Dual Task Performance in early Alzheimer's disease, amnestic mild cognitive impairment and depression

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Abstract

Background: The dual task paradigm (Baddeley et al., 1986; Della Sala et al., 1995) has been proposed as a sensitive measure of Alzheimer's disease, early in the disease process.

Methods: We investigated this claim by administering the modified dual task paradigm (utilising a pencil and paper version of a tracking task) to 38 patients with amnestic Mild Cognitive Impairment (aMCI) and 10 with early Alzheimer's disease, as well as 21 healthy elderly subjects and 17 controls with depressive symptoms. All groups were closely matched for age and pre-morbid intellectual ability.

Results: There were no group differences in dual task performance, despite poor performance in episodic memory tests of the aMCI and early Alzheimer's disease groups. In contrast, early Alzheimer's disease and depressed patients were impaired in Part B of Trail Making Test, another commonly used measure of divided attention.

Conclusions: The dual task paradigm lacks sensitivity for use in the early differential diagnosis of Alzheimer's disease.

Key words: Neuropsychology; Diagnosis; Geriatric Assessment; Memory Disorders; Amnesia, Anterograde; Depressive Disorder; Depressive Disorder, Major; Dysthymic Disorder

Introduction

Alzheimer's disease (AD) is the most common form of dementia, estimated to affect 25 million people around the world with the number of diagnosed cases expected to rise dramatically in the near future (Wimo et al., 2003). Research has focused on developing pharmaceutical interventions for AD, with an increasing emphasis on early accurate diagnosis and intervention. Amnestic mild cognitive impairment (aMCI; Peterson et al., 2001) is associated with an elevated risk of developing dementia. Research on clinic-based samples has suggested that the conversion rate from aMCI to dementia is 10-15% per year (e.g. Petersen et al., 1999, Storandt et al., 2006) compared with between 1-2% in a normal age matched non-clinical sample. AMCI is thus considered a transitional stage between normal ageing and the earliest clinical features of AD (Petersen, 2005; Petersen & O'Brien, 2006).

While it is generally accepted that the primary impairment in very early AD includes episodic memory function, many authors have reported that certain aspects of attention and executive functioning are also vulnerable at this stage (Parasuraman & Haxby, 1993; Perry & Hodges, 1999). In particular, people with early AD exhibit difficulties dividing their attention between two concurrent tasks. A dual task measure was developed by Baddeley and colleagues in order to evaluate the central executive component of working memory (Baddeley et al., 1986). By comparing performance of a synchronous dual task to that of identical task components done separately and consecutively, a deficit in dual performance can be attributed to failure of the central executive that coordinates the simultaneous operation of these components. To our knowledge this dual task paradigm has not been investigated with a sample defined according to recent aMCI criteria (Petersen et al, 1999).

One advantage of this paradigm is that it reduces modality-specific interference between tasks: while the tracking task is presented visually and a manual response is required, information for the digit span task is presented aurally and a verbal response is necessary (Nebes et al., 2001). A further strength of the dual task paradigm is that the task demands can be fixed at individual ability levels, controlling for individual variation in performance in the component parts of the dual task. Therefore, each patient acts as his or her own control, controlling for the generally poorer performance of AD patients in the baseline tasks (Logie et al., 2004).

Research has suggested that failure of this 'coordination' function is characteristic of mild AD in a laboratory setting. Participants with mild AD appear to be impaired, irrespective of task demands, and this impairment has been found to worsen with illness progression (Baddeley et al., 1986; 1991; MacPherson et al., 2004). Proponents of the dual task paradigm suggest such findings are in contrast to normal ageing, which they suggest has a relatively minor effect on dual task performance (e.g. Baddeley et al., 1986; Hartley & Little, 1999; Logie et al., 2004 but see Crossley & Hicock, 1992). Taken together, the above raises the possibility that the dual task may be of use in the early differential diagnosis of AD.

One difficulty with such a proposal is that the equipment for this test has often comprised a computerised tracking device impractical for use in a clinical setting (e.g. Baddeley et al., 1991; Logie et al., 2004). This issue was addressed by Della Sala et al. (1995) who developed a modified pencil and paper version of the tracking component

for the dual task. This has been reported to produce results comparable to the original instrument (Della Sala et al., 1995; Sebastian et al., 2006).

