How the Electrical Activity and Synaptogenesis of Neurons Contribute to the Efficacy of Neurofeedback Therapy

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Abstract

Neurofeedback Therapy (NFT) is a type of biofeedback therapy specifically targeting the brain and nervous system. According to the Mayo Clinic, biofeedback is defined as a technique one can use to learn to control the body’s functions, done usually by connecting one’s body (bio) to electrical sensors that help you receive information about it (feedback). This can help people focus on making subtle changes in their bodies, such as relaxing certain muscles to achieve certain results, such as pain reduction. Subsequently, the Task Force on Nomenclature specified that the presentation of information on the functioning of one’s brain partnered with changes in thinking, emotions, and behavior, support desired physiological changes. By examining a variety of studies, from ones that sought to quantify the changes in white and gray matter after NFT to those that examined the increased neurogenesis of mice living in enhanced environments to those that tried to understand the neural activity underlying brain waves, this review seeks to elucidate the quantifiable evidence that may underlie, and thus explain, the emerging efficacy of neurofeedback therapies. These studies led to the conclusion that there are biological changes taking place during NFT, though only a few have yet come to light. Of these, synaptogenesis and the varied electrical activity of neurons appear to explain how some of this brain modification, or neuroplasticity, occurs.

This paper aims to explore the biological substrates underlying the therapy of neurofeedback, which already has demonstrated to have therapeutic and clinical implications for ailments ranging from Attention Deficit Disorder (ADD) to Carpal Tunnel. According to the International Society for Neurofeedback Research, Neurofeedback Therapy uses monitoring devices to provide individuals with information on the state of their physiological functioning, specifically focusing on the nervous system and the brain (Figure 1).

Discovering how neurofeedback works is significant because the better understanding of it there is, the more precisely it can be used therapeutically. However, though current understanding of it is not very extensive, neurofeedback therapy (NFT) has already been shown to be clinically efficacious. In previous studies using subjects with ADD, it has been shown that NFT aiming to increase beta brainwaves (those associated with concentration and focus) while trying to minimize theta brainwaves (daydreaming, inattention) can lead to a reduction in impulsivity and hyperactivity, thus contributing to an improvement in attention (Monastra, 2002).
While the effects of pharmaceuticals are typically short lived and it can often take weeks for a patient to experience results, NFT can last for months after the training takes place, depending on how intensive the training. It is also much less invasive than any form of surgery. So, though it takes a number of neurofeedback training sessions to see results, it is less invasive, longer term, and has significantly fewer side effects than either pharmaceuticals or surgery.

However, for this type of therapy to be taken seriously, its mechanisms of action need to be understood. Not only should this lead to more accurate and specific usages, but also it should make it more easily accepted as a form of therapy. Firstly, this paper will discuss the methods of recording neural activity and imaging the brain, and how they apply to neurofeedback therapy. The methods included are electroencephalography (EEG), magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion MRI (dMRI), and Diffusion Weighted Imaging (DWI). While EEG and fMRI are used to record more “real-time” data, MRI is usually used to form images and view the internal anatomy of parts of the body (Hollingworth, et al). It is of great utility for measuring volumes in certain areas of the brain, since it can distinguish between white and gray matter and its images are 3-D, measured in units of voxels (like a pixel, but three dimensional). dMRI is typically used to examine white matter (Hagmann et al, 2006), while DWI is more commonly used for gray matter (Le Bihan, et al. 1986).

Secondly, brainwaves and the distinctions between the different types will be explained. Because alpha and beta brainwaves are primarily used in the neurofeedback therapies examined, these will be focused on. These two brainwaves are observed and used more extensively because alpha activity is thought to reflect attentional demands (Basar, 1997) and beta activity is thought to reflect cognitive processes, so they both have clear implications in disorders such as ADD (Cole and Ray, 1985) and general improvement of mental processing.

Lastly, but perhaps most importantly, this article will examine how electrical activity of neurons and synaptogenesis influence the neuroplasticity that underlies the clinical efficacy of neurofeedback therapy (NFT). The term electrical activity refers to the speed of action potentials, or electrical conduction, and the rates at which they occur (Ghaziri, 2013), both factors that influence the type of brainwaves EEGs detect and record. On the biological side of things, it has been shown that changes in electrical activity can influence the myelination of axons (Ghaziri, 2013).

