Prolongation of alpha oscillations in auditory oddball paradigm

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Although an important component of the P300 target response is the “prolonged alpha response”, no relevant analysis is found in the literature. The present study emphasizes the relevance of prolongation of alpha responses in auditory oddball paradigm. Two types of stimuli were applied to twenty subjects. As standard stimuli 80 dB–1500 Hz tones and the target stimuli 80 dB–1600 Hz tones were used. The prolongations of alpha responses were measured in 13 recording sites in the frequency range of 8–13 Hz. At the Cz recording site, the time period for reaching one third (duration of prolongation) of its peak-to-peak amplitude (1/3 latency) of alpha response to target was 446 ms. The prolongation of non-target stimuli was 277 ms. Thus, the alpha response to target was significantly more prolonged than the alpha response to non-target stimuli.

Similarly, at C3, the alpha response to target stimuli was prolonged to 373 ms. The alpha response to non-target stimuli was prolonged to 284 ms. The target alpha response was more prolonged in comparison to the non-target alpha results. The alpha response to target stimuli (431 ms) was also more prolonged in comparison with the alpha response upon non-target stimuli (266 ms) at the C4 recording site.

The results indicate that the alpha responses are prolonged under a certain level of cognitive load and working memory. Alpha prolongation is a significant component of P300 responses. It can be suggested that the cognitive load dependency of alpha responses upon the targets could be related to working memory.

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1. Introduction

The analyses of the electroencephalogram (EEG), event-related potentials (ERPs), and event-related oscillations (EROs) are among the fundamental research tools for understanding sensory and cognitive functions of the brain. The P300 event-related brain potential (ERP) is often obtained with a simple discrimination task in which two different stimuli are randomly presented with one occurring less frequently than the other, the oddball paradigm (Polich, 2003; Polich and Criado, 2006). This paradigm also belongs to the ensemble of important tools in electrophysiology which are used for measuring "working memory".

The dynamics of alpha processes (spontaneous, evoked, induced, and emitted) in relation to memory, movement and sensation provide an outstanding prototype to uncover the universal ‘building blocks’ in the integrated CNS functions. These interrelated, parallel or cognitive processes demonstrate the significant role of the dynamic approach to the understanding of integrative brain functions (Schürmann and Başar, 2001).

There are many recent publications related to the relation between alpha oscillations and attentional processes (Babiloni et al., 2004a,b,c; Dockree et al., 2004; Sauseng et al., 2005a; Klimesch et al., 1998; Irak and Karakaş, 2000) and fMRI (Laufs et al., 2003) studies. The oscillatory responses exhibit differentiations between the modality, stimulus properties, and topology. In the present study, the subjects were required to recognize the target stimuli that are different from the standard (non-target) signals and count them mentally. Even for the simplest conditions of stimuli, which were applied in this study, the cognitive components such as sensory register, working memory, attention, perception, and learning are integrated in overall processing.

A bunch of functions have been assigned to alpha oscillations such as mental imagery, internal attention (Cooper et al., 2003, 2006; Ray and Cole, 1985a,b), inhibitory control of motor programmes (Pfurtscheller and Andrew, 1999; Pfurtscheller et al., 2000), primary sensory perception (Başar, 1998), sensory memory (Başar, 1999, 2004; Dinse et al., 1997; Silva et al., 1991), and cognitive tasks (Başar 2004, Başar et al., 2007; Klimesch, 1996; Goldman-Rakic, 1996; Sauseng et al., 2005b). These results indicate a selective differentiation of alpha responses upon simplest stimuli and cognitive loads. Similarly, there have been publications with regard to changes in the EEG alpha rhythm in response to manipulations of tasks and load discrimination between subjects, applied to groups of subjects with differing skills, age, gender and cognitive function or dysfunction (for example; Başar 2004; Babiloni et al., 2004a; Bucci et al., 2004; Gevins and Smith, 2004;
2000; Doppelmayr et al., 2005; Ramos-Loyo et al., 2004; Stam et al., 2005; Neubauer et al., 2005; Knyazev et al., 2006; Knyazev, 2007; Güntekin and Başar, 2007a,b).

