness dot task, EADT, a modified version of the Hester et al.'s EAT. We did so whilst recording electrophysiological data from our participants. As our protocol was largely

influenced and designed in accordance with Harty et al.'s 2013 study which compared online error awareness with psychometric measures of awareness in everyday function, we also included a multi-domain assessment of current level of cognitive function and a measure of awareness, the CFQ. The findings from this study support previous reports that healthy adults have significantly diminished awareness of their errors. This was not however reflected in discrepancy scores of everyday cognitive function recorded on the CFQ. Interestingly there was a correlation between lower levels of online awareness and lower scores on the MMSE. Amongst our main electrophysiological findings we also found evidence to support previous suggestions of age related attenuation of the for the Pe component (Band et al., 2000; Falkenstein et al., 2000; Leuthold et al., 1999; Mathewson et al., 2005). Whilst we acknowledge that an age-related reduction in processing power has contributed to these findings, the data also suggests that inherent task-related strategies may have augmented performance on the EADT.

We would argue that diminished cognitive function is not entirely responsible the levels of awareness recorded throughout this study. The data would seem to suggest that diminished awareness is, in part at least, related to the strategic approach taken by older adults, overwhelmingly characterized by slower responding. This phenomena leads to an alteration of the underlying cognitive responses normally witnessed in the 'normal' error processing system of younger individuals. One of the main effects of this variation in processing is that older individuals achieve significantly higher levels of accuracy compared to their younger counterparts, due perhaps in no small part

to elevated levels of sustained attention (Carriere et al., 2010). Increased vigilance in this case we believe is driven by elevated task difficulty, due to the embedded staircase method which either elongates or shortens task stimulus presentation time. Both of these elements thus lead our older participants to be “absent minded but accurate” (Shalgi et al., 2007). Their errors therefore can largely be attributed to lapses in sustained attention. As a result of this far fewer errors are committed, and of those that are; a higher percentage fall under the radar. It is at this point that the closely related, predominantly right hemispheric, neural phenomena of sustained attention and intact awareness (Harty et al., 2014; O’Connell et al., 2004; Robertson, 2010; Sturm & Wimes, 2001) may interact to disturb the process of accurate insight. Age-related hypoactivation of the rDLPFC and inevitable lapses of attention may contrive to decrease awareness of errors. Of equal importance are the task related effects on the process of evidence accumulation and consequent decision-making. Older adults have less time and less evidence with which to evaluate an action. This is then reflected electrophysiologically by a significant reduction in the build-up rate (evidence gathering) and amplitude (emergent awareness) of the Pe. It is quite possible therefore, that older and younger adults commit two related but dissociable types of error while performing the same task. Impaired awareness in this particular study may then be characterized as a conglomeration of biological, cognitive and methodological factors.

Hyper vigilance therefore has both a positive and negative impact on behavior. In everyday function one may become so fixated on a certain course

of action that errors may go unnoticed, impairing the ability to assess and modify behavior during the course of an activity. Consider for instance the driver who is so focused on maintaining accurate road position that they miss a red light. The counter argument of course is that fewer errors lead to fewer potential accidents.

An important and perhaps novel finding from this current study is that levels of error awareness are correlated with MMSE scores. The MMSE is quite often used by general practitioners prior to memory clinic referral and is therefore quite an important tool in the diagnostic battery. Some however have suggested that it does not possess the desirable level of sensitivity required to detect early levels of pathological cognitive impairment (Nieuwenhuis-Mark, 2010). For this reason we suggest that the incorporation of a quick 'bedside' test which evaluates patient levels of online error awareness might discern hitherto undetected markers of cognitive decline. It was this hypothesis which was to drive the next phase of our research.

In Chapter 3 we continued our exploration of error awareness by examining the 'online' ability of Alzheimer's disease patients to actively assess their performance on a modified version of the EADT. The tablet error awareness task (TEAT) was adapted to suit the particular needs of a clinical population. Similar to our findings regarding the MMSE, levels of online awareness were significantly correlated with scores on the Montreal Cognitive Assessment. The MoCA is potentially the most widely employed psychometric tool in the early assessment of potential dementia and has been regularly been