However, although divided attention is vulnerable in AD, impairments may not always be present at the earliest stages (Greene et al., 1995; Perry et al., 2000; Crossley et al., 2004). Task complexity appears to mediate a deficit of dual task performance in early AD. While manipulating task demands within a component task may not alter the dual task effect (e.g. Logie et al., 2004), some authors have suggested otherwise. Crossley et al. (2004) compared dual task performance for relatively more automatic tasks and effortful tasks between AD patients and controls. They found that AD patients' impairment was only noticeable when the component tasks were complex and novel. They concluded that dual task impairment with less complex task components will only be found in AD patients after the disease has progressed beyond the early stage.

A potential source for discrepancy in study results is illness severity. Most previous research, both with the original and with modified versions of the dual task, has not separated patients with differing symptom severity (e.g. Baddeley et al., 1986; 1991; Logie et al., 2004). Thus it is possible that the more severely affected participants performed sufficiently poorly to make the whole patient group appear to be impaired. Perry et al. (2000) compared the performance of a minimally impaired AD group (MMSE above 24 points) and a mild AD group (MMSE scores between 18 and 23; Perry et al., 2000). The only significant difference was found between control participants and those in the mild AD group. Similar results have been reported by Greene and colleagues (1995), who also used the modified dual task test.

Impairments of attention and executive functioning have been described in very early AD and aMCI using other measures of attention (Perry, et al, 2000), such as Part B of the Trail Making Test (TMT B – Reitan, 1985). The TMT B assesses the ability to divide attention back and forth between multiple lines of thought (connecting numbers and letters, respectively). This task differs from the dual task paradigm in that its component parts are not drawn from separate modalities, so that performance is more vulnerable to reduced processing capacity. Several previous studies have demonstrated that TMT B is impaired in the very early and even pre-clinical stages of AD (Lafleche & Albert, 1995; Arnaiz et al., 2000; Perry et al., 2000; Nathan et al., 2001; Crowell et al., 2002; Crossley et al., 2004; Alladi et al., 2006; Baudic et al., 2006; Stokholm et al., 2006), although its specificity for AD, as distinct from e.g. depression, has not been established.

To our knowledge, only one study has investigated dual task performance in older adults with minimal cognitive impairment (Holtzer et al., 2004): Cognitively impaired adults, defined by a dementia rating scale (DRS - Mattis, 1988) cut-off score of 123 or less, performed two tasks in different modalities at the same time. Two combinations of tests were used: a visual cancellation task (where participants were required to cross out a specified stimulus type from a field of stimuli) combined with a digit span task, and the same visual cancellation task combined with a verbal fluency task. Adults scoring below 124 on the DRS were significantly worse at carrying out the tasks concurrently compared with controls. However, direct comparisons between these findings and those of previous research is prevented by the fact that patients were identified purely on the basis of their dementia rating score, and the dual task

methodology differed from those used in previous studies. The findings furthermore contrast with previous research that has failed to show a dual task deficit in very early AD (Greene et al., 1995; Perry et al., 2000).

Depression is also associated with attentional deficits. Hasher and Zacks (1979) suggested that people with depression show impaired attention during effortful processing tasks, for instance on measures of divided attention such as the TMT B (Nathan et al., 2001; Mahurin et al., 2006). However, only one study has investigated the effect of depressive symptoms on Baddeley's (1986) original dual task paradigm (Nebes et al., 2001). This indicated that people with depression had a significantly greater decrement in computerised tracking performance and a composite decrement measure than non-depressed controls. To our knowledge, no study to date has reported the effects of clinically depressed mood on the modified version of the dual task paradigm (Della Sala et al., 1995). This issue is of particular importance clinically, as depression is common among healthy elderly and cognitively impaired older adults and clinicians are frequently required to differentiate between the cognitive effects of depressive illness and those attributable to an early neurodegenerative illness (Herrmann et al. 2007).

The aim of this study was to assess dual task performance in aMCI, in order to ascertain whether this measure could be useful in the early diagnosis of Alzheimer's disease. If AD is associated with a specific impairment in the aspect of working memory that coordinates performance of two separate tasks, then we predicted that the performance of people with aMCI and very early AD should be significantly lower than that of aged matched controls. Furthermore, the inclusion of a group of

elderly patients with symptoms of depression would test the specificity of dual task impairments in Alzheimer's disease. On the basis of the previous research, we predicted that the depressed group would show impairment in the dual task compared with controls.

