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Letter to the Editor

Hemoencephalography self-regulation training and its impact on cognition: A study with schizophrenia and healthy participants

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ABSTRACT

Background: Cognitive impairments in schizophrenia are strongly correlated to functional outcome and recovery rates, with no pharmacological agent approved for its treatment. Neurofeedback has emerged as a non-pharmacological approach to enhance neuroplasticity, which consists in inducing voluntary control of brain responses through operant conditioning.
Method: The effects of hemoencephalography neurofeedback (HEG-NFBK) in 4 brain sites (F7, Fp1, Fp2 and F8) was studied in 8 patients with schizophrenia (SCH, mean age 36.5 ± 9.98) and 12 health controls (mean age 32.17 ± 5.6). We analyzed groups' performance (10 sessions) and cognitive differences in 3 time points (baseline, after training and follow-up) with generalized estimated equations. For SCH we also evaluate the impact on psychopathology.
Results: We found a group * time interaction for HEG-NFBK performance in the left hemisphere sites (F7 an Fp1) and a near-to-significant in the right frontotemporal region (F8), with no group differences and a significant time effect. Most of cognitive domains improved after intervention, including information processing speed, attention processing, working memory, executive functioning, verbal and visual learning. No group * time interaction was found. Results suggest that both groups benefit from HEG-NFBK training regardless of cognitive differences at baseline. No significant time effects were found for Calgary and PANSS total scale and subscales (positive, negative neither general).
Conclusion: To our knowledge, this is the first controlled trial showing effects of NFBK on cognitive performance improvement in schizophrenia.
Further research investigating the effects of HEG-NFBK training in schizophrenia should be performed.

Dear editor,

Cognitive impairments are strongly correlated to functionality and recovery rates in schizophrenia (SCH) (Green and Harvey, 2014; Grimes et al., 2017). Reductions in resting-state cerebral blood flow (CBF) and cerebral metabolism (Hill et al., 2004; Hoshi, 2005) have widely associated to these deficits, which are often treated as PFC dysfunction (Lewis and Glausier, 2016; Sakurai et al., 2016).

Currently, no pharmacological agent is approved for the treatment of the cognitive symptoms, evidencing the need for new interventions. Training the voluntary control of brain responses through operant conditioning - known as neurofeedback - has emerged as a non-pharmacological alternative to enhance neuroplasticity and cognition in this scenario, but not much has been explored in deep. For instance, there's a lack of studies on PFC blood perfusion neurofeedback (a simplified NIRs-based brain training popularly known as HEG-NFBK), which in thesis establishes an even closer relation to PFC dysfunction than brain wave training. The aim of this controlled clinical trial is to evaluate HEG-NFBK potential in generating cognitive enhancements in SCH.

Eight SCH patients (DSM-IV-R) (mean age 36.5 ± 9.98; 87.5% males; mean IQ of 95.33 (±11.73)) and 12 health controls (mean age 32.17 ± 5.6; 41.7% males; IQ of 113.92 (±6.71)) provided informed consent (approved by the local IRB). Subjects received HEG-NFBK training for 4 brain sites (F7, Fp1, Fp2 and F8), for 10 sessions, twice a week. Training was performed in eyes-open condition, using a headband containing

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one active channel connected to a Pocket Neurobics device (Biocomp Research Institute). Real-time oscillations in hemodynamics were calculated by a ratio of received red to infrared light (HEGratio = red light/infrared light) for each site separately, and displayed graphically to the participant with Bioexplorer software from CyberEvolution. This variable is called here as *HEG increase*, reflecting the intentional HEG

