

Attentional control in Alzheimer's disease

A. D. Baddeley,¹ H. A. Baddeley,¹ R. S. Bucks² and G. K. Wilcock²

Departments of ¹Experimental Psychology and ²Care of the Elderly, University of Bristol, UK

Correspondence to: Alan Baddeley, Department of Experimental Psychology, University of Bristol, 8 Woodland Road, Bristol BS8 1TN, UK

Summary

Attentional control of executive function declines during the early stages of Alzheimer's disease. Controversy exists as to whether this decline results from a single global deficit or whether attentional control can be fractionated, with some aspects being more vulnerable than others. We investigated three proposed domains of attention, namely (i) focal attention, based on simple and choice reaction times; (ii) the capacity to resist distraction in a visual search task; and (iii) the capacity to divide attention between two simultaneous tasks. For each domain, two levels of difficulty were used to study Alzheimer's disease patients, who were compared with elderly and young control subjects. The unitary attentional hypothesis predicted that the impacts of level of difficulty, age and

disease would be qualitatively similar across the three attentional domains. In fact we observed different patterns for each domain. We obtained no differential impairment for patients in the focal attentional task, whereas patients were somewhat more susceptible than control subjects to the similarity of the distractor items in visual search. Finally, we observed marked impairment in the capacity of Alzheimer's disease patients to combine performance on two simultaneous tasks, in contrast to preserved dual-task performance in the normal elderly group. These results suggest a need to fractionate executive processes, and reinforce earlier evidence for a specific dual-task processing deficit in Alzheimer's disease.

Keywords: Alzheimer's disease; attention; executive processing; working memory

Abbreviations: ANOVA = analysis of variance; MMSE = Mini-Mental State Examination; NART = National Adult Reading Test; NINCDS-ADRDA = National Institute of Neurology and Communication Disorders and Stroke—The Alzheimer's Disease and Related Disorders Association; RT = reaction time

Introduction

In a recent review of attention and executive processes in Alzheimer's disease, Perry and Hodges present evidence for substantial and broad impairment (Perry and Hodges, 1999). Indeed, they suggest that, apart from the episodic memory deficit that is a crucial feature of the diagnosis of Alzheimer's disease, attentional capacities are the first to deteriorate, preceding impairment in perceptual and language function and potentially having a substantial impact on the patient's capacity to cope independently. Their review is based on the increasingly widely held assumption that the concept of attention may be fractionated into a number of potentially separable subsystems. They suggest that these may be differentially sensitive to the effects of the disease, sustained attention (reflected in the capacity to maintain attention over time) being the least affected, and attentional control (the capacity to focus and switch attention) being more susceptible to the disease. However, the strongest evidence for a differentially sensitive aspect of attention is presented by the capacity for divided attention, the ability to perform two distinct tasks simultaneously.

Although the evidence for some kind of deficit in attentional capacity is extremely strong, its theoretical interpretation is much less so. Indeed, despite extended empirical work on attentional deficits in Alzheimer's disease, it remains difficult to rule out the possibility that they simply reflect a broadly based process of cognitive decline that is evident, for example, in a progressive decrease in the speed of some basic cognitive process (Perry and Hodges, 1999; Salthouse, 2000). Tasks that appear to be differentially susceptible to Alzheimer's disease would, in this interpretation, be regarded not as implying a separate subcomponent of attentional control but merely as reflecting particularly sensitive measures of this general capacity. Such an approach continues to be important in attempts to account for the cognitive deficits associated with what Salthouse refers to as a macro-analysis of ageing (Salthouse, 2000), whereby a single basic construct, such as processing speed, is assumed to account for most, though not necessarily all, of the age-related cognitive decline (Salthouse, 1993, 1996, 2000). As Perry and Hodges suggest, such an interpretation has also been applied to the further

cognitive decline associated with Alzheimer's disease (Cerella, 1985; Nebes and Brady, 1992).

The cognitive slowing hypothesis is attractively simple in assuming a single factor underlying the cognitive decline observed with advancing age and, by extension, Alzheimer's disease, namely that the speed of basic neural operations declines systematically. The occurrence of an increased error rate can also be incorporated by assuming that elderly subjects allow insufficient extra time, and hence occasionally respond before adequate processing has occurred. In other situations, such as in the digit span test, the speed deficit may result in an increase in errors through slower—and hence less effective—encoding, slower rehearsal and/or impaired speed of retrieval, allowing more forgetting to occur.

It is, of course, clearly the case that tasks differ in their sensitivity to the effects of both ageing and Alzheimer's disease. The speed hypothesis could interpret this in terms of differences in the basic level of difficulty of the various tasks; difficult tasks require more processing and are hence more affected by age and Alzheimer's disease. Apparent support for this view of ageing came from Cerella, who performed meta-analyses of the available data using a technique known as the Brinley plot, whereby data from a range of tasks are combined (Cerella, 1985). In each case, the performance of the young group on this specific task is plotted as a function of that of the elderly. If the data from a wide range of tasks are combined, a linear function tends to be produced, indicating that the ratio of elderly to young performance remains constant, despite the fact that the absolute difference increases with task difficulty. The data are then typically analysed by fitting a straight line, which tends to account for substantially more than 90% of the variance for most ageing studies. In the case of Alzheimer's disease, it is suggested that the slope of the line changes, with a slope of ~1.9 in the case of mild dementia and 2.6 in moderate cases (Nebes and Brady, 1992).

Unfortunately, although the Brinley plot method of analysis typically produces straight lines that account for an impressively large proportion of the data, it has been criticized as being a highly insensitive method of data analysis that swamps the relatively subtle and complex age-related effects with the very much larger and more reliable differences in performance that can be achieved by varying the difficulty of the underlying tasks (Fisk and Fisher, 1994; Perfect, 1994; Perfect and Maylor, 2000).

The method used most widely by advocates of the general slowing hypothesis involves some form of multivariate analysis. Subjects of different ages are tested on a range of tasks, some of which are assumed to rely principally on speed of processing. Performance in each task is then correlated with age and stepwise regression is used to identify the best predictor. The data may be analysed subsequently by the use of some form of structural equation modelling, combining the various measures into a smaller number of hypothetical underlying processes and seeking the pattern linking these processes that will account for the available

data most economically (Perfect and Maylor, 2000). Using such methods, Salthouse concluded that most, though not all, of the decrement in cognitive performance observed in the process of ageing can be accounted for by a simple systematic decrement in processing speed (Salthouse, 1993, 1996).

Despite its elegant and sophisticated use of psychometric techniques, this approach has met with a number of serious objections. The first concerns the measure of speed that is assumed to lie at the basis of the analysis. Speed is measured in terms of specific tasks, which themselves reflect a range of underlying processes that are typically unspecified. In this absence of specification, it is unclear what a speed measure means. Combining data from a number of different tasks simply broadens the range of operations being sampled. This could be regarded as a positive feature methodologically, as it is likely to increase the generality and reliability of the measure. However, it is less helpful in the task of identifying underlying mechanisms as it has the disadvantage of lumping together a whole range of potentially quite different processes.

Perhaps the most severe problem in this approach to the analysis of behaviour comes from the problem of collinearity, the tendency for many different functions to change at the same time as a result of the processes that underlie normal ageing or the impact of Alzheimer's disease. The seriousness of this problem became clear with the publication of extensive research on a cohort of elderly subjects carried out by Baltes and his group in Berlin (Baltes and Lindenberger, 1997). This group also measured a range of functions, using multivariate analysis to build an overall picture of age-associated cognitive decline. However, whereas Salthouse tended to use measures of speed and reaction time, Baltes and his group looked carefully at a range of basic processes of sensory function and motor output. They were able to account for an impressive amount of age-related variance simply in terms of the accuracy with which their subjects performed a visual discrimination task; they found a similar correlation with auditory discrimination. In addition, however, they found equally good predictiveness for a measure of grip strength. Baltes and colleagues do not, of course, claim that the mental agility of elderly people is driven by the strength of their arms, but accept that the measures they used are reliable indicators of a general process of decline that accompanies ageing. The fact that they are good predictors does not mean that they are causally related to the decline. As Lindenberger and Pötter point out in a detailed analysis of the problem, one of the basic premises of statistics, namely that correlation does not necessarily imply causation, seems to have been forgotten briefly in the field of ageing research (Lindenberger and Pötter, 1998).

How can one avoid the problem of collinearity? It is, of course, also a problem with neuropsychology, in which the greater the degree of brain damage, the greater the likelihood of cognitive deficit; here the answer has been to use dissociations rather than associations. The fact that patient A has poorer long-term memory than patient B says nothing about the specificity of the memory deficit. However, if

another type of memory—short-term memory—is preserved, this indicates that these two types of memory are potentially separable. The provision of a second group of patients in whom the opposite pattern prevails allows one to rule out differences in test sensitivity, arguing more strongly for two separate memory functions (Shallice, 1988). We suggest that a similar approach can be used to investigate decrements in attentional capacity resulting from age and Alzheimer's disease (Baddeley *et al.*, 1991). Using such methods, we hope both to increase our knowledge of the disease and to develop further understanding of normal attentional processes.

The attraction of the cognitive slowing hypothesis lies in its simplicity: age, disease and task complexity all exert their effects through the speed at which the basic operations can be performed. One might therefore expect a given task to be performed more slowly by an elderly person than by a young subject, and yet more slowly by an Alzheimer's disease patient. Suppose one then introduces two levels of difficulty into the basic task. The simplest assumption would be that the more difficult version would simply add a constant amount to the performance time for each of the three groups. This is typically not what is observed in the case of dual-task performance, in which dividing the attention has little effect on the performance of the young or the normal elderly subjects but clearly impairs the performance of Alzheimer's disease patients (Baddeley *et al.*, 1991). One interpretation of this finding is that patients have a specific impairment in the capacity to divide attention between two tasks. Another is to argue that this effect stems from the greater difficulty of the dual-task condition, on the grounds that any task that increases the effect of normal ageing on performance will lead to an even greater impairment in patients.

