

## SELECTIVE ATTENTION IN ALZHEIMER'S DISEASE

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### 1. ABSTRACT

This chapter presents a review of selective attention functioning in Alzheimer's disease (AD). The primary focus is on work conducted into this complex topic within the author and colleagues' laboratories (i.e. studies of simple and conjoined visual search). Findings obtained by the author and colleagues investigating simple and conjoined feature visual search in AD are related to findings obtained in the same laboratories in the healthy elderly and in patients with Parkinson's disease. Selective attention is a complex, multifactorial entity. Impairment of selective attention may be an early feature of AD and a prominent clinical characteristic of some patients. However, there are currently few reliable clinical measures of attentional dysfunction in AD. The experimental literature implicates some aspects of selective attention more reliably in AD than others. With respect to our own empirical studies, more effortful or controlled aspects of selective attention (as characterized by conjoined feature

visual search) are impaired in AD. Furthermore, on the basis of our experimental observations, these aspects of selective attention appear to be disproportionately impaired relative to deficits in other cognitive domains that have previously been reported in the AD literature. By contrast, conjoined feature visual search deficits were not observed in our studies in patients with Parkinson's disease. The selective attention deficits that we have noted in AD patients represent an extension of the types of impairments that we have also observed in healthy aging; that is, compared with the healthy elderly, AD patients were quantitatively but not qualitatively more impaired on conjoined feature visual search. This is an important observation. The ways in which these findings relate to the wider AD selective attention literature are also considered, drawing out several common theoretical strands across a range of empirical studies.

### 2. INTRODUCTION (AND CAVEATS)

Before embarking upon a review of selective attention in Alzheimer's disease (AD), some caveats are warranted. The landscape of attention is complex. All cognitive capacities comprise multiple component processes, some of which are better characterized than others; one thinks, for example, of the distinction between different elements and components of long-term memory, object identification, reading, face and speech processing. However, in the attention literature, we are faced with an array of putative attentional processes (for example, sustained, divided, selective, vigilance) whose relationship to each other is currently poorly defined. A related point is that, empirically, it has proven challenging to operationalise proposed subtypes of attention in a manner that permits individual subtypes to be clearly delineated experimentally.

Another important issue is that the term 'attention' is often used interchangeably with other complex concepts such as 'consciousness' and 'working memory'. Moreover, given their central role in cognition, attentional processes can interact with and modulate many other cognitive capacities (for example, memory and perception). These problematic and multi-faceted aspects of attention are reflected in the use of a number of still widely used metaphors. Researchers often refer to the 'spotlight', 'window', 'filter' or 'bottleneck' of attention (of course, these metaphors may apply better to some aspects of attention than to others). Metaphors may serve as useful approximations and can facilitate understanding, but they never completely suffice as explanatory tools.

Attention is clearly a multifactorial entity, or group of entities. Different subtypes of attention may differ considerably in terms of their functional characteristics and neural bases. I will here be focusing on 'selective attention'. To which capacity am I referring in using this term? I am referring to the aspect of attentional functioning that involves an individual's allocation of his/her cognitive capacity among the myriad array of perceptual inputs presented via the senses. Within an experimental context, selective attention refers to the differential processing of target information, whereby a specified item may be processed with no (or minimal) interference from simultaneously presented distractors.

An eloquent description of selective attention was provided over a century ago, by one of the great-grandfathers of contemporary experimental psychology, William James. James (1) referred to the 'primordial chaos of sensation' with which we continually have to deal. It is the selective aspect of attention that extracts order from this chaos. James writes, "Looking back, then...we see that the mind is at every stage a theatre of simultaneous possibilities. Consciousness consists in the comparison of these with each other, *the selection of some, and the suppression of the rest by the reinforcing and inhibiting agency of attention...* The mind, in short, works on the data it receives very much as a sculptor works on his block of stone." [My italics, 1 pp228-229]

It is arguable to what extent our present day understanding of the mechanisms underlying selective attention has significantly progressed beyond the framework articulated so eloquently by William James at the end of the nineteenth century. This question notwithstanding, in this chapter I will attempt to work within the limitations and constraints imposed by the framework of the current experimental attention literature to provide an overview of the kinds of deficits in selective attention that occur as a consequence of aging and age-related neurodegenerative illnesses. More specifically, the focus of the chapter will be on our studies of selective attention in AD, and the cognitive component processes that may underlie any observed deficits. I will also attempt to relate pertinent findings obtained in our laboratory to those reported in the wider AD literature. By referring to findings from our complementary studies of healthy aging and Parkinson's disease, important issues of continuity, selectivity and specificity will also be considered. In this context, particular questions that will be addressed are as follows: is selective attention significantly impaired in AD? If reliable deficits are observed in AD, how specific are these deficits to the domain of selective attention (compared with other domains of cognitive functioning)? How specific are deficits in selective attention to AD relative to other types of neurodegenerative illness (specifically, Parkinson's disease)? And to what extent do any deficits that are observed in AD related to changes that are observed in selective attention as a consequence of normal aging? In considering these important issues, I will draw primarily upon experimental findings obtained in our laboratory, but I will also refer - where relevant - to other research groups working in this field. The reader is also referred to the work of Perry and Hodges (2), Perry, Watson and Hodges (3) and Johannsen, Jakobsen, Bruhn *et al.* (4) for a consideration of how different elements of attention (sustained, divided, selective) may cluster and fractionate at different stages of severity of AD.

### 3. BACKGROUND TO CURRENT STUDIES: SELECTIVE ATTENTION IN ALZHEIMER'S DISEASE

Dementia is a disorder characterized by memory loss, confusion and lack of orientation in time and place (5). Alzheimer's disease (or Dementia of the Alzheimer Type) is the leading cause of dementia in Western societies. It is an acquired, cognitive impairment resulting from systematic and typically unremitting neural degeneration. AD is a multifactorial entity, affecting a range of cognitive capacities, including attention, memory, language, visuospatial functions, reasoning and language (6). As early as the 1950s, it was noted that "...what the demented patient lacks is not so much the ability to behave in a fitting manner as the ability to *select from his environment the cues to tell him what is fitting*" (7) [My italics]. Nevertheless, until recently there has been a relative dearth of systematic research into selective attentional functions in AD compared with other cognitive domains such as memory. However, there have been recent suggestions that attention is impaired early in the course of AD (2, 8), and that deficits in attention may, indeed, mediate some of the other cognitive impairments noted in AD (9-12),

as well as some of the deficits in activities of daily living observed in the disease (2, 13- 17).

Deficits in attention in AD have been observed in a wide variety of capacities and on a range of different tasks, many of which may be tapping aspects of selective attention. These include both auditory (18) and visual (19) selective processing, attentional orienting (20), visual pursuit tracking (21), visual search (22), attention-shifting (23), uncued reaction time (24), divided attention (25-28) and the generation of antisaccadic eye movements (29). Deficits have also been noted in "attentional grasp" (30), in inhibition of return (31) and with respect to AD-related biases in attentional hemifield (32, 33). In addition, Simone and Baylis (34) observed exaggerated effects of interference in AD patients on a reaching task. On a cued visual search task, Greenwood, Parasuraman and Alexander (35) found that the positive effects of location precues on target detection declined progressively with increasing age and the onset of AD. It has further been suggested that aspects of selective attention such as set-shifting and response selection are especially affected in AD (2). In their work Perry *et al.* (3) observed that impaired episodic memory was present in all AD patients tested, but that deficits in attention were more prevalent than deficits in semantic memory in AD. Rizzo *et al.* (12) noted strong relationships between reduced attention skills in AD and overall cognitive impairment, further attesting to the potential significance of attentional dysfunction in AD. It has additionally been argued that deficits in attention in AD can be related to the characteristic neurochemical (for example, cholinergic) changes that occur in the disease (36). From an anatomical perspective, it has been suggested that the relevant neuropathological changes underlying deficits in attention in AD relate to i) spread of AD pathology from the medial temporal to basal forebrain structures and/or ii) corticocortical tract disconnection (see 2).