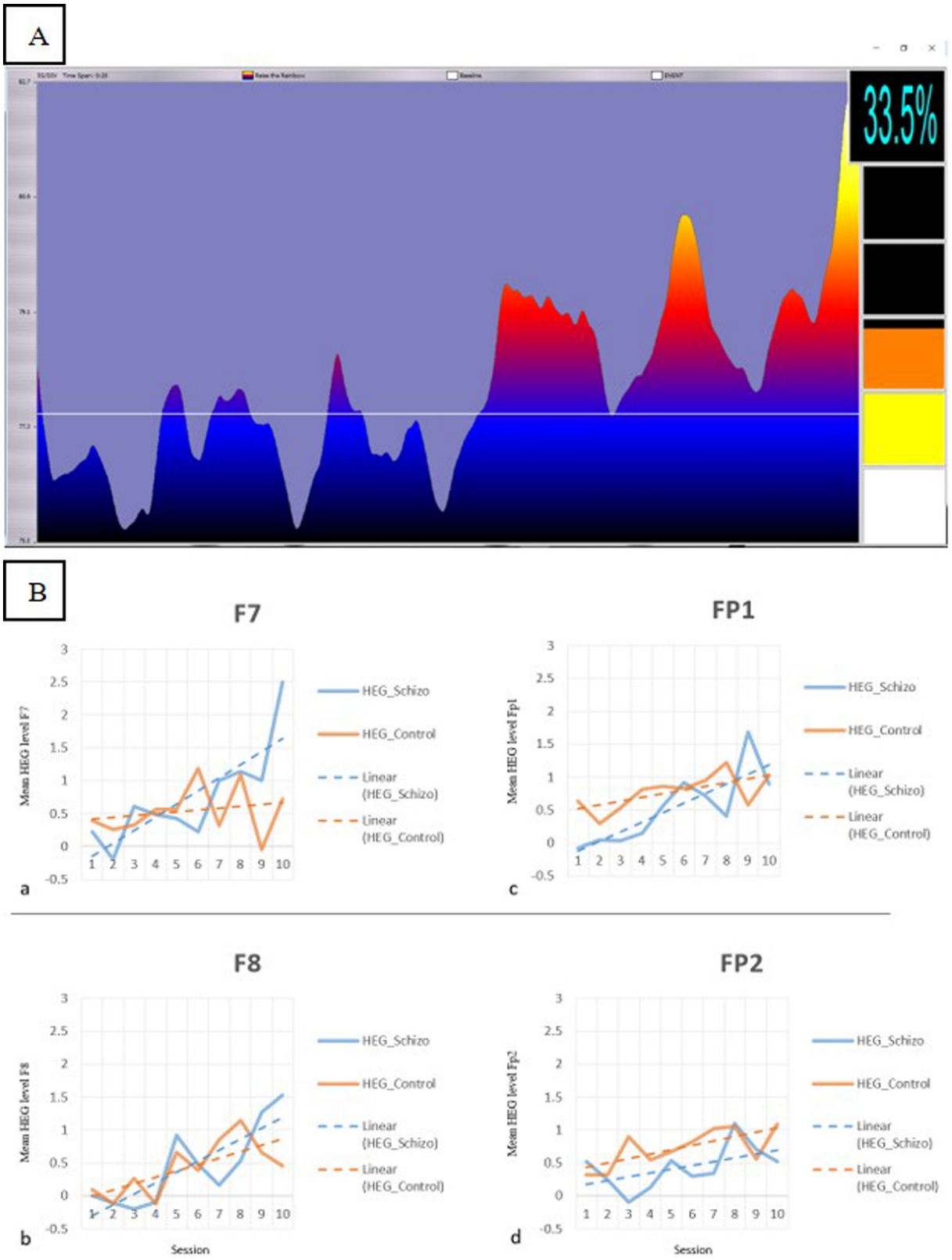

Fig. 1. A. Participant's screen of HEG autobaseline training design on Bioexplorer software; B. Mean HEG level along 10 sessions. Blue line reflects HEG level for SCH group while green line for the CTRL group. Figures a, b, c and d correspond respectively to F7, F8, Fp1 and Fp2 sites. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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ratio augmentation, associated to increase in blood flow oxygenation in the target area (Toomim and Carmen, 2009; Toomim et al., 2004) (see Fig. 1A). Training sessions started with 4 min in each site, increasing one minute every two sessions, achieving 8 min/site by the end.

