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Brain volumetry and self-regulation of brain activity relevant for neurofeedback

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ABSTRACT

Neurofeedback is a technique to learn to control brain signals by means of real time feedback. In the present study, the individual ability to learn two EEG neurofeedback protocols – sensorimotor rhythm and gamma rhythm – was related to structural properties of the brain. The volumes in the anterior insula bilaterally, left thalamus, right frontal operculum, right putamen, right middle frontal gyrus, and right lingual gyrus predicted the outcomes of sensorimotor rhythm training. Gray matter volumes in the supplementary motor area and left middle frontal gyrus predicted the outcomes of gamma rhythm training. These findings combined with further evidence from the literature are compatible with the existence of a more general self-control network, which through self-referential and self-control processes regulates neurofeedback learning.

1. Introduction

Neurofeedback (NFB) is a technique to learn how to control diverse parameters of one's own brain activity and thereby to improve cognitive performance as well as to regulate stress levels, emotional functioning and behavior (Coben & Evans, 2010; Gruzelier & Egner, 2005; Gruzelier, 2013; Kropotov, 2009; Vernon, 2005; Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002). NFB has been employed successfully in the treatment of several clinical disorders such as attention and hyperactivity disorders, depression, autism and post-traumatic stress disorder (e.g. Angelakis et al., 2007; Coben & Padolsky, 2007; Gevensleben et al., 2009; Kluetsch et al., 2014; Lévesque, Beauregard, & Mensour, 2006; Niv, 2013). NFB also is useful in the field of peak/optimal performance training, since healthy persons also can benefit from the ability to control their own brain activity (Gruzelier, 2013, 2014).

NFB is based on neuroplasticity mechanisms capable of inducing short-term as well as long-term changes in brain activity, e.g. reflected in EEG oscillations or BOLD response (Gruzelier, 2014). Along with functional changes, gray matter volumes are an indicator of the potential of the brain to undergo neuroplasticity (Johansen-Berg, 2012; Zatorre, Fields, & Johansen-Berg, 2012). Larger gray matter volumes have been associated with learning performance in many different contexts (Boyke, Driemeyer, Gaser, Büchel, & May, 2008; Driemeyer, Boyke, Gaser, Büchel, & May, 2008; Enriquez-Geppert et al., 2013; Halder et al., 2011; Kühn, Gleich, Lorenz, Lindenberger, & Gallinat, 2013). Therefore, one may expect that gray and white matter features of the brain may predict the outcome of NFB training programs. Positive evidence on this assumption has already been obtained by Halder et al. (2013). These authors found structural integrity and myelination quality of deep white matter structures to be correlated with performance in a brain–computer-interface architecture. Moreover, Enriquez-Geppert et al. (2013) have shown that larger gray matter volumes in the dorsal anterior cingulate cortex are related to stronger theta-NFB effects in healthy young participants. As discussed by Enriquez-Geppert et al. (2013), pre-existing differences in brain morphology such as intra-regional and inter-regional connectivity or regional shapes and volumes may be associated with NFB training success.

The hemodynamic response in the anterior cingulate cortex (Gruzelier, 2014) as well as in other frontal regions also has been associated with EEG NFB performance. Increased BOLD responses have been reported in the dorsal anterior cingulate gyrus, the anterior insula, middle frontal gyrus, and the supplementary motor area when participants undergo NFB training based on slow cortical potentials (Hinterberger et al., 2003), and the sensorimotor rhythm (Halder et al., 2011). Moreover, Ros et al. (2013) reported that after short NFB training in alpha oscillations an increase of

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functional connectivity can be found in a network including the dorsal anterior cingulate gyrus (see also Gilroy et al., 2013). These results suggest that the anterior cingulate cortex, the middle frontal gyrus, the anterior insula and the supplementary motor area may play a more general role in NFB learning and may support different NFB training programs.

