Focused attention deficits in patients with Alzheimer's disease and Mild Cognitive

Impairment

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Abstract

Reaction time (RT) tasks take various forms, and can assess psychomotor speed, (i.e. simple reaction time (SRT) task), and focused attention (i.e. choice reaction time, (CRT) task). If cues are provided before stimulus presentation (i.e. cued choice reaction time (CCRT) task), then a cueing effect can also be assessed. A limited number of studies have addressed the nature of focused attention impairments in Alzheimer's disease (AD). Additionally, it is unknown whether similar impairments occur in Mild Cognitive Impairment (MCI). The current study used three RT tasks to address the nature of focused attention impairments in AD and MCI subjects.   The results suggest that there were significant CRT and CCRT differences in AD subjects when compared to NECs. Furthermore, slowed RTs were also present in the MCI group, which provides evidence for impaired focussed attention and the inability to benefit from a cue in both the MCI and AD groups. The implications of the impairments related to the MCI group could potentially prove useful in early diagnosis of cognitive impairments in the elderly.

Introduction

Typically, tasks used to study attention entail cognitive processes in addition to attention resources. Although impairments in episodic memory performance constitute the earliest type of deficit that occurs during the early onset of Alzheimer's disease (AD), specific cognitive evaluations indicate that deficits in attentional control may occur as well (for review, see Perry & Hodges, 1999). Several studies have examined the nature of attentional impairments related to the capacity to divide and focus attention (Gordon & Carson, 1990; Nestor, Parasuraman, & Haxby, 1991). While these studies present reliable

evidence for the existence of deficits in divided attention in early AD, controversy exists as to whether such deficits necessarily co-occur with impairments of focused attention.

Focused attention can be studied using various forms of reaction time (RT) tasks. In the choice reaction time (CRT) task, participants are required to carry out one of two response options based on the nature of the stimulus that is presented. In the simple reaction time task (SRT), subjects respond as rapidly as possible to a single stimulus. While both tasks entail a component of psychomotor speed, CRT entails an additional choice decision component. If a reliable cue precedes the stimulus, then additional decision-making time is reduced in normal elderly controls (NEC) (Gordon & Carson, 1990).

When NECs are tested on the CRT and SRT tasks, they tend to perform slower than young normal individuals on both the SRT and CRT task (Baddeley, Baddeley, Bucks & Wilcock, 2001). Nestor, et al., (1991) found that AD subjects were slow in responding to the cue in the CRT task, and argued that the slowing was due to impaired focused attention. In contrast, Baddeley et al., (2001) failed to find deficits in AD patients on the CRT task and concluded that slowed CRT performance is not specific in AD, but is rather the result of generalized cognitive slowing from brain damage.

The degree of cognitive impairment associated with AD and aging may play a role in the nature of slowed attentional performance. Previous studies have used mild- to moderately-demented patients. Additionally, there is a sub-group of elderly individuals who manifest subjective and objective memory impairment, and perform worse than NECs on neuropsychological tests of memory, but do not meet the NINCDS-ADRDA criteria for AD (Petersen, 2000). It is also unclear whether cognitive domains in addition

to memory are reliably affected in subjects clinically classified with Mild Cognitive Impairment (MCI).

The purpose of the current study is to twofold. First, we were interested in addressing the controversy as to whether focused attention is reliably impaired in AD, and to what extent the cueing effect is also impaired. Second, we wished to determine whether MCI subjects would show any deficits in these domains when compared to NEC subjects.   We used three RT tasks to determine the extent of focused attention impairments. The SRT task assessed general psychomotor speed, whereas the CRT task assessed focused attention, and the CCRT task assessed whether or not subjects could benefit from the availability of a cue prior to stimulus presentation. We predicted that AD subjects would be significantly slower on CRT and CCRT tasks as compared to NECs. Furthermore, we predicted that in comparison to NECs, MCI subjects would be impaired on the CRT and CCRT tasks.

