GIBA, Aleksandra, NICZYPORUK, Patrycja, ZAJKOWSKA, Izabela, IŁENDO, Kamila, KRÓLIKIEWICZ, Wiktor, MARECKI, Rafał and KICMAN, Aleksandra. Music therapy and repetitive transcranial magnetic stimulation - nonpharmacological interventions in schizophrenia. Quality in Sport. 2025;41:59941. eISSN 2450-3118.

https://doi.org/10.12775/QS.2025.41.59941 https://apcz.umk.pl/QS/article/view/59941

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2025.

This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Torun, Poland. Open Access: This article is distributed under the terms of the Creative Commons Attribution Noncommercial License, which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (http://creativecommons.org/licenses/by-nc-sa/4.0/), which permits unrestricted, non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interest regarding the publication of this paper. Received: 31.03.2025. Revised: 30.04.2025. Accepted: 12.05.2025. Published: 12.05.2025.

MUZYKOTERAPIA I PRZEZCZASZKOWA STYMULACJA MAGNETYCZNA – NIEFARMAKOLOGICZNE INTERWENCJE W LECZENIU SCHIZOFRENII

MUSIC THERAPY AND REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION - NONPHARMACOLOGICAL INTERVENTIONS IN SCHIZOPHRENIA

Aleksandra Giba https://orcid.org/0009-0003-2384-1662 giba.aleksandra99@gmail.com Military Institute of Medicine ul. Szaserów 128, 04-141 Warszawa

Patrycja Niczyporuk https://orcid.org/0009-0001-5834-5277 39916@student.umb.edu.pl Medical University of Bialystok ul. Jana Klinskiego 1, 15-089 Bialystok

Izabela Zajkowska https://orcid.org/0009-0002-8526-7339 36831@student.umb.edu.pl Medical University of Bialystok ul. Jana Klinskiego 1, 15-089 Bialystok

Kamila Hendo https://orcid.org/0009-0004-6646-5350 kamila.ilendo@gmail.coml Medical University of Bialystok ul. Jana Klinskiego 1, 15-089 Bialystok Wiktor Królikiewicz https://orcid.org/0009-0009-2749-3419 wiktorkr97@gmail.com Independent Researcher SPZOZ w Siedlcach, Jana Kilińskiego 29, 08-110 Siedlce

Rafał Marecki https://orcid.org/0009-0002-0815-1244 rafal.marecki@sd.umb.edu.pl Department of Psychiatry, Medical University of Bialystok ul. Wołodyjowskiego 2, 15-272 Bialystok

Aleksandra Kicman https://orcid.org/0000-0002-4933-1893 olakicman@gmail.com Department of Aesthetic Medicine, Medical University of Bialystok, Bialystok, Poland. ul. Akademicka 3, 15-267 Białystok

ABSTRACT

Cel badań:

Muzykoterapia (MT) stanowi obiecującą metodę wspomagania redukcji lęku u pacjentów onkologicznych, jednak jej mechanizmy działania pozostają niejasne. Celem badania jest analiza wpływu MT na oś jelitowomózgową, w tym na mikrobiotę jelitową, regulację cytokin zapalnych oraz poziom neuroprzekaźników.

Materialy i metody:

Przeprowadzono przegląd literatury, analizując badania dotyczące wpływu MT na stan zapalny, skład mikrobioty jelitowej oraz modulację neurochemiczną u pacjentów onkologicznych oraz osób z zaburzeniami neuropsychiatrycznymi, w tym schizofrenią i depresją.

Wyniki:

Badania sugerują, że MT może zmniejszać objawy lękowe u pacjentów z nowotworami poprzez obniżenie poziomu prozapalnych cytokin, takich jak IL-6 i IL-8, oraz modulację neuroprzekaźników związanych z nastrojem, np. serotoniny i dopaminy. Ponadto, istnieją dowody na wpływ MT na mikrobiotę jelitową, co może odgrywać kluczową rolę w regulacji osi jelitowo-mózgowej. Wyniki badań nad schizofrenią wskazują również na potencjalne korzyści MT w redukcji objawów psychotycznych, poprawie interakcji społecznych i zwiększeniu elastyczności poznawczej, choć efekty te często są krótkotrwałe.

Wnioski

MT jest bezpieczną i skuteczną metodą wspierania dobrostanu emocjonalnego oraz funkcji odpornościowej u pacjentów onkologicznych. Jej wpływ na oś jelitowo-mózgową wskazuje na nowy potencjalny mechanizm terapeutyczny, wymagający dalszych badań. Korzyści płynące z MT w zaburzeniach neuropsychiatrycznych podkreślają jej wartość jako terapii wspomagającej w różnych kontekstach klinicznych.

ABSTRACT

Objective:

Music therapy (MT) has emerged as a promising non-pharmacological intervention for alleviating anxiety in cancer patients. However, the mechanisms underlying its effects remain unclear. This study aims to explore the influence of MT on the gut-brain axis, particularly its impact on gut microbiota, inflammatory cytokine regulation, and neurotransmitter levels.

Materials and Methods:

A literature review was conducted, analyzing studies on MT's effects on inflammation, gut microbiota composition, and neurochemical modulation in cancer patients and individuals with neuropsychiatric disorders, including schizophrenia and depression.

Results:

Research suggests that MT can reduce anxiety symptoms in cancer patients by lowering levels of proinflammatory cytokines such as IL-6 and IL-8 while modulating mood-related neurotransmitters like serotonin and dopamine. Additionally, studies indicate that MT may influence gut microbiota composition, which plays a crucial role in the gut-brain axis. Findings from schizophrenia studies further highlight MT's potential in reducing psychotic symptoms, improving social interaction, and enhancing cognitive flexibility, though effects are often transient.

