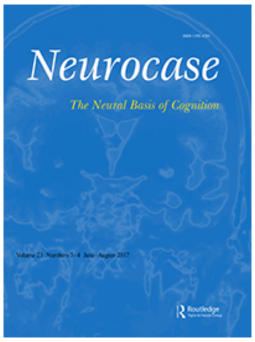
Neurocase
The Neural Basis of Cognition

ISSN: 1355-4794 (Print) 1465-3656 (Online) Journal homepage: http://www.tandfonline.com/loi/nncs20



Enhanced cognition and emotional recognition, and reduced obsessive compulsive symptoms in two adults with high-functioning autism as a result of deep Transcranial Magnetic Stimulation (dTMS): a case report

Keren Avirame, Jimmy Stehberg & Doron Todder

To cite this article: Keren Avirame, Jimmy Stehberg & Doron Todder (2017) Enhanced cognition and emotional recognition, and reduced obsessive compulsive symptoms in two adults with high-functioning autism as a result of deep Transcranial Magnetic Stimulation (dTMS): a case report, Neurocase, 23:3-4, 187-192, DOI: 10.1080/13554794.2017.1361451

To link to this article: https://doi.org/10.1080/13554794.2017.1361451

NEUROCASE, 2017
VOL. 23, NOS. 3–4, 187–192
https://doi.org/10.1080/13554794.2017.1361451

Enhanced cognition and emotional recognition, and reduced obsessive compulsive symptoms in two adults with high-functioning autism as a result of deep Transcranial Magnetic Stimulation (dTMS): a case report

Keren Avirame[a], Jimmy Stehberg[b] and Doron Todder[a,c,d]

[a]Neuroclinic Health center, Ramat Gan, Israel; [b]Laboratorio de Neurobiología, Centro de Investigaciones Biomédicas, Universidad Andres Bello, Santiago, Chile; [c]Beersheva Mental Health Center, Beersheva, Israel; [d]Zlotovsky Center for Neuroscience, Ben-Gurion University, Beersheva, Israel

ABSTRACT

We report reduced repetitive behaviors similar to obsessive compulsive disorder and improved emotional recognition and cognitive abilities in two young patients diagnosed with high-functioning Autism as a result of deep transcranial magnetic stimulation (dTMS). The patients received daily high-frequency (5 Hz) dTMS with HAUT-coil over the medial prefrontal cortex for a period of 5–6 weeks. A computerized cognitive battery, tasks for testing emotional recognition, and clinical questionnaires were used to measure the effects of treatment. TMS might have modulated networks related to metalizing abilities and self-referential processes since both patients reported improved sociability and communication skills.

ARTICLE HISTORY
Received 19 January 2017
Accepted 25 July 2017

KEYWORDS
Autism; obsessive compulsive disorder; transcranial magnetic stimulation; emotion; cognition

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairment in interpersonal relations, communication, cognition, and behavior (Hill & Frith, 2003). It is thought to be primarily a genetic disorder of prenatal and postnatal brain development involving multiple genes (Abrahams & Geschwind, 2008). The neurobiology of ASD reveals a complex picture of abnormal brain growth (DiCicco-Bloom et al., 2006), altered inhibition (Enticott, Rinehart, Tonge, Bradshaw, & Fitzgerald, 2010), and aberrant connectivity (Courchesne & Pierce, 2005). In view of this neurobiological complexity, developing new therapeutic avenues is particularly challenging.

ASD comprises different symptom domains, involving various mechanisms that might be intertwined. Researchers have long emphasized the importance of cognitive abnormalities in ASD due to deficits in executive functions and information processing (Happé, 1999; Ozonoff, Pennington, & Rogers, 1991). However, impaired understanding of emotions has been often correlated with the social difficulties observed in ASD (Adolphs, 2001; Pelphrey, Adolphs, & Morris, 2004) and the disability to represent mental states (Baron-Cohen, 2000; Frith, 2001). These issues are usually addressed especially in childhood and adolescence through therapies focusing on behavior (applied behavioral analysis), information processing (sensory integration), and communication (occupational and speech therapy), achieving limited progress.

ASD is also characterized by repetitive and constricting behaviors, leading to social isolation and high distress. It has been suggested that these stereotyped and rigid behaviors are similar to the obsessions and compulsions characteristic of obsessive compulsive disorder (OCD) (Cath, Ran, Smit, Van Balkom, & Comijs, 2007; Bejerot, 2007). Despite high resemblance, ASD and OCD seem to be associated with different symptoms since frequent OCD symptoms such as cleaning, checking, and counting, are less likely to be reported by patients with ASD (Goodman, Naylor, & Volkmar, 1995).

