

Mirror Neuron Dysfunction and Ego-Boundary Disturbances in Schizophrenia: A Transcranial Magnetic Stimulation Study

Rakshathi Basavaraju, Urvakhsh Meherwan Mehta, Jagadisha Thirthalli, Bangalore N. Gangadhar

ABSTRACT

Background: Ego-boundary disturbance (EBD) is a unique symptom cluster characterized by passivity experiences (involving thoughts, actions, emotions and sensations) attributed by patients to some external agency. The neurobiology of these “first rank” symptoms is poorly understood. Aberrant mirror neuron activation may explain impaired self-monitoring and agency attribution underlying these symptoms. We aim to study mirror neuron activity (MNA) in schizophrenia patients with and without EBD using transcranial magnetic stimulation (TMS). **Materials and Methods:** 50 right-handed schizophrenia patients (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) were evaluated using the Mini-International Neuropsychiatric Interview and the Positive and Negative Syndrome Scale. They completed a TMS experiment to assess putative premotor MNA. Motor evoked potential (MEP) was recorded in the right first dorsal interosseous muscle (FDI) with (a) 120% of resting motor threshold (RMT), (b) stimulus intensity set to evoke MEP of motor threshold 1 mV amplitude (MT1), (c) two paired pulse paradigms (short- and long interval intra-cortical inhibition). These were done in three states: Actual observation of an action using the FDI, virtual-observation (video) of this action and resting state. The percent change of MEP from resting to action-observation states formed the measure of putative MNA. **Results:** MNA measured using MT1 and 120% RMT paradigms was significantly lower in the 18 patients with EBD (thought-broadcast/withdrawal/insertion, made-act/impulse/affect and somatic passivity) than the 32 patients without EBD ($t = 2.431, P = 0.020; t = 2.051, P = 0.04$ respectively for the two paradigms). The two groups did not differ on age, gender, education and total symptom scores. **Conclusion:** Schizophrenia patients with EBD have lower premotor MNA. This highlights the role of MNA dysfunction in the pathophysiology of this unique and intriguing symptom cluster in schizophrenia.

Key words: Ego-boundary disturbances, first rank symptoms, mirror neuron activity, psychosis, transcranial magnetic stimulation

INTRODUCTION

First rank symptoms (FRSs) – a group of intriguing symptoms characterized by a striking breach of “self-versus nonself” boundaries, first described by Schneider,^[1] have had a critical influence on the diagnosis of schizophrenia over the past many decades. This symptom cluster comprises of audible thoughts, voices arguing, voices commenting on one’s action, influence playing on the body (somatic passivity),

Access this article online	
Website: www.ijpm.info	Quick Response Code 
DOI: 10.4103/0253-7176.150821	

Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India

Address for correspondence: Dr. Urvakhsh Meherwan Mehta

Department of Psychiatry, Wellcome Trust/DBT India Alliance Early Career Fellow, National Institute of Mental Health and Neurosciences, Bengaluru - 560 029, Karnataka, India. E-mail: urvakhsh@gmail.com

thought withdrawal, thought insertion, broadcasting of thoughts, made feelings, made impulses, made volitional acts, and delusional perception.^[1,2]

Factor analytical studies have supported a two-dimensional structure of FRS that is stable over time: Symptoms characterized by ego-boundary disturbances (EBDs; delusions of alien control, thought alienation phenomena and somatic passivity) and those characterized by different auditory hallucinations.^[3] Although FRS lack diagnostic specificity, these symptoms provide a well-defined template to study the neurobiological basis of psychotic symptoms from a phenomenological perspective.^[4] The first symptom dimension characterized by EBDs is of particular interest as it represents an alienated feature of the sense of one's own mental or physical activity.^[5]

The neural underpinnings of such EBDs are poorly understood. It has been hypothesized that a dysfunctional mirror neuron network (inferior frontal gyrus, ventral premotor cortex and inferior parietal lobule) leads to functional dissociations between the action imagination, and action enactment, thus resulting in misattribution of agency,^[6] which is seen in symptoms of EBD. Mirror neurons are specialized neurons that are active not only when performing an action oneself, but also while observing someone else perform that action.^[7] Interestingly, there is emerging evidence for dysfunctional mirror neuron activity (MNA) in patients with schizophrenia.^[8,9]

However, there are no studies, which have empirically tested this hypothesis. Transcranial magnetic stimulation (TMS) is a unique, noninvasive, tool having both investigative and therapeutic applications.^[10] It has been extensively used to derive a putative measure of MNA (henceforth referred to as MNA) in humans by detecting changes in the motor evoked potentials (MEP) of hand muscles recorded using electromyography. Enhancement in the MEP amplitude during action observation relative to rest states gives a measure of putative MNA.^[11,12] When compared to functional neuroimaging, TMS has poorer spatial resolution, but better temporal resolution to measure MNA.^[13] In this study, we aim to compare putative MNA, measured using TMS between schizophrenia patients with and without symptoms of EBDs. We hypothesize that patients with EBD will have reduced MNA than patients without EBD.

