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Case Report

Psychiatry/Mental Health Section

Improving Diagnostic and Treatment Precision for Negative Symptoms of Schizophrenia using Quantitative Electroencephalography and Transcranial Direct Current Stimulation: A Case Report

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ABSTRACT

Schizophrenia is a major mental illness associated with significant disability. Negative symptoms represent a key determinant of long-term morbidity and poor functional outcomes. This is a case report of a 22-year-old male presenting with poor functional recovery despite apparent resolution of psychotic symptoms (hallucinations and delusions) on antipsychotics. In follow-up his antipsychotic dose was up titrated along addition of anti-depressants with suspicion of primary negative vs depressive symptoms. He did not show any improvement in his negative symptoms such as avolition, anhedonia, apathy, alogia, asociality. Comprehensive reassessment, including clinical evaluation and Quantitative Electroencephalography (qEEG), showed findings such as frontal dysfunction and raised the possibility of secondary negative symptoms related to antipsychotic treatment rather than a primary deficit state. Based on this, pharmacotherapy was optimised by switching from high-dose risperidone to amisulpride and augmenting with transcranial Direct Current Stimulation (tDCS) targeting the left dorsolateral prefrontal cortex. Significant improvement was observed in affect, speech output, social interaction, and Cognitive Performance (CPT), supported by normalisation of electrophysiological markers. This case highlights the importance of distinguishing primary and secondary negative symptoms and suggests a potential role for qEEG in guiding pharmacological and other interventions. This case study challenges the conventional wisdom that uptitrating antipsychotics in incomplete remission of psychotic illness can be counterproductive leading to secondary negative symptoms. In such cases adequacy of dopamine blockade can be assessed by qEEG.

Keywords: Cognitive dysfunction, Continuous performance test, Electrophysiological biomarkers, Neurostimulation, Precision psychiatry

CASE REPORT

A 22-year-old male, graduate, belonging to a lower socio-economic status, presented with predominantly negative symptoms, including anhedonia, avolition, asociality, apathy, and decreased speech output for past 15 months. The patient had a well-adjusted premorbid personality characterised by good academic performance and adequate social and interpersonal skills. There was no past psychiatric or significant medical history. Developmental history was normal, with no evidence of neurodevelopmental disorders, neurotic traits, or conduct disorder. The illness onset was acute, approximately 15 months prior to presentation, precipitated by a period of sleep deprivation. The initial episode was characterised by sleep disturbance, auditory hallucinations, agitated behaviour, and impaired self-care, for which he was admitted briefly and started on risperidone. Following initiation of treatment, there was significant improvement in positive symptoms. However, negative symptoms persisted. Over the subsequent 15 months, risperidone was gradually titrated up to 6 mg/day for residual symptoms. Trihexyphenidyl 2 mg/day was added prophylactically for extrapyramidal symptoms. Even after adequate dose optimisation and adherence, there was no improvement in negative symptoms [1]. Fluoxetine was initiated at 20 mg/day for nearly a month to address possible depressive features but this did not lead to any clinical benefit. He was presented to the psychiatry department for further management.

The patient was appropriately dressed and well groomed. He was cooperative but showed decreased spontaneity during the interview, making rapport difficult to establish. He was conscious, alert, and oriented to time, place, and person. Psychomotor activity was reduced, and eye contact was intermittent. Speech was characterised by reduced rate, low volume, decreased spontaneity, and increased reaction time. Responses were brief but relevant. Mood was subjectively reported as "fine," with a blunted and apathetic affect. Thought form showed loosening of associations with occasional derailment and reduced goal-directedness. Poverty of thought content was present. The patient denied hallucinations or delusions. Patient had Grade IV insight [2]. Judgment was intact.