In recent years, a number of studies applied transcranial magnetic stimulation (TMS) to improve symptoms of ASD (for review, Oberman, Rotenberg, & Pascual-Leone, 2015). TMS is a noninvasive technique that has been long used in neuropsychiatric disorders to study the dynamics of brain–behavior relations as well as to attain symptomatic improvements (Fox et al., 2014). The premise of these methods is that pathological neural activity in specific regions or networks could be modulated via the excitatory or inhibitory effects of TMS (Dayan, Censor, Buch, Sandrini, & Cohen, 2013; Demirtas-Tatlidede, Vahabzadeh-Hagh, & Pascual-Leone, 2013).

Most TMS studies in ASD focused on frontal stimulation because abnormalities in the frontal cortex have been proposed to play a key role in ASD (Courchesne & Pierce, 2005). For example, Baruth and colleagues (2010) used inhibitory TMS to modulate the hyperexcitability observed in ASD, thus improving not only plasticity, but also behavior (Baruth et al., 2010). In another study, excitatory TMS over parts of Broca's area was used to improve naming skills, thus supporting the hypothesis that language network dynamics is disrupted in ASD which might eventually lead to impaired communication skills (Fecteau, Agosta, Oberman, & Pascual-Leone, 2011).

The efficiency of TMS over the medial prefrontal cortex (mPFC) in ASD has been recently tested using the H-coil which is designed for reaching deep cortical regions with lower magnetic fields (Bersani et al., 2013). The mPFC is an important node within functional networks supporting mentalizing abilities which are crucial for social interactions, and were found to be impaired in adults with ASD (Kennedy, Redcay, & Courchesne, 2006). Enticott and colleagues (2011) showed that 2 weeks of daily excitatory stimulation (5 Hz) over

CONTACT Keren Avirame research@neuroclinic.co.il

mPFC improved social functioning in a 20-year-old woman with high-functioning ASD (Enticott et al., 2011). It is noteworthy that this case report was based solely on self-reported assessments.

A later double-blind placebo-controlled study by the same group found that stimulating the mPFC improved social relation and reduced socially related anxiety (Enticott et al., 2014). However, this placebo-sham-controlled study did not evaluate changes in emotional and cognitive abilities which are essential for proper social behavior. Here, we aimed at comprehensively and objectively measuring the modulation of emotional and cognitive functioning in response to 5-week daily deep transcranial magnetic stimulation (dTMS) in two high-functioning ASD patients.

Materials and methods

Patients

P1 is a 25-year-old Hispanic female. At age 4, she underwent speech therapy and occupational therapy due to speech and motor underdevelopment. At age 15, she was diagnosed with Asperger´s syndrome. Since age 16, she received different antidepressants (Anafranil, Lexapro, Prozac, and Paxil) for only a short period of time because of adverse side effects. At age 18, she was also diagnosed with OCD due to the occurrence of obsessive thoughts, leading to different compulsions such as asking repetitive questions in order to get reassurances, leading to indecisiveness and personal distress. In the 4 months before starting dTMS treatment, P1 started to take Zoloft and Risperidone; no side effects were reported and there was no noticeable improvement. P1 graduated from high school and worked as house helper for a short period. She came to treatment due to high occurrence of OCD-like symptoms, impaired communication skills which was also observed in reduced eye contact, facial and gestural expressions, and social anxiety.

P2 is a 30-year-old Caucasian male. Although P2 suffered from social isolation, anxiety, and OCD since early age, he was first diagnosed with Asperger´s syndrome at age 25. He was unsuccessfully treated in the past for a short period of time with antidepressants (Anafranil) and CBT due to high occurrence of obsessive thoughts, leading to different compulsions such as need for symmetry. P2 completed a 1-year-long course and obtained a professional diploma, and has been working as clerk for 6 years. P2 came to treatment due to high occurrence of OCD-like symptoms and social anxiety which was accompanied by poor communication skills and difficulty in reading social situations leading to social isolation.