A range of "attentional" deficits has therefore been reported in the AD literature to date. However, much previous work is characterized by a rather atheoretical, data driven approach to research, with empirical findings typically being evaluated in a more descriptive rather than analytical manner. Clinical tests of attention suitable for use with AD patients are not well developed and/or tend to confound different aspects of attentional function. With regards to experimental investigations, it is not entirely clear from previous studies that have reported attentional deficits in AD whether impairments should be attributed to reduced target processing, impaired inhibition of distractors, or to a combination of each. While some studies of selective attention in AD (e.g. 37-39) have identified impaired target processing, other investigations have found target enhancement to be preserved in AD (e.g. 40-43). Faust, Balota, Duchek *et al.* (44) suggested that AD patients exhibit impaired inhibitory control, with relative preservation of facilitatory selective processes, as indicated by performance on a sentence comprehension task. This conclusion was supported by the findings of Spieler, Balota and Faust (45), who argued that there is a deficit in inhibitory control in normal aging, which is further exaggerated in AD. Problems in inhibition have also been inferred from AD patients'

impaired performance in other experimental tests, and on clinical measures such as the Stroop, Trails and Wisconsin Card Sorting Tests (22, 28, 35, 43, 46-52). More specifically, it has been suggested that AD patients are unable to inhibit the activation of competing, prepotent responses (28, 30, 51). Other researchers have suggested that AD-related deficits on tests of visuospatial attention often take the form of impaired disengagement from distractor items (33, 51, 53).

There may be considerable overlap among different ways of characterizing impaired visuospatial functions in AD. A common thread of many of these studies is that AD patients are less able than controls to ignore or inhibit distracting information. However, the specific component processes underlying these effects have not yet been clearly identified. It appears that some inconsistencies in previous studies in attributing AD-related deficits to reduced target or increased distractor processing may be due to the possibility that AD patients are able to suppress weakly activated distractors efficiently, but are less able to suppress more strongly activated distractors (see 43). Furthermore, it should be noted that deficits in target and distractor processing are, of course, not mutually exclusive.

The findings of the studies reviewed above have indicated an attentional impairment in AD. However, other past studies of selective attention in AD have revealed no marked deficits, or a more equivocal pattern of findings. AD patients appear to show preserved functioning in detecting, shifting to and engaging target items (28, 40-43, 51, 53-55), although deficits in these capacities have been reported as the disease progresses (56). Alertness and vigilance, as measured by the facilitation in responding to targets provided by a prior warning stimulus (57) or over time (58), may also be preserved in AD. Nebes and Brady (10) found that patients with AD were able to limit their visual search as well as controls to stimulus items sharing a relevant salient feature (see also 35). On a negative priming task, Sullivan *et al.* (43) noted impaired priming in AD, although there was a similar size distractor interference effect to controls on this task.

Nebes and Brady (10) have argued that there is no focused attention impairment in AD (although other researchers have reported that impairment does exist; for example, 11, 59, 60). Using a covert selective attention task, Parasuraman, Greenwood, Haxby and Grady (53) observed disproportionately poor performance in AD patients when they were invalidly cued and had to re-orient their attention to another location in the visual field. By contrast, patients in the mild to moderate stages of AD were generally able to use a valid cue to move visuospatial attention efficiently toward an expected location. Consistent with the position of Nebes and Brady (10), Parasuraman *et al.* (53) suggested that focusing of attention is preserved in AD, but that disengagement mechanisms might be impaired. However, Caffarra, Riggio, Malvezzi *et al.* (61) reported no deficits in disengagement processes in AD: compared with patients with Parkinson-Dementia, Parkinson's disease and matched controls, AD patients showed no differences in performance on the Posner paradigm of covert visuospatial attention. Faust and Balota (54) investigated inhibition of return in AD patients and elderly and young controls on a stimulus

detection task, and found no AD-related deficits in inhibition, in contrast to the findings reported above (for example, 44, 45). However, both an age-related and an AD-related increase in the beneficial effect of a peripheral cue on target detection were observed in the Faust and Balota (54) study. There is also evidence that semantic attentional processing is preserved in AD (e.g. 40, 62).

Sahgal, Galloway, McKeith *et al.* (52) compared attentional processing in AD with Lewy body dementia (LBD). Dementia with Lewy bodies is the second commonest form of degenerative dementia, accounting for up to 20% of cases of dementia in the elderly. It is characterised by fluctuating cognitive impairment, spontaneous Parkinsonism and recurrent visual hallucinations. Sahgal *et al.* (52) found that both AD and LBD patients were impaired on an attentional set-shifting task. By contrast, on a visual search matching-to-sample task, the AD group performed at close to normal levels.

### 4. OUR RESEARCH: RATIONALE

There is therefore a continuing debate concerning the nature and degree of the selective attentional impairment in AD. Much of this debate relates to heterogeneity of tasks and patient samples and inadequate characterization and definition of specific component processes of selective attention. It is against this background of mixed and unclear findings that our own studies have been conducted (63-65). We will now consider the background to our studies, before reviewing our findings to date, and then considering to what extent our findings inform and extend the existing literature of studies of selective attention in AD.

A general objective of our work has been - within a clearly delineated experimental paradigm - to characterize further precisely which component processes of selective attention are impaired or preserved in AD. The simple and conjoined feature visual search paradigms we have used utilize a parametric manipulation of the independent variable (i.e. number of distractor items present in the visual field). This has enabled us to dissociate the generic features of task performance in AD (possibly mediated by non-specific changes in arousal, motivation or sensorimotor functions) from specific cognitive deficits (which are systematically related to changes in the independent variable). We have further examined whether any deficits that are observed in AD are selective for the cognitive domain of visuospatial attention, whether they are selective to AD (specifically compared with Parkinson's disease), and whether they are qualitatively or quantitatively similar to changes in visuospatial attention observed in other populations, such as the healthy elderly.

We have been especially interested to investigate the relationship between "controlled" (or effortful) and "automatic" (or non-effortful) selective attentional capacities in AD (see 9, 66, 67). The distinction between controlled and automatic processing is very well established in the experimental psychology literature. Schneider and Shiffrin (66) and Shiffrin and Schneider (67) have argued that controlled and automatic processing represent qualitatively

different forms of human information processing. More specifically, many tasks of our everyday lives are so well practised that they become *automatic* and require no or very few selective attentional resources for their efficient performance - for example shaving or brushing one's teeth (note the emphasis on the performance of a well learned skill or ability). Other tasks, however, require selective attention (i.e. their performance is *controlled* by attentional limitations) - for example learning to fly or to scuba dive (note the emphasis on the acquisition of a novel skill or ability).

Controlled - as distinct from automatic - processing is sensitive to variations in information load, interferes with other forms of ongoing information processing (assuming that these are not fully automatic) and requires conscious cognitive resources. Automatic processing represents the converse of controlled processing, with respect to the dimensions listed in the preceding sentence. The simple feature search task that we have used in our work is considered by many to be a measure of automatic processing, whereas conjoined feature search is generally regarded as an index of controlled processing (68-70). As originally pointed out by William James (1), selective attention involves focusing on some perceptual inputs while excluding additional interfering stimuli. It is proposed here that the distinction between automatic and controlled processing is orthogonal with respect to selective attention. Therefore, one can talk about automatic selective attention and controlled selective attention (as applied, respectively, to the simple and conjoined feature tasks used in our research).

#### 4.1. Visual search performance

Our research has employed a computer-presented visual search task to investigate selective attention in AD. This paradigm has previously been used extensively in the cognitive psychology literature as a robust index of visuospatial selective attention (68-75). More recently, it has been used as an index of visual search capacity using different target types and in different clinical populations (76-78).

In our work, we have evaluated both simple and conjoined feature search tasks in AD patients, investigating the effects of systematically increasing the size of the background array of distractor items on participants' reaction time (RT) to detect a target in each task. Simple and conjoined feature search tasks involve looking for the same target but among a different set of distractors across the two tasks. According to previous findings (for example, 79, 80 - see below for more detail), we anticipated that the effect of array size on target detection speed would be most pronounced in AD patients on the conjoined feature (i.e. 'controlled') search task compared with the simple feature (i.e. 'automatic') task.

In addition to examining whether a robust selective attentional deficit exists in AD, in our work we have sought to investigate other elements of visual search performance, as outlined below.

#### 4.2. Stimulus location

We have examined target detection by stimulus location, which we have varied across peripheral, intermediate and central areas of space. We have been

especially interested to determine whether there is any constriction in the size of the attentional 'window' in AD (81, 82), as this would have clear functional implications for activities of daily living. To determine whether hemispatial bias is present in AD, we have examined target detection in the left and right hemifield, by dividing stimulus presentation into a left half and a right half of space and analysing separately the response latencies in these two regions. Mesulam (83) has proposed that the right cerebral hemisphere (specifically, the right parietal region) is responsible for subserving attention to both the left and right environmental hemispace, whereas these authors have proposed that the left hemisphere (in particular, the left parietal region) is responsible for subserving attention to the right hemispace only (see also 84-87). (A similar view of anatomically-connected attentional networks has been proposed by Michael Posner and associates, who argue that parietal regions are most important for orienting to spatial locations; see, for example, 88-90.) Pathology in the parieto-temporal region of the brain is a common neurological feature of AD and is thought to underlie the deficits in visuospatial functioning that are often present in the disease (see 5, 91, 92.). The findings of Corbetta, Shulman, Miezin and Petersen (79) and Ashbridge, Walsh and Cowey (80) implicate the superior parietal cortex (especially on the right) in the mediation of conjunction search tasks similar to that used in our investigations, but not in preattentive search or "popout". Therefore, in our studies we expected that conjunction search – but not necessarily simple feature search – would be impaired in AD patients, and that there would be greater likelihood of sparing of attentional function in AD for targets presented on the right side (relative to the left side) of the computer screen.