Conclusions:

MT presents a safe and effective method for improving emotional well-being and immune function in cancer patients. Its impact on the gut-brain axis suggests a novel therapeutic pathway, warranting further investigation. Additionally, MT's benefits for neuropsychiatric disorders reinforce its potential as an adjunctive therapy for broader clinical applications.

Słowa kluczowe: muzykoterapia, schizofrenia, przezczaszkowa stymulacja magnetyczna

Keywords: music therapy, schizophrenia, repetitive transcranial magnetic stimulation

Introduction

Schizophrenia is a chronic mental disorder that significantly impacts patients' functioning, limiting their ability to lead independent lives. Despite advances in pharmacotherapy, achieving full symptom control remains challenging, particularly in treatment-resistant schizophrenia. This has led to the exploration of alternative and adjunctive therapeutic approaches that could enhance treatment efficacy.

One of the non-pharmacological approaches used as an adjunctive therapy for schizophrenia is music therapy (MT). It is increasingly recognized as a valuable intervention for a variety of neurological and psychiatric conditions. Recent research has explored its potential in modulating the gut-brain axis, reducing inflammation, and improving neurotransmitter balance, particularly in cancer patients experiencing anxiety. Studies suggest that MT may influence gut microbiota composition, regulate pro-inflammatory cytokines such as IL-6 and IL-8, and enhance serotonin and dopamine levels, contributing to improved emotional and immune function.

Beyond cancer-related anxiety, MT has been investigated for its therapeutic effects on autism spectrum disorders (ASD), dementia, depression, insomnia, and schizophrenia. In schizophrenia, studies have demonstrated improvements in emotional regulation, social interaction, and quality of life, though long-term benefits remain uncertain. Active MT approaches, such as playing musical instruments and group singing, have been associated with reduced negative symptoms and enhanced cognitive flexibility. Specific interventions, such as listening to Mozart's compositions, have been linked to increased functional connectivity in brain regions associated with sensorimotor integration and mood regulation.

In addition to MT, repetitive transcranial magnetic stimulation (rTMS) is emerging as an adjunct therapy for schizophrenia. This non-invasive neuromodulation technique has shown promise in reducing both positive and negative symptoms by altering neural plasticity. While rTMS does not directly impact gut microbiota, studies indicate that it can modulate brain activity in regions implicated in schizophrenia, such as the dorsolateral prefrontal cortex and temporal-occipital cortex. Research suggests that rTMS, particularly when combined with antipsychotic medication, may enhance cognitive flexibility, reduce auditory hallucinations, and improve social functioning.

Despite these promising findings, both MT and rTMS exhibit variability in their effectiveness depending on the method of application, patient characteristics, and duration of therapy. Some studies indicate short-term benefits, while others suggest that repeated sessions over an extended period are necessary for sustained improvements. Future research should focus on optimizing treatment protocols, identifying patient subgroups that may benefit most, and further elucidating the underlying mechanisms of action for both therapies.

Material and methods

We searched the PubMed, Google Scholar, and Web of Science databases using the following keywords: "schizophrenia", "non-pharmacological interventions", "repetitive transcranial magnetic stimulation", "music therapy" and their combinations. The selected articles were analyzed to assess the role of transcranial magnetic stimulation in schizophrenia, with a particular focus on therapeutic strategies and their impact on clinical outcomes.

This review covers findings on non-pharmacological interventions, such as transcranial magnetic stimulation. It is narrative rather than systematic in nature and, while comprehensive, may not include all relevant studies. Methodological and interpretative limitations should be taken into account.

Aim

This article aims to explore the therapeutic potential of music therapy and repetitive transcranial magnetic stimulation in neurological and psychiatric conditions, with a particular focus on their effects on brain function, emotional well-being, and cognitive flexibility. By reviewing recent studies, we seek to highlight the mechanisms underlying these interventions, their impact on specific disorders, and the challenges associated with their clinical implementation.

Results

Music therapy

Music therapy (MT) is a promising method to support anxiety reduction in cancer patients, but its mechanisms of action are not fully understood. Studies suggest that MT may affect the gut-brain axis by modulating the gut microbiota, regulating levels of inflammatory cytokines (e.g., IL-6, IL-8) and neurotransmitters such as serotonin and dopamine. Disorders of this axis have been linked to both cancer and anxiety symptoms. A study by Sun et al. confirms that MT can reduce anxiety symptoms in cancer patients, which is associated with a reduction in levels of pro-inflammatory cytokines such as IL-6 and IL-8, and effects on mood-regulating neurotransmitters. Importantly, the results indicate a possible effect of MT on the gut microbiota, suggesting its role in modulating the gut-brain axis. These findings underscore the potential of MT as a non-pharmacological, safe method to support both the emotional state and immune function of cancer patients (1).

Gassner et al. reviewed the available literature examining the effects of music therapy in the treatment of autism spectrum disorders (ASD), dementia, depression, insomnia and schizophrenia. For schizophrenia, only active testing methods were used, which included playing music. These interventions resulted in improvements in emotional aspects and sense of well-being, but no significant improvements in patients' overall functioning were found (2)

Yang et al. conducted a study on the effects of music therapy on brain function and schizophrenia symptoms. Patients listening to Mozart's music for 30 days showed an increase in functional activity (FC) in the right medial temporal gyrus (MTG) and increased MTG-island connectivity. In addition, an increase in FC between the MTG and the medial temporal curve indicated better sensorimotor integration. The positive changes FC correlated with a reduction in symptoms on the PANSS scale, although the effect faded after six months (3).

