Sex Differences in Cognition in Alzheimer's Disease

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Publications

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Table of Contents

Index of Tables

Index of Figures

Abstract

Inspection of the published research shows that sex differences in cognition in the general population have been widely cited with the direction of the advantage depending on the domain being examined. The most prevalent claims are that men are better than women at visuospatial and mathematical tasks whereas women have superior verbal skills and perform better than men on tasks assessing episodic memory. There is also some evidence that women are more accurate than men at identifying facial expressions of emotion. A more in-depth examination of the literature, however, reveals that evidence of such differences is not as conclusive as would at first appear. Not only is the direction and magnitude of sex differences dependent on the cognitive domain but also on the individual tasks. Some visuospatial tasks show no difference (e.g. figure copying) whist men have been shown to be better than women at confrontation naming (a verbal task).

Alzheimer's disease is a heterogeneous illness that affects the elderly. It manifests with deficits in cognitive abilities and behavioural difficulties. It has been suggested that some of the behavioural issues may arise from difficulties with recognising facial emotion expressions. There have been claims that AD affects men and women differently: women have been reported as being more likely to develop AD and showing a greater dementia severity than men with equivalent neuropathology. Despite this, research into sex differences in cognition in AD is scarce, and conflicting.

This research was concerned with the effect of sex on the cognitive abilities of AD patients. The relative performance of men and women with AD was compared to that of elderly controls. The study focused on the verbal, visuospatial and facial emotion recognition

domains. Data was collected and analysed from 70 AD patients (33 male, 37 female), 62 elderly controls (31 male, 31 female) and 80 young adults (40 male, 40 female).

Results showed those with AD demonstrate cognitive deficits compared to elderly controls in verbal and visuospatial tasks but not in the recognition of facial emotions. There were no significant sex differences in either the young adults or the healthy elderly controls but sex differences favouring men emerged in the AD group for figure copying and recall and for confrontation naming. Given that elderly men and women perform equivalently for these tasks, this represents a deterioration in women's cognitive abilities, relative to men's. Further evidence of such an adverse effect of AD was apparent in other tasks, too: for most verbal and visuospatial tasks, either an effect favouring women in the elderly is reversed or a male advantage increases in magnitude.

There is no evidence of sex differences in facial emotion recognition for any group. This suggests that the lack of published findings reporting on sex differences in this domain is due to the difficulty in getting null findings accepted for publication. The scarcity of research examining sex differences in other domains is also likely to be due to this bias.

1. Introduction

1.1. ALZHEIMER'S DISEASE

Alzheimer's Disease (AD) is a progressive condition that is the most common neurodegenerative disease associated with aging. In England and Wales around 500,000 people have the condition (http://www.alzheimers-research.org.uk/info/statistics - 9th January, 2009). Alzheimer's Disease International estimate that worldwide in 2010 there were 35.6 million people with dementia (a prevalence rate of 4.7%), with AD being the most common type. The prevalence in Europe and North America are similar (at 6.2% and 6.9%, respectively) and it is lower in less developed regions (e.g. in Africa, it is 2.6%). It is estimated that the worldwide figure will nearly double every 20 years to 60.57 million in 2030 with much of the increase likely to be due to increases in the numbers of people with dementia in low and middle income countries (Ferri, Sousa, Albanese, Ribeiro & Honyashiki, 2009).

1.1.1. DEFINITION/DIAGNOSIS

AD is an insidious illness and it has been estimated that neurodegeneration begins many decades before onset of symptoms (Jack, Albert, Knopman, McKhann, Sperling, Carrillo et al., 2011, Perl, 2010). It causes cognitive, behavioural and psychological symptoms. The most common symptom pattern begins with gradually deteriorating episodic memory. Although diagnosis of AD is made based on medical history, clinical, neurological and psychiatric examination, a definite diagnosis can only be made by neuropathology. It can be difficult to distinguish AD from other Dementias, particularly Vascular Dementia (VD), which is the most common coexisting condition with AD (Perl, 2010). The two core pathological hallmarks of AD are amyloid plaques and neurofibrillary tangles (Ballard, Gauthier, Corbett, Brayne, Aarsland & Jones, 2011). The Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV-TR) states that diagnosis requires the presence of both a memory disorder and impairment in at least one additional cognitive domain, both of which interfere with social function or activities of daily living (ADL).

AD is thought to be caused by deposition of amyloid β caused by an imbalance between the production and clearance of amyloid β in the brain (Blennow, de Leon & Zetterberg, 2006). This deposition leads to neuronal dysfunction and death in the brain (Ballard et al., 2011). The first degenerative changes typically occur in the medial temporal lobe, including the hippocampus and ethnorhinal cortex (Braak & Braak, 1995). It takes several decades before neuropathological damage manifests in symptoms that would allow for a diagnosis of AD (Perl, 2010). Neuropathological degeneration occurs in six stages (Braak & Braak stages). In stages I and II alterations are confined to the transentorhinal region : this stage does not, typically, present with symptoms. In stages III and IV severe involvement of the entorhinal and transentorhinal regions and the hippocampus occurs. The final stages (V and VI) sees devastating neocortical destruction (Braak & Braak, 1995). Cognitive deficits found fit with this pathological staging of AD (Carter, Caine, Burns, Herholz & Lambon Ralph, 2012).

1.1.2. Deficits

AD is characterised by loss of cognitive abilities such as language, in particular memory, resulting in symptoms such as confusion, disorientation, and speech difficulties. There are also neuropsychiatric symptoms such as apathy, agitation, delusions and dysphoria.

NEUROPSYCHIATRIC SYMPTOMS

Neuropsychiatric features of AD, or Behavioural and Psychological Symptoms in Dementia (BPSD), are common in early stages of the disease (Karttunen, Karppi, Hiltunen, Vanhanen, Valmaki, Martikainen, et al., 2010). BPSD include apathy, agitation, anxiety, irritability, dysphoria, motor disturbance, disinhibition, delusions, hallucinations and euphoria (Hart, Craig, Compton, Critchlow, Kerrigan, McIlroy et al., 2003).

The most commonly reported symptom is apathy, which has been found to be present at all stages of the disease (Breun, McGeown,Shanks & Venner, 2008; Lyketsos, Steinberg, Tschanz, Norton, Steffens & Breitner, 2000; Lyketsos, Lopez, Jones, Fitzpatrick, Breitner & DeKosky, 2002) as well as in those identified as having mild cognitive impairment (MCI) (Lyketsos et al., 2002). Present at an early stage are anxiety symptoms, possibly as a result of preservation of insight at this stage of the illness (Breun et al., 2008; Eustace, Coen, Walsh, Cunningham, Walsh, Coakley et al., 2002). Hart et al. (2003) reported a prevalence rate of 53% for this symptom and claimed that it was one of the most persistent behavioural changes, as did Eustace et al. (2002). Other common symptoms (affecting more than one in four) are depression, irritability and agitation (Karttunen et al., 2010, Lyketsos et al., 2002).

COGNITIVE SYMPTOMS

Deficits in episodic memory, verbal and visuospatial abilities are present in the preclinical phase of AD (Backman, Jones, Berger, Laukka & Small, 2005). In their meta-analysis examining pre-clinical cognitive impairment in AD Backman et al. (2005) selected papers where participants were free of clinical dementia at baseline and later received a diagnosis of clinical AD. They reported a large effect size of 1.03 for episodic memory deficits, whilst for verbal (*d* = 0.79)and visuospatial (*d* = 0.64)abilities the effect sizes were moderate. They found that those MCI participants who developed AD three years after testing had displayed a baseline deficit in episodic memory (Backman et al., 2005) and concluded that such an impairment in those with MCI is a core indication of an impending dementia disease.

Individuals progress at different rates and as the disease progresses the individual's cognitive and functional abilities decline (Alzheimer's Association, 2011). It is a progressive illness, and one would expect the level of cognitive impairment to be related to the level of dementia severity. Nevertheless, some research indicates that the degree of cognitive impairment may also be moderated by demographic factors including sex (e.g. Buchanan, Wang, Ju & Graber, 2004) and education level (e.g., Le Carret, Auriacombe, Letenneur, Bergua,Dartigues & Fabrigoule, 2005).

1.2. SEX DIFFERENCES

1.2.1. IN THE GENERAL POPULATION

Sex differences in cognitive abilities in healthy men and women are widely documented. The most prevalent claims being that women have better verbal abilities than men (Hyde & Linn, 1988; Weiss, Kemmler, Deisenhammer, Fleischhacker & Delazer, 2003) and perform better on tasks assessing episodic memory (Herlitz, Nilsson & Backman, 1997, Lewin, Wolgers & Herlitz, 2001) and that men have superior visuospatial skills Herlitz et al., 1997 ; (Voyer, Voyer & Bryden, 1995; Weiss et al., 2003) and are better than women at spatial orientation and maths (de Courten-Myers, 1999). However, in a recent review of the literature Wallentin (2009) found no evidence of sex differences in language processing. Furthermore, Welsh-Bohmer, Ostbye, Sanders, Peiper, Hayden, Tschanz et al. (2009), in a large study of 507 healthy elderly participants aged 65 and over, found that sex did not appear to affect neurocognitive performance to any extent. It would appear, therefore, that evidence of sex differences in cognition in healthy men and women is not necessarily as established as is sometimes claimed.

Another area of cognition in which sex differences have been found in the general population is in facial emotion perception (Hampson, van Anders & Mullin, 2006). Women have been shown to be faster than men in recognition of disgust, fear, sadness and anger (Hampson et al., 2006) and the advantage remained, even after controlling for perceptual speed. Similarly, women are more accurate than men in recognizing fear and disgust emotions (Collignon, Girard, Gosselin, Saint-Armour, Lepore & Lassonde, 2010). Calder, Keane, Manly, Sprengelmeyer, Scott, Nimmo-Smith et al. (2003) reported poorer recognition of fear by male participants (which may be because females spend shorter time fixating on fearful images than men do (Clark, Neargarder & Cronin-Golumb, 2010)). However, other research reported no differences between men and women in their ability to recognize facial emotions of expression (Sullivan, Ruffman & Hutton, 2007; Wong, Cronin-Golomb & Neargarder, 2005).

1.2.2. Sex differences in Alzheimer's disease

Previous research has reported that sex affects the development and presentation of AD, with females generally faring worse: Several authors have reported a higher risk of developing AD in women than in men (e.g. Andersen, Launer, Dewey, Letenneur, Ott, Copeland et al., 1999; Bachman, Wolf, Linn, Knoefel, Cobb, Belanger et al., 1992; Lobo, Launer, Fratiglioni, Andersen, DiCarlo & Breteler, 2000) possibly because women have increased longevity (Hebert, Wilson, Gilley, Beckett, Scherr, Bennett et al., 2001).

Sex differences in Cognition

AD is associated with a marked semantic memory impairment affecting sufferers' knowledge of the world and female AD sufferers manifest greater deficits on tasks assessing semantic memory (e.g. Chapman, Mapstone, Gardner, Sandoval, McCrary, Guillily et al., 2011; Henderson & Buckwater, 1994). They also show a greater degree of dementia severity than men with equivalent neuropathy (Barnes, Wilson, Bienias, Schneider, Evans & Bennett, 2005), which some researchers (e.g. Henderson & Buckwalter, 1994) claim is a result of exhibiting greater language deficits than men with AD (see below).

Visuospatial abilities

Men with AD have been reported to perform better than women with AD at visuoconstructive tasks (Heun & Kockler, 2002) at learning and retaining visuospatial information (Beinhoff, tumani, Brettschneider, Bittner & Riepe, 2008) and in tasks that require active manipulation of visuospatial information (Millet, Raoux, LeCarret, Bouisson, Dartigues & Amieva, 2009). This is in line with research into these abilities in the healthy population. However, other researchers have reported no significant sex differences in visuospatial abilities in participants with AD (Henderson & Buckwalter, 1994, Perneczky, Drzezga,Diehl-Schmid, Yi & Kurz, 2007).

Verbal Abilities

In contrast to the female advantage for language ability cited for the general population, women with AD have been reported to perform worse than men with AD on tasks of language ability (Ripich, Petrill, Whitehouse & Ziol, 1995, Chapman et al., 2011) and some studies have reported no sex differences in verbal skills (e.g. Hebert et al., 2000, Henderson & Buckwater, 1994, Perneczky et al., 2007). If these findings are reliable, then this implies that women deteriorate in their language abilities at a greater rate than men do.

Facial Emotion Recognition

In a review of the literature McLellan, Johnstone, Dalrymple-Alford & Porter (2008) reported that AD patients have poorer recognition of facial emotion expressions than the healthy elderly. Burnham & Hogervorst (2004) posited that the deficit in matching facial expressions in AD patients that they found may be due to visuospatial dysfunction. Given that previous research has reported advantages for men in visuospatial abilities one might expect to find that women do not perform as well as men. However, there has been very little published research on whether or not men and women AD sufferers differ in their ability to recognise facial emotions.

1.2.3. Sex differences in the Elderly

As AD is a disease that affects the elderly, it may be that any sex differences in cognition in AD participants are a result of cognitive aging rather than a function of the disease per se. Therefore, it is important that sex differences in cognition in healthy elderly men and women are examined. Heun and Kockler (2002) tested both AD and non-demented elderly participants and they reported that most of the gender differences in the cognitive impairment of the AD patients they tested reflect gender differences in cognitive functioning that they found in non-demented elderly participants. Furthermore, a similar profile has been reported in the elderly as is found in the young healthy population, i.e. women have better episodic memory (Beinhoff et al., 2008, Chapman et al., 2011) and verbal abilities (Gerstorf, Herlitz & Smith, 2006; Proust-Lima, Amieva, Letenneur, Orgogoze, Jaqmin-Gadd & Dartigues, 2008) and men have better visuospatial abilities (deFrias, Nilsson & Herlitz, 2006; Parsons, Rizzo, van der Zaag, McGee & Buckwalter, 2005). However, others have reported no sex differences in the elderly for verbal skills (Beinhoff et al., 2008; van Hooren, Valentin, Bosma, Ponds, Boxtel & Jolles, 2007). Therefore, the inconsistency in findings reported for healthy men and women is also apparent in the literature for cognitive skills in elderly men and women.

1.3. RESEARCH QUESTIONS

This body of research examined the effect of sex on cognition in AD. To this end, facial emotion recognition, verbal and visuospatial skills in AD patients were examined to explore sex differences in these abilities between patients at the same level of disease severity.

In order to be able to set the findings of the research into sex differences in AD patients into context the extent to which such differences already exist in the general population were examined. However, any differences found between the healthy group and the AD patient group may arise due to age differences: there have been some reports that both phonemic and semantic fluency decline with age (e.g. Moreno-Martinez, Laws & Schulz, 2008). Therefore, the degree to which cognitive performance differs according to age will be explored with an age-matched healthy elderly group as a control.

The following research questions were examined:

1. When analysed at group level, is there any evidence of differences in cognitive abilities between men and women in the general population? Specifically, are there any differences in cognitive abilities between elderly men and women?

2. When analysed at group level, is there any evidence of differences in cognitive abilities between men and women AD sufferers?

3. If differences are found, do the patterns of cognitive deficits found in AD patients reflect those found in an age-matched healthy population?

2. Review of the literature

2.1. INTRODUCTION

Early factor analytic studies that sought to define intelligence found that verbal tests and visuospatial tests formed two distinct factors (see Halpern, 2000). In 1974 Maccoby and Jacklin published a review of the available literature on sex differences in cognitive abilities. They concluded that the strongest evidence for sex differences occurred in the visuospatial and mathematical domains, where men outperformed women, and verbal abilities where women performed better than men. Much of the focus of subsequent research has been on this dichotomy that women perform better on verbal abilities and men on visuospatial abilities. This thesis is concerned with sex differences in verbal and visuospatial abilities and also with facial emotion recognition (FER) in Alzheimer's patients.

Alzheimer's disease (AD) predominately affects the elderly and any cognitive deficits found in people with AD may be a function of the normal aging process rather than the disease itself. Therefore, when examining cognitive abilities in AD the effects of aging need to be taken into account. So, this review first examines how aging affects cognition in the healthy elderly (specifically in the visuospatial, verbal and FER domains) before moving on to examine sex differences in the rate of cognitive decline in the elderly. Then, for each domain, sex differences in the healthy population will be examined, followed by how these differences develop in the elderly before finally exploring sex differences in AD.

2.1.1. COGNITIVE DECLINE

It is well-documented that many aspects of cognitive performance decline with age (Barnes, Schneider, Bienias, Evans & Bennett, 2003; Gerstorf, Herlitz & Smith, 2006; Maylor, Reimers, Choi, Collaer, Peters & Silverman, 2007; Read, Pedersen, Gatz, Berg, Vuoksimaa, Malmbert et al., 2006). This decline is, however, task dependent, as there have been reports of no aging decline for category fluency (Mathuranth, George, Cherian, Alexander, Sarma & Sarma, 2003), spatial perception (water level and plumb line tasks – Robert & Tanguay, 1990) and for recognition of happiness in FER (Sullivan & Ruffman, 2004). Whereas, age-related deficits have been reported for block design tasks (Finkel, Reynolds, McArdle, Gatz & Pederson, 2003), the Rod & Frame task (Robert & Tanguay, 1990), lexical fluency (Lanting, Haugrud & Crossley, 2009) and several emotions in facial emotion recognition (Ruffman, Ng, & Jenkin, 2009). For category fluency, cognitive decline has been shown to be category specific (Moreno-Martinez, Laws and Schultz, 2008): in a test involving 14 categories, young participants scored more highly than the elderly on all non-living categories except for kitchen utensils but only 3 living categories (animals, insects and body parts).

Maylor et al. (2007) reported that men showed a significantly greater age-related cognitive decline than women although their internet-based study had a huge sample size (109,612 men and 88,509 women) which would have enough power to detect even the most trivial difference. Furthermore, participants were required to complete computer tasks over the internet with participants being required to type as many words as possible that fell within a particular category, rather than verbally recall them. The results from this type of test may reflect typing speeds rather than verbal abilities, or may be affected by uncontrolled factors such as cheating by participants. For mental rotation, where the tasks were computerised versions of the usual paper-and-pencil task the authors claimed the findings of a greater decline with age in men than women may be due to the ceiling performance of younger men. However, Wiederholt, Cahn, Butters, Salmon, Kritz-Silverstein & Barrett-Connor (1993) agreed with Maylor et al. (2007) that women had an aging advantage over men. They examined 1,692 participants aged 55 -94 years and found that performance in all tests decreased progressively with age but the decline was slower in women than in men.

Other research, however, has found that men and women decline at similar rates (Barnes et al., 2003; Finkel et al., 2003; Gerstorf et al., 2006; Proust-Lima, Amieva, Letenneur. Orgogoze, Jaqmin-Gadda & Dartigues, 2008). Gerstorf et al., 2006, examined memory, processing speed and knowledge in 368 participants aged between 70 and 100 years at the outset over a 13 year period and found that for all cognitive tests men and women declined in parallel. Proust Lima et al., 2008, however, reported that after adjusting for vascular status, sex differences in cognitive decline did emerge, but only at the oldest age, with women showing a steeper decline than men. Similarly, in a sample of 647 twin pairs (mixed twin pairs and single sex pairs (both dizygotic and monozygotic)) aged between 65 and 98 years, Read et al. (2006) reported larger differences between the sexes in working memory and perceptual speed deficits at later ages, with women faring worse (although what qualifies as the oldest/later age was not specified by the authors in either study).

So, although age-related cognitive decline occurs in all three domains of interest the balance of evidence suggests that men and women decline at a similar rate until the very oldest age, when women appear to be more adversely affected. Therefore, we would expect to find that the sex differences apparent in the younger population are mostly maintained in the elderly. Furthermore, any sex effects in AD patients that differ from that seen in the healthy population are likely to be due to the disease process rather than aging *per se*.

2.2. VISUOSPATIAL ABILITIES

2.2.1. VISUOSPATIAL ABILITIES IN THE GENERAL POPULATION

Visuospatial ability is not a unitary concept and indeed, some (e.g. Caplan, MacPherson & Tobin, 1985) have argued that this makes it difficult to review and compare papers that use different definitions of visuospatial ability. In 1985, Linn and Petersen conducted an extensive meta-analysis on sex differences in visuospatial abilities which addressed this concern. To achieve homogeneity across papers, they partitioned visuospatial tasks into three categories: *mental rotation, spatial perception and spatial visualisation.*

Mental rotation involves the ability to mentally rotate a two or three dimensional figure rapidly and accurately (Linn and Petersen, 1985). Tasks commonly used are the Vandenberg & Kuse (1978) mental rotation task and the Shephard & Metzler (1971) task (see Appendix 2 for description of the cognitive tests used).

Spatial perception tasks are those where participants are required to determine spatial relationships with respect to the orientation of their own bodies in spite of distracting information (Linn & Petersen, 1985). These include such tasks as the rod and frame task (Witkin & Asch, 1948), which requires participants to position a rod within a tilted frame so that the rod is either vertical or horizontal, and the water level test (Piaget & Inhelder (1956) where participants are asked to draw in the water level in a picture of a tilted glass half filled with water.

Linn and Petersen (1985)'s final category was *spatial visualisation*, which they defined as being those tasks that involve complicated multi-step manipulations of spatially presented information. They claimed that these can be distinguished from spatial perception and mental rotation tasks as they have the possibility of multiple solution strategies. The types of tasks that are typically used to test this category of visuospatial abilities are the embedded figures test (Witkin, 1971) (a target figure is hidden in the contours of a larger figure) paper folding (e.g. Ekstrom, French & Harman, 1976) (participants imagine the spatial result of folding a piece of paper in several directions) and the identical blocks test (Stafford, 1962) (participants must indicate which block among a number of alternatives is the same as a standard). However, this distinction is vague – Linn and Petersen put into the spatial category all visuospatial tests that did not fit within the first two categories (Voyer, Voyer & Bryden, 1995).

Sex differences in visuospatial abilities in the general population

It is important to distinguish between different visuospatial categories as they tap into different abilities (Caplan et al., 1985). Furthermore, in their meta-analysis, Linn & Peterson (1985) claimed that effect sizes for sex differences vary according to the type of visuospatial task being examined. The strongest effect size emerged for mental rotation tasks, with 29 effect sizes that fell within this category of task. They calculated a large effect size (Cohen's d = 0.94) on the Vandenberg mental rotation task (which has 3-dimensional (3D) stimuli), favouring men. By contrast, the effect size on the Primary mental abilities (PMA) space task (which involves 2-dimensional (2D) stimuli) was only 0.26 so it is important to consider individual tasks, as well as individual categories.

On the spatial perception tasks, Linn and Petersen identified 62 effect sizes to include in the meta-analysis and calculated a medium overall effect size (d= 0.64), again favouring men. On the last category, spatial visualisation, where they identified the highest number of effect sizes (81), the effect size was small (*d*=0.13) and found not to be significantly different from zero.

A later meta-analysis conducted by Voyer et al. (1995) spanning 50 years of published research confirmed the findings of the Linn and Petersen paper. The largest effect size was found for mental rotation tasks (mean weighted *d* =0.56) favouring men and, in line with Linn & Petersen, they found a difference between 3D (*d* =0.67) and 2D tasks (*d* =0.44). For spatial perception tasks the effect size was medium (*d* =0.44) whilst for the category spatial visualisation the effect size was not significant. Nonetheless, significant sex differences favouring men emerged on two of the spatial visualisation tasks: the paper form board and identical blocks test, which both have an important mental rotation component (Voyer et al., 1995).

It has been suggested that the male advantage in visuospatial abilities has reduced in recent years: Feingold (1988) examined published national test results that spanned around three decades and concluded that the effect size for sex differences in visuospatial abilities reduced by 59% between 1947 to 1980. Although only one visuospatial task was included in the three tests he analysed (Differential Aptitude Test (DAT), Preliminary Scholastic Aptitude test (PSAT) and Scholastic Aptitude Test (SAT)) and that task (the space relations subtest of the DAT) is one that does not usually demonstrate sex differences (Feingold reported a small average effect size for this test *d*=0.24) However, this reduction in effect size in recent years has also been reported by Voyer et al. (1995) who found that participants who were born more recently showed smaller sex differences, albeit this reduction was not significant. Similarly, Schaie (1996) in the Seattle Longitudinal Study, has found young adult females show markedly higher performance on spatial orientation than was the case 35 years earlier. But again, they did not examine those tasks where more robust differences between men and women are consistently found.

More recent research (see Table 2.1) shows that mental rotation tasks continue to yield large effect sizes that have remained largely unchanged across time. Men have consistently been cited as performing better than women on these tasks (e.g. Burton, Henninger & Hafetz, 2005; Campos, Perez-Fabello & Gomez-Juncal, 2004; Collins & Kimura, 1997; Halari, Hines, Kumari, Mehrotra, Wheeler, Ng et al., 2005; Hausmann, Schoofs, Rosenthal & Jordan, 2009; Herlitz, Airaksinen & Nordstrom, 1999, Hirnstein, Bayer & Hausmann, 2009; Janowsky, Chavez, Zambeni & Orwoll, 1998; Jansen & Heil, 2009; Lewin, Wolgers & Herlitz, 2001; Maylor et al., 2007; Naeve, Menaged & Weightman, 1999; Nowak & Moffat, 2011; Parsons, Larson, Kratz, Thiebauz, Bluestein, et al., 2004; Peters, Manning & Reimers, 2007, Rahman & Wilson, 2003; Robert & Savoie, 2006; Sanders, Bereczjeo, Csatho & Manning, 2005; Weiss, Kemmler, Deisenhammer, Fleischacker & Delazer, 2003). In a recent meta-analysis examining performance factors in these tasks, Voyer (2011) found a mean weighted effect size of d = 0.70, demonstrating that effect sizes for sex differences in mental rotation remain large.

In addition to their findings of a better male performance compared to women on mental rotation tasks, Halari et al. (2003) and Maylor et al. (2007) identified a male advantage on a computerized version of the line angle judgment task, a spatial perception task. In fact, a male advantage has been reported on a number of spatial perception tasks including the judgement of line orientation task (Caparelli-Daquer, Oliveira-Souza & Moreira Filho, 2009; Collaer & Nelson, 2002; Collaer, Reimers & Manning, 2007; Goyette, McCoy, Kennedy & Sullivan, 2012; Rahman & Wilson, 2003) and water level test (Lewin et al., 2001). However, a number of other researchers have failed to identify any difference between men and women on these tasks (Herlitz et al., 1999; Neave et al., 1999; Parsons et al., 2004).

TABLE 2.1 SUMMARY OF PREVIOUS RESEARCH CITED IN REVIEW EXAMINING SEX DIFFERENCES IN THE GENERAL POPULATION FOR VISUOSPATIAL TASKS

Paper	N M	N F	Mean Age (Range) M	Mean Age (Range) F	Tasks used	Findings
Goyette et al. (2012)	18	23	(19-22)		JLO JLO with landmark	M >F n.s.
Nowak & Moffat (2011)	58	82	23 ± 6		MR PF	M >F (*d*=.88) n.s. (*d*=.37)
Caparelli-Daquer et al. (2009)	149	194	20.3 ±2.8	20.2 ±2.7	JLO	M >F
Hausmann et al. (2009)	55	59	25.8 ±7.2	23.4 ±4.7	MR	M >F (η^2 = .11)
Jansen & Heil (2009)	75	50	(20-70)		MR	M >F (η^2 = .13)
Hirnstein et al. (2009)	17	17	19.8 ±.7	19.8 ±.6	MR	M >F (η^2 = .30)
Collaer et al. (2007)	130k	120k	29.4 ±11.9		JLAP, internet test	M >F (*d*=.56)
Gallagher & Burke (2007)	60	57	39.84		FC (ROCF)	M >F
Maylor et al. (2007)	110k	89k	(20-65)		MR JLAP, internet test	M >F M >F
Peters et al. (2007)	134k	120k	31.2	28.8	MR	M >F (η^2 = .06)
Clark et al (2006)	514	493	28.7 (6-82)		SVM	n.s.
deFrias et al. (2006)	625		(35-80)		BD	M >F
Robert & Savoie (2006)	50	50	21.8 ±1.7	21.6 ±1.8	MR	M >F
Thilers et al. (2006)	1107	1276	(35-90)		BD	M >F
Burton et al. (2005)	41	93	19.3 ±1.1	20.0 ±4.4	MR	M >F
Halari et al. (2005)	42	42	28.3 ±4.8	27.7 ±4.0	MR JLO CJLO	M >F (ES = .91) M >F (ES = .75) M >F (ES = .91)
Sanders et al (2005)	115	119			MR	M >F (ES = .8-1.4)
Campos et al. (2004)	60	69	(20-60+)		MR	M >F (*d*=.49)
Parsons et al. (2004)	20	24	27.9 ±5.4		MR JLO BD	M >F (*d*=.90) n.s. (*d*=.16) n.s. (*d*=.03)
Postma et al. (2004)	32	32	21.4 ±2.5	21.5 ±2.9	CBT	n.s.
Rahman & Wilson (2003)	120	120	(18-40)		MR/JLO	M >F

Paper	N M	N F	Mean Age (Range) M	Mean Age (Range) F	Tasks used	Findings
Weiss et al. (2003)	51	46	26.2 ±3.0	23.9 ±3.8	MR PF EF	M >F (*d*=.41) n.s. (*d*=.18) F >M (*d*=.43)
Collaer & Nelson (2002)	48	80	18.5 (17-22)		JLAP	M >F
Lewin et al. (2001)	91	94	29.9 ±5.8	28.8 ±6.2	MR PF WL FC (ROCF)	M >F (*d*=.78) M >F (*d*=.64) M >F (*d*=.29) n.s. (*d*=.03)
Meurling et al. (2000)	16	16	23.6 (20-41)		PF	n.s.
Herlitz et al.. (1999)	100	100	28.2 ±6.0	28.0 ±5.5	MR WL	M >F (*d*=.89) n.s. (*d*=.04)
Naeve et al. (1999)	34	28	(18-51)		MR WL	M >F n.s.
Robert & Tanguay (1990)	45	45	(40-84)		WL/PL R&F	M >F n.s.
Collins & Kimura (1997)	29	26	22.1	22.7	MR 3-D MR 2-D	M >F (*d*=.86) M >F (*d*=.43-1.1)
Janowsky et al. (1988)	18	30	28.5 ±3.1	29.8 ±3.2	BD	M >F

Note: d = Cohen's *d*. ES = effect size. M = Male. F = Female. n.s. = not significant. Tasks: BD = Block Design. CBT = Corsi Block Tapping. CJLO = Computerised Judgement of Line Orientation. EF = Embedded Figures. FC = Figure Copying. JLAP = Judgement of Line andPposition. JLO = Judgement of Line Orientation. MR = Mental Rotation. PF = Paper Folding, PL = Plumb Line. R&F = Rod and Frame. ROCF = Rey Osterrieth Complex figure. SVM = Span of Visual Memory. WL = Water Level.

Linn & Peterson (1985) and Voyer et al. (1995) claimed that the effect size for sex differences for spatial visualisation tasks were not significantly different from zero and recent research continues to report this although the presence of sex differences appears to be task dependent: Robert & Tanguay (1990) found that men were better than women on some spatial perception tasks (water level and plumb line tests) but not others (rod & frame task). Postma, Jager, Kessels, Koppeschaar & van Honk (2004) did not find any sex differences in the Corsi Block Tapping task (CBT) and Clark, Paul, Williams, Arns, Fallahpour, Hardmer et al. (2006) found no sex differences for the Span of Visual Memory task, which is similar to the CBT. Although Novak & Moffatt (2011), Meurling, Tonning-Olsen & Levander (2000) and Weiss et al. (2003) all reported equivalent scores for men and women on paper folding tests, Lewin et al. (2001) reported a male advantage. Similarly Parsons et al. (2004) did not find a significant sex difference on the block design test but deFrias, Nilsson & Herlitz (2006) Janowsky et al. (1998) and Thilers, MacDonald & Herlitz (2006) all found that men were better than women on this test.

Interestingly, one paper reported that women were better than men on an embedded figures task – section 10 of the Leistungs-Prufsystem (LPS10: Horn, 1983). The LPS10 is similar to the embedded figures test which requires participants to find specific figures within a larger pattern of figures. Weiss et al., (2003) administered a number of visuospatial tasks and found that men performed better on all of them other than the LPS 10, where women were better. In a factor analysis of all the administered tests three factors emerged: memory, verbal and visuospatial. The LPS10 loaded onto both the verbal and visuospatial factors, and Weiss et al. (2003) claimed that this verbal component may be the reason why women scored higher than men.

The recent published evidence, therefore, consistently reports a large advantage for men on mental rotation tasks and a moderate sex difference, still favouring men, on spatial perception tasks. With regards to the spatial visualisation tasks, the relative performance of men and women depends on which task is being used suggesting that the tasks using this category rely on different processes and abilities to each other. (As Voyer et al., 1995 pointed out, this category of Linn & Peterson (1985)'s is vague and could, perhaps, be further partitioned.) Nevertheless, in those visuospatial tasks where males have been shown to have an advantage over women, the effect sizes remain large and robust.

2.2.2. VISUOSPATIAL ABILITIES IN THE ELDERLY

Generally, cognitive abilities show a decline with aging, but to what extent is this evident on visuospatial tasks? Furthermore, do elderly men maintain the advantage on visuospatial abilities reported in the young?

DECLINE IN VISUOSPATIAL ABILITIES IN THE ELDERLY

Finkel et al. (2003) claimed that the rate of decline in visuospatial abilities depends on the task being used. They compared the rate of decline between middle age and old age (age 65 being the cut-off) and found no difference between these age groups in the decline for mental rotation tasks but for block design there was a steeper decline with old age, possibly related to perceptual speed.

Performance on mental rotation tasks decreases with age (Campos et al.,2004; Finkel et al., 2003; Jansen & Heil, 2009; Peters et al., 2007) with the decline being first apparent in the 31-40 year age group (Peters et al., 2007). Although Robert & Tanguay (1990) identified an aging effect in spatial perception, with age accounting for 12% of the variance in scores on the rod and frame task, the water-level task and the plumb-line task, only the rod and frame task showed a significant deterioration with age.

Spatial visualisation tasks also show an aging effect: older participants score lower on the Rey Osterrieth Complex Task (Gallagher & Burke, 2008; Rosselli & Ardila, 1991) with the largest decrease after the age of 70, and Salthouse (1992) claimed that the average 60 year-old performs at about 0.5 to 1.5 SDs below the average 20 year old in tests of paper-folding. The block design task also shows an aging effect (Fahlander, Wilson, Fastbom, Grut, Forsell, Hill et al., 2000; Ganguli, Snitz, Lee, Vanderbilt, saxton & Chang, 2010 Read et al., 2006;

Yonker, Eriksson, Nilsson & Herlitz, 2003) with older adults being less efficient than young adults at manipulating blocks to the desired positions (Salthouse, 1987).

Sex differences in visuospatial abilities in the elderly

Aging affects visuospatial abilities and, given that men and women do not decline cognitively at different rates (see section 2.1.1), we would expect to find the same pattern of relative performance in the elderly, i.e. that men are better than women on mental rotation and spatial perception tasks, whilst the relative performance of women and men on spatial visualisation tasks depends on the test being used, and this is the case (see Table 2.2).