### 4.3. Variability

A further issue that we have investigated in AD patients concerns the degree of variation in task performance observed across the duration of the test session. Increased fluctuation in task performance has been implicated in both pathological and non-pathological aging (93-95). Moreover, clinically, one of the most puzzling aspects of AD concerns day-to-day fluctuations in behaviour. However, there has been little systematic research into AD patients' ability to sustain their performance over the duration of a cognitive test session. Impaired vigilance has been implicated in AD (96-99), although differential AD-related changes in task performance over time have not been evaluated in the majority of previous experimental studies. Furthermore, in those studies where this question has been examined, inconsistency in performance has tended to be treated as a secondary issue. Instead, it may be more appropriate to treat variability as a primary feature of participants' task performance (see 100). We have adopted this approach in our work, investigating both intra-individual and intra-group variability in responding across testing in order to compare these features of AD patients' task performance with controls.

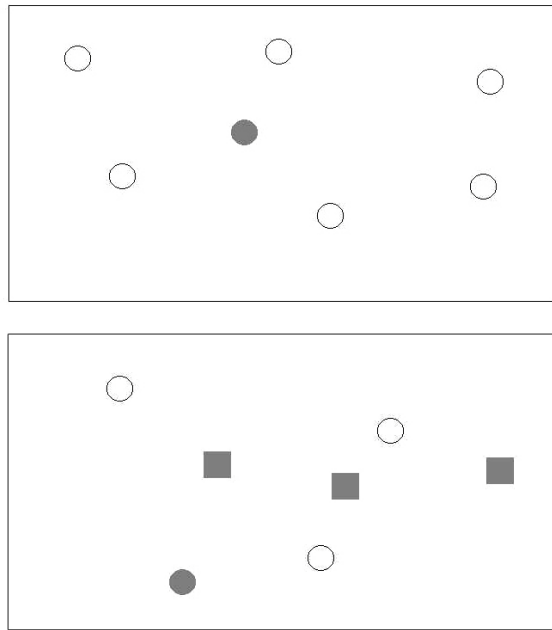
### 4. Generalized cognitive slowing

An important theoretical issue that we have tried to examine in our work is the extent to which any deficits observed on visual search in AD are truly specific to

visuospatial attentional function, or whether, more parsimoniously, they may instead be a product of generalized cognitive slowing (101-105). This central conceptual issue has been investigated extensively in the cognitive aging literature (see, for example, 64). It has not been directly addressed by many previous studies of selective attention in AD, but we have attempted to address this important question in our work (see also 106-108). We here present an overview of this approach, which will be discussed in more detail later in the chapter. Briefly, if it is the case that processing in any given psychological task is qualitatively similar for AD patients and controls, but AD patients are simply slowed by a constant amount for each cognitive operation, a simple linear function should characterize the response data,  $RT_{Alzheimer} = mRT_{old}$ , where  $m$  is a multiplicative slowing factor (greater than 1). However, if the degree of slowing observed in a particular AD research study is substantially greater than that predicted by this linear function (i.e. greater than  $m$ ), then this may be taken as evidence that there is a specific impairment in the cognitive domain being examined in AD (i.e. over and above the deficit predicted on the basis of generalized cognitive slowing). Nebes and Brady (106) conducted a meta-analysis of their own previous work to address the issue of global cognitive slowing in AD. They found that the regression line characterizing the performance of AD patients (compared with young controls) showed a slope within the range 1.87-1.97 for mildly demented patients, and within the range 2.56-2.94 for moderately demented patients.

In our work, we have been interested to compare whether our selective attention data would fall within the numerical range identified by Nebes and Brady (106), so that we can determine whether or not our data can be accounted for in terms of global cognitive slowing mechanisms in AD. As is standard in cognitive aging studies, we used Brinley plots to address this question. This approach was also used by Nebes and Brady (106). The Dementia Rating Scale (DRS) (109) scores of the "mildly demented" and "moderately demented" patients included in the Nebes and Brady (106) analysis were similar to the DRS scores in the Mild and Moderate AD groups tested in our work (65), indicating the viability of the direct comparison of our findings with those of Nebes and Brady (106). Brinley plots involve the plotting of experimental data (which is typically RT data) from the target group or groups (here, mild and moderate severity AD patients) against the reference group (which is usually a group of healthy young controls) across several different levels of the independent variable (here, the visual search array or display size).

To summarize our work into selective attention in AD patients, we have used a well motivated and clearly operationalized test of visual selective attention to try to resolve some of the issues and uncertainties that have existed to date regarding the status of visuospatial selective attentional functions in AD. We have achieved this goal by using a visual search task that is well established in the experimental psychology literature, and which permits the fractionation of attentional component processes underlying distinct elements of task performance (i.e. simple versus conjoined feature search).



**Figure 1.** Examples of positive (i.e. target present) trials in the simple (above) and conjoined (below) feature tasks. In the other experimental conditions, 0, 3 or 12 distractors were present (with an equal number of trials for the 0, 3, 6 and 12 distractor conditions). The distractors comprised empty circles for the simple feature search task and empty circles and filled squares for the conjoined feature search task. For further details concerning the simple and conjoined feature search tasks, see Foster *et al.* (64, 65).

Our work has investigated visual search task performance in AD patients of different levels of disease severity (i.e. Mild and Moderate) with respect to a number of factors. First, we have investigated target detection across stimulus arrays of increasing size, to determine whether there is differential slowing in AD patients with increasing number of distractors. Second, we have systematically varied the location of the target to examine whether there is constriction of the perceptual window or hemispatial bias present in AD patients' performance. Third, we have investigated changes in task performance across the duration of the test session, to determine whether there are significant AD-related changes in variability in performance across visual search testing. Finally, we have examined the possibility that global cognitive slowing represents the critical theoretical mechanism underlying AD-related differences in visual search performance.

In addition to our research into visual search performance in Mild and Moderate AD patients, we have conducted closely related work - using the same visual search paradigm - into the same operationally separable components of visuospatial attention in patients with Parkinson's disease (63) and in healthy elderly individuals (64). The focus of this chapter is selective attention in AD, but where relevant we will also refer to these further investigations. Our complementary work in other populations was undertaken to examine the degree of specificity of our findings to AD compared with Parkinson's disease (PD), and also the degree of continuity

seen in the selective attention profile of AD patients compared with healthy elderly individuals (i.e. in 'pathological' versus 'non-pathological' aging).

Before considering our findings, we now turn briefly to some information regarding our methodology. As already mentioned, in all these sets of investigations (i.e. AD, PD, normal aging), the same visual search paradigm - comprising both simple and conjoined feature search tasks - was used to evaluate levels of selective attentional functioning. In the first simple feature task used, the target (a filled circle) differed from all the background distractors (empty circles) by a single feature. By contrast, in the conjoined feature task, the target (again a filled circle) was differentiated from the background distractors by a conjunction of two features, one of which was embodied by all of the individual distractor items (empty circles and filled squares) [see Figure 1]. In each task, the array of distractors varied in number from 0 to 12, with an equal number of trials presented at each of the four distractor array sizes (0, 3, 6, 12). In these studies, healthy age-matched participants were used as controls for the AD and PD patients (63, 65) and healthy young people were used as controls for the healthy elderly individuals (65). Participants were instructed to respond as quickly as possible if they saw a filled circle on the computer screen. On some of the experimental trials, a target was present on the screen (i.e. 'go' trials), while on an equal number of trials no target was present (i.e. 'no-go' trials).

## 5. OUR RESEARCH: FINDINGS

We here provide an overview of our main experimental findings, before next turning to a consideration of how our findings may be inter-related with the wider literature of studies of selective attention in AD. For further information regarding our findings, the reader is referred to Berry, Nicolson, Foster, Behrmann and Sagar (63), Foster, Behrmann and Stuss, (64) and Foster, Behrmann and Stuss (65).

