The EEG-based local brain activity (LBA-) feedback training

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Abstract

In this paper a training procedure for EEG-based Local Brain Activity (LBA-) Feedback and first highly promising results are presented.

The procedure utilizes multi-channel single trial evoked brain potentials that accompany stimulus-guided cognition. Up to three potential topographies at adjustable latencies are analyzed by means of BEM (boundary element method)-based SMS (simultaneous multiple sources)-LORETA (Pllana & Bauer 2011). If and only if a source can be localized within a predefined region of training (ROT), feedback will be given via a computer screen according to the strongest within-ROT source.

In a screening experiment consisting of 7 session of 2 runs with 120 covert action naming items each, 5 healthy subjects trained to get feedback more frequently and more intensively in order to enhance the activity in their left hemisphere language areas. All subjects gained in both frequency and intensity of feedback, whereas 5 healthy control subjects who got the same instruction but sham feedback (frequency: random, 20% of items; intensity: random) did not learn. Group differences were statistically highly significant. The results are promising with respect to possible applications in rehabilitation, psychotherapy and training of cognitive functions.

Abbreviations:

local brain activity (LBA); electroencephalography (EEG); boundary element method(BEM); simultaneous multiple sources (SMS); low resolution electromagnetic tomography (LORETA); standardized low resolution electromagnetic tomography (sLORETA); quantitative EEG (qEEG); evoked potentials (EP); real time functional magnetic resonance imaging (rtfMRI); blood oxygen level-dependent (BOLD); anterior cingulate cortex (ACC); rostral anterior cingulate cortex (rACC); parahippocampal place area (PPA); slow cortical potential (SCP); functional magnetic resonance imaging (fMRI); region of training (ROT); Brodmann areas (BA); silver/silver chloride (Ag/AgCI); electrooculogram (EOG); 3D photogrammetric head digitizer (3D-PHD)

INTRODUCTION

Various types of neurofeedback – from simple frequency power to quantitative EEG (qEEG) feedback – are in use as therapeutic measures since decades, whereby their efficacies have been assessed empirically on the behavioral and introspective level. However, with all these feedback types it is unclear how and where in the trainees' brains the learning process takes place and whether these processes are alike in all trainees. For all we know, a brain signal, i.e., EEG/ EP components at certain scalp locations or even described as scalp potential topographies, can in principle be generated by different generator (source) configurations in the brain.

During the last two decades a considerable amount of knowledge on the role of cortical structures in various neuronal networks was accumulated by cognitive,

Act Nerv Super Rediviva 2011; 53(3): 107–113

affective and social neuroscience. And, as a matter of fact, all this knowledge could be used by neurofeedback effectively if its actions were more specific and controllable.

Therefore some successful attempts of voluntary regulating brain activity in specific areas by means of real time functional magnetic resonance imaging (rtfMRI) during the past few years have attracted a great deal of attention. Weiskopf et al (2003) were about the first to successfully feed back a single subject's own blood oxygen level-dependent (BOLD) signal in the anterior cingulate cortex (ACC). Despite a considerable delay from image acquisition to visual feedback (about 5 sec), the single subject learned to control his local BOLD response. In a different study using a group of subjects engaged in a motor imagery task, rtfMRI was used to feed back the ongoing level of activation in the somatomotor cortex (deCharms et al 2004). In the course of training, subjects learned to induce fMRI activation in this area that was comparable in magnitude to activation during real movement. Meanwhile, there are several publications that report on successful applications of rtfMRI-feedback suggesting that learning to control local brain activity seems to be possible, e.g., in the rostral anterior cingulate cortex (rACC) (deCharms et al 2005), the anterior insular cortex (Caria et al 2007), the subgenual anterior cingulate cortex (Hamilton et al 2007), the right inferior frontal gyrus (Rota et al 2009), the parahippocampal place area (PPA) (Weiskopf et al 2004), and the auditory cortex (Yoo *et al* 2006).

The idea of using brain-generated signals for control purposes was originally developed in the field of electroencephalography (EEG). However, the approach was rather different, as it was – and still is – almost exclusively based on surface activity. How and where in the cortex the resulting brain activity was produced, has as yet been neglected.

