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Gamma oscillatory activity in relation to memory ability in older adults

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ABSTRACT

Human gamma-band activity (GBA) is widely reported to reflect memory processing. Recent studies suggest that GBA is associated with behavioral performance in memory tasks, but it is not clear whether gamma oscillations are related to individual differences in memory ability. To examine this issue, we recruited participants with low memory ability (mild cognitive impairment, or MCI; n = 16) as well as age-, education-, and sex-matched controls (n = 19) for a study involving a spatial delayed match to sample (DMTS) task. We recorded EEG during task performance and analyzed gamma oscillation changes during the memory maintenance phase of the task. Gamma event-related desynchronization was stronger in the control group than in the MCI group in the mid-frontal area, and mean GBA in this area correlated with clinical memory measures as well as behavioral performance on the DMTS task. These findings suggest that gamma oscillations not only reflect brain activity related to memory processes, but also vary with the memory ability of individuals.

1. Introduction

1.1. Gamma band activity and memory

Oscillatory neural activity in the gamma frequency range (>30 Hz) is involved in numerous cognitive functions, including visual object processing (Gruber and Muller, 2005; Keil et al., 1999), attention (Gruber et al., 1999; Herrmann et al., 1999), and memory (for a review see Nyhus and Curran, 2010). Gamma-band activity (GBA) relates to short-term memory, specifically, as indicated by within-subject studies on the relationship between gamma oscillation and memory performance on two tasks, one requiring cognitive effort and the other not (Herrmann et al., 2004; Nyhus and Curran, 2010; Tallon-Baudry et al., 1998).

Recently, several studies demonstrated that GBA is strongly associated with behavioral performance (reaction time and accuracy) in memory tasks. For example, differential activation of stimulus-specific GBA components to preferred vs. non-preferred stimuli correlates positively with the rate of correct responding (Kaiser et al., 2008b), and a specific gamma band component is enhanced in good performers relative to bad performers (Kaiser et al., 2008a). GBA in the encoding phase of memory tasks is associated with long-term memory retrieval (Gruber et al., 2004; Osipova et al., 2006), and GBA is stronger in participants exhibiting superior recognition memory performance (Busch et al., 2008).

Contemporary researchers are encouraged to correlate EEG and cognitive (Basar and Guntekin, 2007), to facilitate interpretation and improve comparability of their findings. As this literature grows, it may become possible in the future to use EEG to identify cognitive deficits in patients and perhaps even to use EEG findings as a biomarker for certain diseases. However, there is as yet little evidence for an association between gamma oscillatory activity and individual memory ability. Most previous studies subdivided participants into good and bad memory task performers, precluding correlation of GBA with individuals' memory ability. Recently, Lenz et al. (2008) found that evoked gamma activity during stimulus encoding correlates with subsequent recognition performance in a group of healthy children (Lenz et al., 2008). We reported that theta-phase gamma-power coupling correlates with individuals' memory ability in a short-term memory test in elderly participants, consistent with the possibility of an association (Park et al., 2011). Hence, GBA could be an indicator of memory ability. Memory ability declines with age and memory deficits are regarded as an initial symptom of dementia, one of the most prevalent cognitive disorders in older people (Petersen et al., 2001). It is meaningful to determine whether memory-related GBA correlates with memory ability in individuals, as this activity could be a biomarker of memory impairment in older people.

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Stimulus presentation evokes different types of gamma oscillatory activity. There is an early, evoked gamma response that is phase-locked to stimulus onset and occurs within 150 ms of stimulus onset. This response seems to reflect matching of bottom-up signals with memory content at a perceptual processing level. There is also late, induced gamma activity that is not phase-locked to stimulus onset and which appears later than the early evoked response (Herrmann et al., 2004; Tallon-Baudry and Bertrand, 1999). This response might be a signature of utilization processes such as response selection or context updating (Herrmann et al., 2004; Tallon-Baudry and Bertrand, 1999) reported that induced GBA is increased at around 40 Hz during a short-term memory task and is prolonged during the maintenance phase of short-term memory, suggesting that induced GBA is related to actively holding an object representation in short-term memory (Tallon-Baudry and Bertrand, 1999). Because it is believed that neural activity is relatively constant during the maintenance phase of short-term memory, most studies analyze EEG parameters by computing average values across this phase. Beta band synchronization is decreased during the maintenance phase of working memory (Stam et al., 2002), and this decrease is more prominent in patients with Alzheimer's disease (Pijnenburg et al., 2004). In light of these findings, analysis of induced GBA during the maintenance phase of short-term memory could add to our understanding of the relationship between GBA and memory ability. In this study, we analyzed induced (phase-unlocked) GBA during the maintenance phase of a short-term memory task.