The central finding from our AD research was that patients had significant deficits in visual selective attention, as revealed by their differentially slowed target detection speed on the conjoined feature task as the number of distractor items was increased. This differential cognitive impairment in AD patients was observed only in the conjoined feature task, and the degree of the impairment was directly related to the level of the independent variable (i.e. the size of the distractor set). Because the detection speed deficit in AD patients on the conjoined feature task was scaled by the degree of difficulty of the task, this enabled us to rule out the possibility that our findings were in fact due to a fundamental motivational, sensory or motor deficit on the part of the AD patients. The difference in performance that we observed between the AD patients and controls in terms of target detection speed (with a greater impairment in Moderate than Mild AD patients) was also reflected in the error data, with patients making more errors than controls. This was especially notable on the conjunction search task. In addition to being significantly slower Moderate AD patients made more omission and commission errors than

Mild AD patients and Elderly Controls. Taken together, these findings enabled us to discount the possibility that the reaction time RT data we obtained were simply due to shifts in the speed-accuracy trade-off function in AD patients relative to controls. However, the error rates in task performance were low overall (we had designed the simple and conjoined visual search task to be relatively straightforward, in order to avoid a large number of errors in the AD patients, and no individual participant made errors exceeding 5% of the total trials on either the simple or conjoined feature visual search tasks).

Pathology in the parieto-temporal region of the brain is a common neurological feature of AD and is thought to underlie the deficits in visuospatial functioning that are often present in the disease (see 5, 91, 92). Our finding of impaired conjoined visual search in AD patients therefore appears consistent with other work indicating that the superior parietal cortex is specifically involved in mediating conjunction search (79). Other possibly relevant brain regions include the anterior cingulate (which is thought to be involved in selecting target information out from distracting information; see 88-90) and the frontal lobes (which are thought to be involved in resolving response conflict). These additional regions may also be dysfunctional in AD, especially as the disease progresses. Our visual search findings indicate that less resource-demanding capabilities, as tapped by the simple feature search task, remain relatively preserved in AD. Of note, the basal ganglia are thought to mediate the fundamental ability to detect salient targets (see 88-90), and this region is relatively unaffected in AD (110, 111).

The central finding from our location analyses was that in the conjoined feature search task targets on the left were detected faster than those located on the right, and this became even more evident as the array size increased, and in more severely impaired AD patients. There was also evidence from the simple feature search data that AD patients had problems in detecting even highly salient items (i.e. targets in the simple feature search) if these items were presented in more peripheral regions of space. This effect was scaled by severity of the disease, suggesting systematic constriction of the perceptual window in AD. By contrast, on the conjoined feature task AD patients were not differentially slower than controls at detecting peripheral targets.

Of interest, there was some evidence from our variability analyses that the performance of the more severely impaired AD patients on the conjoined feature visual search task may actually have been facilitated more than controls by the beneficial effects of practice. However, this effect was not pronounced. Our finding of the lack of a highly pronounced differential AD-related change in variability in performance over time is consistent with a previous study that systematically evaluated time-related task performance in AD patients (57).

An important theoretical point related to our work derives from the analysis of the Brinley plots [i.e. Young Controls RTs versus a) Old Control RTs, b) Mild AD RTs and c) Moderate AD RTs]. Constructing these plots enabled

us to determine the degree of increased response time observed in the AD patients compared with that expected according to a 'generalized slowing' framework of cognitive decline in AD. The Brinley plots that we constructed revealed that the differential slowing observed on the conjoined feature task in the AD patients was greater than could simply be attributed to the existence of a global (or generalized) cognitive impairment in AD. Furthermore, the increases in target detection time that we identified through the Brinley plots were scaled by severity of the disease, with Moderate AD patients ( $=5.19\text{YoungRT}$ ) being considerably more slowed relative to controls than Mild AD patients ( $=3.64\text{YoungRT}$ ). Recall that in their meta-analysis Nebes and Brady (106) showed a Brinley slope within the range 1.87-1.97 for mildly demented patients, and within the range 2.56-2.94 for moderately demented patients. Our findings therefore imply that the domain of visuospatial selective attention, as measured by conjoined visual search performance, may be differentially impaired in AD relative to other aspects of cognitive functioning, and that this visuospatial selective attention deficit may be systematically related to the severity of the disease in AD patients.

## 6. OTHER RELEVANT STUDIES

How should our findings be integrated with findings of other studies conducted into selective attention in AD? Until comparatively recently, there have been relatively few systematic, experimental studies of attentional functioning in AD. Those experiments that have been reported in the literature have tended to examine an individual independent variable, whereas in our research we have examined several independent variables (namely: task, array size, target laterality and target location). This multifactorial approach permits one directly to inter-relate performance patterns across several participant groups following systematic manipulation of different variables within the same experimental study.

A weakness of many previous studies of selective attention in AD is that attention has been examined in isolation, without attempting to relate attentional status to other cognitive domains in AD (i.e. to consider the cognitive specificity of any significant attentional deficits that are observed). We have avoided this problem in our research by using Brinley plots to compare systematically the performance of AD patients with healthy young and healthy elderly controls on the same visual search tasks, and then to compare the degree of selective attention impairment observed in AD patients with impairments observed in other cognitive domains.

The most closely related previous study to our own work into visual selective attention in AD is that of Parasuraman *et al.* (60). Using a similar visual search task, these researchers reported a finding that was similar to our own for simple feature search (i.e. that AD patients were cognitively unimpaired, although these patients had slower overall target search RTs). On conjoined feature visual search, there was further evidence from the Parasuraman *et al.* (60) study that AD patients were unable to direct their

search as well as controls according to the location of a previously presented spatial cue. However, there was no evidence in the Parasuraman *et al.* (60) study that AD patients became differentially worse at conjoined feature search as the size of the distractor array increased. The difference between these and our findings clearly requires further investigation, particularly given the comparability of patient group sizes across the two studies. However, it should be noted that Parasuraman *et al.* (60) employed a task requiring the conjunction of different features (colour + letter) from those used in our work (where the conjunction of shape + shading was necessary). The task employed by Parasuraman *et al.* (60) additionally involved the use of precues, and only two different stimulus array sizes (10 and 15 items), whereas we have used four different stimulus array sizes (0, 3, 6, 12). Furthermore, all patients in the Parasuraman *et al.* (60) study were categorized as being in the "mild" stage of the disease at the time of cognitive testing. It would therefore be useful to conduct further work in which the different methodologies employed by Foster *et al.* (65) and Parasuraman *et al.* (60) were both evaluated using the same patients, in order to be able to specify further the source of the discrepancies noted above.

### 6.1. Hemifield differences

Caffarra *et al.* (61) used the Posner paradigm of covert visuospatial attention and reported no deficits in disengagement processes in AD: compared with matched controls, AD patients showed no significant differences in performance on this task, and no differences were observed in AD patients across hemifields. In our work, on the conjoined feature task we observed a severity-related left-field advantage in AD patients relative to healthy age-matched controls (65), as we had done previously in the healthy elderly compared with healthy young controls (64). However, in their work Caffarra *et al.* (61) report no significant AD-related differences in task performance between the left and right hemifield. Our finding (65) that on conjunction search AD patients are disproportionately slowed in detecting a target on the right side of the midline perhaps indicates that AD patients have particular problems disengaging and then shifting their focus of selective attention from the 'resting' (in Western cultures?) left side of space, and/or disproportionate difficulty shifting from left-located distractor items. However, using a Posner cued visual search task, Buck (112) observed, by contrast, that AD patients showed a greater deficit for left-presented than right-presented invalidly cued targets (i.e. AD patients were slower to detect a target on the opposite side of space when the invalid cue had previously been presented on the right rather than the left). Furthermore, when Buck (112) examined the SPECT scans of the participants in this study, it appeared that the asymmetry in target detection times (left>right) was correlated with the absolute severity of bilateral parietal damage. Task differences may again be relevant in explaining the discrepancy between our findings and those of Buck (112): perhaps disengage-shift-engage components on one task cannot necessarily be equated with disengage-shift-engage components on another task (i.e. these subprocesses may well be dissociable across the cued valid/invalid [112] and uncued simple/conjoined feature [65] visual search tasks).

