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Cognitive enhancement through real-time fMRI neurofeedback

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Neuroscience has demonstrated that individual differences in cognitive task performance are closely linked to differences in brain activity. Neurofeedback training based on real-time functional magnetic resonance imaging (fMRI) can effectively change specific localized brain activity. Various studies in healthy volunteers and patients have shown that self-regulation of specific brain activity can be learned with fMRI neurofeedback, and leads to specific corresponding behavioral changes. Initial evidence for cognitive enhancement due to fMRI neurofeedback include the domains of perception, motor performance, and memory. Although further conceptual and technical advances are needed to overcome current limitations of this novel method, its non-invasiveness and compatibility with other behavioral or pharmacological approaches promise that it will become a powerful tool for cognitive enhancement.

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Introduction

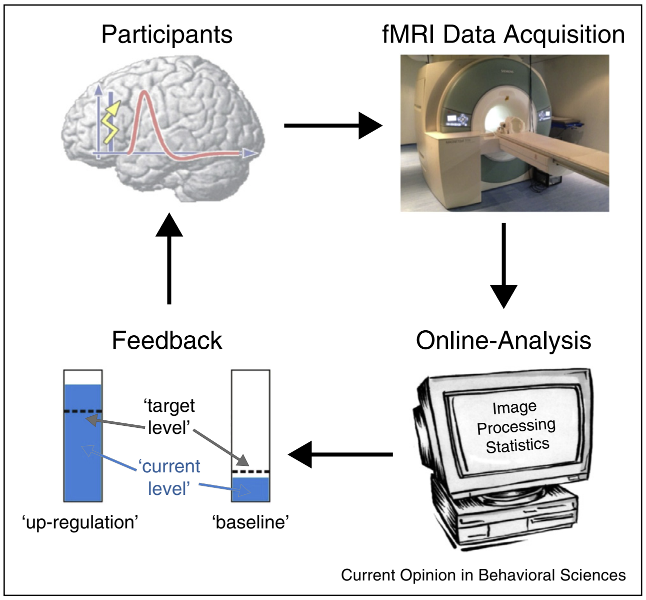
Neuroscientific research has firmly established that individual differences in cognitive task performance are closely linked to differences in brain functioning. For example, the level of activity in specialized brain areas such as the visual cortex, which can change spontaneously and as a function of perceptual training or attention, is associated with improved visual detection [1–3]. This also holds for more complex cognitive functions such as working memory and intelligence, which are associated with specific patterns of activity, in particular the prefrontal cortex [4–8]. Damage to these brain areas can result in severe visual impairment, or memory problems, respectively [1,9,10]. The close link between cognitive task performance and brain states strongly suggests that optimizing brain activity improves cognitive performance. Neurofeedback is a promising approach to manipulating brain states that is non-invasive and does not require pharmacological substances. The rationale behind cognitive enhancement based on neurofeedback is to train participants to reach brain states that have been identified to correspond to optimum levels of task performance. Depending on the task, the optimal brain states that ought to be trained with neurofeedback can be associated with enhanced attention, particular mental strategies, brain patterns evoked by specific stimuli, or any other brain state that might be promising to increase task performance. For example, improved visual sensitivity has been achieved by neurofeedback training of attention-related increases in spontaneous visual cortex activity [11••,12], as well as by training visual cortex activation patterns that corresponded to a specific visual stimulus [13••].

Neurofeedback

Neurofeedback training is accomplished by continuously measuring brain activity, analyzing it in real-time, and then providing feedback regarding the current brain state to the participant [14••,15•,16] (Figure 1). Feedback information is crucial for learning, and neurofeedback makes information about hidden brain states accessible to our consciousness. It thus provides a reinforcement signal to induce conditioning-type learning mechanisms, and also allows individuals to search for appropriate mental strategies to voluntarily control brain activity (Figure 2).

