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Brain oscillatory responses to an auditory-verbal working memory task in mild cognitive impairment and Alzheimer's disease

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Abstract

We report preliminary findings on EEG oscillatory correlates of working memory in mild cognitive impairment (MCI) and Alzheimer's disease (AD). Event-related desynchronization (ERD) and synchronization (ERS) of the 1–20 Hz EEG frequencies were studied using wavelet transforms in elderly controls, MCI patients and mild probable AD patients performing an auditory-verbal Sternberg memory task. Behaviourally, the AD patients made more errors than the controls and the MCI group. Statistically significant differences during the encoding of the memory set were found between the controls and the MCI group, such that the latter group showed ERD in the ~10–20 Hz frequencies. The findings may reflect different, compensatory encoding strategies in MCI. During retrieval, the most obvious differences were observed between the controls and the AD group: the ERD in the ~7–17 Hz frequencies was absent in the AD group particularly in anterior and left temporal electrode locations. This finding might indicate that AD is associated with deficient lexical-semantic processing during the retrieval phase in working memory tasks. Future studies with larger patient groups are needed to establish the diagnostic value of ERD/ERS patterns in MCI and AD.

Keywords: Event-related desynchronization; Event-related synchronization; Mild cognitive impairment; Alzheimer's disease; Memory; 1–20 Hz; EEG

1. Introduction

The aging individual faces an increased risk of developing neurological diseases leading to dementia. The most common form, Alzheimer's disease (AD), accounts for over half of dementia cases. Given the recent developments in drug treatment of early AD, it has become increasingly important to identify these individuals as early as possible. Limited cognitive deterioration, coined as mild cognitive impairment (MCI), has been considered as a risk zone for incipient AD (Petersen et al., 2001). In the present study, we sought for neurophysiological correlates of MCI and early AD by studying the patterns of EEG oscillatory responses during a working memory task performance.

In most EEG studies on AD, quantitative evaluation of fixed periods of spontaneous EEG has been used. This method discards the temporal sequences of task-related EEG changes. Another widely used method is the temporal summation of EEG responses over a number of frequency bands (event-related potentials, ERPs), but in this method the functional significance of the responses in different frequency bands is lost.

It has been proposed that EEG oscillatory responses of different frequency bands of the human EEG reflect different aspects of information processing and that the

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oscillatory changes are basic phenomena in the EEG (Basar et al., 2001a,b; Karakas et al., 2000). One way to assess event-related oscillatory EEG responses is the event-related desynchronization-method (ERD). A relative decrease in the power of any given frequency band during either external or internal stimulus processing is called event-related desynchronization (ERD), while a relative increase in the power is called synchronization (Pfurtscheller and Lopes da Silva, 1999). The ERD/ERS phenomenon is quantified by comparing two different conditions, often a resting state and the presentation of a stimulus, and expressed as a percentage power decrease or increase. The time-resolution of this method is good and it is thus suitable for studying cognitive processes that are dynamic and evolve over time.

Different frequencies in the EEG have been found to stem from different areas in the brain. The hippocampal theta rhythm in rodents has been extensively studied. It has been found to be related to long-term potentiation and learning (Kahana et al., 2001). Theta activity has, however, also been recorded from the neocortex by using intracranial EEG in humans and primates (Caplan et al., 2000; Kahana et al., 1999; Lee et al., 2005; Raghavachari et al., 2001). Even though the neurophysiological mechanisms and generators of the theta rhythm are still debated, the evidence for its role in information processing is mounting. Event-related changes in the scalp-recorded human theta activity (~4–6 Hz) have been found to reflect brain processes associated with both attention (Kahana et al., 2001), working memory (Bastiaansen et al., 2002a; Jensen and Tesche, 2002) and episodic memory (Barbeau et al., in press; Bastiaansen et al., 2002b; Klimesch et al., 1997a, 2001).