Research shows that elderly men performed better than elderly women in mental rotation (Campos et al., 2004; Finkel et al., 2003; Gerstorf, Ram, Hoppman, Willis & Schaie, 2011; Jansen & Heil, 2009; Parsons et al., 2004; Peters et al., 2007; Willis & Schaie, 1988) and a male advantage in the elderly has been reported for spatial perception tasks (Duff, Schoenberg, Mold, Scott & Adams., 2011; Moore, Miller, Andersen, Arndt, Haynes & Moser, 2010; Parsons, Rizzo, van der Zaag, McGee & Buckwalter, 2005; Robert & Tanguay, 1990). However, Barnes et al. (2003) examined 577 women and 271 men (mean age 75.4 years) longitudinally and no significant sex differences emerged on the judgment of line orientation task or the standard progressive matrices both of which usually produce moderate sex differences in favour of young men. This may be because visuospatial ability was assessed as a summary measure rather than analysing data for individual tests. Individual test analysis may have revealed differing performance between men and women on each test. In addition, the participants in this study were Catholic nuns, priests and brothers and it may be that the socioeconomic and lifestyle experiences usually encountered differentially by men and women are substantially less for this population.

TABLE 2.2 SUMMARY OF PREVIOUS RESEARCH CITED IN REVIEW EXAMINING SEX DIFFERENCES IN THE ELDERLY FOR VISUOSPATIAL TASKS

	N		Mean Age (Range)			
Paper	**M**	**F**	**M**	**F**	**Tasks used**	**Findings**
Duff et al. (2011)	300	418	72.9 ±5.5	73.6 ±6.1	FC (RBANS) JLO (RBANS)	n.s. M >F
Gerstorf et al. (2011)	901	1,079	(50-80)		MR:PMA	M >F
Moore et al. (2010)	50	38	68 ±7.8		FC (RBANS) JLO (RBANS)	n.s. M >F
Jansen & Heil (2009)	25	25	64.7 (60-70)		MR	M >F (*d*=.59)
Beinhoff et al. (2008)	28	23	63.5 ±8.9	63.8 ±8.2	FC (WMS-R)	n.s.
Cushman & Duffy (2007)	31	37	73.2 ±7.2		JLO	n.s.
Peters et al. (2007)	2191	1172	(61+)		MR	M >F
Whittle et al. (2007)	108	231	(90+)		FC (CERAD)	n.s.
deFrias et al. (2006)	625		(35-80)		BD	M >F
Read et al. (2006)	1294		65+		BD	M >F
Thilers et al. (2006)	1107	1276	62.2 ±13.5	63.8 ±10.3	BD	M >F
Simpson et al. (2005)	196	191	(55-87)		PRM, SSP	M >F
Campos et al. (2004)	20	20	67.8 ±4.4		MR	M >F (*d*=.54)
Parsons et al (2005)	15	15	74.8 ±6.2	73.4 ±7.5	MR JLO	M >F M >F
Barnes et al. (2003)	271	577	74.0 ±6.5	76.1 ±7.0	JLO/SPM	n.s.
Finkel et al. (2003)	219	339	(44-88)		MR BD	M >F n.s.
Yonker et al. (2003)	18	18	60.3 ±6.3	61.1 ±6.8	BD	n.s. (*d*=.46)
Heun & Kockler (2002)	171	267	66 ±8.9	68.9 ±8.5	FC (SIDAM)	M >F
Fahlander et al. (2000)	43	184	84.4 ±4.9		BD	n.s.
Buckwalter et al. (1996)	52	82	74.8 ±6.5	74.2 ±9.5	BD FC (CERAD)	n.s. n.s.
Portin et al. (1995)	104	135	62	62	BD	M >F
Henderson & Buckwalter (1994)	130	261	69.7 ±6.3	67.1 ±8.0	FC (CERAD)	n.s.

Paper	N M	N F	Mean Age (Range) M	Mean Age (Range) F	Tasks used	Findings
Rosselli & Ardila (1991)	346		(55+)		FC (ROCF)	M>F
Robert & Tanguay (1990)	45	45	(40-84)		WL/PL R&F	M >F n.s.
Willis et al. (1988)	97	132	72.8 (64-95)		MR	M >F

Note: M = Male. F = Female. n.s. = not significant. Tasks: BD = Block Design. CERAD = Consortium to Establish Registry for Alzheimer's Disease FC = figure copying. JLO = Judgement of Line Orientation. MR = Mental Rotation. PL = Plumb Line. PRM = Pattern Recognition Memory. RBANS = Repeatable Battery for Assessment of Neuropsychological Status. R & F = Rod and Frame. ROCF = Rey Osterrieth Complex figure. SIDAM – A Structured Interview for the diagnosis of Dementia of the Alzheimer type, Multi-infarct dementia and dementia of other aetiology. SPM = Standard Progressive Matrices. SSP = Spatial Span. WL = Water Level Task. WMS-R = Wechsler Memory Scale – Revised.

In spatial visualisation the findings are variable: a male advantage has been reported on the block design task (deFrias et al., 2006; Portin, Saarijarvie, Joukamoa & Salokangas, 1995; Read et al., 2006; Thilers et al., 2006), figure copying (Heun & Kockler, 2002) and on a task of visual memory (Simpson, Maylor, Rae, Meunier, Andriollo-Sanchez, Catasta et al., 2004) although equivalent male and female performance has also been reported (Beinhoff, Tumani, Brettschneider, Bittner & Riepe, 2008; Buckwalter, McCleay, Shankle, Dick & Henderson, 1996; Duff et al,, 2011, Fahlander et al., 2000; Finkel et al., 2003; Heun & Kockler, 1994; Henderson & Buckwalter, 1994; Yonker et al., 2003). including on the block design task (Fahlander et al., 2000; Finkel et al., 2003; Portin et al., 1995; Read et al., 2006) where sex differences favouring men are usually found in the young. Although Heun & Kockler (2002) found that elderly men performed significantly better than elderly women drawing a geometric shape, Duff et al. (2011) and Buckwalter et al. (1996) examined figure copying in the elderly and no significant differences emerged.

It would seem, therefore, that as expected the profile of visuospatial abilities in the elderly mirror those found in younger adults. Men are better than women at mental rotation tasks and spatial perception and there are conflicting reports, depending on the task, for spatial visualisation. Furthermore, the male advantage endured: Jansen & Heil (2009) reported a male advantage in all age groups (range 20–70 years old) and deFrias et al. (2006) reported sex differences in cognition to be of similar magnitude throughout the adult life span. However the effect size may reduce in the oldest age (Campos et al., 2004; Peters et al., 2007).

2.2.3. VISUOSPATIAL ABILITIES IN ALZHEIMER'S DISEASE

In addition to the episodic and semantic memory impairments, people with AD demonstrate verbal and visuospatial deficits when compared to the healthy elderly. This section will examine the impact of AD on visuospatial abilities.

As might be expected, people with AD perform worse than the healthy elderly on various visuospatial tasks. Visuospatial deficits are apparent in the years prior to diagnosis: Backman, Jones, Berger, Jonsson, Laukka & Small (2005) found that healthy elderly participants who were later diagnosed as having AD performed more poorly on visuospatial tasks than those who remained free of dementia at follow up and Laukka, MacDonald, Frataglioni & Backman (2012) identified an increase in the rate of visuospatial decline in elderly participants ten years before diagnosis of AD.

Lineweaver, Salmon, Bondi & Corey-Bloom (2005) posited that as mental rotation involved the parietal cortex and AD results in extensive damage to this region, AD patients should be unable to perform the required mental spatial rotation to complete this task. In line with this they found that AD patients were impaired, compared to healthy elderly controls, on a simple mental rotation task (Lineweaver et al., 2005) as did Kurylo, Corkin, Rizzo &

Growdon (1996), Mendola, Cronin-Golomb, Corkin & Growdon (1995) and Mendez, Tomsak & Reimer (1990).

Salmon and Bondi (2009) claimed that visuospatial deficits associated with AD are usually evident in visuoconstructional tasks such as the block design test and visuoperceptual ones such as the judgement of line orientation (JLO) task. In support, AD participants have been shown to be worse than EC on the JLO (Cushman & Duffy, 2007; Lineweaver et al., 2005; Ricker, Jeenan & Jacobson, 1994; Ska, Poissant & Joanette, 1990). Impairments have also been reported for block design (Cahn-Weiner, Sullivan, Shear, Fama, Lim, Yesavage et al., 1999 Ricker et al., 1994) and figure copying (Freeman, Giovannetti, Lamar, Cloud, Kaplan & Libon, 2000; Morris, Heyman, Mohs, Hughes, van Belle, Fillenbaum et al,, 1989). Even participants with mild AD score lower than elderly controls on a figure copying task (Binetti, Cappa, Magni, Padovani, bianchetti & Trabucchi, 1998; deIpolyi, Rankin, Mucke, Miller & Gorno-Tempini, 2007) and on drawing a complex figure from memory (deIpolyi et al., 2007).

In line with the cognitive impairments seen in the disease, there is a deficit in visuospatial abilities on many visuospatial tasks and this is even apparent as early as ten years before diagnosis. Whilst there are a number of studies examining spatial perception and spatial visualisation tasks, very few studies have examined mental rotation tasks, possibly because they are too complex for AD participants.

Sex differences in visuospatial abilities in Alzheimer's disease

It is evident that AD impacts performance on a wide range of visuospatial tasks, but does the performance on these tasks differ between men and women? If AD affects men and women equivalently, then we would expect to see a male advantage on all tests other than figure drawing, as this profile is found in the healthy elderly.

Of the 16 studies that examined sex differences in cognition in AD, only nine included a task that measured visuospatial abilities (see Table 2.3). It is remarkable, given that a male superiority for visuospatial abilities has been consistently reported in the healthy population, that researchers have not investigated whether AD impacts this advantage.

TABLE 2.3 SUMMARY OF PREVIOUS RESEARCH CITED IN REVIEW EXAMINING SEX DIFFERENCES IN AD FOR VISUOSPATIAL TASKS

	N		**Mean Age /(Range)**		**Mean MMSE**			
Paper	**M**	**F**	**M**	**F**	**M**	**F**	**Tasks used**	**Findings**
Millet et al. (2009)	20	20	23.2	22.8			CBT,	n.s.
							CBTb, VPT	M >F
Beinhoff et al. (2008)	26	23	65.7 ±8.1	69.7 ±8.3	25.6 ±2.4	24.7 ±2	FC (WMS-R)	M >F
Cushman & Duffy (2007)	22	12	74.4 ±7.1		24.03 ±3.99		JLO	n.s.
Perneczky et al. (2007a)	50	43	67.5 ±10.5	72.1 ±8.3	23.9 ±1.8	23.0 ±2.6	FC (CERAD)	n.s.
Heun & Kockler (2002)	171	267	66 ±8.9	68.9 ±8.5	15.5 ±7.1	16.3± 6.5	FC (SIDAM)	M >F
Buckwalter et al. (1996)	72	87	70.0 ±7.9	73.2 ±7.6	17.8 ±6.7	16.5 ±7.9	BD	n.s.
							FC (CERAD)	n.s.
Henderson et al. (1996)	26	27	75.3 ±6.2	74.3 ±6.3	13.8 ±7.7	11.8 ±8.3	FC (CERAD)	n.s.
Henderson & Buckwalter (1994) 1	22	24	74.6 ±6.7	73.5 ±6.7	not given		FC (CERAD)	n.s.
Henderson & Buckwalter (1994) 2	270	377	69.9 ±7.8	73.4 ±7.9	17.5 ±5.8	17.3 ±5.8	FC (CERAD)	n.s.

Note: M = Male. F = Female. n.s. = not significant. Tasks: BD = block design. CBT = Corsi block tapping. CBTb = Corsi block tapping (backwards). CERAD = Consortium to Establish Registry for Alzheimer's Disease. EF = embedded figures. FC = figure copying. JLO = Judgment of Line Orientation. SIDAM – A Structured Interview for the diagnosis of Dementia of the Alzheimer type, Multi-infarct dementia and dementia of other aetiology. VPT = Vecchi's Pathway Task. WMS-R = Wechsler Memory Scale - Revised

What has been reported? There was only one paper that used a spatial perception task: Cushman & Duffy (2007) were primarily concerned with navigation but also included the judgement of line orientation task. No significant sex differences emerged. All other papers examined spatial visualisation tasks. Buckwalter et al. (1996) was the only paper to use the block design test and no differences between men and women with AD emerged. However, Beinhoff et al. (2008) reported that males with AD were better than females with AD at another spatial visualisation task - a drawing task measuring visuospatial episodic memory as did Heun & Kockler (2002). However, most other researchers failed to identify any difference between men and women with AD at copying a geometric figure (Buckwalter et al., 1996; Henderson et al., 1996; Henderson and Buckwalter, 1994; Perneczky, Drzezga, Diehl-Schmid, Yi & Kurz., 2007).

Millet, Raoux, LeCarret, Bouisson, Dartigues & Amieva (2009) made the distinction between passive processing, where information on form and location of visual stimuli are temporarily retained, and active processing, which refers to the retention and execution of movement sequences and the ability to operate mental rotation. They identified a sex difference in people with AD, favouring men, on tasks requiring dynamic transformation of the material, i.e. active processing, (Vecchi's pathway task and the backward Corsi block-tapping task), whilst on passive tasks (where they used a computerised version of the Vecchis matrix memory task and the forward CBT task) there were no sex differences in performance.

In summary, the published research would suggest that the visuospatial abilities of men and women with AD do not differ to the same extent as in the healthy population. Nevertheless, none of the papers examining visuospatial abilities in AD patients have used tasks that most commonly reveal normal sex differences (i.e. mental rotation and spatial perception tasks).

It may be that researchers specifically avoid using the mental rotation tasks with AD patients, given the complexity of these tasks. Although some researchers have used simpler mental rotation tasks (Lineweaver et al., 2005) these researchers did not report male and female performance separately.

2.3. VERBAL ABILITIES

2.3.1. VERBAL ABILITIES IN THE GENERAL POPULATION

The term ‘verbal abilities’ relates to cognitive processes that are concerned with words, or language. As with visuospatial abilities, verbal ability is not a unitary concept – the term can apply to all components of language use. Tasks used to measure verbal ability rely on rapid access to, and retrieval of, semantic and phonological information in memory – both episodic and semantic. The extent to which semantic and phonological knowledge is required varies between tests.

Fluency tests measure either semantic (categorical) fluency or phonological (lexical) fluency. Category fluency is a measure of semantic memory in which participants are asked to name as many exemplars of a given category as they can, usually within a time limit (often one minute). The most frequently employed category is animals (Tombaugh,, Kozak & Rees, 1999). Lexical fluency tasks require participants to list as many words as they can, beginning with a given letter of the alphabet, again usually within one minute. It does not require semantic knowledge, but depends on phonological processing. The letters F,A,S are frequently used by researchers and clinicians.

Confrontation naming tasks require participants to name visually presented items – usually line drawings. This test is used as a measure of semantic memory processes, but also depends on visual acuity and phonological processes (in order to retrieve the name). The most frequently used tasks are Boston Naming Test (BNT), Graded Naming Test (GNT) and the Snodgrass and Vanderwart corpus (1980).

SEX DIFFERENCES IN VERBAL ABILITIES IN THE GENERAL POPULATION

In 1988, Hyde & Linn published a meta-analysis on verbal abilities. They claimed that although there was a clear consensus that women were better than men at verbal tasks, some disagreement existed about which types of verbal abilities showed sex differences. Their review examined 165 studies (including dissertations and unpublished papers) originating from the USA or Canada. A 'headcount' of the findings revealed that 27% of studies found a female advantage, 66% reported no significant difference and 7% reported that males were better than females. However, when they examined only those papers that provided analysable data (i.e. data that allowed them to calculate Cohen's *d*), they calculated 120 effect sizes, of which 75% reported a female advantage.

Although their results (75% of effect sizes favouring women) suggest a strong female advantage, Hyde & Linn (1988)'s meta-analysis calculated only a small weighted effect size of d= 0.11 in favour of women. Similarly to the Linn & Petersen (1985) visuospatial meta-analysis (see 2.2) they broke down the analysis by type of test. Hyde & Linn (1988) revealed that the magnitude of sex differences was close to zero for vocabulary, reading comprehension, essay writing and those tests included in the SAT. Whilst for others, the effect sizes were only modest (analogies d =-0.16, i.e. favouring males) speech production d =0.33, anagrams d =0.22 and general/mixed d =0.2).

Although on a count basis the findings of Hyde & Linn (1988) corresponded with the Maccoby & Jacklin (1974) review, the quantitative analysis did not. In order to find out why this might be, Hyde & Linn separately analysed those papers published before and after 1974. The earlier studies had a mean effect size of *d*=0.23, whilst for the 1974 and later studies the effect size was *d*=0.10. Hyde & Linn (1988) suggested that the difference may be because boys had more recently been permitted to engage in (more verbal) activities that were previously reserved for girls. However, Halpern (2000) had an alternative explanation. She claimed that the apparent reduction reflected an increase in the number of non-significant studies published after 1974. When non-significant results were removed from the analysis, the pre-1974 median effect size became *d* = 0.32 and the post -1974 median effect size became *d* = 0.33.

Hyde and Linn (1988) concluded that verbal sex differences were so small as to be close to zero. However, researchers have continued to refer to a female verbal advantage. For example Lewin et al. (2001) stated that "women have repeatedly been shown to be better than men at verbal episodic memory" (Lewin et al., 2001, p 165) and Halari et al., 2005 said that "women score higher than men, on average, on tests of verbal fluency and synonym generation" (Halari et al., 2005 p. 104). So, to what extent are such differences found?

Verbal fluency is one area where sex differences are often cited and women have been reported as scoring higher than men in lexical fluency tasks (Burton et al., 2005; de Frias et al., 2006; Hausmann et al., 2009; Herlitz et al., 1999; Thilers et al., 2006; Weiss et al., 2003, Weiss, Ragland, Brenninger, Bilker, Deisenhammer & Delazer, 2006) (see Table 2.4). However, Wallentin (2009) argued that the evidence for the female advantage in lexical fluency finding is weak, and he criticises the Weiss et al. (2003) study in particular, despite Weiss et al. (2003) reporting a moderate effect size for the lexical fluency of *d*=0.45. Wallentin (2009) also claimed that Weiss et al. (2003) failed to control for IQ and age.

However, in the Weiss et al. (2003) paper men actually scored higher on verbal IQ than did women, so presumably the effect size would increase had the effect of IQ been controlled for. With regards to age, although there was a significant difference between men and women, the mean ages for these groups were early twenties when one would not usually expect to find any age effect. In 2006, Weiss and colleagues again examined verbal fluency and they again found that women generated significantly more words than men on lexical fluency (Weiss et al., 2006). Furthermore, a similar effect size (*d*=0.49) was reported by Herlitz et al. (1999) so the finding by Weiss and colleagues was not an isolated one. (Wallentin (2009) did not discuss the Herlitz paper, even though the sample size (of 200 participants) fell within the criteria for inclusion.)

In 2006, Rodriguez-Aranda & Martinussen explored sex effects in their meta-analysis on age-related differences in lexical fluency. They found no significant differences between men and women at any age, although they were only able to identify five studies that provided appropriate data to examine sex effects. (They only included in their analysis papers that reported original data for at least two different age groups as they were primarily interested in age differences.) Other researchers have reported no significant sex differences in lexical fluency (Brickman, Paul, Cohen, Willimas, MacGregor, Jefferson et al., 2005; Clark et al., 2006; Van der Elst, Van Boxtel, Van Breukelen & Jolles, 2006; Halari et al., 2005; Harrison, Buxton, Husain & Wise, 2000; Janowsky et al., 1988; Lanting et al., 2009; Lewin et al., 2001; Naeve et al., 1999; Nowak & Moffatt, 2011; Rahman, Abrahmas & Wilson, 2003; Robert & Savoie, 2006; Tombaugh et al., 1999). Halari et al. (2005) claimed they may not have had enough participants to detect an effect, however, the effect size they reported was very small (*d*=0.23), so the study was unlikely to have been underpowered. Furthermore, both Tombaugh et al., 1999 and Elias, Elias, D'Agostino, Silbershatz & Wolf, 1997 reported that the variance in lexical fluency accounted for by sex was less than 1%.

TABLE 2.4 SUMMARY OF PREVIOUS RESEARCH CITED IN REVIEW EXAMINING SEX DIFFERENCES IN THE GENERAL POPULATION FOR VERBAL FLUENCY AND CONFRONTATION NAMING

	N		Mean Age (Range)			
Paper	**M**	**F**	**M**	**F**	**Tasks used**	**Findings**
Nowak & Moffat (2011)	58	82	23 ± 6		LF: COWA C,F,L	n.s. (*d*=.24)
Hausmann et al. (2009)	55	59	25.8 ±7.2	23.4 ±4.7	LF: L,P	F >M (η^2 = .06)
Lanting et al. (2009)	29	31	28.8 ±6.2 (18-40)		LF: COWA C,F,L CF: a	n.s. n.s.
Cameron et al. (2008)	30	30	(20-80)		CF: f, fu CF: t CF: a, ve, k, c	F >M M >F n.s.
Moreno-Martinez et al. (2008)	18	18	31.7 ±6.9	29.8 ±7.7	CF: f,t,a,i,tr,v,ve,fu,k c,fl,mi,bp,bg	n.s.
Clark et al. (2006)	514	493	(6-82)		LF: F,A,S	n.s.
deFrias et al. (2006)	625		(35-80)		LF: A, M (5 letters) CF: Professions beg B	n.s. n.s.
Robert & Savoie (2006)	50	50	21.8 ±1.7	21.6 ±1.8	LF: P,R,V, (2mins) CF: f,v	n.s. f = F >M, ve =n.s.
Thilers et al. (2006)	1107	1276	(35-70)		LF: A, M (5 letters)	F >M
Van der Elst et al. (2006)	915	910	(25-80)		LF: M (4 letter words) CF: a CF: p	n.s. n.s. M >F
Weiss et al.(2006)	40	40	25.5	25.0	LF: F,A,S CF: a	F >M n.s.
Brickman et al. (2005)	231	240	(21-82)		LF: F,A,S CF: a	n.s. n.s.
Burton et al. (2005)	41	93	19.3 ±1.1	20.0 ±4.4	LF: sum & S (5mins) C 4 letters (4mins)	F >M n.s.
Coppens & Frisinger (2005)	24	66	(20-92)		CN: S&V	LT: n.s.; NTL: M >F
Halari et al. (2005)	42	42	28.3 ±4.8	27.7 ±4.0	LF: F,A,S CF: a,f,v (sum)	n.s. ES = .23 F >M ES = .61
Connor et al. (2004)	129	107	(30-94)		CN: BNT	M>F
Rahman et al. (2003)[1]	120	120	29.9	26.8	LF: COWA, P,R,W CF: a, f, v (sum)	n.s., *d*= .17 F >M, (*d*=1.12)
Weiss et al. (2003)	51	46	26.2 ±3.0	23.9 ±3.8	LF: B,A,S CF: s,a,ve (sum)	F >M (*d*=.45) n.s. (*d*=.24)
Lewin et al. (2001)	91	94	29.9	28.8	LF: F,A,S	n.s.

Paper	N M	N F	Mean Age (Range) M	Mean Age (Range) F	Tasks used	Findings
			±5.8	±6.2		
Harrison et al. (2000)	166	199	40.2	41.3	LF: COWA, B	n.s.
			±18.1	±18.7	CF: a	n.s.
Capitani et al. (1999)	112	154	53.9 (18-96)		CF: f	F >M
					CF: t	M >F
					CF: a	n.s.
Herlitz et al. (1999)	100	100	28.2	28.0	LF: F,A,S	F >M (*d*=.49)
			±6.0	±5.5		
Lansing et al. (1999)	287	430	(50-98)		CN: BNT	M >F
Naeve et al. (1999)	34	28	(18-51)		LF: L	n.s.
Tombaugh et al. (1999)	559	741	(16-95)		LF: F,A,S	n.s.
					CF: a	n.s.
Janowsky et al. (1988)	18	30	28.5	29.8	LF: F,A,S	n.s.
			±3.1	±3.2	CF: a	n.s.

Note: [1.] Values/results are those for heterosexual men and women. *d* = Cohen's *d*. ES = effect size. F = Female. M = Male. n.s. = not significant. Tasks: CF = Category Fluency. CN = confrontation naming. COWA = Controlled Oral Word Association. LF = Lexical Fluency. S&V = Snodgrass & Vanderwart. Categories: a = animals, b = birds, bg = buildings, bp = body parts. c = clothing, f = fruit, , fl = flowers, fu = furniture, i = insects, k = kitchen utensils, mi = musical instruments, n = first names, s = supermarket items, t = tools, tr= trees, v = vehicles, ve = vegetables. LT = living things, NLT = nonliving things. * 14 categories analysed.

Halari et al. (2005) found that women scored significantly higher than men on semantic fluency but Weiss et al. (2003; 2006) found that although women performed better than men the difference was not significant. Other researchers have reported no significant sex differences in category fluency (Brickman et al., 2005; Harrison et al., 2000; Janowsky et al., 1988; Lanting et al., 2009; Tombaugh et al., 1999 – all of whom examined animal fluency). Janowsky et al. (1998) conceded that they may not have found an (expected) effect due to a small sample size (30 women and 18 men) although Tombaugh et al., 1999 failed to find a significant difference with a sample size of 735. Robert & Savoie (2006) found no significant sex difference on verbal fluency overall, however follow-up analyses revealed a significant female advantage for fruit names (although not for the vehicle category) whilst Van der Elst et al. (2006) found no significant sex difference for animals, but a male advantage for professions. It may be, therefore, that any sex differences found are category specific and no sex differences exist in the most frequently examined category of animals. In support, Capitani, Laiacona & Barbarotto (1999) reported a female advantage in naming fruits whereas males named more tools, but no sex difference in animal fluency. And these findings were also reported by Cameron, Wambaugh & Mauszycki (2008) who examined semantic fluency across eight categories in 30 men and 30 women. However, Moreno-Martinez et al. (2008) included 14 categories in their category fluency study and there were no significant sex differences in 36 young adults (18 males, 18 females) on any category, including fruits and tools where differences have been reported by others. Many researchers did not provide a breakdown by category, such as Weiss et al. (2003) (supermarket items, animals and vegetables), and both Rahman et al. (2003) and Halari et al. (2005) (animals, fruits and vegetables). Sex differences may have been apparent for individual categories had these been analysed separately as averaging across categories can mask differences that would emerge if single categories are examined.

For verbal fluency, then, the findings are variable. Although many published papers reported a female advantage for lexical fluency a large number reported no significant sex differences. The results for semantic fluency were less equivocal: researchers largely failed to find significant sex differences, unless specific categories are analysed separately when sex differences emerged in favour of women for fruit and men for tools.

An advantage for men has been consistently found in one language task: confrontation naming. Although there have been very few papers examining sex differences. (Connor, Spiro, Obler & Albert, 2004; Coppens & Frisinger, 2000; Lansing, Ivnik, Munro, Cullum & Randolph., 1999). Connor et al., 2000 were primarily concerned with aging effects, but included some younger participants and identified a male advantage on the Boston Naming Test (BNT). Lansing et al. (1999) examined the scores of 719 normal participants on different versions of the BNT. They found a significant effect of sex on all forms of the test, with men scoring significantly higher than women even after covarying for age and education. The difference was approximately 2.7 items on the full 60 item test. Coppens & Frisinger (1999) were interested in sex differences in naming living and non-living things and found a male advantage for non-living items but no sex differences for living items, so the presence of sex differences may be category specific for naming, too.

For verbal abilities in the general population, as with visuospatial abilities, the existence of sex differences is task dependent. Men have been reported as being superior on confrontation naming (although there is a scarcity of published findings). For lexical fluency, the findings are mixed with some reports of a female advantage. However, on semantic fluency tasks sex differences are rarely apparent other than on certain specific categories such as fruits (females better) and tools (males better).

2.3.2. VERBAL ABILITIES IN THE ELDERLY

Before examining sex differences in verbal abilities in the elderly we need to consider to what extent do verbal abilities reduce with aging?

DECLINE IN VERBAL ABILITIES IN THE ELDERLY

In a summary of the findings of the Seattle Longitudinal Study, Schaie (1996) stated that verbal abilities show a significant positive age difference until mid-life, with small reductions thereafter, so that those at advanced old age are still at a higher level than the youngest age. Van Hooren, Valentin, Bosma, Ponds, Boxtel & Jolles, 2007 also reported a significant general decline in cognitive functioning between the ages of 64 and 81 years with age groups differing on all cognitive measures examined, including category fluency.

Rodriguez-Aranda & Martinussen (2006) conducted a meta-analysis examining the effect of aging on the Controlled Oral Word Association (COWA) Test, which measures lexical verbal fluency. They observed a constant decline in mean effect size from age 40 until over 80. While the decline between those in their forties and those in their fifties was only small, after age 60 the decrease was considerable, resulting in a large aging effect size of Cohen's *d* = .76 when comparing those in their twenties to those in their eighties. Brickman et al. (2005), Backman & Small (2007) and Lanting et al. (2009) also reported that lexical naming declined with age. In contrast, Bird, Papadopolou, Ricciardelli, Rosser & Cipolotti (2004) reported no correlation between age and lexical fluency scores although as their participants were aged between 40 and 70 years their analysis did not include any very young adults nor any of the oldest old. However, Schmitter-Edgecombe, Vesneski & Jones (1999) also reported no differences in lexical fluency between the age groups and they did include a group of participants who were over 75 years of age.

Although they found the elderly were poorer than the young in animal fluency, van Hooren et al. (2007) claimed that long-term semantic memory was the most resistant to deterioration in age. In support of this, Bird et al. (2004) found no correlation between age and semantic fluency (animals). However, there have been reports of an aging decline in animal naming (Brickman et al., 2005. Lanting et al., 2009; Snitz, Unverzagt, Chang, Vanderbilt, Goo & Saxton, 2009 and Wiederholt et al., 1993). Lanting et al. (2009) reported that younger adults (18-40 years) produced significantly more words than older adults (65-91 years). Capitani et al. (1999) found age to be a significant predictor for semantic fluency overall and for all categories examined in a sample of 26 participants with a mean age of 53.9 years, with older participants scoring lower. Similarly, Backman & Small (2007) reported age-related deficits for supermarket items. Schmitter-Edgecombe et al. (1999) claimed, however, that a deficit in semantic fluency only appeared in the oldest adults, i.e. those over 75 years of age.

Confrontation naming has also been shown to be inversely associated with age (Randolph, Lansing, Ivnik, Cullum & Hermann., 1999; Ross, Lichtenberg & Christensen, 1995). Zec, Burkett, Markwell & Larsen et al. (2007) reported significantly poorer mean scores with successively older age groups, with the size of the decline increasing with each successive decade. Welch, Doisneau, Johnson & King (1996) identified the same association between aging and naming; however when data was grouped according to age the decline was not apparent until aged 75+. Other research also indicates that naming remains stable with age until individuals are in their 70s, after which a significant difference between 70 year olds and all other age groups emerges (Albert, Heller and Milberg, 1988). Although Albert et al. (1988) conducted a cross-sectional study of performance on the BNT with 80 participants ranging from 30 to 80 years and such studies may reflect cohort differences, an aging decline after age 70 has also been reported longitudinally. Zec, Markwell, Burkett & Larsen (2005) studied 541 ‘normal’ elders initially aged between 50 and 99 years over 10 years. In this group, BNT scores did not decline until around 70 years old at which stage an annual decline of 1.3 words was evident. Further support comes from Connor et al. (2004) who, in a study of 236 participants, reported a mean cognitive decline in confrontation naming of 2% per decade, with an accelerated decline over the age range.

In contrast, Cruice et al. (2000) failed to find age-related change in scores on the BNT and Bird et al. (2004) discovered that age did not mediate performance on the GNT, although this latter study did not include any very old participants (188 participants, age range 40-70 years) so a decline may not yet be apparent. The study by Cruice et al. (2000) was longitudinal, but it only spanned four years and Connor et al. (2004), who examined participants over 20 years claimed their analyses were more sensitive to subtle declines with age than those of Cruice et al. (2000). The findings of Schmitter-Edgecombe et al. (1999) concurred with those reporting a decline in naming in the oldest participants, but they found that both groups of old participants (young-old – aged 58-74 and old-old – aged over 75) scored higher than the young group (18-22 years). Analysis of individual items on the full, 60-item, BNT revealed that the young found four of the items particularly difficult (yoke, trellis, abacus and palette). Removing these items from the analysis entirely removed the apparent advantage that the elderly had over the young group (Schmitter-Edgecombe et al., 1999) suggesting a cohort effect.

Verbal abilities do show an aging decline but the age at which such a decline is evident varies according to the task. In lexical fluency a decline is apparent from age 40 with the rate of decline increasing after age 60. Semantic tasks may be the most resistant to deterioration in aging, but category fluency does decline with age, particularly after 75 years. Similarly, confrontation naming shows an age-related reduction which emerges most strongly after 65 years of age.

Sex differences in verbal abilities in the elderly

So, for verbal skills, there is a cognitive decline, but as the rate of cognitive decline is reportedly similar for men and women (see section 2.1.1.), we would expect to find the same pattern of sex differences in the elderly as the younger population, i.e. a male advantage on confrontation naming, mixed reports for lexical fluency and no sex differences for category fluency (see section 2.3.1).

The findings for sex differences in lexical fluency in the elderly do reflect those found in the young (see Table 2.5 for a summary). Some researchers report a female advantage (Elias et al., 1997; Gerstorf et al., 2006, 2011; Monsch, Bondi, Butters, Salmon, Katzman & Thal, 1992; Thilers et al., 2006) whereas others report no difference between men and women (Clark et al., 2006; de Frias et al., 2006; Fahlander et al., 2000; Lanting et al., 2009; Mathuranath et al., 2003; Welsh-Bohmer, Ostbye, Sanders, Peiper, Hayden, Tschanz et al., 2009; Whittle, Corrads, Dick, Ziegler, Kahle-Wrobleski, Paganini-Hill et al., 2007) including the meta-analyis by Rodriguez-Aranda & Martinussun (2006).

Also mirroring the findings in the young, published research into sex differences in the elderly in category fluency provides conflicting evidence. With reports of a female advantage (Duff et al., 2011; deFrias et al., 2006; Fahlander et al., 2000; Marra, Ferracciolo & Gainotti, 2007; Monsch et al., 1992; Moore et al., 2010; Proust-Lima et al., 2008) even for animals (Welsh-Bohmer et al., 2009), no sex differences (Beinhoff et al., 2008; Gerstorf et al., 2006; Henderson & Buckwalter, 1994; van Hooren et al., 2007; Lanting et al., 2009; Mathuranath et al., 2003; Snitz et al., 2009; Whittle et al., 2007) and even a male advantage (Wiederholt et al., 1993). The presence of an effect remains category dependent with some authors reporting both a female advantage and an absence of sex differences (Moreno-Martinez et al., 2008) or both a female advantage and a male advantage (Marra et al, 2007) or all three (Capitani et al., 1999).