Method

Participants

We examined 38 patients with amnestic mild cognitive impairment (aMCI), ten early Alzheimer's disease (AD) patients, 17 control outpatients with depressive symptoms, and 21 healthy elderly controls, following a protocol approved by the local ethics of research committee. All participants also took part in a larger longitudinal study of neuropsychological markers in pre-clinical AD. The aMCI patients were recruited over a 2 year period (September 2003 – September 2005) from tertiary referrals to the local neuropsychological assessment service for older adults and met criteria for aMCI (Petersen et al., 1999). AMCI patients presented with subjective reports of memory difficulty corroborated by an informant and performed at least one standard deviation below the age mean on two or more measures of episodic memory. All aMCI patients underwent comprehensive neuropsychological and psychiatric evaluation, medical screening and neuroimaging prior to study entry. Exclusion criteria for the aMCI group were a diagnosis of dementia or other medical/neurological conditions which may account for memory loss, untreated depressive illness, significant or predominant cerebro-vascular disease on neuroimaging, significant motor and/or visual problems or an age below 58 years. MMSE scores ranged from 24 to 30, with a mean of 28.49. The final aMCI group consisted of 16 males and 22 females with a mean age of 73.1 years (range 58 -85 years).

For the healthy elderly control group (MMSE 28-30), we recruited spouses or carers of patients who had attended the service. Potential participants were excluded if there was a history of medical, psychiatric or neurological conditions (i.e. stroke or

cerebrovascular disease, head injury, alcoholism, schizophrenia, etc.) that could conceivably affect cognitive functioning. The healthy elderly control group was matched as closely as possible to the aMCI and early AD groups in terms of age and estimated premorbid IQ. The final elderly control group consisted of 8 males and 13 females with a mean age of 69.5 years (range 59-81 years).

Ten participants diagnosed with Alzheimer's disease, in accordance with NINCDS-ADRDA (McKhann et al., 1984) and DSM-IV (American Psychiatric Association, 1994) diagnostic criteria, took part in the current study. AD patients were recruited from tertiary referrals to our neuropsychology service or via referrals to the local old age psychiatry service. All early AD patients scored above 23/30 on the Mini Mental State Examination (MMSE) and above 65/100 on the more comprehensive Addenbrooke's Cognitive Examination (ACE; Mathuranath et al. 2000), indicating relatively mild disease. Patients had undergone relevant medical screening and neuroimaging, together with comprehensive psychiatric and neuropsychological evaluation as part of their initial diagnostic workup. The final early AD group consisted of 3 males and 7 females with a mean age of 73.6 years (range 65-81 years).

Seventeen participants with depressive symptoms (MMSE 25-30) were recruited via local psychiatric outpatient clinics and day hospitals. In an attempt to match this patient group with the aMCI group in terms of illness severity, patients with milder forms of depression were included. Fifteen of the 17 participants were receiving treatment for their symptoms at the time of testing; all but 2 of these pharmaceutical in nature. As it has been suggested that type of depression does not influence the magnitude of cognitive deficits (Christensen et al., 1997), participants with a variety

of disorders were included. Eight patients had a history of major depression, 2 of bipolar disorder, 2 were suffering from anxiety disorders with depressive features, 3 were considered dysthymic and 2 were considered to be suffering with a sub-clinical level of depressive symptoms. Mean Geriatric Depression Scale score for this group was 13.2 (range: 0 – 27). We once again excluded patients with any medical, neurological or psychiatric condition with a known potential to affect cognitive function. The final depressive control group consisted of 3 males and 14 females with a mean age of 73.3 years (range 65-84 years). Participants gave informed written consent to the protocol, which was approved by the Lothian Research Ethics Committee; the research was completed in accordance with the Helsinki Declaration.

Neuropsychological Tests

All participants completed a variation of the modified dual task paradigm (Della Sala et al., 1995). This pencil and paper test of divided attention consists of 2 components (a digit span task and a visuospatial tracking task) that are each performed on their own before being performed concurrently. First, participants' digit span was determined. This involved repeating strings of digits read by an experimenter at a rate of approximately 2 per second. Initially, 2-digit strings were presented and these increased one digit at a time if the participant correctly recited 5 of 6 examples of each length. When the participant failed to recite 2 or more of 6 strings of the same span, digit span for that person was considered to be the previous length. No time limit was imposed at this stage. Having determined the participants' individual digit span, participants had 90 seconds to recite as many digit strings, fixed at the individual participants' digit span, as possible (digit span – single). Responses were recorded as correct for each digit recited in the correct order.