Brain stimulation

The magnetic stimulation was delivered by a Magstim Super Rapid^2 stimulator (Magstim Company, Ltd, Carmarthenshire, Wales, UK) with a HAUT-coil (Brainsway Inc.). The HAUT dTMS coil is approved in Israel by the ministry of Health and has been successfully used to treat ASD (Enticott et al., 2011, 2014). In the first session, the optimal spot on the scalp for stimulation of the primary motor cortex and the resting motor threshold (MT), defined as the lowest stimulation intensity capable of inducing a motor response, were determined by involuntary thumb movement measured by evoked potentials using an Electromyography (EMG) of the abductor pollicis brevis muscle. The MT was obtained after gradually decreasing the intensity of single pulses delivered to the motor cortex in an interval of 5 s. The MT was determined as the lowest intensity of stimulation able to produce subtle muscle movement in 5 out of 10 pulses. After the identification of the MT, the coil was placed centrally about 7 cm anterior to the MT to stimulate the bilateral mPFC, similar to previous studies (Enticott et al., 2011, 2014). During stimulation, patients had earplugs to reduce any possible adverse effects on hearing. Each session consisted of 60 trains of 5 Hz given for 10 s, every 20 s, lasting for about 30 min. The stimulation was set to 110% of the individual MT. No adverse effects were reported. P1 received 27 daily sessions of dTMS during 6 weeks at 58% intensity. P2 received 29 daily sessions during 6 weeks at 53% intensity. P1 missed 3 treatments and P2 missed 1 treatment along 6 weeks of intervention due to personal reasons.

Testing

Patients underwent a computerized cognitive battery (Mindstreams, Neurotrax) to measure the possible effects of dTMS on their cognitive abilities. The Mindstreams battery was administrated twice, before and after treatment, testing the same tasks in the same order but with different stimuli (for detailed descriptions, see Dwolatzky et al., 2003). These tasks have been found to be valid and reliable, without significant practice effects (Schweiger, Doniger, Dwolatzky, Jaffe, & Simon, 2003). The Mindstreams battery measures memory (verbal and nonverbal recognition tests), executive function (go-no-go, stroop interference, and catch game), attention (go-no-go and stroop task), verbal function (naming and rhyming), motor skills (finger tapping and catch game), staged information processing speed (single digit, two-digit, and three-digit arithmetic), and visual spatial imagery. Patient's performance is compared to data from cognitively healthy individuals matched according to the patient's age and education. Scores for each of these 7 domains are calculated separately as deviation from the standardized performance and summed together to give the global score. The entire test is administrated in about 60 min. For further details on Neurotrax, see http://www.neurotrax.com and for publications using Neurotrax, see http://www.neurotrax.com/Publications.

Patients were also tested on a comprehensive battery of emotional recognition tasks from the Autism research center in Cambridge, including the eyes test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), the face tests (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997), which are both manual tests, as well as the Cambridge Mindreading (CAM) face-voice battery (Golan, Baron-Cohen, Hill, & Golan, 2006; Golan, Baron-Cohen, Hill, & Rutherford, 2007), using clips and voice records, respectively. In all these tests, the capacity to correctly read emotional cues in the eyes, face, and voice are evaluated.

Questionnaires

In addition to the testing, the patients answered two self-applied clinical questionnaires: (a) Interpersonal Reactivity Index (IRI; Davis, 1980) and (b) the adult Autism Spectrum

Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). The IRI is a brief, self-assessment screening instrument for measuring relational skills. The IRI comprises two cognitive aspects related to metalizing abilities (perspective taking and fantasizing) and two emotional aspects related to recognition and response to emotions (empathic concern and personal distress). The AQ is a brief, self-assessment screening instrument for measuring the degree to which an individual of normal intelligence shows autistic traits. The AQ includes questions about attention to details, social discomfort, and ritualistic behaviors. In addition, obsessive compulsive symptomatology was assessed by the psychiatrist during the baseline and end clinical interviews, using the Yale-Brown obsessive compulsive scale (Y-BOCS). The Y-BOCS is a widespread brief screening instrument for evaluating the severity of obsessions and compulsions in OCD (Goodman et al., 1989). Patients were instructed by the psychiatrist during those sessions on how to fill the Y-BOCS in order to self-report on their condition during the follow-up assessments, which were received via email.

Treatment procedure

The two patients were first examined by an expert psychiatrist who confirmed their diagnosis, assessed their medical state, and verified whether they met the exclusion criteria according to safety guidelines (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). Patients filled in personal and medical questionnaires and signed an informed consent form to undergo the treatment. Patients also received a full explanation on the possible side effects including scalp discomfort, migraine, dizziness, and tiredness. Patients were also informed about the rare occurrence of epileptic seizures. Once the informed consent form was signed, cognitive, emotional, and clinical evaluations were administered by trained psychologists. Evaluations were performed at baseline and after the last dTMS session. The follow-up self-assessment questionnaires were sent via email and were filled by the patients at their home 2 months after the end of treatment. Patients were under the direct supervision of a physician throughout the treatment. The treatment was conducted in accordance with the ethical standards of Helsinki declaration and with the guidelines approved by the Ministry of Health. The records of these two patients with ASD treated in our clinic were retrospectively reviewed. No changes in pharmacological dosage were performed from at least 1 month before treatment and throughout treatment and follow-up.