Synaptogenesis refers to a positive change in synapse number, and sometimes includes changes in morphology (Markham and Greenough, 2004). Because neurofeedback can be seen as a way of enhancing ones environment, it makes sense that there would be increased neuroplasticity, as previous studies have repeatedly shown that mice placed in “enriched environments” containing paper, toys, and nesting materials, had more hippocampal neurons than those who were housed in empty cages (Kempermann, 1997). Both changes in axon myelination and synapse formation have been found as a result of neurofeedback therapy, and thus provide quantifiable evidence that supports the idea that it induces long-term neuroplasticity that is essential to the clinical effects.
Figure 1: The basic components and processes of a neurofeedback paradigm. The transform algorithm is part of the brain-computer interface that transforms neural signals into visual feedback on a screen, such as moving a cursor.

**Methods of Neurofeedback Therapy**

Electroencephalography works through strategically placing electrodes on parts of the scalp and recording electrical activity and quantifying it in terms of brainwaves, the type of which depends on the frequency of the electrical activity. These voltage fluctuations result from the ionic current flows within the neurons of the brain (Niedermeyer, 2004).

Magnetic Resonance Imaging (MRI) uses magnetic fields and radiowaves to form images of and examine the anatomy of different parts of the body. It allows for the diagnosis and treatment of many conditions in the medical field, however, neurofeedback therapy is most concerned with its ability to provide contrast between white and gray matter (Hollingworth, et al). fMRI takes the technology of normal MRIs, and adds a real-time functional capability to it; it measures brain activity by detecting changes in blood flow to different regions of the brain. This technique is based upon the fact that blood flow in the brain and neuronal activity are correlated and that the blood oxygen level changes in areas in which it is being used (Huttel, 2009).

However, the unit of measurement of the fMRI, a voxel, is 3mm x 3mm x 3mm, which is quite large compared to the size of a neuron, and it records data every 1-2 seconds, which is also very slow compared to the speed of electrical transmission along axons and between neurons. For these reasons, it is not a very specific form of measurement, though it has proven successful in some brain training methods (deCharms, 2007). Diffusion MRI (dMRI) is used to provide images of white matter structure and models of brain connectivity by mapping the diffusion process of various molecules, such as water, invivo and non-invasively (Hagmann, et al, 2006). This form of imaging allows researchers to view the changes in white matter by
measuring the volume at the beginning and end of experimental trials. Diffusion weighted imaging (DWI) is similar, except that it is primarily used for measuring gray matter (Le Bihan, et al. 1986).

So, to record activity of the brain and conduct neurofeedback therapy, EEG is used. By connecting the EEG electrodes placed on the scalp to technology that monitors the electrical output and sends it to brain-computer interface software that transforms the neural activity into some form of visual feedback, such as a moving cursor, patients can view and attempt to manipulate their brainwaves and investigators can study the recording patterns (Fetz, E.E., 2007). To record the brain volume in order to measure changes in it, MRI, dMRI, or DWI, are typically used. These methods allow neurofeedback therapy to happen, and for its neuronal effects to be measured and quantified.

**Brainwaves: What are They and What do They mean?**

Currently there are five types of brainwaves known: these are delta, theta, alpha, beta, and gamma. Each represents different frequencies of electrical activity, which are recorded by EEG machines. Gamma waves are the highest frequency waves, usually recorded around 20- 80Hz (Bressler, S.L. 1990), while delta and theta are the slowest, at 0-3Hz and 4-7Hz respectively. However, most neurofeedback therapy targets beta brainwaves, which are recorded at 16-25 Hz and dominate focused waking states when attention is aimed at cognitive tasks and problem solving.

When the brain is awake and alert, but not problem solving, alpha brainwaves, between 8-12 Hz, dominate (Cole and Ray 1986). Not much is known about brainwaves, aside from the fact that they are due to the electrical activity of neurons and that, as previously stated, certain ones correlate to certain mental states. However, by focusing on targeting the brainwave associated with whatever mental state one hopes to practice maintaining (i.e. Beta for paying attention and problem solving), it is possible to use neurofeedback to ameliorate conditions such as ADD.

**Electrical Activity of Neurons and Synaptogenesis**

Synaptic interactions as well as their respective strengths and input signals contribute to setting the conditions necessary for oscillatory neuronal behavior, more commonly known as brainwaves, to occur. According to Lopes da Silva’s observations, where neurons had synergistic oscillations in the beta frequency range, there were patches of enhanced correlations. Because oscillatory effects appear to be a highly effective manner of activating large populations of neurons (Lopes da Silva, 1991), it can be reasoned that, along the lines of Hebb’s postulate, these neurons “fire together” and “wire together”, thus facilitating the pattern of electrical conductance in the future.

