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Single-trial coupling of EEG and fMRI reveals the involvement of early anterior cingulate cortex activation in effortful decision making

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While the precise role of the anterior cingulate cortex (ACC) is still being discussed, it has been suggested that ACC activity might reflect the amount of mental effort associated with cognitive processing. So far, not much is known about the temporal dynamics of ACC activity in effort-related decision making or auditory attention, because fMRI is limited concerning its temporal resolution and electroencephalography (EEG) is limited concerning its spatial resolution. Single-trial coupling of EEG and fMRI can be used to predict the BOLD signal specifically related to amplitude variations of electrophysiological components. The striking feature of single-trial coupling is its ability to separate different aspects of the BOLD signal according to their specific relationship to a distinct neural process.

In the present study we investigated 10 healthy subjects with a forced choice reaction task under both low and high effort conditions and a control condition (passive listening) using simultaneous EEG and fMRI. We detected a significant effect of mental effort only for the N1 potential, but not for the P300 potential. In the fMRI analysis, ACC activation was present only in the high effort condition. We used single-trial coupling of EEG and fMRI in order to separate information specific to N1-amplitude variations from the unrelated BOLD response. Under high effort conditions we were able to detect circumscribed BOLD activations specific to the N1 potential in the ACC ($t=4.7$) and the auditory cortex ($t=6.1$). Comparing the N1-specific BOLD activity of the high effort condition versus the control condition we found only activation of the ACC (random effects analysis, corrected for multiple comparisons, $t=4.4$). These findings suggest a role of early ACC activation in effort-related decision making and provide a direct link between the N1 component and its corresponding BOLD signal.

Keywords: ACC; Mental effort; Multi-modal imaging; EEG–fMRI; Simultaneous EEG–fMRI

Introduction

The anterior cingulate cortex (ACC) has attracted much attention during the last few years, since it is supposed to play an important role in cognitive functions like conflict monitoring (Barch et al., 2001; Botvinick et al., 1999; Carter et al., 1998), action-outcome evaluation (Gehring and Willoughby, 2002; Nieuwenhuis et al., 2004) or reward-based action selection (Bush et al., 2002; Hadland et al., 2003). While the precise role of the ACC is still being discussed, it is important to find a way of linking different aspects of ACC function. A promising candidate for such a link is mental effort: it has been suggested that ACC activity might reflect the amount of effort associated with cognitive processing such as conflict monitoring (Botvinick et al., 2004). This would be in line with the results of a large meta-analysis summarizing 107 PET activation studies with different cognitive paradigms and modalities describing as a main finding increased activity in the ACC in tasks judged as difficult (Paus et al., 1998). Lesion studies in animals have also pointed towards a role of the ACC in effort-related decision making (Rudebeck et al., 2006; Walton et al., 2006). Similarly, in a recent study using event-related potentials, a relationship between mental effort and ACC activation has been shown (Mulert et al., 2005b). In this study, increased ACC activation was found already 100 ms post-stimulus during the timeframe of the auditory N1 potential in a forced choice task. Apart from this study, we do not know much about the temporal dynamics of ACC function in effort-related decision making, since the widely used functional imaging techniques based on hemodynamic changes do not have the required temporal resolution in the range of milliseconds. On the other hand, ERP-based studies of ACC function are handicapped by the limited spatial resolution of ERP source imaging.

So far, our knowledge about ERP components generated in the ACC is limited: The strongest evidence of an ACC generator is

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found for the error-related negativity (ERN), a negative component that occurs about 100 ms after an error was made (Falkenstein et al., 1995; Gehring et al., 1995). For this component an ACC/medial prefrontal cortex generator was suggested not only using ERP source analysis using dipoles (Van Veen and Carter, 2002) or Low Resolution Electromagnetic Tomography/LORETA (Herrmann et al., 2004), but also using single-trial coupling of EEG and fMRI (Debener et al., 2005). The striking feature of single-trial coupling is its ability to separate different aspects of the BOLD signal according to their specific relationship with distinct neural processes. Using this technique Debener and colleagues found ERN-specific hemodynamic changes in the ACC. Single-trial coupling of EEG and fMRI predicts the BOLD signal specifically related to amplitude variations of electrophysiological components (Benar et al., in press; Debener et al., 2006, 2005; Eichele et al., 2005).

Concerning the N1 potential, there is a long and ongoing discussion about the anatomical structures involved in its generation. Since its maximum is found in central electrodes, a central generator for instance in the cingulate gyrus has been suggested early on (Gastaut, 1953) and some support for this idea was provided by studies on monkeys (Hughes and Mazurowski, 1964). However, this view was later challenged since maximal amplitudes in central electrodes are well in line with two or more symmetric sources in the superior surfaces of the temporal lobes (Scherg and von Cramon, 1985; Vaughan and Ritter, 1970). Naatanen and Picton suggested a number of different subcomponents of the N1 potential including obligatory sources in the superior temporal lobe and several facultative subcomponents such as the “attentional supervisor component”, generated probably in frontal regions (Naatanen and Picton, 1987). Recent studies using different source localization techniques have consistently proposed sources of the N1 potential in both the auditory cortex and the anterior cingulate cortex (ACC) in auditory choice reaction tasks (Gallinat et al., 2002; Mulert et al., 2003, 2001, 2005b).