Results

As shown in Table 1, when comparing performance on the MS battery between pre- and post-treatment, both patients improved in a variety of cognitive functions, with a global improvement of 20% (for P1) and 30% (for P2) in the neuropsychological battery. Additionally, patients reported to experience increasing attention and decisiveness along the treatment.

Table 1. Cognitive scores in the Mindstreams battery.

	P1		P2	
	Pre	Post	Pre	Post
Mindstreams global	87	94	83	104
Memory	93	84	71	99
Executive function	93	105	72	94
Attention	88	97	57	96
Speed processing	78	88	87	107
Visual spatial	49	84	114	114
Verbal function	106	99	91	109
Motor skills	99	103	86	108

Standardized scores before treatment (pre) and at the end of treatment (post) in the entire battery (Mindstreams Global) and in each domain.

The emotional recognition tasks also revealed that recognizing emotions in others became easier, most notably in the prosodic task, in which emotions are conveyed through changes in vocal aspects (see Table 2). Moreover, patients reported to be more aware of emotional and social cues already during the first 2 weeks of treatment.

As indicated in Table 3, the self-report questionnaires showed slight improvement in autistic symptoms (AQ) and empathy (IRI). The most noticeable effect was the decrease in OCD-like symptoms at the end of the treatment as measured by the Y-BOCS scale. This decrease was already reported by the patients during the first two weeks of treatment. Follow-up assessment indicated that OCD-related symptoms are still significantly lower than baseline even 2 months after the end of dTMS treatment.

Aside of the objective measures reported above, changes in eye contact, posture, communication skills, and understanding of both self and others were observed by the patients and their family members. For example, P1 reported that she is "more comfortable" in social situations and behaved "more naturally" when meeting new people. She noted that she "had more to say" and generally she expressed her interests and preferences more freely. She also reported an increased capacity for empathy and perspective taking, even for incidents that occurred many years

Table 2. Emotional recognition tasks.

	P1		P2	
	Pre	Post	Pre	Post
Faces test (error rate)	5%	5%	10%	10%
Eyes test (error rate)	30%	25%	47%	28%
CAM face (error rate)	26%	25%	44%	28%
CAM voice (error rate)	32%	13%	44%	19%

Accuracy (error rate) in emotional recognition tasks from the Cambridge Research Center before treatment (pre) and at the end of treatment (post).

Table 3. Questionnaires.

	P1			P2		
Questionnaires	Pre	Post	FU	Pre	Post	FU
AQ	40	37	35	39	23	19
IRI global	61	65	64	26	41	49
Personal distress	24	24	24	13	7	12
Empathic concern	20	23	23	4	7	11
Fantasy scale	4	7	6	5	10	12
Perspective taking	13	11	11	4	17	14
Y-BOCS	27	0	10	18	0	8
Obsessions	14	0	6	10	0	5
Compulsions	13	0	4	8	0	3

Scores in questionnaires before treatment (pre), at the end of treatment (post) and 2 months post-treatment (FU).

AQ: Autism quotient; IRI: interpersonal relation; Y-BOCS: Yale-Brown obsessive compulsive scale.

before. She was more joyful and open to explore. These improvements seemed to remain at the 2 months follow-up.

P2 started to converse more fluently and to feel less intimidated in social situations. He was gradually able to spend more time outdoors (e.g., pool, rock climbing) and in public places (e.g., coffeehouse, restaurant) and chat with strangers. His family noticed that he is more open and chatty. He reported to feel more at ease when he is around people at work and to communicate more fluently with colleagues.

Discussion

The current case report describes the improvement of two patients with high-functioning ASD with OCD symptoms following 5–6 weeks of daily deep TMS to the mPFC. These results are in line with previous studies using a similar intervention protocol, albeit being only 2 weeks long (Enticott et al., 2014, 2011), including one placebo-controlled study on high-functioning ASD (Enticott et al., 2014). The treatment-induced effects were first measured with validated tests for assessing emotional abilities. In order to gain insight into a person's emotional disposition, it is necessary to properly detect and process facial, vocal, and gestural information. Individuals who lack this capacity find themselves seriously disadvantaged in the social arena, unable to correctly read and respond to social signals, as often reported by individuals with ASD (Adolphs, Sears, & Piven, 2001; Golan et al., 2007). Thus, testing the changes in emotional recognition is essential in a therapeutic procedure intending to ameliorate social dysfunction. Here, the two patients improved mostly in the ability to detect complex emotional states in the speakers' voice, known as affective prosody (Schirmer & Kotz, 2006). In addition, P2 exhibited a significant improvement in the ability to recognize simple and complex emotions in faces and eyes.