shown to be more sensitive than the MMSE (Hoops et al., 2009). It has also been shown to be sensitive to cognitive dysfunction in several other clinical populations (Dagenias, Rouleau & Demers et al., 2005; Gluhm, Goldstein, Broen, et al., 2013; De Guise, Alturki & LeBlanc, et al., 2014). Upon fractionation of the MoCA it was discovered that awareness was particularly related to the attention and executive function components of the task, echoing our findings from Chapter 2. This is of particular importance we feel as it was also found that Alzheimer's patients were significantly more accurate than younger individuals and matched levels of accuracy / attention displayed by age matched controls. Further investigation revealed that this preservation of function did not extend to awareness, as AD patients demonstrated significantly lower levels of error awareness compared to both young and older adults. This evidence runs counter to previous reports of preserved awareness in AD populations (Ito et al., 2005; Mathalon et al., 2003). What these findings seem to suggest is that, in certain settings, Alzheimer's patients are capable of maintaining rather high levels of vigilance and sustained attention. What we may derive from this is that diminished awareness in those with a diagnosis of AD is potentially due to increased pathological degradation and hypoactivation of the rDLPC, rather than degraded cognitive processes.

If for a moment we set aside the theoretical consequences of these findings there are several potential real world applications to be derived from these first two chapters. Chief amongst them is the potential to use the error awareness construct early in the diagnostic process. We have seen how both older adults and AD patients endogenously generate heightened levels of

vigilance and sustained attention. We have also witnessed how both of these groups selectively use certain task related attributes, such as slowing of responses, in a different manner to younger adults. It is therefore possible that those in the pre-morbid stages of dementia may successfully negotiate certain diagnostic tools despite the presence of underlying pathology. Regardless of strategy however, what both groups fail to adequately achieve is sufficient error signaling, implying diminished awareness. What the present study then shows, perhaps for the first time, is the level to which AD levels of online awareness are compromised when compared to that of healthy older adults. In isolation, assessment of error awareness may not be sufficient to accurately diagnose dementia or MCI, but it would certainly have the potential buttress existing measures.

Another possible issue arising from this data is the potential to develop rehabilitation methods aimed at ameliorating awareness in AD patients. We have previously mentioned how Harty and colleagues demonstrated a significant improvement in levels of awareness through the application of anodal transcranial direct current stimulation over the rDLPFC (Harty et al., 2014). By furthering this line of enquiry we may be in a position to mitigate both age-related and pathological deterioration of this cortical region.

As in Chapter 2, our findings from Chapter 3 also did not identify a relationship between everyday cognitive function on the PCRS and levels of error awareness. While previous studies have demonstrated this link (Hoerold et al., 2008) there are many potential reasons why this did not materialise in

the current data. It is possible that previously mentioned problems with discrepancy measures, such as caregiver over or underestimation of ability due to level of burden, might have impacted our findings (Mangone, 1991; Starkstein, 2014). It is also quite possible that the specific cortical attributes required for online awareness are dissociable from the metacognitive processes engaged during the execution of ADL's. For instance competency on basic ADL's such as grooming and feeding are highly dependent on intact motor function and coordination (Bennett, 2002;), and therefore are may not overly influence a task such as that employed here. This perhaps suggests that more consideration should be given to instrumental ADL's; complex behaviours such as adhering to medication protocols and managing finances (Cahn-Weiner et al., 2007) as previous studies have suggested that impaired executive and working memory function are more closely related to activities of this kind.

One further possibility is that because of the level of task difficulty on measures of awareness, such as the EAT (Hester et al., 2005), previous findings may better represent the relationship between complex laboratory based tasks and the higher level cognitive processes necessary for the execution of ADL's. On the other hand, due to the relative simplicity of the current measures, performance on the EADT and TEAT may simply reflect an isolated factor of the overall awareness process which does not impact success on ADL's.

What the previous chapters have therefore highlighted is that while there may be identifiable characteristics and well-defined correlates of any

given cognitive function, these signatures are often open to several lines of corruption. These may be methodological, strategic, pathological or age-related.

With Chapter 4 of this thesis delineating matters such as these were perhaps complicated even further by inclusion of questionnaires to record levels of anxiety and depression at the time of testing. This was further supplemented by self-reported measures of action-orientation (Kuhl, 1990), representative of the cognitive approach to everyday activities. The data from this chapter, perhaps unsurprisingly, suggested that individual traits have the ability to either impede or assist task performance.

Electrophysiological evidence emerged to suggest that the more action orientated an individual is, the greater the amplitude and build up rate of the Pe is. That is to say, an older adults personal ability to maintain task goals and avoid ruminative thoughts encourages more efficient evidence accumulation. This finding contradicts previous reports which suggest that the Pe is resistant to change, and is representative of a purely cognitive process (Holmes et al., 2008). Further evidence was also presented to challenge this theory, as high levels of anxiety and depression in younger adults were found to increase the build-rate of the Pe. It is therefore possible that those who are susceptible to anxious thoughts may adopt a state of hyper-vigilance, constantly assessing their environment for potential threats (Aarts et al., 2010). The threat in this case? Task failure. However what we see is that these same individuals actually record lower accuracy levels. As these are novel findings it is difficult to

account for this finding, but there may be merit in the following conceptualization of the process.