Following this, participants completed the tracking task. This involved tracing a line through circles, in a clearly marked order, on an A3 sized sheet of paper, after a short practice session. Participants had 90 seconds for this trial, and the number of circles reached during this time was recorded (tracking – single). The final trial was the concurrent dual task. Here participants had 90 seconds to perform both tasks simultaneously: i.e. recite digit strings fixed at their digit span (digit span – dual) as well as carrying out a tracking task identical to the one used above (tracking – dual). In order to take into account the various strategies one may adopt in performing the two tasks simultaneously, an overall decrement score was calculated using the following formula:

$$\mu = (1-[(P_m + P_t)/2]) * 100$$

where μ is the combined dual task score, P_m is the proportional loss in span performance between single (X_{single}) and dual task (X_{dual}) conditions, $[(X_{single} - X_{dual})/ X_{single}]$ while P_t is the equivalent proportional loss in tracking score. Thus a score of 100 would represent no dual task decrement and lower scores reflect greater dual task decrements.

A number of additional tests were administered as part of the longitudinal investigation of neuropsychological markers. These included measures of general cognitive ability, such as the Addenbrooke's Cognitive Examination (ACE) and the more widely known Mini Mental State Examination (MMSE). The National Adult Reading Test-Revised version (NART-R; Nelson & Willison, 1991) was used to

provide an estimate of the premorbid level of intellectual functioning. Episodic memory was assessed using the Hopkin's Verbal List Test- Revised (HVLT-R; Brandt, 1991) and the Paired Associates Learning test (PAL) from the Cambridge Automated Neuropsychological Test Battery (CANTAB; Swainson et al., 2001). Participants also completed the Trail Making Test Part A and B (TMT A; TMT B; Reitan, 1985), measures of visuo-motor processing speed and speeded divided attention.

The HVLT-R requires participants to recall as many words as possible immediately following presentation of a 12-item word list. The word list is presented on three consecutive learning trials. The participant is also required to recall, and finally recognise, as many words from the list as he or she is able, following a delay of 30 minutes. The PAL is a computerised measure of visuospatial learning requiring participants to learn the locations of an increasing number (i.e. 1, 2, 3, 6 and then 8) of patterns (Swainson et al., 2001). The score of interest was the number of pattern-position errors at the 6 pattern level. The TMT B requires participants to trace a line linking numbers and letters alternatively in ascending order and in this regard requires the participant to divide his/her attention back and forth between multiple lines of thought.

Each of these measures have been shown to be sensitive to very early Alzheimer's disease (Blackwell et al., 2004; Chen et al., 2000; Hogervorst et al., 2002; Nathan et al., 2001; Stokholm et al., 2006; Swainson et al., 2001). Neuropsychological assessments lasted approximately 90 minutes in total. The order of test administration was identical for all assessments.

Statistics

Data were analysed using SPSS 12.0 for Windows. Demographic variables were analysed using univariate ANOVAs, and Tukey HSD pairwise comparisons were carried out on all significant analyses where possible. Between-group differences in gender were tested using a chi square analysis. Where the assumption of homogeneity of variance was not met (Levene statistic $p<0.05$), data were transformed to their natural logarithm. If this did not control the variance, we used Games-Howell post-hoc pairwise comparisons. A univariate ANOVA was carried out on the overall decrement score (see above). Decrement scores broken down into tracking decrement and digit span decrement were also calculated and examined using ANOVAs. Two participants in the early AD group were incapable of completing the TMT B; in these cases a default ceiling score of 500 seconds to completion was applied. Non-specific aspects of the TMT B were removed, using the difference of (TMT B - TMT A) as the new variable controlled for psychomotor speed. For the analysis, especially the logarithmic transformation, two negative difference values were set to 1.

Results

Participant Characteristics

[INSERT TABLE 1 HERE]

Demographic matching characteristics are presented in Table 1. There were no group differences in age [$F_{(3,82)}$=1.72; p=0.17] or estimated pre-morbid full scale IQ [$F_{(3,80)}$=0.40; p=0.75]. The groups were matched for sex [$\chi^2_{(3)}$=3.26; p=0.35]. The mean MMSE score for the early AD group was, as expected, significantly lower than that of the other groups [$F_{(3.82)}$=19.5, p<.0001] (AD vs. CT: p=0.001; AD vs. Depression: p=0.003; AD vs. aMCI: p=0.003). No other group differences in mean MMSE score were noted. As expected, the early AD patients had significantly lower mean ACE scores than did all other groups [$F_{(3,82)}$=27.17; p<0.0001] (post-hoc tests as above in all cases: p<0.0001). The ACE also discriminated between normal elderly control participants and aMCI patients, with the latter group obtaining a significantly lower mean ACE score (aMCI vs. CT: p=0.008).