MATERIALS AND METHODS

A total of 50 right-handed schizophrenia patients (18 with FRS and 32 without FRS) from the inpatient and outpatient services of the National Institute of

Mental Health and Neurosciences, Bengaluru who were recruited as part of a larger study assessing MNA in schizophrenia^[14] were recruited for this analysis. They were diagnosed independently by two qualified psychiatrists according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria, and confirmed using the Mini-International Neuropsychiatric Interview (MINI).^[15] Symptoms were assessed using Positive and Negative Syndrome Scale (PANSS).^[16] Presence or absence of EBD symptoms (though withdrawal, broadcast and insertion, made volition, impulse and affect; and somatic passivity) was determined initially during interviews with PANSS and MINI; which was then confirmed by a comprehensive clinical interview and mental status examination, based on the definitions given by Mellor.^[2]

Patients with substance dependence in the previous 6 months (except nicotine), presence of co-morbid neurological or medical disorder, clinically diagnosable or self-reported visual or auditory impairment, current pregnant or postpartum state and a score of ≤ 19 on the Hindi Mental Status Examination^[17] were excluded from the study. All subjects were assessed with (a) the Edinburgh inventory for handedness^[18] and (b) TMS adult safety screen^[19] to screen for their potential to develop complications. The Institute's Ethics Committee approved the study and all subjects provided written informed consent.

Transcranial magnetic stimulation experiment to assess putative mirror neuron activity

Subjects underwent an experiment to assess motor cortical excitability during goal-directed action observation, relative to rest states, to give a putative measure of MNA.

They were seated comfortably in a chair, in a silent room, 50 cm from the presentation monitor, with their elbows flexed at 90° and hands rested on the armrest of the chair in a prone position.^[11] Single pulse TMS was applied using a 70-mm figure-of-eight coil (MagPro R30 with MagOption; MagVenture, Farum, Denmark) positioned tangentially over the hand area of the left motor cortex, with the handle pointing posterolaterally at a 45° to the sagittal plane.

For each subject, the optimal coil position was determined based on standard methods described in previous studies^[20,21] for localizing the scalp area to stimulate the right first dorsal interosseous (FDI) muscle. This site was marked with a skin marker pen to ensure uniformity of coil positioning throughout the experiment. The coil was held with both hands bracing the coil against the head.^[22] Magnetic pulses activate cortical pyramidal neurons, leading to corticospinal

output that can be measured peripherally as an MEP using electromyography. Initially, all participants underwent a calibration session during which their motor thresholds were established. Resting motor threshold (RMT) was defined as the minimum stimulation intensity (measured in percentage of maximum machine output) required, to evoke a $>50 \mu\text{V}$ MEP in the resting, right FDI muscle in at least 6 out of 10 consecutive trials, measured using electromyography.^[23] Motor threshold of 1 mV (MT1) was defined as the minimum stimulation intensity, evoking 1 mV peak-to-peak amplitude in the resting, right FDI muscle in at least 6 out of 10 successive recordings.^[23] Both RMT and MT1 were calculated using progressive reduction of the stimulator intensity from supra-threshold levels in 1% decrements as described in previous studies.^[20,21]

Next, participants underwent the experiment session. Four stimulus paradigms (two single-pulse and two paired-pulse paradigms) were used to study cortical excitability while the participants watched three different action related visual displays (see below).

Single-pulse paradigms

- 120% of RMT: MEPs obtained with stimulus intensity equal to 120% of RMT were recorded. This stimulus intensity has been the most commonly implemented in studying putative mirror mechanisms using TMS.^[9,22]
- MT1: MEPs obtained with stimulus intensity equal to MT1 were recorded.^[24]

Both 120% RMT and MT1 are a measure of membrane excitability of pyramidal neurons, being influenced by voltage-gated sodium channels.