A study by Pinar et al. examined the effects of music therapy on auditory hallucinations and quality of life in patients with schizophrenia. Patients in the experimental group listened to music in the key of Rast for 15 minutes while they experienced auditory hallucinations. The music was played on an MP3 player through headphones. The results of the study showed that the severity of auditory hallucinations and positive symptoms decreased after hospitalization, and the improvement in the quality of life of patients in the experimental group was significant. No such clear change was observed during hospitalization. Six months after discharge, these patients reported an increase in quality of life in physical, mental and environmental aspects (4).

The Lu et al. study involved group music therapy, which included 10 sessions of active and passive music therapy. Patients participated in activities that included a variety of musical activities: listening to music, singing popular Taiwanese songs, playing percussion instruments, and watching music videos and discussing music. The study showed that group music therapy led to significant improvements in psychotic symptoms (reduced PANSS scale values) and depressive symptoms (lower CDSS scale scores) compared to the control group. However, these effects were short-lived and did not persist after three months (5).

A similar study by Hayashi et al. examined the effectiveness of group music therapy in female patients hospitalized with a diagnosis of schizophrenia or affective schizophrenia. The therapy consisted of regular meetings in which patients participated in a variety of musical activities, such as listening to music, singing in a choir or performing simple exercises with instruments. Improvements in negative symptoms of schizophrenia and interpersonal relationships in the therapy group were observed, but the effect appeared to be short-lived, again suggesting that music therapy may have only a superficial, short-term effect (6).

A study by Tan et al. tested the effectiveness of Cognitive Remediation Therapy (CRT) and music and dance therapy (MDT) in patients with schizophrenia. The CRT therapy consisted of three modules examining the subjects' thinking flexibility, working memory and planning mainly while performing various tasks on a piece of paper. The MDT group participated in activities including learning to play the dulcimer and dance. The results showed that patients in the CRT group showed significant improvements in cognitive function, especially in flexibility of thinking and memory, while the MDT group also showed improvements, but to a lesser extent. Both groups improved social function (7).

A study by Gold et al. tested the effectiveness of MT among patients with low motivation for other forms of therapy. Participants who were assigned to the MT group attended 2 individual sessions per week for 3 months. The therapy was based on a resource-based approach that focused on patients' strengths, expressing emotions through music and jointly setting therapy goals. Through improvisation, playing and creating music together, patients improved their motivation, social skills and emotion regulation. The results of the therapy saw patients reduce negative symptoms of the disease, improve overall functioning and improve relationships with people. The therapy was particularly effective for patients who previously had difficulty engaging in traditional forms of treatment (8).

The study by Tang et al involved 76 patients with the residual subtype of schizophrenia who received standard medication as prescribed by their doctors, but participants in the therapy group additionally benefited from a month-long music therapy program that included both passive music listening and active singing of popular songs in the company of other patients. Music therapy was shown to significantly reduce patients' negative symptoms, improve their ability to interact with others, reduce social isolation and increase interest in the surrounding reality (9).

The first study by Shih et al. examined the effects of music on attention in the context of vocational rehabilitation in people with a chronic form of schizophrenia. Participants were divided into three groups: a control group (quiet atmosphere), a group listening to classical music, and a group listening to popular music. The results showed that the introduction of background music had a positive effect on attention test scores, with the most significant increase observed in the group listening to popular music (10). In turn, five years later, the same author examined the effect of background music tempo on attention performance. Participants were divided into four groups, including one control group with no music and groups that listened to fast and slow

tempo music and white noise. The results confirmed that background music improved attentional performance compared to no music, with significantly better results for slow tempo music compared to fast tempo music (11).

A study by Ulrich et al. involved schizophrenic patients participating in group music therapy, the main form of which was playing rhythmic instruments together. In addition, patients engaged in singing familiar songs and in group discussions. The study showed that music therapy had a positive effect on patients' self-esteem and reduced the severity of negative symptoms of schizophrenia, particularly apathy, alogia and flat affect. No significant differences in quality of life were observed (12).

Peng et al. studied the effect of group musical activity on psychotic symptoms in 67 patients with acute schizophrenia. The music therapy consisted of two parts: the first involved solo and duet singing using a karaoke system, and the second part involved listening to music, including pop songs, folk songs and New Age music. Musical activity significantly reduced the severity of psychotic symptoms and symptoms such as anxiety, disorganized thinking and hallucinations in the experimental group (13).

A study by Leung et al. evaluated the effectiveness of karaoke therapy in the rehabilitation of patients with chronic schizophrenia in Hong Kong. In a six-week double-blind study, patients were divided into two groups: one practiced karaoke and the other Simple singing. The conclusion was drawn that karaoke therapy may be more effective than Simple singing in improving social interaction, while in schizophrenic patients in an unstable emotional state it may also induce feelings of anxiety (14).

Music therapy has shown promise in treating schizophrenia, improving patients' quality of life and social functioning and reducing negative symptoms. Although some studies suggest benefits of music therapy, significant differences in the effectiveness of different methods and the risk of inducing anxiety in emotionally unstable patients indicate the need for further research.

Repetitive extracranial magnetic stimulation (rTMS)

Repetitive extracranial magnetic stimulation (rTMS) is one of the non-pharmacological treatments for schizophrenia as an adjunctive therapy. It is a non-invasive method used to treat a variety of neuropsychiatric disorders that uses a magnetic field to stimulate neurons and affect their plasticity (15).

