An EEG-Driven Brain-Computer Interface Combined With Functional Magnetic Resonance Imaging (fMRI)

Thilo Hinterberger*, Nikolaus Weiskopf, Ralf Veit, Barbara Wilhelm, Elena Betta, and Niels Birbaumer

***Abstract*—Self-regulation of slow cortical potentials (SCPs) has been successfully used to prevent epileptic seizures as well as to communicate with completely paralyzed patients. The thought translation device (TTD) is a brain-computer interface (BCI) that was developed for training and application of SCP self-regulation. To investigate the neurophysiological mechanisms of SCP regulation the TTD was combined with functional magnetic resonance imaging (fMRI). The technical aspects and pitfalls of combined fMRI data acquisition and EEG neurofeedback are discussed. First data of SCP feedback during fMRI are presented.**

***Index Terms*—Slow cortical potentials (SCPs), functional MRI, blood oxygen level-dependent (BOLD), thought translation device (TTD), multi-modal imaging, neurofeedback, physiological regulation.**

I. Introduction

NONINVASIVE brain-computer-interfaces (BCIs) can be operated by learned voluntary control of brain signals such as the μ-rhythm [1], [2] or the slow cortical potentials (SCPs) [3]. SCPs, i.e., shifts in neuroelectric potentials lasting up to a few seconds, are used in BCIs such as the thought translation device (TTD) [4] or BCI2000 (see this issue) for direct brain communication. Several patients suffering from amyotrophic lateral sclerosis (ALS) have learned to self-regulate their SCPs for writing messages using the TTD [3]. However, communication speed is presently restricted to two to three letters per minute which yields an information transfer rate of approximately 15 Bits/min.

Improved self-regulation of SCPs would help to increase transfer rates and speed of communication. However, it is still unclear why some of the patients and healthy subjects achieve better control of SCPs than others. Successful regulators report different strategies for producing a negative or positive shift in neuroelectric potentials (cortical negativity or positivity). This raises the question which brain areas are responsible for self-regulation and which patterns of brain activation characterize this skill. The answer could help to understand the basic psycho-physiological mechanisms of SCP self-regulation and allow to develop new training procedures and paradigms, in particular for those who did not learn to control their SCPs using the present paradigm.

Functional magnetic resonance imaging (fMRI) provides information about the brain metabolism with a high spatial resolution (mm-scale) as reflected by the blood oxygen level-dependent (BOLD) effect. Recently, we reported fMRI results of ten well trained persons who applied their SCP self-regulation skills during fMRI [5]. However, due to interference of fMRI data acquisition with electroencephalography (EEG) an on-line SCP-feedback system was not available and subjects had to rely on their well trained skill. The present article describes how the TTD was adapted to an fMRI environment to provide EEG-feedback inside an MR scanner. We present pilot data of SCP self-regulation monitored by EEG and fMRI which allows for the assessment of the correlations between local BOLD-responses and the SCP changes.

II. Procedure

A. Training of SCP Self-Regulation

Self-regulation was trained outside the MR scanner with feedback of SCPs at the vertex (Cz) referenced to the mastoids in a rhythmic, time-locked trial structure. One block of trials comprised 50 trials with no inter-trial intervals. A training day consisted of about 10 trial blocks. Each trial was divided into a 2-s preparatory interval in which the required task was indicated and a 4 s feedback interval in which feedback was provided [Fig. 1(a)]. At the beginning of each trial a rectangle at either the top or bottom of the screen was high-lighted indicating the direction along which the cursor should be moved during feedback. The top rectangle could be reached by the production of cortical negativity and the bottom rectangle by a positive potential shift. The sign of the average potential during the feedback

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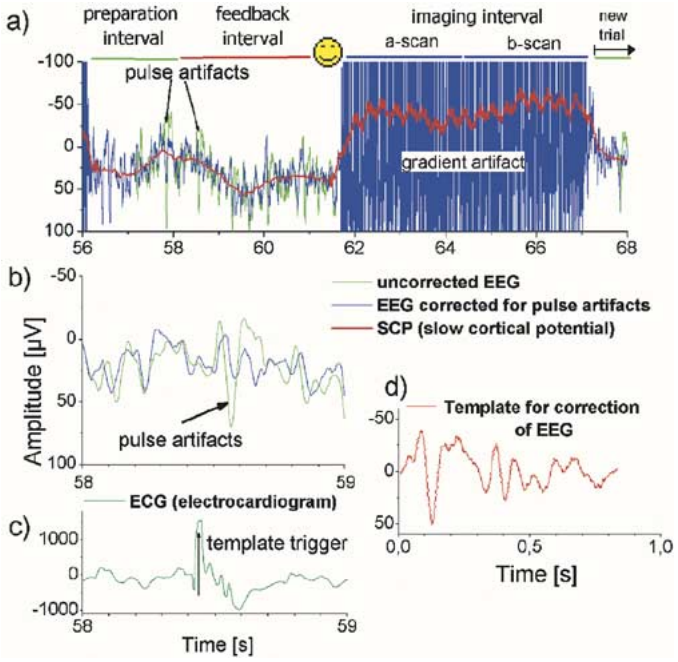

