



Modulation of frontal-midline theta by neurofeedback

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ABSTRACT

Cortical oscillations demonstrate a relationship with cognition. Moreover, they also exhibit associations with task performance and psychiatric mental disorders. This being the case, the modification of oscillations has become one of the key interests of neuroscientific approaches for cognitive enhancement. For such kind of alterations, neurofeedback (NF) of brain activity constitutes a promising tool. Concerning specific higher cognitive functions, frontal-midline theta (fm-theta) has been suggested as an important indicator of relevant brain processes. This paper presents a novel approach for an individualized, eight-session NF training to enhance fm-theta. An individual's dominant fm-theta frequency was determined based on experiments tapping executive functions. Effects of the actual NF training were compared to a pseudo-NF training. Participants of the pseudo-NF training experienced a comparable degree of motivation and commitment as the subjects of the actual NF training, but found the "training" slightly easier. In comparison to the pseudo-NF training, proper NF training significantly enhanced fm-theta amplitude in the actual training sessions, as well as during the whole course of training. However, unspecific changes in the alpha and beta frequency ranges found with both the actual NF and the pseudo-NF training groups emphasize the relevance of active control groups for neurofeedback studies.

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1. Introduction

Cognitive functions are related to synchronous neuronal processes as reflected in electroencephalographic (EEG) oscillations of specific frequencies (Basar and Güntekin, 2008; Engel et al., 2001; Herrmann and Knight, 2001; Herrmann et al., 2004). In the frequency domain, these oscillations appear as "peaks" in spectral analyses (e.g., Klimesch, 1999). Synchronization of oscillations can occur locally between neurons within the same area, but also between neural populations of different areas within a wider network (e.g., Ward, 2003). Thus, synchronous oscillations outline a possible mechanism for communication within the brain. For instance, Varela et al. (2001) postulate that communication between widespread brain areas relies on lower frequency bands whereas higher frequency bands implement local communication. Hence, the size of a functional brain network determines its oscillatory frequency: the more distributed, the slower the underlying oscillation (Von Stein and Sarnthein, 2000). Especially for complex

cognitive tasks more widespread brain regions are supposed to act as networks. Therefore, it is suggested that cognitive events rely heavily on such long-range low frequency mechanisms (e.g., Canolty and Knight, 2010).

The specific relationship between oscillations and cognition is a highly debated topic (Gohse and Maunsell, 1999; Shadlen and Movshon, 1999; Treisman, 1999); however, causality has already been demonstrated in an animal study with rats (McNaughton et al., 2006). McNaughton et al. (2006) demonstrated that precise, restored hippocampal rhythmicity, introduced by electrical stimulation, is crucial for appropriate hippocampal functioning concerning spatial learning and memory. In 2006, slow potential oscillations were reported to have a causal role on memory consolidation during sleep (Marshall et al., 2006). Marshall et al. (2006) instructed their subjects to perform a declarative and a procedural learning task right before sleep. After waking up, only those subjects who received transcranial electrical stimulation at 0.75 Hz during REM sleep showed enhanced memory retrieval. Causality was furthermore demonstrated for the alpha frequency and perception (Neuling et al., 2012). Neuling et al. (2012) applied oscillating transcranial direct current stimulation (tDCS) at 10 Hz and revealed that detection thresholds in an auditory detection task depended on the phase of the entrained oscillation. These examples suggest that oscillations in general are of functional relevance. Therefore, there is a high potential for the

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improvement of cognitive functions by modulating specific neural oscillations.

Currently, two main approaches are used to modulate the amplitude of EEG oscillations: neurostimulation (including transcranial magnetic stimulation (TMS), tDCS, and transcranial alternating current stimulation (tACS)) and neurofeedback (NF; e.g., Egner et al., 2002; Demos, 2004; Hanslmayr et al., 2005; Zoefel et al., 2010). While neurostimulation directly stimulates the brain by means of electrodes mounted on the scalp, NF requires the active engagement of the participant and relies on operant conditioning. Active engagement might facilitate long-term retention as suggested by constructivist learning theories applied in school environments (e.g., Narli, 2011). Moreover, self-efficacy might also be enhanced (e.g., Carlson-Catalano and Ferreira, 2001; Linden et al., 2012) due to the experience of success on regulating one's own brain activity via continuous feedback.

Within the last years, NF has been successfully applied as treatment for patients with intractable epilepsy or attention deficit hyperactivity disorder (ADHD; Birbaumer et al., 2009). Regarding ADHD, NF has been proven to be highly efficient (Arns et al., 2009; Monastra et al., 2003) with induced effects lasting for more than two years (Gani et al., 2008). The protocols used for ADHD are often based on the modulation of the alpha-to-theta ratio. It is important to note that effects can result from either a change in the alpha, in the theta or from a change in both frequency bands. With respect to alpha band NF, Hanslmayr et al. (2005) have demonstrated an association between NF-induced amplitude increases and cognitive performance enhancements in a mental rotation task. These results received further support by a study conducted by Zoefel et al. (2010). However, as ADHD is a disorder showing disrupted executive functions (e.g., Barkley, 1997), and frontal-medial (fm) theta is suggested as a correlate of executive functioning (e.g., Cavanagh et al., 2011; Nigbur et al., 2011; Trujillo and Allen, 2007; Moor, 2005), one might assume that at least part of the effects found for NF in ADHD are due to the influence of theta.