To date, the direct effects of rTMS on the composition and function of the gut microbiota have not been described. However, an available study by Rui Li et al. describes the effect of low-frequency rTMS combined with risperidone on the composition of the gut microbiota in schizophrenic patients. After examining samples from 33 patients with chronic schizophrenia and 37 healthy subjects, they found that a decrease in *Proteobacteria*, *Enterobacteriaceae* and *Escherichia-Shigella*, as well as an increase in the genus *Lachnospiraceae*, may be related to the effect produced by rTMS therapy together with antipsychotic drugs (16).

Wagner et al. showed in their study that rTMS in combination with clozapine may be more effective than drug monotherapy (17). A significant and moderate effect of rTMS on both positive and negative schizophrenia was found in a study by Freitas et al. In addition, Hasan et al. showed that some structural changes in brain areas observed on MRI scans before or after rTMS correlate with improvement of negative symptoms in those who received actual stimulation (18). Also, a study by Rosenberg et al. showed the effectiveness of deep magnetic stimulation of the temporal-occipital cortex as an adjunctive therapy for schizophrenia in patients with delusions and visual hallucinations (19).

In a study, Gornerova et al investigated the effectiveness of low-frequency repetitive magnetic stimulation (LF-rTMS) in treating auditory hallucinations (AHs) in patients with refractory schizophrenia. The results showed a significant improvement in hallucinations in patients receiving LF-rTMS. Analysis of brain electrical activity revealed a decrease in current density in alpha-2 and beta waves in the left hemisphere of the brain in the active group, suggesting that LF-rTMS may inhibit activity in brain areas associated with hallucination processing (20).

Lande et al. in turn examined the effects of 10 Hz rTMS on prefrontal cortex activity in patients with schizophrenia and negative symptoms. The study involved 24 patients who received active or placebo rTMS for three weeks while their brain activity was measured using functional magnetic resonance imaging (fMRI) during the Tower of London (ToL) task (21). The Tower of London (ToL) task is used to assess planning ability and another study has shown that it activates various brain areas, including the dorsolateral prefrontal cortex (DLPFC), medial prefrontal cortex, cingulate cortex, striatum, cuneus, precuneus, supramarginal gyrus, and

angular gyrus in the parietal lobe, as well as the frontal opercular area of the insula (22). After treatment, the research group showed increased activity in the right DLPFC and right medial prefrontal cortex, and there was decreased activity in the left corpus callosum, suggesting that rTMS over the DLPFC may increase activation of task-related brain areas in patients with schizophrenia (23).

And a study by Mittrach et al. evaluated the tolerability and safety of rTMS as an additional treatment in patients with chronic schizophrenia. Participants underwent 10 sessions of 10 Hz stimulation to the left prefrontal cortex for two weeks. Patients experienced a reduction in psychopathological symptoms, improved scores on the Wisconsin Card Sorting Test (WCST), which assesses executive abilities, i.e. cognitive flexibility and the ability to adapt to changing conditions. Improved scores on this test suggest that rTMS may have helped patients better adapt to new situations and change their thinking strategies (24).

A study by Kumara et al evaluated the effectiveness of unilateral magnetic stimulation (rTMS) at 20 Hz on the left prefrontal cortex (DLPFC) in treating negative symptoms of schizophrenia. Participants underwent 20 sessions of rTMS for four weeks, with a total of 2,000 pulses per session. Results showed significant improvement in negative symptoms, as measured by the PANSS and SANS scales. The beneficial effects of rTMS persisted for four months After treatment, even though the lesions were small (25).

In contrast, Schönfeldt- Lecuona et al. investigated the effects of rTMS on auditory hallucinations resistant to drug treatment in patients with schizophrenia. Stimulation was carried out in areas of the cerebral cortex associated with speech, identified by fMRI. Although rTMS did not lead to a significant reduction in the severity of hallucinations, a trend of improvement was noted for stimulation over the superior temporal cortex in patients undergoing fMRI. Stimulation of Broca's area, on the other hand, did not produce significant therapeutic effects, which may suggest that other brain areas may be more central to the pathophysiology of hallucinations (26).

An interesting study by Ji et al. focused on understanding how different changes in brain structure in patients with schizophrenia might affect the effects of rTMS treatment. To this end, they developed individual maps of patients' cerebral atrophy, comparing them with data from healthy individuals and analyzing how these differences affect response to therapy. It was found that despite the diversity in atrophy maps between patients, there is a common network in the brain that is associated with schizophrenia and influences the effectiveness of treatment. A key finding was that stronger functional connections between rTMS therapy targets and areas of the brain that exhibit atrophy had a significant effect on improving schizophrenia symptoms. The results suggest that using a personalized approach to analyze atrophy may improve the effectiveness of rTMS in treating schizophrenia, as it allows better matching of stimulation targets to individual patient brain changes (27).

A study by Hu et al. examined the efficacy of rTMS in treating patients with a first episode of schizophrenia, focusing on the application of 1 Hz rTMS over the right orbitofrontal cortex (OFC). Patients in the rTMS group achieved significant improvements in negative symptoms and cognitive deficits compared to the control group after 20 days of treatment (28).

Also, a study by Wölwer et al. examined the effect of rTMS on facial affect recognition in patients with chronic schizophrenia. Stimulation this time at 10 Hz included 10,000 stimuli applied to the left dorsolateral prefrontal cortex. The results showed a significant improvement in facial affect recognition in the rTMS group. In contrast, there was no correlation with clinical improvement (29).

Another study by Liemburg et al. looked at the effects of rTMS on brain activity in schizophrenic patients in the context of emotion processing. Participants performed a task that involved judging emotions on faces. In some cases, the emotions were clear and easy to recognize, while in others they were less obvious, more difficult to assess. The goal was to see how the brain reacts to these different types of emotions. The task was to activate the areas of the brain responsible for emotion recognition, especially the prefrontal cortex along with the striatum, frontal and parietal cortex. The results showed that after rTMS, brain activity in these regions was lower in patients, which suggests that stimulation can normalize responses to ambiguous emotional stimuli, which may have a role in treating the negative symptoms of schizophrenia (30).