TABLE 2.5 SUMMARY OF PREVIOUS RESEARCH CITED IN REVIEW EXAMINING SEX DIFFERENCES IN THE ELDERLY FOR VERBAL FLUENCY AND CONFRONTATION NAMING

Paper	N		Mean Age (Range)		Tasks	Findings
	M	F	M	F		
Duff et al. (2011)	300	418	72.9 ±5.5	73.6 ±6.1	CF: RBANS CN: RBANS	F >M n.s.
Gerstorf et al. (2011)	901	1079	(50-80)		LF: S (5mins)	F >M
Moore et al. (2010)	50	38	68 ±7.8		CF: RBANS CN: RBANS	F >M n.s.
Albert et al. (2009)	146	138	72.0 ± 7.4		CN: BNT	M >F
Lanting et al. (2009)	29	43	74.7 ±5.8 (65-91)		LF: COWA C,F,L CF: a	n.s. n.s.
Snitz et al. (2009)	655	1230	77.2 ±7.1		CF: a	n.s.
Welsh-Bohmer et al. (2009)	227	280	79.3 ±7.2	80.2 ±7.8	LF: COWA CF: a CN: BNT	n.s. F >M n.s.
Beinhoff et al. (2008)	28	23	63.5 ±8.9	63.8 ±8.2	CF: a CN: BNT	n.s. n.s.
Moreno-Martinez et al. (2008)	17	19	72.6 ±6.2	70.2 ±7.9	CF: k.ve,fl CF: f,i,tr,v,a,t, bp,bg, fu,mi,c	M >F n.s.
Proust-Lima et al. (2008)	815	985	65		CF: Isaacs set, ci,f,a,co (sum)	F>M
van Hooren et al (2007)	292	286	51.4 ±16.8		CF: a	n.s.
Marra et al. (2007)	100	89	72.6 ±10.4	70.5 ±12.4	CF: fu CF: b	F >M M >F
Whittle et al. (2007)	108	231	90+		LF: F CF: a CN: BNT	n.s. n.s. n.s.
Zec et al. (2007)	354	663	68.7 ±8.1	68.0 ±8.9	CN: BNT	n.s.
Clark et al. (2006)	514	493	(6-70+)		LF: F,A,S	n.s.
deFrias et al. (2006)	625		(35-80)		LF: A, M (5 letters) CF: Professions beg B	n.s. n.s.
Gerstorf et al. (2006)	258	258	84.7 ±8.4	85.1 ±8.9	LF CF	F >M n.s.
Thilers et al. (2006)	1107	1276	62.2 ±13.5	63.8 ±10.3	LF: A, M (5 letters)	F >M
Coppens & Frisinger (2005)	17	43	(55-92)		CN: S&V	LT & NLT n.s.
Connor et al. (2004)	129	107	(30-94)		CN: BNT	M >F
Barnes et al. (2003)	271	577	74.0 ±6.5	76.1 ±7.0	Semantic memory: total of VF/CN	M >F
Mathuranath et al. (2003)	62	91	67.3 ±5.4	66.7 ±5.7	LF: P,A CF: a	n.s. n.s.

Paper	N		Mean Age (Range)		Tasks	Findings
	M	F	M	F		
Kent & Luszcz (2002)	410	393	77.6		CN: BNT	n.s.
Fahlander et al. (2000)	43	184	84.41 ±4.89		LF: N,S CF: g	n.s. F >M
Capitani et al. (1999)	112	154	53.9 (18-96)		CF: f CF: t CF: a	F >M M >F n.s.
Lansing et al. (1999)	287	430	73.6 (50-98)		CN: BNT	M >F
Randolph et al. (1999)	287	430	73.6 ±10.3		CN:BNT	M >F
Elias et al. (1997)	742	1063	(55-88)		LF	F >M
Buckwalter et al. (1996)	52	82	74.8 ±6.5	74.2 ±9.5	CN: BNT	n.s.
Welch et al. (1996)	74	102	(60 – 93)		CN: BNT	M >F
Ross et al. (1995)	47	76	75.9 ±7.4		CN: BNT	n.s.
Henderson & Buckwalter (1994)	130	261	69.7 ±6.3	67.1 ±8.0	CF: a CN: CERAD	n.s. n.s.
Wiederholt et al. (1993)	693	999	Range: 55 +		CF: a	M advantage
Monsch et al. (1992)	17	36	71.2 ±7.9		LF: F,A,S CF: s, n CF: a,f,ve (sum)	F >M F >M F >M

Note: *d* = Cohen's *d*. ES = effect size. F = Female. M = Male. n.s. = not significant. Tasks: CF = Category Fluency. CN = confrontation naming. BNT = Boston Naming Test. COWA = Controlled Oral Word Association. LF = Lexical Fluency. RBANS = Repeatable Battery for Assessment of Neuropsychological Status. S&V = Snodgrass & Vanderwart. VF = verbal fluency. CF categories: a = animals, b = birds, bg = buildings, bp = body parts. c = clothing. ci = cities. co = colours. f = fruit, , fl = flowers, fu = furniture, g = grocery store, i = insects, k = kitchen utensils, mi = musical instruments, n = first names, s = supermarket items, t = tools, tr= trees, v = vehicles, ve = vegetables. LT = living things, NLT = nonliving things.

On confrontation naming tasks, there have been more published papers examining sex differences in the elderly than were found for young adults. In their longitudinal study, Connor et al. (2004) found that the rate of decline on confrontation naming was the same for men and women. In line with this, elderly men have been reported to score higher than elderly women (Albert, Spiro, Sayers, Cohen, Brady, Goral et al., 2009; Connor et al., 2004; Lansing et al., 1999; Randolph et al., 1999; Welch et al., 1996) mirroring the male advantage found in young adults. However, a number of researchers failed to find a significant sex difference in this task in the elderly (Beinhoff et al., 2008; Buckwalter et al., 1996; Coppens et al., 2005; Duff et al., 2011; Henderson & Buckwalter, 1994; Kent & Luszcz, 2002; Moore et al., 2010; Ross et al., 1995; Welsh-Bohmer et al., 2009; Whittle et al., 2007; Zec et al., 2007) suggesting either that elderly men lose their advantage in naming or that the apparent male advantage in the young is not a robust finding. Given that only three papers were identified citing a male advantage, the latter may be the case.

The relative performance of men and women in the elderly largely reflects that found in young adults on fluency tasks, i.e. roughly equal performance (until specific categories are examined in which a female advantage for naming fruits emerges). However, although some researchers reported a male advantage for confrontation naming, the majority of papers reported an absence of sex differences.

2.3.3. Verbal abilities in Alzheimer's disease

Semantic memory deficits are found at an early stage in AD (Salmon 2011). Category fluency deficits are apparent five years before diagnosis (Auriacombe, Lechevallier, anieva, Harston, Raoux & Dartigues, 2006) and even mild AD patients were more impaired than both MCI and elderly controls on category fluency (Adlam, Bozeat, Arnold, Watson & Hodges, 2006; Balthazar, Martinelli, Cendes & Damasceno, 2007; Lonie, Herrmann, Tierney, Dohaghey, O'Carroll, Lee et al., 2009). In two meta-analysis studies a significant difference for category fluency emerged, with elderly adults scoring higher than people with AD (Henry, Crawford & Phillips, 2004; Laws, Duncan & Gale, 2010). In the Laws et al. (2010) analysis 92 studies produced a large effect size, Cohen's *d* of 2.10.

In contrast, people with AD have been shown not to be impaired on lexical fluency (Butters, Granholm, Salmon and Grant, 1987; Rogers & Friedman, 2008). However, deficits in lexical fluency in people with AD have been reported (e.g. Lonie et al., 2009, Phillips, Scott, Henry, Mowar & Bell, 2010). Furthermore, Laws et al. (2010)'s meta-analysis included 96 studies examining lexical fluency and an AD deficit emerged with a large effect size at *d* = 1.46. Although, the meta-analysis by Henry et al. (2004) claimed that the performance of people with AD on lexical fluency tests was entirely consistent with the patients' overall level of cognitive functioning.

The elderly also score higher than AD patients on confrontation naming (Adlam et al., 2006, Balthazar, Cendes & Damasceno, 2008, Frank, McDade & Scott, 1996; Lukatela, Malloy, Jenkins & Cohen, 1998, Nicholas, Obler, Au & Albert, 1996, Rogers & Friedman, 2008)). The difference is apparent at a very early stage in the disease process and can be found in mildly affected AD patients (Adlam et al., 2006; Baudic, Barba, Thibaudet, Smagghe, Remy & Traykov, 2006) and amnestic mild cognitive impairment (aMCI) patients (Ahmed, Arnold, Thompson, Graham & Hodges, 2008, Balthazar et al., 2008) although Adlam et al., 2006 did not find a deficit in naming in aMCI patients, and neither did Balthazar and colleagues in an earlier study (Balthazar et al., 2007). In their meta-analysis, Laws et al. (2010) identified a significant difference between Alzheimer's patients and the elderly for naming: the calculated effect size (Cohen's *d*) from 56 studies was 1.54.

Most research has reported an AD deficit on semantic fluency tasks, and the category fluency test has been shown to be the test most sensitive to mild semantic memory impairments although a deficit is also apparent in confrontation naming. A large effect size is also evident in lexical fluency, with AD participants scoring lower than EC.

Elderly men and women show little difference in their performance in verbal fluency tasks, other than for fruit fluency whereas men have been reported as being better than women at confrontation naming. Is there any evidence that the relative performance of men and women with AD is different from that found in the healthy elderly?

Some researchers have concluded that women with AD have worse language abilities than men with AD (McPherson, Back, Buckwalter & Cummings, 1999; Moreno-Martinez et al., 2008; Ripich, Petrill, Whitehouse & Ziol, 1995) whilst others claim that there are no sex differences in verbal abilities (Bayles, Azuma, Cruz, Tomoeda, Wood & Montgomery, 1999; Perneczky et al., 2007) or in the rate of decline of these abilities (Bayles et al., 1999; Herbert, Wilson, Gilley, Beckett, Scherr, Benerr et al., 2000; Ripich et al., 1995). The results, therefore, are conflicting and the results for individual verbal tests need to be examined.

No significant effect for sex has been found for lexical fluency (Bayles et al., 1999; Henderson, 1996; McPherson et al., 1999; Monsch et al., 1992; Ripich et al., 1995). For semantic fluency, men scored significantly higher than women on naming animals (Henderson & Buckwalter, 1994) insects, trees, tools, musical instruments and vehicles (Moreno-Martinez et al., 2008) and birds (Marra et al., 2007). By contrast, no significant sex differences were found in naming animals (Bayles et al.,1999; Beinhoff et al., 2008; Henderson, 1996; McPherson et al., 1999; Moreno-Martinez et al., 2008; Perneczky et al., 2007), fruits (Bayles et al., 1999; Moreno-Martinez et al., 2008), furniture (Marra et al., 2007; Moreno-Martinez et al., 2008) supermarket items or first names (Monsch et al., 1992). Monsch et al. (1992) did, however, report a female advantage in semantic fluency –

in the scores for animals, fruits and vegetables combined although they did not analyse each category separately.

TABLE 2.6 PREVIOUS RESEARCH EXAMINING SEX DIFFERENCES IN AD FOR VERBAL FLUENCY AND CONFRONTATION NAMING

	N		Mean Age (Range)		Mean MMSE			
Paper	**M**	**F**	**M**	**F**	**M**	**F**	**Tasks used**	**Findings**
Beinhoff et al. (2008)	26	23	65.7 ±8.1	69.7 ±8.3	25.6 ±2.4	24.7 ±2	CF: a CN: BNT	n.s. n.s.
Moreno-Martinez et al. (2008)	28	33	73.7 ±6.0	74.9 ±9.3	21.2 ±4.2	18.9 ±4.9	CF: I,tr,v,t,mi CF: a,fl,f,fu,k, c,bg,bp	M >F n.s.
Marra et al. (2007)	85	168	70.7 ±7.6	71.6 ±7.3	19.1 ±4.8	17.6 ±5.2	CF: fu CF: b	n.s. M >F
Perneczky et al. (2007a)	50	43	67.5 ±10.5	72.1 ±8.3	23.9 ±1.8	23.0 ±2.6	CF: a CN: CERAD	n.s. M>F
Bayles et al. (1999)	30	33	77.7 ±9.1	80.1 ±8.3	15.2 ±5.1	15.9 ±6.1	LF: A,S CF: a, f CN	n.s. n.s. n.s.
McPherson et al. (1999)	23	36	73.9 ±9.0	74.9 ±6.4	23.3 ±3.3	22.2 ±3.8	LF: F,A,S CF: a CN:BNT	n.s. ES (R) = .01 n.s. ES (R) = .19 M >F ES (R) = .32
Randolph et al. (1999)	129	196	76.0 ±9.7		not given		CN: BNT	M >F
Buckwalter et al. (1996)	72	87	70.0 ±7.9	73.2 ±7.6	17.8 ±6.7	16.5 ±7.9	CN: BNT	M >F
Henderson (1996)	26	27	75.3 ±6.2	74.3 ±6.3	13.8 ±7.7	11.8 ±8.3	LF: F,A,S, CF: a CN: BNT	n.s. n.s. n.s.
Ripich et al. (1995)	29	31	71.7 ±7.8	74.8 ±7.6	not given		LF: F,A,S CN: BNT	n.s. M>F
Henderson & Buckwalter (1994) 1	22	24	74.6 ±6.7	73.5 ±6.7			CN: BNT	M >F
Henderson & Buckwalter (1994) 2	270	377	69.9 ±7.8	73.4 ±7.9	17.5 ±5.8	17.3 ±5.8	CF: a CN: CERAD	M >F M >F
Monsch et al. (1992)	43	46	72.1 ±6.6		18 ±5		LF: F,A,S CF: s, n CF: a,f,ve (sum)	n.s. n.s. F >M

Note: ES = effect size. F = Female. M = Male. n.s. = not significant. Tasks: BNT = Boston Naming Test. CERAD = Consortium to Establish Registry for Alzheimer's Disease. CF = Category Fluency. CN = confrontation naming. LF = Lexical Fluency. CF categories: a = animals, b = birds,bg = buildings, bp = body parts. c = clothing, f = fruit, , fl = flowers, fu = furniture, i = insects, k = kitchen utensils, mi = musical instruments, n = first names, s = supermarket items, t = tools, tr= trees, v = vehicles, ve = vegetables.

In line with the findings in the healthy elderly, women with AD have been reported as being worse than men at confrontation naming (Buckwalter et al., 1996; Henderson & Buckwalter, 1994; McPherson et al., 1999; Randolph et al., 1999; Ripich et al., 1995). And the magnitude of the effect size for naming was similar for the AD group and the elderly (Randolph et al., 1999). Others reported higher scores by men, but no significant sex differences (Bayles et al., 1999; Beinhoff et al., 2008; Perneczky et al., 2007).

Women with AD do not demonstrate an advantage in verbal fluency, although such an advantage has been reported in the general population, including in the elderly. It would appear, therefore, that women's language abilities are impacted to a greater degree by AD than are men's. Similarly, although elderly men have been shown to score higher than women in CN, much research reports no sex differences, whilst in AD men have an advantage over women, again suggesting a greater female deterioration.

2.4. FACIAL EMOTION RECOGNITION

Facial expressions are the most accessible cue to understanding an individual's affective state (McLellan, Johnston, Dalrymple-Alford & Porter, 2008). Many people with AD suffer in their interpersonal relationships (Shimokawa, Yatomi, Anamizu, Torii, Isono, Sugai et al., 2001) and it may be that impairment in recognition of facial emotions contributes significantly to this.

In studying facial emotion recognition (FER), researchers have identified six global expressions: anger, disgust, fear, happiness, sadness and surprise (Ekman & Friesan, 1971). Sometimes, contempt is also included in studies, but many studies focus on these six universally expressed and recognized emotions because they appear to be race- and culture- independent (Ekman, 1994). A number of different tests are used in the study of FER, almost always using static images. The most widely used are the Facial emotion expression - stimuli and test (FEEST: Young, Perrett, Calder, Sprengelmeyer & Ekman, 2002) and associated tests, the Florida Affect Battery (FAB: Bowers, Blonder & Heidman, 1989) and the Japanese and Caucasian Facial Expressions of Emotion (JACFEE: Matsumoto & Ekman, 1988) and extensions thereof (See Appendix 1 for detailed descriptions of these tests).

2.4.1. FER IN THE GENERAL POPULATION

SEX DIFFERENCES IN FER IN THE GENERAL POPULATION

In 1978, Hall reviewed the literature examining sex differences in identifying emotions from non-verbal communication. Examination of the results presented for each paper shows that, of the 35 studies with adult participants examining facial stimuli, only 7 were identified as having significant sex differences (at $p<0.05$) and for all of these, women were better than men. Furthermore, those that showed no significant sex differences had effect sizes (Cohen's *d*) ranging between 0 and 0.30 and most of the studies had large sample sizes ($n>100$). A qualitative review of the included literature would have concluded that the evidence provided by published research at that time was ambiguous. However a significant sex difference emerged in the meta-analysis: Hall reported a mean effect size (Cohen's *d*) of 0.32 for the visual mode, favouring females (Hall, 1978).

Subsequent research examining sex differences has been limited. Some research has shown that women are more accurate than men at recognizing facial expressions of emotion and that they do so faster than men (e.g., Hall Hutton & Morgan, 2010). Women have even been shown to be more accurate than men when stimuli are presented so fast as to be at the edge of conscious awareness (Hall & Matsumoto, 2004). Montagne, Kessels, Frigerio, de

Haan & Perrett (2005) claimed that men performed worse overall compared to women both for accuracy and sensitivity (the average amount of expression needed to first be able to correctly label the specific emotion). But Scholten, Aleman, Montagne & Kahn (2005) found that although women were more accurate than men at FER overall, there was no sex difference for sensitivity.

Other research, however, reported no differences between men and women in their ability to recognize facial emotions of expression (Clark, Neargarder and Cronin-Columb, 2010; Grimshaw, Bulman-Fleming & Ngo, 2004; Palermo & Coltheart, 2004; Sullivan, Ruffman & Hutton, 2007; Wong Cronin-Golomb & Neargarder, 2005). Clark et al. (2010), found no significant sex differences in healthy controls for any emotion, but they only examined 20 healthy participants. Palermo & Coltheart (2004) stated that there were no effects involving the sex of the rater although they also acknowledge that this may be due to insufficient power (only 24 participants were used). Neither study provided information on the effect size in their paper, so it is difficult to establish if these studies *were* underpowered. Sullivan et al., 2007 did not report whether they analysed sex differences on individual emotions just that they found "no effects for gender for either emotion recognition or scanning" (p.56). Similarly, Grimshaw et al. (2004) reported no main effects or any interactions for sex and Wong et al., 2005 checked for a sex difference for total accuracy scores across all emotions without examining individual emotions. Even if no sex difference emerges for total scores, if men outscore women on some emotions while women outperform men on others, they are likely to cancel each other out.

TABLE 2.7 SUMMARY OF REVIEW OF PREVIOUS LITERATURE ON DIFFERENCES BETWEEN YOUNG MEN AND WOMEN FOR FACIAL EMOTION RECOGNITION OF ANGER, DISGUST, FEAR, HAPPINESS, SADNESS AND SURPRISE

Author(s)	N M	N F	Test Used	Overall	Anger	Disgust	Fear	Happiness	Sadness	Surprise
Clark et al. (2010)	10	10	E&F 1976 - Accuracy	x	na	na	na	na	na	na
Hall et al. (2010)	19	20	E&F 1976 Morphed - Accuracy & RT	M	x	x	x	x	M	x
Mill et al. (2009)	176	431	JACFEE & JACNeuF	M	M	x		M	x	-
Vassallo et al. (2009)	23	27	JACFEE - Accuracy	x	na	na	na	na	na	na
			JACFEE - RT	M	x	x	x	M	x	x
Williams et al. (2009)	470	530	Webneuro	M	x	x	M	x	M	n.s.
Sullivan et al. (2007)	30	30	E&F 1976 Morphed	x	na	na	na	na	na	na
Teng et al. (2007)	39	29	FAB	M	M		M	x	M	
Biele & Grabowska (2006)	14	24	MSFDE	x	x			x		
Calder et al. (2006)	124	103	E&F 1976 - Accuracy	x	na	na	na	na	na	na
	73	62	E&F - Morphing	x	na	na	M	na	na	na
Hampson et al. (2006)	31	31	E&F 1976 - Accuracy	x	x	x	x	x	x	
			E&F 1976 - RT	M	M	M	M	x	M	
Montagne et al. (2005)	28	40	R&P - Accuracy	M	x	x	x	x	M	M
			R&P - Sensitivity	M	M	M	x		x	x
Wong et al. (2005)	19	21	E&F 1976 - Accuracy & RT	x	na	na	na	na	na	na
Scholten et al. (2005)	21	21	R&P - Accuracy	M	na	na	na	x	na	x
Grimshaw et at (2004)	36	37	E&F 1976 – Accuracy	x	x			x	x	
Palermo & Coltheart (2004)	12	12	E&F 1976 – Accuracy & RT	x	x	x	x	x	x	X
Rahman et al. (2004)	120	120	E&F 1976 – Accuracy					x	x	
			E&F 1976 – RT					M	M	
Hall & Matsumoto (2004)	69	27	JACBART		M	M	M	M	M	x

Note: x = no significant difference. M = Men significantly worse. Blank cells indicate that this emotion was not tested. na = not analysed. E&F = Ekman & Friesen. FAB = Florida Affect Battery. R&P = Rowland & Perrett 1995. MSFDE - Montreal Set of Facial Expression of Emotion. JACFEE = Japanese and Caucasian facial expressions of emotion. JACNeuf = Japanese and Caucasian facial expressions of emotion and neutral faces. JACBART = Japanese and Caucasian brief affect recognition test. R&P = Rowland & Perrett. RT = Reaction times

In fact, differences between men and women for particular emotions *have* been reported, but the findings are inconsistent and sex differences are largely contained to negative emotions (see Table 2.7 for a summary of the recent literature). Negative emotions are those of fear, anger, disgust and sadness whilst happiness and surprise are considered to be positive emotions. Scholten et al. (2005) compared male and female scores on negative emotions and then on positive emotions and they found sex differences on the negative emotions only. Montagne et al. (2005) reported that men were significantly less accurate than women for the negative emotion of sadness (but also for surprise). Similarly, Hall et al., 2010 found that although women scored higher than men for each emotion, the difference was only significant for the sadness emotion. Conversely, Vassallo, Cooper & Douglas (2009) did not find a sex difference for either negative or positive emotions, possibly because they only used 3 images for each emotion and this may not be sufficient to allow a sex difference to emerge. Hampson, van Anders & Mullin (2006) also failed to identify any difference between the sexes for *accuracy* on any emotion, although as participants performed at, or near, ceiling for most emotions, sex differences in accuracy could not be analyzed meaningfully.

To remove the ceiling effect, Calder, Keane, Manly, Sprengelmeyer, Scott, Nimmo-Smith & Young (2003) made the task more difficult by using images morphed with neutral faces so that only 75% of the target emotion was included. They failed to find any significant sex differences when 100% faces were used but although there were no sex differences for happiness, disgust, anger, sadness and surprise, significantly poorer recognition of fear by male participants did emerge.

Rahman, Wilson & Abrahams (2004) also failed to find a significant sex difference in accuracy for sadness or for happiness (the only emotions they examined) but they found that women were faster at recognizing these facial emotion expressions than men, albeit the effect size was low (eta squared = 0.029). Hall et al. (2010) reported that women were significantly faster for emotion recognition overall (although examination of individual emotions revealed that only sadness was significant) whereas Hampson, et al. (2006) identified shorter reaction times for women relative to men in recognising disgust, fear, sadness and anger and the advantage remained, even after controlling for perceptual speed. Furthermore, they reported that the female superiority was significantly larger for negative emotions than for positive ones.

In summary, sex differences have been found in FER, but not with any consistency. All those papers that did identify a significant difference in facial emotion recognition reported a female advantage for either accuracy, sensitivity and/or reaction times. A significant male advantage has not been reported anywhere. The same is true when individual emotions are examined. Most papers either did not analyse separate emotions (particularly once they identified that there were no significant sex differences overall) or failed to find an effect for sex for each emotion. The emotions where sex differences have most commonly been reported (again, always with a female advantage) are sadness, anger and fear - all negative emotions. Vassallo et al. (2009) did find that positive emotions (happy, surprised) were more accurately identified than negative ones (sad, angry, fearful and disgusted). It may be that for positive emotions of happiness and surprise sex differences do not emerge because participants score so highly.

2.4.2. FER IN THE ELDERLY

Published research shows that as people age, they have worse accuracy in tasks of facial emotion recognition than younger participants (Mill, Allik, Realo & Valk., 2009; Ruffman, Ng, & Jenkin, 2009; Sullivan et al., 2007) (See Table 2.8). A review by Isaacowitz, Lockenhoff, Lane, Wright, Sechrest, Riedel & Costa in 2007 showed that the aging effect varied by emotion and summarised that most studies identified older adults as worse at recognizing the specific emotions of anger, sadness and fear. Wong et al. (2005) reported this finding as did Suzuki & Akiyama (2012), along with a deficit for happiness and surprise. Although Sullivan & Ruffman (2004) did find the elderly to be significantly worse at recognizing sadness and anger, this was not the case for fear (or happiness) whereas Calder et al. (2003) found that older adults (58-70 years) showed significantly worse recognition of fear and sadness than young adults (18-30 years) but not anger (nor happiness or surprise). Furthermore, in a follow up experiment, accuracy in identifying fear decreased significantly with increasing age beginning at around 40 years old and there was some evidence of worsening performance with age for anger (Calder et al., 2003). Circelli, Clark and Cronin-Golomb (2013), however, found an aging deficit for fear only.

In a longitudinal study, Mill et al. (2009) found that the probability of recognising sadness and anger was highest in the youngest group (18-20 years) and steadily decreased in older age groups. For all other emotions examined (contempt, happiness, fear, disgust and surprise) recognition ability was stable at all ages until 60 years of age after which there was a considerable drop.

TABLE 2.8 SUMMARY OF REVIEW OF PREVIOUS LITERATURE ON DIFFERENCES BETWEEN ELDERLY CONTROL AND YOUNG ADULTS FOR FACIAL EMOTION RECOGNITION OF ANGER, DISGUST, FEAR, HAPPINESS, SADNESS AND SURPRISE

Author(s)	N		Test Used	Anger	Disgust	Fear	Happiness	Sadness	Surprise	EC group criteria
	EC	YA								
Circelli (2013)	16	16	E&F (1976)	x	YA	EC	x	x	x	62-79 years
Suzuki (2012)	36	36	JACFEE and E&F (1976)	EC	YA	EC	EC	EC	EC	65 – 78 years
Mill et al. (2009)	150	448	JACFEE	EC	EC	EC	EC	EC	EC	40 years+
Ruffman et al. (2009)	30	30	MacBrain facial stimulus set	EC	EC			EC	EC	62 years +
Williams et al. (2009)	#1000		Webneuro	EC	EC	EC	EC	EC		6-91 years
Henry et al. (2008)	30	30	E&F (1976)	x	na	x	na	na	na	mean = 76.9 years
Ruffman et al. (2008)	159	448	Meta Analysis	EC	x	EC	EC	EC	EC	
Sullivan et al. (2007)	30	30	E&F (1976) morphed	EC	x	EC	x	x	x	60 years+
Suzuki et al. (2007)	34	34	JACFEE	x	YA	x	x	EC	x	62 years +
Keightley et al. (2006)	30	30	JACFEE			EC		EC		mean = 72.5 years
Wong et al. (2005)	20	20	E&F (1976) Accuracy	EC	YA	EC	x	EC	x	mean = 69.5 years
Sullivan and Ruffman (2004)	30	31	E&F (1976) morphed	EC	-	EC	x	EC	x-	60 years +
Calder et al. (2003)	12	12	1. E&F (1976)	x	YA	EC	x	EC	x	58 years+
	## 227		2a. E&F (1976)	EC	x	EC	x	x	x	Range 17-70 years
	## 227		2b. E&F (1976) morphed	x	YA	EC	x	x	x	Range 18-75 years
Phillips et al. (2002)	30	30	E&F (1976) Accuracy	EC	x	x	x	EC	x	60 years +

Note: x = no significant difference.. EC = Elderly controls worse. YA = young adults worse. Blank cells indicate that this emotion was not tested. na = not analysed. E&F = Ekman & Friesen. FAB = Florida Affect Battery. JACFEE = Japanese and Caucasian Facial Expressions of Emotion. # No EC/YA split provided – data stratified into decades. # #No EC/YA split provided – data stratified 5 age bands.

Some researchers have identified an *improvement* with aging for the disgust emotion (Calder et al., 2003; Circelli et al., 2013; Suzuki & Akiyama, 2012; Wong et al., 2005) and a positive correlation between age and accuracy for recognition of disgust in older adults (Circelli et al., 2013). This improvement was not explained by older participants using the 'disgust' label as a default response when they were unsure (Calder et al., 2003). Although Suzuki & Akiyiama (2012) explained their findings as being due to young adults being hypersensitive to anger and therefore more likely to falsely identify disgust as anger. Wong and colleagues claimed that the effect was due to differences in eye gaze. Older participants fixated more on the bottom half of the face and recognition of disgust relies more on this area than on the eyes, where young adults looked most frequently (Circelli et al., 2013; Wong et al., 2005).

The published literature on the effect of aging on FER largely supports the claim that this ability declines with age. This has been shown for all emotions other than disgust which has been reported to be better in the elderly than the young, however, the findings are inconsistent.

SEX DIFFERENCES IN FER IN THE ELDERLY

Even though there have been a number of papers examining the effects of aging on FER there has been little attention paid to whether or not there are sex differences in emotion recognition in the elderly population. Most papers on aging did not even report the data split by sex. Two papers did examine sex differences in aging. Mill et al.(2009) reported that, generally, women performed better than men and sex was a significant predictor of

FER for anger, happiness and contempt. Furthermore, Scott, Nimmo-Smith & Young (2003) reported poorer recognition of fear by male participants for all ages including the elderly (range 17-75 years).

Given that sex differences have emerged in studies examining the young, and that FER shows an aging decline it is interesting to explore whether such sex differences are maintained in the elderly. However, as only two papers have examined this, there is a clear need for more research in this area.

2.4.3. FER in Alzheimer's disease

It has been suggested that difficulties in recognising the emotions of others may underlie the interpersonal problems found in AD (Shimokawa, Yatomi, Anamiru, Torii, Isono, Sugai et al., 2001). Identification of an FER deficit in AD would provide support for this claim.

A review by McLellan et al. (2008) examined the literature on FER with Alzheimer's patients. They concluded that AD patients show poorer recognition of facial expressions. However, they only reviewed in detail six studies, and two of these did not find any significant difference in overall performance. They also reported that sadness was particularly affected even though only three papers that were reviewed examined each emotion separately, and even though only one of those three reported such a difference.

The literature shows that, generally, AD patients are worse than ECs in FER (e.g. Bediou, Ryff, Mercier, Milliery, Hanaff, D'Amato et al., 2009; Cadieux and Grieve, 1997; Henry, Ruffman, McDonald, O'Leary, Phillips, Brodaty & Rendell, 2008; Phillips et al. 2010; Weiss, Kohler, Vonbank, Stadelmann, Kemmler, Hinterhuber et al., 2008). The research has indicated widely different patterns of deficits when examining each emotion separately (see

Table 2.9). The most frequently reported deficits in recognition compared to elderly controls are fear (Burnham & Hogervorst, 2004; Henry et al. 2008; Lavenu, Pasquier, Lebert, Petit & Van der Linden, 1999; Phillips et al. 2010, Weiss et al. 2008) and sadness (Burnham & Hogervorst 2004; Hargrave, Maddock & Stone, 2002; Phillips et al. 2010; Weiss et al. 2008,). Fear and sadness (along with anger) are those emotions that are most frequently reported as showing an aging decline, so it may be that the deficit in the elderly is exaggerated in people with AD. Some support for this comes from the findings for the emotion of disgust: some researchers have found that the elderly are better than the young in disgust and Henry et al., 2008 reported that recognition of disgust is preserved in AD patients.

Sex differences in FER in AD

Cadieux and Grieve (1997) concluded that impaired performance on FER tasks were the result of a visuoperceptual deficit. They separated participants into low-verbal AD group and low-spatial AD group and found that if there was a difference between these two groups, it was always the low-verbal group that was relatively impaired.

If there was a visuoperceptual deficit in AD that impacts FER, then we would expect to find that women were less accurate at FER than men, given that men have been found to have superior visuospatial skills. However, NONE of the papers found that examine the performance of AD patients on facial emotion recognition have reported whether there are any differences between men and women in their abilities.

TABLE 2.9 SUMMARY OF REVIEW OF PREVIOUS LITERATURE ON DIFFERENCES BETWEEN ALZHEIMER'S PATIENTS AND ELDERLY CONTROLS FOR FACIAL EMOTION RECOGNITION OF ANGER, DISGUST, FEAR, HAPPINESS, SADNESS AND SURPRISE

Author(s)	N AD	N EC	Test Used	Anger	Disgust	Fear	Happiness	Sadness	Surprise
Phillips et al. (2010)	30	30	FEEST (morphing) 100% intensity	AD	x	AD	x	AD	AD
			FEEST (morphing) 75% intensity	AD	AD	AD	AD	AD	AD
Henry et al. (2008)	24	30	E&F (1976)	AD	X	AD	AD	x	x
Weiss et al. (2008)[(1)]	53	35	Penn Emotion Recognition Test (ER40)	x		AD	AD[(3)]	AD	
Bediou et al. (2009)	10	10	Morphing with neutral face – test not named	AD	x	x	x		
Bucks & Radford (2004)	12	12	FAB – Facial affect naming/selection/matching	X		x	x	x	
Burnham & Hogervorst	13	13	E&F (1976) matching	x	x	AD	AD	AD	x
			E&F (1976) labeling	x	x	x	x	x	x
Hargrave et al. (2002)	22	14	JACFEE matching	AD	AD	AD	AD	AD	AD
			JACFEE labeling	X	AD	x	x	AD	AD
Lavenu et al. (1999)[(2)]	20	12	E&F (1986)	x	x	AD	x	x	X

Note: x = no significant difference. AD = Alzheimer's patients worse. Blank cells indicate that this emotion was not tested. E&F = Ekman & Friesen. FEEST = Facial Emotion Expression – Stimuli & Test. FAB = Florida Affect Battery. JACFEE = Japanese and Caucasian Facial Expressions of Emotion. [(1)] AD impaired for neutral faces. [(2)] AD impaired for contempt. [(3)] Moderate AD only: mild AD group not impaired

The previous literature on FER in people with AD supports the claim of a deficit in this ability compared to the healthy elderly. However, the findings with regards to specific emotions vary from study to study. It would be useful to be able to clearly identify which emotions people with AD are impaired at recognising. There is no published literature that reports on sex differences in this domain so there is a clear need for research to be conducted to examine this.

2.5. CONCLUSION TO THE CHAPTER

The literature shows that sex differences in cognition exist, but the evidence is conflicting and it is not as simple as suggested by the frequently cited male advantage for visuospatial skills and female advantage for language abilities.

There is a large male advantage on mental rotation, a moderate one for spatial perceptions tasks and some spatial visualisation tasks but no sex differences on some tasks, such as paper folding and figure copying. For verbal tasks, there is some evidence of a male advantage for confrontation naming, but this has only been examined in two published papers, some reports of a female advantage for lexical fluency but no sex differences in category fluency other than for the specific categories of tools (males better) and fruits (Females better). Furthermore, this profile of sex differences is mirrored in the elderly, although for confrontation naming a large number of papers reported no sex differences.

All reports of a sex difference in FER report a female advantage, most frequently for negative emotions. In the elderly only 2 papers examined sex differences and both found a female advantage for some emotions, but no sex differences in others.

Published research examining sex differences in cognition in AD patients is scarce. In an extensive literature search, only 16 papers could be found reporting data on visuospatial and/or verbal abilities separately for male and female AD patients. The visuospatial abilities of men and women have been shown not to differ, but the tasks used are those where sex differences are usually not found in the healthy elderly (i.e. spatial visualisations ones). For verbal tasks, the only task showing a sex differences is confrontation naming where males perform better than women. With regards to the recognition of emotions from facial expressions, the literature on sex differences in AD is non-existent.

What is apparent from this qualitative review of the literature is that papers reporting on the existence of sex differences in cognitive abilities in AD are scarce and the results are conflicting. Furthermore, the sample sizes in the AD studies are mostly small and non-significant findings may reflect a lack of power in these studies. It was decided to conduct a meta-analysis of the published literature to address these issues. A meta-analysis statistically integrates effect sizes across studies to provide a more rigorous and objective analysis than can be provided by a qualitative review. Pooling the results of several studies with relatively small samples overcomes the problem of insufficient statistical power.