As to the “memory” studies in humans; strong relationships between alpha oscillation activity and memory have repeatedly been demonstrated (Başar, 1999, 2004; Başar et al., 1997a,b,c, 2007; Klimesch, 1996, 1997, 1999; Klimesch et al., 1994,1997, 1999, 2007; Babiloni et al., 2004b; Razumikhina, 2007).

The prolongation of theta and alpha oscillatory responses was first recorded by Başar and Stampfer (1985). However, a methodical account of the “prolonged alpha” has not yet been systematically analyzed by using adequate number of subjects and suitable statistics. Although studies on brain oscillations have been extremely useful in functional analysis of CNS, the manifestation of the prolongation is almost unknown. In order to fill this gap the present study focuses on alpha oscillations in the target responses of P300 subjects and discusses the results jointly with the delayed delta and theta oscillations.

2. Materials and methods

2.1. Subjects

The measurements were performed with twenty subjects (age: 19–27; mean: 22.6; 13 female). Preceding the measurements, basic personal data (name, age, handedness, neurological and psychiatric aspects of the family and individual’s medical history) was acquired during a standardized interview. All subjects had normal hearing and were right-handed. The subjects did not report any neurological and psychiatric deficiencies. They were seated in a sound-proof, dimly illuminated, echo-free room and were instructed to minimize blinking and eye movements.

2.2. Experimental strategy

In the auditory oddball paradigm two types of stimuli were applied. As standard stimuli 80 dB–1500 Hz tones were used and the target stimuli were 80 dB–1600 Hz tones. For electrophysiological recordings an EEG-CAP was used. The EEG was digitized on-line with Nihon Kohden EEG-4421 G apparatus with band limits of 0.1–24 Hz. Filtered according to determined frequency bands in 8–13 Hz.

2.2.1. Data recording set

In auditory oddball experiments, the target and non-target stimuli were applied pseudo-randomly. Total of 120 stimuli were applied with approximately 25% as target signals (31–32/120). The inter-stimulus intervals were randomly set to 3.5–6.5 s (Fig. 1). Auditory stimuli consisted of 1500 Hz non-target tones, for which subjects were asked to ignore, and 1600 Hz target tones, which were asked to be counted. In other words, the task was for the subjects to count the target stimuli mentally. The experimental setup did not have any motor responses (as push buttons).

2.2.2. Electrophysiological recording

According to the 10–20 system (Jasper, 1958), the electroencephalogram (EEG) was recorded from Fz, F4, Cz, C4, T3, T4, T5, T6, P3, P4, O1, and O2 locations. For the reference and EEG recordings Ag/AgCl electrodes were used. Linked earlobe electrodes (A1+2A) served as reference. The EEG was amplified by means of a Nihon Kohden EEG–4421 G apparatus with band limits of 0.1–100 Hz 24 dB/octave.

2.3. Data analysis

The epochs that contained artifacts were rejected by an offline technique, before the averaging procedure. In the off-line procedure, single sweep EOG recordings were visually studied and trials with eye-movement or blink artifacts were rejected. Subject averages and grand averages were calculated for each electrode site. The peak-to-peak maximum amplitudes of alpha (8–13 Hz) responses to stimuli were measured in the 0–500 ms time window following stimulation and the prolongation analysis was conducted in the time window 0–1000 ms. An analysis to evaluate the prolongations of the alpha responses was performed and the peak-to-peak (pp) maximum amplitude’s latency (lat) was measured. In order to assess the duration and the damping of these responses, the time periods for reaching a third (1/3 lat) of the maximum pp amplitudes of the responses was measured. This measure revealed the temporal characteristics of the oscillations, as the onset, duration, and damping of these responses. The same procedures were repeated for both stimuli and 13 locations.

2.3.1. Computation of selectively averaged Event Related Potentials (ERP)

The data was digitally filtered according to determined frequency bands of interest. According to new approaches, the EEG consists of the activity of an ensemble of generators producing rhythmic activity in several frequency ranges. These oscillators are active usually in a random way. However, by the application of sensory stimulation these generators are coupled and act together in a coherent way. This synchronization and enhancement of EEG activity gives rise to “evoked” or “induced rhythms”. Evoked potentials representing ensembles of neural population responses were considered to be a result of transition from a disordered to an ordered state. The compound ERP manifests a superposition of evoked oscillations in EEG frequencies ranging from delta to gamma (“natural frequencies of the brain” such as alpha: 8–13 Hz, theta: 3.5–7 Hz, delta: 0.5–3.5 Hz and gamma: 30–70 Hz) (Yordanova and Kolev, 1998).