The study by Dollfus et al. involved patients with auditory hallucinations undergoing rTMS therapy to the left temporal sulcus. After four sessions of stimulation, 34.6% of patients in the rTMS-targeted group showed improvement, measured as a decrease of more than 30% on the Auditory Hallucination Rating Scale (AHRS). In the placebo group, only 9.1% of patients showed improvement (31).

Also, Kamp et al. investigated the effects of 10 Hz rTMS on hypofrontality in schizophrenic patients using controlled stimulation over the left dorsolateral prefrontal cortex. After 10 sessions of rTMS, they noted a

significant decrease in delta band activity in the right prefrontal cortex, which correlated with improvements in facial affect recognition, but had no direct effect on negative symptoms of schizophrenia (31).

It is worth noting that Freitas et al. in their study showed that a full response to rTMS therapy occurs only after 8 weeks, which may be related to the regulation of neurotransmitter receptors in the brain. The delayed effect of therapy may be due to the need for time for receptors to fully adapt to the changes induced by stimulation (32). In schizophrenia, rTMS may induce "up-regulation" of D1 receptors in the prefrontal cortex, which improves negative symptoms, and "down-regulation" of D2 receptors, which reduces dopaminergic overactivity associated with psychotic symptoms (33).

In contrast, a study by Walther et al. found that rTMS (1-Hz) inhibitors in the supplementary motor field area effectively reduced psychomotor slowing in patients with schizophrenia. After 15 sessions of rTMS, 68% of patients responded to the treatment, compared to lower results in the placebo and intermittent Theta Burst Stimulation (iTBS) groups. Effects were evident after a few sessions, and improvements lasted up to six months. rTMS has been shown to be safe, although effects may occur with a delay (34).

In the study, the authors examined the effects of high-frequency repetitive magnetic stimulation (HF-rTMS) over the left dorsolateral prefrontal cortex (DLPFC) on negative symptoms of schizophrenia in sixteen patients stable on antipsychotic treatment. Despite subjecting the patients to ten sessions of rTMS stimulation at 20 Hz, the results did not confirm a significant effect of this method on negative symptoms. Only the positive PANSS subscales showed a slight increase after eight weeks (35).

Another study to evaluate the therapeutic effects of rTMS on negative schizophrenia symptoms and BDNF levels was conducted by Zhai et al. Patients in the active group took paliperidone at a dose of 3-6 mg/day. Active rTMS stimulation was applied to the left dorsolateral prefrontal cortex for four weeks. Results showed a more significant improvement in negative symptoms on the PANSS scale and higher serum BDNF levels in the active group compared to the control group. They also found that higher BDNF levels were correlated with improvements in negative symptoms. Adverse effects were minimal and did not differ significantly between groups (36).

The Walther et al. study examined the effects of rTMS on gesture performance in patients with schizophrenia, given that social interaction and gesture use are impaired in this group. Participants underwent three rTMS protocols: iTBS over the left inferior frontal gyrus (IFG), inhibitory theta burst stimulation (cTBS) over the right inferior parietal lobe (IPL), and placebo. The results showed that patients improved their performance in the upper limb apraxia test after cTBS over IPL and in the coin flipping task. Single sessions of cTBS on the right IFG significantly improved gestural accuracy and manual dexterity (37).

Campana et al. examined the effect of gender on the efficacy of rTMS in treating negative symptoms in patients with schizophrenia, analyzing data from the RESIS trial for 105 days after the intervention. The analysis showed that gender had no significant effect on treatment effectiveness, nor did baseline motor excitability (RMT) (38)].

Another study addressing this issue, by Huber et al, found that women improved their scores on the Number Call Test after rTMS, while men did not. The gender differences were statistically significant. However, no significant differences were found in other clinical measures i.e. anxiety scores suggesting that the differences were mainly in cognitive function rather than psychopathological symptoms (39).

In contrast, brain responses to subliminal rTMS in patients with schizophrenia were examined by Oxley et al. The results indicated that there were no differences in motor threshold (RMT) between groups at baseline, but patients showed reduced levels of cortical inhibition compared to healthy subjects. After rTMS, healthy participants showed a decrease in motor evoked potentials (MEPs) and an increase in RMT, while patients registered the opposite effects - an increase in MEPs and a decrease in RMT. The results suggest that people with schizophrenia respond abnormally to rTMS, which may be related to reduced cortical inhibition in motor areas (40).

To summarize the research on rTMS for the treatment of schizophrenia, there is much evidence of positive effects, especially in alleviating negative symptoms and hallucinations. However, the effects may appear with a delay, usually after a few weeks of regular sessions. The benefits can last from a few months to a year, but it is important that therapy is continued periodically to ensure long-term effects. It is also worth noting that there are studies that do not support a significant effect of rTMS on schizophrenia symptoms, highlighting the diversity of

results and the need for further studies. Nevertheless, rTMS therapy can be used as a complementary therapy, especially in cases of co-occurring depressive symptoms or to reduce negative symptoms that often occur after treatment with antipsychotic drugs. Such use of rTMS can improve patients' quality of life, especially in terms of improving cognitive and emotional function.

Conclusions

Music therapy presents a promising complementary approach for managing neurological and psychiatric conditions, particularly in reducing anxiety, improving cognitive function, and enhancing social interaction. Similarly, rTMS has shown potential in addressing schizophrenia symptoms by modulating neural activity. While both interventions demonstrate encouraging results, further research is needed to establish standardized treatment protocols and determine long-term efficacy. Integrating MT and rTMS into clinical practice requires a personalized approach, considering individual patient needs and therapy responsiveness to maximize therapeutic outcomes.