Paired-pulse paradigms

- Short interval intra-cortical inhibition (SICI): A sub-threshold conditioning stimulus (80% of RMT) was given 3 ms before a supra-threshold test stimulus (MT1) with the right hand at rest. The sub-threshold conditioning stimulus excites only the cortical interneurons and, therefore, inhibits the MEP response to the test stimulus (conditioned MEP) by 50%-90%.^[25] GABA_A receptor agonists potentiate SICI, thus suggesting that SICI may be mediated by GABA_A receptor-mediated neurotransmission.^[26]
- Long interval intra-cortical inhibition (LICI): A supra-threshold conditioning stimulus (MT1) is given 100 ms before a supra-threshold test stimulus (MT1).^[27] The supra-threshold conditioning stimulus activates GABA_B receptor-mediated inhibitory postsynaptic potentials, thus inhibiting the MEP response to the test stimulus (conditioned

MEP).^[28] Thus, LICI reflects cortical inhibition mediated through GABA_B receptor-mediated neurotransmission, based on findings that baclofen, a specific GABA_B receptor agonist enhances LICI.^[29]

Cortical inhibition was expressed as a percentage of the ratio between the conditioned MEPs and the nonconditioned MEPs with stimulus intensity of MT1; that is, (conditioned MEP/nonconditioned MEP) \times 100.^[30]

Ten MEP recordings using each of these four stimulus paradigms (total of 40 recordings) were elicited in random sequence with 5-s intervals, while the subjects observed each of the following:

- Actual observation of an action with active FDI: The subjects observed the experimenter's hand, holding a key in lateral pinch grip (grasping objects between the side of the index finger and the thumb) to perform locking/unlocking actions. This action requires contraction of the FDI to abduct the index finger.^[31]
- Virtual observation: The subjects observed a video showing the above action [Figure 1a].
- Resting state: The subjects observed a still image of a hand and a lock displayed on the monitor [Figure 1b].

The sequence of displaying these experimental states to each subject was randomized. The percent change of the MEP or CI from resting to action observation states (average of virtual and actual observation) formed a measure of MNA. It was calculated using the following formula, where cortical reactivity refers to MEP (in mV) for single-pulse paradigms and CI (%) in paired-pulse paradigms:

$$\frac{\text{Motor cortical reactivity at action observation} - \text{Motor cortical reactivity at rest} \times 100}{\text{Motor cortical reactivity at rest}}$$

Data acquisition and analysis were done using Signal-4 Software, (Cambridge Electronic Devices, Cambridge, UK).

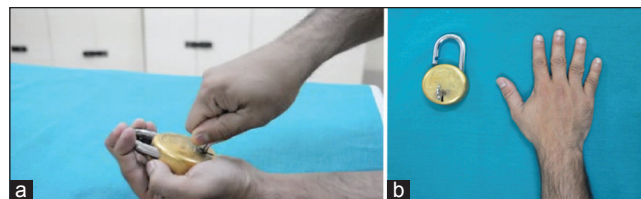


Figure 1: (a) Screen-shot and (b) Photograph of the video (depicting a goal-directed action using the right first dorsal interosseous muscle) and static images of a hand/lock and key, that were used in the experiment to assess putative mirror neuron activity during the virtual observation and rest states respectively

Statistical analyses

Univariate statistics (independent samples *t*-test and Chi-square tests) were used to compare clinical and demographic parameters across the two groups (patients with and without FRS). MNA of the two groups was compared using independent samples *t*-test. All statistical tests were two-tailed, and significance was set at an error $P = 0.05$.

RESULTS

Demographic and clinical variables

As shown in Table 1, the two groups did not significantly differ from each other in terms of age, gender and education, illness duration, medication status (drug-naïve v/s on medication) and symptom scores. Greater proportion of patients with symptoms of EBD had a diagnosis of paranoid schizophrenia. Twelve patients were receiving risperidone, 4 olanzapine, 3 risperidone + olanzapine, 1 olanzapine + amisulpride and 1 aripiprazole. Median duration of treatment with anti-psychotics was 60 days and mean chlorpromazine equivalent was 413.43 ± 226.95 mg/day. The rest were drug-naïve (never treated with any psychotropic medications).

Symptoms of ego-boundary disturbances

A total of 18 (36%) patients experienced symptoms of EBDs as defined. Thought broadcast was the most common symptom, being present in 72% of the patients who experienced symptoms of EBDs [Table 2].

Mirror neuron activity in patients with and without symptoms of ego-boundary disturbances

Independent samples *t*-test on the two groups (patients with and without ego-boundary disturbances) revealed significantly greater MNA in patients without ego-boundary disturbances than in patients with ego-boundary disturbances for MT1 and 120%RMT stimulus paradigms, indicating lesser mirror neuron activity in patients with symptoms of ego-boundary disturbances [Table 3, Figure 2]. Effect sizes (Cohen's *d*)

ranged from 0.52 to 0.62. There was no significant difference in MNA measured using the two paired-pulse paradigms (SICI and LICI) across the 2 patient groups.