Patients were assessed at baseline, after intervention and in a 3-month follow-up. Cognitive assessment was based on the Brazilian version of the Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery (MATRICS), and was performed by two independent psychologists for: speed of processing; attention; working memory; verbal learning; visual learning; reasoning; problems solving and executive function (Fonseca et al., 2017). Patients were clinically assessed using the Positive and Negative Syndrome Scale (Higuchi et al., 2014; Kay et al., 1987), Calgary Depression Scale (Addington et al., 1993) the Global Assessment of Functioning Scale (Endicott et al., 1976) and the Clinical Global Impressions-Severity Scale. Data were analyzed using generalized estimated equations (Gamma distribution and first-order autoregressive correlation structure), except for the Calgary scale, in which linear distribution was adopted. We adopted Sidak adjustment for multiple comparisons. Gender differences were analyzed using chi-squared test, age with *t*-test for independent sample and IQ with non-parametric Mann-Whitney *U* test.

We found a significant group*time interaction for HEG-NFBK performance for the left hemisphere sites (F7, $p < 0.001$; and Fp1, $p < 0.015$) and a near-to-significant for the right frontotemporal region (F8, $p < 0.059$) (see fig. 1B). Most of cognitive domains improved after the intervention: information processing speed (TMA, $p < 0.027$; BACS, $p < 0.001$; CWIT_composite, $p < 0.044$), attention processing (CPT, $p < 0.001$), working memory (SS, $p < 0.009$), executive functioning ($p < 0.026$; CWIT_condition3, $p < 0.001$), verbal (HVLT, $p < 0.001$) and visual learning ($p < 0.001$), with no group $*$ time interaction. Results suggest that both groups benefit from HEG-NFBK training regardless of cognitive differences at baseline.

Our study suggests that patients may be able to increase their HEG levels relative to their own baseline as much as healthy controls. In other words, they tend to respond to the task with the appropriate inner behavior. This is in line with Schneider (Schneider et al., 1992), who suggested that the patients were less efficient then controls in the beginning, but with prolonged training their ability to intentionally control their brain improved significantly.

Albeit exciting for patients and doctors, these findings should be seen as strictly exploratory and some limitations should be noted. The device used for HEG-NFBK only allows training changes in dynamic blood flow; we do not know how cerebral hemoglobin concentrations varied in this regard. The study had a small sample size, was not adjusted for IQ and had no sham group. Its interest relies on the fact of being the first controlled trial showing effects of NFBK on cognitive performance in schizophrenia, on the fact that patients seem to learn how to control their PFC blood flow and that such practice may positively affect their cognitive performance. Further research investigating the effects of HEG-NFBK training in schizophrenia should be performed.

Contributors

Gomes, JS: contributed with definitions of the study design and protocol procedures; she also contributed collecting data and analyzing the results; she contributed in the first draft of the manuscript and in the final version;

Ducos, DV: contributed with definitions of the neuropsychological evaluation procedures; she also contributed collecting data and analyzing the results. She reviewed and contributed in the final version of the manuscript;

Gadelha, A: contributed with definitions of the study design, with psychiatric evaluation procedures and selecting patients; he also contributed collecting data. He reviewed and contributed in the final version of the manuscript;

Ortiz, BB: contributed with definitions regarding the psychiatric evaluation procedures and collecting data; He contributed with the interpretation of results and also reviewed the final version of the manuscript;

Van Deusen, AM: contributed with definitions of the study design and protocol; He reviewed and contributed in the final version of the manuscript;

Akiba, HT: contributed with definitions of the protocol procedures; He reviewed and contributed in the final version of the manuscript;

Guimaraes, LSP: contributed with the statistical analysis and description of the results. He also reviewed and contributed in the final version of the manuscript;

Cordeiro, Q: contributed with definitions of the study. He reviewed and contributed in the final version of the manuscript;

Trevizol, AP: contributed with the interpretation of results, writing the first draft and in the final version of the manuscript;

Lacerda, A: contributed with definitions of the study design. He contributed in interpretation of results and in the final version of the manuscript.

Dias, AM: contributed with definitions of the study design and protocol procedures. He contributed in interpretation of results and in the final version of the manuscript.

Author disclosure

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2017.08.044.

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