Method

Participants

Fifty-two NEC subjects (see Table 1) were recruited from community volunteers as well as the Family Practice Clinic at the Jewish General Hospital in Montreal, Canada. A neuropsychological battery, clinical assessment and neurological exam were carried out in order to determine whether they were neurologically and cognitively normal for their age.   The MCI cohort consisted of 34 participants recruited from the McGill University Memory Clinic at the Jewish General Hospital (see Table 1).   All patients were referred to the clinic after complaints were made about their memory from themselves or their family members. The subjective memory complaints were confirmed

by objective evidence of memory loss on mental status testing as well as neuropsychological test scores at least 1 SD below the norm for their age. Their memory deficits were not severe enough to meet the NINCDS-ADRDA criteria for probable AD (McKhann, et al. 1984).

Thirty AD patients were also recruited from the McGill Memory Clinic at the Jewish General Hospital (see Table 1). Patients met the NINCDS-ADRDA criteria for the diagnosis of probable AD, and the DSM-3 criteria for dementia (McKhann, et al. 1984).   All subjects underwent a clinical evaluation to exclude additional neurological disorders that interfere with normal cognitive functioning. Structural brain diseases were excluded using CT and/or MRI analyses.

[insert Table 1 here]

Procedure

For all three tasks (SRT, CCRT and CRT), each participant completed one block of 50 trials. In the SRT task, participants were told that they would see the word "Ready?" on the screen. After this prompt, they were instructed to press the space bar as soon as a black dot appeared on the screen. In the CCRT participants were told to respond either to the number 1 by pressing the control button on the keyboard, or the number 2 by pressing the keyboard button on the corresponding side of the keyboard. Prior to the stimulus presentation, a cue consisted of the following prompt that prepared the subject for the stimulus and stated: "Are you ready for the number 1?" All such prompts were valid cues, correctly alerting the subject to the number about to appear. In the CRT condition, the stimuli were similar to those of the CCRT but there was no cue

prior to the presentation of the numbers 1 or 2. In all conditions, the prompt consisted of the word "Ready?".

A 400 ms interval separated the cue from the stimulus. After responding, the experimenter pressed the return button to initiate the next trial. Prior to the testing phase, participants were given ten practice trials to familiarize themselves with the procedure. The presentation order of conditions was invariably SRT, CCRT, and CRT in a non-randomized order. Participants were informed to work as quickly as possible without making many errors. RTs were recorded in milliseconds, and all incorrect responses and technical errors were discarded from the analysis.

Results

The AD, MCI and NEC subjects did not differ in terms of age or education (see Table 1). AD subjects were mild in terms of mean dementia severity (mean MMSE score 22.1/30). Error trials were removed from the data of each subject, but were not analyzed since they accounted for less than 5% of the trials for any condition. Outlier correct RTs were also removed from the individual data if they were greater or less than two standard deviations from the mean RTs for that subject. The exclusion of errors and outliers resulted in the removal of less than 5% of the entire set of data points. Four MCI and 5 AD patients were excluded from the sample because their overall mean RT was greater than 1000 msec, suggesting some additional undetected cause of psychomotor slowing. One subject was excluded due to technical malfunction. Figure 1 shows the average RTs for the AD, MCI, and NEC subjects as a function of the SRT, CRT and CCRT conditions.

A 3 x 3 ANOVA was performed on RTs with the between subject factor of Group (AD, MCI, NEC) and the within subject factor of Attention Task (SRT, CRT, CCRT). This analysis revealed significant a significant two-way interaction between Group and Attention Task [$F(2, 114) = 6.2$, $p < 0.003$]. There were also significant main effects of Group [$F(2, 114) = 12.1$, $p < 0.01$] and Attention Task [$F(1, 114) = 335.5$, $p < 0.001$].

These analyses were followed up by an additional series of 2 x 3 ANOVAS, which were planned comparisons involving pairwise contrasts between groups and attention tasks. A significant two-way Group x Attention Task interaction was found when the CRT times were compared with the SRT times [$F(2, 114) = 6.2$, $p < 0.001$]. Furthermore, there were significant main effects of Group [$F(2, 114) = 10.7$, $p < 0.00$], and Attention Task [$F(1, 114) = 335.5$, $p < 0.00$]. There was also a significant Group x Attention Task interaction [$F(2, 114) = 4.7$, $p < 0.01$], and significant main effects of Group [$F(2, 114) = 8.9$, $p < 0.000$] and Attention Task [$F(1, 114) = 29.2$, $p < 0.00$] when the CCRT and SRT tasks were compared. The 2 x 3 comparison of CRT and CCRT tasks revealed no significant Group x Attention Task interaction [$F(2, 114) = 0.4$, *n.s.*]. However, there were significant main effects of Group [$F(2, 114) = 13.5$, $p < 0.00$], and Attention Task [$F(1, 114) = 131.2$, $p < 0.00$].