For example, there are a number of biofeedback techniques applied in healthy (Bauer & Lauber 1979; Bauer & Nirnberger 1980, 1981; Hinterberger et al 2004 a,b), paralyzed (Kübler et al 1999) and epileptic subjects (Rockstroh et al 1993; Kotchoubey et al 1996) which are based on slow cortical potentials (SCPs). SCPs last from several hundred milliseconds to several seconds and are thought to signal changes in the activity level of underlying cortical regions (e.g., Stamm & Rosen 1972; Fuster 1973; Rebert 1973; Rowland 1974; Marczynski & Karmos 1978, Bauer & Rebert 1990; Bauer 1993, 1998). It has been shown that subjects can learn to voluntarily produce positive- and negative-going slow cortical potential shifts if changes of the potential in the desired direction are positively reinforced. The resulting selfcontrol of SCPs has been used for therapeutic purposes, as it can, for example, lead to a significant decrease of the seizure rate in epilepsy patients (Rockstroh et al 1993; Kotchoubey et al 1996, 1999, 2001).

However, one problem with SCP-control is its variability across subjects. For example, even if epileptic

patients learn to control their cortical potentials, the therapeutic effects vary considerably (Kotchoubey et al 2001; Rockstroh et al 1993). One reason for this variability may be that the SCP-changes measured are produced by a variety of different patterns of active cortical structures, most of them unrelated to the emergence of seizure. This is because feedback of SCPs typically involves feedback from a single, centrally located electrode. This, however, does not allow any direct inference about the identity or the spatial location of the neural activity within the cortex that gives rise to the measured potential. As pointed out and proved by Helmholtz (1853), the inverse problem without constraints has no unique solution. That means a specific cortical source configuration produces a unique scalp potential topography, but a given scalp potential topography can be produced by an infinite number of different cortical source configurations. Thus, SCPs measured at a certain electrode site may be generated from various brain regions by using various different strategies. Indeed, a recent fMRI-study in healthy subjects reported that the activations and deactivations associated with the voluntary generation of negative and positive-going SCPs were widely spread across the entire cortex (Hinterberger et al 2003). Moreover, the activation patterns also varied across subjects. The authors speculate that this may be due to the different mental strategies used by the subjects to generate the SCP shifts which ranged from motor imagery and language imagery to emotional strategies.

Similar objections hold for neurofeedback based on sLORETA (standardized Low Resolution Electromagnetic Tomography; Pasqual-Marquis 2002), if feedback simply depends on the sum of estimated current density values of voxels within a predefined region of training (ROT) (Congedo *et al* 2004; Cannon *et al* 2007, 2009). sLORETA solutions are pseudo-tomographic, which can easily be demonstrated by a simple simulation as shown in *Fig. 1.*

The sLORETA solution of a 'scalp' potential distribution generated by the forward solution of a single isolated generator within the central voxel results in non-zero values also in all other voxels of the solution space. Although the central voxel holds admittedly the dipole with maximum strength, this is, however, only a little bit higher than the dipole strengths of the other voxels. That means that the intra-cranial current density values estimated by sLORETA as low resolution inverse algorithm are highly correlated with those of neighboring voxels. Therefore, with sLORETA-neurofeedback, generators outside a ROT can easily cause the intended changes within the ROT.

In general, no procedures are currently available for training to regulate the activity in particular brain areas on EEG-basis. Such a method would, however, be of interest for several reasons. Firstly, the fact that EEG is cheaper and easier available makes it a more practicable method than fMRI. Secondly, EEG is free from acoustic noise and therefore applicable in a wider range of areas. For example, the targeted voluntary activation of particular localized brain areas could be used to enhance attention and learning, without being hampered by noise. Thirdly, the speed of rtfMRI is naturally limited, because hemodynamic coupling leads to a delay between neuronal activation and the BOLD signal changes (Moonen & Bandettini 2000). EEG neurofeedback is not limited by such an inherent delay, thus allowing prompter feedback and probably consequently, faster learning.

General Method

Aiming to utilize and integrate these advantages, a feedback procedure based on multi-channel EEG has been developed that enables to control the activity of specific cortical areas. To accomplish that, two sub-goals had to be addressed and achieved:

А distributed source localization method (sLORETA) had to be adapted to automatically pinpoint the number, location and the strength of identifiable generating sources of a given scalp potential distribution. This conversion to a discrete solution was necessary, on the one hand, since the feedback procedure must decide firstly whether there is a source in the ROT, and only in positive cases give a feedback according to its strength. On the other hand, possible smaller simultaneously active sources within the ROT should not be overlooked - this is important, since learning progress at the beginning of the training fully depends on the spontaneous rate of sources within the ROT which, however, can be low with small ROTs.

A way had to be found to efficiently separate 'single trial signals, i.e., scalp potential distributions' from 'noise' (raw EEG), since we did not aim, in the first place, to base feedback on spontaneous EEG frequency components.

