INPLASY PROTOCOL

Corresponding author:
Wenqian Huang

huangwenqian05@163.com

Author Affiliation:
Beijing Huilongguan Hospital

Efficacy of noninvasive brain stimulation for general psychopathology symptoms in schizophrenia: A meta-analysis

Huang, WQ[1]; Chai, JB[2]; Li, Y[3].

Review question / Objective: Investigating the efficacy of noninvasive brain stimulation (NIBS) on the treatment of general psychopathology symptoms（GPS）in schizophrenia.

Condition being studied: Non-pharmacological interventions, such as noninvasive brain stimulation (NIBS), offers a novel and key approach in the treatment of schizophrenia. Although several meta-analyses have addressed the benefits of NIBS on negative and positive symptoms of schizophrenia, there is little attention paid to general psychopathology symptoms (GPS) treatment for schizophrenia at present. GPS covers a range of symptoms, which are critical to functional outcome. The presence of GPS is likely to affects patients' functional outcome and quality of life. Therefore, the intervention of GPS is also very critical. However, the current NIBS technology focuses more on the main positive symptoms and negative symptoms, and there is a lack of intervention studies on GPS-specific NIBS. Treatment of GPS in schizophrenia is an important and often neglected aspect of the management of schizophrenia. In present study, we aim to investigate efficacy of NIBS on the treatment of GPS in schizophrenia and to explore the possible moderators of NIBS treatment efficacy on GPS in schizophrenia.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 February 2023 and was last updated on 18 February 2023 (registration number INPLASY202320082).

INTRODUCTION

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a novel and key approach in the treatment of schizophrenia. Although several meta-analyses have addressed the benefits of NIBS on negative and positive symptoms of schizophrenia, there is little attention paid to general psychopathology symptoms (GPS) treatment for schizophrenia at present. GPS covers a range of symptoms, which are critical to functional outcome. The presence of GPS is likely to affects patients' functional outcome and quality of life. Therefore, the intervention of GPS is also very critical. However, the current NIBS technology focuses more on the main positive symptoms and negative symptoms, and there is a lack of intervention studies on GPS-specific NIBS. Treatment of GPS in schizophrenia is an important and often neglected aspect of the management of schizophrenia. In present study, we aim to investigate efficacy of NIBS on the treatment of GPS in schizophrenia and to explore the possible moderators of NIBS treatment efficacy on GPS in schizophrenia.

METHODS

Search strategy: Five databases were searched, including PubMed, Web of Science, PsycINFO, Google Scholar, and the China National Knowledge Infrastructure (CNKI).

Participant or population: Adult patients with schizophrenia.

Intervention: The intervention used in this study was non-invasive brain stimulation, which mainly included repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS).

Comparator: The comparator in this study called control group and the control group received placebo treatment. The patients in the control group were stimulated with the coil of the same shape as the real coil. This special coil can produce the same sound as the real coil but gives no stimulation during the treatment.

Study designs to be included: A meta-analysis will be carried out based on the data of published articles to investigate the efficacy of noninvasive brain stimulation on the treatment of GPS in schizophrenia and to explore the possible moderators of NIBS treatment efficacy on general psychopathology symptoms in schizophrenia. All included studies were randomized sham-controlled study design.

Eligibility criteria: Both the inclusion criteria and exclusion criteria were utilized as follows:Inclusion Criteria:1. Randomized sham-controlled study design; 2. Patients diagnosed with schizophrenia according to standardized criteria such as Diagnostic and Statistical Manual of Mental Disorders (DSM), International Statistical Classification of Diseases and Related Health Problems (ICD) or Chinese Classification of Mental Disorders (CCMD);3. Application of rTMS or tDCS interventions; 4. PANSS was used to assess general psychopathology symptoms as outcome measures (Kay et al., 1987); 5. Psychotropic medication dosages were unchanged before the intervention and maintained throughout the trial; 6. Written in English or Chinese.Exclusion Criteria:1. Participants had prominent positive symptoms or negative symptoms; 2. Patients displayed other psychotic symptoms; 3. No data on the general psychopathology symptoms scores were reported; 4. Articles were duplicate records or included overlapping samples; 5. Articles were case reports, editorials, comments, or review papers; 6. There was no control group or a lack of information for the control group (e.g., no symptoms or data on age were reported);7. The age of participants was under 18 years old.

Information sources: Five databases were searched, including PubMed, Web of Science, PsycINFO, Google Scholar, and the China National Knowledge Infrastructure (CNKI). The search terms were as follows: "transcranial magnetic stimulation", "TMS", "transcranial direct current stimulation", "tDCS", "brain stimulation", "schizophrenia", "psychotic disorder", "psychosis", "general symptom",

"general psychopathology", "positive and negative syndrome scale", "PANSS", "randomized controlled trial" and "RCT".

Main outcome(s): Investigated the efficacy of noninvasive brain stimulation (NIBS) on the treatment of general psychopathology symptoms（GPS）in schizophrenia.

Quality assessment / Risk of bias analysis: The quality of each study was assessed using the modified Jadad scale. Each study was evaluated using the following criteria: randomization, blinding strategy, withdrawals/dropouts, inclusion/exclusion criteria, adverse effects, and statistical analysis. Five domains are included in the assessment of risk of bias: bias derived from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported result. The methodological quality of the studies was decided by consensus between the assessment ratings of the first and the corresponding authors.

Strategy of data synthesis: A total of 35 studies were identified. We extracted the following information from the included studies: name of the first author and year of publication, demographic and clinical characteristics (sample size, the number of males and females, mean age), survey area, diagnosis criteria, outcome measurements, groups, and the number of sessions of rTMS or tDCS.

Subgroup analysis: The effects of different types of NIBS on the efficacy of general psychopathology symptoms in schizophrenia were analyzed by subgroup analysis and also the parameters of rTMS was analyzed by subgroup analysis using frequency as variables.

Sensitivity analysis: Sensitivity analysis will be conducted on the extracted data.

Language restriction: English and Chinese.

Country(ies) involved: China.

Keywords: Schizophrenia, PANSS, rTMS, tDCS, general psychopathology, meta-analysis.

Contributions of each author:
Author 1 - Wenqian Huang - The author drafted the manuscript.
Email: huangwenqian05@163.com
Author 2 - Jiabao Chai - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Email: chaijiabao1988@126.com
Author 3 - Ying Li - The author provided statistical expertise.
Email: yyjnly@126.com