#### \*Citation Paper\*

#### Prefrontal Gamma Neurofeedback Improves Emotional State and Cognitive Function

#### Jonathan Cowan, PhD; Estate Sokhadze, PhD

In addition to well known cognitive impairments, there are disruptions in processing emotion in individuals with substance dependence and in those predisposed to drug abuse. Neurofeedback training-based intervention is one of the potentially efficacious non-pharmacological treatment options for substance use disorders. Several neurofeedback protocols (e.g., Peniston, Scott-Kaiser, etc.) have reported success in treating addictive behaviors. However, there are practically no studies on the use of neurofeedback in occasional drug users who have drug use history but have not yet developed substance dependence. We developed a protocol that might be used to prevent drug abuse through self-regulation training aimed to enhance EEG measures associated with positive emotional states. One of the aims of this pilot study was to determine the dynamics of self-reported perceived positive emotional state rating before, during and after twelve 25 min long neurofeedback training courses in two groups of subjects. One group of subjects had documented drug use history [N = 6, most ofthem referred from Louisville Adolescent Network for Substance Abuse Treatment (LANSAT)]; and another one was a group of drugnaïve subjects (N = 6, recruited mostly from graduate students and residents). Our hypothesis was that the prefrontal gamma power increase over 12 training sessions is possible and will be accompanied by an increased rating of positive affect. As a preferred neurofeedback protocol, we used enhancement of gamma range (centered around 40 Hz) activity and inhibition/suppression of other frequencies at the prefrontal site (FPz). Neurofeedback training at the midline prefrontal site after 12 sessions resulted as we hypothesized, as it predicted better performance on MicroCog and IVA+ tasks and improved scores on emotional self-reports (i.e., happiness) and clinical (BDI-II) status. Individual reports of self-received happiness scores assessed during each neurofeedback session using Continuous Response Digital Interface showed significant positive correlation with relative gamma power during individual training sessions. Neurofeedback was accompanied by positively correlated subjective self-reports of positive emotional feelings during sessions, and resulted in improved performance on IVA+ and MicroCog tests during post-neurofeedback evaluations. Post-training evaluations and 3 months follow-up showed decrease in depression scores and increased happiness rating in both groups of subjects in this study.

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Keywords: -Neurofeedback -EEG gamma -Emotion

# **Biofeedback in Coronary Artery Disease, Type 2 Diabetes and Multiple Sclerosis**

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Biofeedback-mediated stress management can be used to train patients to regulate their autonomic nervous system. Particularly in diseases where sympathetic activation has been shown to be excessive and parasympathetic activation insufficient, biofeedback may be a useful method for balancing autonomic nervous system input. Coronary artery disease, type 2 diabetes and multiple sclerosis are all diseases of increasing prevalence in the US population, and all are diseases where heart rate variability (HRV) has been shown to be decreased, suggesting an inappropriate balance of sympathetic/parasympathetic nervous system activation. We hypothesize that biofeedback-assisted stress management can be used to restore a healthy balance of autonomic activation in patients with these three diseases, and that less sympathetic and more parasympathetic input will result in altered symptoms of each disease, as well as enhanced quality of life. In this ongoing study, we are enrolling 180 patients, with 60 in each of the three disease groups, and randomizing them to receive eight sessions of biofeedback-mediated stress management or usual medical care. All participants, regardless of treatment group, receive an initial and final assessment of physiological reactivity to three mental stressors and complete the SF-36, PHQ-9 and GAD-7 questionnaires. In addition to disease-specific markers, we are also measuring HRV, plasma norepinephrine (NE), plasma C-reactive protein (CRP), and plasma tumor necrosis factor alpha (TNF) in all patients before and after the biofeedback training period. Across all three groups of patients, we will test the hypothesis that biofeedback-mediated stress management will result in decreased sympathetic nervous system activity (as evidenced by changes in HRV and plasma NE) and increased parasympathetic nervous system activity (as evidenced by changes in HRV and the inflammatory markers CRP and TNF). The overall goal of the study is to demonstrate that, regardless of disease etiology, biofeedback training can effectively restore a healthy balance of autonomic nervous system input, retard disease progression, and significantly improve clinical status and quality of life.

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Keywords: -Coronary artery disease -Diabetes, multiple sclerosis

## \*Citation Paper\*

### Biofeedback in Heart Failure Patients Awaiting Transplantation

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Biofeedback training can be used to alter the balance of autonomic input to the cardiovascular system. Studies from our own group and others have shown that heart failure is accompanied by over-activation of the sympathetic nervous system, and that decreasing this activation (for example, with a beta blocker or left ventricular assist device) not only has a positive impact on clinical status, but also reverses cellular and molecular alterations associated with the failing myocardium. In this study, we hypothesized that biofeedback-mediated stress management could also be used to remodel the failing myocardium in the direction of normal cardiac muscle function. A total of 25 patients with end-stage heart failure were studied, including 10 stable outpatients awaiting transplantation at home, who were studied in the Clinical Research Unit, and 15 inpatients awaiting transplantation in the hospital, who were studied in their rooms. All patients were subjected to the same protocol, which included an initial assessment of physiological reactivity to mental stress, six sessions of