Another relevant factor may be locus of pathology. As AD patients typically experience bilateral pathology involving both the left and right parietal lobe, especially as the disease progresses (see 5, 91, 92), the attentional deficits of AD patients may in fact be more akin to those seen in patients with Balint's syndrome - many of whom experience simultagnosia and/or bilateral attentional impairment (78, 113) - rather than the more focal left-sided attentional deficits often reported in patients with unilateral parietal lobe dysfunction. Moreover, although the pathology present in AD is typically bilateral, significant stable asymmetries have been reported across AD patients, and this too may influence research findings (see 8, 53, 114). Maruff *et al.* (32) studied covert orienting of selective attention to spatial and nonspatial cues. They classified their AD patients into three different subgroups, according to their abnormally slow attentional biases: the first group showed a significant slowing of RT to all left-sided targets, the second group was significantly slowed to right-sided targets and the third group showed a significant slowing of RT to both left- and right-sided targets. Mendez *et al.* (33) used four different measures of attentional neglect and reported that AD patients were generally impaired in attending to the left hemispace, but that a subgroup of patients reported deficits in attending to the right side of space. In the context of the points noted above, the differences in performance across hemifield that have been noted in groups of AD patients within and across studies (for example, 32, 33, 65, 112) may well have significant neurological underpinnings.

Taken together with the results of our work, findings in the extant literature therefore indicate a considerable degree of individual heterogeneity in hemifield-related attentional biases in AD, perhaps - as noted - related to the acknowledged variability that exists in AD neuropathology across patients (see, for example, 115). This heterogeneity in pathology presumably influences the degree of damage to attentional networks mediating task performance. As anticipated, in our work we saw no group-related difference in target detection across hemifield on the simple feature task. These findings are in line with those of Caffarra *et al.* (61), and indicate that specific task demands (i.e. feature extraction versus feature conjunction) may also have a significant impact on hemifield-related deficits in target detection in AD. The complex issue of AD-related hemifield differences in selective attention clearly requires more research to elucidate the precise mechanisms and processes involved.

### 6.2. Selective attention in AD versus PD

The findings of Caffarra *et al.* (61) also relate to another study - already mentioned (63) - that we have conducted, investigating visual search performance in Parkinson's disease (PD). PD is a degenerative disorder of the brain that is characterized by progressive tremor, bradykinesia (i.e. slowness of movement) and rigidity. Cognitive impairments have also been cited in Parkinson's disease, with suggestions that impaired attentional functions may be an intrinsic feature of PD and may mediate at least some of the other reported cognitive deficits in this disease (116-120).



In our work, patients with PD were indistinguishable from matched controls on simple and conjoined feature visual search tasks (63). By contrast, PD patients with evidence of concomitant frontal lobe dysfunction were significantly and globally slower on both the simple and conjoined feature visual search tasks. It is also noteworthy that Berry (121) has observed a similar pattern of visuospatial selective attention performance to that which we have observed in AD patients in a group of PD patients with concomitant dementia. The interaction of task type and patient group in influencing experimental outcomes clearly requires further empirical investigation.

### 6.3. Selective attention in AD versus healthy aging

One important issue that we have been interested in addressing in our research concerns the question of functional continuity or discontinuity in selective attention between AD and normal aging. In a relevant recent investigation that compared the performance of AD patients and elderly and young controls together in one study, Greenwood *et al.* (35) used a cued visual search task to manipulate the size of the 'attentional spotlight' in AD. The tasks used were related to those used in our own work (i.e. simple and conjoined feature search), although Greenwood *et al.* (35) used precues to indicate (with varying degrees of validity) the size and location of the area to be visually searched. Greenwood *et al.* (35) found that location precues exerted the strongest effects on conjoined feature search and the weakest effects on simple feature search. Furthermore, as the size of the invalid cues decreased, conjunction search was differentially facilitated. These findings seem consistent with the notion that simple feature search may occur "in parallel", with no or minimal shifts in visuospatial attention, whereas conjoined feature search takes place "in series", with shifts of attention from one array element to the next (68, 70). The other findings of the Greenwood *et al.* (35) study were complex. However, the beneficial effects of precuing declined progressively with increasing age and the onset of AD. The greatest group differences were observed when a valid precue was small and precise: this type of cuing benefited the elderly and AD patients considerably less than young controls.

Greenwood *et al.* (35) argued from their findings that both AD and, to a lesser extent, advanced aging reduces control of the spatial focus of attention (see also 60). These researchers also argue that the performance of AD patients is preserved on visual search tasks that require the conjunction of stimulus features (the effects of precues notwithstanding). This clearly conflicts with our own findings (65), and may well have been due to methodological differences across studies; for example, there were only two different array sizes (10 or 15) in the Greenwood *et al.* (35) study, the region of space within which the stimulus arrays were located subtended a smaller visual angle than in our work, there were 8 different possible types of distractor and the AD patients studied by Greenwood *et al.* (35) were all in the "early stage" of the disease.

The findings of Greenwood *et al.* (35) are, however, consistent with those observed in our research (64, 65) in showing a broad functional continuity between

attentional deficits observed in AD and in normal aging. A further consistent observation across these studies is for the performance of 'old-old' participants to fall somewhere in between the performance of 'young-old' and AD participants. Moreover, the findings of Greenwood *et al.* (35) suggest a possible explanation for our findings with AD patients and the elderly (64, 65): if AD patients (and, to some degree, elderly controls) have problems in adjusting the focus of their 'attentional spotlight', then they may have searched the stimulus array in the 'controlled' conjoined feature search task suboptimally, while still being able to process stimuli reasonably efficiently on the 'automatic' simple feature search task (see also 81, 82). If an impairment in reducing the size of the attentional window in AD is also related to a reduced signal-to-noise ratio within the attentionally engaged region of space, this may also explain the higher level of erroneous responding to distractor items which has been reported in AD (e.g. 34, our own error data have also indicated that AD patients make a larger number of omission and commission errors than healthy controls). A lack of flexibility in the allocation of visuospatial selective attention may also explain our observation of differentially slowed detection of targets on the right side of the midline in AD patients on the conjoined feature task (65), as referred to previously in the *Hemifield Differences* section. In simple feature search, it may well be necessary to widen the window of visual 'grasp' for more peripheral targets to achieve optimal task performance. If AD patients again lack this flexibility, this could explain why we observed severity-related differentially worse performance in AD patients in detecting more peripheral targets on simple feature search.

Another relevant finding obtained by Greenwood *et al.* (35) concerns these researchers' "combined search" condition. In this condition, to perform efficiently participants were required to restrict their search within a subset of array items that shared a salient feature with the target. It has been shown that young controls are able to perform this kind of restricted search task well (122), presumably by first selecting out a subset of items sharing the relevant salient property (e.g. colour, form), and then searching for the target within this re-categorized subset of items. Plude and Doussard-Roosevelt (123) have noted that this selection ability was retained in older adults, and indeed we have replicated this finding among the healthy elderly in our own work (64). Greenwood *et al.* (35) have further argued that this restricted search capacity is preserved in AD patients. I will not discuss our findings in detail here, but we have also observed this to be the case in the AD patients we have tested, i.e. we have replicated the findings of Greenwood *et al.* (35) regarding preservation of stimulus categorization abilities in AD patients, where this categorization depends upon the identification of a single feature (specifically, concerning shaded versus non-shaded items in the stimulus display).

What are the likely mechanisms of the deficits in visual search observed in our AD work? It is generally agreed that the allocation of selective attention about the environment involves at least three processes: engage, disengage and shift (to a new location), followed by engagement of that new location or stimulus. We will now

consider each of these processes in turn, with respect to our findings on the simple and conjoined feature search tasks. As we have not monitored eye movements in our work to date, and therefore have not probed engage, disengage or shift mechanisms directly, I will here take the lead from other studies which cast more direct light on the involvement of these three mechanisms in selective attention capacities in AD. It is worth noting that deficits in engage, disengage and shift mechanisms that may be present in AD are not – of course – mutually exclusive. Indeed, several of the studies referred to below cite AD-related deficits in more than one of these component processes within a single study. This is perhaps not surprising when one considers the heterogeneity of cognitive deficits that have been reported across AD patients. This heterogeneity probably reflects the varied distribution of neuropathologic changes in the disease, affecting structures mediating different aspects of attention. Task differences may well also be of central relevance: for example, AD-related deficits in disengagement may be more likely to be revealed on tasks that require stimulus *discrimination* rather than mere stimulus *detection*, and which therefore require a more complex cognitive decision to be made.

### 6.4. Engagement

There is some inconsistency in evidence relating to the engagement of attention in AD. Some studies have noted problems in selective attention in AD with respect to impaired target engagement (28, 37-39, 54, 55, 124). However, other studies have found preserved attentional engagement and target enhancement in AD (for example, 40-43, 51, 53). Another relevant study compared attentional functions in AD and Lewy body dementia (LBD): Sahgal *et al.* (52) found that mild AD patients were impaired, compared with matched controls, on a visual attentional set shifting task, but that on a visual match-to-sample search the AD group performed at close to normal levels of responding. (Mild LBD patients were significantly impaired on both tasks.) The study conducted by Sahgal *et al.* (52) highlights the potential fractionation of different components of attentional engagement in AD patients. This kind of fractionation could account for some of the other discrepancies in this literature, and for the range of findings obtained in our own studies. The findings of Parasuraman *et al.* (60) and Greenwood *et al.* (35) suggest that deficits in the engagement of focused attention in AD may depend critically on the type of task used: when targets are presented in one of several possible locations, and are preceded by cues of different levels of spatial resolution, impairments of engagement in AD may emerge.