Age related characteristics such as speeded responding and diminished inhibition are further exacerbated by anxious feelings and hyper-vigilance, which combined lead these individuals to display decreased levels of accuracy. When an error does occur there may be a tendency to over analyze, interpret or ruminate on incoming task related evidence which may in turn lead to increased electrophysiological activity. This of course is merely speculative. It assumes that the increased build-up rate of the Pe is not solely representative of the quality of evidence or one's confidence regarding a decision; rather it is a measure of the magnitude of computational resources utilised in the evidence accumulation process. While we acknowledge the hypothetical nature of this theory, and accept that anxiety has regularly been linked to cortical hypoactivation (e.g. Bishop et al., 2007), it remains plausible that awareness process is influenced by the hyper-vigilant state of the anxious participant. In terms of emotion then, decreased levels in the build-up rate of the Pe then may be a combination reduced processing power but decreased activity due to heightened emotional control in older adults. As the precise nature of Pe has not been fully elucidated on (Murphy et al., 2013), further investigation would certainly seem to be warranted in order to discount or support this line of thinking.

Chapter 4 also presented us with evidence that performance on the MoCA is influenced by the level of anxiety felt by the participant at the time of

testing, supporting previous findings of a similar nature (Blair et al., 2016; Del Brutto et al., 2014). These findings should not entirely come as a surprise as in the event that one is referred to a memory-clinic; there is a high possibility that a life changing diagnosis may be given. In such circumstance it is highly probable that emotion may impact on performance. If these effects are demonstrable even in a laboratory setting, the level to which they might confound scores in a clinical setting should perhaps form part of the diagnostic protocol. This is of particular importance in light of the difficulty many clinicians already face in separating emotional and cognitive symptoms of potential pathology (Steffens, 2008).

5.2 Methodological Considerations

The series of studies reported in this thesis represent an attempt to uncover underlying error related signatures in a range of populations. The methodologies employed, whilst not entirely novel, included several new modifications. As is quite often the case, the development of new tasks, that reliably and sensitively capture the precise cognitive phenomenon in question, is a complicated venture. One of the main aims of our task parameters was to reduce task difficulty whilst retaining the potential for participants to commit a sufficient number error to support our analysis. As part of this we adopted the staircase method, which varied the stimulus duration in the both the EADT and the TEAT.

While it is possible that these new measures demonstrated the inherent strategic differences between our populations, they may also have affected

awareness levels. As both the AD and older groups displayed significantly higher accuracy levels compared to younger individuals, the subsequent awareness correlates may not precisely represent the of ability in these populations. It is possible that both are actually less aware, however, task related parameters have served to upgrade performance. It may seem odd to suggest that the amelioration of diminished awareness is a negative outcome, however, if we are to truly understand the level of diminution related to the ageing and pathological characteristics of error processing we must consider this finding in such a light. It is only through the development of empirical measures, which precisely recruit the same cognitive processes across all age groups and populations, that we might be able to fully understand this phenomenon as it develops over the lifespan, including its manifestation in pathological domains.

In particular we suggest that the complexity of tasks should consider and reflect upon the wide range of social, cortical and behavioural changes which are observed in older adults. As our own research has highlighted, the dynamic relationship between cortical recruitment and behavioural strategies are constantly developing throughout much of ours lives. If in fact it is these changes that are the main area of interest this does not seem to pose a great problem. However, if the aim of our research is to describe the trajectory of a specific cognitive function as it transforms over the life span, then egalitarian measures that neither hinder nor help specific individuals are essential. Chief amongst these factors in error processing are speed-accuracy, task difficulty and the projected cortical recruitment inherent in our methods.

One notable observation throughout our research is the enormous level of variability across all domains, both between and within age groups. For instance, the failure of five AD participants to complete the TEAT task, despite achieving results comparable to those of other patients on a range of psychometric tests. Though it may be idealistic to envisage a task that is suitable for all participants and patients, it may not be practical. The incredible level of heterogeneity associated with all aspects of human cognition and emotion may mean that the data of certain individuals may be rendered unusable throughout the course of the testing process. The question is; should we expand out tasks to try and bring these individuals back into the fold, or should we accept the loss of this data as 'collateral damage'. Collateral damage? As all tasks are open to any number of exogenous confounding variables attempts therefore to modify, or to put it rather crudely 'dumb down', tasks we are possibly exposing our methods and data to an even greater level of corruption. This is not say that we should not aim to gather evidence from as many individuals as possible, but perhaps not by sacrificing the purity of the cognitive phenomenon we wish to assess.

