

rTMS for Treatment Resistant Schizophrenia

Mikellides Georgios^{1*} and Tantele Marianna²

¹PhD Researcher, Maastricht University, Maastricht, Netherlands

²Consultant Psychiatrist, Cyprus Mental Health Services, Cyprus

*Corresponding Author: Georgios Mikellides, PhD Researcher, Maastricht University, Maastricht, Netherlands.

Received: January 30, 2020; Published: February 14, 2020

DOI: 10.31080/ecpp.2020.09.00656

Abstract

Introduction: Schizophrenia presents with positive and negative symptoms which some of these symptoms are characterised by hearing voices (auditory hallucinations), reduced social engagement and emotional expression, and also lack of motivation. Around 20 percent of patients with Schizophrenia present with treatment resistance to medication where Clozapine treatment is indicated as it could be more effective, if it's to be compared to other antipsychotics. However, Clozapine has more side effects and requires close monitoring due to the potential life-threatening side effect of agranulocytosis and this could present in less than 4 percent of patients receiving clozapine.

Method: In this case series study, five cases are presented which received the theta burst stimulation on the dorsolateral prefrontal cortex followed by combining either an inhibition of the Wernicke's area or inhibition of the right dorsolateral prefrontal cortex.

Results: This study explored the efficacy of rTMS on negative symptoms, delusions and auditory hallucinations by using high frequency rTMS to the dorso-lateral prefrontal cortex and low frequency rTMS stimuli on Wernicke's area on the left temporo-parietal cortex or inhibition of the right dorsolateral prefrontal cortex. The cases described in this study demonstrated excellent results.

Conclusion: It seems that rTMS could have important benefits in a variety of neuropsychiatric disorders and perhaps it should be applied in treatment resistant schizophrenia too.

Our cases could perhaps stimulate the area of research further and develop double blind RCTs in these treatment options.

Keywords: Schizophrenia; Clozapine, rTMS

Introduction

Schizophrenia presents with positive and negative symptoms [1] which some of these symptoms are characterised by hearing voices (auditory hallucinations), reduced social engagement and emotional expression, and also lack of motivation [2,3]. Around 20 percent of patients with Schizophrenia present with treatment resistance to medication where Clozapine treatment is indicated. Clozapine may be more effective if it's to be compared to other antipsychotics [4]. However, Clozapine has more side effects and requires close monitoring due to the potential life-threatening side effect of agranulocytosis [5] and this could present with less than 4 percent of patients receiving clozapine.

The use of rTMS has been explored in treatment of negative symptoms of schizophrenia [6] which in combination with antipsychotics could improve this symptomatology [6] and also as a treatment option for auditory hallucinations [7] with promising effects [7] however further research was recommended.

This study [7] explored the efficacy of rTMS on negative symptoms by high frequency rTMS to the dorso-lateral prefrontal cortex and low frequency rTMS stimuli to Wernicke's area in the left temporo-parietal cortex which showed promising effects.

In this case series study, we will present cases in which we have used the theta burst stimulation in the dorsolateral prefrontal cortex followed by combining the inhibition of the Wernicke's area.

Case 1

A unique case is presented where a young 21-year-old patient with treatment resistant Schizophrenia, with prominent negative symptoms and auditory hallucinations received treatment with a combination of rTMS. On his first assessment in our Cyprus rTMS Clinic he was on a triple high dose antipsychotic regime which included Olanzapine 45 mg daily, Risperidone 9mg daily and Haloperidol 20 mg daily and there was no response to treatment.

We initiated a combination of rTMS treatment which included theta burst stimulation on the Left Dorsolateral Prefrontal Cortex followed by 1 Hz inhibition of the Left Wernicke's Area. Also, during the rTMS treatment which was for 6 weeks initially, 5 sessions per week we gradually reduce the antipsychotic medications and by week six he was only on Olanzapine 10 mg nocte.

He demonstrated a magnificent recovery which started post two weeks into treatment with the auditory hallucinations subsiding completely and with no further negative symptoms. He was able to carry on with his exams and successfully complete the year at his university.

The very interesting points which are demonstrated in this case report is that a combination of stimulation of the DLPFC with theta burst stimulation, 3 minutes FDA protocol for depression and 1 Hz inhibition of Left Wernicke's area could perhaps offer a treatment option of such patients that are faced with such a serious disorder without the need to consider Clozapine treatment.

Case 2

A 26 year old man with psychotic illness and treatment resistant symptoms which included persistent auditory hallucinations and comorbidity disorder, use of THC with social isolation and temper tantrums, he was previously tried on Risperdal 4 mg daily, Haloperidol 40 mg daily, Amisulpride 600 mg BD as well as Aripiprazole 400 mg depot maintena and he continued to experience psychotic symptoms with auditory hallucinations. He received 15 sessions of rTMS treatment which included theta burst stimulation on the Left Dorsolateral Prefrontal Cortex follow by 1 Hz inhibition of the Left Wernicke's Area and the auditory hallucinations subsided completely, he continued with the maintenance of Aripiprazole maintena 400 mg depot.