Although ASD is often diagnosed on the basis of behavioral symptoms, cognitive dysfunctions are also important in characterizing individuals with ASD (Wilson et al., 2014). Here, we observed that 5–6 weeks daily dTMS increased performance in a range of cognitive tasks, most noticeably in speed processing, attention, and executive functions. In fact, executive functions have been proposed to play a key role in Autism and to be associated with frontal abnormalities (Pennington & Ozonoff, 1996). Executive functions are viewed as a central component of the information-processing system responsible for directing attention and monitoring activity, as well as for coordinating and integrating both information and activity (Hill, 2004). According to this approach, frontal abnormalities cause impairment in goal-directed behavior including problem-solving, flexibility, and planning. It is thus possible that regulating frontal activity with daily high-frequency dTMS might enhance adaptability, which enables the individual to expand and diverge his behavior.

Clinical tools assessing symptoms of ASD also revealed considerable gains, with the most noticeable reduction in the Y-BOCS questionnaire which estimates the severity and occurrence of obsessions and compulsions. Interestingly, the first obvious change subjectively experienced by the two patients was the reduction in OCD symptoms. To our knowledge, this is the first study showing that high frequency bilateral stimulation over the mPFC leads to a temporary remission of OCD symptoms. This observation is in line with a recent study which achieved reduction in OCD symptoms by applying low-frequency stimulation over the mPFC (Modirrousta et al., 2015). Still, the rapid remission of OCD-like symptoms observed in the current case report is surprising given the limited results so far achieved with OCD patients (Dell'Osso, Altamura, Allen, & Hollander, 2005; Kumar, Kumar, & Gupta, 2016). This might correspond with the premise that repetitive behaviors in ASD and OCD stem from different impairments (Wakabayashi, Baron-Cohen, & Ashwin, 2012).

High-frequency stimulation over the mPFC was administered here in a manner similar to previous reports using dTMS in ASD (Enticott et al., 2014, 2011). The mPFC is thought to be involved in reasoning about another person's thoughts, later defined as the cognitive component of theory of mind, as well as in representing socially or emotionally relevant information about other people (Krause, Enticott, Zangen, & Fitzgerald, 2012). Moreover, the mPFC was found to critically contribute not only to social cognition but also to self-referential processes (Mitchell, Banaji, & MacRae, 2005). This is in line with increased self-awareness and expression of wishes, opinions, and preferences, which were subjectively reported by patients and family members. In fact, the absence of deactivation in the default-mode network, in which the mPFC is a central node, might imply that self-referential processes that usually occur at rest, are deficient in ASD patients (Kennedy et al., 2006).

Although the present results are promising, data from clinical trials based on a larger sample and including a control group is necessary in order to comprehensively evaluate the potential of dTMS in ASD. If behavioral outcomes could be further combined with imaging methods, it would permit to explore the underlying neural mechanisms of treatment-induced changes. In the current case report, we observed changes in the emotional, cognitive, and social domains, as well as important reduction in OCD-like symptoms in two adult patients. As such, modulating prefrontal activity with dTMS could be crucial for allowing those who suffer from ASD to acquire more adaptive behaviors. Importantly, treatment-induced effects seem to largely persist 2 months post-treatment and to lead to real-life changes (e.g., participation in social activities). Further studies should examine whether these positive effects could persist for long term (e.g., at least 6 months), whether maintenance period could enhance treatment outcomes and whether accumulative effects can be achieved as a result of repeating the treatment procedure.

An overall improvement seems to be one of the major limitations of this study, especially in the absence of control condition. However, improvement was not observed in all tests and clinical scales. It is also important to note that although we have applied in both sessions the same cognitive battery, the items used in each session were different. This design was previously reported to be satisfactory for reducing practice effects in repeated testing (Schweiger et al., 2003). Moreover, all tests were performed 5–6 weeks apart, as commonly implemented in clinical interventions (Avirame et al., 2016; Levkovitz et al., 2009). Importantly, further studies should assess whether dTMS effects on symptoms of anxiety and depressive have contributed to the amelioration of both OCD and cognition in ASD patients.