We therefore concur with the conclusion of Perry and Hodges that although there appears to be *prima facie* evidence for differential impairment of different aspects of attention in Alzheimer's disease, the evidence is at present far from conclusive (Perry and Hodges, 1999). They propose that future studies should (i) study a range of subtypes of attention within the same group of subjects; (ii) use a range of information processing tasks targeted at potential specific deficits, taking account of the general slowing hypothesis in deciding whether the differences between the subtypes of attention are qualitative or merely reflect different levels of overall difficulty; (iii) include young as well as old controls; and (iv) include patients at different stages of the disease so as to provide a more finely graded estimate of the rate of decline of different components of attention.

Fortunately, although the design of our study preceded the review of Perry and Hodges, we share their views on the factors appropriate to designing a study in this area and were able to put them into operation, with one exception. The pattern of patient referral to our clinic does not provide more than a small number of patients suffering from what Hodges and his group term 'minimal dementia', i.e. patients scoring >24 in the Mini-Mental State Examination (MMSE) (Greene

et al., 1995; Perry and Hodges, 1999). Furthermore, patients with scores of ≤ 15 tend to have difficulty understanding and following the instructions for all but the simplest novel cognitive tasks. Hence, rather than opting for two clearly separate groups, our main study included a single patient group, although we subsequently analysed our patient group in terms of severity of dementia as measured by the MMSE.

Our study therefore involved three groups, one comprising patients, the second consisting of age-matched controls and the third of young control subjects. The two older groups were matched for years of education and general socioeconomic level, using a spouse as a control wherever possible. All three groups were tested on a range of baseline measures together with four attentional tasks, each involving two levels of difficulty. One of these tasks was essentially a replication of an earlier dual-task procedure whereby subjects combined a motor task (writing crosses in boxes) with concurrent testing of digit span, and the level of difficulty was determined by whether the subject was performing one task or two simultaneous tasks. A second task also involved dual-task performance but used quite different procedures, combining visual search with concurrent auditory detection. A third involved simple and choice reaction times, difficulty being varied through the number of response alternatives, and a fourth task studied visual search performance, with difficulty determined by the degree of similarity between target and distractor items.

Each task thus involved two levels of difficulty and was performed by three groups: young and elderly subjects and Alzheimer patients. In the case of the reaction time and visual search experiments, we would expect a slowing due to age and a further impairment attributable to the disease, together with differing effect of difficulty across groups. The crucial issue, however, is whether an interaction occurs between subject group and level of difficulty, and the nature of any such interaction. The lack of a significant interaction would be consistent with the general slowing hypothesis.

A slightly more complex version of the general speed hypothesis is that the effect of difficulty is not absolutely equivalent across the various groups but is proportional. For example, the increase might be proportional to the baseline level of performance. If this were the case, then one might expect a logarithmic transform to remove the interaction. If this were not the case, then it would be difficult to give an account of the pattern of data in terms of a single overall factor, such as the speed of processing. If, for example, there was a disproportionate effect of difficulty in the case of the Alzheimer's disease patients, this would suggest a disease-related specific deficit.

Earlier research indicates that the dual-task paradigm offers the possibility of a more striking test of the hypothesis, as it suggests that age, unlike Alzheimer's disease, has little or no impact on the capacity to divide attention. If confirmed, this clearly implies a disproportionate effect of disease on this aspect of attentional control. By including two different versions of this paradigm using very different tasks, we

hoped to ensure that earlier findings were replicable and that they could be extended to the combination of two new tasks.

Methods

Subjects

Patient sample

A total of 41 patients attending the Memory Disorders Clinic at the Department of Care of the Elderly at Bristol were given a diagnosis of probable Alzheimer's disease and fulfilled the following criteria: a score of at least 15 out of a possible 30 on the MMSE (Folstein *et al.*, 1975); not suffering from any other medical or neurological condition or on any medication that would be likely to affect cognitive performance; not clinically depressed; able to hear, see adequately and follow instructions.

Patients attending the Bristol Memory Disorders Clinic are assessed by thorough medical, psychiatric and psychological screening to exclude any other treatable pathology that could explain their dementia. Particular attention is paid to presenting symptoms, onset (sudden or insidious), progression (static, stepwise or gradual) and the presence of memory and other cognitive problems, as well as affective or behavioural difficulties. Their medical history is also evaluated, with emphasis on conditions that might be associated with cognitive impairment, medications and substance abuse (especially alcohol). Any family history of depression or organic or neurological disease is also noted. A depression rating scale is used (Alexopoulos *et al.*, 1988). Patients are referred for assessment by a psychiatrist if there is any clinical suspicion of affective or psychotic illness or if they score above the cut-off on the depression rating scale. Behavioural and functional deficits are measured in an interview with the carer, using the Bristol Activities of Daily Living Scale (Bucks *et al.*, 1996). The Hachinski Ischaemic Scale is also administered (Hachinski *et al.*, 1974) using a modified form designed to improve reliability (O'Neill *et al.*, 1995). A comprehensive physical examination is undertaken, including neurological assessment for signs of apraxia, aphasia or agnosia, extrapyramidal signs and primitive reflexes. Laboratory blood testing and CT brain scans are also carried out. When clinically indicated, some patients are also referred for SPECT (single photon emission computed tomography) or MRI.

The neuropsychological assessment used in the Bristol Memory Disorders Clinic is designed specifically for the clinic and has been validated in a sample of healthy older individuals and samples with probable Alzheimer's disease and vascular dementia (Bucks and Loewenstein, 1999). Each patient's assessment is discussed in a multidisciplinary case conference. A diagnosis of probable Alzheimer's disease is made according to the NINCDS—ADRDA (National Institute of Neurology and Communication Disorders and Stroke—The Alzheimer's Disease and Related Disorders Association) criteria (McKhann *et al.*, 1984) and the Diagnostic and

Statistical Manual—IV (American Psychiatric Association, 1994). Patients with a score of ≥ 5 on the Hachinski scale (Hachinski *et al.*, 1974) were excluded to reduce the possibility of including vascular dementias.

Only patients with unequivocal and stable diagnoses were recruited. Longitudinal evidence from the memory clinic suggests that 70% of diagnoses made by the clinic are stable 6 months later (O'Neill *et al.*, 1992), rising to 90% at the 1-year follow-up. Participants are followed longitudinally for between 6 months and ≥ 2 years. The data of any individual whose diagnosis was subsequently changed were removed. Individuals with depression or taking medications likely to affect cognition (cholinesterase inhibitors or newly prescribed antidepressants) were excluded from the study.

Participants were recruited if they were suffering from very early to moderate impairment, as measured by the MMSE (Folstein *et al.*, 1975). Four of the original patients were subsequently excluded. Of these, two failed to show any further cognitive decline over the subsequent 6-month period, putting their diagnosis of probable Alzheimer's disease in doubt, one patient's diagnosis was changed to Lewy body dementia and the fourth was found subsequently to be partially sighted.

Control samples

Initially, 39 elderly control subjects were recruited and tested. Whenever possible, carers of the patients were invited to act as elderly control subjects (17 carers). A further 22 volunteers aged ≥ 60 years were recruited from the community. Data from three of these volunteers were subsequently excluded in order to match the patient group as closely as possible in terms of age, years of education, occupational category and estimated premorbid intelligence.

Thirty-six young control participants (aged 20–50 years) were also recruited so as to match the other groups in terms of occupational category, and to match the elderly group in verbal intelligence as estimated by the Spot The Word test from the SCOLP (Speed and Capacity of Language Processing) test. This is a test in which subjects are asked to pick the real word out of 60 pairs of items, each of which comprises one real word and one pseudo-word (Baddeley *et al.*, 1992, 1993). All subjects also performed the National Adult Reading Test (NART), a word-reading test in which subjects are required to read aloud phonetically irregular words (Nelson, 1982). Whereas the NART is a relatively robust measure of verbal intelligence, there is evidence that it may be somewhat sensitive to dementia (Stebbins *et al.*, 1990; Fromm *et al.*, 1991). We therefore chose to equate the patients and elderly control subjects for occupational category and years of education rather than NART, and did indeed find a small but significant difference between the patient and elderly control groups on NART, though not on Spot the Word performance. Demographic statistics for the patient and control groups are given in Table 1. Neuropsychological measures included two estimates of premorbid verbal

Table 1 Demographic characteristics of participants (standard deviations are given in parentheses)

	Alzheimer's disease patients	Elderly controls	Young controls
Gender	F 26 M 10	F 18 M 18	F 26 M 10
Age*	76.28 (6.33)	74.36 (8.12)	38.4 (8.79)
Years of education*	10.83 (1.78)	10.42 (1.9)	¶
Social group [†]			
1	3	1	0
2	14	17	21
3	19	18	15
MMSE	19.94 (1.78)		
NART*	108.94 (12.55)	114.94 (9.57)	111.47 (13)
Spot the Word*	45.93 (9.2)	48.27 (8.28)	45.54 (8.86)
Story recall, immediate [§]	5.83 (4.76)	28.88 (8.53)	36.11 (9.60)
Story recall, delayed [§]	1.64 (3.94)	26.77 (8.74)	34.26 (8.92)
Digit span [†]	5.14 (1.10)	5.61 (0.90)	5.61 (1.10)
Kendrick digit copying [§]	98.1 (20.1)	110.68 (20.1)	119.3 (15)
Verbal fluency (FAS) [‡]	33.86 (11.46)	44.71 (14.2)	45.5 (12.7)
Weigl test [‡]	2.93 (1.43)	3.97 (0.17)	3.88 (0.32)

*Patients = elderly controls; [†]patients = elderly controls = young controls; [‡]patients < elderly controls ($P < 0.05$) = young controls; [§]patients < elderly controls ($P < 0.05$) < young controls.