DISCUSSION

This study aimed to explore MNA of a subset of schizophrenia patients with symptoms of EBDs like thought alienation phenomena, made phenomena and somatic passivity. A common link across these symptoms is a breach in the barrier separating the self from one's environment. A dysfunctional mirror neuron system has been proposed to underlie deficits in self-awareness and agency attribution, which may lead to symptoms of EBD.^[6,32] We used TMS to derive a putative measure of mirror mechanisms of the brain as has been used in earlier studies.^[9,11,22] MNA was measured in schizophrenia patients with and without symptoms of EBD.

Thirty-six percent of the patients experienced symptoms of EBDs and thought broadcast was the most common symptom as has been reported in previous studies.^[2,33] We found greater enhancement of MEP during action observation relative to rest states in schizophrenia patients without EBD than those with EBD. That is to say, schizophrenia patients with symptoms of EBD had significant deficits in MNA when compared to patients without symptoms of EBD. The effect sizes ranged from 0.52 to 0.62 indicating moderate to good magnitude of difference across the two groups. The two patient groups did not differ in terms of their age, education, and illness duration or symptom scores assessed using PANSS. Hence the observed differences in MNA may be attributed to presence or absence of EBD symptoms. Not surprisingly, more patients with symptoms of EBD had a diagnosis of paranoid sub-type of schizophrenia. Results were consistent when MNA was measured using single-pulse TMS paradigms (MT1 and 120% RMT). However, when MNA was measured using the paired pulse paradigms (SICI and LICI), there was no significant difference between the two groups, though

Table 1: Demographic and clinical variables

Variables	Patients with EBDs (n = 18)	Patients without EBDs (n = 32)	t/ χ^2	P
Age (years)	33.11 (8.20)	29.97 (8.59)	-1.262	0.213
Gender (females) [#]	9 (50)	18 (56.25)	0.181	0.670
Education (years)	12 (4.16)	9.5 (4.86)	-1.841	0.072
Illness duration (months)	63.55 (56.05)	35.84 (34.78)	-2.161	0.069
Medication status (drug naïve) [#]	9 (50)	20 (62.5)	0.739	0.072
Paranoid schizophrenia (%) [#]	15 (83.3)	17 (53.1)	4.56	0.033
PANSS total score	81.55 (20.96)	91.84 (22.84)	1.573	0.122
PANSS positive symptoms	24.50 (5.33)	23.66 (6.09)	-0.491	0.626
PANSS negative symptoms	20.22 (9.24)	25.10 (9.23)	1.791	0.080

All values in the cells are mean (SD); [#]Except=n (%); SD – Standard deviation; PANSS – Positive and negative syndrome scale; EBDs – Ego-boundary disturbances

the findings were in the expected direction (i.e., patients with EBD had poorer MNA than those with EBD). This

indicates a possible type-2 error as the sub-group with EBD had a small sample size ($n = 18$).

Table 2: Distribution of symptoms of EBDs

EBDs	Number of patients ($n = 18$) (%)
Somatic passivity	2 (11.11)
Thought broadcast	13 (72.22)
Thought withdrawal	1 (5.55)
Thought insertion	1 (5.55)
Made volition	4 (22.22)
Made affect	4 (22.22)
Made impulse	1 (5.55)

EBDs – Ego-boundary disturbances

While an aberrant hyperactive MNA may underlie catatonic^[34] or affective^[35] symptoms, there is emerging evidence for MNA deficits in patients with schizophrenia^[8,9] and its association with deficits in social information processing^[36] and negative symptoms.^[37] To the best of our knowledge this is the first study to demonstrate specific associations of premotor MNA deficits with specific symptom dimensions (EBD) of schizophrenia. Our findings indirectly support existing theoretical formulations of

Table 3: Putative MNA in both groups: The MEP difference between resting and action-observation states (average across virtual and actual action-observation) formed the measure of putative MNA

Variables	Patients with EBDs ($n = 18$)	Patients without EBDs ($n = 32$)	t	P
MNA calculated using MT1 paradigm	3.60 (15.44)	32.12 (63.11)	2.431	0.020*
MNA calculated using 120% RMT paradigm	1.29 (15.91)	26.77 (66.80)	2.051	0.047*
MNA calculated using SICI paradigm	4.65 (28.86)	21.39 (46.22)	1.388	0.171
MNA calculated using LICI paradigm	-3.23 (48.87)	7.11 (69.48)	0.778	0.58

MNA – Mirror neuron activity; SICI – Short interval intra-cortical inhibition; LICI – Long interval intra-cortical inhibition; RMT – Resting motor threshold; MT1 – Motor threshold to obtain motor evoked potential of 1 millivolt peak-to-peak amplitude; MEP – Motor evoked potential; EBDs – Ego-boundary disturbances