2.3.2. Digital filtering

Filtering produces visual displays of the time courses of the oscillatory components within the frequency limits of the utilized filters. Digital filters are advantageous because they do not produce the phase shifts that are a characteristic of electronic filters. The digital filtering was employed in the present study for the digital pass-band filtering of the event related potentials (ERPs) and thus, to demonstrate the event-related oscillations (EROs) in selected frequency-bands (for a detailed explanation of the AFC method see Başar et al., 2001; Karakaş et al., 2000a,b).

2.3.3. Statistical analysis

An SPSS software package was used for statistical analysis. For the auditory target responses, repeated measures ANOVA analysis was applied in order to assess the differentiations between target and non-target responses in the time domain, including the between subjects factor condition (target, non-target) and the within subject factor location (F3, F4, C2, C4, P3, P4, T3, T4, T5, T6, O1, O2). Greenhouse–Geisser corrected ‘p’ values were used. Post-hoc analysis was conducted using the paired samples t test.

3. Results

In Fig. 2 alpha responses as grand average of 20 subjects in 13 distributed scalp locations are illustrated as responses to the target and the non-target stimuli in the alpha frequency windows (8–13 Hz). At first glance, a prolongation of oscillation was observed in most of the locations. In parietal locations a slight increase of the alpha amplitudes was also recorded.
According to Fig. 2, an important feature of the results is the significant differentiation in the prolongation of alpha responses along the time axis. Fig. 3 shows more detailed information for the responses to target stimuli in comparison to standard stimuli at three locations that showed significant results. The duration of the response envelopes indicate prolonged alpha oscillation. This was measured with an approximation calculated by the decay of this envelope into its 1/3 value of pp-max as seen in Fig. 3 (see Özgören et al., 2005).

The repeated measures ANOVA on alpha responses revealed a significant effect for condition \( (F(1,21)=8.45, p<0.01) \) indicating a more prolonged alpha response to target stimulation in comparison with the non-target stimulations. Post-hoc analysis was conducted using the paired samples \( t \) test.

At the Cz recording site, the time period for reaching one third (duration of prolongation) of its pp amplitude (1/3 lat) of alpha response to target was 446 ms. The prolongation of non-target stimuli was 277 ms. Thus, the alpha response to target was significantly more prolonged than the alpha response to non-target stimuli \( (t=3.69, p<0.001) \).

Similarly, at C3, the alpha response to target stimuli was prolonged to 373 ms. The alpha response to non-target stimuli was prolonged to 284 ms. The target alpha response was more prolonged in comparison to the non-target alpha results \( (t=2.32, p<0.05) \).

The prolongation of the alpha response to target stimuli (431 ms) was also more prolonged in comparison with the alpha response upon non-target stimuli (266 ms) at C4 recording site \( (t=3.74, p<0.001) \).

The significant differences are also shown in the histogram in Fig. 4.

The target responses show more prolonged alpha responses in comparison to non-target response in frontal and parietal areas (see Fig. 2). However, these recording sites did not show statistical significant changes.

4. Discussion

Recording event related oscillations could be a good method of approaching the problem both from the neurophysiological and psychological levels since brain oscillations have similar frequency codes in over the whole brain ( Başar, 1999; Başar et al., 2000; Varela et al., 2001; Stein et al., 1993). Furthermore, cognitive inputs evoke in the brain oscillatory responses similar to sensory oscillatory responses both in the same frequency channels of EEG; presenting not only different topological distributions but also the prolongation (Başar, 2004).
4.1. Delay and prolongation of oscillations during working memory processes

The prolongation of the theta responses and delay of the delta response was first described by Stampfer and Bașar (1985, 1988), Bașar and Stampfer (1985). Bașar-Eroğlu et al. (1992), Karakaş and Bașar (1998) gave a detailed account of delta delay and prolongation of oscillations to target stimuli during the oddball paradigm. Later, Bașar-Eroğlu et al. (2000) showed prolonged gamma oscillations during working memory processes. The present study describes the prolongation of alpha oscillations in responses to target stimuli of a P300 response as a first time by using a large number of subjects, systematic analysis and suitable statistics. In the processing of complex functions, a great number of oscillatory networks are involved, the brain works longer and possibly during complex signal processing, delay or prolongation of the oscillatory activities is observed and it is clear that “prolongation” of oscillation can be considered to be an important parameter in dynamic cognitive processing. The difficulty of recognizing a target in the oddball paradigm is manifested by delays and prolongations in different frequency windows (Bașar, 2004).