3. Greater cognitive deterioration in women than men with Alzheimer's disease: a meta analysis

3.1. INTRODUCTION

Alzheimer's Disease International (ADI) estimates that currently 30 million people across the planet have dementia, with 4.6 million new cases annually – indeed, the estimate is one new case every 7 seconds (Ferri, Prince, Brayne, Brodaty, Fratigloni, Ganguli et al., 2005). Alzheimer's disease (AD) manifests in well-documented deficits in cognitive abilities such as semantic and episodic memory, language and spatial orientation as well as interpersonal difficulties. Intriguingly, both the prevalence and the incidence of AD are greater amongst women than men and the discrepancy increases with advanced age (Andersen, Dewey, Letenneur, Ott, Copeland, 1999; Lobo, Launer, Fratigloni, Andersen, DiCarlo & Breteler, 2000). As well as being more likely to be diagnosed with AD, women have been reported as showing greater cognitive deficits than men even in verbal abilities where a female advantage is usually reported in the healthy population (e.g. Maylor, Reimers, Choi, Collaer, Peters & Silverman, 2007; Weiss, Kemmler, Deisenhammer, Fleischacker& Delazer, 2003).

In their post mortem analyses of 141 brains from the Religious Orders Study, Barnes, Wilson, Bienas, Schneider, Evans & Bennett (2005) found that the association between AD pathology and clinical AD was significantly stronger in women than in men. Indeed, each unit of AD pathology increased the odds of clinical AD by more than 20 times in women compared with a 3 times increase in men. The authors concluded that AD pathology is more likely to be clinically expressed as dementia in women than in men. Of course, the incidence of AD has been widely reported to be higher in women than in men (Andersen et al., 1999) - possibly because women have increased longevity (Hebert, Wilson, Gilley, Beckett, Scherr, Bennett et al., 2000).

Sex differences in cognitive abilities are, of course, frequently cited in the 'normal' literature, with women typically reported to have better verbal abilities than men (for recent critical discussion see Wallentin, 2009). In their large meta-analysis of sex differences, Hyde and Linn (1988) reported a small, but reliable female advantage (d=.11) for verbal ability across 165 studies. Hyde and Linn (1988) reported that in 44 studies (27%) females performed significantly better than males, 109 (66%) found no significant sex difference, and in only 12 (7%) males performed significantly better than females. By contrast, men are most frequently reported as having superior visuospatial skills (e.g. Weiss et al., 2003). Voyer, Voyer and Bryden (1995) meta-analysed 286 studies spanning 50 years and found that men significantly outperformed women on visuospatial tasks. Within Cohen's (1988) nomenclature, the effect size was large for mental rotation (d = 0.73), medium for spatial perception (d = 0.44), and small for spatial visualization (d = 0.13). Moreover, some research indicates that these sex differences persist into old age. For example, both de Frias, Nilsson & Herlitz (2006) and Maylor et al. (2006) found better visuospatial skills in healthy elderly men than elderly women and that for this age group, women were better than men on language tasks.

By contrast, studies suggest that sex-based cognitive differences may disappear or even reverse in AD. For example, Perneczky, Drzezga, Diehl-Schmid, Yi & Kurz (2007a) reported no significant sex differences in mildly demented AD patients on either verbal or visuospatial tests. One possible interpretation is that a proportionally greater deterioration of verbal and visuospatial ability occurs for women and men respectively. However, other researchers have reported that the male advantage in visuospatial skills is maintained in AD sufferers. Millet, Raoux, LeCarret, Bouisson, Dartigues & Amieva (2009) found men performed significantly better than women in tasks requiring active manipulation of visuospatial information. Beinhoff, Tumani, Brettschneider, Bittner & Riepe (2008) reported that in AD patients males were better than females at learning and retaining visuospatial information, although no sex differences in visuospatial memory span emerged. Turning to verbal abilities, Chapman, Mapstone, Gardner, Sandoval, McCrary, Guillily et al. (2011) found that AD men performed better than women on the Logical Memory test, which assesses verbal episodic memory, and was a reversal of the profile reported for their healthy elderly controls. Surprisingly, perhaps, men with AD have also been reported to perform better on naming tasks (Buckwalter, Rizzo, McCleary, Shankle, Dick & Handerson, 1996; Henderson & Buckwalter, 1994; McPherson, Back, Buckwalter & Cummings, 1999) and verbal fluency (Buckwalter et al., 1996). Findings relating to cognitive sex differences in AD patients seem somewhat inconsistent, but may be misleading. To quantify any sex differences in the cognitive abilities of AD patients we conducted a meta-analysis.

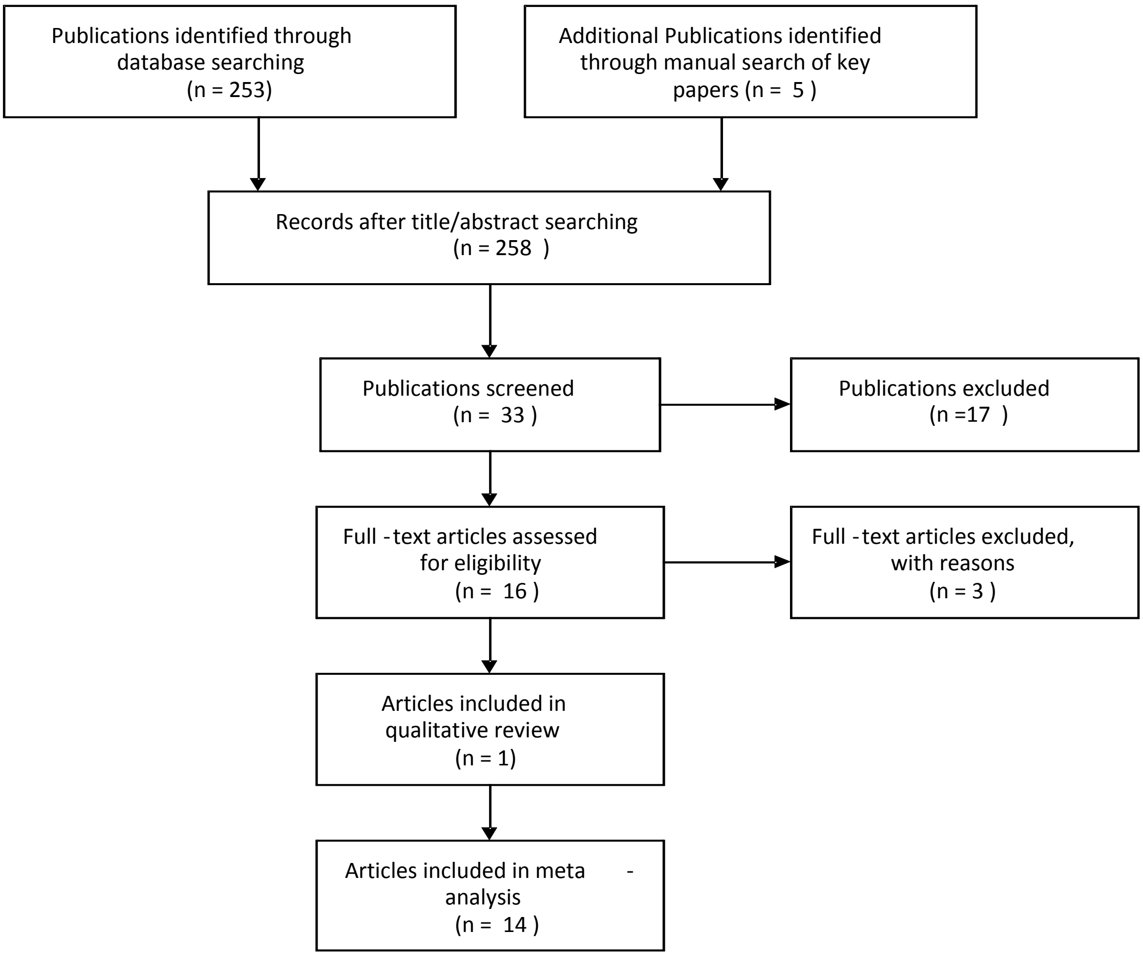
3.2. METHOD

A literature search was carried out using the search engines Scopus and Web of Science. The terms used were “Alzheimer*” combined with “sex differences” or “gender differences” and “Cognition” or “cognitive deficits”. No limits were applied on the dates of publications; however, the search engines go back to 1966 (Scopus) and 1950 (Web of Science).

The resulting 253 titles and abstracts were scrutinised and papers that were obviously not concerned with cognition and Alzheimer's disease in humans were excluded. Also excluded at this stage were papers that were not published in English. The abstracts of the papers not excluded thus far were then consulted to identify those that were likely to include data relevant to the meta-analysis. The papers that remained on the list were read to identify those which satisfied the inclusion criteria (see Figure 3.1 for search details).

The inclusion criteria were that research papers needed to include demographic data and results that allowed for calculation of Cohen's *d* (e.g. mean and standard deviations) of both male and female AD patients on at least one cognitive test. The reference lists for these papers were also then checked to identify any further papers. Finally, we consulted search engines to identify any publications that had cited the papers selected thus far. These additional publications were checked to identify whether they should be included. In total, we located 14 suitable articles for inclusion in the meta analysis, with one article contributing two studies (see Figure 3.1 for details of the literature search).

Data obtained from each study were converted into the effect size 'Cohen's *d*', i.e. the difference between the two groups (females – males) divided by their pooled standard deviation. When means and standard deviations were not provided, *d*-values were computed from *F*-values and *r* values. Hedges' *d* correction (Hedges and Olkin, 1985) was used to correct for upwardly biased estimation of the effect in studies with small sample sizes, which leads to overestimations of the population effect size (Rosenthal, 1991).



Excluded articles:

Publication	Reason for exclusion
Cushman, L.A. & Duffy, C.J.The Sex specificity of navigational strategies in Alzheimer Disease. *Alzheimer's Disease and Associated Disorders*. 21 (2) 122-129, 2007.	Mean and SD scores by sex not provided.
Laws, K.L. , Duncan, A., Gale, T. M. 'Normal' semantic-phonemic fluency discrepancy in Alzheimer's disease? A meta-analytic study. *Cortex* 46 (5) 595-601, 2010.	Meta Analysis
Widmann, C.N., Beinhoff, U., & Riepe, W. (2012). Everyday memory deficits in very mild Alzheimer's Disease. *Neurobiology of Aging* 2010.03.012	Mean and SD scores by sex not provided.

FIGURE 3.1 Literature search

Homogeneity was calculated using the Q_{wi} statistic (Hedges and Olkin, 1985), which tests whether the studies can be taken to share a common population effect size. A significant Q_{wi} statistic indicates heterogeneity of the individual study effect sizes i.e. whether the variability of the effect size is larger than would be expected from sampling error (Lipsey and Wilson, 2001). To test for the significance of the mean effect size confidence intervals were calculated using MetaWin 2.1 (Rosenberg, Adams, and Gurevitch, 2000). Effect sizes are considered significantly different from zero when the confidence interval does not include zero. A random effects model was employed to analyse the effect sizes derived (DerSimonian and Laird, 1986). The nomenclature of Cohen (1988) suggests the following classification of effect sizes (small d =0.20 to 0.49; medium d = 0.50 to 0.79; and large d >0.80).

Test scores that were included in the meta-analysis were those that measured cognitive abilities (see Table 3.1 for a list of the tests analysed). We excluded test scores that measured global cognitive function such as the Mini Mental State Examination (MMSE: Folstein, Folstein, & McHugh, 1975) and scores that were a composite of other tests included in the same paper. The tests were divided into different domains, semantic, non-semantic, verbal, visuospatial and memory (see Table 3.1 for allocation of tests to domains). A mean effect size was calculated according to these domains for each paper, and then across all papers for each domain. In longitudinal studies (Hebert et al., 2000; Ripich, Petrill, Whitehouse & Ziol, 1995), we used the baseline cognitive scores. All effect sizes were independently extracted, compared and verified by two of the authors.

The total sample of AD patients across 15 studies consisted of 828 males and 1238 females. Most of the papers diagnosed patients as having AD according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann, Drachman, Folstein, Katzman, Price & Stadlan, 1984). The two exceptions were Heun and Kockler (2002), who used the DSM-III-R criteria and Henderson and Buckwalter (1994) who did not specify the criteria used for diagnosis.

TABLE 3.1 ALLOCATION OF TASKS TO COGNITIVE DOMAINS

Semantic	Non-Semantic	Verbal	Visuospatial	Memory
Boston Naming Test	Wechsler Block Design	Boston Naming Test	Wechsler Block Design	CERAD Immediate Recall
Narrative Writing	CERAD Drawing	Narrative Writing	CERAD Drawing	CERAD Delayed Recall
Verbal fluency	Praxis	Verbal fluency	SIDAM visuoconstuction	SIDAM immediate recall
WAIS-R Vocab	Memory – immediate/delayed	WAIS-R Vocab	WMS-R visuospatial reproduction	SIDAM STM
WAIS-R Info	SIDAM visuoconstuction	Category Naming	Wechsler spatial span	SIDAM LTM
Category Naming	Wechsler LM	Wechsler Logical Memory	CERAD constructional praxis	Wechsler LM2
Peabody picture vocab	Wechsler verbal span	Peabody picture vocab	Corsi block tapping task	CVLT
Body part identification	Wechsler spatial span	Wechsler verbal span	Vecchis matrix memory task	Wechsler verbal span
Responsive naming	CVLT	CVLT	Vecchis mental pathway task	Wechsler spatial span
	WMS-R visuospatial	CERAD word list learning		Visual memory span – non
	CERAD word list learning	Commands		Verbal span
	CERAD constructional praxis	Word repetition		Verbal EM recall
	Corsi block tapping task	Phase repetition		Verbal STM digit span
	Vecchis matrix memory task	Body part identification		Corsi block tapping task
	Vecchis mental pathway task	Responsive naming		Vecchi's matrix memory task
	Commands			
	Word repetition			
	Phase repetition			

Note: WAIS-R = Wechsler Adult Intelligence Scale, Revised. CERAD = Consortium to Establish a Registry for Alzheimer's Disease. SIDAM = A Structured Interview for the diagnosis of Dementia of the Alzheimer type, Multi-infarct dementia and dementias of other aetiology according to ICD-10 and DSM-III-R. CVLT = California Verbal Learning Test. WMS-R = Wechsler Memory Scale, Revised. STM = short term memory. LTM = long term memory. EM = episodic memory. LM = Logical memory.

3.3. RESULTS

The mean effect sizes for each domain on each paper for the AD participants is shown in Table 3.2 from which it can be seen that a significant male advantage emerged for every effect size in every domain with the exception of three: verbal abilities (Millet et al., 2009) , non-semantic abilities (Hebert et al., 2000) and visuospatial abilities (Perneczky, 2007a).

TABLE 3.2 MEAN EFFECT SIZES FOR EACH DOMAIN IN EACH STUDY

	Number of participants			Semantic	Non-semantic	Verbal	Visual-Spatial	Memory
	M	F	Total	*d*	*d*	*d*	*d*	*d*
Bayles et al (1999)	30	33	63	-0.10		-0.10		
Beinhoff et al (2008)	26	23	49	-0.07	-0.44	-0.22	-0.60	-0.37
Buckwalter et al (1996)	72	87	159	-0.46	-0.24	-0.46	-0.24	
Hebert et al (2000)	119	245	364	-0.23	0.04	-0.09		
Hendersen &Buckwalter	22	24	46	-0.37	-0.37	-0.37	-0.18	
Hendersen &Buckwalter	270	377	647	-0.30	-0.12	-0.30	-0.11	-0.12
Hendersen et al (1996)	26	27	53	-0.26	-0.22	-0.09	-0.44	-0.15
Heun & Kockler (2002)	17	76	93		-0.18		-0.62	-0.04
Laiacona et al (1998)	11	15	26	-0.29		-0.29		
Marra et al (2007)	85	168	253	-0.23		-0.23		
McPherson et al (1999)	23	36	59	-0.24	-0.54	-0.35		-0.71
Millet et al (2009)	20	20	40		-0.40	0.08	-0.63	-0.40
Moreno-Martinez et al	28	33	61	-0.42		-0.42		
Perneczky et al (2007a)	50	43	93	-0.24	-0.12	-0.20	0.02	-0.17
Ripich et al (1995)	29	31	60	-0.74		-0.74		
Total	828	1,238	2,066					

Note: M = Male, F = Female. *d* = effect size (Hedge's *d*). Negative effect size indicates male advantage.

The meta-analysis revealed a small, but significant, effect size across all domains, with a consistent and significant deficit for women across all five domains. The effect sizes for semantic (*d*=-0.25), verbal (*d*= -0.27) and visuospatial (*d*=-0.24) domains are small and for non-semantic (*d*=-0.14) and memory (*d*=-0.17) are very small. The studies were not heterogeneous for any domain (see Table 3.3).

The male and female means for age, MMSE and level of education were extracted from each study and used to calculate overall means to check for sex differences in these potential moderating variables. Independent samples t-tests showed no significant differences between men and women for age (t[26] = -1.98, p=0.06: women 74.18± 2.52; men 71.86± 3.58),MMSE (t[20] = 0.49, *p*=0.63: women Mean MMSE 18.82± 3.90 and men 19.65± 4.02) or Level of Education (t[22] = 0.84, *p*=0.41: women mean 10.74 years± 2.98 and men 11.76± 2.96). Nevertheless, moderator regression analyses showed that age, level of education and MMSE did not significantly predict the male cognitive advantage in any cognitive domain.

TABLE 3.3 MEAN EFFECT SIZES AND 95% CONFIDENCE INTERVALS FOR EACH DOMAIN

Domain	*d*	95% CI	Test of Heterogeneiity
Semantic	-0.25	-0.42 to -0.07	Qwi = 8.71, df=12 p = 0.73
Non Semantic	-0.14	-0.26 to -0.02	Qwi = 7.17, df=9 p = 0.62
Verbal	-0.27	-0.37 to -0.16	Qwi = 9.51, df=13 p = 0.73
Visual-spatial	-0.24	-0.43 to -0.05	Qwi = 6.89, df=7 p = 0.44
Memory	-0.17	-0.33 to -0.01-	Qwi = 4.89, df=6 p = 0.56

Note: A negative effect size denotes a male advantage and a positive effect size a female advantage. d = effect size (Hedge's *d*).

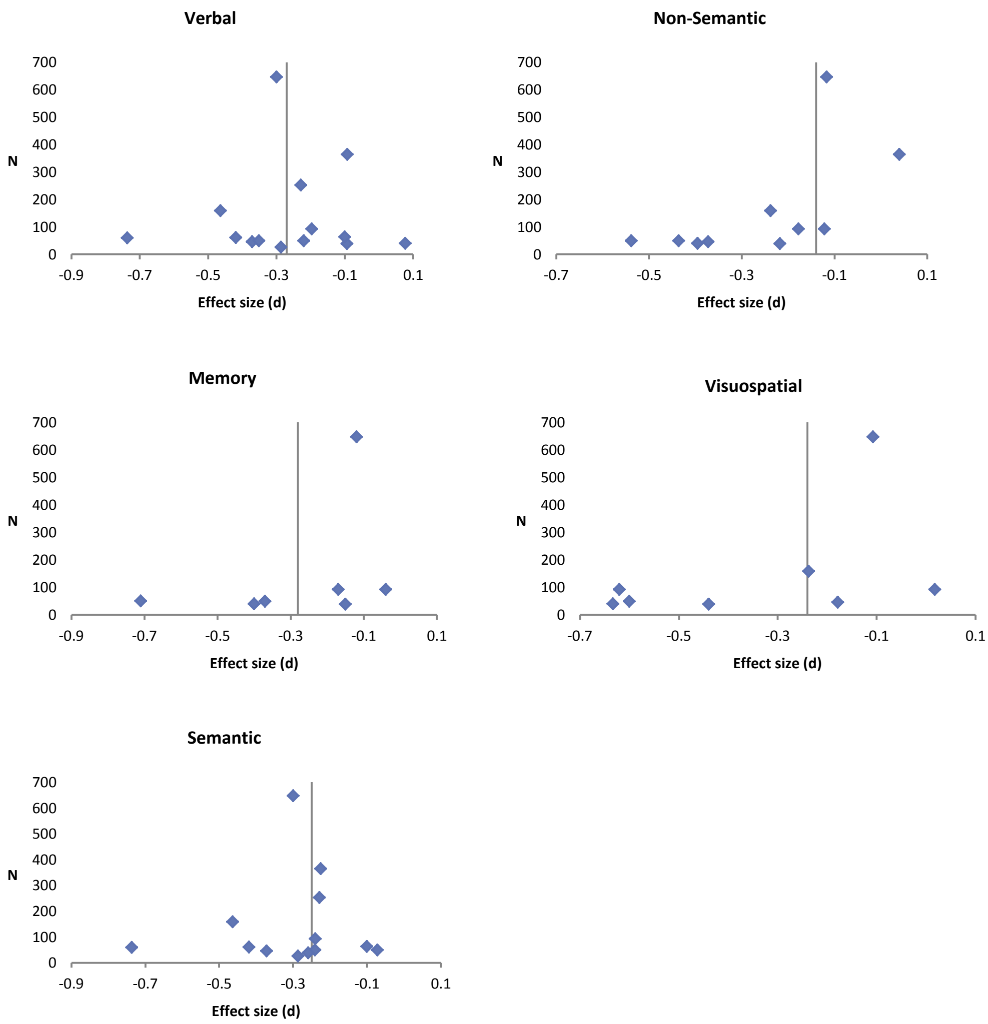


FIGURE 3.2 FUNNEL PLOTS FOR EACH DOMAIN FOR AD PARTICIPANTS. VERTICAL LINE REPRESENTS MEAN EFFECT SIZE. A NEGATIVE EFFECT SIZE DENOTES A MALE ADVANTAGE AND A POSITIVE EFFECT SIZE A FEMALE ADVANTAGE. D = EFFECT SIZE (HEDGE'S D).

3.3.1. PUBLICATION BIAS

One potential problem with any meta-analysis, and especially perhaps in the area of sex differences, is publication bias. Papers reporting significant sex differences are, of course, more likely to be published than non-significant results and may bias in favour of the presence of an effect[1]. We calculated the fail-safe statistic (Rosenthal, 1979), which showed that for the semantic domain, 28 unpublished non-significant studies are required to produce a non-significant mean effect size. For the non-semantic domain the number was 35, for visuospatial it was 26 and for verbal there would need to be 114 unpublished non-significant studies before the mean effect size would become non-significant. We also used funnel plots for sample sizes against effect size to check for bias. Figure 3.2 shows plots for each domain examined and generally a male advantage emerges and, as expected, large studies cluster around the mean effect size.

3.4. DISCUSSION

The main finding from this meta-analysis of AD patients is that men modestly but significantly outperform women in all of the cognitive domains that we examined. Most papers report better male performance within every domain (only three reported female superiority in any single domain and the effect sizes were very small [less than 0.08]). Differences in dementia severity (as measured by MMSE) and age did not explain the male advantage. Overall, these findings indicate that cognitive functions are both more severely and more widely affected in women than men with AD.

Memory problems are, of course, a defining characteristic of Alzheimer's disease and our analysis for AD patients revealed a small, but significant male advantage on memory tasks. Some work shows that healthy elderly women have better immediate word learning (van Hooren, Valentin, Bosma, Ponds, Boxtel & Jolles, 2001), verbal memory and episodic

[1] As a rough estimate, we entered 'sex difference" AND 'language" AND 'significant' into Scopus for title, abstract and keywords for past 10 years – this produced approximately 1000 hits; entering 'nonsignificant' instead 'significant' produced 10 hits

memory than comparable men (Gerstorf, Herlitz & Smith, 2006). Others have, however, reported no sex differences in the elderly for verbal memory (Parsons, Rizzo, van der Zaag, McGee & Buckwalter, 2005) or for delayed word learning (van Hooren et al., 2001). Nonetheless, some also report better visual memory (Proust-Lima, Amieva, Letenneur, Orgogoze, Jacqmin-Gadda & Dartigues, 2008), working memory (Read, Pedersen, Gatz, Berg, Vuoksimaa, Malmbert et al., 2006) and episodic memory (Read et al., 2006) in elderly men than women. So, no clear pattern of sex advantage emerges for memory in the healthy elderly and any sex differences appear to be task dependent. Despite this, we found a consistent memory advantage for men with AD on memory tasks *per se*. Unfortunately, too few studies have currently analysed memory in more fine-grained detail i.e. visual versus verbal, short-term memory vs. long-term memory, and so on.

Turning to visuospatial abilities in AD, men clearly outperform women, thus mirroring the male advantage documented in the general population (e.g. Lewin, Wolgers & Herlitz, 2001; Weiss et al., 2003) and the healthy elderly (e.g. de Frias et al., 2006; Maylor et al., 2006). For verbal abilities in AD, men also outperform women, and in this domain, the male advantage runs contrary to the generally reported normative profile.

Why might women with AD lose their verbal advantage? Cognition does of course decline *normally* with age across many domains, including verbal recall (van Hooren et al., 2007), episodic memory and spatial reasoning (Read et al., 2006) and some evidence suggests a faster decline in women. For example, Parsons et al. (2005) reported that elderly male subjects retained visuospatial superiority, but that the female advantage on language tasks was lost. Nevertheless, de Frias et al. (2006) conducted a 10 year longitudinal study of over 600 non-demented adults, aged 35–80, and found stable sex differences across 5 age groups - women outperformed men on verbal memory, verbal recognition and semantic fluency tasks, while men demonstrated better visuospatial ability. Others, however, (Coffey, Lucke, Saxton, Ratcliffe, Unitas, Billig et al., 1998; Larrabee & Crook, 1993; Maylor et al., 2007; Zelinski & Stewart, 1998) report greater age-related cognitive decline in males than in females, or no differences in the rate at which cognitive abilities are lost (de Frias et al., 2006; Gerstorf et al., 2006; Mathuranath, George, Cherian, Alexander, Sarma & Sarma, 2003; van Hooren et al., 2007). In a large study spanning 13 years, Proust-Lima et al. (2008) reported that, at 65 years of age, cognitive decline was similar for the sexes, but amongst the oldest participants, women showed a slightly steeper decline than men. Similarly, Read et al. (2006) reported that greater age was related to lower performance on a range of cognitive tasks, with a greater relative deterioration for women of a higher age on perceptual speed and working memory tasks. It may therefore be the case that women suffer differentially greater deterioration than men, but only at advanced ages.

A broader examination of the literature reveals some reports of a female advantage in the healthy elderly for episodic memory (Beinhoff et al., 2008; Chapman et al., 2011; Gerstorf et al., 2006), verbal fluency (Gerstorf et al. 2006; Proust-Lima et al., 2008) and semantic fluency (de Frias et al., 2006; Proust-Lima et al., 2008), while others report no such differences in verbal fluency (Beinhoff et al., 2008; van Hooren et al., 2007; Mathuranath et al., 2003) or semantic memory (Beinhoff et al., 2008; Henderson & Buckwalter, 1994; Mathuranath et al., 2007). Of course, with a large sample, then a small effect may be more readily detected as significant; however the Beinhoff et al. (2008) and Chapman et al. (2011) studies both report female verbal advantages with *total* sample sizes below 50, with roughly equal sized groups of each sex. Studies reporting no sex differences do not appear to have included groups of very old participants. Whatever the case, the literature on verbal abilities in the elderly reveals either an advantage for women or no sex difference - crucially, not one paper reports a male advantage in this domain. This would strongly support the conclusion that female AD patients are more adversely affected, cognitively, than men.

Some researchers have suggested that, following the menopause, cognitive abilities in healthy elderly women are adversely affected by loss of estrogen (Maki, Zonderman & Resnick, 2001; Phillips & Sherwin, 1992; Robinson, Friedman, Marcus, Tinklenberg & Yesavage, 1994; Sherwin, 1988) albeit only on verbal tasks. Moreover, a role for estrogen in both the pathobiology and prevention of AD has been reported (Wharton, Gleason, Lorenze, Markgraf, Ries, Carlsson et al., 2009). Consistent with these notions, Henderson (1996) found that female AD patients on estrogen hormonal therapy performed significantly better on a naming task and two verbal short-term memory tasks than women with AD who were not having hormone therapy; moreover, no significant differences emerged between hormonal therapy group and male AD patients on these tasks indicating that sex differences in verbal abilities may arise via an estrogen deficiency in women with AD. Supporting this idea further, Barnes,, Wilson, Schneider, Bienas, Evans & Bennett (2003) found that duration of estrogen use was related to the rate of global cognitive decline and visuospatial ability in non-demented elderly women but not to semantic or episodic memory. Nevertheless, the literature on cognitive decline in the non-demented elderly shows that men and women decline at a similar rate (deFrias et al., 2006; Gerstorf et al., 2006; van Hooren et al., 2007) no sex differences in verbal abilities emerge or elderly women are better than elderly men. If loss of estrogen underpinned the poorer cognitive performance of AD women than men, then we would expect to see the same deficits for verbal fluency and verbal episodic memory in the healthy elderly as are seen in women with AD and that has not been reported.

It may be that AD pathology affects cognition differently in women than in men (Cushman & Duffy, 2007). For example, females with AD may deteriorate more rapidly than men. Chapman et al. (2011) compared sexes on the Logical memory test, finding that the decline in performance from the healthy controls to the AD group was 1.6 times greater in women than men. By contrast, Ripich et al. (1995) reported that the rates of decline for language abilities in male and female AD patients were steady across time; however, they did not report the severity of dementia in their patients. Hebert et al. (2000) also found no sex difference in rate of decline either globally or for any specific domain, but once again, dementia severity was not reported. It may be that women deteriorate faster early on, and then at a similar rate thereafter. This idea would be consistent with the findings of Chapman et al. (2011), since their AD group was only mildly demented (inclusion criteria were for MMSE score >22).

A faster decline for females in the early stages of AD could be explained by the concept of *cognitive reserve*. Neuroimaging studies reporting sex differences in brain function for males and females at the same stage of the disease are consistent with a reserve hypothesis. Perneczky et al. (2007a,b) found that despite being at the same disease stage and showing no significant differences in general cognitive scores, men with AD had more pronounced and extensive pathology affecting the frontal, temporal and insular cortex, as well as the hippocampus in the right hemisphere. Moreover, women were more likely to clinically express reductions of regional cerebral metabolic rate as dementia. The authors suggest that this could be because the brain reserve capacity serves as a stronger counterweight to neurodegeneration in men than in women.

Another possible explanation for the sex differences in AD patients relates to the apolipoprotein E (APOE) ε4 allele, which is an established genetic risk factor for AD (Corder, Saunders, Strittmatter, Schmechel, Gaskell, Small et al., 1993). Several studies have indicated that the APOE genotype affects the aprobability of developing AD for women to a greater extent than for men (Bretsky, Buckwalter, Seeman, Miller, Poirer, Schellenberg et al., 1999; Gomez Isla, West, Rebeck, Harr, Growdon, Locascio et al., 1996; Payami, Zaresparsi, Montee, Sexton, Kaye, Bird et al., 1996). The effect exerted by APOE genotype on cognitive performance in the general population is more pronounced in women than men (Bartres-Faz, Junque, Moral, Lopez-Alomar, Sanchez-Aldegner & Clemente, 2002; Hyman, Gomez-Isla, Briggs, Chung, Nichols, Kohout et al., 1996) and may impact on hippocampal atrophy in female sufferers of Mild Cognitive Impairment (Fleisher, Grundman, Jack, Petersen, Taylor, Kim et al., 2005). A large post mortem study (n=729) reported that AD-related abnormalities such as neurofibrillary tangle and senile plaque is affected by a complex interaction between the aging process, sex, and genetic (ApoE 4) risk factors (Ghebremedhin, Schultz, Thal, Rub, Ohm, Braak et al., 2001). These findings are consistent with a relatively greater semantic and verbal impairment in female AD sufferers that differs from and is greater than any pre-existing sex differences in cognition (Heun & Kockler, 2002).

One surprising discovery of this study was the small number of relevant studies we could identify. Although many studies have examined cognitive function in AD, it is only recently that data have been reported separately for males and females, making the number of papers available to include in the analysis somewhat limited. Another limitation is the broad categorisation of tests into verbal and visuospatial tasks. Within the category of visuospatial tasks, sex differences have emerged for some categories of test e.g. those measuring mental rotation, but not others, e.g. those measuring spatial visualisation (Linn & Petersen, 1985, Voyer et al., 1995). So, ideally, a meta-analysis should examine these tasks separately. However, none of the papers included those tests that produce the largest, and most consistent, effect sizes (those involving mental rotation). Despite this, our analysis still showed a small effect for sex in this domain.

In conclusion, this meta-analysis shows that men with AD outperform women with AD across all five cognitive domains examined. Most strikingly, the female deficit for language is at odds with the profile reported for the general population. These findings are inconsistent with studies examining cognitive decline under normal aging, suggesting something specific about AD neuropathology that disadvantages females. Some limited evidence suggests that females deteriorate faster than males in the earlier stages of the disease. Possible explanations are for a hormonal influence, possibly due to estrogen loss in women (Henderson, 1996) or a greater cognitive reserve in males, which provides protection against the disease process (Perneczky et al., 2007 a,b). Future studies which examine sex differences on a longitudinal basis, may provide greater clarity on these issues.

4. Sex differences in visuospatial abilities in people with Alzheimer's disease

4.1. INTRODUCTION

Sex differences in visuospatial abilities have been widely reported in the general population. Meta-analyses by Linn & Peterson (1985) and Voyer, Voyer & Bryden (1995) both reported large effect sizes, favouring men. However, it is important to distinguish between different visuospatial categories as they tap into different abilities (Caplan, McPherson & Tobin, 1985) and the magnitude of sex differences varies greatly according to the type of task being examined.

Mental rotation (the ability to mentally rotate a two or three dimensional figure rapidly and accurately) produces the largest, and most consistent, effect sizes (Linn and Petersen, 1985; Voyer et al., 1995). Spatial perception tasks (participants are required to determine spatial relationships with respect to the orientation of their own bodies) also produce reasonable effect sizes (Linn & Peterson, 1985). But, in spatial visualisation tasks (those tasks that involve complicated multi-step manipulations of spatially presented information) differences in performance between men and women often fail to emerge, with effect sizes close to zero (Linn & Peterson, 1985).

The existence of sex difference within each category varies according to specific tasks. For example, mental rotation tasks that have 3D stimuli produce larger effects than those with 2D stimuli, albeit the differences consistently favour men (e.g. Campos, Perez-Fabello & Gomez-Juncal, 2004; Halari, Hines, Kumari, Mehrotra, Wheeler, Ng et al., 2005; Hirnstein, Bayer & Hausmann, 2009

, Janowsky, Chavez, Zamboni & Orwoll, 1998; Jansen & Heil, 2009; Nowak & Moffat, 2011; Peters, Manning & Reimers, 2007). Researchers have identified a male advantage on the judgement of line orientation (JLO) task (Caparelli-Daquer, Olivera-Souza & Moreira Filho, 2009; Collaer, & Nelson, 2002; Goyette, McCoy, Kennedy & Sullivan, 2012; Halari et al., 2005; Maylor, Reimers, Choi, Collaer, Peters & Silverman, 2007; Rahman & Wilson 2003) and the water level (WL) test (Lewin, Wolgers & Herlitz, 2001). In a meta-analysis significant sex differences favouring men emerged on two spatial visualisation tasks: the paper form board and identical blocks test (Voyer, Voyer & Bryden, 1995). (See Appendix 2 for a description of tasks cited.)

