

TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

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SUMMARY

Attention Deficit Hyperactivity Disorder (ADHD) is a common neuropsychiatric disorder, which affects children as well as adults and leads to significant impairment in educational, social and occupational functioning and has associated personal and societal costs.

Whilst there are effective medications (mostly stimulants) as well as some psychobehavioural treatments that help alleviate symptoms of ADHD, there is still need to improve our understanding of its neurobiology as well as explore other treatment options.

Transcranial Magnetic Stimulation (TMS) and repetitive transcranial magnetic stimulation (rTMS) are safe and non-invasive investigative and therapeutic tools respectively.

In this short article, I will explore their potential for improving our understanding of the neurobiology of ADHD as well consider its as a possible treatment option.

Key words: ADHD – TMS - rTMS

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ADHD

The core features, namely, inattention, hyperactivity and impulsivity of *Attention Deficit Hyperactivity Disorder (ADHD)* cause significant impairment in social, academic and occupational functioning. This often leads to poor educational and vocational outcomes, an increased risk for antisocial behaviour and drug abuse (Harpin 2005).

Genetics plays a significant role (Bobb 2006) along with its complex interplay with environmental factors in the etiology of ADHD.

Attention deficits, impulsiveness and hyperactivity appear to relate to disordered executive functions, disturbed motor control with abnormalities in the fronto-striatal-cerebellar circuits.

PET and fMRI studies suggest atypical function of right fronto-striatal circuits, reduced blood flow in striatum and in frontal-cerebral circuits in individuals with ADHD.

Moreover, Evoked Potential studies have described shorter amplitude and longer latencies correlating with attentional dysfunction whilst steady state visual EP have supported right frontal dysfunction in ADHD.

Meta-analysis of fMRI studies have shown reduced/increased activation in attentional networks and reduced activation in inhibitory networks (Hart 2013).

Large body of evidence suggests that there is dysregulation of neuromodulators, noradrenaline (NA) and dopamine (DA) in ADHD sufferers (Pliszka 2005).

To date methylphenidate (MPH), one of the most prescribed drug for ADHD has shown response rate of up to 80%. MPH increases the striatal and frontal activation capturing DA transporter. Number of other drugs (including atomoxetine) are also used along with psychobehavioural therapies for the management of symptoms in both children and adults with ADHD.

TMS

Transcranial Magnetic Stimulation (TMS) is a non-invasive, safe tool to investigate pathophysiological abnormalities in neuropsychiatric disorders. It uses alternating magnetic fields to induce electric current, which leads to firing off cortical neurons. Developed first by Barker and colleagues in Sheffield, England in 1985, TMS successfully modulated the human motor cortex (Barker 1985).

With further development, TMS machines were able to deliver repetitive stimulation of low and high frequencies (low frequency, ≤ 1 Hz, high frequency, > 1 Hz). Described as repetitive transcranial magnetic stimulation, also known as rTMS it has led to exploration of therapeutic applications in number of neuropsychiatric disorders including, depression (Loo 2005), bipolar affective disorder (Michael 2004), Obsessive compulsive disorder (Greenberg 1997) and schizophrenia (Hoffman 2000, Zaman 2008).

The potential therapeutic effects in neuropsychiatric disorders depend upon the cortical regions being stimulated and their interconnectivity with other cortical areas as well as deeper regions of the brain. Other factors that play a role include, frequency and number of stimulations and the length of period of stimulation.

There have been numerous studies that have yielded positive therapeutic results in depression, which have led to approval of rTMS as clinical treatment by FDA in USA as far back as 2008. Yet despite the fact that TMS was first successfully carried out in Sheffield, UK (Barker 1985), the National Institute of Clinical Excellence (NICE) of UK have yet to approve its clinical use in depression.

The use of TMS in ADHD has so far been significantly limited when compared with its use in neuropsychiatric disorders such as depression both as investigative and potential therapeutic tool.

As an investigative tool, TMS has demonstrated a delay in the maturation of the cortico-motoneuronal system (Ucles 2000). Whilst, Moll et al. (2000) reported that ADHD children have significantly reduced intra-cortical inhibition with normal intra-cortical facilitation when compared with normal controls and that this improved with treatment with MPH (Moll 2000).

In a study comparing 49 children with and without ADHD, Gilbert and colleagues described use of TMS to measure short interval cortical inhibition (SICI) in the motor cortex. They showed reduction of mean SICI by 40% in children with ADHD, as well as a correlation with ADHD severity. These results led to suggestion by the authors that TMS could aid ADHD diagnosis, measure symptom severity as well as reflect upon motor skill development in children (Gilbert 2011).

As is the case in use of TMS as an investigative tool in ADHD, the therapeutic use of rTMS in ADHD lags far behind its use in neuropsychiatric disorders such as depression.

Amongst the earliest therapeutic use of rTMS for ADHD was reported by Weaver and colleagues. They described randomized, sham-controlled, crossover study of 9 adolescents and adults with ADHD. The subjects undergoing the study received 10 Hz rTMS, for 10 sessions (2000 stimulation per session) over 2 weeks on to their right Dorsolateral prefrontal cortex (DLPFC) which led to improvement of clinical global impression and the ADHD-IV scales. However, this positive result applied both to active and sham rTMS, suggested that larger controlled studies were needed to see if there indeed are differences in effects of real and sham rTMS (Weaver 2008).

During the same year, Niederhofer (2008) published a case report utilizing low frequency rTMS (1Hz), for five days on the “impending scalp additional motor area”, in ADHD subject and reported “significant improvement” that lasted 4 week. However, he reported that the placebo control did not show any improvement (Niederhofer 2008).