4.2. The working memory contribution in the P300 potentials

Working memory is essential for the detection of a target signal during a P300 type of experiment as several reports strongly confirmed (Baddeley, 1992; Collette et al., 1999; Cowan, 1999; Klimsch, 1999; Miller et al., 2002). During the experiment the subject has to confirm the information concerning the target (for example, nature of the target, shape, color and frequency, depending on the type of the experiment). According to reports of authors mentioned above; working memory is a system of higher cognitive functions such as reasoning, planning, and problem solving and that it is modulated by (pre-) frontal brain activations.

The theoretical and empirical investigations have provided evidence that both mnemonic processes (such as storage and rehearsal) and non-mnemonic processes (such as strategy selection, error monitoring, updating, inhibition, attention shifting) are mediated by the prefrontal and medial frontal cortex (Frith and Dolan, 1996; Passingham and Sakai, 2004; Walton et al., 2004, Schmiedt et al., 2005). Further, the link between P300 amplitude and latency measures, and working memory processes has been already established (Sanquist et al., 1980; Howard and Polich, 1985; Pratt et al., 1989; Fabiani et al., 1990; Scheffers and Johnson, 1994). The matching processes after the detection of the target should depend, in this case, on working memory or the success of this type of memory, P300 versus N100 (Bașar, 2004).

Fig. 3. The central evoked potentials and alpha (8–13 Hz) oscillatory responses (I) The evoked responses recorded from the central electrodes (C3, Cz, and C4, respectively). The vertical axes are amplitudes in μV and the x axis shows the time scale in milliseconds. The upper wave forms (gray color) represent the non-target and the lower waves (black) represent the target responses. (II) The prolongation of alpha responses at central electrodes, A left central, B central and C right central electrodes as a grand average of 20 subjects. The envelopes of the waveforms guide the measurement of the time frame (respecting prolongation times: P1 and P2) which is required to achieve the one-third of the maximum peak-to-peak values. Lower plots (dark) indicate the target and upper plots (gray) of the panels indicate the non-target alpha responses.

Fig. 4. Significant differences between the prolongation of alpha responses to target stimuli and non-target stimuli at three electrode sites (C3, Cz, C4) for alpha oscillations (means of 20 subjects results). The prolongation time to target stimuli are represented by black bars and to non-target by gray bars.
The subjects differentiate the target signals from the non-target signals and count them mentally; therefore, they have to pay more attention to the target signals. The processes of for example, remembering, matching, counting need more time. It has been demonstrated that the oscillatory activities, in alpha, gamma, theta, and delta do reflect “work of the brain” In cases of novelty or doubt the brain works with “delays or prolonged behavior” requiring more time to work longer (Başar, 2004).

Several publications indicate that working memory is processed in (pre-) frontal and parietal locations (Baddeley, 1992; Frith and Dolan, 1996; Collette et al., 1999; Cowan, 1999; Klimesch, 1999; Miller et al., 2002; Passingham and Sakai, 2004; Walton et al., 2004; Schmiedt et al., 2005; Başar-Eroğlu et al., 2007; Mathes et al., 2006). However, by analyzing event related oscillations in order to describe functional correlates and their links to various locations an essential advantage of this concept is emerging: In a number of cases in compound evoked potentials often an oscillatory component is obscured by other components. In the case of a P300 complex potential the theta and delta components have much larger amplitudes and make it difficult to detect alpha changes in central locations. However, if we confine our attention to new results of the alpha oscillatory response it is clear that during this working memory process central locations are also contributing to the working memory process. This type of refinement manifests the most important advantage of the oscillatory analysis. Accordingly, one of the most important messages from the present study is to show that central locations are also involved in the working memory process.