To conclude, the current case report suggests that 5–6 weeks of daily deep TMS to the mPFC may show beneficial effects in high-functioning ASD patients with OCD symptoms. Although placebo-controlled studies are required to determine if the observed effects are indeed significant against placebo, this report might encourage to further study the role of the mPFC in ASD patients with OCD symptoms. Finally, understanding the difference in repetitive behaviors between OCD and ASD could help distinguish between these two seemingly overlapping conditions, possibly leading to more adapted pharmacological and behavioral treatments.

Disclosure statement

No potential conflict of interest was reported by the authors.

Compliance with Ethical Standards

The study was performed in accordance with the 1964 Helsinki declaration.

Informed consent was obtained from the patients included in the study.

References

Abrahams, B. S., & Geschwind, D. H. (2008). Advances in autism genetics: On the threshold of a new neurobiology. *Nature Reviews Genetics*, *9*, 341–355. doi:10.1038/nrg2346

Adolphs, R. (2001). The neurobiology of social cognition. *Current Opinion in Neurobiology*, *11*, 231–239. doi:10.1016/S0959-4388(00)00202-6

Adolphs, R., Sears, L., & Piven, J. (2001). Abnormal processing of social information from faces in autism. *Journal of Cognitive Neuroscience*, *13*, 232–240. doi:10.1162/089892901564289

Avirame, K, Stehberg, J, & Todder, D. (2016). Benefits of deep transcranial magnetic stimulation in alzheimer disease: case series. *ECT,32(2) ECT,32 (2) 32*, 127-133. doi:10.1097/YCT.0000000000000286

Baron-Cohen, S. (2000). Theory of mind and autism: A fifteen year review. *Understanding other minds: Perspectives from developmental cognitive neuroscience*, 2, 3–20.

Baron-Cohen, S., Jolliffe, T., Mortimore, C., & Robertson, M. (1997). Another advanced test of theory of mind: Evidence from very high functioning adults with autism or asperger syndrome. *Journal of Child Psychology and Psychiatry*, *38*, 813–822. doi:10.1111/jcpp.1997.38.issue-7

Baron-Cohen, S, Wheelwright, S, Hill, J, Raste, Y, & Plumb, I. (2001). The "reading the mind in the eyes" test revised version: a study with normal adults, and adults with asperger syndrome or high-functioning autism. *Journal Of Child Psychology And Psychiatry*, *42*, 241–251. doi: 10.1111/jcpp.2001.42.issue-2

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "reading the mind in the eyes" test revised version: A study with normal adults, and adults with asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry*, *42*, 241–251. doi:10.1111/jcpp.2001.42.issue-2

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders*, *31*, 5–17. doi:10.1023/A:1005653411471

Baruth, J. M., Casanova, M. F., El-Baz, A., Horrell, T., Mathai, G., Sears, L., & Sokhadze, E. (2010). Low-frequency repetitive transcranial magnetic stimulation modulates evoked-gamma frequency oscillations in autism spectrum disorder. *Journal of Neurotherapy*, *14*, 179–194. doi:10.1080/10874208.2010.501500

Bejerot, S. (2007). An autistic dimension: a proposed subtype of obsessive-compulsive disorder. *Autism*, *11*(2), 101-110. doi:10.1192/bjp.176.4.357

Bersani, F.S., Minichino, A., Enticott, P.G., Mazzarini, L., Khan, N., Antonacci, G., Raccah, R.N., Salviati, M., Delle Chiaie, R., Bersani, G. & Fitzgerald, P.B. (2013). Deep transcranial magnetic stimulation as a treatment for psychiatric disorders: A comprehensive review. *European Psychiatry*, *28*, 30–39. doi:10.1016/j.eurpsy.2012.02.006

Cath, D. C., Ran, N., Smit, J. H., Van Balkom, A. J., & Comijs, H. C. (2007). Symptom overlap between autism spectrum disorder, generalized social anxiety disorder and obsessive-compulsive disorder in adults: A preliminary case-controlled study. *Psychopathology*, *41*, 101–110. doi:10.1159/000111555

Courchesne, E., & Pierce, K. (2005). Why the frontal cortex in autism might be talking only to itself: Local over-connectivity but long-distance disconnection. *Current Opinion in Neurobiology*, *15*, 225–230. doi:10.1016/j.conb.2005.03.001

Dayan, E., Censor, N., Buch, E. R., Sandrini, M., & Cohen, L. G. (2013). Noninvasive brain stimulation: From physiology to network dynamics and back. *Nature Neuroscience*, *16*, 838–844. doi:10.1038/nn.3422