Disclosure

Author's contribution

Conceptualization: Patrycja Niczyporuk, Rafał Marecki; Methodology: Patrycja Niczyporuk; Software: Izabela Zajkowska; Wiktor Królikiewicz; Check: Izabela Zajkowska; Formal analysis: Patrycja Niczyporukt; Investigation: Patrycja Niczyporuk; Resources: Patrycja Niczyporuk, Kamila Iłendo; Data curation: Izabela Zajkowska, Kamila Iłendo; Writing-rough preparation: Aleksandra Giba.; Writing-review and editing: Aleksandra Kicman, Rafał Marecki; Visualization: Aleksandra Giba; Supervision: Aleksandra Kicman, Rafał Marecki; Project administration: Aleksandra Kicman, Rafał Marecki

Funding Statement

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This research was funded by Medical University of Bialystok, grant number: B.SUB.25.237/01.S

Institutional Review Board Statement

Not Applicable.

Informed Consent Statement

Not Applicable.

Data Availability

Statement Not Applicable.

Acknowledgements

This research has not received any administrative or technical support.

Conflict Of Interest

The authors declare no conflict of interest.

All authors have read and agreed with the published version of the manuscript.

References:

- 1. Sun C, Sang S, Tang Y, Niu X, Yoo HS, Zhou P, et al. Effects of music therapy on anxiety in patients with cancer: study protocol of a randomised controlled trial. BMJ Open [Internet]. 2023 May 29 [cited 2025 Mar 19];13(5). Available from: https://pubmed.ncbi.nlm.nih.gov/37247967/
- 2. Gassner L, Geretsegger M, Mayer-Ferbas J. Effectiveness of music therapy for autism spectrum disorder, dementia, depression, insomnia and schizophrenia: update of systematic reviews. Eur J Public Health [Internet]. 2022 Feb 1 [cited 2025 Mar 19];32(1):27–34. Available from: https://pubmed.ncbi.nlm.nih.gov/34595510/
- 3. Yang M, He H, Duan M, Chen X, Chang X, Lai Y, et al. The Effects of Music Intervention on Functional Connectivity Strength of the Brain in Schizophrenia. Neural Plast [Internet]. 2018 [cited 2025 Mar 19];2018. Available from: https://pubmed.ncbi.nlm.nih.gov/29853841/
- 4. Ertekin Pinar S, Tel H. The Effect of Music on Auditory Hallucination and Quality of Life in Schizophrenic Patients: A Randomised Controlled Trial. Issues Ment Health Nurs [Internet]. 2019 Jan 2 [cited 2025 Mar 19];40(1):50–7. Available from: https://pubmed.ncbi.nlm.nih.gov/30111213/
- 5. Lu SF, Lo CHK, Sung HC, Hsieh TC, Yu SC, Chang SC. Effects of group music intervention on psychiatric symptoms and depression in patient with schizophrenia. Complement Ther Med [Internet]. 2013 Dec [cited 2025 Mar 19];21(6):682–8. Available from: https://pubmed.ncbi.nlm.nih.gov/24280478/