¶Not comparable because of change in the law on obligatory education.

intelligence [the NART and Spot the Word tests], immediate and delayed prose recall and digit span (Coughlan and Hollows, 1985), the Kendrick digit-copying test (Kendrick, 1985) (a simple measure of speed of processing) and two tests of executive function [verbal fluency requiring subjects to produce words beginning with the letter F, followed by A words and then S words (Spreen and Strauss, 1991) and the Weigl block-sorting test (Weigl, 1941)].

Patients were tested in their homes, which involved a session taking ~2 h in total, excluding time for breaks. For some patients, testing extended over two sessions to avoid overtiredness. Of the patients approached, all but one agreed to participate and provided their own and their carer's written informed consent. Younger subjects were tested either at home or in a quiet room at their place of work. All control subjects gave informed consent. The study was approved by the Ethics Committee of the University of Bristol.

Three aspects of executive dysfunction were assessed. The capacity to focus attention and respond rapidly was assessed using simple and choice reaction time; visual search against similar and dissimilar backgrounds was used to indicate the capacity to reject irrelevant material; and the capacity to divide attention was measured by requiring the subjects to perform two tasks simultaneously.

Experiment 1: simple and choice reaction times (RT)

We chose simple and choice RTs as measures of focused attentional processing. In each case the subject had to watch a VDU screen for a stimulus and then press a key as rapidly as possible. Because choice RT involves the additional tasks

of discriminating between two stimuli rather than one, and selecting the appropriate response, it seemed reasonable to assume a higher level of difficulty. This assumption should be testable by its prediction of longer choice time than simple reaction time.

Procedure

RT was tested using a portable computer (Macintosh Powerbook). The test of simple RT required the subject to respond as rapidly as possible to the presentation of a circle (diameter 5 cm) displayed on the screen. Circles were presented in blocks of 20 trials, with individual trials separated by a delay ranging from 1.33 to 4.00 s (mean 2.35 s). The subject was required to press a computer key as rapidly as possible, whereupon, after a quasi-random delay, the next circle appeared. To test choice RT we used identical conditions, except that half the items were circles and half were squares (5 cm), the subject being required to press separate keys for each. The key for simple RT was numerical key 2 and those for choice RT were keys 2 and 1. Four blocks of 20 stimuli were used. The subjects started with simple RT followed by two trial blocks of choice RT and a final simple RT block. Simple RT and choice RT to both stimuli were recorded, as were choice RT errors.

Results

Figure 1 shows mean performance for the three groups on simple and choice RT. Analysis of variance (ANOVA) indicated a significant effect of group [$F(2,104) = 48.9$, $P < 0.0001$], an effect of condition [$F(1,104) = 238.3$,

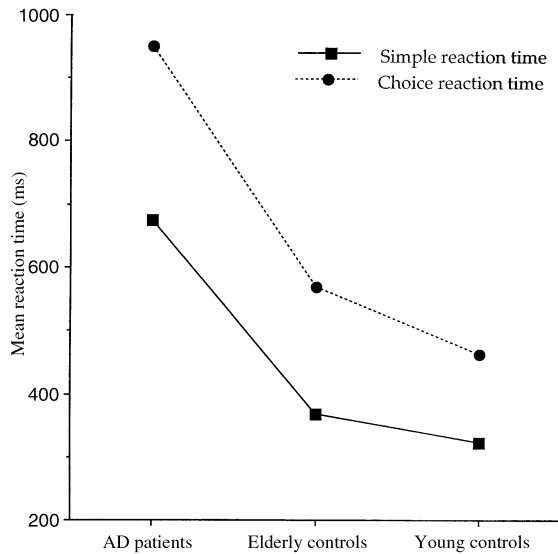


Fig. 1 Simple and choice reaction time in Alzheimer's disease (AD) patients and in age-matched and young control subjects.

$P < 0.0001$] and a significant interaction between the two [$F(2,104) = 8.3, P < 0.001$]. The extent to which the interaction was attributable to age versus disease effects was assessed by re-analysing the data with the patient group removed. There proved to be a significant group effect [$F(1,70) = 7.34, P < 0.01$], an effect of condition [$F(1,70) = 375.6, P < 0.001$], together with a significant interaction, [$F(1,70) = 11.00, P < 0.005$], indicating a greater age effect for choice than simple RT. The young group was excluded from the overall analysis in order to separate the effect of disease from that of age. In this case, there was a significant group effect [$F(1,69) = 49.8, P < 0.0001$] and a significant effect of condition [$F(1,69) = 145.8, P < 0.0001$], but the interaction failed to reach significance [$F(1,69) = 3.59, 0.05 < P < 0.1$]. When the data were logarithmically transformed, the significance levels of the main effects were unchanged, but all the interactions fell below the 0.05 significance level, only the interaction between condition and age approaching significance [$F(1,70) = 3.06, 0.05 < P < 0.1$].

Somewhat surprisingly, therefore, although the patients were slowed overall substantially more than the elderly controls, the effect of moving from simple to choice RT was broadly equivalent for the two groups in absolute terms. Indeed, when results were expressed as a percentage of simple RT, moving from one response to two added a mean of 44.3% for the young controls, 54.7% for the elderly controls and 41.0% for the patients. This pattern of results is not, of course, consistent with either a general slowing interpretation of Alzheimer's disease, or with specific vulnerability to an increase in the number of response alternatives.

All three groups made some errors in the choice RT condition, ranging from a mean of 1.1% (SD = 0.84) for

the young control subjects, through 1.6% (SD = 1.38) for the elderly group to 2.9% (SD = 3.17) in the Alzheimer's disease patients. There was an overall group difference [$F(2,104) = 7.62, P < 0.001$], the patients showing a higher error rate than the two control groups ($P < 0.01$ in each case), which did not differ ($P > 0.1$).

In order to assess the effect of progress of the disease, we split the group at the median MMSE score of 19, omitting those whose scores fell on the median. This gave us a sample of 17 patients who scored above the median (mean MMSE = 22.3, range 20–26) and 15 who scored below the median (mean MMSE = 17.1, range 15–18). The two groups did not differ significantly in years of education, age or premorbid intelligence, as estimated by the NART or the Spot the Word test. ANOVA indicated a significant effect of subject group [$F(1,29) = 7.57, P < 0.01$], task and whether simple or choice RT [$F(1,29) = 46.33, P < 0.0001$], together with a significant interaction [$F(1,29) = 4.37, P < 0.05$]. Whereas the higher-performing group showed an increase of 29.9% between simple (612 ms) and choice RT (795 ms), the lower MMSE group increased by a mean of 44.3% when moving from simple (775 ms) to choice RT (1119 ms).

Discussion

Our results overall suggest that both normal ageing and Alzheimer's disease impair RT performance, choice RT being slower and more sensitive to the effects of age. Somewhat surprisingly, however, the Alzheimer's disease patients were not significantly more impaired by the increase in difficulty than the normal elderly, although comparison within the patient groups suggests that greater sensitivity may be starting to emerge as the disease progresses. This may explain the somewhat mixed pattern of previous results, some of which show no evidence of significant slowing in mildly impaired patients (Lafleche and Albert, 1995), whereas others found significant impairment in simple RT (Reid *et al.*, 1996) or an impairment in choice but not simple RT (Pate *et al.*, 1994). The pattern of results is, however, broadly consistent with an earlier study by Baddeley and colleagues using a semantic categorization task, which again found no evidence to suggest that patients were disproportionately slowed down by an increase in the number of response alternatives (Baddeley *et al.*, 1991).

Considered overall, the pattern of results does not fit a hypothesis of general slowing. Although the patients were slower than the elderly control subjects, who in turn were slower than the young subjects, the additional slowing due to shifting from simple to choice RT was not proportionate; indeed, on a percentage basis it was less for the patients than for the elderly controls (41.0 versus 54.7%), although within the patient group there did seem to be a tendency for further decline to be shown most clearly in the choice RT task. This will be discussed later.

Experiment 2: visual letter search

Our second task involved visual search through rows of letters, subjects being required to cross out the letter Z. The level of difficulty was manipulated by embedding the Zs among either curved letters, a relatively easy discrimination, or other angular letters, a task that has been demonstrated to lead to slower processing and a higher error rate (Neisser, 1964).

Subjects were required to scan blocks of underlined upper case letters, comprising 10 lines of 15 letters, and to cross out examples of the letter Z. Each block contained 20 Zs distributed quasi-randomly across the 10 lines. Subjects began by being given untimed practice runs, continuing until it was clear that they fully understood the task. They were encouraged to work as quickly as possible without missing targets. In half the sets (version A), the background letters were dissimilar, comprising items in which the features were predominately curved (B C D G O P Q R S U). Version B comprised similar distracter letters, consisting principally of straight-line features (K L M N T V W X Y). Subjects were then tested using four blocks of each version, presented in the order A, B, B, A – B, A, A, B. The time taken to complete each block was measured by a stopwatch, and errors of omission and commission were subsequently scored.