Dell'Osso, B., Altamura, A. C., Allen, A., & Hollander, E. (2005). Brain stimulation techniques in the treatment of obsessive-compulsive disorder: Current and future directions. *CNS Spectrums*, *10*, 966–979,983. doi:10.1017/S1092852900010531

Demirtas-Tatlidede, A., Vahabzadeh-Hagh, A. M., & Pascual-Leone, A. (2013). Can noninvasive brain stimulation enhance cognition in neuropsychiatric disorders? *Neuropharmacology*, *64*, 566–578. doi:10.1016/j.neuropharm.2012.06.020

DiCicco-Bloom, E., Lord, C., Zwaigenbaum, L., Courchesne, E., Dager, S. R., Schmitz, C., et al. (2006). The developmental neurobiology of autism spectrum disorder. *The Journal of Neuroscience*, *26*, 6897–6906. doi:10.1523/JNEUROSCI.1712-06.2006

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *Psychology*. 10, 85

Dwolatzky, T., Whitehead, V., Doniger, G. M., Simon, E. S., Schweiger, A., Jaffe, D., & Chertkow, H. (2003). Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatrics*, *3*, (1). doi:10.1186/1471-2318-3-4

Enticott, P. G., Fitzgibbon, B. M., Kennedy, H. A., Arnold, S. L., Elliot, D., Peachey, A., Zangen, A. & Fitzgerald, P. B. (2014). A double-blind, randomized trial of deep repetitive transcranial magnetic stimulation (rTMS) for autism spectrum disorder. *Brain Stimulation*, *7*, 206–211. doi:10.1016/j.brs.2013.10.004

Enticott, P. G., Kennedy, H. A., Zangen, A., & Fitzgerald, P. B. (2011). Deep repetitive transcranial magnetic stimulation associated with improved social functioning in a young woman with an autism spectrum disorder. *The Journal of ECT*, *27*, 41–43. doi:10.1097/YCT.0b013e3181f07948

Enticott, P. G., Rinehart, N. J., Tonge, B. J., Bradshaw, J. L., & Fitzgerald, P. B. (2010). A preliminary transcranial magnetic stimulation study of cortical inhibition and excitability in high-functioning autism and asperger disorder. *Developmental Medicine & Child Neurology*, *52*, e179–e183. doi:10.1111/j.1469-8749.2010.03665.x

Fecteau, S., Agosta, S., Oberman, L., & Pascual-Leone, A. (2011). Brain stimulation over Broca's area differentially modulates naming skills in neurotypical adults and individuals with asperger's syndrome. *European Journal of Neuroscience*, *34*, 158–164. doi:10.1111/ejn.2011.34.issue-1

Fox, M. D., Buckner, R. L., Liu, H., Chakravarty, M. M., Lozano, A. M., & Pascual-Leone, A. (2014). Resting-state networks link invasive and non-invasive brain stimulation across diverse psychiatric and neurological diseases. *Proceedings of the National Academy of Sciences*, *111*, E4367–E4375. doi:10.1073/pnas.1405003111

Frith, U. (2001). Mind blindness and the brain in autism. *Neuron*, *32*, 969–979. doi:10.1016/S0896-6273(01)00552-9

Golan, O., Baron-Cohen, S., Hill, J. J., & Golan, Y. (2006). The "reading the mind in films" task: Complex emotion recognition in adults with and without autism spectrum conditions. *Social Neuroscience*, *1*, 111–123. doi:10.1080/17470910600980986

Golan, O., Baron-Cohen, S., Hill, J. J., & Rutherford, M. D. (2007). The "reading the mind in the voice" test-revised: A study of complex emotion recognition in adults with and without autism spectrum conditions. *Journal of Autism and Developmental Disorders*, *37*, 1096–1106. doi:10.1007/s10803-006-0252-5

Goodman, W. K., Naylor, S. T., & Volkmar, F. R. (1995). A case-controlled study of repetitive thoughts and behavior in adults with autistic disorder and obsessive-compulsive disorder. *The American Journal of Psychiatry*, *152*, 5.