The Positive and Negative Syndrome Scale (PANSS) [3] scores showed Positive: 13, Negative: 43, and General Psychopathology: 28, indicating a predominant negative symptom burden. Cognitive function was assessed using the Continuous Performance Test (CPT) [4]. The patient demonstrated marked vigilance deficits, with omission errors of 50 and reaction time variability of 143 ms, showing poor attention and reduced cognitive control. Electrophysiological assessment was performed using the Muse 2 wearable EEG device in association with the Myndlift platform to obtain neurophysiological measures. Muse 2 facilitates the acquisition of research-grade EEG data as supported by several published studies [5-8]. EEG data serves as adjunctive information alongside comprehensive clinical assessment rather than as standalone diagnostic marker. Relative elevations in theta/beta ratios in the central (Cz) and left frontal (F3) regions as well as altered alpha recovery patterns suggested possible frontal network dysregulation and reduced cortical adaptability.

Pharmacological intervention included cross-titrating risperidone with amisulpride over a five-day period during which risperidone was

gradually tapered and stopped while amisulpride was increased to a target therapeutic dose of 600 mg/day to leverage its specific D2/D3 receptor affinity profile. Concurrently, trihexyphenidyl and fluoxetine were completely discontinued to eliminate potential secondary confounding effects. To target the persistent negative and cognitive symptoms, non invasive neuromodulation was initiated via a localised tDCS protocol. Utilising stimulation parameters derived from established randomised controlled trials [9-11], anodal stimulation was applied to the left dorsolateral prefrontal cortex (F3) and cathodal stimulation to the right supraorbital region (Fp2) , with a current intensity of 2.0 mA and a session duration of 20 minutes administered twice daily for a total of 20 sessions.

Following informed consent, the patient tolerated the intervention well over the full course, reporting only a minimal, transient mild tingling sensation over the electrode site with no significant adverse effects noted. Simultaneously, adjunctive occupational therapy and structured activity scheduling were integrated to translate these neurophysiological improvements into functional, real-world social interactions and improved daily routines.

There was progressive improvement in speech output, social interaction. Patient brief replies improved to coherent speech. The patient also showed increased interest in participating in group activities.

Accuracy improved from 85% to 99% (absolute improvement: +14 percentage points; relative improvement: +16.5%). Omission errors were reduced from 50 to 3 (-94.0%), indicating improvement in sustained attention and vigilance. Reaction time variability decreased from 143 ms to 79 ms (-44.8%), showing improvement in response consistency [Table/Fig-1].

Parameter	Baseline (Risperidone)	After intervention (Amisulpride+tDCS)	Absolute change	Relative change
Accuracy	85%	99%	+14	+16.5%
Omission errors	50	3	-47	-94.0%
RT variability	143 ms	79 ms	-64 ms	-44.8%

[Table/Fig-1]: Neurocognitive evaluation (CPT performance).

Central (Cz) theta/beta ratio decreased from 2.45 to 1.76 (–28.2%), indicating restoration of cortical arousal. Alpha recovery improved from -1% to +6%, indicating improvement in neuroplasticity and adaptability. The frontal (F3) theta/beta ratio decreased from 2.81 to 1.63 (–42.0%), this demonstrates reversal of hypofrontality. Interhemispheric asymmetry (L/R theta-beta ratio) improved from 1.28 to 0.86 (–32.8%), indicating better hemispheric balance [Table/Fig-2].

Region	Metric	Baseline (Pre)	Outcome (Post)	Magnitude of Change
Central (Cz)	Theta/Beta Ratio	2.45	1.76	-28.2%
	Alpha Recovery	-1%	+6%	Normalised
Frontal (F3)	Theta/Beta Ratio	2.81	1.63	-42.0%
Symmetry	Theta/Beta (L/R)	1.28	0.86	-32.8%