Many researchers, however, claim that spatial visualisation tasks do not demonstrate sex differences (Meurling, Tanning-Olsen & Levander, 2000; Nowak & Moffat, 2011; Postma, Jager, Kessels, Koppeschaar & van Honk, 2004; Robert & Tanguay, 2006) even on those that the meta-analyis of Voyer et al., 1995 identified as demonstrating a male advantage: neither Parsons, Larson, Kratz, Theibaux, Bluestein, Buckwalter et al. (2004) nor Yonker, Eriksson, Nilsson & Herlitz (2003) found a significant sex difference on the block design (BD) test. However, deFrias, Nilsson & Herlitz (2006) did find that men were better than women on BD as did Janowsky et al. (1998) and Thilers, MacDonald & Herlitz (2006). Furthermore, men have been reported as scoring higher than women on the spatial span test (SSP), a computerised version of the Corsi block-tapping test (CBT), a paper folding task (Lewin et al., 2001) and the Rey-Osterrieth Complex Figure (ROCF) task (Gallagher & Burke, 2007) although Lewin et al. (2001) failed to identify a significant male advantage on this latter task.

Although performance on visuospatial tasks decreases with age (Campos et al., 2004; Finkel, Reynolds, McArdle, Gatz & Pedersen, 2003; Jansen & Heil, 2009; Peters et al., 2007), with the decline being first apparent in the 31-40 year age group (Peters et al., 2007), men and women decline at similar rates (Barnes, Wilson, Bienias, Schneider, Evans & Bennett, 2005; Proust-Lima, Amieva, Letenneur, Orgogoze, Jacqmin-Gadda & Dartigues, 2008). So, one would expect to see a male advantage in the elderly in line with that found in the young.

Healthy elderly men perform better than women in mental rotation (Campos et al., 2004; Finkel et al., 2003; Gerstorf, Ram, Hoppman, Willis & Schaie, 2011; Jansen & Heil, 2009; Parsons, Rizzo, van der Zaag, McGee & Buckwalter et al., 2005; Peters et al., 2007; Willis & Schaie, 1988) and in spatial perception (Duff, Schoenberg, Mold,Scott & Adams, 2011; Moore, Miller, Andersen, Arndt, Haynes & Moser, 2010; Parsons et al., 2005; Robert & Tanguay, 1990). In spatial visualisation, in line with what is found in the young, the findings are variable: a male advantage has been reported on the BD task (Portin, Saarijarvie, Joukamaa & Salokangas, 1995; Read, Petersen, Gatz, Berg, Vuoksimaa, Malmberg et al., 2006; Wahlin, Robins Wahlin, Small & Backman, 1998) and on the SSP and Pattern Recognition memory (PRM) tasks (Simpson, Maylor, Rae, Meunier, Andriollo-Sanchez, Catasta et al., 2004) although equivalent male and female performance has also been reported (Beinhoff, Tumani, Brettschneider, Bittner & Riepe, 2008; Duff et al.,, 2011, Fahlander, Wahlin, Fastbom, Grut, Forsell, Hill et al., 2000; Heun & Kockler, 1994).

As expected, people with AD perform worse than the healthy elderly on mental rotation (Kurylo, Corkin, Rizzo & Growdon, 1996; Lineweaver, Salmon, Bondi & Corey-Bloom, 2005) the JLO task (Cushman & Duffy, 2007; Lineweaver et al., 2005), the CBT (Baudic, Barba, Thibaudet, Smagghe, Remy &Traykov, 2006) and figure copying (Freeman, Giovannetti, Lamar, Cloud, Kaplan & Libon, 2000; Morris, Heyman, Mohs, Hughes, van Belle, Fillenbaum et al., 1989). Binetti, Cappa, Magni, Padovani, Bianchetti & Trabucchi (1998) reported that people with mild AD scored lower than elderly controls on both a figure copying task (ROCF) and on spatial perception. Furthermore, the AD participants showed a worsening performance in a follow-up test 8 months later, although no such deterioration was evident in the verbal tests they conducted.

With regards to sex differences in AD, Cushman & Duffy (2007) found no difference on the JLO task. Equivalent performance for men and women with AD has also been reported on spatial visualisation (Buckwalter, Rizzo, McCleary, Shankle, Dick & Henderson, 1996; Henderson 1996; Henderson & Buckwalter, 1994; Perneczky, Drzezga, Diehl-Schmid, Yi & Kurz, 2007). Therefore, the published research would suggest that the visuospatial abilities of men and women with AD do not differ to the same extent as in the healthy population. Nevertheless, very few of the papers examining visuospatial abilities in AD patients have used tasks that most commonly reveal the usual sex differences (i.e. mental rotation and spatial perception tasks). It may be that researchers specifically avoid using the mental rotation tasks with AD patients, given the complexity of these tasks to avoid floor effects.

Individual factors other than sex and age have also been shown to influence cognitive abilities: IQ has been shown to influence scores on cognitive tests (Albert, Heller & Milberg, 1988; Gallagher & Burke, 2007; Harrison, Buxton, Husain & Wise, 2000). Similarly, authors have identified an association between level of education (often used as a proxy for IQ) and visuospatial abilities (Harrison et al., 2000; Wiederholt, Cahn, Butters, Salmon, Kritz-Silverstein & Barrett-Connor, 1993). Furthermore, in the elderly, a higher level of education is advantageous for visuospatial tasks such as figure copying (Unverzagt, Hall, Torke, Rediger, Mercado, Gureje et al., 1996) including the ROCF (Rosselli & Ardila, 1991) and the JLO task (Caparelli-Daquer et al., 2009).

As it was expected that women are more adversely affected than men by AD, visuospatial tests were selected which would normally demonstrate no sex differences in the healthy population, i.e. spatial visualisation ones. These tasks are also somewhat easier than those in other categories, such as mental rotation, where one might expect to find floor effects in AD patients.

Young adults would be expected to perform better than the elderly on these tasks and the healthy elderly should score higher than those with AD. With regards to sex differences, it was expected that there would be no difference between men and women in either of the healthy groups, but a male advantage in the group of people with AD. As previous literature suggests that IQ and level of education are important mediating factors in the performance of cognitive abilities in both the elderly and those with AD. It was decided, therefore to conduct multiple regression analyses to identify the relative effects of each of the variables of sex, IQ, age and dementia severity on the cognitive tests examined.

4.2. METHOD

4.2.1. PARTICIPANTS

There were three groups of participants and demographic details are presented in Table 6.1.

AD PATIENTS

71 participants (34 male, 37 female) were recruited via outpatient clinics at the QEII Hospital (in Welwyn Garden City) and Lister Hospital (in Stevenage). All participants had been assessed for probable AD under NICE criteria (NICE, 2007) which includes elimination of other possible pathologies by means of a detailed assessment of the history/onset, detailed

neuropsychological assessment and, in some cases, neuroimaging. Inclusion criteria were that participants have a score on the Mini Mental State Examination (MMSE: Folstein, Folstein & McHugh, 1975) between 13 and 28 and must be judged by their treating clinician to have the capacity to give informed consent. Patients scoring above 28 or below 13 on the MMSE were excluded on the basis of showing very mild cognitive impairments or too severe a cognitive impairment respectively. Moreover, it has been shown that an MMSE score of 13/14 is the optimal cut-point for assessing capacity to consent (Whelan, Oleszek, Macdonald & Gaughran, 2009). One participant was removed from this group as he was identified as suffering with young-onset dementia (aged 52 years) leaving 70 participants.

Controls

There were 2 control groups: an elderly control group and a younger group.

Elderly Controls (EC)

The elderly group was recruited from a list of healthy elderly individuals who have previously volunteered through local GP surgeries and also included spouses or partners of AD patients (who should be suitable matched controls for the AD patients). There were 62 participants in this group (31 male and 31 female).

Young Adults (YA)

The young group was mainly recruited from the psychology department at the University of Hertfordshire through the research participation system for which they received course credit. However, due to shortage of men available in this group, male participants were also recruited via friends and family of the researcher. There were initially 104 participants in this group (45 male and 59 female) but the mean age for men was significantly higher than for women. In order to try and address this imbalance, the oldest 5 men and the youngest 19 women were removed, resulting in 40 men and 40 women.

For all groups, participants had normal, or corrected to normal, vision, and spoke English as their first language.

TABLE 4.1 MEAN ± SD FOR AGE, IQ, YEARS OF EDUCATION, MMSE AND HADS SCORES OF THE PARTICIPANTS

Group	AD		EC		YA	
	Male	Female	Male	Female	Male	Female
N	33	37	31	31	40	40
Age	80.48 ±6.56	81.81 ±6.92	76.52 ±7.32	75.77 ±6.50	27.68 ±8.45	23.58 ±8.23
IQ	106.30 ±8.06	108.54 ±8.64	115.84 ±7.22	115.32 ±7.25	112.15 ±5.11	110.50 ±6.66
Years of Education	10.64 ±2.52	11.41 ±2.19	11.61 ±1.84	11.39 ±1.67		
HADS	6.85 ±5.02	5.59 ±4.99	6.23 ±4.51	6.42 ±4.11		
MMSE	22.03 ±5.32	21.27 ±4.15	28.74 ±1.44	29.16 ±0.97		

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults. HADS = Hospital Anxiety and Depression Scale. MMSE = Mini-Mental State Examination.

Independent t-tests were used to check whether there were any differences between groups (AD, EC and YA) and within each group, between men and women on possible confounding factors of age, IQ, level of education and HADS scores. Where such differences emerge, those variables were covaried in subsequent analyses, to control for the confounding effect.

There was a significant difference between AD and EC groups for age, with the AD group being older ($t(130) = 4.25$, $p<0.001$), IQ ($t(130) = -5.92$, $p<0.001$), with the EC scoring higher and (as expected) MMSE scores (EC scoring higher) (t (130) = -11.87, *p*<0.001). So the analysis comparing the AD and EC groups included age and IQ as covariates. There was no significant difference between these groups on level of education (t (130) = -1.25, *p*=0.21) or HADS score (t (130) = -0.17, *p*=0.87)).

Obviously the YA and EC differed significantly on age (t(140) = 37.93, *p*<0.001) but also on IQ (t(140)=3.86, *p*<0.001) where the Elderly scored higher. So the analysis comparing the YA and EC groups included IQ as a covariate.

Independent t-tests showed that for both the AD and EC groups there were no significant differences between men and women for age, IQ, level of education, MMSE scores or HADS scores (see Table 5.1 for demographic details). (AD group: age t(68) = -0.82, *p*=0.42, IQ t(68) = -1.12, *p* =0.27, level of education t(68) = -1.37, *p* =0.18, MMSE t(68) = 0.67, *p* = 0.51, HADS t(68) = 1.05, *p* =0.30. EC group: age t(60) = 0.42, *p* =0.68, IQ t(60) = 0.28, *p* =0.78, level of education t(60) = 0.51, *p* =0.61, MMSE t(60) = -1.35, *p* =0.18, HADS t(60) = -0.18, *p* =0.86)

In the YA group there was no significant difference between men and women on IQ t(78) = 1.24, *p*=0.22), however males were significantly older (mean age 27.68 (8.45)) than females (mean age 23.58 (8.28)): t(78) = 2.19, *p*=0.03). Therefore age was included as a covariate in the MANCOVA examining sex differences in the young group.

4.2.2. Materials

Mini Mental State Examination (MMSE: Folstein, Folstein & McHugh,1975)

Elderly participants (AD and EC) were screened using the MMSE to determine the degree of disease severity in the AD group and to control for undiagnosed memory deficits in the EC group. The MMSE is composed of questions measuring cognitive impairment and is used as a measure of dementia severity by clinicians. The maximum score is 30.

Visual Acuity test of The Cortical Vision Screening Test (CORVIST: James, Plant & Warrington, 2001)

The CORVIST was used to check visual acuity in the Elderly participants. The test consists of six rows which contain two each of three shapes (circle, square, triangle). A viewing window is used to reveal only one shape at a time, and participants are required to move along each row saying out loud the name of the shape. If participants hesitated, the researcher reminded the participant what the names of the shapes were (i.e. they were asked whether the shape was a circle, square or triangle). This was to ensure that an incorrect answer was not due to naming difficulties. The rows decrease in size. If a participant was unable to read the top row, then testing was stopped.

National Adult Reading Test (NART: Nelson, 1978)

This was used to estimate IQ or pre-morbid IQ. This test requires participants to read aloud a list of 50 unusual and/or irregular words. It has been shown to be a valid estimator of premorbid ability in mild to moderate dementia (McGurn, Starr, Topfer, Pattie, Whiteman, Lemmon, et al., 2004).

Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983)

As depression is associated with poor performance on cognitive tests (Weiss, Kohler, Vonbank, Stadelmann, Kemmler, Hinterbauer & Marksteiner, 2008), elderly participants were screened for depression and anxiety using the HADS.

Rey Osterrieth Complex Figure task – copy and recall

(All participants were administered these tasks.)

This task is a visuoperceptual one. Participants are asked to draw a complex figure which is in front of them. At the end of the testing session, participants are unexpectedly asked to draw the figure from memory. A point is given for every element of the diagram that has been included, with another point for that element being in the correct position. If an element has been drawn as incomplete or distorted 0.5 is awarded. The total possible score is 36.

The Cambridge Neuropsychological Test Automated Battery (CANTAB: Robbins, James, Owen, Sahakian, McInnes & Rabbitt, 1994)

This is a battery of computerised cognitive tests. It was presented to participants on a touch-screen tablet. Participants were advised that they could either respond by touching the appropriate button on the screen or verbally to the researcher.

(This battery of tests was administered to the AD and EC groups only.)

Paired associates learning (PAL)– assesses visual memory and new learning. It is primarily sensitive to changes in medial temporal lobe functioning. Participants are presented with six boxes which open, one at a time, to reveal a pattern in one of them. Once all the boxes have been opened, the pattern appears in the middle of the screen. Participants are required to identify where they saw the pattern. The measure used is the total number of errors, adjusted to allow for those stages that were not attempted due to previous failure.

Pattern Recognition Memory (PRM) – assesses visual pattern recognition memory in a 2-choice forced discrimination paradigm. The test is sensitive to medial temporal areas of the brain. Participants are shown a series of 12 patterns. In the recognition phase they are required to choose between a pattern they have already seen and a novel one. The outcome measure is the percentage correct.

Spatial Span (SSP) – a computerised version of the CBT. Assesses working memory capacity. A pattern of white boxes is displayed on the screen. Some of these will change colour and participants are required to repeat the sequence using the touch screen. The task gets progressively harder beginning with a sequence of 2 changes up to a total span of 9. The outcome measure is the largest sequence successfully completed by the participant.

4.2.3. Procedure

The study was approved by the National Health Service National Research Ethics Service.

Participants were recruited via clinical staff who ensured that patients fell within the criteria for the study. If so, they introduced patients to the researcher. Participants were then given detailed information on the research, including an information sheet to read. They were given the opportunity to ask questions and, if they agreed to take part, an appointment was made for the testing.

All patients and elderly controls completed the task in their own homes. At the testing session, participants were once again told about the research and were given the opportunity to ask questions. If they agreed to take part, they were asked to sign the consent form.

The first tasks were the CORVIST, the HADS and the NART. There then followed a series of cognitive tests (some of which will not be considered within this chapter) including tests assessing visuospatial abilities that are the subject of this chapter (see Appendix 1 for a list of all the tests that were administered). The battery of computerised tests was administered at a separate testing session.

4.2.4. Data Analysis

Statistical analyses were performed using SPSS for Windows v.19.0.

Multivariate Analyses of Covariance (MANCOVA) were conducted for all groups to identify any interaction between group and sex on visuospatial scores. Subsequently, separate multivariate analyses of variance (MANOVA) or MANCOVAs were conducted for each main effect. As the difference between the AD group and young adults was of no interest, it was decided to run two separate MANCOVAs (i.e., between EC and YC and AD and EC) to detect group differences. A separate MANOVA/MANCOVA was also run for each group to identify sex differences.

Regression analyses were conducted to explore the extent to which demographic factors might influence the dependent variables. Sex, IQ, age, level of education and MMSE scores were entered

4.3. RESULTS

4.3.1. ROCF task

Descriptive statistics are presented in Table 4.2, from which it can be seen that men with AD scored higher than women with AD on both tasks. In the healthy participants there was very little difference between men and women on either task. People with AD show a clear deficit compared to the elderly, and the elderly score somewhat lower than the young group.

TABLE 4.2 DESCRIPTIVE STATISTICS (MEAN, ±SD) FOR SCORES ON ROCF TASK BY GROUP AND BY SEX.

Group	AD			EC			YA		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
N	31	36	67	30	30	60	40	40	80
ROCF Copy	26.69_a ± 8.68	21.92_a ± 10.74	24.13_b ±10.05	33.55 ±2.81	33.98 ±2.63	$33.77_{b,v}$ ±2.71	35.55 ±0.96	35.78 ±0.53	35.66_v ±0.78
ROCF Recall	4.71_d ±4.68	1.76_d ±2.73	3.13_e ±4.01	15.83 ±6.90	15.07 ±5.74	$15.45_{e,f}$ ±6.30	23.35 ±5.82	22.86 ±5.88	23.11_f ±5.82

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults. Scores sharing subscripts are significantly different (at p<0.001). (Difference between AD and YA were not tested.)

Assumption of equality of covariance matrices was not violated (Box's test p >0 .001). The MANCOVA did not reveal a significant interaction for group and sex so these factors were examined separately.

Group Differences

AD and EC groups

As the groups differed on age and IQ, these were added to the MANCOVA as a covariate. The EC group scored significantly higher than the AD group on both the copy and recall tasks (copy, $F(1,123) = 20.91$, p<0.001, Recall, $F(1,123) = 88.97$, p<0.001) (See Table 6.3 for effect sizes for these comparisons).

EC and YA groups

A MANCOVA was conducted, with IQ as a covariate as there was a significant group difference for this variable. The YA group scored significantly higher than the EC group on both the copy and recall tasks (copy, $F(1,137) = 63.65$, $p<0.001$, Recall, $F(1,137) = 73.11$, $p<0.001$).

TABLE 4.3 EFFECT SIZES (COHEN'S *D*) FOR GROUP DIFFERENCES ADJUSTED FOR AGE AND IQ

ROCF Task	AD vs EC[1]	EC vs YA[2]
Copy	0.90***	1.40***
Recall	1.86***	1.51***

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults. * $p<0.05$, ** $p<0.01$, *** $p<0.001$.
1 – Negative value indicates an AD advantage. 2 – Negative value indicates an Elderly advantage.

SEX DIFFERENCES

AD group

Males scored significantly higher than women on the copy task ($F(1,65)= 3.90$, $p =0.05$). and on the recall task ($F(1,65) = 10.23$, $p <0.01$).

TABLE 4.4 EFFECT SIZES (COHEN'S *D*) FOR SEX DIFFERENCES

ROCF task	AD	EC	YC
Copy	-0.49*	0.16	0.28
Recall	-0.80**	-0.12	-0.04

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults * $p<0.05$, ** $p<0.01$. Negative value indicates a male advantage.

EC

No significant sex differences emerged for the EC group in either the copy ($F(1, 58) = 0.38$, $p = 0.54$) or recall ($F(1, 58) = 0.22$, $p = 0.64$) test.

YA

As there was a significant difference between men and women for age, this was covaried in the MANCOVA. No significant sex differences emerged in this group in either the copy ($F(1, 77) = 1.49$, $p = 0.23$) or recall ($F(1, 77) = 0.03$, $p = 0.87$) test. (See Table 4.4 for effect sizes for these comparisons).

4.3.2. CANTAB TESTS

The scores for men and women for PAL total errors in the EC showed a substantial difference (men: mean 61.64 ±50.43, women: 32.34, ±27.52) and resulted in an unexpected significant difference between men and women $F(1.29) = 4.26$, $p<0.05$, effect size d =0 .77). Examination of the results revealed that one male participant had an extremely high score of 188, compared to the mean for males of 51.92 when his score is excluded. Although there was nothing unusual or notable about this participant as his score was so extreme, he was removed from the data file. All subsequent results and discussions reflect the removal of this participant from the data.

Descriptive statistics are presented in Table 4.5, from which it can be seen that women with AD made more errors on the PAL than men, although elderly women performed better than elderly men. For the PRM test, there is a small female advantage in the EC group which is again reversed in the AD group. The scores for the SSP test are very similar for men and women in both groups.

TABLE 4.5 DESCRIPTIVE STATISTICS (MEAN ±SD) FOR SCORES ON CANTAB TESTS BY GROUP AND BY SEX.

Group		AD			EC	
	Male	Female	Total	Male	Female	Total
N	30	33	66	13	17	30
PAL Total Errors (Adjusted)	137.87 ± ±45.76	144.76 ±34.14	141.48_a ±39.91	51.92 ±36.36	32.24 ±27.52	40.77_a ±32.61
PRM percentage correct	59.72 ±13.59	57.45 ±13.21	58.53_b ±13.33	77.89 ±9.38	77.94 ±14.34	77.92_b ±12.24
SSP Span	3.47 ±1.76	3.61 ±1.12	3.54_c ±1.45	4.77 ±0.83	4.71 ±0.99	4.73_c ±0.91

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults PAL = Paired Associate Learning, PRM = Pattern Recognition Memory, SSP = Spatial Span. Scores sharing subscripts are significantly different (at $p<0.001$).

Assumption of equality of covariance matrices was not violated (Box's test $p > 0.001$). The MANOVA revealed a significant interaction for group and sex on the PAL scores, reflecting the reversal of the elderly female advantage in the AD group.

4.3.3. GROUP DIFFERENCES

As the groups differed on age and IQ, these were added to the MANCOVA as a covariate. The EC group scored significantly higher than the AD group on the PAL ($F(1,89) = 96.51$, $p<0.001$), PRM ($F(1,89) = 22.28$, $p<0.001$) and SSP span ($F(1,89) = 11.03$, $p<0.001$)) (See Table 4.6 for effect sizes for these comparisons).

TABLE 4.6 EFFECT SIZES (COHEN'S *D*) FOR GROUP DIFFERENCES

CANTAB test	AD vs EC
PAL	2.35***
PRM	1.13***
SSP	0.79***

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults. PAL = Paired Associate Learning, PRM = Pattern Recognition Memory, SSP = Spatial Span. * p<0.05, **p<0.01, ***p<0.001. Negative value indicates an AD advantage.

4.3.4. SEX DIFFERENCES

AD GROUP

There were no significant sex differences on any of the tasks in this group: PAL F(1,61) = 0.46, *p*=0.50, PRM F(1,61) = 0.45, *p*=0.50 and SSP (F(1,61) = 0.14, *p*=0.71).

EC

No significant sex differences emerged for this group: PAL (F(1, 30) = 2.86, *p* =0.10), PRM (F(1,30) <0.01, *p*=0.99) and SSP (F(1,30) = 0.04, *p*=0.85). (See Table 4.7 for effect sizes for sex differences.)

TABLE 4.7 EFFECT SIZES (COHEN'S *D*) FOR SEX DIFFERENCES

CANTAB test	AD	EC
PAL	-0.17	0.64
PRM	-0.17	0.14
SSP	0.10	0.00

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults PAL = Paired Associate Learning, PRM = Pattern Recognition Memory, SSP = Spatial Span. * p<0.05, **p<0.01. Negative value indicates a male advantage.

POST HOC ANALYSIS

As performance on the ROCF task relies on visual perception, a correlation analysis was run and although significant correlations between visual acuity and ROCF copy (r=0.29, p=0.001) and acuity and ROCF recall (r=-0.28, p= 0.001) emerged there were no significant differences between men and women on acuity in either elderly group (AD: t=-0.48, p=0.63; EC: t=-1.53, p=0.13).

4.3.5. REGRESSION ANALYSES

In order to evaluate the relative importance of other individual differences, multiple regression analyses were run including the independent variables of sex, age, IQ, and MMSE scores. Tolerance was at an acceptable level (lowest 0.55) for all predictors, therefore there was no multicollinearity. The results are shown in Table 4.8.

AD GROUP

The total amount of variance in the ROCF copy task accounted for by the four predictors entered was 19.2% (F(4,62)=3.69, p=0.01). Of these predictors, Sex and MMSE scores were significant uniquely explaining 8% and 9% of the variance respectively. While IQ scores explained 1% of the variance the contribution of age was zero. Similarly for ROCF Recall, where the model was significant (F(4.62)=5.92, p<0.001), explaining 27.6% of the variance and sex and MMSE were significant predictors contributing 12% and 13% of the variance in scores. For all the CANTAB tasks, only MMSE was a significant predictor. This variable explained 31% of the variance in PAL errors made, 10% of the variance on PRM and 18% of the variance in spatial span. For all tasks, sex contributed 1% or less and IQ did not contribute to the variance in scores at all.

Elderly Controls

The total amount of variance in the ROCF copy task accounted for by the four predictors entered was 39.7% ($F(4.55)=9.05$, $p<0.001$). Of these predictors, IQ scores (10%) and MMSE scores (11%) were significant whereas sex failed to explain any of the variance in scores. However, for ROCF Recall, the model was not significant ($F(4,55)=2.01$, $p=0.11$), explaining only 12.7% of the variance. Sex independently accounted for only 1% of this amount.

The model for PAL total errors was significant, explaining 51.4% of the variance ($F(4,26) = 6.88$, $p=0.001$). By far the most important predictor was MMSE scores (20%). The PRM model was also significant ($F(4,26) = 3.72$, $p<0.001$, $R^2=0.364$) but the only significant individual predictor was age (explaining 18% of the variance). Lastly, the model for SSP span failed to reach significance, ($F (4,26) = 0.72$, $p=0.59$, $R^2=0.099$). For all three computerised tasks (i.e. PAL, PRM and SSP), the contribution of sex was minimal, accounting for 1% or less of the variance.

Young adults

The total amount of variance in the ROCF copy task accounted for by the three predictors entered was 21.4% ($F(3,76)=6.91$, $p<0.001$). Both IQ scores and age were significant explaining 19% and 6% of the variance, respectively while sex only accounted for 2% of the variance. The model for ROCF Recall was also significant ($F(3,76)=4.22$, $p<0.01$), explaining 14.3% of the variance but for this test only IQ scores was a significant predictor contributing 13% of the variance in scores. Sex accounted for less than 1%.

TABLE 4.8 RESULTS OF MULTIPLE REGRESSION ANALYSIS FOR YOUNG ADULTS, ELDERLY CONTROLS AND AD PATIENTS ON VERBAL TESTS.

Test	Predictor											
	Sex[1]			IQ			Age			MMSE score		
	SP	SP^2	t	SP	SP^2	t	SP	SP^2	t	SP	SP^2	t
AD												
ROCF Copy	-0.23	0.08	-1.99*	0.09	0.01	0.79	-0.04	0.00	-0.34	0.30	0.09	2.63*
ROCF Recall	-0.34	0.12	-3.15**	-0.04	0.00	-0.40	-0.01	0.00	-0.11	0.36	0.13	3.31**
PAL	0.05	0.00	0.46	-0.07	0.00	-0.70	0.05	0.00	0.50	-0.55	0.31	-5.41***
PRM	-0.08	-0.01	-0.65	0.22	0.05	1.85	0.00	0.00	0.00	0.31	0.10	2.63*
SSP	0.10	0.01	0.80	-0.04	0.00	-0.35	0.10	0.01	0.82	0.42	0.18	3.56**
Elderly Controls												
ROCF Copy	0.04	0.00	0.34	0.32	0.10	3.02**	0.01	0.00	0.07	0.34	0.11	3.22**
ROCF Recall	-0.08	0.01	-0.61	0.19	0.04	1.53	-0.21	0.05	-1.69	0.09	0.01	0.74
PAL	-0.12	0.01	-0.75	0.17	0.03	1.10	0.20	0.04	1.26	-0.41	0.16	-2.56*
PRM	-0.12	0.01	-0.73	0.26	0.07	1.65	-0.42	0.18	-2.67*	0.09	0.01	0.56
SSP	-0.11	0.01	-0.60	0.00	0.00	0.02	-0.14	0.02	-0.75	0.19	0.04	1.03
Young Adults												
ROCF Copy	0.14	0.02	1.38	0.44	0.19	4.32***	-0.25	0.06	2.49*			
ROCF Recall	-0.02	0.00	-0.16	0.36	0.13	3.43**	-0.12	0.02	-1.15			

Note: SP = semi-partial correlation. * p< 0.05, ** p<0.01, *** p<0.001. [1] Negative value indicates a male advantage. PAL: lower scores indicate a better performance.

4.4. DISCUSSION

The elderly performed better than the young on both the ROCF copy and recall tasks and people with AD were impaired on all tests, compared to the healthy elderly. Men with AD scored significantly higher than women for ROCF copy and recall tasks but there were no sex differences in the healthy groups (both young and elderly) on either of the ROCF tests. There were no sex differences in the PAL, PRM or SSP tasks in either the EC or AD groups.

These findings are in line with those previously reported. Gallagher & Burke, 2007 found the elderly scored higher than the young for the ROCF and people with AD are worse than elderly controls for this task (Binetti et al., 1998; Freeman et al., 2000; deIpolyi, Rankin, Mucke, Miller & Gorno-Tempini, 2007), the PRM and PAL tasks (Sahakhian, Morris, Evenden, Heald, Levy, Philpot et al., 1985) and the CBT (Baudic et al., 2006; Toepper, Beblo, Thoma & Driessen, 2008) (the SSP is a computerised version of the CBT).

Although the ROCF copy task was found by Gallagher & Burke (2007) to elicit a male advantage in young participants, other researchers found no sex difference as participants perform at, or close to, ceiling (Lewin et al., 2001). This is what was found in the current study. Figure copying in the elderly generally fails to demonstrate any sex differences (e.g. Duff et al., 2011; Henderson & Buckwalter, 1994 Moore et al., 2010) and the current study supports this finding.

A male advantage has previously been reported on figure copying tasks in AD patients (Beinhoff et al., 2008; Heun & Kockler, 2002) although some researchers found there to be no difference (Buckwalter et al., 1996; Henderson, 1996; Henderson & Buckwalter 1994; Perneczky et al., 2007). The current findings concur with the former studies, but, as far as I am aware, this is the first time that a male advantage in AD has been reported for the ROCF tests.

The absence of significant sex differences in the AD group for PAL, PRM and SSP reflects the pattern found in healthy elderly men and women and agrees with previous research. Although Simpson et al. (2005) reported a male advantage in the elderly for both the PRM and SSP tasks the participants in their study were from a number of different European countries and significant sex differences did not emerge in UK participants. Similarly, Millet et al. (2009) failed to identify a difference between men and women with AD on the forward CBT. The literature search failed to find any paper that examined sex differences in the PAL in either the elderly or those with AD.

There was a (non-significant) female advantage in the elderly for PAL which was not apparent in the AD group where men scored higher than women. This apparent reduction in women's performance relative to men is also evident in the PRM and the ROCF tests. What the ROCF recall, PRM and PAL have in common is that they are measures of visual memory and new learning. However, the sex differences found were not due to differences between men and women in visual acuity. These processes are mediated in the temporal lobe whereas the SSP relies more heavily on short-term working memory processes which are frontal lobe oriented. The frontal lobes are affected by AD at a later stage than the temporal lobes (Braak & Braak, 1985). Therefore, if AD has a greater impact on women's cognitive abilities than men's, this should first become apparent in those tasks involving the temporal lobe, which is what was found in this study. It may be that a worse performance by women on frontal lobe tasks would emerge at a later stage in the disease than those examined here.

There is some evidence that women are more susceptible to the pathological changes seen in AD than are men. Chapman, Mapstone, Gardner, Sandoval, McCrary, Guillily et al. (2011) reported a decline in performance from the healthy controls to the AD group that was 1.6 times greater in women than in men, although they used a verbal memory task. It may be that brain reserve capacity serves as a stronger counterweight to neurodegeneration in men than in women: Perneczky et al. (2007) found that despite being at the same disease stage (as measured by MMSE scores) and showing no significant differences in general cognitive scores, men with AD had more pronounced and extensive pathology in regions of the frontal, temporal and insular cortex as well as the hippocampus in the right hemisphere.

The characteristics of the young group present an important limitation to this study. The majority of the women were psychology undergraduates whereas the male participants were recruited via friends and colleagues of the author resulting in the men in this group being significantly older than the women. Although the effect of age was controlled for in the MANCOVA, the men and women differed on other characteristics such as occupation. Another limitation is that the study is cross-sectional, so the apparent worsening of women's performance seen by comparing the EC and AD participants may not be a true effect, rather a result of cohort differences. Only examining participants pre-morbidly and following them longitudinally would address this question.

This is the first time that a male advantage has been reported for the ROCF tasks in AD participants, but no other paper has been published examining sex differences for this specific task. It is unclear whether this is because researchers have not examined this previously, or because non-significant results are unlikely to be accepted for publication.

What is evident from the current study is that sex does not play a large role in the visuospatial tasks examined, particularly in the healthy population. The regression analysis showed that IQ uniquely explained far more variance than sex, particularly for the ROCF tasks, whereas for the elderly groups MMSE scores were the most important factor, even in the healthy group. However, in the meta-analysis of sex-differences reported in chapter 3, a reversal of the female advantage in verbal abilities normally reported even in the elderly emerged. What was not apparent from that analysis was that women are similarly affected in the visuospatial domain: in the current study a higher score by elderly women than men for PAL was reversed in the AD group where men had the advantage and a similar effect also emerged in the PRM and ROCF tests.

5. Sex differences in verbal abilities in people with Alzheimer's disease

5.1. INTRODUCTION

Conflicting reports exist concerning the presence of differences in the verbal abilities of healthy men and women (see Section 2.3 for detailed review). Although papers often cite females as having a verbal advantage over men, closer examination of the literature reveals that the sex differences may be task dependent. In 1988, Hyde & Linn claimed that although there was a clear consensus that women had better verbal abilities than men, the effect size was only small (Cohen's *d*= 0.11), albeit with a huge sample, and was not apparent on all tasks.

Women have been reported as scoring higher in lexical fluency tasks (Burton, Henninger & Hafetz, 2005; de Frias, Nilsson & Herltz, 2006; Hausmann, Schoofs, Rosenthal & Jordan, 2009; Herlitz, Nilsson & Backman, 1999; Thilers, McDonald & Herlitz, 2006; Weiss, Kemmler, Deisenhammer, Fleishacker & Delazer, 2003), although other researchers have found no such difference (Brickman, Paul, Cohen, Williams, MacGregor, Jefferson et al., 2005; Halari, Hines, Kumari, Mehrotra, Wheeler, Ng & Sharma, 2005; Lewin, Wolgers & Herlitz, 2001; Nowak & Moffat, 2011; Robert & Savoie, 2006; Tombaugh, Kozak & Rees, 1999). Similarly there have been competing claims with regards to semantic fluency with some researchers failing to detect sex differences (Brickman et al., 2005; Janowsky, Chavez, Zamboni, & Orwoll, 1998; Lanting, et al., 2009; Tombaugh, Kozak & Rees, 1999) and others reporting a significant female advantage (Cameron, Wambaugh & Mauszycki, 2008; Halari et al., 2005). Sex differences in semantic fluency may be category specific, however: Robert & Savoie

(2006) found no sex difference on verbal fluency overall, but a significant female advantage for fruit names. Capitani, Laiacona & Barbarotto (1999) and Cameron et al. (2008) also reported a significant female advantage in naming fruits, though Moreno-Martinez, Laws & Schulz (2008) found no sex differences in young adults on any category, including fruits. A consistent advantage for men in one language task – confrontation naming - has been found (Connor, Spiro, Obler & Albert, 2004, Lansing et al., 1999), although these are the only two papers examining sex differences in the young in this task.