1.2. Aims of the study

We tested the relationship between induced GBA and individual differences in memory ability by comparing older adult participants with low memory ability (mild cognitive impairments, or MCI) with age-, education-, and sex-matched controls on a spatial delayed match to sample (DMTS) task with simultaneous EEG recording. We hypothesized that memory ability is associated with altered gamma oscillations. Hence, we examined correlations between GBA and clinical memory measures and between GBA and behavioral performance on the DMTS task. We were particularly interested in differences between the MCI group (MCIs) and controls in the gamma oscillatory changes during the memory maintenance phase of the DMTS task.

2. Materials and methods

2.1. Participants

The participants in this study comprised 16 MCIs (seven males, nine females; 66.63 ± 4.88 [mean ± SD] years of age; 7.94 ± 3.92 years of education) and 19 age- sex-, and educational level-matched controls (nine males, 10 females; 67.05 ± 4.92 years of age; 8.79 ± 4.13 years of education) who were enrolled in a program for the early detection and management of dementia at Gongju-National Hospital. The criteria for MCI were as follows: memory complaint, preferably corroborated by an informant; objective memory impairment for age and level of education (see below); normal general cognition; preserved activities of daily living; and lack of dementia (Doppelmayr et al., 1998). We were particularly interested in amnestic MCIs with multiple memory domain impairments. The MCIs exhibited objective impairment (at least 1.5 standard deviations below the age- and educational level-adjusted mean) in at least one memory domain and/or other cognitive domain (i.e., language, visuo-spatial function, and frontal lobe function).

We assessed the controls and MCIs using neuropsychological instruments developed by the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) (Lee et al., 2002; Mao et al., 1999). The CERAD instruments are standardized clinical and neuropsychological assessment batteries for the evaluation of patients with Alzheimer's disease (Morris et al., 1989), but the CERAD assessment packet can facilitate the standardized evaluation of dementia and mild cognitive disorders in many clinical and research settings, including cross-cultural investigations (Heyman and Fillenbaum, 1997). We used the CERAD-K, a Korean language translation and standardization of these instruments (Lee et al., 2002).

The exclusion criteria for both groups were as follows: significant hearing or visual impairment that made participation in the interview difficult; history of neurological disorder (e.g. stroke, Parkinson's disease, or active epilepsy); psychiatric illness (e.g. schizophrenia, mental retardation, severe depression, or mania); use of psychotropic medication; current or previous uncontrolled or complicated systemic disease (including diabetes mellitus); and history of significant abuse of alcohol or other substances.

This study was conducted in compliance with the ethical guidelines of the Institutional Review Board of Gongju National Hospital and the Declaration of Helsinki (Rickham, 1964).

2.2. Memory tests

We used two clinical memory measures to assess memory impairment: a letter–number sequencing test and a spatial span test. In the letter–number sequencing test, each trial involves a different combination of numbers and letters. The letters consist of seven syllables signifying days of the week in Korean. The participants are asked to repeat them, saying the numbers first in ascending order and then the letters in the order of Monday to Sunday (Gold et al., 1997; Wechsler, 1997). In the spatial span test, there is a board featuring 10 cubes with numbers printed on the sides oriented towards the examiner. The examiner taps the cubes in a specified sequence and then asks the participant to tap them in either the same sequence (spatial span forward) or in reverse order (spatial span backward). A total score is generated based on the sum of the forward and backward scores (Song and Chey, 2006; Wechsler, 1997). We also used the following subscales of the CERAD-K: verbal fluency, modified Boston naming, Mini-Mental State Examination (MMSE), word list memory, constructional praxis, word list recall, word list recognition, and constructional recall (Lee et al., 2002).

2.3. Short-term memory task with simultaneous EEG recording

To assess short-term memory, we used a DMTS task (Fig. 1). At the beginning of each trial, a small red cross was presented at the center of a computer screen to achieve eye fixation. During the encoding period, three black circles (6.8° × 6.8° maximum visual angle; distance from monitor = 100 cm) located randomly among 16 points (a 4 × 4 matrix) were presented for 2000 ms. Following a 3000-ms delay period, a probe (one black circle) was presented for 3000 ms. As a test of memory maintenance, participants judged whether the black circle was in the same location as one of the three black circles presented earlier. Participants were asked to respond as quickly and accurately as possible by pressing one of two buttons (one by the right and the other by the left index finger) signifying “yes” or “no.” Assignment of right and left sides to “yes” and “no” responses was counterbalanced across participants. Feedback on correct/incorrect responses and accuracy rates was presented at the end of each trial for 1500 ms. The next trial then began after an inter-trial interval of 2000–3000 ms. There were two blocks of 80 trials each (160 trials in total), half of which were matches and half were non-matches. Accuracy and reaction time were the behavioral performance measures that we compared to gamma oscillations.

2.4. EEG measurement and data preprocessing

During the DMTS task, we took EEG measurements from the scalp using a NeuroScan SynAmps2 amplifier and 64 Ag–AgCl electrodes mounted in a Quik-Cap using a modified 10–20 placement scheme