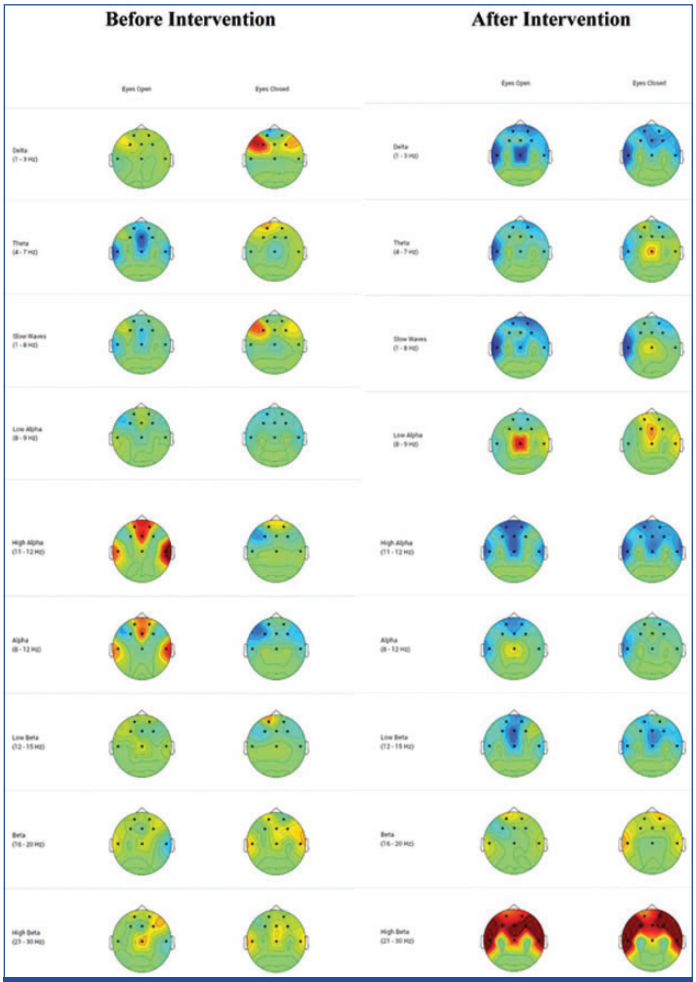
[Table/Fig-2]: Mechanistic Electrophysiological Shifts (qEEG).

Psychopathology improved following optimisation with amisulpride and adjunctive tDCS. The PANSS positive symptom score decreased from 13 to 9, indicating further reduction in residual positive symptoms. A more significant improvement was noted in the PANSS negative symptom score, which decreased from 43 to 19, indicating improvement of negative symptoms such as avolition, anhedonia, apathy, and reduced speech output. The PANSS general psychopathology score also decreased from 28 to 23 [Table/Fig-3]. These findings indicate that the intervention was associated with improvement, particularly in the negative symptoms domain, which was the primary therapeutic target in this patient.

Brain maps of qEEG activity are presented, with blue representing lower-than-normal activity and red representing higher-than-normal activity [Table/Fig-4]. At the one-month follow-up, the patient

Variables	Before Intervention	After Intervention
Positive	13	9
Negative	43	19
General	28	23

[Table/Fig-3]: Difference in PANSS score before and after interventions.



[Table/Fig-4]: Representative qEEG brain maps before and after intervention.

maintained the clinical improvement, with sustained reduction in negative symptoms and continued improvement in social interaction and speech output.

DISCUSSION

Schizophrenia is a chronic psychiatric disorder with a global prevalence of approximately 0.3-0.7%. It contributes substantially to long-term morbidity and functional impairment [9]. Approximately 40-60% of individuals with schizophrenia exhibit clinically significant negative symptoms, with nearly half presenting at illness onset. Although negative symptoms often emerge early, including during the prodromal phase, their course is heterogeneous [12].

This case highlights the clinical challenge of differentiating primary (deficit) negative symptoms from secondary negative symptoms in schizophrenia. Persistent negative symptoms lead to long-term morbidity, poor functional recovery, and reduced quality of life. Early identification of primary deficit syndrome is vital as they show poor response to conventional pharmacotherapy whereas the secondary negative symptoms are usually reversible [10,12]. In this case, the persistence of negative symptoms despite resolution of positive symptoms raised the possibility of secondary causes which include antipsychotic induced extrapyramidal symptoms, depression.