Taken together, several functional studies investigating NFB processes (Gilroy et al., 2013; Halder et al., 2011; Hinterberger et al., 2003; Ros et al., 2013) as well as sham NFB (Ninaus et al., 2013) have found activation in the network including the anterior cingulate cortex, the anterior insula, the middle frontal gyrus, and the supplementary motor area. Therefore, one may assume that the gray matter/white matter features in this network predict NFB outcomes. Furthermore, it remains elusive to which extent the predictive value of gray/white matter features depends on the specific NFB training protocol at hand. In the present study, the association between NFB learning rates and gray matter/white matter features of the brain, particularly in those regions dedicated to cognitive control, were investigated. To identify neural circuits related to NFB in a more general way, two functionally independent EEG frequency bands (sensorimotor rhythm and gamma oscillations) were trained in two separate groups of participants. If the anterior cingulate cortex, the anterior insula and the supplementary motor area are related to NFB in a more general manner, gray matter/white matter features in these regions should predict NFB outcomes not only for the theta rhythm (Enriquez-Geppert et al., 2013) or sensorimotor rhythm (Halder et al., 2013) but also for the gamma oscillations.

2. Methods

2.1. Participants

A total of twenty participants were recruited for this study [10 male, 10 female; age range 40–63 years; mean age = 46.4 years; standard deviation (*SD*) = 5.14] and randomly assigned to one of two different NF-training protocols (SMR- or Gamma-training). One participant was excluded from statistical analysis due to excessive EEG artifacts during the NFB-training sessions. Thus, data for nine participants in SMR-group (4 males, 5 females; mean age = 47, *SD* = 6.65) and ten participants in Gamma-group (5 males, 5 females; mean age = 46, *SD* = 3.97) were available. The participants were not aware of the aims of the study at the time of data collection and gave their written informed consent. Participants had normal or corrected to normal vision and presented no history of major medical illness, psychiatric or neurological disorders. The study was approved by the ethics committee of the University of Graz.

2.2. Neurofeedback-protocols

2.2.1. Training

In this study, two different NFB-training protocols were employed. That is, one group was positively reinforced whenever their SMR (12–15 Hz) power exceeded a predefined power-threshold (SMR-group). The other group was rewarded whenever their Gamma (40–43 Hz) power exceeded a predefined threshold (Gamma-group). Each participant had to complete ten NFB training sessions within 3 weeks. Each NFB training session started with a baseline run followed by six feedback runs á 3 min each ($n = 7$ runs).

The visually displayed feedback consisted of three vertical moving bars on a computer monitor, each bar reflected a specific absolute EEG band power in real-time. The height of the bar in the middle reflected absolute SMR (12–15 Hz) band power for the SMR-group and absolute Gamma (40–43 Hz) band power for the Gamma-group and was used as an enhance band. Two smaller flanking bars reflected absolute band power between 4–7 Hz (left bar) indicating eye blinks, and absolute band power between 21–35 Hz (right bar) indicating movements and other high frequency disturbances (Doppelmayr & Weber, 2011; Weber, Köberl, Frank, & Doppelmayr, 2011). These two smaller bars were used as inhibit bands to prevent augmentation of SMR or Gamma signal by artifacts, such as eye blinks or movements, and should be kept as small as possible during training. If the bar in the middle exceeded an individually defined threshold (mean SMR/Gamma power of previous runs) and the two control bars were below their predefined thresholds (mean power of baseline run + 1 *SD*), participants were rewarded by getting points. Additionally, a midi tone signaled this fulfillment of requirements. In contrast, during the baseline runs participants were instructed not to interact with the feedback.

The bandwidth of the Gamma and SMR band was made identical to prevent possible effects due to bandwidth difference (Keizer, Verschoor, Verment, & Hommel, 2010; Kober, Witte, Ninaus, Neuper, & Wood, 2013). Furthermore, although the typical range of gamma is from 30 to 100 Hz (Fries, Nikolić, & Singer, 2007), we used a gamma band around 40 Hz (40–43 Hz) for NFB training, since it seems to be a widely accepted and often referred to indicator of gamma band (e.g. Bird, Newton, Sheer, & Ford, 1978; Keizer, Verschoor, et al., 2010; Kober et al., 2013; Reichert, Kober, Neuper, & Wood, 2015; Rubik, 2011; Tallon-Baudry & Bertrand, 1999). Moreover, a rather narrow band of gamma is frequently used in gamma NFB studies: 40 Hz (Bird et al., 1978; Rubik, 2011); 40–43 Hz (Kober et al., 2013); 36–44 Hz (Keizer, Verment, & Hommel, 2010; Keizer, Verschoor, et al., 2010; Staufenbiel, Brouwer, Keizer, & van Wouwe, 2014).