In order to further examine the nature of the significant 2 x 3 interactions, a series of planned comparisons using 2 x 2 ANOVAs were conducted between Group and Attention Tasks. A significant interaction was found when the AD and NEC subjects were compared on SRT and CRT tasks [$F(1, 81) = 11.3$, $p < 0.001$]. There was a significant main effect of Group [$F(1, 81) = 17.9$, $p < 0.00$], indicating that the AD subjects were slower than the NECs. There was also a significant main effect of

Attention Task [F(1, 81) = 218.0, $p < 0.00$], which implied that performance on the CRT was slower than performance on the SRT. When AD and NEC subjects were compared on SRT and CCRT tasks, there was a significant two way interaction of Attention Task x Group [F(1, 81) = 6.9, $p < 0.01$]. Furthermore, the AD subjects were significantly slower than the NECs, [F(1, 81) = 16.2, $p < 0.00$] and performance on the CCRT task was significantly slower than performance on the SRT task [F(1, 81) = 14.1, $p < 0.00$].

The NECs were also compared to the MCIs. There was a significant Group x Attention Task interaction [F(1, 84) = 4.5, $p < 0.00$] when the SRT and CRT tasks were compared. Additionally, there was a significant effect of Attention Task [F(1, 84) = 287.4, $p < 0.00$], but no significant difference between Group performance [F(1, 84) = 0.8, n.s.]. When NEC and MCI groups were compared on SRT and CCRT tasks there was a significant interaction between Group and Attention Task [F(1, 84) = 7.31, $p < 0.00$]. The main effect of Attention Task [F(1, 84) = 18.2, $p < 0.00$] was statistically significant. However, the main effect of Group was not statistically significant [F(1, 84) = 1.7, n.s.].

Group comparisons between MCI and Ads on CRT and SRT tasks were also compared. A 2 x 2 ANOVA conducted to examine pairwise contrasts indicated that there was no significant interaction of Group x Attention Task [F(1,63) = 2.1, n.s.], but there were significant main effects of Group [F(1,63) = 10.3, $p < 0.00$] and Attention Task [F(1,63) = 182.2, $p < 0.00$]. Similarly, a comparison of MCI and AD subjects on CCRT and SRT tasks failed to show a significant Group x Attention Task interaction [F(1, 63) = 0.4, n.s.], but there was a significant Group effect [F(1, 63) = 6.7, $p < 0.01$] and a significant effect of Attention Task [F(1, 63) = 25.2, $p < 0.00$].

[insert Figure 1 here]

Discussion

We used three RT tasks to determine whether focused attention is impaired in AD. Additionally, we examined whether AD subjects could benefit from the presence of a cue in the CCRT task. We also sought to determine whether MCI subjects would also manifest impairments in focussed attention similar to those seen in AD subjects. The results indicated that the AD subjects were slower than the MCI and NEC subjects (see Figure 1), reflecting an effect of generalized cognitive slowing that is related to the extent of brain damage in the AD subjects (Benton, 1986).

The results also suggest that all subjects were slower on the CRT task when compared to the SRT task (see Figure 1). However, there was a pronounced difference on the CRT task amongst the AD subjects when compared to NECs, which suggests that AD patients are impaired on tasks of focussed attention. In contrast to the current results, Baddeley et al. (2001), concluded that their cohort of AD subjects did not perform any slower than the NECs in their study and therefore did not have impaired focused attention deficits. There are several explanations for these inconsistent findings between Baddeley et al. and the current results. First, the SRT task in this experiment used a constant inter-stimulus interval. In contrast, Baddeley et al. (2001) used a varied inter-stimulus interval. This manipulation might have caused further slowing on the SRT task, thus reducing the potential group differences in RTs between the SRT and CRT tasks. Furthermore, subject group differences might also explain the contrasting results of the current study from those of Baddeley et al.

In addition to the focused attention impairment related to AD, the MCI subjects performed the CRT task in a manner similar to the AD subjects. These results suggest that there is a clear attentional impairment in focused attention also present amongst the MCI group that cannot be elicited on standard neuropsychological testing.