- 6. Hayashi N, Tanabe Y, Nakagawa S, Noguchi M, Iwata C, Koubuchi Y, et al. Effects of group musical therapy on inpatients with chronic psychoses: a controlled study. Psychiatry Clin Neurosci [Internet]. 2002 [cited 2025 Mar 19];56(2):187–93. Available from: https://pubmed.ncbi.nlm.nih.gov/11952923/
- 7. Tan S, Zou Y, Wykes T, Reeder C, Zhu X, Yang F, et al. Group cognitive remediation therapy for chronic schizophrenia: A randomized controlled trial. Neurosci Lett [Internet]. 2016 Jul 28 [cited 2025 Mar 19];626:106–11. Available from: https://pubmed.ncbi.nlm.nih.gov/26314508/
- 8. Gold C, Mössler K, Grocke D, Heldal TO, Tjemsland L, Aarre T, et al. Individual music therapy for mental health care clients with low therapy motivation: Multicentre randomised controlled trial. Psychother Psychosom. 2013;82(5):319–31.
- 9. Tang W, Yao X, Zheng Z. Rehabilitative effect of music therapy for residual schizophrenia. A one-month randomised controlled trial in Shanghai. Br J Psychiatry Suppl [Internet]. 1994 Aug 1 [cited 2025 Mar 19];164(24):38–44. Available from: https://europepmc.org/article/med/7946230
- 10. Shih YN, Chen CS, Chiang HY, Liu CH. Influence of background music on work attention in clients with chronic schizophrenia. Work [Internet]. 2015 Jun 9 [cited 2025 Mar 19];51(1):153–8. Available from: https://pubmed.ncbi.nlm.nih.gov/24594536/
- 11. Shih YN, Chu KH, Wu CC. The effects of background music tempo on the work attention performance of workers with schizophrenia. Work [Internet]. 2020 [cited 2025 Mar 19];66(1):119–23. Available from: https://pubmed.ncbi.nlm.nih.gov/32417819/
- 12. Ulrich G, Houtmans T, Gold C. The additional therapeutic effect of group music therapy for schizophrenic patients: a randomized study. Acta Psychiatr Scand [Internet]. 2007 Nov [cited 2025 Mar 19];116(5):362–70. Available from: https://pubmed.ncbi.nlm.nih.gov/17919155/
- 13. Peng SM, Koo M, Kuo JC. Effect of group music activity as an adjunctive therapy on psychotic symptoms in patients with acute schizophrenia. Arch Psychiatr Nurs [Internet]. 2010 Dec [cited 2025 Mar 19];24(6):429–34. Available from: https://pubmed.ncbi.nlm.nih.gov/21111297/
- 14. Leung CM, Lee G, Cheung B, Kwong E, Wing YK, Kan CS, et al. Karaoke therapy in the rehabilitation of mental patients. Singapore Med J [Internet]. 1998 Apr 1 [cited 2025 Mar 19];39(4):166–8. Available from: https://europepmc.org/article/med/9676147
- 15. Klomjai W, Katz R, Lackmy-Vallée A. Basic principles of transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS). Ann Phys Rehabil Med [Internet]. 2015 Sep 1 [cited 2025 Mar 19];58(4):208–13. Available from: https://pubmed.ncbi.nlm.nih.gov/26319963/
- 16. Li R, Fu R, Cui Z quan, Guo L, Chen Y huan, Bai J, et al. Effects of low-frequency rTMS combined with risperidone on the gut microbiome in hospitalized patients with chronic schizophrenia. Brain Res [Internet]. 2023 Nov 15 [cited 2025 Mar 19];1819. Available from: https://pubmed.ncbi.nlm.nih.gov/37598899/
- 17. Wagner E, Wobrock T, Kunze B, Langguth B, Landgrebe M, Eichhammer P, et al. Efficacy of high-frequency repetitive transcranial magnetic stimulation in schizophrenia patients with treatment-resistant negative symptoms treated with clozapine. Schizophr Res [Internet]. 2019 Jun 1 [cited 2025 Mar 19];208:370–6. Available from: https://pubmed.ncbi.nlm.nih.gov/30704862/
- 18. Koutsouleris N, Kambeitz-Ilankovic L, Ruhrmann S, Rosen M, Ruef A, Dwyer DB, et al. Prediction Models of Functional Outcomes for Individuals in the Clinical High-Risk State for Psychosis or With Recent-Onset Depression: A Multimodal, Multisite Machine Learning Analysis. JAMA Psychiatry [Internet]. 2018 Nov 1 [cited 2025 Mar 19];75(11):1156. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6248111/
- 19. Rosenberg O, Roth Y, Kotler M, Zangen A, Dannon P. Deep transcranial magnetic stimulation for the treatment of auditory hallucinations: a preliminary open-label study. Ann Gen Psychiatry [Internet]. 2011 Feb 9 [cited 2025 Mar 19];10(1). Available from: https://pubmed.ncbi.nlm.nih.gov/21303566/
- 20. Gornerova N, Brunovsky M, Klirova M, Novak T, Zaytseva Y, Koprivova J, et al. The effect of low-frequency rTMS on auditory hallucinations, EEG source localization and functional connectivity in schizophrenia. 19];794. Neurosci Lett [Internet]. 2023 Jan 18 [cited 2025 Mar Available from: https://pubmed.ncbi.nlm.nih.gov/36427815/
- 21. Dlabac-de Lange JJ, Liemburg EJ, Bais L, Renken RJ, Knegtering H, Aleman A. Effect of rTMS on brain activation in schizophrenia with negative symptoms: A proof-of-principle study. Schizophr Res [Internet]. 2015 Oct 1 [cited 2025 Mar 19];168(1–2):475–82. Available from: https://pubmed.ncbi.nlm.nih.gov/26187147/
- 22. Dlabac-De Lange JJ, Bais L, Van Es FD, Visser BGJ, Reinink E, Bakker B, et al. Efficacy of bilateral repetitive transcranial magnetic stimulation for negative symptoms of schizophrenia: results of a multicenter double-blind randomized controlled trial. Psychol Med [Internet]. 2015 Apr 18 [cited 2025 Mar 19];45(6):1263–75. Available from: https://pubmed.ncbi.nlm.nih.gov/25354751/
- 23. Dlabac-de Lange JJ, Liemburg EJ, Bais L, Renken RJ, Knegtering H, Aleman A. Effect of rTMS on brain activation in schizophrenia with negative symptoms: A proof-of-principle study. Schizophr Res [Internet]. 2015 Oct 1 [cited 2025 Mar 19];168(1–2):475–82. Available from: https://pubmed.ncbi.nlm.nih.gov/26187147/