Results

Figure 2A shows the mean search time per list for the three subject groups as a function of similarity of distractor letters. ANOVA (three groups \times two levels of difficulty) indicated significant effects of group [$F(2,101) = 41.3, P < 0.001$] and condition [$F(1,101) = 252.8, P < 0.001$] and a significant group \times condition interaction [$F(2,101) = 21.0, P < 0.001$]. The nature of the interaction was further explored by first excluding the patient group to investigate the effect of age. Age group proved to be significant [$F(1,68) = 19.7, P < 0.001$], as did condition [$F(1,68) = 275.2, P < 0.001$] and the age \times condition interaction [$F(1,68) = 7.2, P < 0.01$]. Similarly, when the young control group was omitted, the effects of disease [$F(1,67) = 27.0, P < 0.001$] and condition [$F(1,67) = 179.4, P < 0.001$] were highly significant, as was the interaction [$F(1,67) = 16.6, P < 0.0001$]. Logarithmic transformation left the significance level of the main effects virtually unchanged while reducing that of the interaction, but not eliminating it [$F(92,101) = 3.7, P < 0.05$]. When the analysis of transformed data was broken down to separate the effects of age from those of disease, the age \times condition interaction was abolished [$F(1,68) < 1$] and the condition \times disease interaction became marginal [$F(1,67) = 3.37, 0.05 < P < 0.1$].

The pattern of omission errors is shown in Fig. 2B (errors of commission, in which a letter other than Z was crossed out, were extremely rare). ANOVA indicated significant effects of group [$F(2,101) = 11.0, P < 0.001$] and distractor similarity [$F(1,101) = 39.5, P < 0.001$] and a

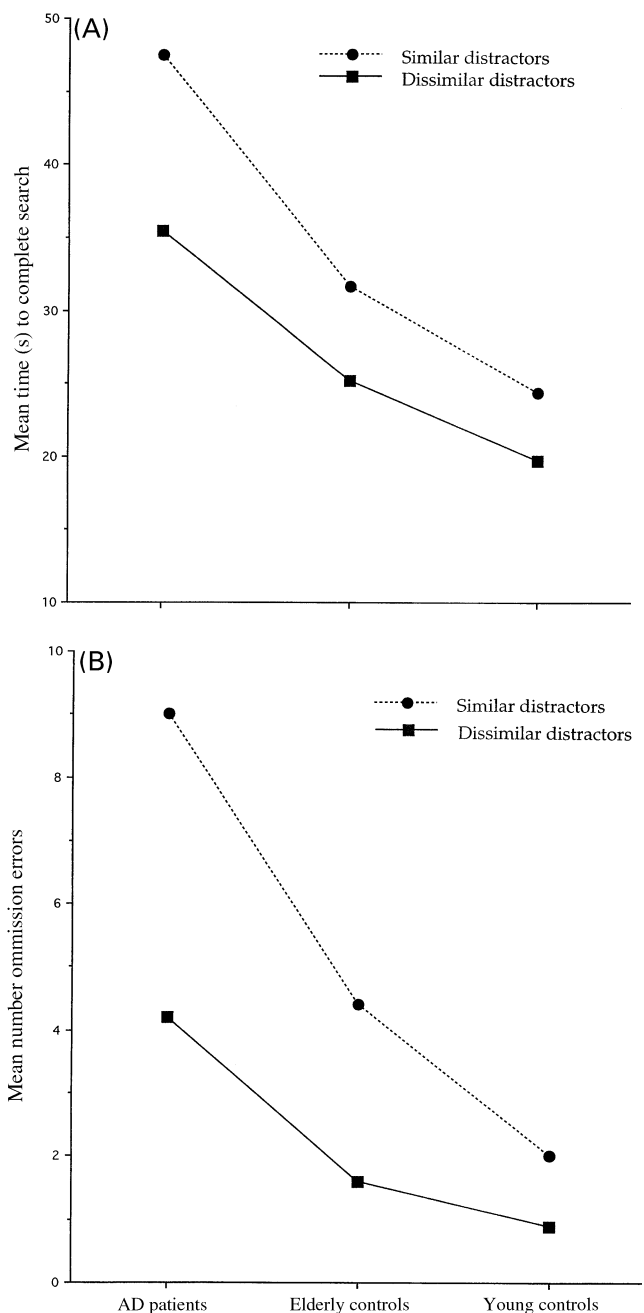


Fig. 2 Visual letter search with similar and dissimilar distractors. (A) Mean search time. (B) Mean number of omission errors. AD = Alzheimer's disease.

group \times similarity interaction [$F(2,101) = 5.5, P < 0.005$]. When the patient group was omitted, there was no significant effect of age [$F(1,68) = 3.17, 0.05 < P < 0.1$]. The effect of condition remained highly significant [$F(1,68) = 18.2, P < 0.001$], whereas the interaction, like the group effect, just failed to reach conventional significance [$F(1,68) = 3.76, 0.05 < P < 0.1$]. When the young group was excluded in order to study the effect of disease, there proved to be a significant effect of group [$F(1,67) = 8.12, P < 0.01$] and of condition [$F(1,67) = 37.0, P < 0.001$], whereas the

group \times condition interaction again failed to reach significance [$F(1,67) = 2.51, P > 0.1$].

Our final analysis involved dividing the patients on the basis of their MMSE scores into those above and below the median in order to assess the effect of disease stage on performance. There was a non-significant tendency for the higher-scoring group to search at a faster rate (38.1 versus 47.0 s per list), an effect that was of borderline significance [$F(1,28) = 3.49, 0.05 < P < 0.1$]. The effect of distractor similarity remained highly significant [$F(1,28) = 87.8, P < 0.001$] and the interaction between group and distractor type was also significant [$F(1,28) = 7.80, P < 0.01$], indicating that the effect of disease stage was reflected principally in performance on the more difficult discrimination; the high-performing group took an average of 26.8% longer to search the similar letters, whereas the group with poorer MMSE scores took a mean of 42.4% longer. In the case of errors, neither the effect of group nor the interaction between group and condition reached statistical significance.

Discussion

As Della Sala and colleagues reported, the speed and accuracy of letter search are highly sensitive to the effects of Alzheimer's disease (Della Sala *et al.*, 1992). However, both are also sensitive to age, making interpretation more complicated. Is it simply the case that replacing a dissimilar with a similar letter background will slow down performance to an equivalent extent for all three groups, or is the effect of increasing difficulty in this way disproportionately large for Alzheimer's disease patients? The effect of increasing background similarity on visual search did seem to be roughly equivalent across the young and elderly control groups, increasing performance by 23.9% for the young and 25.8% for the elderly compared with a difference of 34.4% for the Alzheimer's disease patients.

The staging analysis lends further weight to the suggestion that Alzheimer's disease patients may have a particular problem in resisting interference from similar material, as the progress of the disease is reflected principally in lower performance in the similar background condition. A single experiment is clearly insufficient for firm conclusions to be drawn, but this aspect of attentional control would appear to be well worth further investigation.

As discussed earlier, a more powerful source of evidence for the fractionation of attentional control would be provided by a demonstration that there was no effect of age, together with a clear impact of Alzheimer's disease, producing results that would be inconsistent not only with a hypothesis of general slowing but also with a more complex version of this hypothesis that argues for a slowing effect that is proportional across groups. On the other hand, if a given source of attentional difficulty is not influenced by age but is highly sensitive to the effects of Alzheimer's disease, this would be a strong argument for the fractionation of attention.

As noted by Perry and Hodges, the strongest candidate for such a dissociation is offered by the capacity to divide attention between two distinct tasks (Perry and Hodges, 1999). Our last two experiments examine this claim in more detail, first by attempting to replicate earlier effects using similar design and materials, and secondly by extending the paradigm to other quite different tasks. Whereas further direct replication may seem unnecessary (Della Sala *et al.*, 1992; Greene *et al.*, 1995), as Perry and Hodges point out, comparisons across paradigms within the same study are likely to allow much more firm conclusions than those that depend on the assumption that subjects and procedures from different studies are equivalent. Hence, were we to carry out our fourth experiment using different modalities and new material and find no evidence for the predicted dissociation, we would not be certain whether the failure to replicate stemmed from changing the paradigm or changing the subject sample. Furthermore, running both dual-task studies in the same group gave the opportunity of comparing sensitivity between the two studies, which may in turn give hints as to how the technique might be developed for possible clinical use.

In Experiment 3, therefore, a motor task in which subjects crossed out a chain of boxes was combined with a concurrent immediate serial verbal memory task (Baddeley *et al.*, 1997), and the fourth study attempted to extend the range of dual-task studies by combining visual search with auditory detection.