The tDCS is a non-invasive neuromodulation technique that modulates cortical excitability and has shown promise in addressing negative and cognitive symptoms [13]. qEEG provides objective insights into brain function, with schizophrenia commonly

associated with increased slow-wave activity, altered beta activity, and frontal hypofunction. These electrophysiological patterns may help in differentiating primary deficit states from secondary negative symptoms by identifying potentially reversible network dysfunction [11]. In addition, cognitive assessment using CPT, as implemented through platforms such as Myndlift, allows objective quantification of attention and vigilance deficits, enabling correlation with clinical and electrophysiological findings [14]. Together, these tools may aid in clinical phenotyping and guide targeted, individualised intervention.

Exploratory EEG-derived measures provided supplementary physiological information that complemented the clinical assessment; however, these findings should not be interpreted as validated biomarkers capable of differentiating primary from secondary negative symptoms. Baseline findings showed increased theta/beta ratio and impaired alpha recovery which is suggestive of cortical hypoarousal and disrupted thalamocortical regulation. These patterns are consistent with frontal network dysfunction rather than a fixed deficit state [11,15]. Following intervention, normalisation of these electrophysiological markers paralleled clinical improvement (as seen in PANSS and CPT outcomes). This temporal association supports the utility of qEEG as a state marker, aiding in distinguishing potentially reversible secondary negative symptoms from primary deficit syndrome.

Negative symptoms are associated with dysfunction of mesocortical dopaminergic pathways, particularly involving the dorsolateral prefrontal cortex and midbrain connections [16,17]. D3 receptors also play an important role in motivation, cognition, and social functioning. Preclinical studies suggest that improvement in negative symptoms and cognition occur through D2/D3 modulation [18,19]. Based on the findings, risperidone was cross-titrated with amisulpride because of its D2/D3 receptor affinity [20,21].

Anodal tDCS was given over the left DLPFC as it is involved in executive function, motivation and goal-oriented behaviour. Dysfunction of the DLPFC has been consistently associated with negative symptoms and hypofrontality in schizophrenia [16,22]. Anodal tDCS increases cortical excitability and enhances neural plasticity. In this case, targeted stimulation resulted in improvements in affect, speech output, and social engagement, along with objective gains in CPT and electrophysiological normalisation (qEEG findings). These findings are consistent with prior randomised controlled trials that demonstrate that tDCS reduces negative symptoms [13,23].

When compared directly to the existing literature, improvements observed in this patient are robust. In a major randomised controlled trial by Valiengo L da CL et al., active tDCS over a 6-week period yielded a statistically significant but clinically modest reduction in PANSS negative scores among patients with schizophrenia [23]. By contrast, this patient achieved a reduction in PANSS negative scores from 43 to 19. This response highlights the therapeutic benefit of intensive, twice-daily tDCS along with optimisation of the medication through amisulpride cross-titration. Furthermore, the patient's cognitive improvement is demonstrated by a 94% drop in CPT omission errors The patient also demonstrated steadier reaction times. Similar improvements in attention and working memory were previously reported by Jeon DW et al. [24] using adjunctive prefrontal tDCS. qEEG showed a 42% reduction in the frontal (F3) theta/beta ratio which may be compared with the clinical series published by Surmeli T et al., on qEEG-monitored interventions [14], reinforcing the hypothesis that reversals of cortical hypoarousal and frontal network imbalances can provide meaningful functional recovery.

Improvement was noted across multiple domains, including a reduction in PANSS negative scores (43 → 19), marked decrease in omission errors and reaction time variability, reduction in theta/beta ratio and improved alpha dynamics.

CONCLUSION(S)

Negative symptoms in schizophrenia remain a major therapeutic challenge. This case demonstrates that integration of qEEG-guided assessment with targeted neuromodulation using tDCS, along with pharmacological optimisation, may offer meaningful clinical benefits. Further research is needed to establish the role of such personalised approaches in routine clinical practice.

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