While discrepancy measures provide us with an valuable insight into the perceived level of functioning, of both patient and healthy participants, it is important to acknowledge them for what they are; subjective perceptions. This is also true of the accounts provided by significant others, particularly in clinical studies. Over the course of our own programme we suggest that on more than one occasion, familial carers, who seemed anxious or overburdened

by the stress of caring for a loved one, were seen to underestimate patient functionality. While this is subjective and speculative, it certainly warrants further discussion.

5.3 Future Research

A potential exciting path to embark upon in this field of research is the establishment of a model which predicts diminished error awareness. There is overwhelming evidence to suggest that the rDLPFC plays an important role in compromised insight in both everyday and laboratory based cognitive insight. And while the electrophysiological and behavioural evidence related to error awareness has illuminated this process, we believe that the inclusion of both functional and volumetric neuroimaging techniques may propel this research to another level. If indeed the rDLPFC is fundamental to this process, it follows then that a volumetric reduction due to age-related or pathological atrophy may be partly responsible for impaired function. Longitudinal studies, which assess both age-related degradation of the rDLPFC and behavioural measures of online insight, can perhaps offer an insight into the diminution of awareness so often reported in older adults. Hypothetically, cytoarchitectural stability or atrophy and decreased activity of this region, measured at different intervals, may correlate with reduced or preserved awareness. This model may also inform us as to the specific types of cognitive activities and ADL's that are associated with rDLPFC function. While some attempts have been made to explore this process (e.g. Cahn-Weiner et al 2007), a coherent model has yet to be created.

We have already alluded to the fact that diminished online awareness has been shown to correlate with lower scores on the MMSE and the MoCA. However, it is important to reiterate our belief that by exploring this phenomenon at the earliest possible phase of the diagnostic process clinicians, patients and their families will benefit. This is of particular importance when one considers the enormous benefits bestowed by accurate early diagnosis.

5.4 Final Thoughts

When the late Francis Crick employed the reductive “nothing but a bunch neurons” maxim (Crick, 1994), the at times controversial theorist Steven Rose suggested that he had “splendidly missed the point”, as he ignores the fact that ‘We are...by virtue of possessing these neurons...humans with agency...history’ - we are ‘biosocial organisms’ (Rose, 2006). Cognitive science now pervades almost every aspect of daily life; from the classroom to the your car. Perhaps more importantly, it has played a significant role in discovering the underlying causes for several clinical conditions and has further assisted in the development of remedial therapies. For this reason it is imperative that we resist the temptation to succumb to the bunch of neurons axiom and embrace the interdependent bio-psycho-social model of human behavior. For it is only by taking such an approach that we can hope to truly develop a coherent model of cognitive psychology. Psychological study is also not immune to the process of stereotyping, and so researchers must challenge the narrative that those in society who are older are on a psychological and physiological downward

spiral. For this to happen perhaps it is time for the psychology of healthy ageing to coalesce within the development framework.

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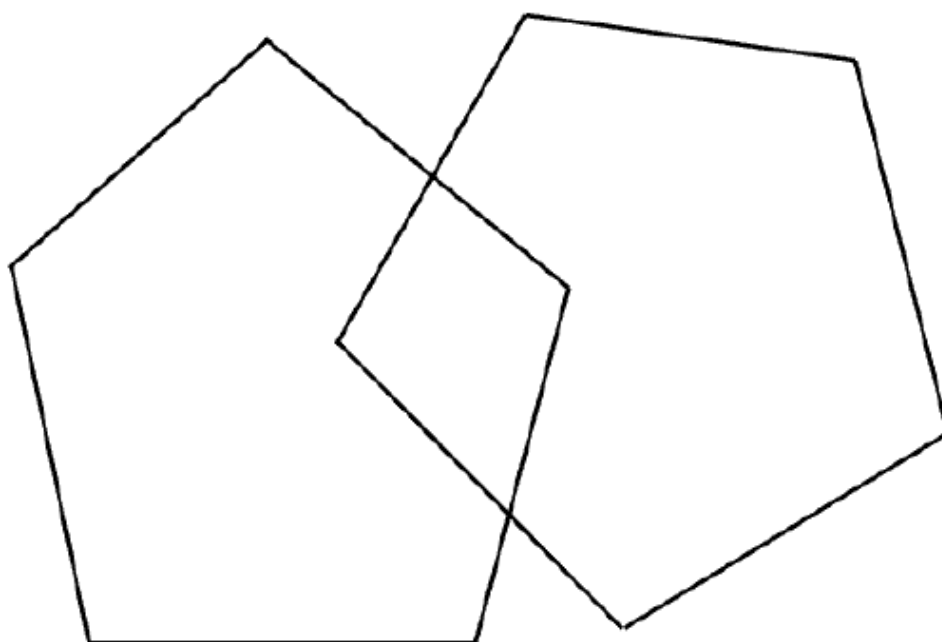
Appendices