Men and women have been shown to decline in their cognitive abilities at a similar rate (Barnes, Wilson, Schneider, Bienas, Evans & Bennett, 2003; Gerstorf, Herlitz & Smith, 2006 Proust-Lima, Amieva, Letenner, Orgogoze, Jacqmin-Gadda & Dartigues, 2008) and although verbal abilities have been shown to improve with age, after mid-life there is some decline (van Hooren, Valentin, Bosma, Ponds, Boxtel & Jolles, 2007, Schaie, 1996). An aging decline in category fluency, in particular for animal naming, has been widely reported (Brickman et al., 2005. Lanting et al., 2009, Laukka, MacDonald, Fratiglioni & Backman, 2012; Snitz, Unverzagt, Chang, Vander Bilt, Goo, Saxton, Hall et al., 2009, Wiederholt, Cahn, Butters, Salmon, Kritz-Silverstein & Barrett-Connor, 1993). Furthermore, Capitani et al. (1999) found age to be a significant predictor for semantic fluency overall and for all categories, not just animal naming. In a meta-analysis on lexical fluency, the elderly were shown to perform worse than the young (Rodriguez-Aranda & Martinussen, 2006) but again there is some conflict: others (e.g. Bird, Papadopoulou, Ricciardelli, Rossor & Cipolotti, 2004; Fahlander, Wahlin, Fastbom, Grut, Forsell, Hill et al., 2000) reported no correlation between age and lexical fluency scores. Confrontation naming, however, appears to remain stable with age until individuals are in their 70s (Albert, Heller & Milberg, 1988, Welch, Doineau, Hohnson & King, 1996; Zec, Markwell, Burkett & Larsen, 2005)

In line with the reports of an absence of sex differences in the young and a similar rate of cognitive decline for men and women (see section 2.1.1), many researchers have reported equivalent performance for elderly men and women on lexical fluency (Mathuranath, George, Cherian, Alexander, Sarma & Sarma, 2003; Gerstorf et al., 2006; Wahlin, Robins Wahlin, Small & Backman, 1998; Welsh-Bohmer, Ostbye, Sanders, Peipers, Hayden, Tschanz et al., 2009; Whittle, Corrada, Dick, Ziegler, Kahle-Wrobleski, Paganini-Hill et al., 2007). However, as with the young, conflicting reports are found in the elderly. Some researchers have reported a significant female advantage in lexical fluency (Elias, Elias, D'Agostino, Silbershatz & Wolf, 1997; Lanting et al., 2009; Monsch, Bondi, Butters, Salmon, Katzman & Thal, 1992). For semantic fluency there have been reports of a male advantage (Marra, Ferraccioli & Gainotti, 2007; Wiederholt et al., 1993), no sex differences (Beinhoff, Tumani, Brettschneder, Bittner & Riepe, 2008; Gerstorf et al., 2006; Henderson & Buckwalter, 1994; van Hooren et al., 2007 Snitz et al., 2009; Wahlin et al., 1998; Whittle et al., 2007) and a female advantage (Duff, ASchoenberg, Mold, Scott & Adams, 2011; Marra et al., 2007; Moore, Miller, Andersen, Arndt, Haynes & Moser, 2011; Welsh-Bohmer et al., 2009).

Elderly women have been reported as impaired on confrontational naming tasks relative to men (Buckwalter, Rizzo, McCleary, Shankle, Dick & Henderson, 1996; Connor et al., 2004; Randolph, Lansing, Ivnik, Cullum & Hermann, 1999; Welch et al., 1996), reflecting the male advantage found in young adults, although many researchers failed to find a significant sex difference in this task in the elderly (Beinhoff et al., 2008; Coppens & Frisinger Duff et al., 2011; Henderson & Buckwalter, 1994; Moore et al., 2011, Welsh-Bohmer et al., 2009, Whittle et al., 2007, Zec et al., 2007).

Deficits in semantic memory appear early in the course of Alzheimer's disease (AD). Consequently, most research has reported an AD deficit on semantic fluency tasks (see the meta-analyses by Henry, Crawford, & Phillips, 2004 and Laws, Duncan & Gale, 2010). Adlam, Bozeat, Arnold, Watson & Hodges (2006), Lonie, Herrmann, Tierney, Donaghey, O'Carroll, Lee et al. (2009) and Balthazar, Nartinelli, Cendes & Damasceno (2007) all reported that even mild AD patients were more impaired than both mild cognitive impairment (MCI) participants and elderly controls on category fluency. The evidence on lexical fluency is more conflicting: people with AD have been shown to be unimpaired on lexical fluency, compared to the healthy elderly (Butters et al., 1987; Rogers & Friedman, 2008) although deficits in lexical fluency in people with AD have been widely reported (e.g. Lonie et al., 2009; Monsch et al., 1992; Phillips, Scott, Henry, Mowat & Bell, 2010). Henry et al. (2004) and Laws et al., 2010 both conducted meta-analyses and each showed that performance on lexical fluency tests was impaired compared to the elderly.

Elderly controls also score higher than AD patients on confrontation naming (Adlam et al., 2006, Balthazar et al., 2008, Frank, McDade & Scott, 1996, Lukatela, Malloy, Jenkins & Cohen, 1998, Nicholas, Obler, Au & Albert, 1996, Rogers & Friedman, 2008)). As would be expected given the semantic nature of this task, the difference is apparent at a very early stage in the disease process and can even be found in mildly affected AD patients (Adlam et al., 2006) and amnestic MCI (aMCI) patients (Ahmed, Arnold, Thompson, Graham & Hodges, 2008, Balthazar et al., 2008).

With regards to the relative performance of men and women AD on verbal tasks, there have not been any reports of sex differences in AD for lexical fluency. Furthermore, Bayles, Azuma, Cruz, Tomoeda, Wood & Montgomery (1999), McPherson, Back, Buckwalter & Cummings (1999), Monsch et al. (1992) and Ripich, Petrill, Whitehouse & Ziol (1995) have all found no significant difference between men and women on this task. For semantic fluency the existence of sex differences is category dependent: men with AD have been reported as scoring significantly higher than women on naming animals (Henderson & Buckwalter, 1994) insects, trees, tools, musical instruments and vehicles (Moreno-Martinez et al., 2008), and birds (Marra et al., 2007). By contrast, Monsch et al. (1992) found that women scored significantly higher than men when the numbers of animals, fruits and vegetables were totalled (although they did not analyse these categories separately) whereas for supermarket items and first names, there were no significant differences. Similarly, no significant sex differences in animal naming in AD were found by Bayles et al. (1999), Beinhoff et al. (2008), Henderson et al., 1996; McPherson et al. (1999) or Perneczky, Drzezga, Diehl, Schmid, Yi & Kurz (2007).

The published research on sex differences in confrontation naming is also conflicting, with some finding that women with AD are worse than men at confrontation naming (Buckwalter et al., 1996; Henderson & Buckwalter, 1994; McPherson et al., 1999; Randolph et al., 1999; Ripich et al., 1995) and others reporting higher scores by men, but no significant sex differences (Bayles et al., 1999; Beinhoff et al., 2008; Perneczky et al., 2007).

The evidence for sex differences in verbal cognition, therefore, is ambivalent. The most consistent finding is for a male advantage for confrontation naming (found in the healthy, including the elderly, and people with AD) but there are still a number of published papers that have reported no sex differences. The picture for verbal fluency is much less clear. In semantic fluency there is evidence that sex differences are category specific, with the most widely examined category (animals) showing no sex difference and the most widely reported differences being a female advantage for fruit and a male advantage for tools. However, only one paper has reported a female advantage for semantic fluency in AD. No studies have reported superior male performance for lexical fluency, but a female advantage has been reported in both the young and old. However, the only (five) published papers examining this task in AD have all failed to identify any difference between the sexes. If the findings for verbal fluency were robust, it would suggest that women's verbal abilities are affected differently by the course of AD than are men's.

What about the role of demographic factors other than age and sex? There is a strong association between verbal IQ and both verbal fluency (Bolla, Lindgren, Bonaccorsy & Bleecker, 1990; Crawford, Moore & Cameron, 1992; Harrison, Buxton, Husain & Wise, 2000) and confrontation naming (Albert et al., 1998; Bird et al., 2004; Harrison et al., 2000). Similarly, authors have identified an association between level of education (often used as a proxy for IQ)and verbal abilities (Capitani et al., 1999; van Hooren et al., 2007).

In the elderly, a higher level of education results in higher scores in verbal fluency (Van der Elst, Boxtel, van Breukelen & Jolles., 2006; Ganguli, Snitz, Lee, Vanderbilt, Saxton & Chang, 2010; van Hooren et al., 2007). Similarly, some authors have identified an advantage in confrontation naming with higher levels of education (Ganguli et al., 2010; Lansing, Ivnik, Cullum & Randolph, 1999; Kent & Luszcz, 2002), although others found no such effect (Cruice, Worrall & Hickson, 2000; Tsang & Lee, 2003).

In AD, as with the elderly, a positive correlation between level of education and confrontation naming has been identified (Randolph et al., 1999; Weintraub, Salmon, Mercaldo, Ferris, Graff-Radford, Chui et al.., 2009). However, other authors found no effect of education on naming (Moreno-Martinez et al., 2008) or on the rate of cognitive decline (Ballard, Patel, Oyebode & Wilcock, 1996).

This chapter of this dissertation is concerned with trying to clarify and add to the literature on sex differences in verbal abilities in people with AD. Given previous findings, it was expected that people with AD would perform worse than elderly controls on all verbal tests, whilst the young were expected to score higher than the elderly on verbal fluency tasks, but not on confrontation naming. With regards to sex differences, given the conflicting reports previously published and the scarcity of research it is difficult to make a prediction. However, it was expected that males would perform better than females in all groups on confrontation naming. For lexical fluency, a female advantage should emerge in both healthy groups, but this would disappear in the group with AD. For semantic fluency the expectation was that a female advantage for fruits, a male advantage for tools and no sex difference for animals would emerge. Furthermore, as previous literature suggests that IQ/ level of education are important demographic factors in verbal abilities in both the elderly and those with AD multiple regression analyses were conducted to identify the relative effects of sex, age and IQ on the cognitive tests examined.

5.2. METHOD

5.2.1. PARTICIPANTS

There were three participant groups. Demographic details of each group are given in Table 5.1.

ALZHEIMER'S PATIENTS

71 individuals (34 male, 37 female) were recruited via outpatient clinics at the QEII Hospital (in Welwyn Garden City) and Lister Hospital (in Stevenage). All participants had been assessed for probable AD under NICE criteria (NICE, 2007) which includes elimination of other possible pathologies by means of a detailed assessment of the history/onset, detailed neuropsychological assessment and, in some cases, neuroimaging.

Inclusion criteria were that participants have a score on the Mini Mental State Examination (MMSE: Folstein, Folstein & McHugh, 1975) between 13 and 28 and must be judged by their treating clinician to have the capacity to give informed consent. Patients scoring above 28 or below 13 on the MMSE were excluded on the basis of showing very mild cognitive impairments or too severe a cognitive impairment respectively. Moreover, it has been shown that an MMSE score of 13/14 is the optimal cut-point for assessing capacity to consent (Whelan, Oleszek, Macdonald & Gaughran, 2009). One participant was removed from this group as he was identified as suffering with young-onset dementia (aged 52) leaving 70 participants.

CONTROLS

There were 2 control groups: an elderly group (EC) and a younger group (YA).

Elderly Controls

The EC group was recruited from a list of healthy elderly individuals who have previously volunteered through local GP surgeries and also included spouses or partners of AD patients (who should be suitable matched controls for the AD patients). There were 62 participants in this group (31 male and 31 female).

Young Adults

The YA group was recruited from the psychology department at the University of Hertfordshire through the research participation system for which they received course credit. However, due to shortage of men available in this group, male participants were also recruited via friends and family of the researcher. There were initially 104 participants in this group (45 male and 59 female) and the mean age for men was significantly higher than for women. In order to try and address this imbalance, the oldest 5 men and the youngest 19 women were removed from the analyses, resulting in 40 men and 40 women.

For all groups, participants had normal, or corrected to normal, vision, and spoke English as their first language.

TABLE 5.1 MEAN ±SD FOR AGE, IQ, LEVEL OF EDUCATION, MMSE AND HADS SCORES OF THE PARTICIPANTS

Group	**AD**		**EC**		**YA**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
N	**33**	**37**	**31**	**31**	**40**	**40**
Age	80.48 ±6.56	81.81 ±6.92	76.52 ±7.32	75.77 ±6.50	27.68 ±8.45	23.58 ±8.23
IQ	106.30 ±8.06	108.54 ±8.64	115.84 ±7.22	115.32 ±7.25	112.15 ±5.11	110.50 ±6.66
Years of Education	10.64 ±2.52	11.41 ±2.19	11.61 ±1.84	11.39 ±1.67		
HADS	6.85 ±5.02	5.59 ±4.99	6.23 ±4.51	6.42 ±4.11		
MMSE	22.03 ±5.32	21.27 ±4.15	28.74 ±1.44	29.16 ±0.97		

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults. HADS = Hospital Anxiety and Depression Scale. MMSE = Mini-Mental State Examination.

Independent t-tests were used to check whether there were any differences between groups (AD, EC and YA) and between men and women on possible confounding factors of age, IQ, level of education and hospital anxiety and depression (HADS) scores. Where such differences emerge, those variables were covaried in subsequent analyses, to control for the confounding effect.

There was a significant difference between AD and EC groups for age, with the AD group being older (t (130) = 4.25, $p<0.001$), IQ (t(130) = -5.92, $p<0.001$), with the EC scoring higher and (as expected) MMSE scores (EC scoring higher) (t (130) = -11.87, $p<0.001$). So the analysis comparing the AD and EC groups included age and IQ as covariates. There was no significant difference between these groups on level of education (t (130) = -1.25, *p*=0.21) or HADS score (t (130) = -0.17, *p*=0.87)).

Obviously, the YA and EC differed significantly on age (t(140) = 37.93, *p*<0.001) but also on IQ (t(140)=3.86, *p*<0.001) where the Elderly scored higher. So the analysis comparing the YA and EC groups included IQ as a covariate.

Independent t-tests showed that for both the AD and EC groups there were no significant differences between men and women for age, IQ, level of education, MMSE scores or HADS scores (see Table 5.1 for demographic details). (AD group: age t(68) = -0.82, *p*=0.42, IQ t(68) = -1.12, *p* =0.27, level of education t(68) = -1.37, *p* =0.18, MMSE t(68) = 0.67, *p* = 0.51, HADS t(68) = 1.05, *p* =0.30. EC group: age t(60) = 0.42, *p* =0.68, IQ t(60) = 0.28, *p* =0.78, level of education t(60) = 0.51, *p* =0.61, MMSE t(60) = -1.35, *p* =0.18, HADS t(60) = -0.18, *p* =0.86)

In the YA group there was no significant difference between men and women on IQ t(78) = 1.24, *p*=0.22), however males were significantly older (mean age 27.68 ±8.45) than females (mean age 23.58 ±8.28): t(78) = 2.19, *p*=0.03). Therefore age was included as a covariate in the MANCOVA examining sex differences in the young group.

5.2.2. MATERIALS

MINI MENTAL STATE EXAMINATION (FOLSTEIN, FOLSTEIN & MCHUGH,1975)

Elderly participants (AD and EC) were screened using the MMSE to determine the degree of disease severity in the AD group and to control for undiagnosed memory deficits in the EC group. The MMSE is composed of questions measuring cognitive impairment and is used as a measure of dementia severity by clinicians. The maximum score is 30.

Visual Acuity test of The Cortical Vision Screening Test (CORVIST: James, Plant & Warrington, 2001)

The CORVIST was used to check visual acuity in the Elderly participants. The test consists of six rows which contain two each of three shapes (circle, square, triangle). A viewing window is used to reveal only one shape at a time, and participants are required to move along each row saying out loud the name of the shape. If participants hesitated, the researcher reminded the participant what the names of the shapes were (i.e. they were asked whether the shape was a circle, square or triangle). This was to ensure that an incorrect answer was not due to naming difficulties. The rows decrease in size. If a participant was unable to read the top row , then testing was stopped.

National Adult Reading Test (NART: Nelson, 1978)

This was used to estimate IQ or pre-morbid IQ. This test requires participants to read aloud a list of 50 unusual and/or irregular words. It has been shown to be a valid estimator of premorbid ability in mild to moderate dementia (McGurn, Starr, Topfer, Pattie, Whiteman, Lemmon, Whalley & Deary, 2004).

Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983)

As depression is associated with poor performance on cognitive tests (Weiss, Kohler, Vonbank, Stadelmann, Kemmler, Hinterbauer et al. 2008), elderly participants were screened for depression and anxiety using the HADS.

The Graded Naming Test (GNT: McKenna and Warrington, 1983)

Participants are shown a series of line drawings and asked to name the object on the card. There is no time limit set on their response and one point is awarded for each correct answer. The items are graded in order of difficulty, and the test is stopped once participants make 6 consecutive incorrect responses. The maximum obtainable score is 30.

Lexical fluency

This was assessed by asking participants to say aloud as many words as they can, in one minute, beginning with a particular letter of the alphabet. They were instructed not to say any word more than once, not to give the same word with different endings and not to give proper nouns. The initial letters used were F,A,S. If participants hesitated, they were prompted with “Can you think of anymore?”

Category fluency

Category fluency was assessed by asking participants to name aloud as many exemplars from a given category, in one minute. The categories used were animals, tools and fruit. If participants hesitated, they were prompted with “Can you think of anymore?”

5.2.3. Procedure

The study was approved by the National Health Service (NHS) National Research Ethics Service.

Participants were recruited via clinical staff who ensured that patients fell within the criteria for the study. If so, they introduced patients to the researcher. Participants were then given detailed information on the research, including an information sheet to read. They were given the opportunity to ask questions and, if they agreed to take part, an appointment was made for the testing.

All patients and elderly controls completed the task in their own homes. The young controls, recruited via the University of Hertfordshire, completed the study in a study cubicle.

At the testing session, participants were once again told about the research and were given the opportunity to ask questions. If they agreed to take part, they were asked to sign the consent form.

5.2.4. DATA ANALYSIS

Statistical analyses were performed using SPSS for Windows v.19.0.

Multivariate Analyses of Covariance (MANCOVA) were conducted for all groups to identify any interaction between group and sex on verbal scores. Subsequently, separate multivariate analysis of variance (MANOVA) or MANCOVAs were conducted for each main effect. As a comparison between the AD group and young adults was of no interest, it was decided to run two separate MANCOVAs (i.e., between EC and YC and AD and EC) to detect group differences. A separate MANOVA/MANCOVA was also run for each group to identify sex differences. Lastly, the categories of animals, tools and fruits were examined separately as some effects may emerge only when the analysis focuses on separate categories: some evidence suggests that differences may be category specific (Capitani et al., 1999).

In order to evaluate the relative importance of other individual differences, multiple regression analyses were run including the independent variables of sex, age, IQ and MMSE scores.

5.3. RESULTS

Descriptive statistics are presented in Table 5.2, from which it can be seen that men scored higher than women in all groups for GNT. However, the relative performance of males and females is inconsistent on the fluency tasks and dependent on the groups.

TABLE 5.2 DESCRIPTIVE STATISTICS (MEAN ±SD) FOR SCORES ON VERBAL TESTS BY GROUP AND BY SEX.

Group	AD			EC			YA		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
N	33	37	70	31	31	62	40	40	80
GNT	11.06_a ±7.75	7.14_a ±5.82	8.99_b ±7.03	22.23 ±4.12	20.71 ±5.92	$21.47_{b,c}$ ±5.12	16.05 ±5.24	15.48 ±6.03	15.76_c ±5.62
Category Fluency	19.80 ±10.46	19.38 ±10.07	19.53_d ±10.19	41.48 ±10.59	44.94 ±7.10	$43.21_{d,e}$ ±9.11	47.72 ±10.09	46.25 ±9.96	46.99_e ±9.99
Lexical fluency	19.06 ±12.03	22.27 ±14.08	20.76_f ±13.16	38.23 ±15.13	35.29 ±12.81	$36.76_{f,g}$ ±13.98	42.83 ±10.98	36.67 ±9.53	39.75_g ±10.67

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults. GNT = Graded Naming Test. Scores sharing subscripts are significantly different (at p<0.01). (NB, difference between AD and YA groups not tested.)

Assumption of equality of covariance matrices was not violated (Box's test p >0 .001). The MANCOVA did not reveal a significant interaction for group and sex so these factors were examined separately.

5.3.1. GROUP DIFFERENCES

A MANCOVA was conducted examining mean differences between the EC group and the AD group, covarying age and IQ. The EC group scored significantly higher than the AD group on the GNT ($F(1,128) = 58.72$, $p<0.001$), lexical fluency ($F(1,128) = 10.35$, $p<0.01$) and category fluency ($F(1,128) = 98.57$, $p<0.001$)) (See Table 5.3 for effect sizes for these comparisons).

Examination of specific categories revealed an EC advantage for animals (F(1,128) = 64.30, *p*<0.001 (Cohen's *d* =1.54), tools (F(1,128) = 57.34, *p*<0.001) Cohen's *d* = 1.45) and fruit (F(1,128) = 75.74, *p*<0.001 Cohen's *d* = 1.67).

TABLE 5.3 EFFECT SIZES (COHEN'S *D*) FOR GROUP DIFFERENCES, ADJUSTED FOR AGE AND IQ (AD VS EC) AND IQ (EC VS YA)

Verbal test	AD vs EC[1]	EC vs YA[2]
GNT	1.47***	-0.81***
Category fluency	1.91***	0.69***
Lexical fluency	0.62**	0.68***

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults. GNT = Graded Naming Test. * p<0.05, **p<0.01, ***p<0.001. 1 – Negative value indicates an AD advantage. 2 – Negative value indicates an EC advantage.

A MANCOVA was conducted examining mean differences between the EC group and the YA group, covarying IQ. YA scored significantly higher than EC on category fluency (F(1,139) = 15.42, *p*<0.001) and the lexical fluency task (F(1,139) = 15.13, *p*<0.001). However, the elderly scored significantly higher than YA on the GNT (F(1,139) = 21.82, *p*<0.001). Inspection of specific categories for semantic fluency revealed a significant group difference for animals only (F(1,139) = 26.44, *p*<0.001, effect size *d* = 0.90).

5.3.2. SEX DIFFERENCES

AD GROUP

There was a significant male advantage on the GNT (F(1,68) = 5.82, p=0.02). No significant differences emerged between men and women on lexical (F(1,68) = 1004, p=0.31) or category fluency (F(1,68) = 0.02, p=0.90). (See Table 5.4 for effect sizes for these comparisons). Nor were there any sex differences in the individual category scores: animals (F(1,63) = 0.02, p=0.88), tools (F(1,63) = 2.08, p=0.15) and fruits (F(1,63) = 1.04, p=0.31).

TABLE 5.4 EFFECT SIZES (COHEN'S D) FOR SEX DIFFERENCES ADJUSTED FOR AGE IN YOUNGER PARTICIPANTS

Verbal test	AD	EC	YA
GNT	-0.59*	-0.30	0.17
Category fluency	-0.03	0.39	-0.01
Lexical fluency	0.25	-0.21	-0.45

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults. GNT = Graded Naming Test. * p<0.05, **p<0.01. Negative value indicates a male advantage.

ELDERLY CONTROLS

No significant sex differences emerged for the EC group: GNT F(1,60) = 1.37, *p*=0.25, lexical fluency F(1,60) = 0.68, *p*=0.41 and category fluency F(1,60) = 2.27, *p*=0.14. However, examination of specific categories revealed a sex difference in the this group on the fruit category, with females scoring higher than males (F(1,60) = 7.03, *p*=0.01, effect size, *d* =

0.69). There were no sex differences on either the animals (F(1,60) = 1.93, *p*=0.17) or tools (F(1,60) = 0.50, *p*=0.48) categories.

YOUNG ADULTS

As men and women in this group differed significantly in age, a MANCOVA was conducted with age entered as a covariate. No significant sex differences emerged on any task: GNT (F(1,77) = 0.56, *p*=0.46), lexical fluency (F(1,77) = 3.86, *p*=0.053) and category fluency (F(1,77) = 0.001, *p*=0.98). .Examination of specific categories revealed a significant female advantage for the category of fruit (F(1,77) = 4.71, *p*=0.03, effect size, *d* = 0.50) but no significant differences between men and women for animals (F(1,77) = 0.71, *p*=0.40) or tools (F(1,77) = 0.93, *p*=0.34).

POST HOC ANALYSIS

It has been suggested that difficulties in naming in the elderly may be due to deficits in visual perception (e.g. Kirshner, Webb & Kelly, 1984). A correlation between visual perception and naming (AD: r=0.38, *p*<0.001; EC: r=-.39, *p*<0.01) was found and although there were no significant differences between men and women on acuity in either group (AD: t=-0.48, *p*=0.63; EC: t=-1.53, *p*=0.13) ANCOVAs were run for each group of elderly participants with acuity as a covariate and the findings remained the same, i.e. men scored higher than women in the AD group (F(1,65) = 10.23, *p*<0.01) and there was no significant difference in the EC (F(1,57) = 0.14, *p*=0.72).

5.3.3. REGRESSION ANALYSES

Regression analyses were conducted to examine the relative roles of disease severity, sex and aging alongwith IQ. The results are presented in Table 5.5.

AD GROUP

The model for GNT naming was significant ($F(4,65) = 10.06$, $p<0.001$), and explained 38.2 % of the variance in GNT naming. The most important predictor was MMSE score which explained 14% of the variance in this test for this group. sex and IQ were also significant predictors, explaining 8% and 7% of the variance, respectively. For lexical fluency, the model was again significant ($F(4,65) = 7.62$, $p<0.001$) explaining 31.9% of the variance. Although MMSE scores was again a significant predictor, explaining 5% of the variance in lexical fluency, IQ was the most important predictor, accounting for 17% of the variance. Sex only explained 1% of the variance in lexical fluency. Finally, the model for category fluency was significant ($F(4.65) = 6.98$, $p<0.001$) and accounts for 30.0% of the variance. MMSE was the only significant predictor, explaining 19% of the variance. The contribution of sex and IQ to the overall variance in category fluency was close to zero.

TABLE 5.5 RESULTS OF MULTIPLE REGRESSION ANALYSIS FOR AD PATIENTS, ELDERLY CONTROLS AND YOUNG ADULTS ON VERBAL TESTS.

	Predictor											
	Sex[1]			IQ			Age			MMSE score		
Test	SP	SP^2	t	SP	SP^2	t	SP	SP^2	t	SP	SP^2	t
AD												
GNT	-0.28	0.08	-2.91**	0.27	0.07	2.73**	0.01	0.00	0.13	0.38	0.14	3.89***
Lexical fluency	0.08	0.01	0.78	0.42	0.17	4.06***	0.00	0.00	-0.02	0.22	0.05	2.11*
Category fluency	-0.01	0.00	-0.14	0.17	0.01	1.65	0.11	0.01	1.10	0.44	0.19	4.22***
Elderly Controls												
GNT	-0.14	0.02	-1.59	0.62	0.38	6.97***	-0.06	0.00	-0.64	0.08	0.01	0.94
Lexical fluency	-0.09	0.01	-0.90	0.55	0.31	5.47***	0.01	0.00	0.09	0.05	0.00	0.48
Category fluency	0.16	0.03	1.42	0.30	0.09	2.58*	-0.24	0.06	-2.15*	0.13	0.02	1.10
Young Adults												
GNT	0.08	0.01	0.91	0.46	0.21	5.51***	0.18	0.03	2.13*			
Lexical fluency	-0.20	0.04	-2.00*	0.21	0.04	2.10*	0.17	0.03	1.66			
Category fluency	0-.00	0.00	-0.01	0.31	0.10	2.96**	0.07	0.01	0.69			

Note: SP = semi-partial correlation. * p< 0.05, ** p<0.01, *** p<0.001. [1] Negative value indicates a male advantage.

ELDERLY CONTROLS

The model for GNT naming was significant ($F(4,57) = 17.45$, $p<0.001$), and explained 55.10 % of the variance in GNT naming. MMSE scores explained very little of the variance in verbal test scores because the performance of elderly controls on the MMSE was at ceiling providing very little variance in MMSE scores. The most important predictor was IQ score which explained 38% of the variance in this test for this group. Sex only explained 2% of the total variance in this task. For lexical fluency, the model was again significant ($F(4,57) = 10.16$, $p<0.001$) explaining 41.6% of the variance. Again, only IQ was a significant predictor, and this factor explained 31% of the variance whereas sex only explained 1% of the variance in lexical fluency. Finally, the model for category fluency was also significant ($F(4,57) = 5.07$, $p=0.001$) and accounts for 26.3% of the variance. IQ scores and age were bothsignificant predictors, explaining 9% and 6% of the variance, respectively. The contribution of sex to the overall variance in category fluency is again very small – accounting for only 3% of the variance.

YOUNG ADULTS

The model for GNT naming was significant ($F(3,76) = 22.84$, $p<0.001$), and explained 47.40 % of the variance in GNT naming. The most important predictor was IQ score which independently explained 21% of the variance in this test for this group. Age was also a significant predictor, explaining 3% but sex only accounted for 1%. For lexical fluency, the model was again significant ($F(3,76) = 8.01$, $p<0.001$) explaining 24.00% of the variance. IQ scores and sex were significant predictors and each accounted for 4% of the variance. Finally, the model for category fluency was significant ($F(3,76) = 5.62$, $p<0.01$) and accounts for 18.1% of the variance. IQ scores was the only significant predictor, explaining 10% of the variance. Although IQ is approaching significance (*p*=0.06) and explained 5%. Sex again accounted for less than 1%.

5.4. DISCUSSION

This study showed that the AD group scored significantly lower than EC on all three verbal tests and, with respect to category fluency, in each category when examined separately. Further, a decline in aging was evident in verbal fluency, but the EC scored higher in the naming task. With regards to sex differences in AD, these did not emerge in either lexical or semantic fluency but a male advantage in confrontation naming was found.

As expected, the AD group scored significantly lower than EC for all tasks, and this was reflected in the regression analysis which showed MMSE scores to be the most important predictor in the AD group. These results support previous research which has identified an impairment for people with AD for all three tasks (Adlam et al., 2006, Henry et al., 2004, Laws et al., 2010) and are consistent with the neuroanatomical staging of the disease and neurological correlates of the processes underlying these tasks. Category fluency and confrontation naming tasks are dependent on semantic memory processes which research shows occur in the temporal lobe (Melrose, Harwood, Osata, Mandelkern & Saltzer, 2009; Pihlajamaki, Ranila, Janninen, Kononen, Laakso, Portanen et al., 2000; Ryan, Carriere, Scali, Ritchie & Ancelin, 2009) and the medial temporal lobe has been shown to be involved in generating exemplars in confrontation naming (Ryan et al., 2009), The temporal lobe is the site of primary pathological deficits in AD (Braak & Braak, 1991; Keilp et al., 1999): there is a severe reduction in grey matter volume and significant cortical atrophy in this area (Grossman, Robinson, Biassou, White-Devine & D'Esposito, 1998; Ohnishi, Matsuda, Tabira, Asado & Uno, 2001; Rombouts, Barkhof, Witter & Scheltens, 2000), including the fusiform gyrus (Harasty, Halliday, Kril & Code, 1999). Moreover, research has shown a strong correlation between regional cerebral blow flow in the fusiform gyrus and category fluency (Kitbayashi, Ueda, Tsuchida, Iizumi, Narumoto, Nakamura et al., 2001). Lexical fluency, on the other hand, involves selecting and retrieving information based on orthography and is less reliant on semantic memory (Birn, Kenworthy, Case, Cararella, Jones, Bandettini et al., 2010). Such phonological processes, specifically lexical fluency, activate areas in the frontal lobe (Melrose et al., 2009) which is affected by AD later in the disease process (Aries, Le Bastard, Debruyne, Van Buggenhout, Nagels, De Deyn & Engelborghs, 2010; Scahill, Schott, Stevens, Rossor & Fox, 2002). Hence, one would expect to see relatively greater deficits in semantic memory tasks (such as confrontation naming and category fluency) than those found in other cognitive tasks (such as lexical fluency) that do not depend on the semantic network, and this is what was found.

A decline with aging was evident in both fluency tasks, supporting previous reports that performance on fluency tasks reduce with age (Brickman et al., 2005, Lanting et al., 2009). However, the EC scored higher than YA in the naming task, which was not what was expected as most research reported either no age effect (Cruice et al., 2000, Welch et al., 1996) or a decline once people were in their 70s (Albert et al., 1988, Zec et al., 2005). As the mean age of the participants in the current study was 76 years, see some decline with naming in this group should be apparent. The regression analysis does indicate that, in the elderly, there is a negative relationship between aging and naming scores, although less than 1% of the variance in scores was explained by this variable.

In summary, as expected, people with AD score lower than the healthy elderly on all tasks. The elderly produced lower scores on verbal fluency, which concurs with previous research, but were better than the young for confrontation naming, in contrast to what was expected.

No significant lexical fluency differences emerged between the sexes in any group. The findings with regards to the absence of sex differences in this task in people with AD is entirely consistent with that previously reported (Bayles et al., 1999; McPherson et al., 1999; Monsch et al., 1992; Ripich et al., 1995). However, they are in contrast to those findings that show a female advantage in the young (e.g., Burton et al., 2005; Elias et al., 1997; Weiss, Ragland, Brenninger, Bilker, Deisenhammer & Delazer, 2006) but concur with others reporting no sex differences in this task (e.g. Brickman et al., 2005; Halari et al., 2005; Robert & Savoie, 2006). Closer examination of the previously published research, however, reveals that in those studies where a female advantage emerged, the participants had been required to *write down* their responses whereas those where no sex difference was apparent had asked for verbal responses. The current study instructed participants to respond aloud so, given the previous findings, no significant sex difference should have been apparent, and this was the case.

An absence of sex differences in this task in the EC group mirrors the findings in the YA and agrees with much of the published research, although a female advantage has previously been reported by Elias et al. (1997), Gerstorf et al. (2006) and Monsch et al. (1992). Elias et al. (1997), however, found that although men performed better than women sex only accounted for 1% of the variance in this test a figure that also emerged on the regression analysis herein. Furthermore, their study included 1,805 participants and they failed to adjust for multiple testing, even though they performed a large number of comparisons.

Therefore, they were more likely to detect even a small effect size as significant and they increased the chances of making a Type-I error. Gerstorf et al. (2006) found no significant sex differences until after adjusting for education which resulted in a female advantage, although other researchers failed to find any differences even after adjusting for education (e.g., Mathuranath et al., 2003).

When examining the total scores in semantic fluency there were no sex differences in any of the groups. This is what was expected, based on previous research (e.g. Robert & Savoie, 2006 (young); Gerstorf et al., 2006 (EC); Bayles et al., 1999 (AD)). However, a female advantage for fruit did emerge in both the EC and YA. A female advantage for fruit has previously been reported in the young (e.g. Cameron et al., 2008; Capitani et al., 1999; Robert & Savoie, 2006) but not in the elderly. There were no sex differences in animal naming which, again, largely concurs with previous research. Although Wiederholt et al., 1993 reported a male advantage in the elderly for naming animals (the only study that has) and Welsh-Bohmer et al. (2009) reported a female advantage, most researchers reported no sex difference for animal fluency in EC (e.g. Beinhoff et al., 2008; van Hooren et al., 2007; Lanting et al., 1999; Snitz et al., 2009). Cameron et al. (2008) and Capitani et al. (1999) found that young men were better than young women at naming tools but the current study found no such effect and nor did Moreno-Martinez et al. (2008). Cameron et al. (2008) did not impose a time restriction on their participants and this may have had a differential effect on men and women: perhaps women were more likely than men to stop early.