Same author later published another case report, utilizing rTMS (low frequency, 1Hz, 1200 stim/day for five days) and applied on the impending scalp in the motor additional area of a patient suffering from combined type ADHD who was also receiving methylphenidate (MPH). Niederhofer reported significant improvement in hyperactivity lasting for at least three weeks leading to final reduction in dosage of MPH to 10 mg (Niederhofer 2011).

Bloch and co-investigators, in what was described as crossover, double blind, randomized, sham controlled pilot study evaluated the effect of single session of high frequency rTMS (real and sham) upon the right prefrontal cortex in 13 adults with ADHD. They noted improvement in attention after 10 minutes with real rTMS with no change in anxiety and mood measures. The sham rTMS had no effect (Bloch 2010).

Clearly our knowledge concerning the utilization of TMS/rTMS as investigative and therapeutic tool in ADHD is very much in its infancy. There is great potential to use TMS as investigative tool either on its own (for example as a diagnostic tool) or in combination with others (for example EEG, MRI, fMRI, DTI etc) in order improve our understanding of the neurobiology of ADHD.

As for investigating the potential of rTMS as a therapeutic tool in ADHD, there is little doubt, that there is need for larger studies, utilizing standardised protocols (such as cortical regions being targeted, frequency of stimulation, number and length of stimulation sessions used) as has been the case in many depression studies. Only then we could be in position to draw more satisfactory conclusions concerning the use of rTMS as potentially effective therapeutic option for ADHD.

In addition, studies are needed to explore whether rTMS could be used to augment medications such as in individuals who are resistant to usual ADHD medications or indeed as an alternative treatment in those who either can not take medications (due to intolerance or side-effects) or in those who are not suitable for stimulant medications due to the risk of abuse.

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References

1. Barker AT, Jalinous R, Freeston IL: *Non-invasive magnetic stimulation of the human motor cortex. Lancet. 1985; 1:1106–7.*
2. Bobb AJ, Castellanos FX, Addington AM, Rapoport JL: *Molecular genetic studies of ADHD: 1991 to 2004. Am. J. Med. Genet. B Neuropsych Genet 2006; 132:109–125.*
3. Bloch Y, Harel EV, Aviram S, Govezensky J, Ratzoni G, Levkovitz Y: *Positive effects of repetitive transcranial magnetic stimulation on attention in ADHD Subjects: a randomized controlled pilot study. World J Biol Psychiatry 2010; 11:755-8.*
4. Gilbert DL, Isaacs KM, Augusta M, Macneil LK, Mostofsky SH: *Motor cortex inhibition: a marker of ADHD behavior and motor development in children. Neurology 2011; 76:615-21.*
5. Greenberg BD, George MS, Martin JD, Benjamin J, Schlaepfer TE, Altman M, et al: *Effect of prefrontal repetitive transcranial magnetic stimulation in obsessive-compulsive disorder: A preliminary study. Am J Psychiatry 1997; 154:867–9.*
6. Harpin VA: *The effect of ADHD on life an individual, their family, and community from preschool to adult life Arch Dis Child 2005; 90:i2-i7.*
7. Hart H, Radua J, Nakao T, Mataix-Cols D, Rubia K: *Meta-analysis of functional magnetic resonance imaging studies of inhibition and attention in attention-deficit/hyperactivity disorder: exploring task-specific, stimulant*

- medication, and age effects. *JAMA Psychiatry* 2013; 70:185-98.
8. Hoffman RE, Boutros NN, Hu S, Berman RM, Krystal JH, Charney DS: Transcranial magnetic stimulation and auditory hallucinations in schizophrenia. *Lancet* 2000; 355:1073–5.
 9. Loo Colleen K and Philip B Mitchel: A review of the efficacy of transcranial magnetic stimulation (TMS) treatment for depression, and current and future strategies to optimize efficacy. *Journal of affective disorders* 2005; 88:255-267.
 10. Michael N and Erfurth A: Treatment of bipolar mania with right prefrontal rapid transcranial magnetic stimulation. *Journal of affective disorders* 2004; 78:253-257.
 11. Moll GH, Heinrich H, Trott G, Wirth S, Rothenberger A: Deficient intracortical inhibition in drug-naïve children with attention-deficit hyperactivity disorder is enhanced by methylphenidate. *Neurosci Lett* 2000; 284:121-5.
 12. Niederhofer H: Effectiveness of repetitive Transcranial Magnetic Stimulation (rTMS) of 1 HZ for Attention-Deficit Hyperactivity Disorder (ADHD). *Psychiatr Danub* 2008; 20:91-2.
 13. Niederhofer H: Additional biological therapies for attention-deficit hyperactivity disorder: repetitive transcranial magnetic stimulation of 1 Hz helps to reduce methylphenidate. *Clin Pract* 2011; 2:e8.
 14. Pliszka SR: The neuropsychopharmacology of attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2005; 57:1385–1390.
 15. Uclés P, Serrano JL, Rosa F: Central conduction time of magnetic brain stimulation in attention-deficit hyperactive disorder. *J Child Neurol* 2000; 15:723-8.
 16. Weaver L, Rostain AL, Mace W, Akhtar U, Moss E, O'Reardon JP: Transcranial magnetic stimulation (TMS) in the treatment of attention-deficit/hyperactivity disorder in adolescents and young adults: a pilot study. *J ECT*. 2012; 28:98-103.
 17. Zaman R, Thind D, Kocmur M: Transcranial magnetic stimulation in schizophrenia. *Neuro Endocrinol Lett* 2008; 29(Suppl 1):147-60.

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