The first goal has been achieved by developing 'BEMbased SMS-LORETA' ('Boundary Element Method based Simultaneous Multiple Sources LORETA'; Pllana & Bauer 2008, 2011). SMS-LORETA applies sLORETA iteratively after subtracting the forward solution of the dipole with maximum strength that was estimated in the previous step (all other voxels zeroed) from the remaining scalp potential distribution, until the potential distribution is depleted. The frequency of occurrence of those voxels that showed maximum values during this process determines the number and location of identifiable sources using a specifically developed spatial cluster analysis. This way it is possible to automatically localize all identifiable generators of a given scalp potential distribution (topography). This means that BEM-based SMS-LORETA gives discrete results using realistic head models although its core algorithm is a distributed source estimation method.

To accomplish the second sub-goal the fact has been taken into account that for most, if not all possible

applications of neurofeedback training, i.e., rehabilitation, psychotherapy and training of cognitive functions, some specific tasks can be designed where particular task-involved cortical structures can be trained. Therefore, the intended 'Local Brain Activity (LBA-) Feedback' procedure has been made task-linked. As can be seen in *Fig. 2*, trainees will be presented with a series of particular task stimuli where multi-channel scalp potential distributions will be extracted from the measured signal during each task execution using a regression based algorithm. If BEM-based SMS-LORETA identifies a source within the predefined ROT, then feedback will be given accordingly and consecutively updated after each task execution.

SCREENING EXPERIMENT

Experimental design

As a first step of verification, a screening experiment with five subjects and five control subjects was performed. All participants were healthy, right-handed males within an age range of 19 to 30 years. The study



Fig. 1. sLORETA output resulting from a topography that was generated via forward solution by a single generator (dipole strength of 1.4) located in the central voxel of the solution space of a spherical 3 shell head model.

Herbert Bauer, Avni Pllana and Uta Sailer

was conducted in accordance with the Declaration of Helsinki and local guidelines of the University of Vienna. Informed written consent was obtained from each participant prior to the experiments. All participants were presented with visual items of an action naming task (simple sketches of actions) and were instructed to speak the corresponding verbs covertly during the presentation time of 3 sec. Items were presented on computer screen with a visual angle of about 10° using a display size of 412×412 pixels and an ISI of 5 sec. Visual feedback was given via a grey frame that bordered the display area and turned green in various intensities according to the ongoing analyses. The whole experiment consisted of 7 sessions containing 2 runs each whereof the very last one was a transfer run without feedback. Each run consisted of 120 shown items. The left-hemispheric Brodmann areas (BA) 6, 21, 22, 40, 44 and 45 comprised the ROT. Subjects were given feedback exclusively for all within-ROT-sources according to the source with the maximum strength. Control subjects got sham feedback at a rate of 20% with random intensity. All participants got the same instruction, i.e., "please find the adequate verb and speak it covertly as clearly as possible and also try to make the grey frame around the display area as often and as intensively green as possible. This works best if the covert speaking is done repeatedly and highly concentrated during presentation time."

Physiological recordings

The EEG was recorded via 59 Ag/AgCl electrodes referenced to a balanced sterno/vertebral electrode, digitized at a rate of 125 samples per sec, corrected for vertical and horizontal eye movement artifacts and low

pass filtered at 30 Hz. Eye movement artifact correction was done by subtraction of the weighted ongoing vertical and horizontal EOG signals from the EEG signals; channel-specific weights were estimated in trials of voluntary eye movements preceding every session (Bauer & Lauber 1979; Bauer 1998).

Source localization and feedback calculation

Source localization was done by means of BEM-based SMS-LORETA (Pllana & Bauer 2011) using individual electrode coordinates projected radially to a standard 3-shell realistic head model. This model was derived from averaged T1-weighted magnetic resonance head images, provided by the Montreal Neurological Institute (MNI), available in FSL (http://www.fmrib.ox.ac. uk/fsl/) standard data folder (MNI152_T1_2mm.nii. gz). Electrode coordinates were measured by means of a photogrammetric 3D head digitizer (3D-PHD, Bauer et al 2000). With each stimulus presentation, scalp potential distributions were extracted at 3 predefined latencies (200 msec [EP component; N2], 700 msec [EP late positive complex; LPC] and 2600 msec [cognitive potential; CP]) using a regression based algorithm and fed into the BEM-based SMS-LORETA procedure. If and only if one or more sources were localized within the ROT, feedback was given according to the strongest 'within source' for subjects in the experimental group and the training runs only. This feedback was updated immediately after the end of each stimulus presentation.

With control subjects identical online calculations were done but not used to provide feedback since they got sham feedback, which was pre-defined for each run and randomly generated with the frequency limit of 20% of all trials; its intensity was random.



Fig. 2. Data and information flow during EEG-based LBA-Feedback training.

All online calculations were also done during transfer runs at the end of the training; however, these runs were feedback free. All participants knew that and were instructed to do the same they did in the training run before.

