Orbital-Thalamic Network for the Regulation of Cortical Synchronization

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Abstract

We investigated the contribution of orbital frontal cortex to cortical synchronization in the alpha band. Orbito-frontal cortex differentially affects the synchronicity of alpha EEG activity in response to visual stimuli over frontal areas. Control subjects and patients with orbital frontal damage detected infrequent target-triangles which were preceded by novel stimuli. Increases in evoked (phase-locked) alpha and decreases in induced (non phase-locked) alpha power were observed in normals in response to detected targets. Evoked alpha activity over lateral frontal cortex was significantly higher in patients than in age-matched controls. The decrease of induced alpha in response to stimuli was suppressed for patients. These findings indicate a higher degree of cortical synchronicity subsequent to orbital frontal cortex damage. These findings support the previously formulated hypothesis that frontal cortex regulates the thalamic driving of cortical alpha activity in the human EEG. A neuroanatomical model for orbital-thalamic EEG synchronization is proposed.

Introduction

When a primary cortical area receives no or little input from its thalamic gate, it in turn oscillates predominantly in the alpha frequency range at relatively high amplitude which is considered to reflect cortical idling (Pfurtscheller, 1996). It has therefore been proposed that this type of alpha activity in the human EEG reflects cross-modality shifts of attention (Pfurtscheller, 1996). If, on the other hand, the inhibition to a thalamic gate is turned off, the input is put through and the alpha oscillations of the respective primary cortical area are suppressed in amplitude while their phase is reset. This leads to an increase of evoked (phase-locked) alpha activity and a simultaneous decrease of induced (non phase-locked) alpha activity (Klimesch, 2000). While the decrease of induced alpha after visual stimulation is most prominent over occipital cortex (Basar, 1997) the increase of evoked alpha is strongest over frontal cortex (Kolev, 2001). This frontal increase of evoked alpha has been associated with cognitive function during task processing and has been shown to be enhanced in elderly subjects (Yordanova et al., 1998). Since the frontal cortex is most sensitive to aging, it has been argued that frontal cortex is also responsible for this enhancement of frontal alpha in elderly subjects (Yordanova et al., 1998).

In order to test this hypothesis, we investigated the electroencephalogram of 5 patients with orbito-frontal brain lesions and 10 age-matched healthy control subjects. All subjects had to perform a visual target detection taks. We presented novel stimuli followed by triangles pointing up- or downwards. Subjects had to press a button indicating in which direction the triangle pointed.

Methods

We investigated 5 patients aged from 26 to 65 years (mean 49.4) with orbito-frontal lesions and 10 age-matched healthy control subjects aged from 25 to 75 years (mean 51.9). Each of the subjects gave their consent according to university guidelines. The subjects were seated in a sound-attenuated room 1m in front of a computer screen. Subjects were instructed to fixate on a cross in the middle of the screen.

Subjects discriminated between upright and inverted triangles (target; 150 ms duration). Targets were randomly presented in the left or right visual hemifield. A brief novel picture (150 ms duration) selected from the International Affective Picture System was presented centrally 350 ms prior to the subsequent target. Subjects were instructed to ignore the pictures and respond to the targets as quickly and accurately as possible. On 18% of the trials the targets were not preceded by a picture and on 27% of trials the pictures were not followed by a target. The novel pictures offset was 200 ms prior to the onset of the target. The response hand was counterbalanced.

Brain electrical activity was recorded with Ag-AgCl electrodes placed at 30 scalp sites and referred to left mastoid. Impedances were maintained below 5 kW. The EEG was sampled at 250Hz and digitally stored for off-line analysis. Trials containing blinks, horizontal eye movements or EMG artifacts were automatically rejected from further analysis. To selectively investigate the alpha activity of our EEG recordings, we applied a wavelet analysis with a center frequency of 10 Hz (Herrmann et al., 1999).

Results

Figure 1 shows horizontal brain slices of the 5 patients taken with magnetic resonance tomography (MRT). The degree of overlap is displayed in color. All lesions lie within the orbital part of pre-frontal cortex.