Appendix A

Mini Mental State Exam (MMSE)

MINI MENTAL STATE EXAM	
Participant ID: _____	Date: ____/____/____
ONE POINT FOR EACH CORRECT ANSWER	SCORE
ORIENTATION	
• What is today's date? ____ • What year is it? ____ • What month is it? ____ • What day is it today? ____ • What time is it? ____	____/ 5
• What country are we in? ____ • What county are we in? ____ • What city? ____ • What institution? ____ • What floor are we on? ____	____/ 5
IMMEDIATE RECALL/REGISTRATION	
• Examiner names three objects (eg <i>apple, table, penny</i>) - Participant is then asked to repeat these words. - If the participant cannot remember ask them to repeat the sequence up to six times until they get it right.	____/ 3
ATTENTION & CALCULATION	
• Ask the participant to subtract 7 from 100 and then repeat from the result, continue five times scoring 1 for each correct response 100 / 93 / 86 / 79 / 72 / 65.	____/ 5
• Alternative: Spell "WORLD" backwards – "DLROW".	
RECALL	
• Ask the participant to repeat the three words learned earlier	____/ 3
LANGUAGE	
• Show and ask the participant to name a watch and a pencil.	____/ 2
• Repeat "No ifs, ands, or buts"	____/ 1
• Give a three stage command and ask the participant to complete the action. "Place the index finger of your right hand on your nose and then on your left ear".	____/ 3
• Ask the patient to obey the written command "CLOSE YOUR EYES"	____/ 1
• Ask the patient to write a sentence. Score the sentence if it is sensible and has a subject and a verb.	____/ 1
COPYING	
• Ask the participant to copy a pair of intersecting pentagons:	____/ 1
Researcher: _____	TOTAL SCORE: ____/ 30

CLOSE YOUR EYES



Appendix B

Cognitive Failures Questionnaire (Broadbent, et al., 1982)

The following questions are about minor mistakes which everyone makes from time to time, but some of which happen more often than others. We want to know how often these things have happened to you in the past 6 months.

Please circle the appropriate number.

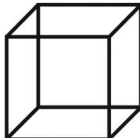
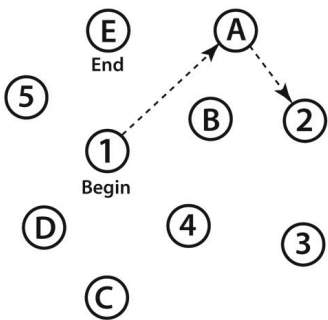
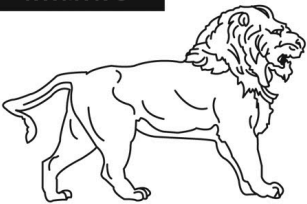
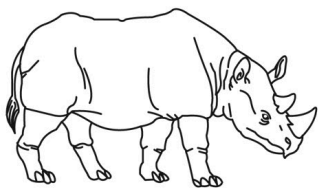
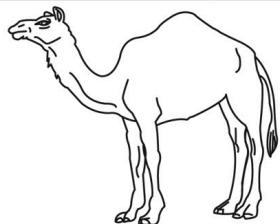
		Very often	Quite often	Occasion - ally	Very rarely	Never
1.	Does he/she read something and find they haven't been thinking about it and must read it again?	4	3	2	1	0
2.	Does he/she find they forget why they went from one part of the house to the other?	4	3	2	1	0
3.	Does he/she fail to notice signposts on the road?	4	3	2	1	0
4.	Does he/she confuse right and left when giving directions?	4	3	2	1	0
5.	Does he/she bump into people?	4	3	2	1	0
6.	Does he/she forget whether they've turned off a light or a fire or locked the door?	4	3	2	1	0
7.	Does he/she fail to listen to people's names when they are meeting them?	4	3	2	1	0
8.	Does he/she say something and realize afterwards that it might be taken as insulting?	4	3	2	1	0
9.	Does he/she fail to hear people speaking to them when they are doing something else?	4	3	2	1	0
10.	Do you lose your temper and regret it?	4	3	2	1	0
11.	Does he/she leave important letters unanswered for days?	4	3	2	1	0
12.	Does he/she find they forget which way to turn on a road they know well but rarely use?	4	3	2	1	0
13.	Does he/she fail to see what they want in a supermarket (although it's there)?	4	3	2	1	0
14.	Does he/she find himself/herself suddenly wondering whether they've used a word correctly?	4	3	2	1	0

