Spotlight

Closed-loop cognition: the next frontier arrives

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A new study trains attention by implementing a closed-loop neurofeedback approach that monitors attention status in the whole brain using real-time fMRI. Offline analyses underscore information carried by the fronto-parietal attention network as most relevant for the training-driven behavioral improvements.

We humans are inherently adaptive in our interactions with the environment, flexibly up-regulating and down-regulating our level of engagement and depth of cognitive processing based on task demands. But what if the tasks we engage in could also monitor our cognitive and underlying neural states and continuously adapt and update task stimuli and demands based on these real-time states? This dynamic task updating based on an individual's neuro-cognitive state is referred to as the 'closed-loop' approach [1]. Closed-loop technologies and experiments can be hugely beneficial for both basic science investigations and for translational research. In the basic neurosciences, if we can harness specific neural network dynamics in a closed-loop task, we can better understand how these networks contribute to task performance. Hence, real-time closed-loop neural control over a cognitive task provides deeper insights into the neural mechanisms underlying cognition and behavior. Additionally, closed-loop methods represent a very important tool for translational research; if we can accurately and continuously monitor our neural activity patterns we can learn to self-regulate them. Indeed, this is the very conceptual basis for the field of neurofeedback, which has been clinically used as a therapeutic approach to train patients to self-regulate deviant neural rhythms [2]. Further, neural activity patterns can not only be harnessed for computerized digital feedback and interactivity, but also for control of robotic sensors, which is the foundation of the field of neuroprosthetics [3]. Neural activity can also be used to drive electrical stimulation of certain brain regions to boost or silence impaired function, which underlies closed-loop development efforts in deep brain stimulation [4]. Finally, in the burgeoning field of cognitive training, custom video game training approaches are designed to track real-time on-task behavior, accuracy and response times, and dynamically adapt game difficulty based on current behavior [5,6]. We predict that real-time neural metrics guiding cognitive training approaches are the future of closed-loop neuro-cognitive training [7].

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Recently, deBettencourt *et al.* used neural signals derived from real-time fMRI (rtfMRI) to modulate stimuli in an attention task [8]. The participants viewed overlapping face/scene images in the scanner with the task of attending to one of the two stimulus categories. Then, multivariate pattern analysis (MVPA) was applied in real-time to decode whole-brain blood oxygen level-dependent (BOLD) rtfMRI responses, contrasting attention to the task-relevant vs. irrelevant stimuli. The output of the MVPA classifier then updated the percent composition of the stimulus on the next trial. Successful attention to the task-relevant stream was rewarded with proportionally greater representation of the task-relevant category in the next trial's overlapping image, whereas lapses in attention were reprimanded with a greater proportion of the task-irrelevant category in the next overlapping image. Remarkably, the authors found that engaging in only one session of this rtfMRI closed-loop neurofeedback training could significantly improve on-task attention. However, there were no assessments measuring transfer to other untrained attention tasks or cognitive abilities.

As it is important for intervention studies to control for generic practice and placebo effects, the authors additionally confirmed their main experimental findings by running four control groups: (i) a yoked-neurofeedback group was matched to the main experimental group in all regards, except their images during training were modulated by the neural response profile from another participant in the experiment group; (ii) a no-feedback group performed the task without feedback; (iii) A response time (RT) feedback group was rewarded for slow RTs (cautious responding) with greater representation of the task-relevant category image on the next trial whereas fast RTs were reprimanded with more task-irrelevant content in the next trial; and (iv) a yoked-RT group whose task stimuli composition was modulated by the RTs from participants in the RT-feedback group. None of the control groups showed behavioral gains in the post- vs. pre-training attention assessment, emphasizing the role of the closed-loop neurofeedback approach in the main rtfMRI experimental group.

In subsequent offline analyses of the rtfMRI training session, the authors showed that frontal cortex, ventral temporal cortex (especially fusiform gyri that encode faces and parahippocampal gyri that encode scenes) and basal ganglia all came to represent attention states more distinctively, that is, their activity patterns for the attended vs. unattended state, as classified by MVPA, became more separable from the beginning to the end of training. Finally, a network classifier applied over the fronto-parietal attention network reliably correlated with the whole-brain classifier output that was used during training, and this reliance on the attention network also predicted the improvement in performance from pre- to post-training. Thus, even though the authors used neural network non-specific whole-brain neurofeedback during training, follow-up analyses underscored activity modulations in the frontoparietal network, but notably not within occipitotemporal sites, as most crucial to the observed behavioral gains.

This study sets the stage for new experiments that investigate closed-loop cognition. This is a challenging endeavor because cognition is dictated by distributed neural network activity that is changing at the millisecond scale, representing the various sub-components of cognition: stimulus perception, attention, decision-making, response planning and motoric responding. Thus, although a whole-brain classifier approach as used by deBettencourt *et al.* makes sense as a first study, new studies should push the limits of spatio-temporal network specificity that can be achieved by such closed-loop approaches. Both fMRI and electroencephalography are suitable for this purpose, with the latter providing the much needed millisecond temporal resolution as well as the scalability of a low-cost method. Finally, although the use of rtfMRI in combination with MVPA-based activity classification is not new, this study is different in that it fuses updating of the stimulus and reward aspects of the task such that the adaptive response to sustaining attention is an easier stimulus. This is in contrast to successful cognitive training approaches that implement behavioral closed-loops by keeping stimuli and reward adaptations independent, which simultaneously allows provision of increasing rewards and increasing stimulus-based task challenge when behavioral performance is improving [5,6]. Thus, new closed-loop studies must carefully evaluate how behavioral/neural performance metrics tie into task difficulty progressions to achieve maximal training gains as well as transfer to untrained cognitive abilities.

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