Neurofeedback Training in Schizophrenia: A Study on Executive Functioning

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Abstract

The present study was designed to investigate the viability of neurofeedback training which entails the acquisition of effortful learning skills to gain volitional control on electrocortical activity in order to ameliorate executive function of schizophrenic patients. In this pre-test post-test design 30 schizophrenic male inpatients were selected out of which fifteen were trained to inhibit delta and theta at frontal cortex and reward SMR at vertex. Wisconsin Card Sorting Test was administered prior and after the training stage. Descriptive methods were used and P-value <0.05 was considered statistically significant. The results revealed significant improvement in executive functioning measures in experimental group relative to the control group. Our finding suggests that being the prime feature of the disorder does not necessarily imply intractability. It was once believed that schizophrenic patients could not learn to modify their bioelectrical functioning while the findings of the current research prompted a re-thinking.

Keywords: Neurofeedback, training, schizophrenia, functioning

Introduction

With its annihilating effect, schizophrenia has always been regarded as the most devitalizing psychiatric illness (Clark, 2001). Affecting about 1% of the population (Tandon, Nasrallah & Keshavan, 2009), this variegated disease, enervates the caregivers(Clark, 2001) and leaves the clinicians prostrated with its chronic course and deteriorating feature as is evident by Kraepelin's nomenclature (1919) "dementia praecox". The disease process results in aberrant clinical presentations such as positive and negative clusters, as well as cognitive dysfunctions (Tandon, Nasrallah&Keshavan, 2009). Kraepelin acknowledged the latter one as the uncontested salient features of the disorder. Innumerable numbers of evidence converge to demonstrate that cognitive impairments are present in this disorder (Klonoff et al, 1970; Saykin et al, 1991; Heinrichs&Zakzanis, 1998; Mohamed, O'Leary & Andreasen, 1999; Heaton et al, 2001; Nuechterlein, 2004). Being detectable even in premorbid level of disease (Fuller et al, 2002) first-onset schizophrenia and prior to the administration of antipsychotics (Saykin, 1994), this phenomena correspondingly increases the imperative to devise an optimum treatment. Among the extensive arrays of cognitive domains being studied, executive function, the term under the shadow of which series of cognitive abilities such as goal-orientation, planning (Velligan& Bow-Thomas, 1999), inhibition (Smith &Jonides, 1999) and cognitive flexibility (McCabe et al, 2010) are included, continues to be the crux of treatment.

Despite extensive endeavors to alleviate cognitive decays, dearth of investigations has taken the advantage of utilizing a technique placed between behavioral and physiological realms in the rehabilitation of these decrements. In prioritizing the treatment paradigms, pharmacotherapy has

always been the benchmark of treatment (Sadock&Sadock, 2007); however, marginal effects of conventional antipsychotics (Medalia et al., 1988; Spohn&Strauss, 1989), side effect of second generation (Sadock&Sadock, 2007) and even modest benefits of other medication options in conjunction with antipsychotics such as bupropion (Rezaee,Masafi, Mohamadreza&Akbarpour, 2012),lack of insight and therefore lack of compliance (Buckley et al, 2007) prompt the clinicians to consider alternative non-pharmaceutical modalities such as neurofeedback.Based on the behavioral approach and operant conditioning paradigm, NF is termed as "internal cerebral exercise" (Tansey, 1983). Benefiting from shaping procedure (Leslie, 2011), the ultimate goal of this technique as Vernon (2005) aptly stated is the "re-creation of cortical activity patterns". This appealing strategy, not only heightens awareness by means of eliciting desirable brain activity and inhibiting abnormal electrocortical activity (Kouijzer et al, 2009), but also reinforces voluntary control on electrophysiological components. There has been reports about beneficial effects of NF on an assortment of psychiatric illnesses such as attention deficits (Lubar&Lubar, 1984), seizure (sterman& Friar, 1972) autism (Kouijzer et al, 2009), depression (Saxby &Peniston, 1995), and even schizophrenia. However, relevant attempts mostly evolve around the symptomatology of this disorder.

In the most preliminary study Schneider et al (1992) ameliorated attention breakdown of schizophrenics through regulating the slow cortical potentials.