The existing evidence is therefore equivocal on whether or not engagement of target items is impaired in AD. As we have already seen, a mixture of significant and non-significant group differences is a recurring theme in the AD selective attention literature. Overall, however, there is no strong evidence from the preceding literature that the findings we have obtained using visual search in AD patients should be attributed to impaired engagement processes. This is particularly the case when one considers that many of the AD-related engagement deficits noted in the existing

literature have been observed in the context of explicitly cued target presentation (a procedure which was not employed in our work). Furthermore, the AD patients that we have studied are, for the most part, apparently able to engage target items as well as control participants when the target is denoted by the presence of a single feature. (Although note that even on the simple feature task, AD patients responded globally more slowly than controls; this observation may be indicative of a deficit in 'engaging' with the task, but could also be due to retarded perceptual input or motor output processes).

### 6.5. Disengagement

Caffarra *et al.* (61) used the Posner covert attention paradigm to investigate "disengagement" processes across the left and right sides of space in AD. From their findings, Caffarra *et al.* (61) concluded that AD patients show no impairment in attentional disengagement, and discuss their findings in terms of Kinsbourne's framework of interhemispheric balance. By contrast, in our laboratory, PD patients revealed a distinctly different pattern of performance to AD patients on the simple and conjoined feature tasks. More specifically, in our work patients with PD without further brain damage did not show cognitive deficits on either the simple or conjoined feature task (63). The contrast with the findings of the Caffarra *et al.* (61) study may well be related to differences in the visuospatial selective attention task and/or the degree of concomitant brain damage present in PD patients tested in the Caffarra *et al.* (61) study.

Parasuraman *et al.* (53) used cue-directed shifts of spatial attention with a letter-discrimination task in mild-moderate AD patients and age-matched controls. RT benefits for cues that were valid did not differ between the AD group and the controls, whereas reaction times costs incurred by cues that were invalid were significantly greater in the AD group than in the controls. This suggested problems in disengaging from an invalid cue in the AD patients. Very similar findings have been reported in AD by Oken *et al.* (51) using a closely related disengagement task. 124 measured eye movements while subjects were instructed a) to attend to and fixate a target appearing randomly to the right or left of a central marker and b) to direct attention to and fixate a target appearing randomly in one of four peripheral locations. The increased number of perseverative responses recorded by AD patients in this study is suggestive of problems with disengagement. Mendez *et al.* (33) tested AD patients on 4 measures of neglect (visual search of a complex picture, letter cancellation, Schenkenberg line bisection and computerized line bisection) and concluded that hemispatial neglect on visual search tasks in AD may relate to difficulties in disengaging attention or in visual exploration.

Parasuraman *et al.* (53) have concluded that focusing of attention to location is intact in early AD, but that disengagement of visuospatial attention is impaired. Parasuraman *et al.* (53) have further suggested that intact focusing and impaired disengagement of visuospatial functioning in AD may be linked to dysfunction of cortico-cortical attentional networks linking the posterior parietal and frontal lobes. Indeed, other researchers have suggested that

the parietal lobe - which typically shows reliable pathological changes in AD (5, 91, 92) - may be intimately involved in the disengagement of spatial attention (see, for example 88-90). However, the findings of Parasuraman *et al.* (53) clearly conflict with those of Caffarra *et al.* (61) and other studies (28, 54, 55) which indicate that disengagement processes are *not* necessarily impaired in AD.

In summary, the evidence concerning whether our data should be interpreted in terms of impaired disengagement processes in AD is again somewhat equivocal. However, the balance of findings in the literature seems to indicate that disengagement deficits may mediate at least some of our own data, although the precise interplay between disengagement mechanisms and the detailed task requirements of simple and conjoined feature search has yet to be resolved. This important issue needs to be investigated by using similar tasks in clearly defined groups of patients at similar stages of disease across different research laboratories.

### 6.6. Shift

There has been relatively little work conducted into attentional shift mechanisms in AD. In a study of normal aging, However, the ability to shift appropriately the 'window' or 'spotlight' (125) of selective attention (assuming it has - if necessary - been adequately disengaged from a previous location) appears to be well preserved in AD (28, 51, 53-55). Greenwood, Parasuraman and Haxby, (126) argued that whereas healthy aging had only a weak effect on voluntary attention shifts, dementia affects both voluntary and involuntary modes of attentional shifting. Overall, however, it seems unlikely that our visual search data should be interpreted in terms of impaired shift mechanisms. Furthermore, although impairments in shift mechanisms may - on the surface - appear to provide a convenient explanation of the deficits in conjoined feature search performance that we have noted in AD patients, impaired shift mechanisms cannot easily account for other aspects of our findings (for example, deficits in processing more peripherally located simple feature search targets in some AD patients in the absence of differentially slowed processing of more peripheral targets on conjoined feature search).

### 6.7. Inhibition

We will now consider the extent to which impaired inhibition of distractors could explain the pattern of visual feature search performance that we have observed in AD patients. The reader may care to reflect on the relationship between the concept of 'inhibition' and the notions of 'engage', 'disengage' and 'shift' of attention that were considered in the previous sections. The interplay between these processes has not been adequately explored to date, although one reasonable argument might propose that inhibition acts to prevent the initial engagement of distractors by the 'spotlight' of selective attention and/or facilitates disengagement from distractors if they are inappropriately engaged by the attentional spotlight.

In a relevant study, Simone and Baylis (34) examined the ability of young controls, elderly controls and

elderly individuals suffering from AD to perform a selective reaching task. Normal aging did not increase the degree of interference caused by distractors on this task. The finding of this selective reaching task is therefore similar to the pattern we have previously observed on the simple feature task in elderly individuals, but not on the conjoined feature task, where normal aging did differentially affect performance (see 64). Simone and Baylis (34) did, however, demonstrate exaggerated effects of interference on their selective reaching task in AD patients. This seems somewhat similar to our own findings of a greater effect of distractors on conjoined feature search in AD patients. Simone and Baylis interpreted their findings in terms of AD patients' inability to use inhibitory processes, and suggested that this inability increased with the severity of AD. This conclusion is supported by the work of Faust *et al.* (44), who observed impaired inhibitory control in AD patients on a sentence comprehension task, and by the findings of Spieler *et al.* (45), who observed impaired inhibitory functioning in AD on the Stroop task. Grande *et al.* (19) and Sullivan *et al.* (43) have also cited evidence of reduced inhibitory capacities in patients with AD. Problems with inhibition and/or interference in AD have also been suggested by a range of other studies that have reported difficulties in resolving stimulus-response conflict, using both novel experimental and established psychometric procedures (for example 22, 35, 47, 49-52). This is consistent with our own error data (65), in which we noted that AD patients were more likely to make errors of both commission and omission, although this was much more evident for Moderate than for Mild AD patients. Previous studies indicate that distractor inhibition is less severely affected than stimulus-response conflict resolution in AD, but more affected than target processing, for which there appears to be least evidence in the existing AD literature (see also reviews of changes in attention in AD presented by 127, 128).

Findings of impaired inhibitory functioning in AD seem consistent with the notion that at least some of the deficits that we have noted in AD patients in our work into visuospatial selective attention are related to reduced inhibition of distractor items during visual search. However, Faust and Balota (54) used a simple detection task to examine covert orienting of visuospatial attention in AD and reported no evidence for inhibitory deficits. More specifically, these researchers noted equivalent inhibition of return (i.e. a slowing in the response to previous spatially cued locations) in AD patients and in young and elderly controls. However, Faust and Balota (54) noted both an age-related and an AD-related increase in the beneficial effect of a peripheral cue on target detection, perhaps indicating an impairment in spontaneous attentional engagement in AD. The findings of Faust and Balota (54) also provide an interesting comparison with the data obtained in our studies, as our own findings indicate that, on the simple feature task (but, surprisingly, not on the conjoined feature task), peripheral targets were detected more poorly by AD patients. This is perhaps again indicative of impaired spontaneous engagement of peripheral targets in AD. Furthermore, by comparison with the findings of Simone and Baylis (34), the findings of preserved inhibition of return reported by Faust and Balota (54) imply some fractionation of impaired inhibitory processes in AD.