Fig. 1. (a) The EEG trace of the feedback electrode Cz is depicted over one trial. Each trial consists of a two seconds preparation interval, a 2.5 seconds feedback interval followed by 0.5 seconds for presentation of the result, and the reinforcing smiley in case of successful regulation. The final six seconds are used for the acquisition of two whole brain images. During image acquisition the EEG is heavily distorted by the switching magnetic gradient fields. Due to a delay time of the BOLD response with respect to electric brain activity by approx. 5 s, imaging can be accomplished after each EEG-feedback period. Thus, the first image (a-scan) represents the neuroelectric activity during the preparation interval and the second image (b-scan) reveals the BOLD correlates of electrical potential shift during the feedback interval. The pulse artifact (b) is corrected on-line by subtracting a template (d) from the EEG which is created from the EEG epochs triggered by the R-peaks (c) of the electrocardiogram (ECG).

interval compared to a baseline amplitude immediately before the start of the feedback interval decided about the outcome of a trial, i.e., a positive sign is regarded as positivity and a negative as negativity. A correct cursor movement was rewarded at the end of each trial by a smiling face. The SCPs were on-line corrected for artifacts caused by vertical eye movements.

B. SCP Feedback in an fMRI-Environment

To record neuroelectric potentials we used the EEG amplifier EMR16/32 (Schwarzer, Munich, Germany) which was specifically designed for use in the MR environment. The amplifier box, located close to the subject, sends the digitized EEG signal via an optical fiber to a DSP-board in the measurement-PC in order to avoid artifacts by electric induction. The TTD software interfaced the DSP-board to configure and read out the EMR-amplifier in real time. Interference of the switching gradient fields during imaging [see Section II-D and Fig. 1(a)] with the EEG feedback signal could be avoided by acquisition of the MRI scans between the feedback intervals (see Section II-C). For the fMRI study the feedback interval was shortened from 5 s to 3 s and the echo-planar imaging (EPI) was performed during a subsequent 6 s period. To synchronize the trial structure of the feedback paradigm with image acquisition, the TTD software was triggered by the MR scanner.

In addition to the 7 EEG-channels and the vertical EOG, two ECG channels (electrocardiogram) were recorded from the chest for pulse artifact correction (see Section II-D). The low-pass filters were set to 40 Hz, the high-pass filters to 0.01 Hz for EEG and EOG and to 10 Hz for the ECG. As in the preceding feedback training, SCP at Cz versus mastoids, corrected for eye-blinks, served as feedback signal. For the fMRI study, additionally to the negativity and positivity task, a third neutral control task was introduced to compare the results of the two tasks with a no-task condition. During the control condition the persons should passively view the screen which showed the targets but none of them was high-lighted and no feedback signal was presented.

C. Functional Imaging

Imaging was performed with a 1.5 T Magnetom Sonata (Siemens, Erlangen, Germany) whole body MRI system equipped with a volume head coil. A modified echo-planar imaging protocol (EPI; flip angle 90°, TE 40 ms, FOV 180×240 mm, matrix 48×64, 36 slices, slice thickness 3 mm, gap 1 mm) was used that allowed us to measure two volumes (2×2.7 s, referred as a-scans and b-scans respectively) per trial during the 6 s period after SCP-feedback (Fig. 1(a)). The TR was therefore variable, i.e., $\mathrm{TR1} = 8.3$ s and $\mathrm{TR2} = 2.7$ s.

Previous studies have shown that the hemodynamic response is delayed with respect to the underlying neuroelectric activity (e.g., [6], [7]), resulting in an approx. lag of 6 s of the peak BOLD response. Therefore, the first scan (a-scan) reflects mainly the EEG activity during the preparation interval. The second scan (b-scan) reflects mainly the feedback interval, i.e., the BOLD correlates of SCP self-regulation. Since the delay of the BOLD response depends on different factors including the location in the brain, this distinction is only an approximation. However, the variation in the delay was reported to be smaller than 1–2 s (e.g., [6]).

D. Handling of Artifacts

1) Artifacts in MR Images: Inhomogeneities in the magnetic field caused by the electrode cream might lead to signal dropouts in the EPI at the site of the electrodes [8]. These image artifacts were minimized by testing different kinds of electrode gel. The EC2™ electrode (Astro-Med, Inc.) cream showed no visible artifacts ranging below the skullcap and it was, therefore, used for the present study.