By adopting the model of functional hemispheric imbalance, Gruzelier et al (1999) trained 16 patients to shift negativity in the opposite directions with respect to the symptom pictures they exhibited. In an in-depth case study, Schummer (2008) uncovered favorable effects of NF in a protracted process. Ruiz (2011) trained nine schizophrenic patients to volitionally up- and down-regulate anterior insular cortex activity in an attempt to improve face emotion recognition. Bolea's report (2010) provides suggestive evidence that alpha enhancement and inhibiting delta and fast beta reduce some schizophrenics' disturbances.Surmeliet al (2012) further showed significant improvement of clinical symptoms and attention with personalized protocols after NF. On the framework of previous reports and observations aboutneuropsychophysiological features and consequent neurobehavioral dysfunctions in schizophrenia, Rocha et al (2009) offered new directions for protocol designation. The findings of these authors in 2011 in an experimental setting, yield measurable cognitive benefits after NFT in 3 schizophrenic patients who were trained to inhibit theta and high beta while rewarding SMR. All in all, the work of Rocha (2011) and Surmeli could be regarded as the only studies of NFT in cognition spheres of schizophrenics. Given the scarcity of results involving the effects of NF on cognitive decrements of schizophrenic patients and exiguousness of data on the effects of NF on executive dysfunctions, more scientific exploration is warranted as a laboratory experiment. The present study is conducted to fulfill this need.

Materials and Methods

The study recruited 30 institutionalized male inpatients ranged in age 18-60 (mean age=41.60 years)(Table 1). Establishment of diagnoses was based on semi-structured interviews which were conducted by an expert psychiatrist according to the criteria of fourth edition of the diagnostic and statistical manual of mental disorders (DSM-IV-TR) (Table 2). Informed consent was obtained after full explanation of purpose and procedure of the study. Positive and Negative Syndrome Scale was used for the sake of psychopathological evaluation as well as ruling out depression. Inclusion criteria are as follows: (1) Diagnosis of mental retardation (2) concurrent substance abuse (3) neurological damage (4) comorbid psychiatric illnesses and (5) experience of electroconvulsive therapy 3 months prior to the experiment. Patients were also excluded if they were on clozapine and olanzapine medication since their influence on EEG parameters and cognitive

functions have been previously reported.(Centorrino, 2002; Pillmann, 2000).Subjects were allocated randomly into two groups.The study consisted of a 4-month successive training period. All patients were on antipsychotic medication during training course. The experimental group completed 30 sessions, each lasting approximately 50-minutes with 2 intervals of 5 minutes in between. In a complete sham debriefing session, patients were acclimatized with the experimental setting. The experiment was performed in a sound-attenuated, electrical shield room to circumvent any artifact. NFT was administered using NEXUS 4 channel device. Resting baseline was carried out in 2 minutes with eyes open. They were instructed to reduce muscle activity and control eye blinks. The amplitudes were calculated in delta (0–4 Hz), theta (4–7 Hz) and SMR (12-15 Hz) bands for each participant. EEG was recorded over right hemisphere (F4) with reference placed on the right earlobe and ground electrode on the left earlobe throughout the first 10 sessions. During the middle 10 sessions, F3 (left hemisphere) was selected with symmetrical pattern. In the course of the last 10 sessions data were acquired via electrode situated at Cz with reference on the left ear and ground on the right ear. Manual threshold setting was used. Feedback displays contained different animation with melodious sounds accompaniment. Experimental group were trained to inhibit delta and theta at F3 and F4 and reinforce SMR at Cz while simultaneously inhibited theta.

Table 1. Demographic characteristics of schizophrenia patients

	Mean(SD)	
	Experimental group (n=15)	Control group (n=15)
Age	42.06 (2.36)	41.13 (2.86)
Education	11.26 (0.529)	11.06 (0.520)
Age at onset	25.26 (1.37)	25.40 (1.58)
Duration of illness	16.80 (2.14)	15.73 (2.71)

Table 2. Statistics of assessments with clinical scale (PANSS)

	Mean(SD)	
	Experimental group N=15	Control group N=15
PANSS score	38.26 (2.08)	39.40 (2.63)
Panss negative subscale	5.53 (0.893)	4.60 (0.681)
Panss positive subscale	10 (1.27)	11.33(1.25)

Table 3. Normality of distribution (Shapiro-wilks)

	Experimental		Control	
	F	Sig value	F	Sig
Completed category	.748	.051	.805	.114
Perseverative responses	.952	.558	.857	.052
Correct responses	.888	.062	.868	.061
Errors	.888	.062	.868	.061
Percentage of conceptual level	.728	.151	.596	.089
Failure to maintain a set	.859	.084	.749	.171

Statistical analysis

In this pre-test post-test design, multivariate analysis of covariance (MANCOVA) was used with pre-test as the between-group factor for controlling the test-wise effects, and six EF composite function scores as the dependent variables. Statistical analyses were performed using SPSS (version 21). Shapiro-Wilks test was applied to test for the normality of the distribution of the data (Table 3). The significance level was set at two-tailed p<0.05. Table 4 displays thatLevene's Test of homogeneity of variances is non-significant (the group variance is equal), therefore it is inferred that the assumption of homogeneity of regression is met allowing for the administration of MANCOVA. Statistical analysis of experimental and control group patients performance are presented in Table 6.