Alpha activity (~7–13 Hz) has been suggested to be generated in thalamo-cortical networks. The lower alpha components reflect alertness and attention, and the upper alpha is modulated mainly by stimulus-related aspects and semantic memory processes (Jensen et al., 2002; Klimesch, 1999; Klimesch et al., 1997a). Utilizing cognitive tasks with auditory stimuli (words, instrument sounds), Karrasch et al. (1998, 2004) and Krause et al. (1999, 1996, 2001) have repeatedly demonstrated that memory encoding typically elicits alpha frequency ERS in the EEG, whereas retrieval and stimulus comparison elicits alpha ERD.

EEG beta activity has been extensively studied in relation to motor processing (Pfurtscheller and Klimesch, 1991). Imagining, planning and execution of movement has repeatedly been found to elicit ERD and ERS in the ~14–35 Hz frequency range over the sensorimotor areas (Neuper and Pfurtscheller, 2001). Recent findings have, however, indicated that beta oscillations also might play a role in working memory processing and attention (Vazquez Marrufo et al., 2001). Short memory retention intervals has been reported to elicit synchronization in the ~13–20 Hz frequencies (1–2 s), whereas retention of material during longer delays (10 s) elicits desynchronization (Peterson and Thaut, 2002; Tallon-Baudry et al., 1999). Lowered amplitudes in the 20–24.5 Hz frequency and desynchronization in the 10–20 Hz frequency range have also been reported during recognition and working memory performance (Düzel et al., 2003; Karrasch et al., 2004).

The effects of normal aging on oscillatory responses during auditory working memory performance have been reported in a recent study (Karrasch et al., 2004). In that study, it was observed that encoding elicited ERS in the ~1–8 Hz frequency ranges irrespective of age. However, in the elderly subjects, the ERS in the ~10 Hz frequency was greater than in the young subjects and the ERS in the ~4–6 Hz frequency was attenuated. During retrieval, ERS in the ~1–5 Hz frequency bands, as well as ERD in the ~8–20 Hz frequencies, were observed in all subjects, but these responses were weaker in the elderly subjects. The results indicated that the working memory-related oscillatory processes especially during retrieval are somewhat modulated by aging even though no age-related effects were observed at the behavioural level.

AD patients are known to present with “slowing” of the EEG (Besthorn et al., 1997). The peak frequency in the extended alpha range has been reported to be ~1 Hz lower in mild AD when compared to age-matched controls (Lehtovirta et al., 1996). In moderate AD, the peak frequency in the power spectrum has been found to be below 6 Hz (Signorino et al., 1995). Generally, it has been thought that the earliest AD-related changes in the EEG include an increase in theta activity and decrease in beta activity, which is later on followed by a decrease in alpha activity (Bennys et al., 2001; Claus et al., 1998; Coben et al., 1983; Jeong, 2004; Kowalski et al., 2001). An increase in relative theta power has been found to predict which MCI patients will progress to AD (Jelic et al., 2000). The functional reactivity of EEG oscillations in MCI and AD has, however, mostly been studied in relation to eye opening (Claus et al., 1999), tone stimulation (Müller et al., 1991) and movement (Babiloni et al., 2000).

1.1. The aim of the study

The aim of the present preliminary study was to explore the event-related desynchronization and synchronization patterns in the 1–20 Hz frequency bands during the encoding and retrieval phase of an auditory-verbal working memory task in mild cognitive impairment and Alzheimer’s disease. A similar auditory working memory paradigm have repeatedly demonstrated that encoding elicits ERS and retrieval ERD in the 8–12 Hz alpha frequency band in young subjects (Krause, 2002; Krause et al., 1996, 2001). Moreover, encoding and even more so retrieval has typically elicited ERS in the 4–6 Hz theta band. A recent study indicated that normal aging is associated with weakened ERD in the 8–20 Hz frequencies and ERS in the 1–5 Hz frequencies during retrieval (Karrasch et al., 2004). As memory disturbances play a key role in AD (and MCI), it is of interest to explore the ERD/ERS responses in the 1–20