None of the categories showed a sex difference in the AD group, a finding partly consistent with other researchers (Bayles et al., 1999 (fruits and animals); Beinhoff et al., 2008 (animals), Cameron et al., 2008 (animals); McPherson et al., 1999 (animals); Perneczky, 2007 (animals)). However, Henderson et al. (1994) and Moreno-Martinez et al. (2008) both reported a male advantage for animal naming in people with AD. It is unclear why the results of these studies would differ from other published papers and the current one, especially as the sex difference is not even close to being significant – the effect size is practically zero (*d*=-0.02). The effect size derived from the Henderson paper is small (*d* =0.20) but they had a large sample size of 377 females and 270 males making it more likely that a small effect is found to be significant. However, the Moreno-Martinez study (33 females and 28 males) produced a moderate effect size of *d*=0.60. The AD patients in the Henderson and Moreno-Martinez papers were more severely affected by the disease than the current study (mean MMSE 17 in the former and 19 for females, 21 for males in the latter) so it may be that sex differences, favouring males, in animal naming would emerge at later stages of the disease process.

The findings of the current study are consistent with imaging research which showed no gross differences in the pattern of activation during verbal fluency tasks between male and female participants (Schlosser et al., 1998)

A significant male advantage in confrontation naming was apparent in in the AD group, with a moderate effect size (d = -0.62) and this was not due to acuity differences. Furthermore, sex was a significant predictor, accounting for 8% of the variance in scores in this task. This supports Buckwalter et al. (1996), Henderson et al., (1994), McPherson et al., (1999) and Ripich et al., (1995)who all reported a male advantage, albeit on the Boston Naming Test (BNT). Interestingly, these researchers claim this advantage to be contrary to expected findings although no female advantage had been previously reported in this test. In contrast, Bayles et al. (1999) Beinhoff et al. (2008) and Perneczky et al. (2007) found no sex differences in naming in AD participants. The test used by Bayles et al. (1999) only contained 18 items which may not be enough for a difference to emerge. Whilst Perneczky et al. (2007)'s male participants did score higher than women and this was approaching significance (p=0.06). The Beinhoff et al. (2008) study only included participants with mild AD (mean = 25.1). Furthermore, although they do not indicate which version of the BNT they used, the mean scores even in the healthy group are low (14.8) suggesting that they used a short version of this test.

Contrary to previous research, where a male advantage for confrontation naming has been reported in both the young and the old, a sex difference in this task did not emerge in either of these groups. The previous findings may reflect a sex bias in the BNT. Randolph et al. (1999) identified 18 items on the BNT (out of 60) where men performed significantly better than women and four where the opposite was true. They claimed that the sex difference they found was due to the preponderance of these male-biased items. It is standard practice that the test is stopped once participants get six consecutive incorrect responses. Randolph et al. (1999) claimed that the items favouring women were to be found near the end of the test, so they were less likely to reach these items before the test is stopped, again systematically biasing the results. The results of the current study do appear to show an aging deterioration in naming scores of women relative to men, however: young women scored higher than young men but in the EC group the men scored higher.

With regards to sex differences, therefore, very few of these emerged. The absence of any significant sex differences in any group for verbal fluency supports the notion of a similar pattern of cognitive deficits for men and women. However, the emergence of a male advantage for confrontation naming in AD suggests at least one domain in which women are more adversely affected by the disease than are men. There is also some evidence for a female disadvantage in AD in category fluency: both young and elderly women score significantly higher than men for fruit naming, but this difference was not significant in the AD group. Furthermore, the effect sizes for sex differences in the elderly for category fluency overall was d = 0.39 favouring women but was practically zero in the AD group, suggesting that women's scores are declining relative to men's.

So how does the role of sex compare to other factors examined in predicting verbal scores? The regression analysis shows IQ to be far the most important predictor of scores in the tasks examined, explaining as much as 38% of the variance in some cases. This is hardly surprising given that the test used measures verbal IQ, nevertheless the NART has been shown to be a good assessment of overall IQ. In the AD group, disease severity is also a strong predictor of verbal abilities explaining between 6 and 19% of variance. However, neither age nor sex contribute significantly to scores on most tests indicating that aging and sex differences do not play an important role in verbal abilities.

The make-up of the young group presents an important limitation to this study. The majority of the women included in this group were psychology graduates at the University of Hertfordshire. The proportion of men available from this population was small and a disproportionate number of male participants were recruited in this way. Instead, they were obtained via friends and colleagues of the author. Hence the men in this group were significantly older than the women. The effect of age was controlled for in the MANCOVA but the current study still produced unexpected findings in the young group (the young performing worse than the elderly in confrontation naming and the absence in YA of sex differences in this task). These results may reflect some, other, difference(s) between the sexes in this group such as experience, level of education and/or occupation. This possible influence of confounding variables demonstrates the importance of achieving equivalence in male and female participants when examining sex differences.

As already discussed, the BNT is more widely used than the GNT and the former may have a sex bias favouring males which is reflected in previous findings. A study comparing scores on BNT and GNT would address this question. Alternatively, it may be that there are no sex differences in this task. There were only two published studies examining sex differences in the young for naming, hardly a robust finding. Studies that support a null hypothesis are not so likely to be published (the file drawer problem). It may be, therefore, that other research also failed to find any sex differences in this task but the results have not been disseminated. The absence of sex differences in a domain is of as much interest as the appearance of them, especially as claims of a female advantage for verbal tasks have been made for many decades.

This study aimed to identify sex differences in people with AD on verbal tests, and to examine whether the relative performance of men and women on such tests mirrored those found in the healthy population, in particular in the elderly. Despite claims by some authors that women with AD show a greater deficit in verbal tasks than do men with AD, this claim has not been supported by the current study. The absence of sex differences in verbal fluency in the AD group reflects that found in the elderly and in the young. Furthermore, the significant sex difference in the AD group for confrontation naming was in the same direction as found in the elderly (i.e. favouring males), albeit in the elderly the difference was not significant. The results for confrontation naming are in contrast to those previously reported and it would be interesting to examine whether previous findings of a male advantage were due to a sex bias in the BNT, particularly as the test is so widely used as a measure of cognitive decline in the elderly and those with AD.

6. Sex differences in facial emotion recognition in Alzheimer's disease

6.1. INTRODUCTION

Previous chapters have illustrated that differences in cognitive abilities between men and women have been widely reported. Less extensively researched is the extent to which such differences are found in the recognition of facial emotions and, if present, whether such sex differences are also found in people suffering from Alzheimer's disease (AD).

It has long been reported that there are sex differences in cognitive abilities, the most common claims being that men have better visuospatial abilities (e.g., Hirnstein, Bayer & Hausmann, 2009; Voyer, Voyer & Bryden, 1995) whilst women have better verbal skills (e.g., Lewin, Wolgers & Herlitz, 2001, Torniainen, Suvisaari, Partonen, Castaneda, Kuha, Perala et al., 2010; Weiss, Kemmler, Deisenhammer, Fleishacker & Delazer, 2003). However, these putative sex differences have been questioned, particularly in the domain of verbal abilities (see Review chapter for a full review of the literature).

If sex differences in cognitive abilities do exist, does it then follow that the manifestation of cognitive deficits associated with AD present differently for men and women? The research into sex differences in AD is scarce but suggests that men with AD maintain their abilities on visuospatial tests whilst women lose their verbal advantage (for a review see Chapters 2 and 3).

Facial expressions have been said to provide the most accessible information about an individual's affective state (McLellan, Johnston, Dalrymple-Alford & Porter, 2008).

Consequently, it has been suggested that the poor interpersonal behaviour seen in dementia patients may arise from difficulties in facial emotion recognition (FER: Shimokawa, Yatomi, Anamiu, Torii, Isono, Sugai et al., 2001). Deficits in FER have important consequences in the quality of life for people with AD and their carers. In a regression analysis, Phillips, Scott, Henry, Mowat, & Bell (2010) identified FER as a significant predictor of quality of life, using the Quality of life in Alzheimer's Disease Scale (Logsdon, Gibbons, McCurry & Teri, 2002). Moreover, a recent study has shown that one of the most significant predictors of caregiver burden is FER deficits in patients (Miller, Miosh, Savage, Lah, Hodges & Piguet, 2012).

Most studies of FER focus on six universally expressed and recognized expressions: anger, disgust, fear, happiness, sadness and surprise. In line with other cognitive deficits, AD patients are impaired in FER (e.g., Bediou, Ryff, Mercier, Milliery, Hanaff, d'Amato et al., 2009; Phillips et al., 2010, Henry, Thompson, Ruffman, Leslie, Withall, Sachdev et al., 2009, Weiss, Kohler, Vonbank, Stadelmann, Kemmer, Hinterbauer et al., 2008) with the most frequently reported deficits in recognition being for the emotions of fear (Burnham & Hogervorst, 2004; Henry, Ruffman, McDonald, O'Leary, Phillips, Brodaty et al., 2008; Lavenu, Pasquier, Lebert, Petit & Van der Linden, 1999; Phillips et al., 2010, Weiss et al., 2008) and sadness (Burnham & Hogervorst 2004; Hargrave, Maddock & Stone, 2002; Phillips et al., 2010; Weiss et al., 2008) (See Table 2.9).

Limited research has been published examining sex differences in FER and the findings are inconsistent (see Table 2.7). In the general population some studies have shown that women perform better, being more accurate and faster at FER relative to men (e.g., Hall Hutton & Morgan, 2010; Williams, Mathursul, Palmer, Gur,Gur & Gordon, 2009).

Montagne, Kessels, Frigerio, de Haan & Perrett (2005) examined accuracy and sensitivity in FER, with women performing better than men on both. However, Scholten, Aleman, Montagne & Kahn (2005) did not find women to be more sensitive to FER than men although they were more accurate. Sex differences in accuracy are mostly contained to negative emotions such as fear (Hall & Matsumoto, 2004; Williams et al., 2009), anger (Mill, Allik, Realo & Balk, 2009; Teng, Lu & Cummings, 2007), sadness (Hall et al., 2010; Williams et al., 2009) and disgust (Hall & Matsumoto, 2004). Moreover, women have been shown to be faster than men in recognition of these negative emotions (Hampson, van Anders & Mullin, 2006; Williams et al., 2009) even after controlling for perceptual speed (Hampson et al., 2006). However, there have been reports of equivalent performance by men and women in FER (Grimshaw, Bulman-Fleming & Ngo, 2004; Sullivan, Ruffman & Hutton, 2007; Wong, Cronin-Golomb & Neargarder, 2005) although these researchers only analysed total scores and this may have masked sex differences on individual emotions if men scored higher on some emotions and women on others.

AD is a condition that predominantly affects the elderly so it is necessary to interpret any sex differences found in AD in light of those that may exist in the elderly population. Research shows that as people age, they have lower accuracy in tasks of FER than younger participants (Ruffman, Ng, & Jenkin, 2009; Sullivan et al., 2007; Williams et al., 2009) other than for the disgust emotion where the elderly regularly outperform YA (Circelli, Clark, & Cronin-Golomb, 2013; Suzuki & Akiyama, 2012; Wong et al., 2005). However, there has been little interest in whether sex differences emerge for FER in the elderly: only two papers have examined this. Mill et al. (2009) reported that in the elderly being female was a significant predictor of FER for anger, happiness and contempt but not for fear, disgust sadness or surprise whereas Calder et al. (2003) reported poorer recognition of fear by men that continued into old age. Research in AD is even scarcer with no papers reporting data on sex differences in this domain.

The aim of this study, therefore, was to examine how AD impacts FER, specifically to identify whether there is a deficit in AD compared to the elderly and whether there are deficits in FER between men and women with AD. To set these findings in context, this study was also interested in whether sex differences in FER exist in the healthy elderly and young.

6.2. METHOD

6.2.1. PARTICIPANTS

There were three participant groups. Demographic details of each group are given in Table 6.1.

PATIENTS

Fifty-two AD patients (26 male, 26 female) were recruited via outpatient clinics at the QEII Hospital (in Welwyn Garden City) and Lister Hospital (in Stevenage). All participants had been assessed for probable AD under NICE criteria (NICE, 2007) which includes elimination of other possible pathologies by means of a detailed assessment of the history/onset, detailed neuropsychological assessment and, in some cases, neuroimaging. Inclusion criteria were that participants have a score on the Mini Mental State Examination (MMSE: Folstein, Folstein & McHugh, 1975) between 13 and 28 and were judged by their treating clinician to have the capacity to consent. Patients scoring above 28 or below 13 on the MMSE were excluded on the basis of showing very mild cognitive impairments or too severe a cognitive impairment respectively. Moreover, an MMSE score of 13 is viewed as the cut-off point for capacity (Whelan, Oleszek, Macdonald & Gaughran, 2009). One participant was removed from this group as he was identified as suffering with young-onset dementia and was much younger than the rest of the group (52 years of age) leaving 51 participants.

TABLE 6.1 MEAN ±SD FOR DEMOGRAPHIC FACTORS AND MMSE SCORES OF THE PARTICIPANTS

Group	**AD**		**EC**		**YA**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
N	**25**	**26**	**28**	**26**	**13**	**57**
Age	80.04 ±6.62	80.04 ±7.57	76.21 ±7.37	76.54 ±5.45	22.46 ±7.34	21.65 ±7.18
IQ	106.79 ±8.41	106.58 ±7.78	116.25 ±7.03	116.23 ±5.82	111.62 ±6.09	108.95 ±6.49
Years of Education	10.80 ±1.87	11.27 ±2.39	11.64 ±1.83	11.38 ±1.70		
HADS	7.20 ±5.46	6.38 ±5.58	6.54 ±4.64	6.50 ±4.42		
MMSE	20.80 ±4.91	21.00 ±4.29	28.89 ±1.26	29.27 ±0.67		

Note: AD = Alzheimer's disease. EC = Elderly Controls. YA = Young Adults. HADS = Hospital Anxiety and Depression Scale. MMSE = Mini-Mental State Examination.

Controls

There were 2 control groups: an elderly control group (EC) and a young group (YA).

Elderly Controls

The EC group was recruited from a list of healthy elderly individuals who had volunteered through local GP surgeries to participate in research; some spouses/partners of AD patients also volunteered. There were 54 participants in this group (28 male and 26 female).

Young Adults

The YA group was recruited from the undergraduate population at the University of Hertfordshire through their research participation system for which they received course credit. There were 70 participants in this group (13 male and 57 female).

For all groups, participants had normal, or corrected to normal, vision, and spoke English as their first language.

There was a significant difference between AD and EC groups for age ($t\ (103) = 3.24$, $p<0.01$), with the AD group being older; IQ ($t(102) = -6.75$, $p<0.001$), with ECs scoring higher and MMSE scores ($t\ (103) = -12.84$, $p<0.001$). There was no significant difference between the groups on level of education ($t(102) = -1.26$, $p= 0.31$) or Hospital Anxiety and depression (HADS) score ($t(102) = 0.27$, $p=0.79$). Therefore, age and IQ were added to the subsequent multivariate analysis of covariance (MANCOVA) analyses to control for these variables.

There was a significant difference between YA and EC groups for age, as expected, ($t\ (122) = 43.88$, $p<0.001$) and IQ ($t(122) = 5.83$, $p<0.001$), with the EC scoring higher. Therefore, IQ was added to the subsequent MANCOVA analyses to control for this variable.

Independent t-tests showed that there were no significant differences between men and women in any group for age, IQ, level of education, HADS scores or MMSE scores (see Table 6.1 for demographic details).

6.2.2. MATERIALS

MINI MENTAL STATE EXAMINATION (MMSE)

Elderly participants (AD and EC) were screened using the MMSE to determine the degree of disease severity in the AD group and to control for undiagnosed memory deficits in the EC group. The MMSE is used to measure cognitive impairment and is used as a measure of dementia severity by clinicians. The maximum score is 30.

VISUAL ACUITY TEST OF THE CORTICAL VISION SCREENING TEST (CORVIST: JAMES, PLANT & WARRINGTON , 2001)

The CORVIST was used to check visual acuity in the Elderly participants. The test consists of six rows which contain two each of three shapes (circle, square, triangle). A viewing window is used to reveal only one shape at a time, and participants are required to move along each row saying out loud the name of the shape. If participants hesitated, the researcher reminded the participant what the names of the shapes were (i.e. they were asked whether the shape was a circle, square or triangle). This was to ensure that an incorrect answer was not due to naming difficulties. The rows decrease in size. If a participant was unable to read the top row , then testing was stopped.

NATIONAL ADULT READING TEST (NART: NELSON, 1978)

The NART was used to estimate IQ or pre-morbid IQ. This test requires participants to read aloud a list of 50 unusual and/or irregular words. It has been shown to be a valid estimator of premorbid ability in mild to moderate dementia (McGurn, Starr, Topfer, Pattie, Whiteman, Lemmon, Whalley & Deary, 2004).

Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983)

Elderly participants were screened for depression and anxiety using the HADS to rule these out as possible confounding factors since depression can be associated with poor performance on FER (Weiss et al. 2008).

The Facial Expressions of Emotions: Stimuli and Test (FEEST: Young, Perrett, Calder, Sprengelmeyer, 2002)

This was the measure of FER. A total of 60 pictures were presented showing 10 different models (six female four male) each showing the 6 basic emotions (happiness, surprise, fear, sadness, disgust, anger) from the Ekman and Friesen's pictures of facial effect series (see Figure 6.1).

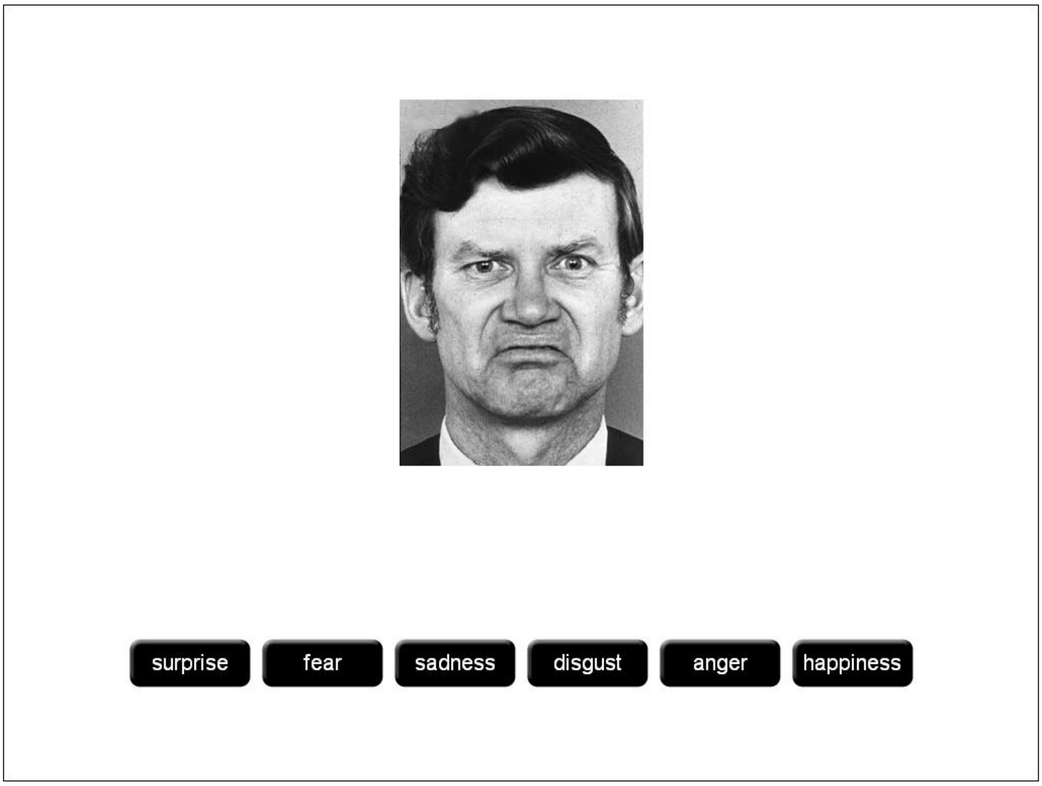


FIGURE 6.1 EXAMPLE OF IMAGE PRESENTED TO PARTICIPANTS (THIS ACTOR IS EXPRESSING THE EMOTION DISGUST)

6.2.3. Procedure

The study was approved by the National Health Service National Research Ethics Service.

Once patients had been identified as being potentially suitable, clinical staff introduced them to the researcher. Participants were then given detailed information on the research, including an information sheet to read. They were given the opportunity to ask questions and, If they agreed to take part, an appointment was made for the testing.

All patients and elderly controls completed the task in their own homes, seated comfortably at a table. The Young Adults, recruited via the University of Hertfordshire, completed the study in a study cubicle containing a desk and a computer. At the testing session, participants were once again told about the research and were given the opportunity to ask questions. If they agreed to take part, they were asked to sign the consent form.

The first tasks were the CORVIST, HADS and the NART. There then followed a series of cognitive tests (most of which will not be considered within this paper) including the FEEST. (See Appendix 1 for a list of all the tests that were administered.) The FEEST was administered on a computer with a touch screen. Faces were presented in a random order and participants were asked to select which label (out of six) best described the emotion displayed. Each face appeared for 5 seconds but participants could take as long as they liked to make their selection. Participants could either touch the label on the computer screen or tell the researcher which emotion was being displayed.

6.2.4. Data Analysis

Statistical analyses were performed using SPSS for Windows v.19.0.

Participants' total scores on the FEEST across all emotions were analysed using a 2 (sex: male, female) x 3 (group: AD, EC, YA) analysis of variance (ANOVA). Subsequently, separate MANCOVAs were conducted to detect differences on individual emotions between EC and YC and AD and EC and then for each group to identify sex differences. Covariates were those that had been identified in the t-tests as showing significant group differences.

In order to evaluate the relative importance of other individual differences, multiple regression analyses were run including the independent variables of sex, age, IQ and MMSE scores.

6.3. RESULTS

Descriptive Statistics are presented in Table 6.2. For all groups combined, women were more accurate than men at identifying facial emotions with a mean score of 45.78/60 (±6.92) for women compared to 42.20/60 (±7.96) for men. However, this varied across groups and across emotions. In the AD group women were more accurate than men for all emotions other than anger and fear. And in the EC group women outperform men on all emotions other than happiness and sadness. For the YA, women score higher than men for anger, disgust, sadness and surprise.

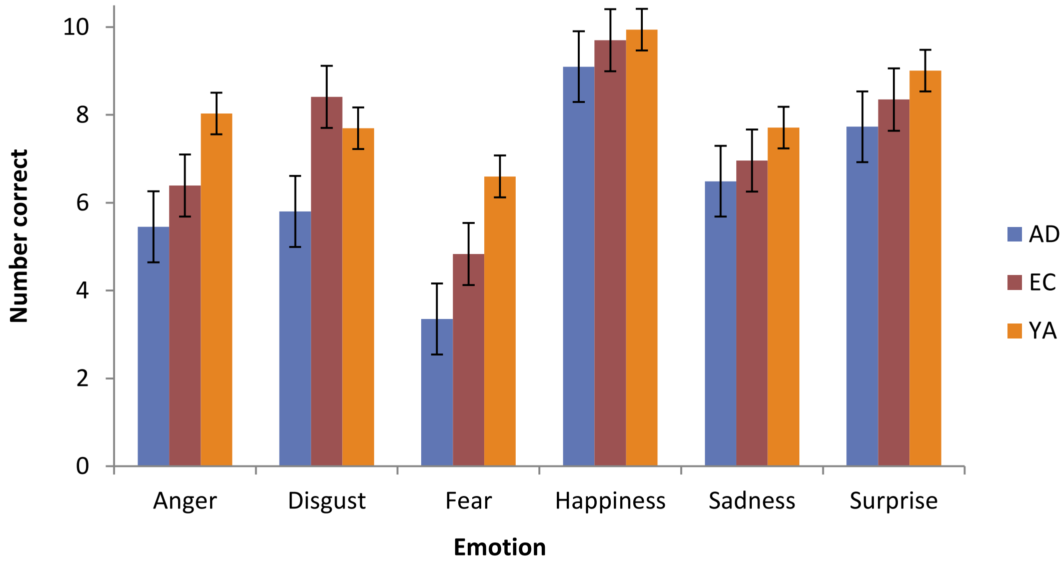


FIGURE 6.2 MEAN SCORES FOR EACH EMOTION, BY GROUP (MAXIMUM SCORE = 10)

TABLE 6.2 DESCRIPTIVE STATISTICS: MEAN ±SD FOR FACIAL EMOTION RECOGNITION BY GROUP AND BY SEX.

	AD		**EC**		**YA**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
N	**25**	**26**	**28**	**26**	**13**	**57**
Overall	37.12 ±8.17	38.69 ±6.39	44.14 ±6.64	45.19 ±5.87	47.77 ±3.75	49.28 ±4.77
Anger	5.52 ±1.87	5.38 ±2.30	5.93 ±2.12	6.88 ±1.97	7.31 ±1.32	8.19 ±1.47
Disgust	5.76 ±2.37	5.85 ±2.62	8.39 ±1.67	8.42 ±1.50	7.22 ±1.88	7.81 ±1.74
Fear	3.44 ±2.00	3.27 ±2.03	4.79 ±2.04	4.88 ±2.01	7.15 ±1.86	6.47 ±2.38
Happiness	8.92 ±1.41	9.27 ±1.22	9.71 ±0.54	9.69 ±0.84	10.00 ±0.00	9.93 ±0.26
Sadness	6.16 ±2.51	6.81 ±2.00	7.25 ±1.74	6.65 ±2.40	7.23 ±2.35	7.82 ±1.70
Surprise	7.32 ±2.41	8.12 ±1.34	8.07 ±1.54	8.65 ±0.94	8.85 ±1.28	9.05 ±1.08

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults

Neither the ANOVA nor the MANOVA revealed any significant group by sex interactions so these factors were examined separately.

6.3.1. GROUP DIFFERENCES

The ANOVA revealed a significant group effect on total FEEST scores (F (2, 172) = 50.35, p<0.001), with significant differences between the AD and EC groups (EC scoring higher) and the EC and YA groups (YA scoring higher).

As there were significant group mean differences on age and IQ (between the AD and EC groups) and age (between the EC and YA groups) MANCOVAs were conducted to examine individual emotions including these variables as covariates (see Table 6.3 for details of effect sizes). A significant difference emerged between the AD and EC groups for disgust only (F (1, 100) = 10.02, p<0.01) with the EC scoring higher than the AD group.

The young and elderly groups differed significantly at recognizing anger (F (1, 121) = 35.97, p<.001), fear (F(1,121) = 44.32, p<0.001), happiness (F (1, 121) = 11.48, p<0.001), sadness (f(1,121) = 16.09, p<0.001) and surprise (F(1,121) = 10.01, p<0.01) with the YA scoring higher than EC. Although the EC scored higher than YA on disgust recognition, this difference was not significant (F(1,121)= 0.79, p=0.38).

TABLE 6.3 EFFECT SIZES (COHEN'S *D*) FOR GROUP DIFFERENCES ON THE MANCOVA FOR EACH EMOTION.

Emotion	AD vs EC(1)	EC vs YA(2)
Anger	0.10	1.16***
Disgust	0.70**	-0.17
Fear	0.23	1.28***
Happiness	0.09	0.65***
Sadness	0.42	0.78***
Surprise	0.08	0.61**

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Adults ** $p<0.01$, ***$p<0.001$. (1)negative value indicates an AD advantage. (2) negative value indicates an EC advantage.

6.3.2. SEX DIFFERENCES

A MANOVA revealed no significant effect for sex on correct scores on FEEST overall or for any specific emotion in any group (See table 6.5 for effect sizes).

TABLE 6.4 EFFECT SIZES (COHEN'S *D*) FOR MEN VS. WOMEN WITHIN EACH OF THE THREE GROUPS.

Emotion	AD	EC	YA
Anger	-0.07	0.47	0.62
Disgust	0.04	0.02	0.33
Fear	-0.09	0.05	-0.30
Happiness	0.27	-0.03	-0.30
Sadness	0.29	-0.29	0.33
Surprise	0.42	0.46	0.18

Note: AD = Alzheimer's Disease. EC = Elderly Controls. YA = Young Controls. A negative figure indicates a male advantage

6.3.3. Regression analyses

AD Group

The model for total scores was significant ($F(4,45)=3.50$, $p=0.01$), explaining 23.7% of the overall variance in FER. Only IQ score was a significant predictor, explaining 8% of the variance. Age explained 3%, MMSE scores 3% and sex explained 2%.

Elderly Controls

The model for total scores was significant ($F(4,49)=11.07$ $p<0.001$), explaining 47.5% of the overall variance in FER. IQ score was the most significant predictor, explaining 44% of the variance, whereas sex only explained 1% of the variance in overall scores.

Young Adults

The model for total scores was significant ($F(3,66)=3.79$, $p=0.01$), explaining 14.70% of the overall variance in FER. Only IQ score was a significant predictor, explaining 8% of the variance. Age explained 1%, and sex explained 3%.

6.4. DISCUSSION

AD patients were poorer at FER than elderly controls for all emotions combined and specifically for disgust whereas the elderly were impaired, relative to the young, for all emotions other than disgust. No sex differences emerged in any of the group for any emotion.

The current findings support previous research showing poorer FER overall in AD patients (e.g., Phillips et al., 2010 and Henry et al., 2009) but not that for the emotion disgust. A deficit for disgust was reported by Hargrave et al. (2009) however, most published research has shown there to be no AD deficit for the disgust emotion (Burnham & Hogervorst, 2004; Henry et al., 2008; Phillips et al., 2010) unless faces are morphed (Phillips et al., 2010).

Our findings for FER of disgust in the elderly group also contradicts previous research which showed that recognition of this emotion improves with age (Calder, Keane, Manly, Sprengelmeyer, Scott, Nimmo-Smith et al., 2003; Circelli et al., 2013; Suzuki & Akiyama, 2012; Wong et al., 2005). While the elderly scored higher on this emotion than the young, the difference was not significant and the effect size was small. However, it is the only emotion where an aging decline was not evident. There is converging evidence from neuropsychology and imaging studies that recognition of disgust involves the basal ganglia and the insula (Calder, Young, Keane & Dean, 2000; Phillips et al., 1996; Sprengelmeyer, Rausch, Eysel & Przuntek, 1998). Furthermore, the globus pallidus (in the insula) has been shown to be the structure most commonly activated in response to disgust (Murphy, Nimmo-Smith & Lawrence, 2003). The globus pallidus is relatively insensitive to aging (Calder et al., 2000) hence recognition of disgust is spared in EC.

It may be that AD does not specifically affect FER, per se, and that the FER problems seen in AD are a result of the aging process. This would explain why there was no AD impairment for any emotion other than disgust. Perhaps AD patients do not benefit from the relative sparing of the globus pallidus during aging so that their impairment in recognition of disgust when compared to the young is of the same magnitude as for other emotions? In fact, AD patients were significantly worse than the young on all emotions, including disgust and the effect sizes ranged between 0.55 and 1.58, with the effect size being 0.91 for the disgust emotion (data not shown).

Sadness and fear are those emotions that are most frequently reported to be susceptible to AD (see Table 2.9). Why did the current study differ from previous research with regards to these emotions? One reason may be that the current study made an adjustment for age and IQ. The regression analysis revealed IQ to be a significant predictor of overall FEEST scores so it is important to control for differences in IQ between the groups as was done in the current study. However, IQ was not controlled for in any previous study although Weiss et al. (2008) and Burnham and Hogervorst (2004) did covary age in their analysis. Weiss et al. (2008) used the Penn Emotion Recognition test, rather than the FEEST, and they had more than twice as many women as men in their sample and this may have confounded their results, particularly if women scored lower than men. Hargrave et al., 2002 found a deficit in AD for *matching* for both fear and sadness, but only for sadness in the emotion labeling task (the interest of the current study). Similarly, Burnham & Hogervorst (2004) found a difference for fear and sadness when participants were asked to match emotions but they found no differences in labeling these emotions.

In line with previous research, such as Ruffman et al. (2009) and Williams et al. (2009), the results showed that compared to young adults, elderly controls displayed impaired recognition of facial emotions overall. Furthermore, after controlling for IQ, elderly controls were worse than young adults at recognizing all emotions other than disgust. This concurs partly with previously published findings: in their review, Isaacowitz, Lockenhoff, Lane, Wright, Sechret, Riedel et al. (2007) claimed that the most reported deficits in the elderly were anger, sadness and fear (see Table 2.8 which confirms this).

This study found no sex differences overall and no significant emotion specific sex differences in any of the groups. There were no published papers that specifically examined sex differences in AD and only two papers concerned with the sex differences in the elderly. Some papers that investigated facial emotion recognition in these groups reported that their data showed no sex differences (e.g. Wong et al., 2007, Sullivan et al., 2007) and the findings of the present study concur with this finding.

Although previous research has identified sex differences in the young in the recognition of various emotions, the findings are inconsistent. Some previous studies report that the female advantage is larger for the negative emotions (Hampson et al., 2006; Scholten et al., 2006) which are less accurately identified than positive emotions (Vassallo, Cooper & Douglas, 2009). Consistent with this, the negative emotions of anger, fear and sadness were those for which sex differences have most frequently been reported, with about half of the papers examining these emotions reporting differences. The current analysis, however, does not concur with this as the effect sizes in the young are similar (around .3) for all emotions other than surprise and anger. Some previous studies report a female advantage for reaction times for anger, sadness and fear but not for accuracy (Hampson et al., 2006, Rahman, Wilson & Abrahams, 2004) which was the interest herein. Females have been shown to have faster processing skills than men (Hampson et al. 2006) and it may be that this more generic advantage is what was measured rather than a specific emotion processing effect. Nonetheless, Hampson and colleagues co-varied processing speed and reported that the sex differences in reaction times remained overall, though they did not report if the emotion specific differences remained.

Differences in the findings of the current study and other research may reflect task demands. Montagne et al. (2005) found a significant sex difference, favouring females, on sadness (but not on anger or fear) using a colour test with more modern faces than the

FEEST. Similarly, some findings of sex differences only become apparent using morphed faces, e.g. Calder et al. (2003) and Hall et al. (2010). Different findings may also arise due to methodological issues. Teng et al. (2007) reported male deficits on fear and sadness however their analysis of emotion specific sex differences included all their participants, including those with Mild Cognitive Impairment – multiple domain (MCI –MD). They identified that MCI-MD men were disproportionately poor at emotion recognition so their overall findings may reflect the poorer performance of these men. Three of the studies that report sex differences have very large sample sizes which are more likely to detect even small effect sizes as being significant. Mill et al. (2009) (176 males/431 females) reported female superiority on anger and happiness, Williams et al. (2009) (470 mean/530 women) a female advantage for fear and sadness and Hall & Matsumoto (2004) (126 males/237 females) a female advantage for anger, disgust, fear, happiness and sadness. However, the Mill et al. (2009) and Williams et al. (2009) papers did fail to detect any significant sex difference for several emotions.

One of the aims of conducting research is to examine areas where there appears to be no previous research undertaken. The lack of published papers reporting on sex differences in AD and the elderly, despite such differences being apparent in the young suggested a gap in the knowledge. Unfortunately it may be that research has been undertaken, but no effect found, in which case it is difficult to get published (the file-drawer effect). In the current case it might be that the reason why there has been no published research on sex differences in facial emotion recognition in Alzheimer's patients is not because it has not previously been examined, but that no sex differences exist. The effect sizes identified for sex differences in AD and the elderly are in most cases very small (all less than d = 0.50) so the non-significant finding probably reflects the true absence of any differences between men and women. However, in the young group, the effect size for sex differences for anger was moderate, at *d*=.62, but this was not found to be significant. Therefore there may be a lack of power in this study, alternatively it may reflect the imbalance in the ratio of males to females (13/57).