Table 4.Equality of Variances. (Leven's Test)

	F	Sig value
Completed category	1.403	.252
Perseverative responses	1.896	.213
Correct responses	.175	.679
Errors	.004	.952
Percentage of conceptual level	3.060	.091
Failure to maintain a set	.413	.526

Results

As table 5 indicates, the control group did not appear to show significant changes in post-test on any of the EF measures. By contrast, in table 6, scores changed significantly in the experimental group for the number of categories attained *(f = 11.986, df = 1, p <0.02)*. Also, Scores declined significantly for number of preservative errors*(f = 8.197, df = 1, p <.008)*. The experimental group also improved significantly more than the control group in terms of correct responses *(f = 6.294, df = 1, p <.018)* indicating heightened accuracy after treatment. Receivers responded to WCST with significantly less errors compared to non-receivers *(f =8.164, df = 1, p <.008)*. Percentage of conceptual level revealed the improved changes in patients conceptualization during test performance *(f =4.801, df = 1, p <.037)*.Comparisons in terms of failure to maintain a set showed an additional group difference between receivers and non-receivers implying the effectiveness of NF on WCST performance. The experimental group showed the most improvement on failure to maintain a set and completed category measures regarding the Eta squares (30%, 77%).

Table 5.Performance of experimental and control group on WCST.

	Experimental				Control			
	Pre-test		Post- test		Pre-test		Post- test	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Completed category	1.66	0.89	3.33	1.67	1.80	.94	1.66	.81
Perseverative responses	14.0	4.6	8.8	2.8	16.	8.0	14.6	7.4
Correct responses	26.4	5.1	32.2	5.05	27.	5.0	27.6	4.98
Errors	33.6	5.1	27.0	4.09	33.0	5.01	31.8	5.0
Percentage of conceptual level	24.7	35.61	55.73	44.7	20.1	33.4	22.40	38.3
Failure to maintain a set	13.4	2.13	1.93	1.8	10.4	5.3	11.8	3.4

Table 6.Performance of experimental group (Multivariate analysis of covariance)

	Sum of squares	Df	Mean square	F	sig	Partial Eta square	Power
Completed category	20.833	1	20.833	11.986	.002	.300	.916
Perseverative responses	258.133	1	258.133	8.197	.008	.226	.789
Correct responses	158.700	1	158.700	6.294	.018	.184	.678
Errors	172.800	1	172.800	8.164	.008	.226	.788
Percentage of conceptual level	8333.333	1	8333.333	4.801	.037	.146	.562
Failure to maintain a set	740.033	1	740.033	96.526	.000	.775	1.000

Discussion

Although the neurophysiological mechanisms being affected by this technique need full elucidation, it is tempting to surmise about such mechanisms contributing to our results. The underlying rational of inhibiting delta at Broadman area 46 and 9 (right and left dorsolateral prefrontal cortex) is the findings extracted from studies suggesting that functional EEG anomalies in schizophrenia are predominantly polarized around frontal areas (Mukundan, 1986;Schellenberg et al, 1990;Saletu et al, 1990; Takeuchi et al., 1995; Knott et al, 2001). Notable reliance of executive variables such as inhibition (Diamond, 1990a) or regulation of behavior (Braver, Barch&cohen, 1999) on DLPFC has been documented. Abnormal perfusion termed "hypofrontality" has been observed in prefrontal cortex during performance of the WCST (Weinberger, Berman &Zec, 1986). Frontal hypofusion is explained by delta excess (Miyauchi et al, 1990; Morihisa, Duffy & Wyatt, 1983) of which increase has been reported at F3 and F4 leads (Begic, 2011). We hypothesize that the observed viability of this protocol, chiefly relies on the improved perfusion to DLPFC. In other words, down-regulation of delta power may have modulated DLPFC's functionality believed to support cognitive control (Cohen, Braver, Oreilly, 1996), hence the improved performance in WCST.

