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Letter to the Editor

Transcranial random noise stimulation for the treatment of negative symptoms in schizophrenia

Dear Editors,

Recently, studies applying transcranial direct current stimulation (tDCS) have shown promising results for the treatment of auditory hallucinations and negative symptoms in schizophrenia (Homan et al., 2011; Brunelin et al., 2012a, 2012b). The rationale for these studies was functional neuroanatomical alterations observed in schizophrenia, i.e. reduced frontotemporal functional connectivity, left temporoparietal hyperactivity and hypoactivity within the prefrontal cortex (left dorsolateral prefrontal cortex, DLPFC, and anterior cingulate regions) (Silbersweig et al., 1995; Sanfilipo et al., 2000; Lawrie et al., 2002). As anodal tDCS exerts excitatory and cathodal tDCS inhibitory effects on cortical excitability in the motor system (Nitsche and Paulus, 2000), Brunelin et al. hypothesized that cathodal tDCS of the temporoparietal junction can reduce persistent auditory hallucinations and anodal tDCS of the DLPFC can improve negative symptoms (Brunelin et al., 2012b). However, specific effects of anodal vs. cathodal stimulation in non-motor regions are experimentally difficult to differentiate and the further development of tDCS may be hampered by a lack of regional specificity.

Another new non-invasive brain stimulation technique which does not have these shortcomings is transcranial random noise stimulation (tRNS). tRNS produces a randomly oscillating current within defined thresholds, following the Gaussian curve around a midpoint, called "offset" (Terney et al., 2008; Chan et al., 2012). Switching the offset from zero towards positive current strength, e.g. 0.5 or 1 mA, inhibits negative polarisation during the oscillations and provides a unidirectional current flow analogously to tDCS. tRNS uses a rapidly changing current strength, in this case within the excitatory frequency of 100–640 Hz (Paulus, 2011). This is supposed to elicit more pronounced plasticity changes than tDCS which could be counteracted by homeostatic plasticity, reducing tDCS-induced excitability shifts (Monte-Silva et al., in press). The underlying neuronal correlate probably is a prolonged opening of the voltage-gated sodium channels (Nitsche et al., 2012; Monte-Silva et al., in press). To our knowledge, the treatment of psychiatric disorders with tRNS has only been addressed by Chan et al. (2012) so far in one patient with major depressive disorder.

Here, we report the case of a 29 year old male patient suffering from paranoid schizophrenia (DSM-IV) for 12 years. The first episode began at the age of 17 after daily cannabis abuse over two years. In the age of 25, he was able to stop drug abuse and maintained abstinence up to now. In the first episode, delusions and hallucinations subsided after treatment with antipsychotics. However, over the past years, there were at least two further psychotic episodes and the patient suffered from increasing negative symptoms (emotional withdrawal, blunted affect, poor rapport, and lack of spontaneity) and cognitive symptoms (disorganization, difficulties in abstract thinking, stereotyped thinking, and disturbance of volition), as well as feelings of depression and anxiety. During actual hospitalisation he was treated with clozapine 150 mg/day and haloperidol 10 mg/day for over all 10 weeks with constant dose for at least 4 weeks. For the treatment of affective symptoms he received lamotrigine 200 mg/day mg and pregabaline 375 mg/day without noteworthy impact on feelings of guilt, depression, and anxiety. The latter medications were stable for at least three weeks prior to add-on tRNS and clozapine serum levels were measured during the treatment (avg. 380 ng/ml). tRNS was delivered by the Eldith Plus Stimulator (neuroConn, Ilmenau, Germany) with 2 mA amplitude, offset at 1 mA, frequency 100–640 Hz, for 20 min with 15 s ramp-in/ramp-out, deriving from tDCS safety criteria (Paulus, 2011). Electrodes (35 cm^2) were coated by saline-soaked sponges and stimulation was performed twice daily for ten days with the anode over the left DLPFC and the cathode over the right orbitofrontal region (Keeser et al., 2011). Clinical assessment and cognitive tasks were performed by the same rater blinded for the treatment before first (baseline) and after the 20th stimulation.

At baseline, the patient presented with a Positive and Negative Symptom Scale (PANSS) score of 102 (subscales: positive 9, negative 34, cognition 32, excitement/hostility 4, depression/anxiety 23), a Scale for the Assessment of Negative Symptoms (SANS) score of 73, and a Calgary Depression Scale in Schizophrenia (CDSS) score of 6. For the Trail Making Test (TMT), he needed 19 s (TMT-A) and 55 s (TMT-B). After 20 stimulations he showed a modest clinical improvement in the domain of negative symptoms (i.e. emotional withdrawal, poor rapport, lack of spontaneity), cognition (i.e. disorganization, difficulties in abstract thinking, and disturbance of volition) and depression/anxiety: PANSS score 68 (subscales: positive 5, negative 21, cognition 25, excitement/hostility 4, depression/anxiety 13), SANS score 48, CDSS score 5, TMT-A 17 s, TMT-B 38 s. tRNS was well tolerated and there were no adverse effects. However, there are some limitations: clinical improvement could also be due to non-specific effects of the treatment or a delayed onset of medication effects. Furthermore, information processing (TMT-A) and executive functioning (TMT-B) were intact at baseline and the modest improvement could be due to learning effects. There also may be several factors limiting the efficacy of tRNS, e.g. chronicity of the disease, short duration of treatment and concomitant medication (Fertonani et al., 2011). For example, lamotrigine and pregabaline may potentially decrease the neuromodulatory effects of tRNS by blocking the opening of voltage-gated sodium channels (lamotrigine) or voltage-gated calcium channels (pregabaline) (Nitsche et al., 2012). However, this case report supports the findings of cognitive enhancement by excitatory non-invasive electrical brain stimulation (Kuo and Nitsche, 2012; Nitsche et al., 2012). Thus, therapeutic effects of tRNS in psychiatric disorders merit systematic investigation.

Statement of interest

The authors declare no conflict of interest.

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