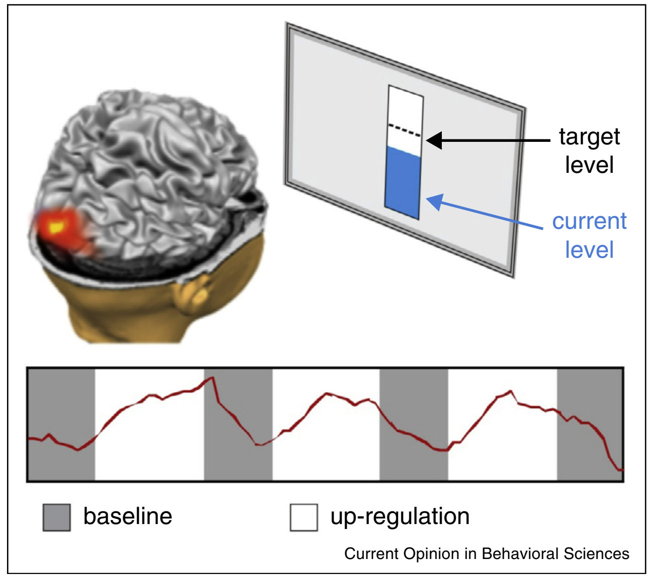
Until recently, neurofeedback was mainly used to train self-regulation of autonomic functions [17–19] or of specific electroencephalography (EEG) components. Such EEG-based neurofeedback training has been used clinically, in order for example to suppress epileptic activity [20], or to treat symptoms of attention deficit hyperactivity disorder (ADHD) [21–23]. It has also been used to optimize performance in healthy volunteers, for example improving vision [24], memory [25–27], motor learning [28], musical performance [29], and cognitive processing speed [30] (see [31,32•] for an overview). The main advantages of EEG as a tool for neurofeedback are that it is portable, relatively inexpensive, and that it has a very high temporal resolution. However, neurofeedback with EEG offers a limited spatial specificity and choice of brain regions that can be targeted. Recent technological

Figure 1



Schematic setup and data flow in real-time fMRI neurofeedback experiments. Participants are instructed to regulate brain activity. Local brain activity is measured using an MRI scanner. Real-time data pre-processing and analysis is performed with dedicated software. Feedback is provided to the participant in the scanner via a projector (e.g. in the form of a thermometer icon, with the temperature reading indicating the current level of brain activity). With the help of the feedback information, participants can learn to voluntarily control brain activity in the targeted brain areas.
Adapted from [11••].

Figure 2



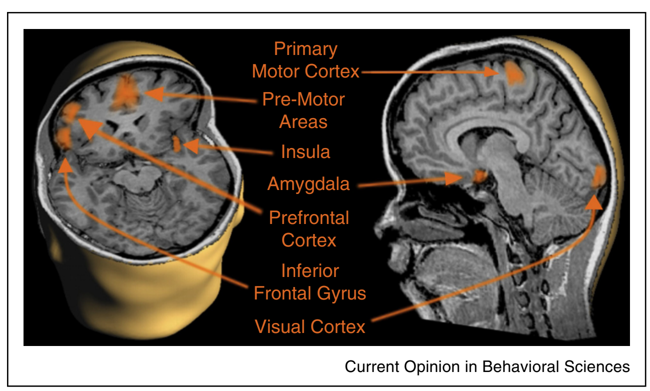
Example neurofeedback training. Participants perform several training runs of approximately 10 min duration, which are composed of baseline blocks and up-regulation blocks. During the up-regulation blocks the target-level indicator of the thermometer display moves up, which indicates to the participants that they should increase activity in the targeted brain region. Participants are presented feedback about their success via, for example, a thermometer icon. With the help of the feedback signal and by trial and error, participants learn voluntary control of activity in the targeted brain region.
Adapted from [52].

advances in the field of functional magnetic resonance imaging (fMRI) have made it possible to analyze fMRI data in real-time and thus to provide online neurofeedback of the functional blood oxygen level dependent (BOLD) signal related to neuroelectric local field potentials [33,34]. Neurofeedback based on real-time fMRI allows for targeting specific brain regions with millimeter resolution and across the entire brain [16,35–37,38•,39].