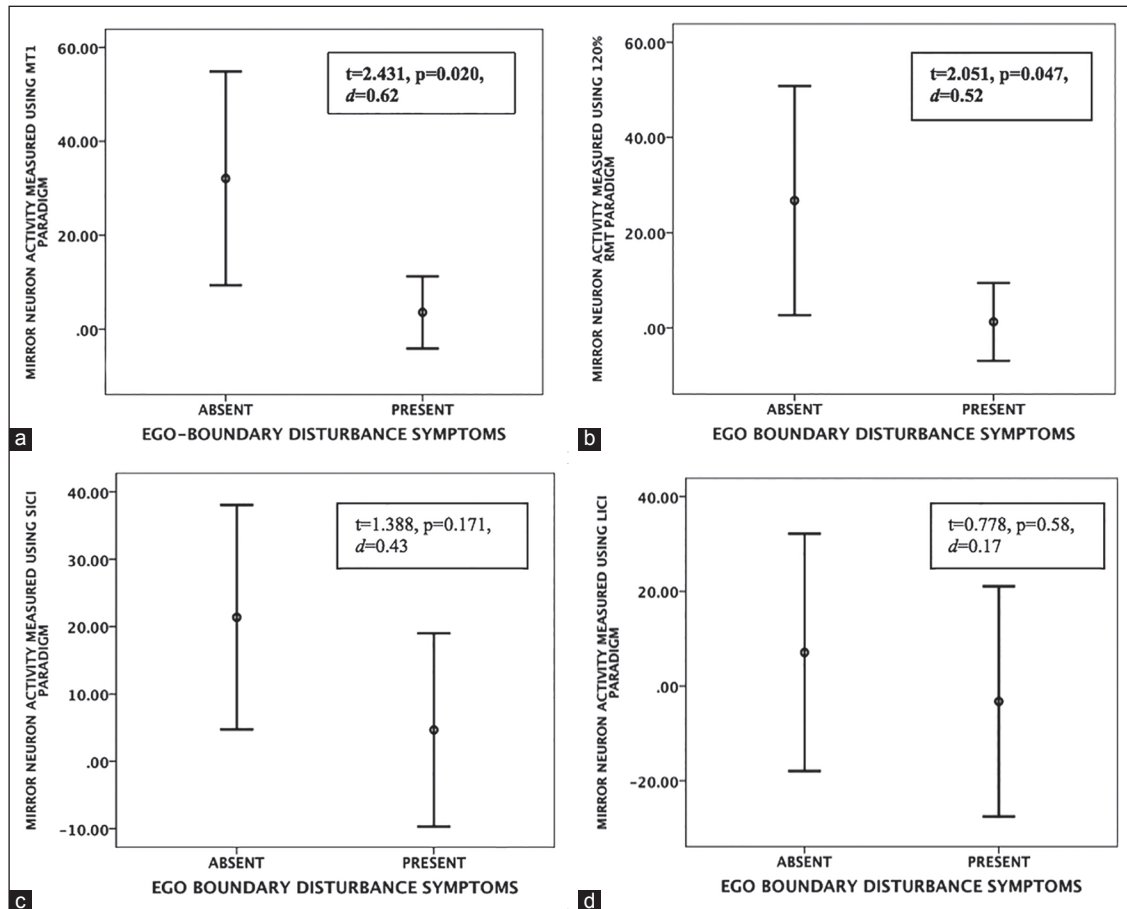


Figure 2: (a) Error bars representing differences in means (95% confidence interval) of mirror neuron activity (y axis) assessed using motor threshold-1, (b) 120% resting motor threshold, (c) Short interval intra-cortical inhibition and (d) Long interval intra-cortical inhibition stimulus paradigms, across patients with and without symptoms of ego boundary disturbances (x axis). Note: d represents effect size (Cohen's d)

the neurobiological substrates of Schneiderian “FRSs of schizophrenia. Aberrant hyperactivity,^[38] deficient cortical thickness^[39] and reduced volume^[40] of the inferior parietal lobule have been demonstrated in schizophrenia patients with FRSs. Interestingly, the inferior parietal lobule is one of the brain regions most consistently shown to have mirror mechanisms in humans.^[41] Our study showing deficient putative MNA in schizophrenia patients with EBD indirectly supports these findings.

According to Frith *et al.*^[42] whenever an action is intended an “efference copy” of the intended action diminishes responses to sensations of limb movements because of which the action is anticipated, the response does not come as a surprise to the person and his self-monitoring is, therefore, intact. When this attenuation does not happen, it leads to parietal cortex hyperactivity; the person perceives the action as an event not under his/her control and goes further to confabulate the agency as external. Mirror neurons could provide a physiological substrate of the “efference copy,”^[43,44] thus playing an integral role in self-monitoring. In schizophrenia patients with EBD, deficient MNA may result in the absence of this attenuation of the responses to sensations of limb movements, thus resulting in a sense of alien control.

