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EEG Neurofeedback therapy: Can it attenuate brain changes in TBI?

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Abstract.
BACKGROUND: Electroencephalogram Neurofeedback therapy (EEG-NFT) has several potential beneficial effects in terms of improving cognition and electrophysiological regulation among patients with brain injury. However, *in vivo* structural and functional changes remain less explored.
OBJECTIVE: The aim of the present study is to explore EEG-NFT induced *in vivo* changes in traumatic brain injury (TBI) patients.
METHOD: Two patients with mean age of 15 years with moderate head injury who had more than seven post concussion symptoms and poor cognitive performances (<5 percentile) were subjected to 20 sessions of EEG-NFT. The neuropsychological test scores, post concussion symptoms and MRI scan of the brain were recorded pre-post to EEG-NFT.
RESULTS: During EEG-NFT the cognitive scores and concussion symptoms improved significantly ($p < 0.05$). The EEG-NFT has shown significant increase in cortical grey matter (GM) volumes ($p < 0.0001$) and fractional anisotropy (FA) of cortical white matter (WM) tracts ($p < 0.0001$, voxel max 60 and above). There was a significant decrease in global, local efficiency, cost and clustering coefficient of functional connectivity (Wilcoxon Sign Rank Test $p < 0.05$). Interestingly there was a significant increase in thalamo-cortical connection (increase FA value) after EEG-NFT.
CONCLUSION: The EEG-NFT therapy has shown significant changes in structural and functional connectivity among young moderately injured TBI patients.

Keywords: EEG-NFT, TBI, MRI scan, neuropsychological scores, *in vivo* changes

1. Introduction

Traumatic brain injury (TBI) is a dynamic process that is caused by force impact. The resulting characteristic pathological process causes structural and functional abnormalities in neural networks that are responsible for cognitive and somatic impairments (Podell, Gifford, Bougakov, & Goldberg, 2010). Electroencephalogram Neurofeedback therapy (EEG-NFT) is a potent technique that modifies the structural and functional abnormalities in cortico-cortical and cortico-subcortical neural network. It acts through operant conditioning where altering the intrinsic firing pattern of neural networks in hypocoupling range for better information acquisition, complex mental activity and

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attention (Lubar, 1997). There are very few studies that have looked into the structural and functional reorganization in the TBI following EEG-NFT.

The aim of the present study is to examine EEG-NFT cause changes in structural [grey matter (GM) and white matter (WM)] and functional neural networks among cognitively improved neuro trauma patients.

2. Methods

Patient 1: Twenty year old male with history of road traffic accident (RTA) presented with the loss of consciousness lasting approximately one hour and had left ear bleed. The computered tomography (CT) scan taken 12 hours following injury indicates normal brain parenchyma and bone architecture with a possibility of diffuse axonal injury (DAI). Patient 2: Twelve year old female with history of RTA presented with loss of consciousness (LOC) for approximately one week with both ears bleed and traumatic amnesia. CT scan had taken within 24 hours show features of DAI.

Both patients were moderately disabled as per Glasgow outcome score (GOS) (Jennett & Bond, 1975) and extended GOS (Levin et al., 2001). They had concussion symptoms such as headache, dizziness, intolerance to noise and light, poor concentration, anger outburst, fatigue and memory disturbances (Rivermead concussion symptoms scale) (King, Crawford, Wenden, Moss, & Wade, 1995). They were unable to interact with their family members and relatives (Rivermead follow up questionnaire) (King, et al., 1995). The detailed neuropsychological evaluation on the National Institute of Mental Health and Neurosciences (NIMHANS) Neuropsychology Battery revealed deficit (<5 percentile) in motor speed, mental speed, category fluency, visuospatial working memory, set shifting ability, verbal encoding and retrieval as well as visual memory. The pre and post neuropsychological scores and brain Magnetic resonance imaging (MRI) scan was acquired one week before and after EEG-NFT respectively.

The MRI scans were acquired using the Siemens 3T Magnetom Skyra Scanner. The T1-weighted Magnetization Preparation Rapid Acquisition Gradient Echo (MP-RAGE) sequence used for morphometric analysis provided excellent gray-white matter contrast. The sequences of resting state functional Magnetic resonance imaging (rfMRI) and 30 directions Diffusion tensor imaging (DTI) were analyzed for functional connectivity and white matter integrity respectively.

Both patients underwent 20 sessions of quantitative EEG-NFT, 40 min/day, 3 days a week for a period of 2 months. EEG-NFT protocols were contingent on the production of 4–7 Hz theta and 8–12 Hz alpha wave frequencies.