Experiment 3: dual-task performance: box-crossing and memory span

Procedure

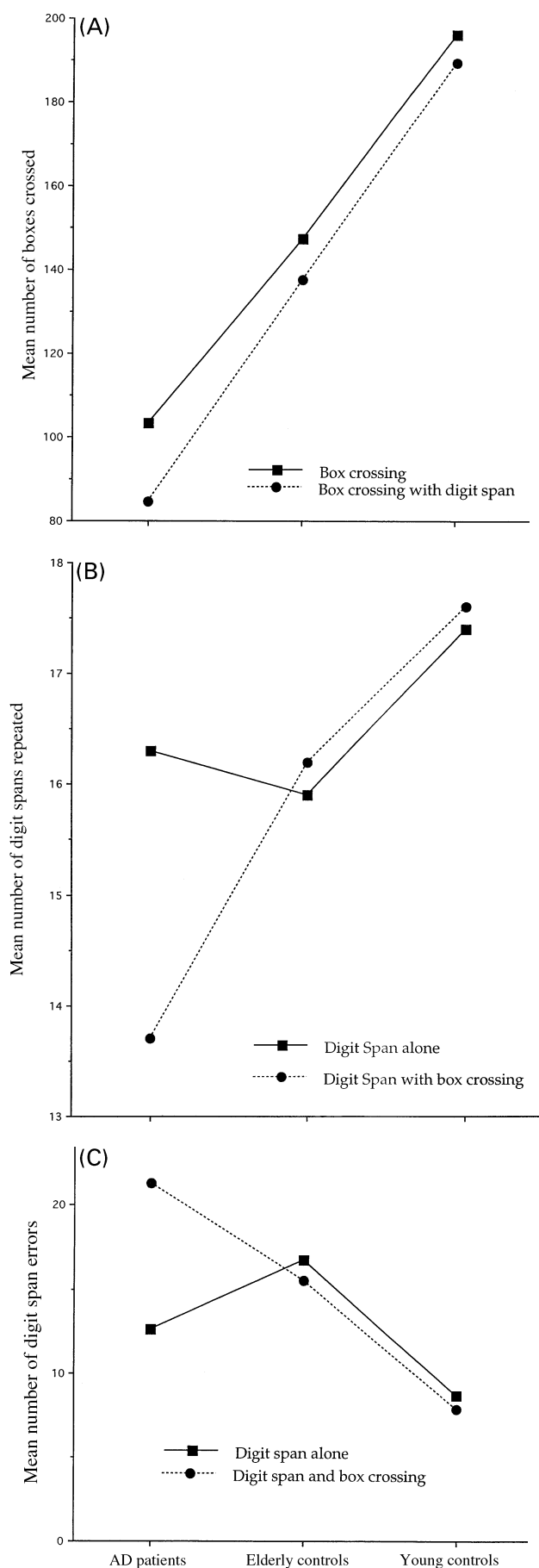
The dual-task paper and pencil measure developed previously was used. In this task, subjects combined crossing out a chain of boxes with repeating span-length sequences of random digits read out by the experimenter (Greene *et al.*, 1995; Baddeley *et al.*, 1997).

Box-crossing

A total of 160 1 cm² boxes joined by lines and arranged along a winding path were printed on A3 sheets of paper. Subjects had available as many sheets as they could complete during each 2-min trial. Although the box-crossing task was sufficiently straightforward to be performed virtually perfectly by both control groups, patients occasionally made errors, either by failing to follow the chain of boxes and switching to an adjacent box or, occasionally, by writing digits rather than crosses in the boxes. When this occurred, it was immediately corrected by the experimenter and scored as a single error.

Digit span

Each subject's forward digit span was determined by presenting three sequences of two digits followed by



sequences of three and four until a length was reached at which the subject failed at least once. Digits were spoken at the rate of one per second. The highest level at which performance was perfect was then selected and used during a 2-min session during which each subject's recall was immediately followed by the presentation of another sequence at that length. Performance was measured both in terms of the number of sequences attempted in 2 min and the percentage correct.

Dual-task performance

After digit span had been determined, subjects were asked to perform both tasks concurrently. Two or three practice trials were allowed if necessary. Patients typically had no difficulty in performing the individual tasks but often had problems with combining them. Two patients proved capable of performing only one of the two simultaneous tasks, in which case they were assigned a zero score for the second. One patient was unable to carry out either task when attempting to do both at the same time. In this case, no score was assigned and the test abandoned. Performance was measured in terms of the number of boxes crossed in 2 min, errors of omission or deviation from the path, the number of digit-span sequences attempted during the 2-min test and the percentage of erroneous digit span sequences.

Results

Figure 3A shows the performance of the three groups on the motor component of the task in terms of the number of boxes crossed out under both the single- and the dual-task condition. Analysis indicated a significant effect of group [$F(2,104) = 75.4, P < 0.001$] and of condition [$F(1,104) = 23.6, P < 0.001$] but no significant interaction [$F(2,104) = 2.19, P > 0.1$]. Although errors in box-crossing were infrequent, they did occur sufficiently often to allow analysis, which indicated a significant effect of group [$F(2,105) = 5.19, P < 0.01$]. However, although errors tended to be more common under the dual-task condition [0.84% (SD 2.65) versus 0.03% (1.01)], the difference did not reach significance ($F < 1$).

Figure 3B shows the effects of age and Alzheimer's disease on the number of digit-span sequences attempted with and without concurrent box-crossing. There proved to be a significant main effect of group [$F(2,104) = 4.2, P < 0.05$] and of condition (single versus dual task) [$F(1,104) = 6.5, P < 0.01$], together with a highly significant interaction between group and condition [$F(2,104) = 13.8, P < 0.0001$].

Fig. 3 Dual-task performance. (A) Mean number of boxes crossed out as a single task and in combination with digit span. (B) Mean number of digit spans processed during the 2-min test. (C) Mean percentage of digit-span errors. AD = Alzheimer's disease.

As Fig. 3B suggests, the interaction was due principally to the dual task performance of the patients. When this group was excluded, the main effect of age failed to reach significance [$F(1,70) = 3.47, 0.05 < P < 0.1$]; the effect of dividing attention also failed to reach significance, as did the interaction between age and condition ($F < 1$ in both cases). When the young subject group was omitted, there was no overall effect of group [$F(1,69) = 1.59, P > 0.1$], but the effect of condition [$F(1,69) = 8.88, P < 0.01$] and the interaction between group and condition [$F(1,69) = 15.9, P < 0.0001$] both reached significance.

Figure 3C shows the mean percentage digit-span error rate across the three groups for single- and dual-task performance. ANOVA indicated a significant effect of group [$F(2,104) = 5.21, P < 0.01$] and no reliable effect of single versus dual task [$F(1,104) = 2.05, P > 0.1$], but a significant group \times task interaction [$F(2,104) = 4.57, P < 0.05$]. When the interaction was further investigated by excluding the patient group, there proved to be a significant overall effect of age [$F(1,70) = 10.5, P < 0.01$] but no effect of condition, and no interaction between condition and group ($F < 1$ in both cases). When the disease effect was investigated further by eliminating the young subjects, there was no overall effect of group ($F < 1$) or category [$F(1,70) = 3.01, 0.05 < P < 0.1$]. However, the interaction between group and condition reached significance, again reflecting the susceptibility of the patients to the dual task demands [$F(1,69) = 5.6, P < 0.05$].

When two tasks are combined, any decrement may be reflected in either of the individual tasks or in both. Relying on either of the measures, however, runs two risks, the first being a trade-off between speed and error whereby the subject is simply favouring one task at the expense of the other; if subjects differ in which task they favour, then neither task may show a reliable change. If these problems are to be avoided, it is necessary to combine scores from the two tasks. In the absence of a thorough theoretical understanding of the way in which the two tasks are performed, any combination must be to some extent arbitrary. However, a method that is plausible and appears to work reasonably well is that proposed by Baddeley and colleagues (Baddeley *et al.*, 1997), who defined the combined score *mu* as follows:

$$mu = [1 - (pm + pt)/2] \times 100,$$

where *pm* is the proportional loss of memory performance under dual-task conditions and *pt* is the proportional loss in tracking score (for a more detailed account, see Baddeley *et al.*, 1997). A score of 100 indicates no decrement, whereas a score of < 100 implies impaired performance as a result of combining the two tasks.

Neither the young subjects nor the elderly controls showed any marked decrement on this measure [mean score 98.78 (SD 6.82) and 98.64 (15.34), respectively], in contrast to a clear decrement shown by the Alzheimer's disease patients [mean 86.93 (17.3)]. The patients scored significantly less than the elderly controls [$F(1,69) = 11.45, P < 0.01$], whereas the two control groups did not differ ($F < 1$).

Our final analysis involved splitting the patient group into those above and below the median in MMSE score. This showed an overall difference in the rate of box-crossing [mean 109.0 (SD 44.4) for the high-scoring group versus 76.5 (33.2) for the low scorers; $F(1,29) = 5.86, P < 0.05$] and a significant effect of single versus dual task [$F(1,29) = 18.27, P < 0.001$], but no significant interaction between these measures. The percentage of errors did not differ significantly between the two patient groups [mean for high scorers 16.14 (SD 18.37), for low scorers 14.96 (SD 18.22)]. Neither this difference nor the interaction with condition approached significance, although the difference between single- and dual-task performance was significant [$F(1,29) = 5.15, P < 0.05$]. However, when speed and errors were combined to give an overall *mu* score, there was no significant difference between the high and low groups (mean 89.98, SD 14.96) and the low MMSE group [mean 81.49, SD 15.56; $F(1) = 2.39, P > 0.1$]. Logarithmic transformation of the *mu* score left the pattern of results unchanged, with an overall group difference [$F(2,104) = 11.93, P < 0.0001$], no effect of age [$F(1,70) = 0.05 < P < 0.1$] and a clear affect of Alzheimer's disease [$F(1,70) = 12.04, P < 0.001$].

Discussion

The results obtained replicate earlier observations: there was no apparent decline in the capacity to divide attention with age, whereas there was a clear impairment in the dual-task performance of Alzheimer's disease patients. As is commonly the case (Baddeley *et al.*, 1986, 1991, 1997), the effect occurs principally in the digit-span task, although this is not the case universally (Greene *et al.*, 1995). As in previous studies, the combined score *mu* provided clear evidence for a dual-task decrement for the patients but not for either of the two control groups. The pattern resulting from the estimated stage of disease was somewhat different; the speed of box-crossing differed between the high- and low-MMSE groups, whereas differences in error rate and in the combined *mu* score failed to reach significance. This would appear to be at variance with the study of dual-task performance by Baddeley and colleagues, which used a longitudinal design and found the principal decline to be in error rate (Baddeley *et al.*, 1991). It is possible that this may reflect a difference in the procedure for the motor task. The present study used the same box-crossing task for all subjects, assuming that they would adjust their speed of performance to their processing capacity. The study of Baddeley and colleagues explicitly adjusted the speed and hence the demand of their tracking task to a point at which all subjects showed equivalent performance, possibly resulting in a more sensitive measure.