2) Movement Artifacts in EEG: Small displacements of the electrode wires in the magnetic field can cause large induction artifacts in the low-frequency range of the SCPs. Therefore, the radio frequency shielded wires were carefully fixed and tightened together to reduce motion and the inductive area. The amplifier box was placed outside the magnet to avoid vibrational artifacts of the scanner on the amplifier. For the same reason, the helium-pump was temporarily switched off while recording the EEG.

3) Scanning Artifacts in EEG: During image acquisition switching magnetic gradients induce currents in the electrode wires leading to broad-band EEG distortion with amplitudes in the millivolt range [Fig. 1(a)]. Those artifacts could not be

corrected on-line and, thus, EEG-feedback in combination with fMRI was realized in a sparse sampling paradigm [Fig. 1(a)] which is applicable due to the delayed hemodynamic response as described in the previous Section II-C.

4) Correction of Pulse Artifacts: The small pulsations of blood vessels on the scalp can be a major source of artifacts when measuring EEG in a strong static magnetic field. The amplitude of those pulse artifacts in the EEG might affect the SCP feedback signal when electrodes are placed above an artery [Fig. 1(b)]. An on-line pulse artifact correction algorithm has been developed based on a report by Allen *et al.* [9]. To obtain a reference signal for the heart beat, the electrocardiogram (ECG) was recorded simultaneously with the EEG amplifier [Fig. 1(c)]. Assuming that the measured EEG is a linear superposition of the EEG and the time-locked pulse artifact, the R-peak of the ECG served as trigger for the construction of a template that represents the EEG activity correlated to the pulse. This template was continuously updated taking into account the previous 10 s of the ongoing EEG signal and subtracted from the EEG with every pulse [Fig. 1(d)].

III. Pilot Study

Three well-trained subjects (each participant attended 60 to 70 runs á 50 trials) performed SCP self-regulation in the MRI scanner. They participated in one simulation session outside the scanner to get accustomed to the modified paradigm and the scanner noise which was recorded was presented with loudspeakers to the subject. The subsequent fMRI session comprised four runs consisting of 48 trials each.

The subjects achieved an overall correct response rate of 87% and differential SCP amplitude of 17 μV yielding a standardized SCP amplitude difference of 1.6 for the SCP regulation.

The two time series (a and b scans) were separately preprocessed and analyzed using SPM99 (Wellcome Department of Cognitive Neurology, London, U.K.) [10]. The EPI were motion corrected, spatially normalized and smoothed with a Gaussian kernel (16 mm full width at half maximum). A general linear model was used with negativity and positivity as conditions—resembling the task—and the corresponding SCP amplitudes as additional regressors—resembling the performance. The no-task condition was used as reference condition. The small sample size allowed for a fixed effect analysis only. The main effect of negativity and positivity during the preparation and feedback interval was computed by contrasting the tasks against the no-task condition. Furthermore, the reverse contrasts were determined that tested for higher cortical activation during the no-task condition. Additional contrasts were computed to identify areas showing a positive or a negative covariation with the SCP amplitudes independent of the task. Only clusters of activation exceeding a height threshold of $p < 0.05$ (corrected for the multiple comparisons within the whole brain) and a spatial extent of 10 voxels were considered significant.

Sites of significant task-specific BOLD responses during the SCP-feedback are shown in Fig. 2. In the *preparatory interval* the activation pattern around centrally located brain areas matched the contingent negative variation (CNV) in the EEG during the preparation interval (Fig. 2). Covariation analysis of the BOLD responses and SCP revealed a positive covariation (BOLD increase accompanied with positive EEG deflections) in the parietal cortex, whereas a negative covariation (BOLD increase with negative EEG deflection) was found in superior temporal regions bilaterally and the thalamus.