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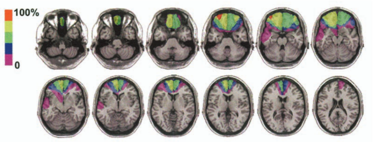

Figure 1: Spatial extent of the brain lesions of 5 patients as degree of overlap.

The event-related potentials comprise prominent peaks in reponse to the novel pictures (cf. Fig. 2). An ANOVA of the evoked alpha activity (cf. Fig. 3A) yielded a significant interaction topography x hemisphere x group (F(1,13)=13.2, p<0.005). Post-hoc tests revealed significant differences between patients and controls in the right anterior region (F(1,13)=4.58, p=0.05) and the left posterior region (F(1,13)=4.45, p=0.05). Amplitudes of the evoked alpha activity are larger in patients (anterior right: 0.72 µV, posterior left: 0.4 µV) than in controls (anterior right: 0.24 µV, posterior left: 0.1 µV). An ANOVA of the induced alpha activity (cf. Fig. 3B) yielded a significant main effect of group (F(1,13)=5.12, p<0.05). Amplitudes of the induced alpha activity were more negative for the controls than for the patients. The topographical distributions of the alpha activity over the scalp in Figure 3 reveal the fronto-central focus of the increase of evoked alpha (cf. Fig. 3 C) and the occipital decrease of induced alpha (cf. Fig. 3 D).

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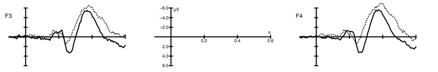

Figure 2: ERPs in response to the visual stimuli. Orbito-frontal patients (dotted) and age-matched healthy control subjects (solid) both show a P250 and N370 component in their ERPs. The differences are not statistically significant.

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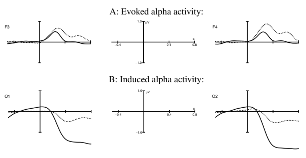

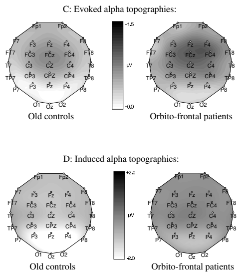

Figure 3: A: The peak of evoked alpha activity in anterior electrodes is enhanced for orbito-frontal patients (dotted) as compared to old controls (solid). B: Induced alpha (absolute alpha power) shows a clear suppression after stimulation which is less prominent for patients (dotted). C: The topographical distribution of the evoked alpha peak (200-300 ms) shows a maximum over fronto-central electrodes (FCZ, FZ, FC4). D: The suppression of induced alpha in response to visual stimuli (400-600 ms) is strongest over occipital electrodes and less prominent in orbito-frontal patients.

Discussion

Our findings report a peak of the evoked alpha activity in response to visual stimulation (synchronization) and a simultaneous suppression of induced alpha activity (suppression of alpha power). The opposite effects of the two measures may at first sound controversial and have been reported as the alpha paradox (Klimesch2000). The potential paradox results from a decrease in alpha power as compared to baseline with a simultaneous synchronization of alpha phase, which is known as phase resetting in response to stimulation (Brandt, 1997). While the amplitude of the alpha oscillations is suppressed after stimulation, the phase resetting leads to a temporary increase only of the evoked response, since phase-locked activity adds up in an average over multiple trials (cf. Fig. 4).

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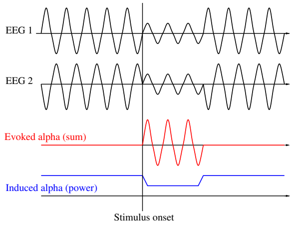

The alpha rhythm of the human EEG is one of the indicators of normal aging (Polich, 1997). Moreover, it has been found recently that evoked frontal alpha oscillations after auditory stimulation are significantly higher in older subjects and it was speculated that frontal cortex is responsible for this synchronization (Yordanova, 1998). We present the first proof for this hypothesis by showing that orbito-frontal brain lesions indeed lead to an even higher degree of alpha synchronicity in frontal brain regions. We found a simultaneous peak of evoked alpha activity and a suppression of induced alpha activity after visual stimulation. The evoked peak was larger and the induced suppression weaker in patients. Both effects are consistent across the whole scalp, but the increse of evoked activity became significant only at right anterior electrodes.