Case 3

A 25 year old lady with persistent auditory hallucinations while she was on treatment on Risperidone 2 mg and Venlafaxine 37.5 mg, risperidone was increased to 3 mg nocte and Venlafaxine 37.5 mg was stopped, she has received 30 sessions of rTMS included theta burst stimulation on the Left Dorsolateral Prefrontal Cortex follow by 1 Hz inhibition of the Left Wernicke's Area and the auditory hallucinations subsided while her mood also improved.

Case 4

A 28-year-old man with treatment resistant Schizophrenia, attended our Cyprus rTMS clinic, while he recently had an admission for 45 days as an inpatient to help him treat his auditory hallucinations with no response. He was on Haloperidol 40 mg daily, Aripiprazole 30 mg daily, Sodium Valproate 500 mg daily. We gradually initiated a reduction of the medications to Haloperidol 20 mg daily and Aripiprazole 20 mg with the aim to stop Aripiprazole and to start Amisulpride 400 mg BD within 5 days to increase it to 600 bd and we also initiated

rTMS treatment which included theta burst stimulation on the Left Dorsolateral Prefrontal Cortex followed by 1 Hz inhibition of the Left Wernicke's Area and the auditory hallucinations subsided completely after 30 sessions.

Case 5

A 21 year old man with a family history of schizophrenia and persistent delusional beliefs of persecution and mild thought disorder who was refusing to take oral antipsychotic medications, he received three Abilify maintena 400 mg depot monthly injections as well as 30 sessions of rTMS which included theta burst stimulation on the Left Dorsolateral Prefrontal Cortex followed by 1 Hz inhibition theta burst on Right Dorsolateral Prefrontal cortex. He continued with 2 rTMS sessions on a monthly basis and he refused to continue with the Abilify maintena depot injections. All his symptoms subsided and went to full remission, currently free from antipsychotic medications for two months even though it was recommended to continue with the antipsychotic regime.

It's important to consider that as previously stated that rTMS could have a valid purpose in a variety of neuropsychiatric disorders and even where ECT was not successful [9]. Even when it is to be used as a combination treatment with medications to treat migraines and anxiety disorders [10].

Conclusion

It seems that rTMS could have important and useful benefits in a variety of neuropsychiatric disorders and we should initiate a new way of thinking of its broader applications into our day to day work in Neuropsychiatry.

These case reviews demonstrated that rTMS could have excellent results in treatment resistant schizophrenia where previous treatments with psychotropic medications did not demonstrate sufficient results.

Our cases should stimulate the area of research further and develop double blind RCTs in these treatment options which were discussed above.

Bibliography

1. Sims A. "Symptoms in the mind: an introduction to descriptive psychopathology". Philadelphia: WB Saunders (2002).
2. "Schizophrenia Fact sheet N°397". WHO (2015).
3. "Schizophrenia". National Institute of Mental Health (2016).
4. Taylor DM and Duncan-McConnell D. "Refractory schizophrenia and atypical antipsychotics". *Journal of Psychopharmacology* 14.4 (2000): 409-418.
5. van Os J and Kapur S. "Schizophrenia". *Lancet* 374.9690 (2009): 635-645.
6. Lin XD., et al. "Effects of Repetitive Transcranial Magnetic Stimulation Treatment on Event-Related Potentials in Schizophrenia". *Chinese Medical Journal* 131.3 (2018): 301-306.
7. Cole JC., et al. "Efficacy of Transcranial Magnetic Stimulation (TMS) in the Treatment of Schizophrenia: A Review of the Literature to Date". *Innovations in Clinical Neuroscience* 12.7-8 (2015): 12-19.
8. Georgios Mikellides. "rTMS (Repetitive Transcranial Magnetic Stimulation) could be used as a First Line Treatment for Depression". *Global Journal of Intellectual and Developmental Disabilities* 5.1 (2018): 555655.

9. Georgios M and Marianna T. "A Case of Treatment Resistant Depression Who Did Not Respond to ECT (Electroconvulsive Therapy) and Responded to rTMS (Repetitive Transcranial Magnetic Stimulation)". *Biomedical Journal of Scientific and Technical Research* 8.1 (2018): 001582.
10. Mikellides G., *et al.* "rTMS for Migraine with a Generalised Anxiety Disorder-A Combination Treatment with Duloxetine". *Journal of Psychiatry* 21.5 (2018): 458.

Volume 9 Issue 3 March 2020

©All rights reserved by Mikellides Georgios and Tantele Marianna.