Apart from that, we intended to decrease theta power at Cz. Medial prefrontal brain regions including the anterior cingulate cortex (ACC) has been postulated to be the locus of theta generation (Tsujimoto, Shimazu, &Isomura, 2006). The pivotal role of different parts of Acc in theta generation in central brain regions has also been reported by Luu and Tucker (2001). There exists clear inverse correlation between the activation of this area and theta production .The observed excess of theta activity in schizophrenia (Sponheim, 1994) on one hand and abnormal Acc function with its contribution to cognitive control abilities and cognitive conflict tasks(Bush, Luu, & Posner, 2000; Henderson et al, 2006), on the other hand, led to our speculation that NFT aiming at reducing theta power at vertex may have given a rise to improved activation of Acc areas believed to be involved in regulating cognitive functions. This might have culminated to better task performance in its own right. This is in harmony with predictions byKouijzer (2008) who declared that better performance of executive requiring mechanisms originates from improved activation of Acc and down-regulation of theta activities.

In addition to theta inhibition at Cz, synchronous SMR enhancement was required concerning the reported effects of SMR up-training on working memory (Vernon et al, 2003), its relation to inhibition (Budzinsky, 2009), and its impact on attentional states (Kaiser, 2000) as well as cortex stabilization (sternman 2000b). Furthermore, SMR reinforcement has been linked to reduction of impulsive behavior (Thompson, 1998). . EF has been introduced to have a role in integration of temporal times and rendering people to direct behavior in goal directed manner (Vaziri, Rezaei&Dolatshahi, 2012).The increased number of categories is a document of patients' improved ability to monitor self, plan and coordinate behavior in a goal-oriented fashion which are collectively in contradiction with impulsion. In this context, it is reasonable to assume that SMR activity might have led to functional changes of these areas following stimulation. This supposition is in broad concordance with researchers' speculation about the impact of manipulation of the brain's neural processes following SMR training (Finley et al, 1975; Lubar&Bahler, 1976; Sterman, 1977).

Deficiency in inhibition which manifests itself in failure to suppress the proneness to react (milner, 1963) is conceptually associated to perseverative errors (steinmentz, 2011). Notable reduction in the number of perseverations made authors to posit that NFT directly enhanced activation of areas governing inhibition. Alternatively, it might have consolidated the network included within the areas involved in cognitive control (Cohen et al, 2000) thus, enabled patients to inhibit their tendency to respond and reflect on the strategies to adopt in the next classification, which may have contributed to improved set-shifting and consequently diminished number of perseverations.

Improved set-shifting skill is also reflected in augmented number of categories. Pantelis et al (2009) believe that set shifting requirement is shifting attention across various stimulus dimensions considering the feedback received. In set-shifting paradigms, such as WSCT, subjects are required to shift attention between different stimulus dimensions on the basis of reinforcing feedback. The most likely explanation for the observed improvement may be the already learned strategies. In fact, the most basic skill leading to mastery in NF complications is profiting from received feedback. Likewise, it seems that task accomplishment in WCST arises from the subjects' alertness to benefit from feedbacks while attempting to sort cards. Given this, we hypothesize that getting familiarized with this efficient strategy to regulate self during the training sessions, rendered patients more vigil to check errors and monitor self in exposure to feedbacks and as a result adopt novel strategies in the new situation (rule change).

Beside neurophysiological interpretations, it is worth considering self-confidence enhancing effects beneath the learning experience. Pharmacothery, despite being invaluable, is not regarded as a self-confidence bolsterer. Active participation and engagement in a novel visually absorbing training and interactive context in which they are entitled with rights to select the programs may have boosted a sense of control for a population who have elapsed great proportion of their lives in a rigidly-structured setting. This would mean that NFT aided to challenge the passivity that is a characteristic of some negative symptom patients. Moreover, the sense of success gained after mastery of games may have led to intrinsic motivation which in turn donates more activation, energy and direction to the behavior (Velligan, Kern & Gold, 2006).

Like several studies, potential limitations make the reader cautious in interpreting the results. First, it was not possible to make the study a fully blinded design. Second, small number of subjects in each group obviously makes reaching to conclusive results difficult. Third, the insufficient control of the contaminating influence of medication on EEG parameters must be considered a complication, thus executing a drug -washing procedureremains the domain of future researches. Another shortcoming was the inaccessibility to Quantitative electroencephalogram device to

measure the distinct individualized EEG patterns. Thus, it is suggested to customize individualized treatment protocols in further studies. There is a need for further studies to address other cognitive functions. Moreover, suitability of NFT on schizophrenia spectrum disorders, females and other subtypes of schizophrenia could be goals for future studies.

Conclusion

It was once believed that schizophrenic patients cannot learn to modify their bioelectirical functioning, thus this may seem a startling claim that schizophrenic patients can learn, however the findings of the current research prompt a re-thinking. Not only are these patients able to exert some control over their electroencephalographic waves but are also capable to apply these techniques in other situations. Our findings may allure those who impugned the trainability of schizophrenic patients.

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