Other recent studies have examined the question of inhibition and 'interhemispheric balance' in AD; for example, Wright *et al.* (28) used a modified version of the Posner covert attention task (in which cues were either 'valid', 'invalid', 'neutral' or 'No-Go'), similar to the task used by Faust and Balota (54). Wright *et al.* (28) noted that - compared with controls - AD patients showed increased benefits of valid cues and reduced costs of invalid cues. Wright *et al.* (28) concluded from their findings that this represented evidence for an AD-related impairment in dividing attention between left and right-sided target locations.

Therefore, the question of whether impaired inhibition from distractors characterizes selective attention performance in AD patients again appears somewhat open. This question is further complicated by the fact that findings using the same or similar experimental paradigms are not always replicated in the AD literature, as noted previously between the findings of Foster *et al.* (65) and Parasuraman *et al.* (60) using a similar conjoined feature visual search task. If - as Faust and Balota (54) contend - AD patients do not manifest impairments on attentional inhibition, then the deficits that we observed in our work on the simple and conjoined feature task may be due to problems in processing the filled circle target itself, rather than in inhibiting or disengaging from distractor items. Nevertheless, the balance of evidence seems to be in favour of the notion that impaired inhibition (i.e. of distractors in the present context) may have some role in the pattern of our findings with AD patients. How this point relates to our previous discussion concerning the role of 'disengage'/'shift'/'engage' processes remains open. Perhaps impaired inhibition mechanisms manifest themselves in the form of slower disengagement from distractors on the Treisman conjoined feature visual search task? This issue waits future investigation.

### 6.8. Summary: engagement/disengagement/shift, inhibition

The findings reviewed above are complex, and the implications are currently far from clear-cut. However, to attempt to summarize: while some existing findings suggest that the ability to disengage attention is selectively impaired in AD (with preservation of shift and engage capacities), other experiments indicate that selective attentional deficits in AD are not limited to disengage processes. Therefore, there does not appear to be a clear consensus from the existing literature indicating whether our findings should be interpreted more in terms of impaired engagement of and/or movement towards the target, or more in terms of a deficit in disengagement from distractors. Nevertheless, for the reasons discussed above, our preferred interpretation of our findings is primarily in terms of impaired disengagement mechanisms in AD, with disinhibitory mechanisms also possibly implicated.

At least some of the existing lack of clarity in the AD attention literature may be due to the fact that - by contrast with our work - few previous studies have attempted to determine whether apparent deficits in disengagement, shift, engagement or inhibition processes transcend 'global cognitive slowing' deficits that may exist in AD. We consider this important theoretical concept further in a subsequent section of this chapter.

As mentioned earlier, on the basis of Posner's influential theory of anatomically-linked attentional networks (88-90), it has been predicted that there are impaired disengagement processes in AD (corresponding to damage in the parietal region; see 5, 91-92), with preserved shift and engagement processes (because of relatively limited neuropathology in AD in the superior colliculus and pulvinar, respectively). Furthermore, it has been proposed that the superior parietal cortex is specifically involved in mediating conjunction search (79). The basal ganglia are thought to mediate the fundamental ability to detect salient targets (see 88-90), and this capacity may underlie simple feature search. The basal ganglia are relatively unaffected in AD (110, 111).

Taken together, these lines of evidence provides support for the notion that damage to the parietal cortex in AD mediates impaired disengagement processes, which - at least partially - underlie the deficits in conjoined visual feature search observed in our work. Of course, the true picture is unlikely to be so simple, and other mechanisms are also likely to be involved (for example, inhibitory processes). Furthermore, this framework does not take into account other important aspects of our findings, such as impaired simple feature search with peripheral target location in more severe AD patients. However, future investigations should help us to refine this working model; for example, studies using non-invasive imaging techniques in individuals undertaking simple and conjoined feature search tasks.

### 6.9. Automatic versus controlled processing

As noted, several research groups have interpreted their findings of exaggerated effects of interference in AD patients in terms of impaired inhibitory processes (for example, 34). Another possible interpretation of these findings is that tasks that draw upon "automatic" functioning in healthy controls may be subserved by "controlled" processing in AD patients. There was the suggestion of a similar effect in our own work, with performance slowing somewhat in the moderate AD patients at the largest distractor array size, even on the simple feature search task. In addition, AD patients showed deficits locating targets in more peripheral locations on the simple feature search task. However, in other respects, the AD patients who participated in Foster *et al.* (65) study did not manifest significant cognitive impairment on the "automatic" simple feature search task. Instead, the AD patients showed a more exaggerated pattern to that observed in our previous work into normal aging (64), with cognitive impairment focused upon the "controlled" conjoined feature search task.

Our finding of generally preserved "automatic" attentional functioning but impaired "controlled" attentional processing in AD would seem to conflict somewhat with the findings of a recent PET study (86). This PET study indicated that "automatic" and "controlled" attentional processing might be mediated via a similar network of anatomical regions. However, the key issues here may be the level of spatial resolution of PET, and the extent to which the "controlled" and "automatic" attentional systems show graceful deterioration after brain damage. For example, it is possible that - although mediated by similar anatomically

distributed regions - the network of structures and processes mediating "automatic" attentional processing may be more resilient following brain damage than the structures subserving "controlled" attentional processing. Techniques offering greater spatial and temporal resolution - such as event-related fMRI and MEG - may help to address these issues in future.

### 6.10. Generalized slowing

Are the deficits in visual selective attention that have been reported in the AD literature specific to selective attentional processes, or should the default explanation be favoured, i.e. that these deficits reflect a more general decline in cognitive functioning in AD? Unfortunately, as previously mentioned, a common feature of many previous studies of attention in AD is their failure to obtain appropriate data to address this question adequately, or - if their data are appropriate - to fail to apply an appropriate quantitative analysis to their data (such as the Brinley plot approach used in our work). Without the use of such a technique, one is unable logically to attribute any deficits reported on selective attention tasks specifically to the domain of selective attention (of course this caveat also applies to other cognitive domains if data are not appropriately obtained and analysed; for example, when deficits are reported in memory in AD without considering to what extent such deficits are truly specific to the domain of memory). That is, in the absence of a Brinley plot (or other similar quantitative tool), one is unable to disregard the possibility that one's data are merely indicative of a general cognitive decline or slowing, which may exist across a whole array of cognitive functions.

Similar concerns have also been voiced within the cognitive aging literature (see 64). Although the construct of global slowing is less well established in the neuropsychology literature than in studies of normal aging (see 101-106), we believe that the failure to evaluate chronometric data in terms of possible global slowing mechanisms represents a fundamental oversight in many previous studies of cognitive functioning in AD. Because of its theoretical importance, the central question of whether "generalized cognitive slowing" can account for our own visual search data will now be considered.

In an important meta-analysis of their own wide-ranging investigations into cognitive functioning in AD, Nebes and Brady (106) directly addressed the impact of global cognitive slowing. The authors plotted a Brinley function of the performance of AD patients and healthy old participants against the performance of young controls across more than 100 psychometric and experimental tests. Nebes and Brady (106) proposed that one could validly infer that a particular cognitive task was selectively impaired only if the data from this particular task lay two or more standard deviations from the regression line fitted to their complete data sample.

This has been interpreted by others as a somewhat stringent criterion for selective cognitive impairment in AD (see 127). However, when our own data are superimposed on the Brinley-type regression function derived by Nebes and Brady (106), there is clear evidence for significant deviation

from this regression function in the conjoined feature search task (65). In the Mild AD group, this deviation is notable at the largest array size, while in the Moderate group such a deviation is apparent at all array sizes, with the extent of the deviation from the regression line increasing approximately in proportion to the level of the independent variable (i.e. in this case, the number of distractors). The Mattis Dementia Rating Scale (DRS) [109] scores of the "mildly demented" and "moderately demented" patients evaluated in the Nebes and Brady (106) review were similar to the DRS scores in the Mild and Moderate AD groups tested in our work (65), indicating the viability of such a direct data comparison.