		Very often	Quite often	Occasion - ally	Very rarely	Never
15.	Does he/she have trouble making up their mind?	4	3	2	1	0
16.	Does he/she forget appointments?	4	3	2	1	0
17.	Does he/she forget where they put something like a newspaper or a book?	4	3	2	1	0
18.	Does he/she find they accidentally throw away the thing they want and keep what they meant to throw away – as in the example of throwing away the matchbox and putting the used match in your pocket?	4	3	2	1	0
19.	Does he/she daydream when they ought to be listening to something?	4	3	2	1	0
20.	Does he/she forget people's names?	4	3	2	1	0
21.	Does he/she start doing one thing at home and get distracted into doing something else (unintentionally)?	4	3	2	1	0
22.	Does he/she find they can't quite remember something although it's "on the tip of their tongue"?	4	3	2	1	0
23.	Does he/she forget what they came to the shops to buy?	4	3	2	1	0
24.	Does he/she drop things?	4	3	2	1	0
25.	Do he/she find they can't think of anything to say?	4	3	2	1	0

Participant: _____

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Montreal Cognitive Assessment (MoCA)

MONTREAL COGNITIVE ASSESSMENT (MOCA)				NAME : _____		Date of birth : _____	
Version 7.1 Original Version				Education : _____		Sex : _____	
VISUOSPATIAL / EXECUTIVE				 Copy cube [] []		Draw CLOCK (Ten past eleven) (3 points) [] [] [] Contour Numbers Hands ____/5	
 [] [] []							
NAMING							
 []				 []		 [] ____/3	
MEMORY							
Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.				FACE VELVET CHURCH DAISY RED		No points	
1st trial							
2nd trial							
ATTENTION							
Read list of digits (1 digit/ sec.).				Subject has to repeat them in the forward order [] 2 1 8 5 4		____/2	
				Subject has to repeat them in the backward order [] 7 4 2			
Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors				[] FBACMNAAJKLBFAKDEAAAJAMOFAAB			
Serial 7 subtraction starting at 100 [] 93 [] 86 [] 79 [] 72 [] 65				4 or 5 correct subtractions: 3 pts , 2 or 3 correct: 2 pts , 1 correct: 1 pt , 0 correct: 0 pt		____/3	
LANGUAGE							
Repeat : I only know that John is the one to help today. []						____/2	
The cat always hid under the couch when dogs were in the room. []							
Fluency / Name maximum number of words in one minute that begin with the letter F [] ____ (N ≥ 11 words)						____/1	
ABSTRACTION							
Similarity between e.g. banana - orange = fruit [] train – bicycle [] watch - ruler						____/2	
DELAYED RECALL							
Has to recall words WITH NO CUE [] [] [] [] []						Points for UNCUED recall only	
Category cue							
Multiple choice cue							
Optional						____/5	
ORIENTATION							
[] Date [] Month [] Year [] Day [] Place [] City						____/6	

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Normal ≥ 26 / 30

TOTAL

____/30

Administered by: _____

Add 1 point if ≤ 12 yr edu

Appendix D

Patient Competency Rating (Patient's Form)

Source: Prigatano, G. P. and Others (1986). Neuropsychological Rehabilitation After Brain Injury. Baltimore: Johns Hopkins University Press.

Identifying Information

Patient's Name: _____

Date: _____

Instructions

The following is a questionnaire that asks you to judge your ability to do a variety of very practical skills. Some of the questions may not apply directly to things you often do, but you are asked to complete each question as if it were something you "had to do." On each question, you should judge how easy or difficult a particular activity is for you and mark the appropriate space.

Competency Rating

1	2	3	4	5
Can't do	Very difficult to do	Can do with some difficulty	Fairly easy to do	Can do with ease

- | | |
|-------|---|
| _____ | 1. How much of a problem do I have in preparing my own meals? |
| _____ | 2. How much of a problem do I have in dressing myself? |
| _____ | 3. How much of a problem do I have in taking care of my personal hygiene? |
| _____ | 4. How much of a problem do I have in washing the dishes? |
| _____ | 5. How much of a problem do I have in doing the laundry? |
| _____ | 6. How much of a problem do I have in taking care of my finances? |
| _____ | 7. How much of a problem do I have in keeping appointments on time? |