Due to neuro-anatomical and electrophysiological considerations, we believe an orbital-thalamic network to be responsible for this effect. Single cell and PET studies have found the thalamus to be correlated with the generation of cortical alpha EEG (Lindgren, 1999). Even though cortical generators are responsible for oscillatory EEG activity, it has been shown that thalamic nuclei drive the cortical areas to oscillate in the alpha frequency range (Steriade et al., 1990). Oscillatory sleep spindles with alpha frequency can be recorded from cortex and thalamus, but when cortex and thalamus are disconnected, the thalamus still oscillates while the oscillations in the cortex cease (Steriade et al., 1985). It has been argued that, even though sleep spindles and waking alpha activity are not the same, the neural generators are probably identical (Steriade & Dechenes, 1984). Partial correlations of various cortical areas and different thalamic nuclei revealed that, among the many thalamic nuclei, the pulvinar shows the strongest influence on cortical alpha EEG (Lopes da Silva, 1991). Neuroanatomical tracing of cortico-thalamic connections in the macaque monkey revealed that orbito-frontal cortex is strongly interconnected with the pulvinar (Cavada et al., 2000). The pulvinar is connected to the lateral pre-frontal cortex and to occipital and temporal cortical areas (Steriade, 1997). Since it has been previously found that frontal cortex can modulate attention (Knight 1997 & 1999), these findings motivated us to propose the follwing model for a cortical top-down modulation of thalamic alpha generation:

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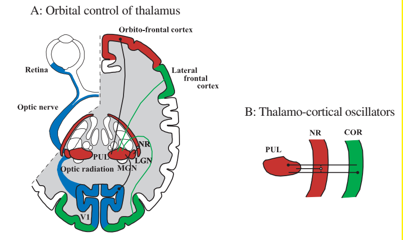

Figure 5: Proposed anatomical model for the orbital-thalamic network regulating synchronization of the human alpha EEG response (a). Main visual pathway (blue), control structures (red) and generators of alpha activity (green). Excitatory neurons have black, inhibitory ones white somata. Cognitive processes in orbito-frontal cortex regulate the pulvinar (PUL) in healthy old subjects to drive the thalamo-cortical alpha oscillator (b, green connections in a). When orbito-frontal cortex is lesioned, occipital cortex regulates the pulvinar in a more automatic fashion, leading to a higher degree of time-locking. The medial and lateral geniculate nuclei (MGN, LGN) serve as relays in the visual and auditory pathway, respectively. Both are inhibited by the nucleus reticularis (NR) which is inhibited by the pulvinar. (Anatomical structures adapted from Nieuwenhuys, 1988.)

Thalamo-cortical feedback loops through the nucleus reticularis (NR), as depicted in Figure 5 B, have been proposed to serve as the driving source for cortical alpha generators (Destexhe et al., 1993). These oscillatory thalamocortical connections are depicted in green in Fig. 5 A. In healthy controls, orbito-frontal cortex controls this feedback loop to generate a short burst of synchronous alpha oscillations in lateral frontal cortex after visual stimulation. The input from frontal cortex represents a cognitive function which inherently operates at a variable time scale and therefore occurrs with slight latency jitter across multiple stimulations. When the orbito-frontal input decreases or is completely lost, automatic mechanisms of primary visual cortex, which operate with the same timing for every stimulation, control the oscillatory mechanism. This leads to an increase in synchronicity from trial to trials and, hence, to the observed increase in evoked alpha activity. Therefore, our model demonstrates a frontal regulation of thalamo-cortical oscillators.

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