When we proceeded to construct formal Brinley plots from our data, the slopes of the Brinley functions relating young participants' target detection times to AD patients' target detection times on the conjoined feature search task were systematically greater in the Mild group, and greater still in the Moderate group, than the slope of the regression function derived for AD patients derived by Nebes and Brady (106). In their meta-analysis Nebes and Brady found that the best fitting regression line for their data showed a slope within the range 1.87-1.97 for mildly demented patients, and within the range 2.56-2.94 for moderately demented patients (when comparing the performance of each set of AD patients with young controls). By contrast, in our work these values were exceeded by both sets of AD patients: Mild AD patients showed a slope of 3.64, while Moderate AD patients showed a slope of 5.19 (see 65). We interpret these values as reflecting the specific central processing demands of the conjoined feature task, revealing impairments in AD patients over and above those predicted according to global cognitive slowing mechanisms. Moreover, we saw a greater increase in the slope of the target detection function in conjunction search in Moderate compared with Mild AD patients, suggesting that the slowing in target detection in conjoined feature search that we observed was systematically related to AD severity. Note also from the data reported in Foster *et al.* (65) that the degree of slowing of healthy Elderly Control participants (slope=2.55 from the relevant Brinley plot, i.e. relative to young controls) on the conjoined feature search task was considerably greater than that which would be predicted from the normal cognitive aging literature ( $<2.0$ ). This is consistent with what we have observed previously in a larger sample of healthy elderly (64). Moreover, a similar (albeit less exaggerated) pattern of findings has been observed in our studies of selective attention in the healthy elderly (64, 65) as we have observed in or research into selective attention in AD patients (65) when the performance of each of these groups was compared with the performance of young controls.

In summary, the findings of the Brinley analyses conducted on the data reported in Foster *et al.* (65) indicated that visuospatial selective attention is affected in AD patients over and above the degree of cognitive impairment expected according to the notion of global or generalized cognitive slowing (see 101-106). Our Brinley analyses (65) also indicated that the AD patients studied showed a qualitatively similar but quantitatively steeper slope on the conjoined feature task than we have observed in normal aging (64).

Greenwood *et al.* (35) have also tried to relate their findings of AD-related reductions in the control of the spatial focus of attention to the explanatory concept of global cognitive slowing. More precise cuing (which the authors argued should make their visual detection task less complex) actually made AD patients perform differentially worse relative to controls. This was interpreted by Greenwood *et al.* (35) as evidence against the applicability of a cognitive slowing model to their data. However, formal Brinley plots were not employed in the Greenwood *et al.* (35) study to evaluate the cognitive slowing hypothesis more rigorously. Furthermore, it could be argued that the cognitive slowing hypothesis requires elaboration and refinement before it is properly evaluated in the context of a task using differentially located and variably sized valid and invalid stimulus cues.

### 6.11. Diagnostic considerations

Early studies of selective attention function in AD tended to use small groups of patients that were often assumed to be in the early stages of the disease. Important questions in this literature have therefore been raised concerning the nature and degree of selective attentional dysfunction in more advanced stages of AD, and whether findings obtained with small numbers of relatively mild patients can be generalized to AD patients as a whole. The AD patients that we have studied all fell within either the Mild or Moderate categories of AD, according to the criteria of the Global Deterioration Scale (GDS). However, most of the Mild patients appeared to fall within category 2 or category 3 of the GDS, while the majority of the Moderate patients seemed to fall within category 5; i.e. within each of the main categories of "Mild" and "Moderate", our patients were located towards the more severely impaired end of the diagnostic range. Although it would have been preferable for us to have tested a greater number of mild AD patients, the number of patients that were tested raises a genuine problem in the field: diagnosis of AD is currently probabilistic and made by exclusion, so that it is much more difficult to find clearly-diagnosed AD patients in the earliest stages of the disorder to participate in research. This consequently raises problems in attempting to define the earliest possible "cognitive markers" for the disease, and in conducting follow-up studies across the widest possible spectrum of disease severity.

In our work, analysis of the performance of individual participants indicated that there was a significant amount of intra-group variability on both the simple feature and conjoined feature selective attention tasks. (See previous sections for a consideration of heterogeneity in the cognitive and neurological profiles across different AD patients.) Furthermore, there was a substantial amount of inter-group overlap both between the performance of participants in the Mild and Moderate AD groups, and between the AD patients and the Elderly Controls. Performance on these visual search tests cannot therefore be used as definitive cognitive markers for the occurrence and level of severity of AD. However, the simple and (especially) the conjoined feature tasks may prove to be valuable when used – perhaps in the context of a multiple regression model – with data from other standardized psychometric tests, in the context of a full clinical work-up, and/or when the level of selective attention

is of particular diagnostic significance. These tasks may also be useful in clinicopathologic subtyping of patients, particularly concerning the already noted heterogeneity of cognitive deficits observed in AD.

Of interest, whereas selective attentional differences between AD patients and controls have been noted in our studies on the conjoined feature task, no such group differences were noted in our work on the "attention" sub-scale of the Mattis Dementia Rating Scale [DRS] (although significant differences between AD patients and controls were noted in our studies on the global DRS score and on the "memory" sub-scale of the DRS). This finding indicates that – in our work – the conjoined feature visual search task is tapping into a decline in selective attentional functioning to which the attention subscale of the DRS is apparently insensitive. A similar observation was made by Simone and Baylis (34), who noted that cognitive screening instruments typically used in the clinic to measure AD severity are often sensitive to memory impairment in AD but not to attentional impairment (as indexed by performance on their experimental delayed response task).

## 7. CONCLUDING COMMENTS

Our work indicates that AD patients have cognitive impairments on a resource-demanding, controlled visual selective attention task, namely conjoined feature search, and that these deficits were more apparent in the right rather than the left hemifield. Moreover, the severity of the deficit in AD patients that we observed on this task was greater than that expected from a meta-analysis of a wide range of previous cognitive studies of AD (106). There was also some indication from our work that more severely impaired AD patients may begin to show deficits on an automatic, non-effortful visual search task, especially with more peripherally located targets.

The findings of our work therefore indicate that AD affects selective attentional abilities. The impairments noted may have important knock-on effects for performance in other cognitive domains. There was no suggestion in our work that AD patients performed the conjoined feature search task in a fundamentally different manner than healthy elderly controls; indeed, our findings largely indicated a functional continuity between the performance of patients with AD and healthy old participants on both of the visual search tasks that we studied (cf 64, 65). The differences that we observed between AD patients and controls were therefore quantitative rather than qualitative. However, the central slowing that we noted on conjoined feature search was specific, in that it exceeded the degree of impairment predicted on the basis of a generalized cognitive slowing impairment in AD (106). These theoretical distinctions between quantitative versus qualitative differences and specific versus global cognitive impairments are important, and need to be further delineated in future studies.

Our findings are consistent with other studies of selective attention in AD, which – as previously noted – have indicated that dementia may impair some attentional processes while sparing others (see 127-129 for reviews).

More specifically, our findings indicate that AD patients are as effective as healthy old or young participants in using a salient physical feature to restrict their processing of information (see 130), as long as that feature uniquely defines the item of interest, and it is not presented in a peripheral region of space. In addition to their theoretical significance, our findings may therefore have practical implications for the day-to-day functioning of AD patients within their natural environment (see 17).

Several questions for future research have been raised by our work. Would the use of pre-target cues permit AD patients to compensate for the deficits that these individuals apparently experience in detecting targets located on the right hand side of the midline (in conjunction search) or in peripheral regions of space (in simple feature search)? What is the mechanism underlying our somewhat paradoxical finding (given the array size effects on visual search that we noted) that AD patients are not differentially impaired in detecting more peripherally located targets on the conjoined feature task, but they are more impaired with peripheral targets on simple feature search? Future investigations should also consider in more detail the possible cognitive mechanisms underlying the deficits we have observed on conjoined feature search in AD patients. For example, by monitoring participants' eye movements, it should be possible to determine whether deficits observed in visual search in AD patients are predominantly due to difficulties in disengaging from erroneously engaged stimuli, shifting attention between stimuli or in processing stimuli once they have been engaged. As we have seen, the current AD literature is far from clear on this issue. Future longitudinal follow-up studies of selective attention will also enable researchers to specify in more detail the time-related nature of the attentional changes taking place in AD. Patients need to be rigorously classified according to disease stage, severity and the local vs global nature of their clinically manifested impairments, so that visuospatial selective attentional performance can be examined as a function of these factors in a carefully controlled manner.

It is clear that selective attention is not a unitary process, and only certain specific components of attention are likely to be impaired in AD, at least in the early stages of the disease. The findings discussed in this chapter on the simple and conjoined feature search tasks indicate some specificity in the attentional performance of AD patients relative to the task demands and the level of severity of the disease. More specifically, our findings indicate probable deficits in AD patients in conjoining features (especially on the right side of hemispace), in detecting even highly salient targets when they are presented in more peripheral regions of space, and in determining whether it is appropriate to respond or withhold from responding (65). In future, the precise visuospatial selective attentional mechanisms that are affected in AD need to be studied more systematically, testing well worked up patients samples (for whom structural and if possible functional brain imaging data are available), and using clearly defined experimental paradigms that have been devised to tease apart fundamental cognitive processes mediating task performance.

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