In the literature there are few publications on prolongation of oscillations (Table 1). Cognitive targets significantly influence the alpha responses in P300, using an oddball paradigm, prolonged event-related alpha oscillations up to 400 ms were observed (Başar, 1998, 1999). EEG rhythmicities showed event-related prolongations, in experiments with certain cognitive tasks (Başar-Eroğlu et al., 1992; Stamper and Başar, 1985; Başar, 1999).

In the target response, the number of generators giving rise to oscillatory responses was not increased. The prolongations might be therefore due to (i) later activated secondary generators or due (ii) to reverberation effects between association networks.

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### 4.3. Prolongation in complex functional processing

In face recognition experiments, the prolongation of beta responses was shown by Özgören et al. (2005). According to their results the largest prolongation of familiar face stimuli is in the central areas followed by the frontal areas. In the present study, the alpha prolongation to target stimuli was recorded in central sites. Başar-Eroğlu and her group submitted a series of publications which were based on the differentiation of oscillatory responses related to working memory load. The authors compared healthy subjects with schizophrenic patients (Başar-Eroğlu et al., 2007; Schmiedt et al., 2005). Schmiedt et al. (2005) emphasized the differences in late theta windows under working memory and matching processes task. Late theta responses have distinguished the healthy and patient groups. Başar-Eroğlu et al. (2007) pointed out that gamma prolongation exists in same experimental group. The prolongation of gamma oscillation disappeared in schizophrenic patients during an arduous working memory task. For these reasons, the late oscillatory responses are not only important as an indicator for cognitive processes but also these indicators can be used as important tools in diagnosing clinical disorders, have been proved with schizophrenic patients. Thus, alpha prolongation activity can be possibly useful for clinical studies.

### 4.4. Working memory and the Attention, Perception, Learning and Remembering (APLR) Alliance

According to Baddeley (1996), working memory provides a crucial interface between perception, attention, memory and action. During experiments involving learning and working memory processing EEG oscillations manifest continuously evolving dynamics. Empirical results lead to a model of the “hierarchy of memories as a continuum” and a brain theory covering the concerted action of function and memory in the “whole brain”.

Hayek (1952) presents his concept of cortical memory network in the context of the main topic, which is not memory itself, but, significantly, perception, as the source of memory and as the product of memory. Fuster (1995) offered an interesting memory model related to this concept. Neural memory is special in several ways; including its capacity not only to retain information but also to utilize it for adaptive purposes. In this sense neural memory becomes conatural with learning, from which it is operationally difficult to distinguish, although the terms learning usually refer to the process of acquiring memory (Fuster, 1995).

The concept of the APLR-Alliance was introduced as a consequence of the measurements. It is not a theoretical construct, but it is derived from the empirical evidence (Başar, 2004).

According to Goldman-Rakic (1996) working memory is the ability to hold an item of information transiently in the mind in the service of comprehension, thinking and planning. Working memory encompasses both storage and processing functions. It serves as a workspace for holding items of information in the mind as they are recalled, manipulated, and/or associated with other ideas and incoming information. When the whole brain is involved in the remembering process, or in dynamic reciprocal acting of APLR-Alliance, the reverberation of signals between brain structures upon sensory stimulation is most probable. Therefore, it is expected that the process of matching takes longer. There are probably cross-talks or reverberations between different structures.

### 5. Conclusion

The analysis of the alpha responses in this study can be concluded as follows;

1) During the oscillatory alpha activation of target and non-target stimuli, the topological distribution of alpha responses is
significantly differentiated by showing “varying degrees of amplitude enhancements and prolongations”. During oddball experiments by applying simple stimuli, which also involve memory processes, a parallel processing in the alpha frequency range takes place. It can be suggested that the cognitive load dependency of alpha responses of the targets can be related to working memory.

2) The whole brain manifests alpha responses that are time-locked to stimuli.

3) The alpha responses are prolonged only on a certain level of cognitive load and working memory (target condition).

4) Even in the presence of the simplest stimuli, there are selectively distributed alpha oscillatory responses.

Alpha prolongation is an important component of P300 responses.

6) Alpha prolongation measurements can be used to understand pathological processes as well as theta and gamma oscillations.

This study clearly showed that in the oddball paradigm, central locations contribute to the working memory process such as frontal and parietal locations.

The above mentioned results should be combined with other frequency analyses, which in turn can be applied to studies in sensory and cognitive prospects of EEG.

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