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Decrease of delta oscillatory responses is associated with increased age in healthy elderly

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ABSTRACT

Background: The purpose of this study was to investigate changes in delta event-related oscillations (EROs) in younger and older healthy elderly subjects. We hypothesized that delta EROs were affected by age-related changes, which could be reflected in a visual oddball paradigm.
Method: The study included two groups of subjects, 17 younger healthy elderly (mean age: 63.1 ± 2.8 years) and 17 gender- and education-matched older healthy elderly (mean age: 79.6 ± 5.2 years), who performed a visual oddball paradigm. EEG was recorded from F_3, F_z, F_4, C_3, C_z, C_4, P_3, P_z, P_4, O_1, O_z and O_2 locations. Peak-to-peak amplitude of delta (0.5–3 Hz) target ERO responses during the post-stimulus 0–800 ms time window was measured. Repeated measures of ANOVA was used to analyze four locations (frontal, central, parietal, occipital), at three sagittal (left, midline, right) sites. Independent *t*-tests were applied for post-hoc analyses.
Results: The older healthy elderly group had 16–25% lower values for the maximum peak-to-peak amplitudes of delta ERO compared with the younger healthy elderly group over frontal ($p < 0.003$), central ($p < 0.0001$) and parietal ($p < 0.007$) locations [$F_{3,96} = 4.396$, $p = 0.015$]. Furthermore, there was a moderate negative correlation between age and C_z peak-to-peak amplitude of target delta responses [$r = -0.401$, $p < 0.02$], indicating the notion that peak-to-peak amplitude of C_z decreases as age increases.
Conclusion: In the present study younger healthy elderly showed significantly higher event-related delta responses than older healthy elderly at frontal, central and parietal locations. Moreover, delta ERO responses decreased in accordance with age.

1. Introduction

The present study was undertaken to assess the effect of aging on visual event-related delta oscillations in younger and older healthy elderly subjects. EEG and event-related potentials (ERPs) undergo substantial change during aging.

It is generally accepted that spontaneous EEG delta oscillations is not the same wave with event related delta oscillations (EROs) (Başar et al., 1999; Knyazev, 2012; Schurmann et al., 2001). Many studies have shown that delta and theta event-related oscillations (EROs) are the primary contributors to the P300 ERP component (Başar-Eroglu et al., 1992; Bernat et al., 2007; Demiralp et al., 2001; Ishii et al., 2009; Jones et al., 2006; Karakaş et al., 2000; Schurmann et al., 2001; Stampfer and Başar, 1985), which is an event-related response to stimuli that are unexpected, rare, or motivationally salient.

Delta oscillations have been related to motivational processes associated with reward mechanisms (Knyazev, 2012), cognitive processes related to attention allocation, working memory and the detection of rare stimuli (Başar et al., 2001; Harmony et al., 1996; Lakatos et al., 2008; Polich and Kok, 1995; Schroeder and Lakatos, 2009; Will and Berg, 2007), and behavioral inhibition (Knyazev, 2007; Putman, 2011). Increased power in the delta band during mental calculation has been shown by many researchers (Fernández et al., 1995; Harmony, 2013; Harmony et al., 1996) and has been related to internal concentration. Several investigators have reported that inhibition strength declines during adult aging, and reduced inhibitory strength has been related to impaired selective attention and increased distractibility, which are common complaints of the elderly (Dempster, 1992; Dustman et al., 1996; Hasher and Zacks, 1988; Hasher et al., 1991; Kinsbourne, 1980; McDowd and Oseas-Kreger, 1991).

Influences of age on ERPs have been described as decreased amplitude and prolonged latency of P300 (Goodin et al., 1978; Polich, 1991)

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and N200 (Bertoli and Probst, 2005; Pfefferbaum et al., 1980) by many researchers. In aging studies, it has been shown that brain electrical activity from multiple recording sites becomes more homogeneous (Dustman et al., 1996), a dedifferentiation occurs between target and standard stimuli (Mott et al., 2014), and the distribution of P300 changes into a more equipotential manner across the midline in older as compared to young adults (Dustman et al., 1990; Goodin et al., 1978; Pfefferbaum et al., 1984).

One of the common parameters seen in ERO studies in different pathologies is the decrease in delta activity upon cognitive load (Başar and Güntekin, 2013). Previous studies related to brain pathological states indicate that the amplitude of event-related delta oscillations decreases in Alzheimer's disease (Yener et al., 2008), mild cognitive impairment (Kurt et al., 2014; Yener et al., 2013), schizophrenia (Ergen et al., 2008; Ford et al., 2008), bipolar disorder (Atagün et al., 2014) and alcoholism (Kamarajan et al., 2004). However, there are few studies in the literature investigating delta ERO in healthy elderly (Schmiedt-Fehr and Başar-Eroglu, 2011; Schmiedt-Fehr et al., 2011). In order to examine the effect of aging on event-related delta oscillations, we compared two healthy elderly subgroups—younger and older healthy elderly. This investigation will shed a light on previous studies as well as any further research related to the neurophysiology of aging or age-related neurodegenerative diseases. From this point of view, we hypothesized that older healthy elderly would show decreased amplitude of event-related delta oscillations.