The identification of a particular oscillation reliably associated with cognition is of crucial importance for the development of effective neurocognitive training. For a putative modulation of executive functions, fm-theta might serve as an ideal parameter. In accordance with the nomenclature of Klimesch (1999), fm-theta represents a phasic oscillation in terms of a task-related modulation of the EEG, in contrast to tonic theta, that is not task-related and associated with a rather diffuse topography. Most often, enhanced cognitive processing is associated with an increase of fm-theta (e.g., Mitchell et al., 2008). Furthermore, high fm-theta amplitude has been linked to improved task performance (e.g., Klimesch et al., 1996). In addition, fm-theta shows a high degree of inter-individual variability (e.g., Mitchell et al., 2008).

More specifically, fm-theta oscillations have been associated with specific event-related brain potentials (ERPs), the so called fm-negativities in cognitive control (e.g., Cavanagh et al., 2011; Gruendler et al., 2011). Regarding response inhibition tasks, for instance, increased fm-theta amplitude can be observed at around 200–600 ms post stimulus presentation, thereby falling well into the time range of the pronounced N200/P300-complex as seen in no-go and stop as trials (for a review refer to Huster et al., 2012). Besides response inhibition, Nigbur et al. (2011) probed various tasks involving interference and showed that fm-theta relates to the N200 and the response-locked error-related negativity (ERN; Falkenstein et al., 1991). The ERN was further demonstrated to correspond to fm-theta generated in the midcingulate cortex (MCC; Luu and Tucker, 2001). More specifically, recent results support the view that the ERN and the N200 are generated by partial phase resetting and amplitude enhancement of theta activity (e.g., Trujillo and Allen, 2007; Cohen et al., 2008). Cavanagh et al. (2011) suggested fm-theta to be the universal source of fm-negativities,

indicating a general biophysical processing mechanism for the coordination of performance-relevant information associated with MCC functioning.

A (further) prerequisite for the modulation of oscillations in order to affect cognition is to demonstrate its trainability which refers to testing if the spectral effects within the trained frequency band are modulated by NF or neurostimulation. In general, only oscillations at biologically relevant frequencies can be modified (Hutcheon and Yarom, 2000). Beyond that, studies have demonstrated that individual peaks within specific frequency bands vary across subjects as a result of age, neurological diseases, task performance or brain volume (e.g., Klimesch, 1999; Moretti et al., 2004). Hence, it has been suggested to estimate individually determined frequency bands. Based on such an individualized procedure, trainability should be even more enhanced (e.g., Hanslmayr et al., 2005; Zoefel et al., 2010).

Here, we report a novel approach of an individualized, eight-session, gap-spaced NF training to enhance an individual's fm-theta amplitude. NF incorporates several advantages in contrast to neurostimulation. An active engagement of the participants, as well as associated long term effects (e.g., Gani et al., 2008; Monastra et al., 2003), are among the potential advantages. Here, we calculated the individual fm-theta peak frequency from four executive functions (task-switching, memory updating, response inhibition, and conflict monitoring), known to be the important and independent representatives of executive functions (Miyake et al., 2000; Fisk and Sharp, 2004). Each 30-min training session was further subdivided into six training blocks with brief gaps (similarly as with Van Boxtel et al., 2012; Zoefel et al., 2010). To control for repetition-related, as well as non-specific effects, we included an active control group. This so-called pseudo-NF group received a pseudo-feedback not related to the actual EEG activity, which was matched in its basic characteristics to those of the actual training group. Self reports of all subjects were used to assess the comparability of both subject groups with respect to motivation, commitment and perceived training difficulty. The aim of the study is to vigorously assess the trainability of fm-theta, focusing on its enhancement. We expected that fm-theta amplitude should be enhanced via the actual NF training as compared to the pseudo-NF training.

2. Materials and methods

2.1. Participants

Thirty-one healthy participants (15 men, mean age: 25 years; standard deviation: 3 years) took part in the NF experiment. All were right-handed, as indicated by the Edinburgh Handedness Inventory (Oldfield, 1971) and had normal or corrected-to-normal vision. Prior to the measurements, all participants were informed about the schedule and goals of the study and gave written informed consent to the protocol approved by the ethic committee of the University of Oldenburg. The study was conducted in accordance with the Declaration of Helsinki. Sixteen participants were randomly assigned to the experimental NF group (7 men), and the other 15 to the pseudo-NF group (8 men). Subjects received a monetary reward (8€ per hour) for their participation.

2.2. Calculation of the individualized fm-theta

For the individualized fm-theta NF training, the participants' task-induced EEG was measured during processing of a cognitive test battery the day before the actual training started. The dominant fm-theta frequency of each individual was estimated for four executive functions and respective tasks (task-switching, memory updating, response inhibition; Miyake et al., 2000; Fisk and Sharp, 2004). (1) For task-switching a visual number-letter task was used. Dependent on the background color, participants were instructed either to classify the number (even vs. odd) or the letter (vowels vs. consonants) via button presses. That is, dependent on the switch cue participants had to change between number and letter task processing (switch condition) or to continue with the same task set (no switch condition). (2) For memory updating, a visual three-back task was performed. Subjects were instructed to indicate per button press whenever a letter was presented three trials before the current one. Whenever this was the case, the trials were assigned to the updating condition, otherwise to the no-updating condition. (3) For response inhibition, a visual stop-signal task was utilized. On the majority of trials, participants had to react as fast

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