Goodman, W. K., Price, L. H., Rasmussen, S. A., Mazure, C., Fleischmann, R. L., Hill, C. L., Heninger, G. R. & Charney, D. S. (1989). The Yale-Brown obsessive compulsive scale: I. Development, use, and reliability. *Archives of General Psychiatry*, *46*, 1006–1011. doi:10.1001/archpsyc.1989.01810110048007

Happé, F. (1999). Autism: Cognitive deficit or cognitive style? *Trends in Cognitive Sciences*, *3*, 216–222. doi:10.1016/S1364-6613(99)01318-2

Hill, E. L. (2004). Evaluating the theory of executive dysfunction in autism. *Developmental Review*, *24*, 189–233. doi:10.1016/j.dr.2004.01.001

Hill, E. L., & Frith, U. (2003). Understanding autism: Insights from mind and brain. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *358*, 281–289. doi:10.1098/rstb.2002.1209

Kennedy, D. P., Redcay, E., & Courchesne, E. (2006). Failing to deactivate: Resting functional abnormalities in autism. *Proceedings of the National Academy of Sciences*, *103*, 8275–8280. doi:10.1073/pnas.0600674103

Krause, L., Enticott, P. G., Zangen, A., & Fitzgerald, P. B. (2012). The role of medial prefrontal cortex in theory of mind: A deep rTMS study. *Behavioural Brain Research*, *228*, 87–90. doi:10.1016/j.bbr.2011.11.037

Kumar, N., Kumar, S., & Gupta, R. (2016). An update of the application of Repetitive Transcranial Magnetic Stimulation (rTMS) in patients with obsessive compulsive disorder. *Journal of Neuropsychiatry*, *06*. doi:10.4172/Neuropsychiatry.1000111

Levkovitz, Y., Harel, E. V., Roth, Y., Braw, Y., Most, D., Katz, L. N., … Zangen, A. (2009). Deep transcranial magnetic stimulation over the prefrontal cortex: Evaluation of antidepressant and cognitive effects in depressive patients. *Brain Stimulation*, *2*, 188–200. doi:10.1016/j.brs.2009.08.002

Mitchell, J. P., Banaji, M. R., & MacRae, C. N. (2005). The link between social cognition and self-referential thought in the medial prefrontal cortex. *Journal of Cognitive Neuroscience*, *17*, 1306–1315. doi:10.1162/0898929055002418

Modirrousta, M., Shams, E., Katz, C., Mansouri, B., Moussavi, Z., Sareen, J., & Enns, M. (2015). The efficacy of deep repetitive transcranial magnetic stimulation over the medial prefrontal cortex in obsessive compulsive disorder: Results from an open label study. *Depression and Anxiety*, *32*, 445–450. doi:10.1002/da.22363

Oberman, L. M., Rotenberg, A., & Pascual-Leone, A. (2015). Use of transcranial magnetic stimulation in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *45*, 524–536. doi:10.1007/s10803-013-1960-2

Ozonoff, S., Pennington, B. F., & Rogers, S. J. (1991). Executive function deficits in high-functioning autistic individuals: Relationship to theory of mind. *Journal of Child Psychology and Psychiatry*, *32*, 1081–1105. doi:10.1111/jcpp.1991.32.issue-7

Pelphrey, K., Adolphs, R., & Morris, J. P. (2004). Neuroanatomical substrates of social cognition dysfunction in autism. *Mental Retardation and Developmental Disabilities Research Reviews*, *10*, 259–271. doi:10.1002/(ISSN)1098-2779

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry*, *37*, 51–87. doi:10.1111/jcpp.1996.37.issue-1

Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. & Safety of TMS Consensus Group. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, *120*, 2008–2039. doi:10.1016/j.clinph.2009.08.016

Schirmer, A., & Kotz, S. A. (2006). Beyond the right hemisphere: Brain mechanisms mediating vocal emotional processing. *Trends in Cognitive Sciences*, *10*, 24–30. doi:10.1016/j.tics.2005.11.009

Schweiger, A., Doniger, G. M., Dwolatzky, T., Jaffe, D., & Simon, E. S. (2003). Reliability of a novel computerized neuropsychological battery for mild cognitive impairment. *Acta Neuropsychologica*, *1*, 407–413.

Wakabayashi, A., Baron-Cohen, S., & Ashwin, C. (2012). Do the traits of autism-spectrum overlap with those of schizophrenia or obsessive-compulsive disorder in the general population? *Research in Autism Spectrum Disorders*, *6*, 717–725. doi:10.1016/j.rasd.2011.09.008

Wilson, C. E., Happé, F., Wheelwright, S. J., Ecker, C., Lombardo, M. V., Johnston, P., Daly, E., Murphy, C. M., Spain, D., Lai, M. C. & Chakrabarti, B. (2014). The neuropsychology of male adults with high-functioning autism or asperger syndrome. *Autism Research*, *7*, 568–581. doi:10.1002/aur.1394