2. Methods

2.1. Subjects

This was an open prospective study in healthy elderly controls. Out of a total of sixty healthy elderly subjects, we examined 17 subjects over 75 years of age (mean age: 79.6 years, age range of 75–91 years), here named as older healthy elderly, and a younger healthy elderly group consisting of 17 individuals who were matched for gender, cognitive scores and education (mean age: 63.1, age range of 59–68 years). The age limit of 75 for older healthy elderly was chosen arbitrarily. Mean education level was 10.0 years in the younger group and 11.4 in the older group ($p = 0.39$). There were twelve females in the younger group and eleven in the older group. The groups did not differ in terms of cognitive capacity measured by neuropsychological tests or performance on the given task such as accuracy in counting of the target stimuli.

All subjects underwent complete neurological, neuro-imaging (magnetic resonance imaging) and laboratory examinations, including blood glucose, electrolytes, liver and kidney function tests, full blood count, erythrocyte sedimentation rate, thyroid hormone, vitamin B12, HIV, and VDRL. The neuropsychological assessment, which was performed in order to exclude dementia, included episodic memory (Öktem, 1992), non-verbal memory (Wecshler Visual Reproduction Test), attention (WMS-R Digit Span Test), orientation, executive functions (Stroop Test, Clock Drawing Test, Verbal Fluency Test), language (Boston Naming Test), the Mini-Mental State Examination (MMSE) and Clinical Dementia Rating Scale (CDR). Depressive co-morbidity was excluded on the basis of a geriatric depression scale score higher than 11 (Yesavage et al., 1983).

The groups' characteristics are shown in Table 1. Participants had no history of major neurological, psychiatric, or medical disorders. All had normal or adjusted to normal vision. All participants with regular use of anti-dementia drugs, antidepressants, neuroleptics, anti-epileptic medications, stimulants, opioids and beta-blockers were excluded from the present study. All participants provided written informed consent prior to voluntary participation and the study was approved by the local ethical committee.

The present paper analyzed the event-related target delta oscillatory responses in younger and older healthy elderly controls by two different methods (phase locking and filtered oscillatory responses). We analyzed delta, theta, beta and alpha oscillatory responses of some of these subjects as control groups for our studies on mild cognitive impairment (Güntekin et al., 2013; Kurt et al., 2014; Yener et al., 2013).

2.2. Electrophysiological recording and stimulation

EEG was recorded from F_3, F_z, F_4, C_3, C_z, C_4, P_3, P_z, P_4, O_1, O_z and O_2 locations with 30 Ag/AgCl electrodes mounted in an elastic cap (Easy-cap) according to the international 10–20 system. Additionally, two linked earlobe electrodes (A1 + A2) served as references. The EOG from the medial upper and lateral orbital rim of the right eye was also registered. For the reference electrodes and EOG recordings, Ag/AgCl electrodes were used. All electrode impedances were less than 10 kΩ. The EEG was amplified by means of a Brain Amp 32-channel DC system machine with band limits of 0.01–250 Hz. The EEG was digitized on-line with a sampling rate of 500 Hz.

A classical visual oddball paradigm was used for eliciting event-related oscillations (EROs). Subjects sat in a dimly lit, isolated room during recordings. The classical visual oddball paradigm consisted of 40 deviant stimuli and 80 standard stimuli. A white screen with a luminance of 40 cd/cm^2 for standard signals and 10 cd/cm^2 for deviant stimuli was used. In the paradigm, the deviant stimuli were embedded randomly within a series of standard stimuli. All signals were applied randomly and the inter-stimulus interval varied from 3 to 7 s. Mental counting of the target stimuli was required and all subjects displayed sufficient accuracy.

2.3. Data analysis

All epochs containing artifacts were rejected by a manual off-line technique. The epoch numbers of target visual stimulation condition were equalized randomly between two groups. Subject averages and grand-averages were then calculated for each electrode site.

2.3.1. Digitally filtered event-related delta oscillatory responses

At this stage, the delta frequency range (0.5–3 Hz) was chosen for investigating the age effect on ERO, since marked differences were observed in delta range in previous studies of our group (Başar et al., 2013; Kurt et al., 2014; Yener et al., 2008, 2013). Peak-to-peak amplitude of delta target ERO responses during the post-stimulus 0–800 ms time window of two groups of elderly was measured.

Table 1
The group characteristics of subjects.

	Younger healthy elderly (n = 17)	Older healthy elderly (n = 17)	p
Age (SD)	63.12 (2.76)	79.65 (5.19)	0.000[a]
Education (SD)	10 (4.83)	11.4 (4.69)	0.394[a]
Gender (M/F)	5/12	6/11	0.714[b]
MMSE (SD)	29.3 (0.99)	29.2 (1.09)	0.870[a]

SD: standard deviation, M: male, F: female, MMSE: Mini Mental State Examination.
[a] Independent sample *t*-test.
[b] Chi-square.

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