With respect to the cueing effect, the results indicate that NECs benefit from the presence of a cue, which essentially changes the CCRT task into an SRT task (see Figure 1). However, neither the MCI or AD subjects achieve this cueing benefit. This suggests an impairment in the cueing effect amongst the two patient groups, which we believe is related to impaired frontal lobe functioning.

Finally, the pairwise comparisons that were made between the MCI and AD subjects failed to show any significant two-way interactions when the SRT task was compared with the CRT task, and when the SRT task was compared with CCRT task. Consequently, this implies that there is a specific impairment in both focused attention and cueing present in both MCI and AD groups as compared to NECs. These results suggest that there are previously unsuspected attention deficits in MCI subjects that cannot be elicited in standard neuropsychological tests. Subsequently, in the future, similar RT experiments could prove useful in detecting early diagnosis of cognitive impairments in the elderly.

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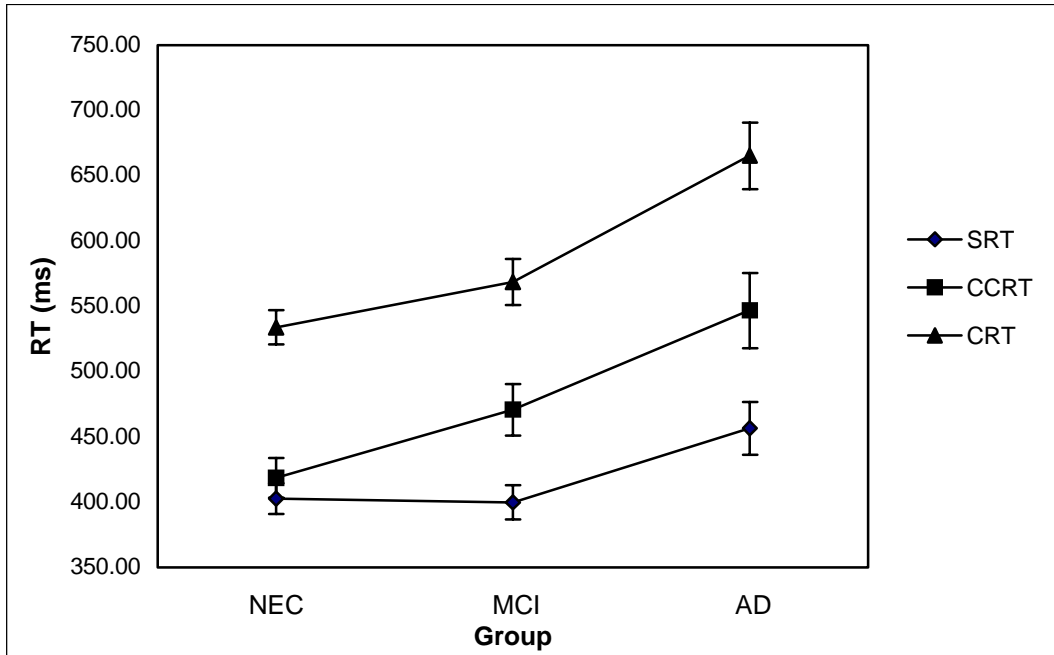
Figure 1. RTs (ms) for all groups (NEC, MCI and AD) on all tasks (SRT, CRT, CCRT)

Table 1. Means (SDs) for demographics and RTs on focussed attention tasks

	NEC ($\underline{N}$ = 52)	MCI ($\underline{N}$ = 34)	AD ($\underline{N}$ = 31)
Age (yrs)	74.0 (5.6)	74.1 (7.1)	73.9 (9.4)
Education (yrs)	11.7 (3.0)	10.5 (3.6)	10.8 (3.3)
MMSE*	29.1 (1.0)	27.7 (2.1)	22.1 (4.1)
SRT (ms)	402.6 (85.3)	399.9 (70.1)	456.5 (117.1)
CCRT (ms)	418.6 (109.1)	470.8 (115.1)	546.7 (168.6)
CRT (ms)	533.9 (95.5)	568.4 (98.5)	665.2 (149.9)

*Denotes significant group difference ($p < 0.00$)