Experiment 4: dual-task performance: visual search and auditory detection

Visual search

Eight pictographs of what were assumed to be clearly discriminable representations of objects were selected from

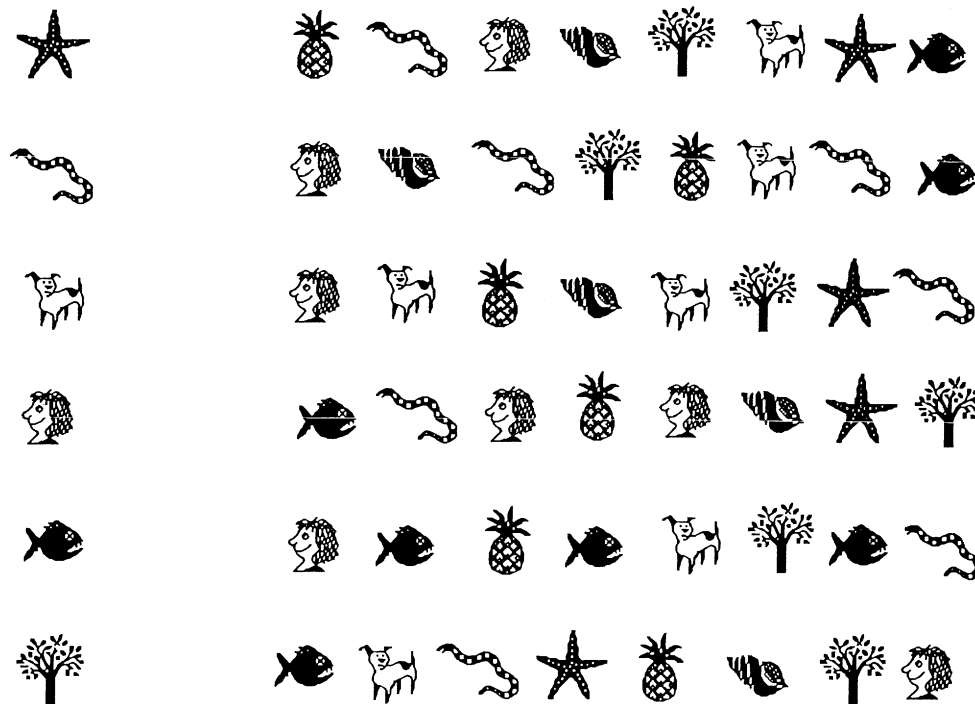


Fig. 4 Example of visual search task as used in Experiment 4.

the range provided by HyperCard (Art Bits) (Apple Computer, 1987). These were used to create 10 test sheets; each comprised 12 lines, with a target item on the left followed by eight items to be scanned. Each line had at least one target, but sometimes two or occasionally three targets (Fig. 4). The subject was required to scan each line and mark examples of the target for that line. Subjects were required to perform the task continually for 2 min, timed with a stopwatch. If a sheet was completed, the watch was stopped and a new sheet was provided, after which timing began again. Performance was scored in terms of the number of lines completed in 2 min, together with errors of omission and of commission.

Auditory detection

Subjects listened to a tape-recorded recitation of 12 well-known British town names (Swindon, Cardiff, Derby, Swansea, Norwich, Durham, London, Belfast, Sheffield, Brighton, Glasgow and Bristol) recorded at a rate of one name per second. Subjects were required to listen for the name Bristol, the city in which the testing typically occurred, and to repeat it back to the experimenter immediately it was detected. The 2-min test sequence contained 12 such targets. Subjects first practised at the rate of 2 s per item in order to ensure that they understood the task, before moving on to the test rate of one per second.

Dual-task performance

Subjects were asked to carry out both tasks concurrently and performance was measured in terms of lines of pictographs

completed in 2 min, the numbers of errors of omission and commission and the number of occurrences of the word 'Bristol' detected. As with Experiment 3, the subjects were given further practice if necessary in combining the two tasks. Patients who nevertheless could perform only one of the two tasks ($n = 3$) were given a score of zero on the other task, and patients who were unable to perform either task when asked to carry them out together ($n = 1$) were excluded.

Results

This study combined a relatively complex task in which performance was scored in terms of speed of search, but which also yielded scores in terms of errors of omission and commission, together with a much simpler concurrent name-detection task for which performance was measured in terms of omissions, there being virtually no false detection responses. Figure 5A shows the mean number of lines searched over the test period of 2 min across the three groups under single- and dual-task conditions. There was a significant effect of group [$F(2,102) = 85.9, P < 0.001$], no significant overall difference between single- and dual-task performance [$F(1) < 1$] and a significant interaction between group and condition [$F(2,102) = 7.00, P < 0.01$]. When the age effect was further examined by excluding the patient group, a very clear group effect was observed [$F(1,70) = 49.88, P < 0.0001$], together with a small but significant dual-task effect, indicating slightly faster performance under dual-task conditions [$F(1,70) = 4.48, P < 0.05$]; the interaction between age and condition failed to reach significance

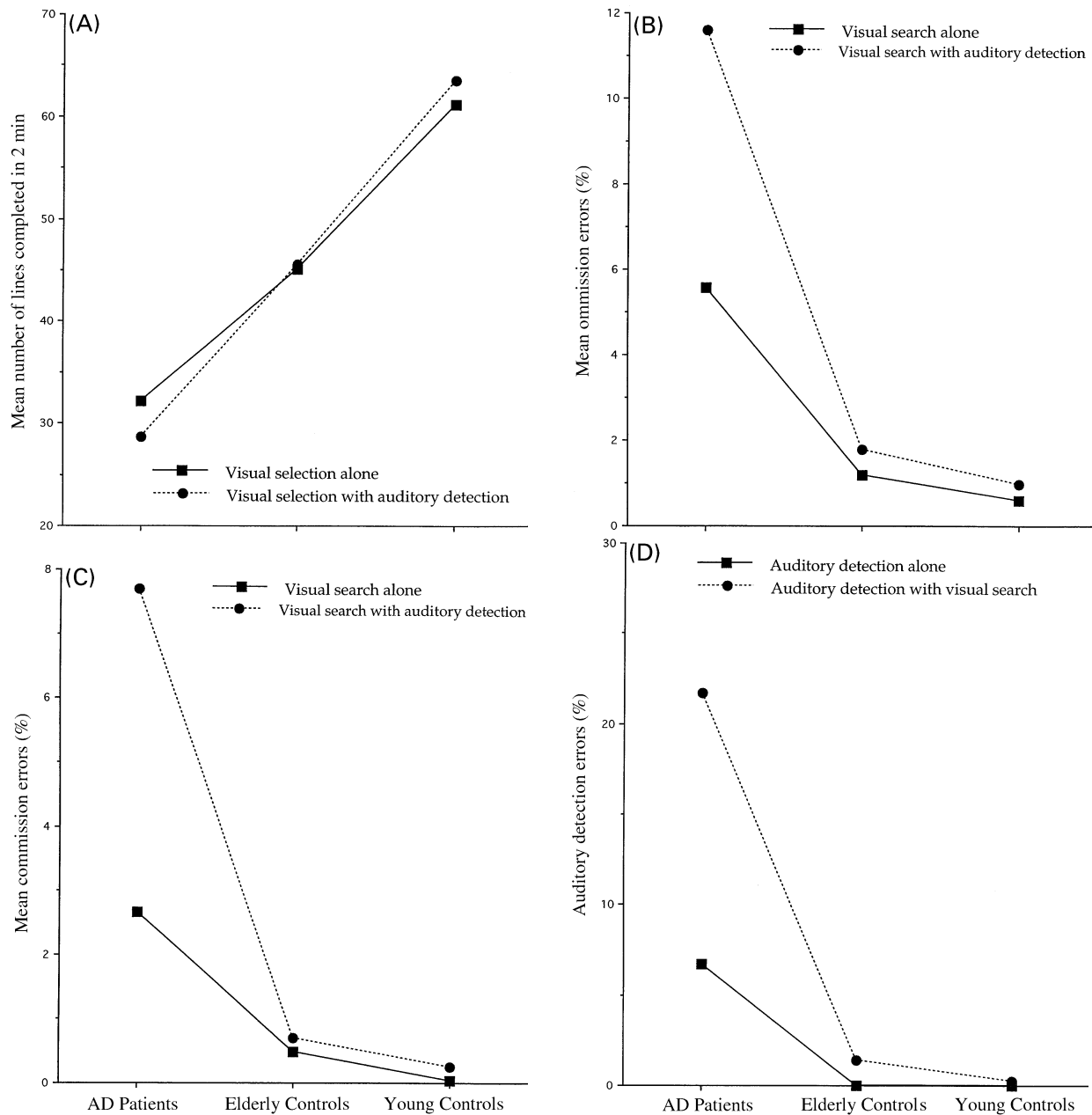


Fig. 5 Visual selection with auditory detection. (A) Mean number of lines inspected in 2 min under single- and dual-task conditions. (B) Mean number of search omission errors. (C) Mean number of commission errors. (D) Mean percentage of errors of auditory detection, in each case under single- and dual-task conditions; all were errors of omission. AD = Alzheimer's disease.