EEG signals were acquired using the 10-channel system NeXus-10 MKII (MindMedia BV, Herten, The Netherlands). The NFB protocols were created using the BioTrace+ software (MindMedia BV). In both groups Cz (international 10–20 EEG placement system) was used as feedback electrode. The acquired signal was referenced to the right mastoid. The ground electrode was placed at the left mastoid. One EOG channel, with the positive electrode placed above and the negative electrode placed below the left eye, was used to measure eye movement related artifacts (e.g. eye blinks).

2.3. EEG data analysis

Data preprocessing and analysis were performed with the Brain Vision Analyzer software (version 2.01, Brain Products GmbH, Munich, Germany). Ocular artifacts were manually rejected by visual inspection. After ocular artifact correction, automated rejection of other EEG artifacts (e.g. muscles) was performed (criteria for rejection: >50 μV voltage step per sampling point, absolute voltage value >±120 μV). All data points with artifacts were excluded from the EEG analysis (15% of data). For the EEG data analysis, absolute SMR (12–15 Hz) and Gamma (40–43 Hz) band power was extracted by means of complex demodulation (Brain Products GmbH, 2009).

2.4. Neurofeedback-performance

To assess the performance in the NFB training in both SMR and Gamma group, the power was averaged per run of training across all ten sessions. This approach gives insight into the participants' ability to modulate EEG frequencies for short periods of time during each training session (Gruzelier, 2014). According to Dempster and Vernon (2009) within session changes may be a more useful approach in identifying alterations from NFB training than identifying possible changes across sessions, which are may be confounded by shifting baselines. Moreover, averaging the data over the sessions and showing an increase of SMR/Gamma power over the runs demonstrates the reliability of participants' ability to modulate the trained frequency at a time and simultaneously reduces the effects of individual natural and random fluctuations. To assess training effects in detail and analyze the time course of SMR/Gamma power over the training runs within sessions, we conducted linear regression analyses (predictor variable = run; dependent variable = SMR/Gamma power). This statistical method allows for a twofold characterization of the time course of training effects on performance. The first one is the characterization of the slope of the power obtained in an average across all participants over the different runs. Furthermore, this method allows the statistical evaluation of the average improvement in performance contrasted with the average error observed across different runs of training. Additionally, it has been shown that this index is a valid approach to assess the NFB performance of individuals (Kober et al., 2015).

2.5. Image acquisition

Neuroimaging data were acquired before the first EEG NFB-session with a 3.0 T Siemens Skyra MRI scanner at the MRI-Lab Graz (Austria; http://bioimaginggraz.at/). The participating individuals were positioned in supine orientation with their head located in a 32 channel head coil. Structural images were collected using a three-dimensional T1-weighted magnetization prepared gradient-echo sequence (MPRAGE) protocol with 176 contiguous slices (TR = 2530 ms; TE = 2.07 ms; acquisition matrix = 256 × 256 × 176; flip angle = 9°; 1 × 1 × 1 mm voxel size; distance factor = 50%; TI = 900 ms). Diffusion weighted images were acquired using a single-shot echo-planar imaging sequence with 64 diffusion directions (TR = 6600 ms; TE = 95 ms; flip angle = 90°; slice thickness = 2 mm; 2 × 2 × 2 mm voxel size; 50 slices; distance factor = 25%; field of view 240 × 240; base resolution = 122; b-factor = 1000; bval = 1000 s/mm^2; b0-bval = 0 s/mm^2).

To minimize head movements of the participants, foam padding was used around the head within the head coil. Additionally, participants were given earplugs to reduce discomfort due to scanner noise.

2.6. Image analyses

2.6.1. Voxel based morphometry

The structural T1-images were processed using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) and the SPM8 software package (http://www.fil.ion.ucl.ac.uk/spm). The VBM8 toolbox provides automated gray matter segmentation pathways with very high accuracy and very high reliability (Eggert, Sommer, Jansen, Kircher, & Konrad, 2012). In a first step the structural T1-images of each participant were manually reoriented with the coordinates system's origin set to the anterior