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Executive function deficits in early Alzheimer's disease and their relations with episodic memory

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Abstract

Previous research suggests that patients with Alzheimer's disease (AD) are impaired on executive function early in the course of disease, but negative findings were reported. To evaluate the performance on executive tasks in early AD and to determine the involvement of memory on the outcome of executive tasks. Thirty-six AD patients were divided into two subgroups on the basis of the MMSE: very mild and mild. The comparison with 17 normal controls shows that very mild AD patients had deficits on visuospatial short-term memory, episodic memory, flexibility and self-monitoring abilities, concept formation and reasoning. The mild AD patients showed additional deficits on the Similarities test. Episodic memory and executive deficits occur in the very early stage of AD and precede impairment in constructional praxis, language and sustained attention. With the progression of the disease, additional deficit is observed in abstract thinking. In mild AD, memory failure is also related to executive impairment.

Keywords: Alzheimer's disease; Early stage; Executive function; Episodic memory

1. Introduction

In recent years, the literature has reported that Alzheimer's disease (AD) patients are impaired on a variety of tasks that have commonly been considered a measure of executive function (Collette, Delrue, Van Der Linden, & Salmon, 2001; Lambon, Patterson, Graham, Dawson, & Hodges, 2003; Logie, Cocchini, Della Sala, & Baddeley, 2004). According to some authors (Anderson & Tranel, 2002), executive function encompasses a number of cognitive abilities which are generally conceived of controlling or guiding behavior in a top–down fashion such as decision-making, planning, self-monitoring, and behavior initiation, organization and inhibition. Baddeley, Bressi, Della Sala, Logie, and Spinnler (1991) showed that AD patients were particularly impaired on dual-tasks even when the difficulty of the tasks, performed separately, was equated across the groups and when the subjects did not have to store presented

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information. Bhutani, Montaldi, Brooks, and McCulloch (1992) showed deficits on a series of executive tasks (verbal fluency test, delayed alternation, Self Ordering Pointing Test and Wisconsin Card Sorting test) administered to very mild, mild and moderate AD patients. Lafleche & Albert (1995) found that their very mild AD patients differed significantly from controls on executive tasks (Self-Ordering task, Hukok Logical Matrices, Trail Making Test and verbal fluency test) that required concurrent manipulation of information, i.e., set shifting, self-monitoring, or sequencing tasks.

Some reports, however, are in contradiction with executive dysfunction in the early stage of the disease. For Broks et al. (1996), executive function is relatively spared in the early stage of the disease. Executive impairment was related to the severity and duration of AD. Similarly, Pillon, Dubois, Lhermitte, and Agid (1986) claimed that executive deficits simply reflect a moderate or severe cognitive deterioration. Another controversy lies in the implication of memory failure in the outcome of executive deficits in AD. Broks et al. (1996) clearly attributed executive deficits in their AD patients to memory impairment. The authors suggest that failure in executive function reflects a selective vulnerability within limbic–cortical networks secondary to a temporal lobe dysfunction. In contrast, Lafleche and Albert (1995) failed to show a relation between memory and executive deficits in their very mild AD patients, despite a variety of statistical analyses.

Moreover, it must be pointed out that variability across studies in both tasks used to examine aspects of executive function, and in the disease severity, makes it difficult to determine which aspects of attention are affected earliest in AD, and how executive impairment is related to other cognitive modules. Consequently, we selected executive tasks which are more "universally" accepted like those mentioned in following studies (Grady et al., 1988; Lafleche and Albert, 1995; Bhutani et al., 1992). The objective was to avoid to further clouding the issue by introducing additional measures.

These conflicting results lead us to conduct the current study. The aim of our study was to provide a more detailed analysis of the cognitive effects of AD in the earliest stages and, therefore to throw light on the relationships between the executive function and episodic memory.

2. Methods

2.1. Subjects

Between January 1997 and December 1998, patients were referred for diagnostic investigation of dementia to the Notre Dame de Bon Secours Hospital, Paris, France. The evaluation procedure consisted in detailed medical history, physical and neurological examinations, cognitive evaluations, appropriate laboratory tests and neuroimaging. All patients underwent brain computed tomography (CT) or magnetic resonance imaging (MRI). History of medical, neurological and psychiatric troubles were obtained from the patient and family members (usually the patient's spouse or children) or other caregivers. The Mini Mental State Examination (MMSE) (Folstein, Folstein, & Mc Hugh, 1975) was used to characterize global cognitive level. Signoret's Battery of Cognitive Efficacy (B.E.C. 96; Signoret et al., 1989) was employed to diagnose AD using DSM IV and NINCDS-ADRDA criteria. None of these tests were used in the total battery. In order to allow for inclusion of mildly impaired patients, inclusion criteria were set arbitrarily to an MMSE score equal to or higher than 20/30.

Among the 216 patients fulfilling the DSM-IV criteria for Dementia (Diagnostic and Statistical Manual of Mental Disorders, 1994), patients were excluded because of the following: (1) probable AD (McKhann et al., 1984) MMSE < 20 ($n = 56$); (2) possible AD (McKhann et al., 1984), or possible vascular dementia (VaD, Roman et al., 1993) ($n = 49$), or AD with cerebrovascular disease (CVD) ($n = 38$); (3) probable VaD (Roman et al., 1993) ($n = 14$); (4) other forms of dementia ($n = 30$) and (5) coexisting dementia and major depression (Diagnostic and Statistical Manual of Mental Disorders, 1994) ($n = 42$). The reminding 36 consecutive patients met DSM-IV criteria for Dementia of the Alzheimer's Type (Diagnostic and Statistical Manual of Mental Disorders, 1994) and the NINCDS-ADRDA criteria (McKhann et al., 1984) for probable AD. At inclusion, the patients were divided into two subgroups on the basis on their scores on the MMSE. An upper cut-off of 24 was chosen to divide the two groups: very mild (corresponding to minimal cognitive impairment, very mild or possible AD in other classifications; 24–30 of MMSE) and mild (20–23 of MMSE) (Perry, Watson, & Hodges, 2000). Eighteen patients presented mild AD and 18 minimal AD. The choice of the score of 24 as the split point is based on relevant theoretical grounds (Morris et al., 2001; Salmon et al., 2002).

None of the AD patients demonstrated focal neurological signs or radiological evidence of stroke. In order to exclude, as much as we could, "mixed" (i.e., AD with CVD) (Roman et al., 1993) cases, patients who fulfilled NINCDS-ADRDA