[$F(1,70) = 2.13, P > 0.1$]. When the effect of disease was studied by omitting the young subjects, there was a large effect of group [$F(1,67) = 38.61, P < 0.0001$], a marginal overall tendency for performance to decline under dual-task conditions [$F(1,67) = 3.06, 0.05 < P < 0.1$] and a significant interaction between group and condition [$F(1,67) = 5.72, P < 0.05$]. Overall, this pattern of results indicates a dual-task decrement for the patients but not for the elderly controls.

Figure 5B shows the mean frequency of omission errors in the visual search task across the three groups. Overall analysis indicated a significant effect of group [$F(2,101) =$

18.11, $P < 0.0001$], a significant effect of condition, errors being more frequent when scanning was combined with auditory detection [$F(1,101) = 5.57, P < 0.05$], and a significant condition \times task interaction [$F(2,101) = 4.04, P < 0.05$]. When the patient group was omitted to study the effect of age, there proved to be a significant overall group effect [$F(1,70) = 2.67, P > 0.1$] and no interaction ($F < 1$). The effect of disease was studied by omitting the young subjects, which yielded a group effect [$F(1,66) = 16.77, P < 0.001$], an effect of condition [$F(1,66) = 5.04, P < 0.05$] and a

significant condition \times group interaction [$F(1,66) = 3.97$, $P = 0.05$].

As Fig. 5C indicates, patients also made errors of commission, crossing out the wrong target. These appeared to reflect either visual errors, in which the item crossed out was somewhat similar to the target (typically the shell was confused with the fish; Fig. 4), or errors of perseveration, in which the subject crossed out targets from the previous line. As the data indicate, such errors were confined almost entirely to patients. Overall analysis showed a significant group effect [$F(2,102) = 19.47$, $P < 0.001$], a significant effect of condition [$F(1,102) = 11.62$, $P < 0.001$] and a significant interaction [$F(2,102) = 9.07$, $P < 0.001$]. Although the errors occurred predominantly in the patient group, when these subjects were omitted there was a significant effect of age [$F(1,70) = 4.67$, $P < 0.05$], whereas the tendency for errors to be more frequent under dual-task conditions did not reach significance [$F(1,70) = 1.93$, $P > 0.1$] and condition did not interact with age ($F < 1$). When young subjects were eliminated in order to study the effect of disease, there proved to be a highly significant group effect [$F(1,67) = 16.94$, $P < 0.001$] together with an effect of condition [$F(1,67) = 10.85$, $P < 0.01$] and a significant group \times condition interaction [$F(1,67) = 8.79$, $P < 0.01$]. The group effect appeared to be attributable principally to the dual-task condition. It is clear, therefore, that the visual scanning task is highly susceptible to the effects of Alzheimer's disease, not only in speed of performance but also in the tendency for errors of both omission and commission to occur under dual-task conditions.

The auditory detection task virtually never evoked false alarm responses, hence performance simply reflected the frequency of errors of omission. These are shown in Figure 5D. ANOVA indicated a significant overall effect of group [$F(2,102) = 10.61$, $P < 0.0001$] and an effect of condition, representing the overall decrement due to the dual-task combination [$F(1,102) = 14.19$, $P < 0.001$], and a significant interaction [$F(2,102) = 11.13$, $P < 0.0001$]. The effects were then broken down into those of age and disease by the elimination of groups. When the patients were omitted, the difference between single- and dual-task performance just achieved significance [$F(1,102) = 2.00$, $P = 0.05$], whereas neither the group effect nor the interaction reached the conventional significance level [$F = 2.0$, $P > 0.1$]. It should be borne in mind that these data are constrained by a floor effect, all conditions other than dual-task performance in elderly subjects resulting in minimal errors. The equivalent analysis with young subjects omitted indicated a clear difference between the elderly control and Alzheimer's disease groups [$F(1,67) = 10.17$, $P < 0.01$] together with an effect of condition [$F(1,67) = 13.81$, $P < 0.001$] and a condition \times group interaction [$F(1,67) = 10.21$, $P < 0.01$], indicating a clear tendency for errors to be more frequent in the patient group, particularly in the dual-task condition. Once again, however, it should be noted that the elderly

control subjects under single-task conditions were performing perfectly, hence placing constraints on interpretation.

Finally, search speed and auditory detection errors were combined to give a single *mu* score for each object. Once again, *mu* was calculated on the basis of the ratio of performance between single and dual conditions for the two combined tasks using the formula:

$$\mu = (1 - (pv + paud)/2) \times 100,$$

where *pv* is the visual search performance on dual-task performance as a proportion of single-task performance and *paud* is the equivalent for auditory performance. Once again, a score of 100 would indicate a total lack of decrement. Both the young and the elderly controls were able to combine the two tasks without apparent cost [mean *mu* scores 99.7 (SD 1.1) and 99.3 (2.6), respectively], whereas a clear decrement was found for the patients [81.3 (25.2)]. This was confirmed by one-way ANOVA [$F(2,105) = 17.35$, $P < 0.0001$], a result that was not substantially changed when the data were transformed logarithmically.

Our final analysis returned to the question of disease stage, comparing the patients high and low in MMSE score. There proved to be a significant difference between the two groups in speed of search [$F(1,30) = 5.74$, $P < 0.05$] with a significant effect of condition, indicating a dual-task effect [$F(1,30) = 10.97$, $P < 0.01$], and a marginally significant group \times condition interaction [$F(1,30) = 3.34$, $0.5 < P < 0.1$]. Whereas visual search errors tended to be more frequent under dual-task conditions, neither group effects nor group \times condition interactions approached significance. The detection of town names did not show any difference between the two groups [$F(1,29) = 1.10$, $P > 0.1$]. Although the condition effect remained strong [$F(1,29) = 16.40$, $P < 0.001$], the interaction between group and condition was again absent [$F(1,29) = 1.21$, $P > 0.1$]. When search speed and auditory detection scores were combined to give *mu* scores, the high- and low-MMSE groups differed significantly [$F(1,30) = 4.90$, $P < 0.05$], suggesting that the potentially more sensitive combined measure may be able to detect an effect of the progress of the disease.

Discussion

Despite changing the constituent tasks from those used successfully in earlier studies, the results of the last study replicate those obtained previously. Whereas the age of the control groups affected the speed at which subjects performed the visual search task, adding a concurrent auditory detection task had no effect on speed or accuracy of search; however, detection errors were only minimally influenced by age. In contrast, when required to perform both tasks simultaneously, patients not only scanned more slowly than age-matched control subjects but also showed an effect of the concurrent task on speed and accuracy of scanning, as well as detecting fewer auditory targets. When the patient group was split on

the basis of MMSE, there was some evidence for poorer combined performance in the low-scoring subgroup.

An interesting feature of Fig. 5A is the tendency for young subjects to scan more rapidly under dual-task conditions. This seems most likely to reflect a practice effect, as this condition, expected to be the most difficult, was always presented last. The fact that the elderly control subjects did not show this improvement could be interpreted as suggesting an age difference in dual-task performance. However, one cannot rule out the possibility that the young subjects were simply more ready to speed up whereas the elderly subjects were more cautious. In principle, this could have been detected by a difference in error rate, but errors in the control groups were too infrequent to provide useful information.

General discussion

The purpose of our study was twofold—to provide a more detailed analysis of the cognitive effects of Alzheimer's disease and, in doing so, to throw light on the nature of the attentional control of executive processes. We did this by generating hypotheses based on attempts to fractionate the executive control of working memory and contrasting these hypotheses with a simple unitary hypothesis of a type that is influential in the literature of normal ageing. This proposes that any factor increasing the difficulty of normal performance will have a proportionately greater effect on the performance of the elderly and will lead to even more substantial impairment in Alzheimer's disease patients. This hypothesis has been expressed most frequently in terms of speed, but is equally applicable to other measures of performance (Cerella, 1985; Nebes and Brady, 1992; Salthouse, 1993, 1996). Set against this hypothesis is the proposal that some subcomponents of attention, such as the capacity to divide attention between two concurrent tasks, may be particularly susceptible to the effect of Alzheimer's disease, while other attentional processes may be relatively preserved (Baddeley *et al.*, 1991; Perry and Hodges, 1999).

We set out to test this by selecting three experimental paradigms that might reasonably be regarded as drawing upon different attentional resource systems, varying the level of difficulty within each and comparing the performance of young and normal elderly subjects and Alzheimer's disease patients. In order to test the hypothesis, we first needed to demonstrate that our basic measures were sensitive to both age and disease effects and that our two levels of difficulty were reflected in our measures of performance. Our results indicate that these preconditions were indeed achieved. We found highly significant intergroup differences in overall RT, in the speed and accuracy of visual search and on the baseline level of performance on both the dual-task paradigms. Similarly, we were successful in varying the level of difficulty in the RT task through the number of response alternatives, in visual search through the similarity of the distractor items, and in dual-task performance through the requirement to combine the constituent parts.

However, although these effects satisfied important preconditions, they were consistent with both the simple slowing hypothesis and the more complex proposal of separable attentional subprocesses. A more crucial issue concerns the pattern of disruption across groups and, more specifically, whether there is an interaction between group and level of difficulty, and the precise nature of any such interaction. The simplest pattern would be indicated by the absence of any interaction, implying that the effects of task difficulty are independent of the effects of ageing and disease. If this were found across the range of tasks, it would be somewhat problematic for both hypotheses. A second possibility is that there is an equivalent interaction between the group and level of difficulty across all four tasks and all three groups. Such a pattern would be broadly consistent with the simple slowing hypothesis. A variant on this pattern would occur if an interaction were present in the analysis but disappeared when a log transform was applied to the data. This would imply an effect of increasing level of difficulty that was proportional to the level of performance in the baseline condition. Such a result would be compatible with a more complex version of the speed hypothesis proposed by Salthouse and Somberg (Salthouse and Somberg, 1982). A third possibility is that the pattern differs across the three paradigms studied, dual-task performance being sensitive to Alzheimer's disease but not to age, a result that would support the proposed fractionation of executive processes.