Real-time fMRI-based neurofeedback

Being able to train localized and functionally specific brain activity allows for enhancing perception and behavior that is associated with the targeted brain area (Figure 3). For example, visual perception has been enhanced with real-time fMRI neurofeedback training of the visual cortex. In one recent study, participants learned to voluntarily increase activity in a particular region of the visual cortex using neurofeedback [11••]. Up-regulation was mediated by increased top-down control of attention-related parietal cortex regions over the trained visual cortex region [12]. When participants exercised that voluntary control over visual cortex they did not only effectively up-regulate spontaneous activity in that region but also improved visual sensitivity. This goes well beyond previous demonstrations of enhancing visual perception through perceptual learning because the improved visual sensitivity can be voluntarily switched on and off by the trained participants, and it does not require

Figure 3



Examples of target regions for fMRI neurofeedback. Studies have so far successfully modulated motor performance by training primary motor and pre-motor areas [36,40••,41•,42,43], emotions by training the anterior insula and the amygdala [47•,49], working memory by training the prefrontal cortex [44], linguistic processing by training the inferior frontal gyrus [45•], and visual sensitivity by training the visual cortex [11••,13••].

repeated exposure to a specific visual stimulus but generalizes to previously unseen stimuli.

Rather than training spontaneous visual cortex activity, another study trained participants' visual cortex activation patterns that corresponded to a specific visual stimulus [13••]. Such training enhanced perceptual sensitivity specifically for that stimulus. The sensitivity remained improved even when participants did not actively self-regulate their visual cortex activity any more.

Also motor performance has been enhanced with neurofeedback training. For example, training to voluntarily increase primary motor cortex activity caused faster motor responses [40••]. Similar studies that successfully trained to increase activity in pre-motor areas also found faster motor responses [36,41•], as well as improved performance in a visuo-motor tracking [42], and a motor execution task [43]. These training effects were mediated by altered connectivity of the trained pre-motor areas with other motor-related brain areas, and significantly greater behavioral enhancement was achieved with neurofeedback than with sham neurofeedback and motor imagery training [43].

In addition to visual perception and motor function, also more complex cognitive functions such as working memory, and linguistic processing have been enhanced through real-time fMRI neurofeedback training. For example, learning to voluntarily up-regulate the dorsolateral prefrontal cortex, which is a brain area involved in working memory, improved performance in a digit span and a letter memory task [44]. Similarly, learning to voluntarily increase activity in the right inferior frontal gyrus, which is a brain area involved in understanding the speaker's intentions, improved detecting emotional intonations [45•]. Interestingly, at the beginning of training, the inferior frontal gyrus showed dense connections to a widespread network of frontal and temporal areas, which decreased and lateralized to the right hemisphere with training [46].

Finally, real-time fMRI neurofeedback training has also been shown to affect emotions positively and negatively. For example, neurofeedback training related activity increases in the left anterior insula, which is a brain area associated with appraisal of emotional stimuli, caused more negative valence ratings of aversive stimuli [47•]. Conversely, more positive valence ratings were achieved through learning to increase the top-down connectivity from cognitive control areas onto emotional limbic areas using connectivity-based neurofeedback [48,49].

Limitations of neurofeedback-based cognitive enhancement

These examples illustrate that real-time fMRI neurofeedback training can improve task performance. Participants that had been trained with this new method could see better, responded faster, showed enhanced memory, and exhibited changed emotions. Although such findings are very promising, several limitations of this novel method have to be further researched and eventually overcome. One such limitation is the relatively small effect size of neurofeedback training. Although no study so far directly compared neurofeedback training with other means of cognitive enhancement, the motor, perceptual, memory-related, and emotional enhancements that have been achieved with neurofeedback training might be somewhat lower than that achieved with high dosage psychopharmacological interventions (but see [50]). On the other hand, at least for clinical populations, neurofeedback training has resulted in effect sizes similar to that obtained with deep brain stimulation [51].

The relatively small effect sizes may be partly due to the limited amount of training that participants receive. So far, most neurofeedback studies included only one training session of approximately 1 h. The most extensive training consisted of approximately 3 h of neurofeedback training spread over the course of several days [11••, 36,41•,52]. This is far less training than is provided with, for example, videogame or mindfulness training [53,54]. The reasons for the limited amount of training offered to the participants are the high scanning costs in the range of approximately 500$ per hour, and the limited availability of MRI scanners. Because maximal performance (i.e. plateauing of the learning curves) has not been reached in most neurofeedback training studies, it is likely that additional training sessions would further improve self-regulation abilities and cognitive enhancement.