	1	2	3	4	5
	Can't do	Very difficult to do	Can do with some difficulty	Fairly easy to do	Can do with ease
_____	8. How much of a problem do I have in starting conversation in a group?				
_____	9. How much of a problem do I have in staying involved in work activities even when bored or tired?				
_____	10. How much of a problem do I have in remembering what I had for dinner last night?				
_____	11. How much of a problem do I have in remembering names of people I see often?				
_____	12. How much of a problem do I have in remembering my daily schedule?				
_____	13. How much of a problem do I have in remembering important things I must do?				
_____	14. How much of a problem would I have driving a car if I had to?				
_____	15. How much of a problem do I have in getting help when I'm confused?				
_____	16. How much of a problem do I have in adjusting to unexpected changes?				
_____	17. How much of a problem do I have in handling arguments with people I know well?				
_____	18. How much of a problem do I have in accepting criticism from other people?				
_____	19. How much of a problem do I have in controlling crying?				
_____	20. How much of a problem do I have in acting appropriately when I'm around friends?				
_____	21. How much of a problem do I have in showing affection to people?				
_____	22. How much of a problem do I have in participating in group activities?				

1	2	3	4	5
Can't do	Very difficult to do	Can do with some difficulty	Fairly easy to do	Can do with ease

- _____ 23. How much of a problem do I have in recognizing when something I say or do has upset someone else?
- _____ 24. How much of a problem do I have in scheduling daily activities?
- _____ 25. How much of a problem do I have in understanding new instructions?
- _____ 26. How much of a problem do I have in consistently meeting my daily responsibilities?
- _____ 27. How much of a problem do I have in controlling my temper when something upsets me?
- _____ 28. How much of a problem do I have in keeping from being depressed?
- _____ 29. How much of a problem do I have in keeping my emotions from affecting my ability to go about the day's activities?
- _____ 30. How much of a problem do I have in controlling my laughter?

Appendix E

Action Control Scale (ACS-90) (English version of the German HAKEMP-90)

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Unit of "Differentielle Psychologie und Persönlichkeitsforschung"

The action control scale consists of three subscales:

1. Action orientation subsequent to failure vs. preoccupation (AOF)
2. Prospective and decision-related action orientation vs. hesitation (AOD)
3. Action orientation during (successful) performance of activities (intrinsic orientation) vs. volatility (AOP)

Each scale consists of 12 items which describe a particular situation. Each item has two alternative answers (A or B), one of which is indicative of action orientation and the other of state orientation.

For scoring the test values, using the action-oriented answers is recommended. The sum of the action-oriented answers for each scale is between 0 and 12.

The items are numbered from 1-36. Which items belong to which scale, and which choice alternative is indicative of **action orientation**, can be found in the following key:

1. Failure-related action orientation vs. preoccupation (AOF)
1B, 4B, 7A, 10A, 13B, 16B, 19A, 22B, 25B, 28B, 31B, 34A
2. Decision-related action orientation vs. hesitation (AOD)
2B, 5B, 8B, 11A, 14B, 17B, 20B, 23A, 26A, 29B, 32A, 35A
3. Performance-related action orientation vs. volatility (AOP)
3B, 6B, 9A, 12B, 15A, 18B, 21A, 24B, 27A, 30B, 33B, 36A

When scoring the questionnaire, the three scales should be scored separately, since each scale deals with a different behavioral aspect of action orientation. If a case arises where giving the entire 36 item questionnaire is not possible, then two of the three scales should be given, rather than only part of the three scales. Since the AOP scale can be affected by several variables other than action/state orientation, this scale can be left out if this particular behavioral aspect has no special importance in the planned study. The scales AOF and AOD should always be administered together.

Action Control Scale (ACS-90)

Choose the one of the possible answers (A or B) that is most like you and give an answer for every question on the supplied answer sheet. Please don't make any marks on this questionnaire.

1. When I have lost something valuable and can't find it anywhere:
☐ A) I have a hard time concentrating on anything else.
☐ B) I don't dwell on it.
2. When I know I must finish something soon:
☐ A) I have to push myself to get started.
☐ B) I find it easy to get it done and over with.
3. When I have learned a new and interesting game:
☐ A) I quickly get tired of it and do something else.
☐ B) I can really get into it for a long time.
4. When I've worked for weeks on one project and then everything goes completely wrong:
☐ A) It takes me a long time to get over it.
☐ B) It bothers me for a while, but then I don't think about it anymore.
5. When I don't have anything in particular to do and I am getting bored:
☐ A) I have trouble getting up enough energy to do anything at all.
☐ B) I quickly find something to do.
6. When I'm working on something that's important to me:
☐ A) I still like to do other things in between working on it.
☐ B) I get into it so much th I can work on it for a long time.
7. When I'm in a competition and lose every time:
☐ A) I can soon put losing out of my mind.
☐ B) The thought that I lost keeps running through my mind.
8. When I am getting ready to tackle a difficult problem:
☐ A) It feels like I am facing a big mountain that I don't think I can climb.
☐ B) I look for a way that the problem can be approached in a suitable manner.
9. When I'm watching a really good movie:
☐ A) I get so involved in the film that I don't even think of doing anything else.
☐ B) I often want to get something else to do while I'm watching the movie.