This chapter examined FER accuracy in AD patients relative to elderly controls and more specifically, whether any sex differences in the ability to recognize specific facial emotions emerged. There is evidence that facial emotion recognition deteriorates with age but AD patients seem not to demonstrate any additional deficits. With regards to sex differences, none were found in the either of the healthy populations or the Alzheimer's group. Nor was there any evidence to suggest that, for FER, women show the more adverse impact of AD apparent in visuospatial and verbal domains. The small effect sizes for sex differences that emerged in the elderly and AD groups suggest that the current findings may be indicative of the true position. Such an absence is as important to disseminate to the research community as a significant difference would be.

7. Conclusion

7.1. INTRODUCTION

This thesis is concerned with cognitive deficits in Alzheimer's disease (AD), specifically for verbal, visuospatial and facial emotion recognition (FER) tasks and, in particular, whether or not AD affects men and women differently. In any examination of cognitive performance in AD, the results need to be considered in light of that found in the healthy population; hence this thesis has examined the relative performance of elderly men and women.

Previous research has identified deficits in AD, compared to elderly controls, for the semantic tasks of confrontation naming and category fluency and these are apparent even in those mildly affected commensurate with the early damage to the temporal lobes. Lexical fluency deficits are not apparent until later, as these largely rely upon frontal lobe processes which are affected later in the disease process. A deficit in AD for visuospatial tasks has been shown as early as ten years before diagnosis. Lastly, AD patients are reported as being impaired on FER compared to elderly controls, but the results are conflicting, particularly when individual emotions are examined: deficits in recognition of fear and sadness are the most widely reported while recognition of disgust appears to be preserved.

Claims of sex differences capture the public's information with books on the subject, such as *Men are from Mars, Women are from Venus* by John Gray becoming bestsellers. However, if sex differences in cognition in the healthy population exist then there are important implications, e.g. in the areas of education, health and social policy. Sex differences in various cognitive domains in the healthy population have been extensively researched with the most widely held (and often cited) belief being that women are better than men at verbal tasks and males are better at visuospatial ones. However, close inspection of the literature reveals that evidence for sex differences in cognition is conflicting and dependent on the task used (see Chapter 2 for an extensive review).

Sex differences in the incidence of AD have been reported: several authors have reported a higher risk of developing AD in women than in men (e.g. Bachman et al, 1992; Andersen et al, 1999, Lobo et al, 2000) so it would not be surprising to find the cognitive performance of men and women are also affected differently by AD.

In fact, it is remarkable how few studies have reported comparisons of neurocognitive performance of men and women with AD. An extensive literature search identified only 15 published studies presenting data for men and women with AD in the domains of verbal and/or visuospatial abilities, and no studies comparing male and female performance in AD for FER. It was this apparent lack of interest in sex differences in AD that was the motivation for this research.

7.2. SUMMARY OF CURRENT FINDINGS

7.2.1. COGNITIVE DEFICITS IN AD

This body of work has largely supported previous research briefly outlined above (and in more detail in Chapter 2). As expected, participants with AD were worse than EC on all verbal and visuospatial tasks examined. However, although AD participants scored significantly lower than elderly controls when total FER scores were examined, the only specific emotion on which an AD deficit emerged was disgust – for all other emotions the difference was not significant. The FER findings would suggest that AD does not affect FER per se, but that there is something in particular about the disgust emotion which is vulnerable to the effects of AD.

7.2.2. SEX DIFFERENCES IN COGNITION

Sex differences were not apparent in the healthy groups for visuospatial, verbal or FER domains, and this is mostly consistent with what has been reported previously for those tasks used herein.

VISUOSPATIAL DOMAIN

Sex differences favouring men were found in the AD group for the ROCF copy and recall tasks. As the EC did not show any sex differences for the ROCF tasks, this represents a worsening of women's visuospatial abilities relative to men's. Further support for this was found even in those tasks where no significant sex differences emerged: with the exception of SSP (where the effect size is practically zero) either elderly women perform better than elderly men, but in the AD group men have the advantage, or the effect size for a male advantage found in the elderly increases in magnitude in the AD group (see Figure 7.1).

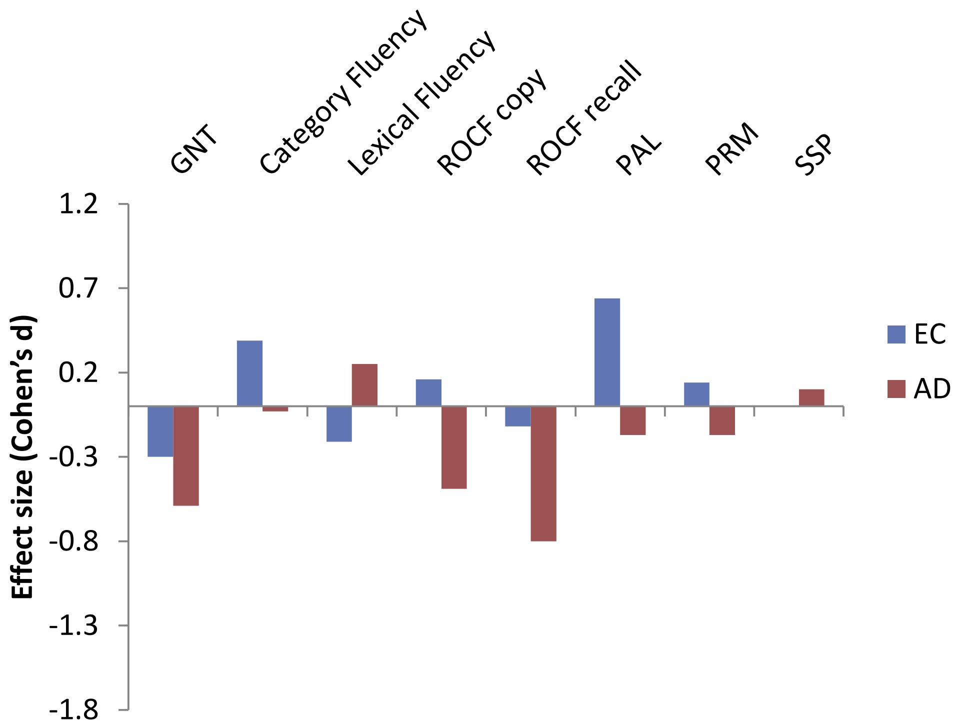


FIGURE 7.1 COMPARISON OF EFFECT SIZES (COHEN'S D) FOR SEX DIFFERENCES FOR EC AND AD GROUPS FOR VERBAL AND VISUOSPATIAL TASKS. A NEGATIVE FIGURE INDICATES A MALE ADVANTAGE. AD = ALZHEIMER'S DISEASE. EC = ELDERLY CONTROLS. GNT = GRADED NAMING TEST. PAL – PAIRED ASSOCIATES LEARNING. PRM = PATTERN RECOGNITION MEMORY. ROCF = REY-OSTERRIETH COMPLEX FIGURE. SSP = SPATIAL SPAN.

VERBAL DOMAIN

A Sex difference, favouring men, was found in the AD group for the confrontation naming task. Given the absence of sex differences in the healthy elderly, this suggests that women with AD demonstrate cognitive deficits over and above those found in men. Although category fluency did not show any significant sex differences, in the EC women scored higher than men, but in the AD group the mean score was practically identical. This trend was not found for Lexical fluency, however, where there was a superior male performance in the EC group but a higher mean score by women in the AD group.

There was a total absence of significant sex differences in FER in all both elderly groups. For most emotions the effect size was close to zero. There was no evidence that the performance of women with AD was declining to a greater extent than men (see Figure 7.2).

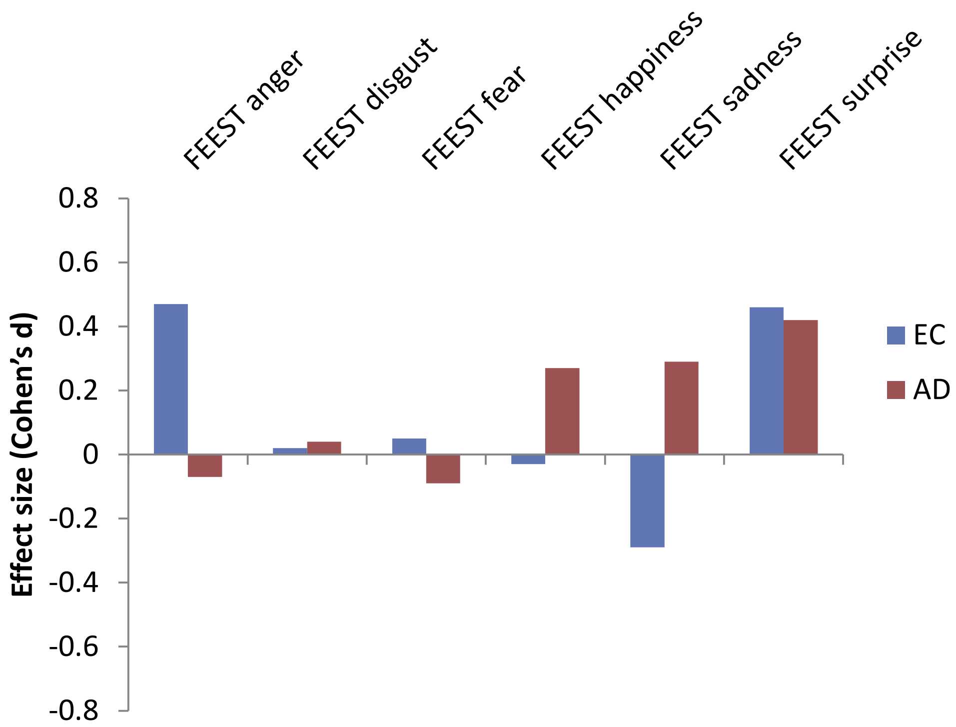


FIGURE 7.2 COMPARISON OF EFFECT SIZES (COHEN'S D) FOR SEX DIFFERENCES FOR EC AND AD GROUPS FOR FACIAL EMOTION RECOGNITION. A NEGATIVE FIGURE INDICATES A MALE ADVANTAGE. AD = ALZHEIMER'S DISEASE. EC = ELDERLY CONTROLS. FEEST = FACIAL EMOTION EXPRESSION: STIMULI AND TEST.

What is interesting is that there appears to be a worse impact of AD on women's abilities relative to men's on those tasks which appear early in the disease process, i.e. the visuospatial tasks and the semantic ones. These are also those tasks that demonstrate large group effect sizes (i.e. $d \geq 0.90$).

7.3. THE ROLE OF INDIVIDUAL FACTORS OTHER THAN SEX

What about the role of individual factors other than sex? In this dissertation, in running the inferential analyses, we have used co-varying as a tool to control for the possible confounding influence of IQ and age, where these have differed between groups and of course age has been examined throughout this thesis.

7.3.1. AGE

Previous research showed a decline in cognitive abilities with aging, so that, in general, the elderly perform less well than the young for both verbal and visuospatial domains, furthermore, the elderly are worse than the young for FER overall (see Chapter 2 for a review). The findings of the current study support these findings as the elderly were impaired compared to the young for FER (see Chapter 6), all visuospatial tasks (Chapter 4) and for verbal fluency (Chapter 5). However, a surprising advantage in the elderly for confrontation naming emerged: although previous research showed that this ability does not decline until participants are in their 70s an improvement was unexpected.

The regression analysis revealed age to be a significant predictor for category fluency with scores reducing with age in the elderly but increasing with age in the young. It explained 6% of the variance in EC and 3% in YA. It was the most important predictor of paired associates learning in the elderly, explaining 18% of the variance in this task, while in the YA it significantly predicted scores on the ROCF copy task. However, it was not a significant predictor in any domain and on any task in the AD group.

7.3.2. IQ

IQ has been shown to influence scores on cognitive tests (Albert, Heller & Milberg, 1988; Bird, Papadopoulou, Ricciardelli, Rossor and Cipolotti, 2004; Gallagher & Burke, 2007; Harrison, Buxton, Husain & Wise, 2000). Unsurprisingly, there is a strong association between verbal IQ and both verbal fluency (Bolla et al., 1990; Crawford et al., 1992) and confrontation naming (Albert et al., 1998; Bird et al, 2004) but IQ scores also lead to higher scores on the ROCF Copy and recall tasks (Gallagher & Burke, 2007).

In the AD participants, IQ was an important predictor of verbal and visuospatial performance, much more so than either age or sex, but not as much as for MMSE scores. However, on the FEEST IQ was the only significant predictor, possibly due to the verbal component in this task, i.e. the labels. Across all groups, the regression analysis revealed IQ to be the most important predictor (understandable given that the NART is a test of verbal IQ). However, it was also a significant predictor of scores on the ROCF copy task in the elderly both the ROCF copy and recall tasks in the young.

7.3.3. EDUCATION

Level of education Is often used as a proxy measure for IQ and authors have identified an association between level of education and visuospatial (Harrison et al.,2000; Wiederholt, Cahn, Butters, Salmon, Kritz-Silverstein & Barrett-Connor, 1993) and verbal (Harrison et al.,2000; van Hooren, Valentin, Bosma, Ponds, Boxtel & Jolles, 2007) abilities.

The initial regression analyses were run including level of education as a predictor for the AD and EC groups (these data were not collected for the young adults as most of them were educated to the same level). Level of education was not a significant predictor for any of the tests, for either group, so it was removed from the final analyses. The highest amount of variance explained by this factor was 3% (on the PAL and SSP tasks for both groups and on the ROCF copy task in the EC group) suggesting level of education does not contribute significantly to verbal, visuospatial or FER tasks in these groups.

The Regression analysis revealed that, in AD, sex was not the most important predictor of cognitive scores, when the individual variables of IQ, age and MMSE scores are also taken into account. Unsurprisingly MMSE score was the most important predictor closely followed by IQ for the verbal and FER tasks and sex for the visuospatial ones. Neither age nor level of education appear to have any great influence on cognitive performance.

7.4. REASONS FOR A MORE ADVERSE IMPACT OF AD ON WOMEN

What are the possible reasons for AD affecting women to a greater extent than men?

7.4.1. COGNITIVE RESERVE

One possibility is that men have greater cognitive reserve than men. Cognitive reserve has been defined as the amount of brain damage an individual can tolerate before reaching a clinical threshold for impairment (Katzman, 1993).

Individuals with greater reserve are hypothesized to sustain more AD-related neuronal damage before onset of symptoms and clinical diagnosis. Consistent with this hypothesis, several recent neuroimaging studies have reported differences in brain function for male and female AD patients who are at the same disease stage. The early neuropathological progression appears to be independent of sex, but female mild cognitive impairment patients showed an increased vulnerability to cognitive impairment earlier in the illness course than males and women with AD had greater cognitive impairment than men, despite an apparent equivalence in brain atrophy (Bai, Zhang, Watson, Yu, Shi, Zhu et al., 2009). Similarly, Perneczky et al (2007) found that men with AD had more pronounced and extensive pathology than women affecting the frontal, temporal and insular cortices as well as the hippocampus in the right hemisphere despite being at the same disease stage and showing no significant differences in general cognitive abilities.

Further support comes from post-mortem studies. Barnes et al. (2005) claimed that AD pathology is more likely to be clinically expressed as dementia in women than in men, as they found that each unit of global AD pathology increased the odds of clinical AD by more than 20 times in women compared with a 3 times increase in men. The association between AD pathology and clinical AD was significantly stronger in women than in men.

Intelligence, education and occupational level are believed to be major active component of cognitive reserve (Whalley, Deary, Appleton & Starr, 2004). In this study, men and women did not differ in their levels of education or IQ. But, perhaps there is something about the differences between the employment histories of men and women that is causing them to have less cognitive reserve?

It has been shown that people with lower mental demands at work show stronger cognitive decline than those with many mental demands at work (Bosma et al., 2003). Also, AD patients with more demanding occupations (Stern et al., 1994) had greater extent of brain pathology when dementia severity was controlled. The cohort of women currently presenting with AD did not work in the same way as men did. They were largely at home with their families. Of course, some women did work and it would be useful to examine whether there are any differences in cognitive performance between women who had demanding jobs and those who were mainly homemakers.

Data on work experience was collected from a limited number of participants. In order to identify whether the reason why women are more adversely affected than men is to do with their occupation history, female participants were split into those that were either homemakers or did work that fitted in with being a mother, such as school assistant, etc., and those that followed a career. The distinction was a crude one because the data was not recorded rigorously and the veracity of some of the self -reports, particularly with the AD participants, was not entirely clear. An ANOVA was run for each of the elderly groups which revealed no significant difference in mean scores on any task between those who had careers outside the home and those who were mainly homemakers so any difference in male and female performance seems unlikely to arise due to different working histories, although a more rigorous collection and analysis of data would address this question better.

7.4.2. Performance factors

In the current research, there were no sex differences in any group for the lexical fluency task. Previous research has in some cases reported a female advantage in this task whilst in others there was no sex difference (see Section 2.3.1). Closer examination of the published studies revealed that, where the authors identified how participants were asked to respond, in those studies reporting a female advantage participants had been asked to write down their answers (see Table). In those studies where participants had been asked to respond verbally (as in the current study) men and women had equivalent scores, with one exception - Weiss (2006).

TABLE 7.1 DETAILS OF HOW PARTICIPANTS WERE ASKED TO RESPOND (ORALLY OR IN WRITING) IN STUDIES REPORTING SEX DIFFERENCES IN LEXICAL FLUENCY.

Study	Letters Used	Oral/Written	Result	Notes
Nowak (2011)	C,F,L	Oral	F=M	COWA
Hausmann (2009)	L,P	Written	F>M	LPS
Lanting (2009)	C,F,L	Oral	F=M	COWA
Clark (2006)	F,A,S	Oral	F=M	Computerised battery
deFrias (2006)	A, M (5 letters)	Oral	F=M	
Robert (2006)	P,R,V	Oral	F=M	(2 mins)
Thilers (2006)	A, M (5 letters)	Not specified	F>M	
Van der Elst (2006)	M (4 letters)	Not specified	F=M	
Weiss (2006)	F,A,S	Oral	F>M	COWA
Brickman (2005)	F,A,S	Oral	F=M	Computerised battery
Burton (2005)	S 4 letters, C	Written	F>M	Thurstone (1962) S (5 mins) C (4 mins)
Halari (2005)	F,A,S	Oral	F=M	
Rahman (2003)[1]	P,R,W	Oral	F=M	COWA
Weiss (2003)	B,A,S	Written	F>M	
Lewin (2001)	F,A,S	Written	F=M	
Harrison (2000)	B	Oral	F=M	COWA
Herlitz (1999)	F,A,S	Written	F>M	
Neave (1999)	L	Not specified	F=M	
Tombaugh (1999)	F,A,S	Oral	F=M	
Janowsky (1998)	F,A,S	Oral	F=M	

Note: [1]. Results are those for heterosexual men and women. COWA = Controlled Oral Word Association COWA. LPS = Leistungsprufsystem.

The absence of a sex difference for confrontation naming in the young population in the current study did not concur with previous reports of a male advantage. However, there were only two published papers reporting on male and female performances. Both these papers used the Boston Naming Test (BNT) for their study whilst the GNT was used here. It has been suggested that the BNT is biased in favour of men and this is the reason for the apparent male advantage (REF –Randolph?). Those items that men were more likely to name correctly than women appeared early in the test and those favouring women towards the end. It is the convention that the test is stopped after six errors so women may be disadvantaged by having those items they found more difficult early in the test. Alternatively, it may be that there are, in fact, no sex differences in naming but that this finding has not been disseminated as it is difficult to get null results accepted for publication: given the interest in differences between the sexes it seems unlikely that no others have examined the relative performance of men and women on this task.

7.5. LIMITATIONS OF THE CURRENT RESEARCH

The intention when this body of research was designed was to recruit young participants from the University of Hertfordshire's psychology undergraduates. In line with other universities, undergraduates are required to participate in psychology research as part of their course. This proved to be problematic with regards to the recruitment of male participants. The data for the FER phase of the research was analysed first. At that stage there were 57 female and 13 male participants, a big imbalance that may have affected the power of the study and could explain why apparently large effect sizes were not significant. When it became apparent that it was going to be difficult to recruit any more male undergraduates male participants were sought from staff at the Metropolitan Police Training college. Although this reduced the imbalance (there were now 45 males and 59 females), the mean age for men in this group was significantly higher than for women. This was addressed by removing the oldest 5 men and the youngest 19 women, leaving 40 of each with no significant difference between the sexes for age. However, this group of men were experienced officers, so not only were they older than the rest of the young group but probably differed from them in other, qualitative ways, having more life experience for example. Therefore, although there are now equal numbers of men and women and the mean age is similar, other confounding variables may be influencing the results for sex differences. Some of these were identified and statistically controlled for, such as IQ, but others may not have been.

For most of the tests used in this research, previous studies have reported no sex differences. However, those tasks where sex differences are most frequently found (such as mental rotation) often produce floor effects, which would not allow for sex differences to emerge. Previous research into sex differences in cognition in AD has used the same tasks that were selected for the current research. It was expected that because people with AD would show deficits on the selected tasks compared to the healthy elderly, there would be an opportunity for any sex differences that exist in these tasks to emerge. So, sex differences may exist in some verbal and visuospatial tasks, but this study may have failed to identify such differences by selecting tests where they do not exist.

7.6. IMPLICATIONS FOR FUTURE RESEARCH

The BNT is widely used in neurocognitive testing, so it is important to establish whether it has an inherent bias which favours men. It might be useful to compare results on the BNT and GNT to identify whether females are disadvantaged by the use of the former.

It would be interesting to identify whether reports of a female advantage on lexical fluency only emerge when participants are asked to write down their responses, as the previous research suggests. Using this task in those with AD usually requires participants to orally respond, but this is not always the case when the test is used to examine the relative performance of healthy men and women, so it would be of interest to establish whether it is writing down the responses that favours women and future research could address this issue. Then, researchers could bear this in mind when designing future studies.

What has become apparent from this research is that although there was very little evidence of a sex difference in cognition in any group examination of the magnitude of the effect sizes for verbal and visuospatial abilities reveals that women's performance is deteriorating relative to men's. The participants examined herein were mild to moderately affected and it would be interesting to examine whether such a deterioration continues so that later in the disease, a significant female deficit emerges. Many of the tasks examined could still be used with those most severely affected without encountering floor effects. Ideally, to rule out a cohort effect, it would be useful to follow participants longitudinally through the course of the disease and compare the rate of deterioration on tasks between the sexes.

Given that there are no sex differences in young adults for the tests used herein (and in previous AD research) future research should use easier versions of tests that show sex differences, such as mental rotation or block design tasks. This would avoid floor effects that would make it difficult for sex differences to emerge.

7.7. CONCLUSION

The results of this study showed that, as expected, those with AD show cognitive deficits compared to elderly controls in verbal and visuospatial tasks, but not in the recognition of facial emotions.

The intention of the research was to address the following research questions:

1. *When analysed at group level, is there any evidence of differences in cognitive abilities between men and women in the general population? Specifically, are there any differences in cognitive abilities between elderly men and women?*
2. *When analysed at group level, is there any evidence of differences in cognitive abilities between men and women AD sufferers?*
3. *If differences are found, do the patterns of cognitive deficits found in AD patients reflect those found in an age-matched healthy population?*

The pattern that has emerged is that there are no sex differences in the healthy population, both young and old. Although sex differences in AD only emerged for the ROCF tasks and confrontation naming, both favouring men, it is apparent that women are differently and more deleteriously affected by AD than men. Of course, it may be that the apparent deterioration in female performance relative to men is a cohort effect and that sex differences remain low or even zero for the cognitive tests used. If, however, the apparent adverse effect of AD on women is a genuine one it becomes of interest to identify why women are so badly affected. There is converging evidence to suggest that greater cognitive reserve in men is responsible for this, but it seems unlikely that women's historical lack of occupational opportunities contributes to this.

Only 15 studies were found reporting sex differences in cognitive abilities in AD even though there has been extensive research into cognitive abilities in AD and into sex differences in cognition. It seems hard to believe that researchers have not previously studied sex differences in AD. In which case, it is probable that studies have been done, but that there are no sex differences in cognition for this group and the lack of published evidence reflects a publication bias whereby those papers that support the null hypothesis fail to be published. It is of as much interest to know that there are no differences between men and women as it is to identify where they do exist. It is surely time that publishers accept papers reporting an absence of an effect so that the putative sex differences that continue to be so widely (and perhaps erroneously) cited are recognised as being non-existent.

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Appendix 1. Order of tasks administered to participants

Tasks were administered across two sessions. The screening/general abilities tasks were always administered at the first session. The computerised tasks were administered at one session and the pen and paper tasks at the other.

Task administered	
Screening/General Abilities	
	Information Sheet
	Consent Form
	MMSE
	NART
	CORVIST
	HADS
Computer based tasks	
	CANTAB – PAL
	CANTAB – PRM
	CANTAB – SSP
	FEEST
Pen and paper tasks	
	ROCF copy
	CANTAB – GNT
	Verbal Fluency Task
	Category Fluency Task
	ROCF recall

Note: CANTAB =The Cambridge Neuropsychological Tests Automated Battery. FEEST = Facial Expressions of Emotion: Stimuli and Test. CORVIST = cortical Vision Screening Test. HADS – Hospital Anxiety and Depression Scale. MMSE = Mini Mental State Examination. NART = National Adult Reading Test. PAL = Paired Associates Learning. PRM = Pattern Recognition Memory. ROCF = Rey-Osterreith complex figure . SSP = Spatial Span.

Appendix 2. Description of Cognitive Tasks

Task	First Author (year)	Description
Test Batteries		
CANTAB	Robbins (1994)	Computerised, non-linguistic and culturally neutral tests of cognition including tests of attention, executive function, memory.
CERAD	Morris (1989)	A brief, comprehensive battery of clinical nad neuropsychological tests for assessment of patients with AD.
DAT	Bennett (1947)	8 paper and pencil tests. Large scale administration in schools. Measures verbal reasoning, numerical ability, spatial visualisation, language/spelling, clerical speed/accuracy, mechanical reasoning and abstract reasoning.
MMSE	Folstein (1975)	Measures level of cognitive impairment. Maximum score is 30.
PSAT/SAT	Donlon (1984)	Large scale administration in schools. SAT are used to assess college admissions in USA and are self-selecting.
RBANS	Randolph (1998)	Used as a screening instrument in the elderly. Measures several cognitive domains. Tests include figure copying/line orientation/.confrontation naming/semantic fluency.
SIDAM	Zaudic (1991)	An instrument used to diagnose dementia containing a range of neuropsychological tests.
General Abilities		
NART	Nelson (1978)	Used to measure pre-morbid intelligence
Standard progressive matrices	Raven (1992)	A non-verbal IQ test that presents a series of geometric figures with one missing. Participants are required to select the missing figure from a set of answer choices.
WAIS - R	Wechsler (1981)	Measures intelligence
Visuospatial Tests		
Block design subtest of WAIS	Wechsler (1981)	Participants must use sets of red and white coloured 3-dimensional blocks to reconstruct shapes of increasing complexity
Card rotations	Ekstrom (1976)	Two-dimensional task with 28 target items.. Participants have to determine whether each of eight items to the right of the target was a rotation of the target or a different figure.
CERAD drawing task	Morris (1989)	Involves copying four line drawings
Corsi Blocks	e.g. Lezak (2004)	Measures STM capacity. A series of 2 to 9 blocks shown. The examiner taps each block in random order and the participant is required to report the sequence.
DAT spatial relations subtest	Bennett (1947)	Participants are required to indicate what an unfolded shape would look like when folded
Embedded Figures	Witkin (1971)	A target figure is hidden in the contours of a larger one.
Identical Blocks	Stafford (1962)	Participants must indicate which block among a number of alternatives is the same as a standard, given a variety of cues (letters and numbers on the faces of the blocks)

Task	First Author (year)	Description
JLO	Benton (1978)	Participants are required to estimate the position and angle of target lines by matching each to an identical line from a semi-circular array of choices.
JLAP	Collaer (2002)	Participants have to match target line segments with a numbered line arrayed in a semi-circle below it. This task requires finer line discrimination than the JLO test, and has a time limit.
Lines Test	Caparelli-Daquer (2000)	Participants are required to cross out all lines in a column that are at the same angle as the stimulus line (which appears at the top of the column). There are between two and four correct answers in each column (out of 11).
PAL subtest of CANTAB	Robbins (1994)	Participants are shown a number of boxes (initially 6) which 'open' one at a time. One of these boxes contains a pattern and participants are required to remember which box contained the pattern. The task gets progressively harder, with two boxes containing a pattern, then 3 and so on.
Paper Folding	Ekstom (1976)	Participants imagine the spatial result of folding a piece of paper in several directions
Paper form Board	Likert (1941)	Participants must decide which of five 2-dimensional line drawings of shapes can be made out of a set of fragmented parts.
Peters MR	Peters (1995)	Paper and pencil test using two sets of 12 items with a target item on the left and four sample stimuli on the right. Participants have to select 2 out of 4 that are identical, but rotated.
Plumb-Line	Piaget (1956)	Requires participants to draw how a plumb-line would appear if hanging from a tilted surface.
PMA MR	Thurstone (2002)	Comprises 20 elements, each of which consists of a two-dimensional geometric figure and six similar figures. Participants must identify the figures that are identical to the target.
PRM subtest of CANTAB	Robbins (1994)	Assesses visual pattern recognition memory in a 2-choice forced discrimination paradigm. Participants are shown a series of 12 patterns. In the recognition phase they are required to choose between a pattern they have already seen and a novel one.
ROCF	Lezak (1995)	Participants are asked to draw a complex figure which is in front of them. In some cases, participants are asked to draw the figure from memory, at varying intervals.
Rod and Frame	Witkin (1948)	requires participants to position a rod within a tilted frame so that the rod is either vertical or horizontal. The test reflects participant's spatial skill or field dependence - cues in the environment for making judgements – or both.
Shepherd & Metzler MR	Shepherd (1971)	Paper and pencil test using 3 – dimensional cube figures. Participants have to select which of 20 pictures are mirros of the 3d target blocks.
SIDAM drawing task	Zaudic (1991)	Involves drawing geometric figures
Span of Visual Memory	Milner (1970)	Variation of Corsi Blocks Task.

Task	First Author (year)	Description
Spatial Span subtest of CANTAB	Robbins (1994)	Computerised version of Corsi Block Tapping. Assesses working memory capacity. A pattern of white boxes is displayed on the screen. Some of these will change colour and participants are required to repeat the sequence using the touch screen. The task gets progressively harder beginning with a sequence of 2 changes up to a total span of 9.
Vandenberg & Kuse MR	Vandenberg (1978)	Paper and pencil test using 3 – dimensional cube figures. Participant must choose which two (of four) items are rotated copies of the target.
Vecchi's pathway task	Vecchi (1998)	Participants are shown a 3x3 matrix with a dot in bottom left-hand corner and mentally imagine a series of moves given by the examiner (e.g. up, right, right, up). They are then asked to point to the square that would now contain the dot.
Water level	Piaget (1956)	Requires participants to draw in the water level in a picture of a tilted glass that they are told is half filled with water.
Verbal Tasks		
Categorical verbal fluency		Measures semantic fluency -participants have to name as many exemplars of a given category as they can within the time frame without repetition. Typical categories used are animals,tools,fruit.
Confrontation Naming		Assesses verbal semantic memory. Participants are shown a series of line drawings and asked to name what they can see
• Boston Naming Test	Kaplan (1983)	Contains 60 line drawings that vary in difficulty (although there are shorter versions). Participants may be required to correctly identify the drawing within a certain time (often20 seconds). If a participant cannot identify the item within the time, they may be given phonemic or conceptual cueing. Stopped after 6 consecutive errors. There are various methods of scoring, depending on whether cueing is used.
• Graded Naming Test	McKenna (1983)	Contains 60 line drawings that vary in difficulty (although there are shorter versions). Participants may be required to correctly identify the drawing within a certain time (often20 seconds). If a participant cannot identify the item within the time, they may be given phonemic or conceptual cueing. Stopped after 6 consecutive errors. There are various methods of scoring, depending on whether cueing is used.
Lexical Verbal Fluency	e.g. Benton (1989)	Measures phonological fluency - participants have to recall, within the time frame, as many words as they can beginning with a particular letter of the alphabet without repetition or proper nouns.
Facial Emotion Recognition Tasks		
Ekman & Friesen pictures of facial affect	Ekman (1976)	Contains 110 black and white images of Caucasian actors. Six universal emotions (anger, disgust, fear, happiness, sadness, suprise) plus neutral faces. Includes morphed images.
FAB	Bowers (1989)	Designed for use with neurological populations to assess interpretation of emotion caused by facial expressions and voice. Facial expressions use females only. Expressions are happiness,

Task	First Author (year)	Description
		sadness, anger, fear and neutral.
FEEST	Young (2002)	Consists of 60 pictures of 10 models (six female four male) showing the six basic emotions from the Ekman and Friesen's pictures of facial effect series. Faces are presented for 5 seconds in a random order and participants are asked to select which label (out of six) best described the emotion displayed.
JACBART	Matsumoto (2000)	Seven universal facial expressions (as JACFEE) presented for 0.2 seconds embedded in a 1-second presentation of the same actor's neutral face.
JACFEE	Matsumoto (1988)	Includes seven basic emotions (anger, contempt disgust, fear, happiness, sadness, surprise). The posers are Caucasian and Japanese. Each picture is shown for 10 seconds.
JACNEUF	Matsumoto (1988)	Includes seven basic (anger, contempt disgust, fear, happiness, sadness, suprise) or neutral emotion. The posers are Caucasian and Japanese. Each picture is shown for 10 seconds.
MacBrain facial stimulus set	#	Uses 43 actors from a range of ethnic backgrounds in 646 pictures. Includes fearful,happy, sad, angry, surprised, calm, neutral and disgusted expressions.
MSFDE	Beaupre (2005)	Consists of facial expressions of people of European, Asian and African descent. Expressions are happy, sad, angry, fearful, disgusted and embarrassed plus neutral. Expressions are morphed into 5 levels of intensity.
Penn Emotion Recognition Test	Kohler (2003)	Computer based test that includes 40 colour photos (8 each) of happy, sad, angry, fearful and neutral faces balanced for mild and extreme expressions. Presented with a single photo and 5 emotion labels. No time limit.
R&P	Rowland (1995)	Real-time interactive morphing from neutral (05) to 100% emotion within 20 image steps using colour photos.
Webneuro	Silverstein (2007)	Internet-based task. Uses 72 facial expression stimuli. 6 males and 6 females depicting neutral, happiness, sadness, fear, anger and disgust.

Note: AD = Alzheimer's disease. COWAT = Controlled Oral Word Association Test. FEEST = Facial Expressions of Emotion: Stimuli and Test. JACFEE – Japanese And Caucasian Facial Emotins of Emotion. JACNEUF = Japanese and Causian Facial Expressions of Emotion and Neutral Faces. JLAP = Judgement of Line Angle and Position test. JLO = Judgement of Line Orientation test . MMSE = Mini Mental State Examination. MR = Mental Rotation. MSFDE = Montreal Set of facial displays of emotion. NART = National Adult Reading Test. PAL = Paired Associates Learning. PMA = Primary Mental Abilities. PSAT= Preliminary Scholastic Aptitude Test. R&P = Rowland and Perrett. RBANS = Repeatable Battery for Assessment of Neuropsychological Status. ROCF = Rey-Osterreith complex figure . SAT = Scholastic Aptitude Test. SIDAM = A Structured Interview for the diagnosis of Dementia of the Alzheimer type, Multi-infarct dementia and dementia of other etiology. STM = Short-term memiry. WAIS –R = Wechsler Adult Intelligence Scale – Revised . # Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at ott0006@tc.umn.edu for more information concerning the stimulus set.