It is crucial to note that TMS is an indirect measurement of mirror neuron processes in the brain. Intracranial depth electrodes^[45] give the most direct evidence of MNA, but their use in humans, especially in those with psychiatric disorders, is extremely challenging. Further, MNA mediation using TMS presumably reflects mirror properties of the premotor cortex, which through corticocortical connections to the motor cortex^[11] or cortico-spinal connections to the spinal cord,^[46] result in greater MEPs from the hand muscle during action observation when compared to rest states. Measuring MNA from the motor cortex limits the generalizability of these experiments to possible premotor/inferior frontal gyrus mirror properties. Functional neuroimaging studies are better suited to produce an indirect measure of MNA in other parts of the core mirror system (inferior parietal lobule) and the extended mirror system (insular cortex, superior temporal sulcus, primary, and secondary motor and somatosensory cortices).^[47]

Our results need to be interpreted in the light of them being preliminary findings from a larger study.^[14] The results indicate possible mirror neuron dysfunction in schizophrenia patients with symptoms of EBD, and are not definitive. Replication of these findings in studies with larger sample sizes is necessary to derive conclusive deductions. Future studies should focus on assessing

MNA in a trans-diagnostic group of patients with symptoms of EBDs using combined TMS-functional neuroimaging methods to achieve optimal spatial and temporal resolution. FRSs of schizophrenia have been associated with a heightened social threat perception during emotion processing tasks.^[48] Assessing the relationship between mirror neuron mechanisms, social cognition and EBDs would certainly enhance our understanding of this complex and intriguing symptom cluster of psychosis.

CONCLUSION

Schizophrenia patients with EBD symptoms showed lower MEP enhancement during action observation relative to rest states, than patients without EBD. This reflects a possible deficit in mirror neuron activation in schizophrenia patients who experience symptoms characterized by a breach in their ego-boundary. Given the emerging evidence for the role of mirror neurons in psychiatric disorders in general,^[49] these findings contribute to the already existing understanding of the neurophysiology of FRS in schizophrenia patients, thus providing novel treatment targets^[50] to be explored in future research.

ACKNOWLEDGMENTS

This study was supported by a grant to Dr. Urvakhsh Meherwan Mehta from the Department of Biotechnology, Ministry of Science and Technology, Government of India, (Grant number BT/PR14311/Med/30/470/2010).

REFERENCES

1. Schneider K. *Clinical Psychopathology*. Translated by Hamilton MW. 5th ed. New York: Grune & Stratton; 1959.
2. Mellor CS. First rank symptoms of schizophrenia. I. The frequency in schizophrenics on admission to hospital. II. Differences between individual first rank symptoms. *Br J Psychiatry* 1970;117:15-23.
3. Heering HD, van Haren NE, Derks EM, GROUP Investigators. A two-factor structure of first rank symptoms in patients with a psychotic disorder. *Schizophr Res* 2013;147:269-74.
4. Nordgaard J, Arnfred SM, Handest P, Parnas J. The diagnostic status of first-rank symptoms. *Schizophr Bull* 2008;34:137-54.
5. Waters FA, Badcock JC. First-rank symptoms in schizophrenia: Reexamining mechanisms of self-recognition. *Schizophr Bull* 2010;36:510-7.
6. Arbib MA, Mundhenk TN. Schizophrenia and the mirror system: An essay. *Neuropsychologia* 2005;43:268-80.
7. Rizzolatti G, Fadiga L, Matelli M, Bettinardi V, Paulesu E, Perani D, *et al.* Localization of grasp representations in humans by PET: 1. Observation versus execution. *Exp Brain Res* 1996;111:246-52.
8. Kato Y, Muramatsu T, Kato M, Shibukawa Y, Shintani M, Mimura M. Magnetoencephalography study of right parietal