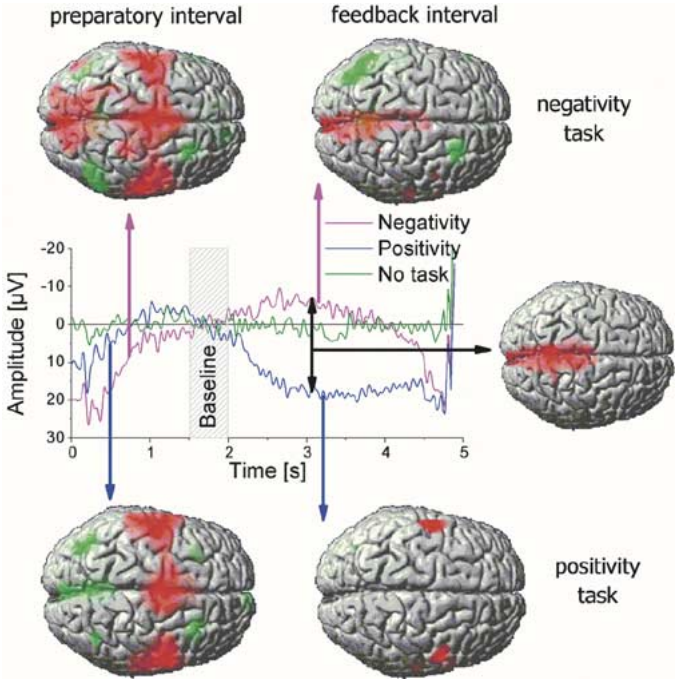

Fig. 2. Center: EEG trace of a trial averaged over 3 participants separately for each task condition ($3 * 192$ trials were averaged). The amplitude from 1.5 to 2.0 s served as baseline after which the feedback task (to produce electro-cortical negativity or positivity) should be performed. The task was presented at the beginning of the trial and evoked a CNV during the first second.
The top row illustrates the activation sites in the negativity condition during the preparatory interval (represented by the first image [a-scan] acquired immediately after feedback) and during the feedback interval (represented by the second image [b-scan]). The bottom row shows the same for the positivity task. The right centered image illustrates the difference in the BOLD response between the negativity and the positivity task. Red indicates a higher activation during the task condition and green indicates a higher activation during the neutral condition.

In the *feedback interval*, activations during required cortical negativity were observed in the supplementary motor area (SMA) and paracentral lobule accompanied with increased activation in the no-task condition in frontomedial and middle temporal regions. In the positivity task, a shift of activations from vertex to temporal regions was observed. The differentiation between negativity and positivity was most pronounced in the SMA and paracentral lobule.

IV. Conclusion

A setup combining fMRI and EEG-feedback has been established that allows to further investigate the processes underlying the self-regulation of SCP. The quality of the EEG recording in the lower frequency range is comparable to the recording outside the MR scanner and the average SCP curves show the same typical shape. The BOLD activities in this pilot study are roughly in line with a previous report on activation

patterns during SCP self-regulation without feedback [5]. Currently, this is further investigated with a larger sample size. In future studies, this approach might be extended to the assessment of other EEG components, such as evoked responses or spectral components, and their respective BOLD activity.

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REFERENCES

[1] J. R. Wolpaw and D. J. McFarland, "Multichannel EEG-based brain-computer communication," *Electroencephalogr. Clin. Neurophysiol.*, vol. 90, pp. 444–449, 1994.

[2] G. Pfurtscheller, D. Flotzinger, M. Pregenzer, J. R. Wolpaw, and D. McFarland, "EEG-based brain computer interface (BCI)," *Med. Prog. Through Technol.*, vol. 21, pp. 111–121, 1996.

[3] N. Birbaumer, H. Flor, N. Ghanayim, T. Hinterberger, I. Iverson, E. Taub, B. Kotchoubey, A. Kübler, and J. Perelmouter, "A spelling device for the paralyzed," *Nature*, vol. 398, pp. 297–298, 1999.

[4] T. Hinterberger, J. Mellinger, and N. Birbaumer, "The thought translation device: Structure of a multimodal brain-computer communication system," in *Proc. 1st Int. IEEE EMBS Conf. Neural Engineering*, Mar. 2003, pp. 603–606.

[5] T. Hinterberger, R. Veit, U. Strehl, T. Trevorrow, M. Erb, B. Kotchoubey, H. Flor, and N. Birbaumer, "The relationship between BOLD-signal of fMRI with slow cortical potentials," *Exp. Brain Res.*, vol. 152, pp. 113–122, 2003.

[6] J. C. Rajapakse, F. Kruggel, J. M. Maisog, and D. Y. von Cramon, "Modeling hemodynamic response for analysis of functional MRI time-series," *Human Brain Map.*, vol. 6, pp. 283–300, 1998.

[7] N. Logothetis, J. Pauls, M. Augath, T. Trinath, and A. Oelterman, "Neurophysiological investigation of the basis of the fMRI signal," *Nature*, vol. 412, pp. 150–157, 2001.

[8] K. Krakow, P. J. Allen, M. R. Symms, L. Lemieux, O. Josephs, and D. R. Fish, "EEG recording during fMRI experiments: Image quality," *Human Brain Map.*, vol. 10, pp. 10–15, 2000.

[9] P. J. Allen, G. Polizzi, K. Krakow, D. R. Fish, and L. Lemieux, "Identification of EEG events in the MR scanner: The problem of pulse artifact and a method for its subtraction," *NeuroImage*, vol. 8, pp. 229–239, 1998.

[10] K. J. Worsley and K. J. Friston, "Analysis of fMRI time-series revisited again," *NeuroImage*, vol. 2, no. 3, pp. 173–181, 1995.

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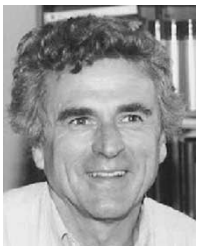

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