Dual Task Performance

Group means and standard deviations for the digit span task and the tracking measures of the modified dual task paradigm are presented in Table 2. Mean percentage scores for performance on the concurrent tasks, the digit span tasks and the visuospatial tracking tasks for each of the 4 groups are presented in Table 3. On carrying out a one-way non-repeated ANOVA on the overall decrement score, no group difference was found [$F_{(3,82)}$=0.62; p=0.60]. Similarly, no significant group differences were found for any of the other component tasks or decrement scores.

[INSERT TABLE 2 HERE]

[INSERT TABLE 3 HERE]

Other Cognitive Functions

Group mean scores and standard deviations for the HVLT-R, the number of errors at the 6 pattern level of the PAL and the TMT B are presented in Table 4. There was a significant group difference for the HVLT-R delayed recall data [$F_{(3,82)}$=10.8, p<0.0001]. AD patients recalled significantly fewer words than the aMCI (p=0.04), who in turn recalled fewer than the healthy control (p=0.009) and depression groups (p=0.02). The performance of the elderly control and depression groups on the HVLT-R delayed recall did not differ. However, the AD group made significantly more errors at the 6 pattern stage of the PAL compared with all other groups [$F_{(3,80)}$=22.11; p<0.0001; post hoc tests comparing AD with other groups were p<0.0001]. The aMCI group's error scores fell between those of the healthy control and AD groups, and significantly differed from both of these (aMCI vs. CT: p=0.03). A significant group effect was also found for the TMT B [$F_{(3,82)}$=9.5; p<0.0001], but not the TMT A [$F_{(3,82)}$=1.3, p=0.30]. Specifically, early AD and depressed participants required significantly more time to complete this task than did healthy controls (p<0.001 and p=0.03, respectively). In addition, patients with AD performed worse than the aMCI patients (p=0.01). The overall effect was maintained when time to completion on TMT A (a measure of psychomotor speed) was subtracted from TMT B [$F_{(3,82)}$=3.7; p<0.02]. Both healthy controls (p=0.05) and aMCI patients (p=0.02) performed better than early AD patients. The previous effect on TMT B in depressed patients was removed by controlling for impairment of psychomotor speed.

[INSERT TABLE 4 HERE]

Discussion

This study investigated the claim that the dual task paradigm can be used in the early diagnosis of dementia of the Alzheimer's type. We assessed the concurrent performance of a visuospatial tracking task and a forward digit span task in four diagnostic categories: amnestic Mild Cognitive Impairment (MMSE 24-30), early Alzheimer's Disease (MMSE 23-29), depressive symptoms (MMSE 25-30) and healthy elderly controls (MMSE 28-30). Our results show that aMCI is not associated with impaired dual task performance; those with aMCI had comparable performance to healthy older adults and older adults with depressive symptoms. Our early AD group were similarly unimpaired on the modified dual task paradigm relative to depressive and non-depressive elderly control groups and the presence of depressive symptoms appeared to have no effect on dual task performance. By contrast, and indeed by definition, episodic memory impairments were present in the aMCI and early AD groups. Particularly the early AD patients (compared with controls and aMCI), but also the depressed group (compared with the controls) exhibited an impaired ability to divide their attention at pace, as indexed by part B of the TMT. This could be accounted for by reduced psychomotor speed only in the depressive symptoms group. After subtracting the Trails A score, early AD patients continued to be slowed as compared with the aMCI and the control groups, implying an additionally reduced processing capacity.

These results shed some light on previous findings. One line of research has suggested that dual task performance is vulnerable to the influence of AD, even early in the disease course (Baddeley et al., 2001; Logie et al., 2004). However, such studies generally involve participants varying in severity of illness. Accordingly, other

researchers have shown that when participants with AD are divided by severity using a simple bedside screening measure, only those later in the disease process are impaired on the dual task paradigm, for example those scoring 23 or below on the MMSE (Greene et al., 1995; Perry et al., 2000). Such findings are in agreement with the observed lack of support for an early AD impairment in the dual task measure. Thus, dual task impairments are generally not observed early on in the Alzheimer disease process, with MMSE scores above 23/30 (as in the current aMCI and early AD sample).