The neurofeedback training is not effective in all participants. Behavioral effects may not be achieved, because participants fail to learn self-regulation of brain activity or the voluntary self-regulation does not result in the intended behavioral improvement. Like with all skill learning, learning with neurofeedback requires motivation, repeated practice, and good training conditions. More rewarding feedback designs, better MRI scanner availability, and improved image quality and real-time signal processing algorithms will facilitate learning success, as does a better understanding of its neuroscientific and psychological underpinnings [14••,55••]. Likewise, an increasingly better understanding of brain function through rapid advances in conventional neuroimaging research and improved sensitivity of the behavioral tests will facilitate the specificity and the detection of neurofeedback training effects. So far, most studies trained self-regulation of functionally specific brain areas, but they did not train to achieve brain states that corresponded to optimum levels of task performance.

Finally, in order to achieve cognitive enhancement, the effects of neurofeedback training need to transfer from the neurofeedback training environment to situations outside the MRI scanner lacking neurofeedback. They also need to be stable and maintained for longer periods of time. So far, studies that included transfer runs without neurofeedback showed mixed results. Some failed to show transfer of learned self-regulation [38•,56–58], while other studies reported successful transfer runs [11••,36,42,49,52,59]. The generalization of learned self-regulation might be facilitated by interleaving transfer runs already during the neurofeedback training, rather than merely testing for transfer effects after training has been completed [52]. Another potentially effective measure to improve transfer might be to practice self-regulation at home or with a coach outside of the scanner. Finally, classical conditioning can be used to associate a stimulus with increased brain activity during neurofeedback training, and to subsequently use that conditioned stimulus for promoting self-regulation outside the scanner [60]. The maintenance of learned self-regulation for longer periods of more than 1 year has not been reported yet, but evidence from EEG Neurofeedback studies support the long-term maintenance of self-regulation [61–65].

Advantages of neurofeedback-based cognitive enhancement

Although neurofeedback based on real-time fMRI is a rather recent development and thus requires further exploration, it clearly offers certain advantages and benefits over conventional cognitive enhancement approaches. Based on previous studies and conceptual arguments, the neurofeedback method is considered safe [66]. As an intervention it empowers the volunteers, since they learn voluntary control. Another advantage of real-time fMRI neurofeedback is that it is fully compatible with other approaches for cognitive enhancement such as psychopharmacology, brain stimulation techniques, and cognitive training. Combining different approaches that have their specific strengths might lead to performance increases beyond simple additive effects. For example, interleaving individual neurofeedback training sessions might make standard cognitive training more directed and efficient. Neurofeedback can also be personalized to the individual needs of each participant in terms of the training objectives, and the target brain areas/networks.

Further, a unique benefit of neurofeedback training is that it may provide insights into how the performance improvement is achieved. Because the training takes place in the MRI scanner, changes in brain activity that underlie successful cognitive enhancement training are automatically recorded, and can be evaluated in order to further improve the effectiveness of this new approach. Another unique advantage of neurofeedback is that it integrates both biological as well as psychological factors underlying cognitive enhancement. Unlike psychopharmacology and cognitive training, which predominantly address either biological or psychological aspects, respectively, neurofeedback training directly changes brain states and enhances mental self-regulation competencies. Finally, neurofeedback is non-invasive in the sense that it is based on a fundamental human capacity: our ability to learn. It therefore does not require interventions from the outside such as with psychopharmacology or brain stimulation techniques.

Conclusions

Neurofeedback based on real-time fMRI is a novel method for cognitive enhancement, and the technology required for it is advancing rapidly. The initial success of neurofeedback training in fields such as perception, motor performance, and memory are promising, although further advances are needed to overcome current limitations of this novel method. The unique advantages offered by neurofeedback training promise that it will be a powerful tool for cognitive enhancement.

Conflict of interest statement

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