10. If I had just bought a new piece of equipment (for example, a laptop) and it accidentally fell on the floor and was damaged beyond repair:
- () A) I would get over it quickly.
- () B) It would take me a while to get over it.
11. When I have to solve a difficult problem:
- () A) I usually get on it right away.
- () B) I have trouble sorting out things in my head so that I can get down to working on the problem.
12. When I have been busy for a long time doing something interesting (for example, reading a book or working on a project):
- () A) I sometimes think about whether what I'm doing is really worthwhile.
- () B) I usually get so involved in what I'm doing that I never think to ask about whether it's worthwhile.
13. When I have to talk to someone about something important and, repeatedly, can't find her/him at home:
- () A) I can't stop thinking about it, even while I'm doing something else.
- () B) I easily forget about it until I can see the person again.
14. When I have to make up my mind about what I am going to do when I get some unexpected free time:
- () A) It takes me a while to decide what I should do.
- () B) I can usually decide on something to do without having to think it over very much.
15. When I read an article in the newspaper that interests me:
- () A) I usually remain so interested in the article that I read the entire article.
- () B) I still often skip to another article before I've finished the first one.
16. When I've bought a lot of stuff at a store and realize when I get home that I paid too much - but I can't get my money back:
- () A) I can't concentrate on anything else.
- () B) I easily forget about it.
17. When I have work to do at home:
- () A) It is often hard for me to get started.
- () B) I usually get started right away.
18. When I'm on vacation and I'm having a good time:
- () A) After a while, I really feel like doing something completely different.
- () B) I don't even think about doing anything else until the end of my vacation.

19. When I am told that my work has been completely unsatisfactory:
() A) I don't let it bother me for too long.
() B) I feel paralyzed.
20. When I have a lot of important things to do:
() A) I often don't know where to begin.
() B) I find it easy to make a plan and stick with it.
21. When one of my co-workers brings up an interesting topic for discussion:
() A) It can easily develop into a long conversation.
() B) I soon lose interest and want to go do something else.
22. When I'm stuck in traffic and miss an important appointment:
() A) At first, it's difficult for me to start doing anything else at all.
() B) I quickly forget about it and focus on something else.
23. When there are two things that I really want to do, but I can't do both of them:
() A) I quickly begin one thing and forget about the other.
() B) It's not easy for me to put the thing that I couldn't do out of my mind.
24. When I am busy working on an interesting project:
() A) I need to take frequent breaks and work on other projects.
() B) I can keep working on the same project for a long time.
25. When something is very important to me, but I can't seem to get it right:
() A) I gradually lose heart.
() B) I just forget about it and go do something else.
26. When I have to carry out an important but unpleasant task:
() A) I do it and get it over with.
() B) It can take a while before I can bring myself to do it.
27. When I am having an interesting conversation with someone at a party:
() A) I can talk to him or her the entire evening.
() B) I prefer to go do something else after a while.
28. When something really gets me down:
() A) I have trouble doing anything at all.
() B) I find it easy to distract myself by doing other things.
29. When I am facing a big project that has to be done:
() A) I often spend too long thinking about where I should begin.
() B) I don't have any problems getting started.

30. When it turns out that I am much better at a game than the other players:
() A) I usually feel like doing something else.
() B) I really like to keep playing.
31. When several things go wrong on the same day:
() A) I don't know how to deal with it.
() B) I just keep on going as though nothing had happened.
32. When I have a boring assignment:
() A) I usually don't have any problem getting through it.
() B) I sometimes just can't get moving on it.
33. When I read something I find interesting:
() A) I sometimes still want to put the article down and do something else.
() B) I will sit and read the article for a long time.
34. When I have put all my effort into doing a really good job on something and the whole thing doesn't work out:
() A) I don't have too much difficulty starting something else.
() B) I have trouble doing anything else at all.
35. When I have an obligation to do something that is boring and uninteresting:
() A) I do it and get it over with.
() B) It usually takes a while before I get around to doing it.
36. When I am trying to learn something new that I want to learn:
() A) I'll keep at it for a long time.
() B) I often feel like I need to take a break and go do