Only one other study has investigated the dual task performance of a group of older adults with cognitive impairment without a diagnosis of dementia (Holtzer et al., 2004). These researchers report that their cognitively impaired group exhibited a significantly larger dual task decrement than age matched controls. We would argue that the current study is methodologically stronger than the Holtzer study and facilitates greater comparison with previously undertaken dual task research. Specifically, the cognitively impaired group in the Holtzer study was identified solely on the basis of a dementia severity rating score (DRS) cut off score falling at or below levels that are indicative of an underlying dementia. It is for this reason difficult to be certain of, or to compare, disease severity of this 'minimally cognitively impaired' group to other studies, which commonly use well established clinical and research criteria to define patient groups. Furthermore, the cognitively impaired group in Holtzer and colleague's study were significantly less well educated than the control groups, whereas in the current study participant groups were well matched both in terms of their age and estimated levels of pre-morbid intelligence. Furthermore, Holtzer et al. (2004) do not investigate the potential influence of depression on dual

task performance. This is crucial where consideration is being given to the early and differential diagnostic value of a neuropsychological measure.

A further strength of the current investigation relates to the availability of additional neuropsychological data demonstrating the existence of significant episodic memory impairments in aMCI and early AD. In contrast, the Holtzer study only compared the dual task performance of minimally cognitively impaired participants with their performance in tests comprising the single task conditions (i.e. visual cancellation, digit span and letter fluency). These tests are not, generally speaking, associated with impairments in very early and pre-clinical AD and it is therefore not surprising that they are insensitive to cognitive deficits in the minimally impaired group, as was the case in the current study. Further, the presence of abnormalities in the depressed group at least for the TMT B task suggests that tasks measuring the ability for speeded divided attention may not be specific for AD.

One important factor that may have influenced the current results is task novelty and complexity. While those studies reporting general dual task impairment in early AD used dual task measures with both computerised and pencil-and-paper versions of the tracking task, only the modified version using the pencil-and-paper tracking task (Della Sala et al., 1995) has been used in studies which separate participants by symptom severity. Thus, while patients who are minimally affected do not show impairments on the modified version of the task, it remains possible that they would show impairments if the test were more taxing – for instance if the dual task paradigm included the original computerised version of the tracking task. This more novel task requires increased effort and attention as participants are required to adjust to an

external influence (i.e. the speed of the light dot on the screen) rather than working at a self-defined rate. It may therefore be sufficiently taxing to identify those who are not picked up by the more straight forward pencil-and-paper tracking task, although its impracticality in a clinical setting would likely remain an issue for clinicians.

Variability in the methods of dual task administration leads to difficulty comparing findings across different studies. In the current study, we administered each of the 3 trials in blocks of 90 seconds; however some previous studies have set the trial time at 120 seconds (e.g. Perry et al., 2000). Most previous dual task studies have utilised pencil-and-paper tracking tasks that require participants to cross out boxes on an A4 size sheet of paper to form a chain (eg. Baddeley et al., 1997). The current task required participants to trace a line through linked circles on an A3 size sheet. While the initial dual task paradigm involved recording the number of completely correct digit strings (Baddeley et al., 1986), many subsequent studies, including the current investigation, have calculated the number of digits recalled in the correct order for this measure. The significance of such minor alterations to dual task administration requires further investigation.

A possible alternative explanation for our negative results is that a majority of individuals forming our aMCI group will fail to convert to AD in the future. If this proves to be the case, then the absence of dual task impairment in the aMCI group would not be surprising. This issue will be fully resolved through longitudinal follow-up of the participants with aMCI. However, the sound performance of our early AD group on the dual task measure would suggest that the negative findings for the aMCI group are not explicable in terms of an absence of underlying AD pathology. Rather,

the impaired performance of the early AD group on an alternative popular measure of speeded divided attention would imply that the dual task measure lacks sensitivity to the very early changes of an attentional/executive nature in AD.