In the present study, we used simultaneous EEG and fMRI to address three questions: 1) Is there an impact of mental effort to the amplitude of the N1 potential in a forced choice task? 2) Can we detect ACC activation in the fMRI analysis under high effort conditions, but not under low effort conditions? 3) Is there a link between N1 amplitude and ACC activation under high effort conditions? To answer the third question we used the single-trial variations of the N1 potential in order to predict the specifically related BOLD signal.

Methods

Subjects

Ten healthy volunteers (seven men, three women, range 21–32 years, mean age 22.6) with no history of neurological and psychiatric disturbance or reduced hearing were recruited from an academic environment. Volunteers were paid for their participation. The study was approved by the local ethics committee of the Ludwig-Maximilians-University of Munich and written informed consent was obtained from each subject.

Paradigm

We used a simple experimental design including low versus high mental effort conditions. Using this design, the impact of mental effort on the N1 potential has been demonstrated earlier (Mulert et al., 2005b). In the present study we used the same paradigm measuring EEG and fMRI simultaneously. The experimental task was a choice reaction paradigm as previously used (Mulert et al., 2005b): 152 tones of different pitches (50%: 800 Hz and 50%: 1300 Hz) with a duration of 250 ms were presented by earphones at 85 dB SPL with pseudo-randomized sequence and interstimulus intervals (ISI: 2.5–7.5 s). In the experimental runs, the subjects had to press one of the two buttons. The two buttons were assigned in advance to the high and low tone, respectively. The low tone had to be responded to by pressing the left button with the left hand and the high tone by pressing the right button with the right hand. Three runs were carried out: One with the instruction to respond with a button press to the tones in a relaxed way (low effort condition), one with the instruction to press the respective button as fast and as precisely as possible (high effort condition), and one control run with no action required at all (control condition). The three runs were performed in a pseudo-randomized order to avoid effects of unspecific vigilance reduction. Between the runs, only a short break of about 1–2 min was taken. Each run took about 13 min. Auditory stimuli were generated on a personal computer using the BrainStim software package (Brain Products, Munich) and conducted through a pair of plastic tubes into a set of headphones placed over the subject's ears.

Acoustic environment, sound system, and headphones

The details of the acoustic environment and the sound system are described in more detail elsewhere (Mulert et al., 2005a, 2004). For the measurement of the sound pressure level inside and outside the scanner we used the following equipment: A 1/2 inch microphone (B&K 4313, Brüel & KJAER, Denmark) attached to a preamplifier (B&K2639) with extension cable (B&K A027) connected to a measuring amplifier (B&K) serving as sound level recording unit. To enable offline recording, the AC output of the measuring amplifier was connected to the line input of a digital audio tape (DAT) recorder (SONY 300 ES, Japan). The measuring amplifier and the DAT recorder were placed outside the shielded MR room and the microphone cable was routed via an opening shielded by copper tubes to suppress radio frequency (RF) induction. Prior to the recordings a calibration procedure was performed using an acoustic calibrator (B&K 4230). The signals were recorded at the position of the human head in the isocenter of the MR system and the second one, at a distance of 1.2 from the opening of the MR. Due to the impulse characteristic of the MR noise, a large difference between averaging measurements applying ‘fast’ time constant and peak detection occurred. The Echo Planar Imaging (EPI) sequence used in our study produced a sound measured in SPL (sound pressure level) of 90.5 dB (dB = decibel) (fast) and of 106.5 dB (peak) inside the MR system. The background noise (due to the vacuum pump) inside the MR system was 76 dB. At 1.2 m in front of the opening of the MR a background noise of 62 dB was measured. Binaural sound transmission was performed using an air tubing sound delivery system (Resonance Technology, Inc. Van Mays, USA). The personal computer was placed outside the shielded MR room. The sound delivery system was evaluated using standardized equipment (microphone 4144, preamplifier 2619, calibrator 4230 and an artificial ear with 2 cm coupler 4152; Bruel & Kjaer, Danemark). Because we combined an invert earphone with circum-aural ear muffs, a high attenuation against the noise of the MR (20 dB at low and 50 dB in the high frequencies) was attained. Due to the tube-based sound transportation and the sound driver characteristics, a rippled band pass frequency response occurred. Therefore, the desired level of 85 dB SPL was achieved by means of a digital attenuation at the correct intensity.