It has been shown that electrical activity within an axon can modulate its myelination over a period of weeks (Ghaziri, et al, 2013), so it can be theorized that focusing on achieving a particular brainwave, for prolonged periods of time, the most common of which is around 30-40 minutes for NFT (Ghaziri, et al 2013), can induce an increase in white matter. Ghaziri, et al. used an NFT protocol that called for three sessions per week, at 30 minutes each, for 13.5 weeks. By comparing the results of the con group (no neurofeedback, and no guidance from researcher), sham group (fake neurofeedback, and guidance from researcher), and experimental group (accurate neurofeedback and guidance from researcher), it was found that NFT led to a significant increase in both white and gray matter. EEG was used for the neurofeedback, while MRI was used to image both white and gray matter volume, and dMRI was used to more specifically examine the white matter.

The idea that the electrical activity of neurons within the CNS affects the myelination of axons, and thus the volume of white matter, is further supported by studies that show that myelin can be inhibited or enhanced by either blocking the action potentials of neighboring axons, or by enhancing
their electrical activity. Administration of tetrodotoxin (TTX), and action potential inhibitor, can also induce a dramatic inhibition of the level of myelination, and its subsequent removal allows for recovery of electrical activity that allows myelination to proceed again (Demerens, 1996).

Any type of sensory experience alters the brain in some way. However, it has been shown that experiencing repeated neurofeedback therapy can induce measurable, morphological changes. Alterations in gene expression and the physiology of the associated neurons often accompany environment-induced reorganization of brain connectivity. This all goes hand in hand with the evidence supporting that electrical activity influences neuroplasticity. Because action potentials cause the release of neurotransmitters, and these neurotransmitters often trigger second messenger cascades within the cell that ultimately affect gene expression, it is very possible that changing patterns of electrical activity can alter genes. In fact, several activity dependent axon signals have been proposed to initiate myelination, including ATP and the neurotransmitters glutamate (Butt and Tutton, 1992).

The results that show increases in both white and gray matter from Ghaziri et. al. support that neuroplasticity remains possible well into adult life – a relatively new concept given that not too long ago people believed the brain to be analogous to a computer and unable to change. The change observed in gray matter is thought to be due to synaptogenesis, or the formation of new synapses. It has been shown that experience can modify the morphology of synapses and contribute to the formation of new ones or loss of old ones (Marham, 2004), so neurofeedback therapy could very well function in this way. Furthermore, changing the shape of dendritic spines can often influence a change in their conductive properties (Markham, 2004), which could ultimately tie into the subsequent modification of myelination. This possibility implies that changes in gray matter can influence changes in white matter.

Brain-derived neurotrophic factor (BDNF) also likely plays a role in the neuroplasticity accompanying NFT. Referring back to the brains of the mice housed in enriched environments, along with their increased numbers of hippocampal neurons, it has been found that these rats also showed increased levels of BDNF. Though the correlational relationship has been found, the causational relationship between BDNF and neurogenesis is still being determined. However, Markham and Greenough found that BDNF is critical for use-dependent synaptic plasticity, and Mizuno et al have found that it regulates both short and long-term potentiation (Mizuno, 2007). This data all support the idea that neurofeedback therapy works by causing changes in white and gray matter that are due to neuroplasticity, which is generated by a myriad of biological mechanisms.

**Conclusion**

The neuroplasticity thought to underlie the clinical efficacy of neurofeedback therapy is likely due to synaptogenesis and varied electrical activity of neurons. This review intended to analyze the relationship between how neurofeedback therapy is conducted and the neural substrates underlying how and why it works. By examining a variety of research articles, it can be concluded that NFT has concrete biological underpinnings that are slowly but surely becoming elucidated. A more thorough understanding of how this therapy works should lead to an increase in its popularity, and hopefully an increase in precision of treatment methods.

The implications of this type of therapy are vast and appear highly beneficial in clinical settings. The risks are much lower and the benefits much longer-term than pharmaceutical or surgical therapies. The brain has an amazing ability to adapt and change itself to environmental demands, and NFT aims to utilize this. Research in this field should continue towards gaining a deeper understanding of how neurofeedback works in the brain and how to accurately use it to manipulate neuroplasticity. It should also examine how pharmaceuticals might be able to enhance the effects of NFT, and how NFT can enhance pharmaceutical use or recovery after surgery. By doing so, the amount of clinical therapies to choose from when faced with ailments of the brain will be greatly expanded.
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References