Finally, in all runs the raw EEG and the actual feedback parameters were stored trial per trial for post experimental analyses.

Transfer runs at the end of the training were feedback free. All participants knew that and were instructed to do the same they did in the training run before.

RESULTS

Score extraction

Two scores per run were calculated:

Frequency: percentage of trials with feedback and, *Intensity*: percentage of the feedback intensity over all trials.



Fig. 3. Individual courses of *Frequency* and *Intensity* scores across runs separated for subjects in the experimental group (solid lines) and the control group (dashed lines).

Descriptive results

Fig. **3** shows the individual courses of feedback Frequency and Intensity scores of all experimental and control subjects across runs. Scores of control subjects were calculated online in the same way as for experimental subjects but were not used to provide the actual feedback since control subjects got random feedback. To enable statistical group comparisons of possible

feedback training effects individual difference scores between the first training run and the transfer run at the end of the whole training were calculated for both scores Frequency and Intensity – see **Tab. 1**.

Inference statistics

Mann-Whitney U tests comparing the individual difference scores of both groups revealed highly significant results (*p*-values <0.01). The frequency of trials with feedback as well as the percentage of feedback intensity was higher in the experimental than in the control group.

DISCUSSION

According to these results we can conclude that the feedback based on the brain activity within the ROT was consistent and informative since learning took place. This means that EEG-LBA-Feedback as described works in principle – experimental subjects gained on average 20% in feedback *Frequency* and 16% in feedback *Intensity*, whereas control subjects remained at about the same level in *Frequency* and in *Intensity*. Since these dif-

Tab. 1. Individual difference scores between the final transfer run and the 1st training run separated for subjects and controls and *Frequency* and *Intensity*.

Experimental Subjects	Frequency	Intensity
1	37.5	29.5
2	10.8	6.7
3	21.6	14.0
4	19.1	20.1
5	11.6	12.4
Mean	20.1	16.5
Median	19.1	14.0
Control Subjects		
1	5.8	0.7
2	8.3	3.9
3	-21.6	-11.7
4	-13.3	-11.9
5	10.0	5.9
Mean	-2.1	-2.6
Median	5.8	0.7

Herbert Bauer, Avni Pllana and Uta Sailer

ferences were statistically significant the brain activity within the ROT of experimental subjects was obviously more prominent after training. The fact that not just the feedback *Frequency* but also the feedback *Intensity* became higher over training, speaks for a real augmentation of brain activity in the ROT during task execution.

Present results are already highly promising for the various applications. With the EEG-LBA-Feedback trainees get immediately informed that they are doing something right and involve the correct and significant cortical structures for a certain cognitive or motor task. In addition to any behavioral or cognitive training, EEG-LBA-Feedback training provides the most specific information, since it comes directly from task relevant cortical structures. Moreover, there is also no transfer of 'feedback-learned brain behavior' to real applications necessary since EEG-LBA-Feedback training is already task linked.

With all these results, EEG-LBA-Feedback as described appears to be basically comparable with rtfMRI-Feedback and, it is a lot more practicable. However, present results have been achieved using a standard head model with individual 3D electrode coordinates projected radially onto a standard head model's scalp surface neglecting varying head sizes and shapes of different individuals. Naturally, this way the accuracy of the localizations was moderate and presumably different cortical structures were trained in different individuals. This problem, of course, needs to be solved in order to really reach comparability with rtfMRI-Feedback. For practical reasons it would make sense deriving individual head models from the standard head model warped to fit exactly individual 3D electrode coordinates. This way the voxel-electrode distances that vary among individuals would go into all further calculations with no MRI scans necessary. Independence from MRI, as already mentioned, would guarantee broad use of this training method. However, it needs to be shown that this ensures indeed sufficient accuracy, otherwise individual head models need to be derived from individual T1-weighted MR scans.

In any case, a preprocessing module of the computer program used in such an upcoming study accepts either a set of 3D electrode coordinates or the data set of an already segmented individual head (producible by means of e.g. the NFT toolbox of the EEGLAB software; (Acar & Makeig 2010) Swartz Center for Computational Neuroscience, UCSD; http://sccn.ucsd. edu/nft/). Depending on the input the preprocessing module either warps the standard head model to the individual shape or starts immediately calculating the grid of voxels (solution space) and transfer matrices for sLORETA.

It also needs to be shown whether the activity increase over training observed in the screening experiment occurred actually within the ROT or resulted indirectly from attenuated activity in structures outside the ROT. An experiment that takes into account all these aspects and uses 'warped individual head models' is already in progress, where ROT-activity will be assessed pre- and post-training in transfer-like trials by means of fMRI.

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