- 24. Mittrach M, Thünker J, Winterer G, Agelink MW, Regenbrecht G, Arends M, et al. The tolerability of rTMS treatment in schizophrenia with respect to cognitive function. Pharmacopsychiatry [Internet]. 2010 [cited 2025 Mar 19];43(3):110–7. Available from: https://pubmed.ncbi.nlm.nih.gov/20127616/
- 25. Kumar N, Vishnubhatla S, Wadhawan AN, Minhas S, Gupta P. A randomized, double blind, sham-controlled trial of repetitive transcranial magnetic stimulation (rTMS) in the treatment of negative symptoms in schizophrenia. Brain Stimul [Internet]. 2020 May 1 [cited 2025 Mar 19];13(3):840–9. Available from: https://pubmed.ncbi.nlm.nih.gov/32289715/
- 26. Schönfeldt-Lecuona C, Grön G, Walter H, Büchler N, Wunderlich A, Spitzer M, et al. Stereotaxic rTMS for the treatment of auditory hallucinations in schizophrenia. Neuroreport [Internet]. 2004 Jul 19 [cited 2025 Mar 19];15(10):1669–73. Available from: https://pubmed.ncbi.nlm.nih.gov/15232304/
- 27. Ji GJ, Zalesky A, Wang Y, He K, Wang L, Du R, et al. Linking Personalized Brain Atrophy to Schizophrenia Network and Treatment Response. Schizophr Bull [Internet]. 2023 Jan 1 [cited 2025 Mar 19];49(1):43–52. Available from: https://pubmed.ncbi.nlm.nih.gov/36318234/
- 28. Hu Q, Jiao X, Zhou J, Tang Y, Zhang T, Song C, et al. Low-frequency repetitive transcranial magnetic stimulation over the right orbitofrontal cortex for patients with first-episode schizophrenia: A randomized, double-blind, sham-controlled trial. Psychiatry Res [Internet]. 2023 Dec 1 [cited 2025 Mar 19];330. Available from: https://pubmed.ncbi.nlm.nih.gov/37992513/
- 29. Wölwer W, Lowe A, Brinkmeyer J, Streit M, Habakuck M, Agelink MW, et al. Repetitive transcranial magnetic stimulation (rTMS) improves facial affect recognition in schizophrenia. Brain Stimul [Internet]. 2014 [cited 2025 Mar 19];7(4):559–63. Available from: https://pubmed.ncbi.nlm.nih.gov/24857264/
- 30. Liemburg EJ, Dlabac-De Lange JJ, Bais L, Knegtering H, Aleman A. Effects of bilateral prefrontal rTMS on brain activation during social-emotional evaluation in schizophrenia: A double-blind, randomized, exploratory study. Schizophr Res [Internet]. 2018 Dec 1 [cited 2025 Mar 19];202:210–1. Available from: https://pubmed.ncbi.nlm.nih.gov/29954702/
- 31. Dollfus S, Jaafari N, Guillin O, Trojak B, Plaze M, Saba G, et al. High-Frequency Neuronavigated rTMS in Auditory Verbal Hallucinations: A Pilot Double-Blind Controlled Study in Patients With Schizophrenia. Schizophr Bull [Internet]. 2018 Apr 6 [cited 2025 Mar 19];44(3):505–14. Available from: https://pubmed.ncbi.nlm.nih.gov/29897597/
- 32. Li Z, Yin M, Lyu XL, Zhang LL, Du XD, Hung GCL. Delayed effect of repetitive transcranial magnetic stimulation (rTMS) on negative symptoms of schizophrenia: Findings from a randomized controlled trial. Psychiatry Res [Internet]. 2016 Jun 30 [cited 2025 Mar 19];240:333–5. Available from: https://pubmed.ncbi.nlm.nih.gov/27138827/
- 33. Ben-Shachar D, Gazawi H, Riboyad-Levin J, Klein E. Chronic repetitive transcranial magnetic stimulation alters beta-adrenergic and 5-HT2 receptor characteristics in rat brain. Brain Res [Internet]. 1999 Jan 16 [cited 2025 Mar 19];816(1):78–83. Available from: https://pubmed.ncbi.nlm.nih.gov/9878693/
- 34. Walther S, Alexaki D, Weiss F, Baumann-Gama D, Kyrou A, Nuoffer MG, et al. Psychomotor Slowing in Psychosis and Inhibitory Repetitive Transcranial Magnetic Stimulation: A Randomized Clinical Trial. JAMA Psychiatry [Internet]. 2024 Jun 5 [cited 2025 Mar 19];81(6):563–71. Available from: https://pubmed.ncbi.nlm.nih.gov/38416468/
- 35. Saba G, Verdon CM, Kalalou K, Rocamora JF, Dumortier G, Benadhira R, et al. Transcranial magnetic stimulation in the treatment of schizophrenic symptoms: A double blind sham controlled study. J Psychiatr Res. 2006 Mar 1;40(2):147–52.
- 36. Zhai WH, Li MC, Su Z, Ji QM, Xiong ZJ, Zhao YJ, et al. The effect of repetitive transcranial magnetic stimulation on the negative symptoms of chronic schizophrenia and serum brain-derived neurotrophic factor. Psychiatr Pol [Internet]. 2023 [cited 2025 Mar 19];57(6):1293–303. Available from: https://pubmed.ncbi.nlm.nih.gov/38564527/
- 37. Walther S, Kunz M, Müller M, Zürcher C, Vladimirova I, Bachofner H, et al. Single Session Transcranial Magnetic Stimulation Ameliorates Hand Gesture Deficits in Schizophrenia. Schizophr Bull [Internet]. 2020 Mar 1 [cited 2025 Mar 19];46(2):286–93. Available from: https://pubmed.ncbi.nlm.nih.gov/31634401/
- 38. Campana M, Schneider-Axmann T, Wobrock T, Malchow B, Langguth B, Landgrebe M, et al. Assessing the impact of sex on high-frequency repetitive transcranial magnetic stimulation's clinical response in schizophrenia results from a secondary analysis. World J Biol Psychiatry [Internet]. 2024 [cited 2025 Mar 19];25(4):233–41. Available from: https://pubmed.ncbi.nlm.nih.gov/38493362/
- 39. Huber TJ, Schneider U, Rollnik J. Gender differences in the effect of repetitive transcranial magnetic stimulation in schizophrenia. Psychiatry Res [Internet]. 2003 Aug 30 [cited 2025 Mar 19];120(1):103–5. Available from: https://pubmed.ncbi.nlm.nih.gov/14500119/
- 40. Oxley T, Fitzgerald PB, Brown TL, De Castella A, Jeff Daskalakis Z, Kulkarni J. Repetitive transcranial magnetic stimulation reveals abnormal plastic response to premotor cortex stimulation in schizophrenia. Biol Psychiatry [Internet]. 2004 Nov 1 [cited 2025 Mar 19];56(9):628–33. Available from: https://pubmed.ncbi.nlm.nih.gov/15522245/