- lobe dysfunction of the evoked mirror neuron system in antipsychotic-free schizophrenia. *PLoS One* 2011;6:e28087.
9. Enticott PG, Hoy KE, Herring SE, Johnston PJ, Daskalakis ZJ, Fitzgerald PB. Reduced motor facilitation during action observation in schizophrenia: A mirror neuron deficit? *Schizophr Res* 2008;102:116-21.
 10. McClintock SM, Freitas C, Oberman L, Lisanby SH, Pascual-Leone A. Transcranial magnetic stimulation: A neuroscientific probe of cortical function in schizophrenia. *Biol Psychiatry* 2011;70:19-27.
 11. Fadiga L, Fogassi L, Pavesi G, Rizzolatti G. Motor facilitation during action observation: A magnetic stimulation study. *J Neurophysiol* 1995;73:2608-11.
 12. Strafella AP, Paus T. Modulation of cortical excitability during action observation: A transcranial magnetic stimulation study. *Neuroreport* 2000;11:2289-92.
 13. Gangitano M, Mottaghy FM, Pascual-Leone A. Phase-specific modulation of cortical motor output during movement observation. *Neuroreport* 2001;12:1489-92.
 14. Mehta UM, Thirthalli J, Basavaraju R, Gangadhar BN, Pascual-Leone A. Reduced Mirror Neuron Activity in Schizophrenia and its Association With Theory of Mind Deficits: Evidence From a Transcranial Magnetic Stimulation Study. *Schizophr Bull* 2013.
 15. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, *et al.* The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59 Suppl 20:22-33.
 16. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 1987;13:261-76.
 17. Ganguli M, Ratcliff G, Chandra V, Sharma S, Gilby J, Pandav R, *et al.* A Hindi version of the MMSE: The development of a cognitive screening instrument for a largely illiterate rural elderly population in India. *International Journal of Geriatric Psychiatry* 1995(10):367-77.
 18. Oldfield RC. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 1971;9:97-113.
 19. Keel JC, Smith MJ, Wassermann EM. A safety screening questionnaire for transcranial magnetic stimulation. *Clin Neurophysiol* 2001;112:720.
 20. Fitzgerald PB, Brown TL, Daskalakis ZJ, Kulkarni J. A transcranial magnetic stimulation study of inhibitory deficits in the motor cortex in patients with schizophrenia. *Psychiatry Res* 2002;114:11-22.
 21. Daskalakis ZJ, Christensen BK, Chen R, Fitzgerald PB, Zipursky RB, Kapur S. Evidence for impaired cortical inhibition in schizophrenia using transcranial magnetic stimulation. *Arch Gen Psychiatry* 2002;59:347-54.
 22. Maeda F, Kleiner-Fisman G, Pascual-Leone A. Motor facilitation while observing hand actions: Specificity of the effect and role of observer's orientation. *J Neurophysiol* 2002;87:1329-35.
 23. Wasserman E. Inter- and intra-individual variation in the responses to TMS. In: *Oxford Handbook of Transcranial Magnetic Stimulation*. Oxford: Oxford University Press; 2008.
 24. Trevillion L, Howells J, Bostock H, Burke D. Properties of low-threshold motor axons in the human median nerve. *J Physiol* 2010;588:2503-15.
 25. Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, *et al.* Corticocortical inhibition in human motor cortex. *J Physiol* 1993;471:501-19.
 26. Ziemann U, Lönnecker S, Steinhoff BJ, Paulus W. Effects of antiepileptic drugs on motor cortex excitability in humans: A transcranial magnetic stimulation study. *Ann Neurol* 1996;40:367-78.
 27. Valls-Solé J, Pascual-Leone A, Wassermann EM, Hallett M. Human motor evoked responses to paired transcranial magnetic stimuli. *Electroencephalogr Clin Neurophysiol* 1992;85:355-64.
 28. Daskalakis ZJ, Farzan F, Barr MS, Maller JJ, Chen R, Fitzgerald PB. Long-interval cortical inhibition from the dorsolateral prefrontal cortex: a TMS-EEG study. *Neuropsychopharmacology* 2008;33:2860-9.
 29. McDonnell MN, Orekhov Y, Ziemann U. Suppression of LTP-like plasticity in human motor cortex by the GABAB receptor agonist baclofen. *Exp Brain Res* 2007;180:181-6.
 30. Patuzzo S, Fiaschi A, Manganotti P. Modulation of motor cortex excitability in the left hemisphere during action observation: A single- and paired-pulse transcranial magnetic stimulation study of self- and non-self-action observation. *Neuropsychologia* 2003;41:1272-8.
 31. Geere J, Chester R, Kale S, Jerosch-Herold C. Power grip, pinch grip, manual muscle testing or thenar atrophy - which should be assessed as a motor outcome after carpal tunnel decompression? A systematic review. *BMC Musculoskelet Disord* 2007;8:114.
 32. Arbib MA. Other faces in the mirror: A perspective on schizophrenia. *World Psychiatry* 2007;6:75-8.
 33. Peralta V, Cuesta MJ. Diagnostic significance of Schneider's first-rank symptoms in schizophrenia. Comparative study between schizophrenic and non-schizophrenic psychotic disorders. *Br J Psychiatry* 1999;174:243-8.
 34. Mehta UM, Basavaraju R, Thirthalli J. Mirror neuron disinhibition may be linked with catatonic echo-phenomena: A single case TMS study. *Brain Stimul* 2013;6:705-7.
 35. Mehta UM, Basavaraju R, Thirthalli J. Mirror Neuron Activity and Symptom Severity in Drug-naïve Mania - A Transcranial Magnetic Stimulation Study. *Brain Stimul* 2014.
 36. Mehta UM, Basavaraju R, Thirthalli J, Gangadhar BN. Mirror neuron dysfunction-a neuro-marker for social cognition deficits in drug naïve schizophrenia. *Schizophr Res* 2012;141:281-3.
 37. Lee JS, Chun JW, Yoon SY, Park HJ, Kim JJ. Involvement of the mirror neuron system in blunted affect in schizophrenia. *Schizophr Res* 2014;152:268-74.
 38. Franck N, O'Leary DS, Flaum M, Hichwa RD, Andreasen NC. Cerebral blood flow changes associated with Schneiderian first-rank symptoms in schizophrenia. *J Neuropsychiatry Clin Neurosci* 2002;14:277-82.
 39. Venkatasubramanian G, Jayakumar PN, Keshavan MS, Gangadhar BN. Schneiderian first rank symptoms and inferior parietal lobule cortical thickness in antipsychotic-naïve schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2011;35:40-6.
 40. Danivas V, Kalmady S, Arasappa R, Behere RV, Rao NP, Venkatasubramanian G, *et al.* Inferior parietal lobule volume and schneiderian first-rank symptoms in antipsychotic-naïve schizophrenia: A 3-tesla MRI study. *Indian J Psychol Med* 2009;31:82-7.
 41. Molenberghs P, Cunnington R, Mattingley JB. Brain regions with mirror properties: A meta-analysis of 125 human fMRI studies. *Neurosci Biobehav Rev* 2012;36:341-9.
 42. Frith CD, Blakemore S, Wolpert DM. Explaining the symptoms of schizophrenia: Abnormalities in the awareness of action. *Brain Res Brain Res Rev* 2000;31:357-63.
 43. Buccino G, Binkofski F, Fink GR, Fadiga L, Fogassi L, Gallese V, *et al.* Action observation activates premotor and parietal areas in a somatotopic manner: An fMRI study. *Eur J Neurosci* 2001;13:400-4.
 44. Pacherie E, Dokic J. From mirror neurons to joint actions. *Cogn Syst Res* 2006;7:101-12.