We will consider the four experiments in turn. As we saw, in the RT paradigm there were clear effects of both group and number of response alternatives, with a significant interaction between these. However, when the effects of age and disease were separated, age significantly interacted with the number of alternatives ($P < 0.005$), whereas removal of the young control group removed the significant interaction. However, these results should be interpreted with caution because, when logarithmically transformed, the main effects were unaffected in overall significance level, whereas the interactions all fell below the 0.05 probability level, only the age interaction approaching significance. The pattern of results therefore suggests that the two RT measures are affected broadly proportionally by age, while the additional effect of disease approximates more closely to an additive effect. Such a pattern of results is not consistent with a general slowing hypothesis, which would predict the opposite, namely greater impairment on the more difficult choice RT measure in the Alzheimer's disease group.

Our analysis of the visual search task indicates clear effects of both group and distractor background, together with a highly significant interaction. The logarithmic transformation, however, suggests that the effect of difficulty level is proportional to baseline performance in the case of age, whereas there is a marginally significant suggestion that Alzheimer's disease patients may be disproportionately sensitive to the effects of distractor similarity. The age effect is thus in line with the more complex version of a general speed hypothesis, while there is a suggestion that the

Alzheimer's disease group may not fit this pattern. The question of whether Alzheimer's disease patients are more sensitive to distraction merits further investigation using a wider range of tasks.

Our third study combined box-crossing with concurrent testing of digit span, and as such was essentially a replication of earlier work. As found previously, given that the constituent tasks were adjusted across groups, task combination failed to have a significant impact on overall performance for either the young or the elderly control group. In contrast, dual-task performance was very markedly impaired in the patient group, an effect that was unchanged by logarithmic transformation.

A general impairment hypothesis would suggest that if task combination simply reflects an increase in general difficulty, there should be a clear age effect. As this does not occur, we can think of no plausible transform that would allow these results to fit the simple slowing hypothesis. We are not, of course, claiming that under no circumstances will age affect the capacity to combine tasks. A number of demonstrations of such a dual-task decrement have in fact been produced; however, typically these do not equate the level of difficulty of the two constituent tasks. If the elderly subjects perform more poorly on each of these, then it is hardly surprising that they will be even more impaired when the two are added. A discussion of this, together with evidence of a small age effect on dual-task performance, is provided by Salthouse and colleagues (Salthouse *et al.*, 1995). However, our evidence does suggest that any such age effect is very much less marked than that observed in our Alzheimer's disease patients.

Our final experiment further extends the evidence for a minimal cost of combining tasks in the elderly coupled with a marked impairment in Alzheimer's disease patients, using the two quite different tasks of visual search and auditory detection. Again, this experiment showed no reliable effect of age on the capacity to combine tasks, together with a clear effect of Alzheimer's disease on dual-task performance, whether measured as *mu* or $\log \mu$. Thus, it reinforces our earlier conclusions and supports the hypothesis that the impairment found in Alzheimer's disease patients affects a more general capacity to divide attention rather than anything specific to manual skill or immediate recall of digits, a conclusion that is supported by a range of evidence from normal subjects (Bourke *et al.*, 1996).

Taken overall, our results show a different pattern of findings for each of the three paradigms we studied. Performance on the two RT tasks, which we assumed to depend on the capacity to focus attention, is affected by age, with a much less clear additional impact of Alzheimer's disease. Our visual search task shows effects of both age and disease, that of Alzheimer's disease being greater than that predicted by a simple additive speed model, and marginally greater than that predicted by a more complex speed model that assumes proportionality rather than additivity. Finally, the two dual-task performance measures give the clearest indication of a dissociation. When the level of single-task

performance is adjusted appropriately, the combination of tasks has a minimal effect on the two control groups but has a major impact on the performance of patients. We suggest that this pattern of performance is difficult to accommodate within either an additive or a proportional speed model of the executive deficit in Alzheimer's disease.

We conclude by commenting on our attempts to provide information on the staging of the disease. As Perry and Hodges (Perry and Hodges, 1999) and Perry and colleagues (Perry *et al.*, 2000) point out, it is useful to have measures of the extent to which performance on given tasks changes as the disease progresses. This is valuable both in understanding the nature of the cognitive impairments and in monitoring the effects of treatment. Ideally, staging should be studied using a longitudinal design in which the same subject is studied at different points during the development of the disease. An alternative to this can be provided by studying groups that are separated on a measure of disease severity that is known to change as the disease progresses, typically MMSE, or a dementia rating scale. However, both of these have the drawback that they are likely to be influenced by factors other than disease stage; a patient with high intelligence and good social skills may well be capable of compensating for the effects of disease, at least during its early stages. Consequently, patients who are matched on MMSE or rating measures are not necessarily at the same stage of the disease.

Nevertheless, we felt that a division into high- and low-MMSE patients might at least provide some guidance on possible staging effects. However, we point out that the difference in MMSE scores was considerably narrower in our study (15–18 and 20–26) than that used by Perry and colleagues, who contrasted a group scoring between 17 and 23 with one scoring between 24 and 29 (Perry *et al.*, 2000). As they point out, inclusion of the higher-scoring group was somewhat controversial, given the conventional cut-off score of 23 that is often regarded as necessary for a clear diagnosis (Albert, 1996; Haroutunian *et al.*, 1998); they suggest, however, that their assumptions are well supported by other work from their group.

Perry and colleagues (Perry *et al.*, 2000) obtained a significant difference between the performance of their minimal Alzheimer's disease and control groups on two of the eight attentional tests they studied, namely the Stroop test, in which subjects have to name the colour of the ink in which colour words are printed, and in a component of the Test of Everyday Attention (Robertson *et al.*, 1994) entitled Elevator Counting With Distraction, in which subjects are required to count a sequence of high tones while ignoring low tones. The authors conclude that the most sensitive aspect of attentional control is the capacity to resist distraction and rapidly switch attention, and that the ability to sustain and divide attention both deteriorate at a later stage in the disease.

Our own *post hoc* attempt at MMSE-based staging used a rather narrower range of scores, virtually all of them falling

within the range categorized by Perry and colleagues (Perry *et al.*, 2000) as 'mild'. On the RT task, our two patient groups differed markedly in overall speed of performance and also showed a significant interaction between subgroup and task difficulty. This suggests that low-scoring subjects respond more slowly and are also more sensitive to the number of alternatives, which in turn suggests that the effect of the number of response alternatives may become more important as the disease progresses, despite its failure to distinguish between patients and age-matched control subjects. In contrast, our letter-search analysis failed to find a significant overall time difference but did show a highly significant interaction, suggesting that the capacity to resist interference from similar distractors may be very sensitive to disease stage, a result that is consistent with the conclusions of Perry and colleagues (Perry *et al.*, 2000).

The data from our two divided attention tasks were equivocal; we did find a significant difference between subgroups on the crucial *mu* switching measure for combining visual search with auditory detection, but not for the digit-span and box-crossing test. This latter result is consistent with that of Perry and colleagues, who used this specific version of the task (Perry *et al.*, 2000). It is perhaps noteworthy that this form of the task tends to lack reliability, principally, it is believed, because of the relatively crude level of control over the digit-span component (Baddeley *et al.*, 1997). However, it is interesting to note that, using a longitudinal design, there was clear evidence of a decline of dual-task performance in the presence of relatively stable performance on the component measures (Baddeley *et al.*, 1991). There is clearly a need for more longitudinal studies to supplement existing cross-sectional designs. Meanwhile, the interaction between scanning and distractor similarity lends some support to the suggestion of Perry and colleagues that Alzheimer's disease patients may have particular difficulty in inhibiting responses to inappropriate stimuli (Perry *et al.*, 2000). Whether, as they suggest, attention switching is also sensitive to disease stage is less clear, particularly given the absence in their study of a staging effect on the Wisconsin Card Sorting Test, which is often assumed to reflect the capacity to switch attention. This suggests a need to look closely at the task-switching component of the attentional deficit.

It is important to bear in mind that our study is concerned with a different question from that of Perry and colleagues (Perry *et al.*, 2000). Their principal concern is with the identification of attentional tests that are sensitive to the early stages of Alzheimer's disease. Our concern is less with sensitivity than with specificity. Hence, the pattern of deficit obtained with dual-task performance is of interest because it appears to be qualitatively different from the pattern found with normal ageing, in contrast to simple and choice RT, which are highly sensitive to both age and Alzheimer's disease. This contrast is consistent with the view that the capacity to divide attention is a separable subcomponent of attention.

Our results and those of Perry and colleagues (Perry *et al.*, 2000) suggest more tentatively that the capacity to select wanted signals from a background of similar or strongly competing unwanted items may also reflect a potentially fractionable subcomponent of attention. In contrast, a simple speeded measure, such as RT, may be highly sensitive to Alzheimer's disease but lack specificity, as it is also sensitive to a wide range of other factors, including the influence of normal ageing. Such sensitive tests will, of course, continue to play an important role in the practical task of diagnosing and monitoring Alzheimer's disease. Less sensitive but more specific tests, on the other hand, are initially more likely to contribute to our theoretical understanding of the underlying processes. When better understood, however, they may well play an increasing role in the clinic.

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