The statistical analysis was carried out between pre and post data for both quantitative EEG and imaging. The quantitative EEG was analyzed using Loreta software. The MP-RAGE data was analyzed with Freesurfer version 5.1.0 (Freesurfer) to obtain cortical and subcortical volumes, which was normalized to Intra cranial volume (ICV). The rfMRI data was preprocessed using statistical parametric mapping SPM8 and further processed using connectivity (CONN) toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). The variables of volumetric and functional connectivity parameters (false discovery rate (FDR) <0.05) were analyzed using the Wilcoxon Sign ranked test in Statistical package for the Social Sciences (SPSS) version 15.0 using ($p < 0.0001$). The DTI data was analyzed using tract based spatial statistics (TBSS) the significance was considered for ≥ 60 voxel with $p < 0.0001$.

3. Results

Results showed that both the patients improved significantly in cognitive functions. Post Neuropsychological assessment showed significant improvement in motor speed, mental speed, and category fluency, visuospatial working memory, set shifting ability, verbal encoding and retrieval of visual memory. Their concussion symptoms reduced significantly.

3.1. Following EEG-NFT

Quantitative EEG – there was a significant decrease in the theta waves but no changes in alpha wave. Indicating that, the theta/alpha ratio reduced significantly.

Structural GM changes – a significant increase in cortical volume (mean difference +0.000104, $p < 0.0001$).

Structural WM changes – the significant FA value appears in Thalamocerebral connections (Thalamic projections with Primary motor, Sensory, Occipital, Pre-frontal, Pre-motor, Posterior parietal, Temporal), Insula and Fornix (uncorrected $p < 0.0001$, voxel max 60 and above). Improvement in FA value in white-matter tracts and cortical structures are appreciated as compared with pre scan.

Functional connectivity – Global and local efficiency, cost and clustering coefficient reduce significantly in

Table 1
Comparison of changes in pre and post resting functional imaging parameters

Functional connectivity parameters	Cerebral hemispheres	Paired mean difference (Pre-post)	WSRT $p < 0.05$
Global efficiency	Left	0.058	0.028
	Right	0.041	0.028
Local efficiency	Left	0.059	0.027
	Right	0.066	0.028
Clustering coefficient	Left	0.118	0.027
	Right	0.135	0.028
Cost	Left	0.111	0.028
	Right	0.070	0.028

WSRT - Wilcoxon Sign Rank Test.

both cerebral hemispheres (Wilcoxon Sign Rank Test $p < 0.05$). The pre-post mean difference values are depicted in Table 1.

4. Discussion

The EEG-NFT has significant potential to change functional and structural connectivity at neocortical and thalamo-cortical neural networks. The study results suggest that young head injured patients with severe cognitive impairment and moderate disability can benefit by EEG-NFT. Two months of EEG-NFT is associated with a significant decrease in theta waves. The cortical GM volume is significantly increased and the WM integrity is well established (significant increase in FA value). The functional hyper connectivity reduced significantly in both cerebral hemispheres.

Studies have demonstrated that EEG-NFT has made quantitative changes in both GM and WM volumes and resting connectivity among these conditions (Johanne Levesque and Mario Beauregard; Lubar, 1997). There are very few or no studies that attempt to understand structural and functional reorganization following EEG-NFT. Hence the present study has attempted to explain EEG-NFT *in vivo* changes for clinical improvements among trauma patients.

The trauma impact causes imbalance at structural and functional level that leads to cognitive and somatic impairments. EEG-NFT has a beneficial role among this group (Rima, Albert, Henry, & Michel, 2002; Timothy & Kathleen, 2000). In the present study EEG-NFT has shown significant improvement in both of the patients in somatic and cognitive functions.

The increased global and local efficiency and decreased FA value is associated with hypercoupling state of neural networks leading to lower frequency waves like theta activity (increased theta activity is associated with decreased attention and concentration) (Lubar, 1997). After 20 sessions of NFB therapy, there is a significant reduction in theta activity. The continuous learning is associated with an increase in GM volume (Johanne Levesque and Mario Beauregard) where it causes changes at neuronal synaptic and dendritic level. The repeated NFT has made significant decrease in global, local efficiency, degree and cost parameters of functional connectivity. Thus EEG-NFT has made *in vivo* changes by the reorganization of structural and functional connections by decreasing the low frequency waves of the brain.

There are significant thalamo-cortical connections as reflected by increased FA value indicating increased WM calibre and integrity. This implies that there is activation of thalamo-cortical dynamic loop that refines the intrinsic neural network. Dopamine as a neuromodulator plays a very important role in different neural loop producing hypocoupling state (Johanne Levesque and Mario Beauregard; Lubar, 1997) and is a potential marker for future studies in this field. It can be summarized that these intrinsic modulations are responsible for significant improvement in the somatic and cognitive function which are corroborated by clinical evidence.

5. Conclusion

The EEG-NFT has a significant potential to change and regulate impaired neural networks among TBI patients. The quality of life of young head injured individuals with moderate disability and poor cognitive performance can be significantly improved using EEG-NFT. However the study has to be replicated on larger sample.

Declaration of interest

None.

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