

Revisiting the Potential of EEG Neurofeedback for Patients With Schizophrenia

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Schizophrenia (SCZ) is a neurodevelopmental disorder that can present as early as late adolescence with symptoms such as hallucinations, delusions, social withdrawal, anhedonia, and deficits in attention and memory. Treatment generally consists of pharmacotherapy with dopamine antagonists, which are highly effective in reducing positive symptoms, especially during acute episodes of psychosis. However, negative symptoms (eg, social withdrawal, anhedonia) and cognitive deficits tend to persist and are associated with profound functional decline. Given these realities, novel approaches are required to develop new treatments for patients with schizophrenia, especially those targeting unmet therapeutic needs. Recent developments suggest that within the emerging field of neuromodulation exists a potentially promising old, yet new, approach.

Neuromodulation refers to treatments that directly target neural or brain signals. For instance, direct and alternating current stimulation, deep brain stimulation, vagal nerve stimulation, transcranial magnetic stimulation, electroconvulsive therapy, and neurofeedback (NFB) are examples of neuromodulatory interventions. In this category of treatments that include both newer and older modalities, NFB occupies a unique position. NFB, or biofeedback to brain targets, was first introduced (separately) in the 1960s by Joseph Kamiya¹ and Barry Sterman.² Kamiya discovered that subjects could modulate their brain activity (as measured by electroencephalography, or EEG) in response to simple rewards. Sterman initially trained cats to control their brainwaves,² and subsequently went on to use NFB to train patients with epilepsy to lower seizure activity.³ In the years since, many different, primarily EEG-guided, protocols have been developed to address several disorders, including attention deficit hyperactivity disorder (ADHD), depression, post-traumatic stress disorder,

and schizophrenia, among others.⁴ In brief, these NFB protocols generally enable individuals to practice modulating their own brain activity, by consciously manipulating visual or auditory representations of their EEG activity.⁵ NFB is unique in that an individual uses his or her own strategy to achieve success, which inherently allows for individual differences and a flexible, personalized treatment approach. Furthermore, NFB is associated with structural changes in brain composition, such as increase in grey matter volume of the target area,⁶ suggesting that treatment effects likely involve cortical growth and plasticity.

Thus, in light of NFB's unique ability to unlock the brain's neuroplasticity in an individualized manner, our group is developing NFB based treatments for cognitive symptoms in SCZ. As part of this project, we conducted a systematic review of the literature for studies of NFB in patients with schizophrenia, the details of which are presented in our accompanying paper in *Schizophrenia Bulletin Open*. To date, few NFB studies have been conducted in schizophrenia spectrum disorders. Nonetheless, as a whole, available studies suggest that NFB influences neural processing, connectivity, and metabolism in the brain and that the effects last well beyond the treatment period. The effects also appear to generalize to related behavioral, biological, and clinical outcomes and are observed even during periods when subjects are asked to reproduce the neuromodulatory skills they have learned outside of formal feedback. Finally, of special importance for patients with complex treatment requirements, NFB is generally well tolerated and has a good safety profile.

Another major strength of NFB and other neuromodulation techniques comes from the fact that they can be designed to target specifically and objectively defined biological targets. By identifying and treating

network- or circuit-specific impairments, treatments are no longer symptom- or syndrome-centric, and can therefore be applied across DSM diagnostic categories. Furthermore, careful study of the brain's responses to these treatments can also advance mechanistic understanding of brain-based disorders and treatments, potentially unlocking novel therapeutic approaches. The review also revealed that current knowledge of NFB comes from small, case control studies, and that larger, randomized, placebo-controlled trials are needed.

Thus, given the potential promise of NFB and related neuromodulatory approaches as discussed above, we hope our proposal helps other investigators to further develop their own research programs to bring neuroscientifically driven, clinically feasible treatments closer to patients in the real world—ultimately improving speeds and rates of recovery, and the lives of patients suffering from these disabling and costly, disorders.

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