In conclusion, patients with early AD and aMCI do not display impaired performance on the modified version of the dual task paradigm at a time when episodic memory, and in the case of early AD, speeded divided attention, are significantly impaired. The findings imply that the dual task paradigm is insufficiently sensitive for use as an adjunctive cognitive tool in the early diagnosis of AD. Future research is needed to investigate the use of dual task tests of varying demand in aMCI and very early AD participants in an effort to determine the potential influence of task demands and complexity on performance.

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Table 1: *Demographic data [Means (SD)]*

Variable	Controls (n=21)	Depression (n=17)	aMCI (n=38)	Early AD (n=10)	Post-hoc tests
Age	69.5 (7.3)	73.3 (6.6)	73.1 (6.3)	73.60 (5.8)	-
Gender	8M:13F	3M:14F	16M:22F	3M:7F	-
NART	118.2 (2.9)	116.8 (6.2)	116.5 (8.1)	115.60 (5.5)	-
MMSE	29.10 (0.7)	28.59 (1.5)	28.47 (1.6)	25.00 (2.3)	CT, Dep, aMCI > AD
ACE	94.57 (3.3)	91.71 (5.0)	89.87 (5.9)	76.70 (6.6)	CT, Dep, aMCI >AD CT > aMCI

M = Male; F = Female AD = Alzheimer's disease; aMCI = Amnestic Mild Cognitive Impairment; ACE = Addenbrooke's Cognitive Examination.

Table 2: *Digit Span and individual component measures of the dual task (Span & Tracking, performed separately and together) [Means (SD); all ANOVAs n.s.]*

Task	Control (n= 21)	Depression (n= 17)	aMCI (n= 38)	Early AD (n=10)
Digit Span (DS)	5.5 (0.68)	5.8 (0.97)	5.7 (0.96)	5.1 (0.74)
DS (Single)*	1.0 (0.03)	0.9 (0.05)	1.0 (0.05)	1.0 (0.03)
DS (Dual)*	0.9 (0.05)	0.9 (0.08)	0.9 (0.08)	1.0 (0.02)
Tracking (Single)	141 (56.5)	140 (51.7)	133 (50.4)	120 (46.3)
Tracking (Dual)	122 (46.0)	126 (58.3)	121 (46.1)	107 (35.6)

* Proportion of digits recalled in the correct position (where 1.0= all correct)
AD = Alzheimer's disease; aMCI = Amnestic Mild Cognitive Impairment.

Table 3: *Percentage loss of performance in component tasks and overall decrement score during the dual task [Means (SD); all ANOVAs n.s.]*

Task	Control (n= 21)	Depression (n= 17)	aMCI (n= 38)	Early AD (n=10)
Digit Span	96 (3.8)	97 (8.6)	97 (7.2)	100 (3.3)
Tracking	90 (22.8)	88 (16.8)	92 (15.0)	93 (17.6)
Overall decrement	93 (11.1)	92 (8.2)	95 (8.4)	97 (9.1)

AD = Alzheimer's disease; aMCI = Amnestic Mild Cognitive Impairment. Percentage loss of performance scores were calculated as $\{1- [(X_{single} - X_{dual})/ X_{single}]\} * 100$ and the overall decrement score as $\mu = (1-[(P_m + P_t)/2]) * 100$, as described in the Methods section.

Table 4: *Other cognitive domain measures [Means (SD)]*

Task	Controls (n=21)	aMCI (n=38)	Depression (n=17)	Early AD (n=10)	Post-hoc Group Differences
HVLT-R	8.1	5.3	8.1	2.1	CT, Dep > aMCI > AD
Delay	(2.8)	(3.3)	(3.3)	(3.7)	
PAL errors	7.8	15.1	10.9	40.7	CT, Dep, aMCI < AD
	(6.9)	(12.9)	(7.8)	(10.6)	CT < aMCI
TMT A	40.3 (11.2)	47.7 (34.7)	54.1 (23.1)	57.6 (25.3)	-
TMT B	87.6 (31.5)	101.6 (48.9)	134.2 (53.6)	216.7	CT, aMCI < AD
				(157.7)	CT < Dep^{+}

CT = Healthy Controls; Dep = Controls with depressive symptoms; aMCI – amnestic Mild Cognitive Impairment; AD = Alzheimer's disease; HVLT-R = Hopkins Verbal Learning Test-Revised; PAL Errors = 6 Pattern Stage errors from the Paired Associates Learning Test; TMT A = Trail Making Test Part A; TMT B = Trail Making Test Part B.
$^{+}$Not significant after control for TMT A effects (see text)