45. Mukamel R, Ekstrom AD, Kaplan J, Iacoboni M, Fried I. Single-neuron responses in humans during execution and observation of actions. *Curr Biol* 2010;20:750-6.
46. Dum RP, Strick PL. The origin of corticospinal projections from the premotor areas in the frontal lobe. *J Neurosci* 1991;11:667-89.
47. Pineda JA. Sensorimotor cortex as a critical component of an 'extended' mirror neuron system: Does it solve the development, correspondence, and control problems in mirroring? *Behav Brain Funct* 2008;4:47.
48. Behere RV, Venkatasubramanian G, Arasappa R, Reddy NN, Gangadhar BN. First rank symptoms and facial emotion recognition deficits in antipsychotic naïve schizophrenia: Implications for social threat perception model. *Prog Neuropsychopharmacol Biol Psychiatry* 2011;35:1653-8.
49. Buccino G, Amore M. Mirror neurons and the understanding of behavioural symptoms in psychiatric disorders. *Curr Opin Psychiatry* 2008;21:281-5.
50. Meherwan Mehta U, Agarwal SM, Kalmady SV, Shivakumar V, Kumar CN, Venkatasubramanian G, *et al.* Enhancing putative mirror neuron activity with magnetic stimulation: A single-case functional neuroimaging study. *Biol Psychiatry* 2013;74:e1-2.

How to cite this article: Basavaraju R, Mehta UM, Thirthalli J, Gangadhar BN. Mirror neuron dysfunction and ego-boundary disturbances in schizophrenia: A transcranial magnetic stimulation study. *Indian J Psychol Med* 2015;37:58-65.

Source of Support: Nil, **Conflict of Interest:** None.

New features on the journal's website

Optimized content for mobile and hand-held devices

HTML pages have been optimized of mobile and other hand-held devices (such as iPad, Kindle, iPod) for faster browsing speed.

Click on [**Mobile Full text**] from Table of Contents page.

This is simple HTML version for faster download on mobiles (if viewed on desktop, it will be automatically redirected to full HTML version)

E-Pub for hand-held devices

EPUB is an open e-book standard recommended by The International Digital Publishing Forum which is designed for reflowable content i.e. the text display can be optimized for a particular display device.


Click on [**EPub**] from Table of Contents page.

There are various e-Pub readers such as for Windows: Digital Editions, OS X: Calibre/Bookworm, iPhone/iPod Touch/iPad: Stanza, and Linux: Calibre/Bookworm.

E-Book for desktop

One can also see the entire issue as printed here in a 'flip book' version on desktops.

Links are available from Current Issue as well as Archives pages.

Click on  View as eBook