**Manifest disease and motor cortex reactivity in twins discordant for schizophrenia**

MARTIN SCHÜRMANN, JUHA JÄRVELÄINEN, SARI AVIKAINEN, TYRONE D. CANNON, JOUKO LÖNNQVIST, MATTI HUTTUNEN and RIITTA HARI

**Summary** Schizophrenia is often associated with difficulties in distinguishing between actions of self and of others. This could reflect dysfunction of the mirror neuron system which directly matches observed and executed actions. We studied 11 people with schizophrenia and their co-twins without manifest disease, using stimulus-induced changes in the magnetoencephalographic ~20 Hz rhythm as an index of activation in the motor cortex part of the mirror neuron system. During action observation and execution, motor cortex reaction was weaker in those with schizophrenia than in their co-twins, suggesting a disease-related dysfunction of motor cognition.

**Declaration of interest** None. Funding detailed in Acknowledgements.

During psychotic episodes people with schizophrenia often have difficulties with awareness of their own actions and recognition of other individuals’ actions, evident from beliefs of alien control (Daprat et al., 1997). Such difficulties, like echopraxia (see e.g. Chapman & McGhie, 1964) and activity delusions (patients feel that they influence others to act; Stanghellini & Rossi Monti, 1993), could be related to dysfunction of the mirror neuron system, which matches executed and observed motor actions (Rizzolatti et al., 1996). The core system comprises the inferior frontal gyrus (Broca’s region in the left hemisphere), the inferior parietal lobule and the primary motor cortex.

Here we tested whether people with schizophrenia would show abnormalities in the motor cortex part of their mirror neuron system during observation and execution of finger movements. Earlier studies have indicated abnormal motor cortex function in patients with schizophrenia compared with healthy participants (reviewed by Spence, 2003). We applied a well-established method to monitor motor cortex ~20 Hz magnetoencephalographic (MEG) activity (Hari et al., 1998). In response to electrical median nerve stimuli, this ~20 Hz rhythm is first transiently and bilaterally suppressed, and then 200–400 ms later is strongly enhanced (Fig. 1A), probably reflecting cortical inhibition (Salmelin & Hari, 1994; Chen et al., 1999). Consequently, the size of the ‘rebound’ reflects the functional state of the primary motor cortex; for example the rebound is abolished when the person manipulates an object (Hari et al., 1998).

We compared motor cortex reactivity within schizophrenia-discordant twin pairs, thereby controlling for a portion of the genetic influences on brain physiology. Some of the non-affected co-twins resembled their twin in possessing features of schizotypal personality, which further increased the suitability of this comparison for pinpointing brain abnormalities related to manifest schizophrenia.

**METHOD**

Participants were derived from a randomly selected subset of 335 schizophrenia-discordant twin pairs, identified (for another study) in a cohort of all 9562 pairs of same-sex twins born in Finland between 1940 and 1957 (Cannon et al., 2000). The Structured Clinical Interview for DSM-III-R Axis I Disorders (patient or non-patient edition; Spitzer et al., 1989) served for verification of the diagnoses in all participants. Interviewers were masked to zygosity and diagnostic status. A diagnosis of schizoaffective disorder, affective type in a twin with manifest disease or a psychotic disorder diagnosis in a non-affected twin led to exclusion of that twin pair (Cannon et al., 2000). Eleven twin pairs (aged 49–64 years, mean age 54.4 years, s.d. ± 4.8, five monozygotic and six dizygotic) participated in the study after informed consent and ethics committee approval. All the participants with manifest disease were out-patients in stable clinical condition (further details in a data supplement to the online version of this report). For all pairs, zygosity was determined by DNA analysis (for details see Cannon et al, 2000).

Neuromagnetic data were acquired during three experimental conditions: (a) rest – the participants rested in a relaxed state; (b) observation – the participants observed the experimenter manipulate a small object with her right-hand fingers; (c) action – the participants manipulated the small object with their right-hand fingers without seeing their own hand.

The left and right median nerves were stimulated alternately at the wrists (0.2 ms constant current pulses at intensities exceeding the motor threshold), once every 1.5 s. Signals from 204 planar gradiometers of a helmet-shaped whole-scalp neuromagnetometer (Vectorview, Neuromag, Helsinki, Finland) were analysed. Stimulus-related changes in the level of the ~20 Hz rhythm were quantified by first filtering signals through 14–30 Hz, then rectifying them and finally averaging them time-locked to the median nerve stimuli (approximately 100 signals averaged per condition). The strength of the rebound in each condition was then quantified (from the MEG channel with the strongest rebound suppression during action observation) as the mean level from 300 ms to 1300 ms after stimuli (Salmelin & Hari, 1994).

**RESULTS**

Figure 1A shows the ~20 Hz motor cortex level for one participant. The rebound, peaking at 700 ms, was abolished during object manipulation and significantly suppressed during observation, as shown previously (Schnitzler et al, 1997; Hari et al., 1998). Figure 1B and 1C illustrate the ~20 Hz reactivity in all twin pairs. For both hemispheres and for both observation and action conditions, the twins with schizophrenia showed weaker reactivity of the ~20 Hz rhythm than their non-affected co-twins (binomial test for n = 11 pairs: rest-action P = 0.033 and rest-observation NS in left hemisphere; rest-action P = 0.006 and rest-observation P = 0.006 in right hemisphere).

The rest levels of the ~20 Hz rhythm did not differ between affected and non-affected
co-twins, nor was there any statistically significant difference between the groups in the strengths of cortical responses peaking in the primary somatosensory cortex 20 ms and 35 ms after median nerve stimuli (t-test, \( P > 0.2 \)). The \( ~20 \text{Hz} \) reactivity and the dosages of antipsychotic medication were not correlated (Pearson’s \( r = 0.43 \), \( P = 0.19 \)) (further details in a data supplement to the online version of this report).

**DISCUSSION**

The \( ~20 \text{Hz} \) motor cortex rhythm in the twins with schizophrenia was systematically less reactive than in their non-affected co-twins, both during action observation and execution, with no sign of an additional mirror neuron system abnormality. Since the observed effects were not correlated with medication, we attribute them to the disease itself. The similar somatosensory cortical responses and the comparable resting levels of the rhythmic activity in non-affected and affected participants render implausible any general dysfunctioning of cortical responsiveness in the patient group. The weakened \( ~20 \text{Hz} \) reactivity, specific to clinically manifest disease in the affected twins, could be related to a deficit in motor cognition affecting both the command and the experience of action, both important for delusions of control (Frith, 2005). Further studies should test more extensively the functionality of motor and sensory mirroring in people with schizophrenia, focusing on subgroups displaying special abnormalities in the experience of action.

**ACKNOWLEDGEMENTS**

Supported by the Academy of Finland (National Centers of Excellence Programme 2006–2011), Sigrid Juselius Foundation, and the National Institute of Mental Health, USA (MHS2857). We thank Ulla Mustonen for help in recruiting the participants.

**REFERENCES**


Clinical details of the 11 pairs of affected and non-affected co-twins

Duration of medication was estimated from hospital records. None of the co-twins without manifest schizophrenia had bipolar disorder. Schizotypal personality disorders were present in several co-twins, in line with expectations for this sample. A sample of 23 twin pairs (out of the original sample of 335 pairs) were approached and asked to take part in the study. Ten pairs refused, for example because they would have had to travel a long distance to the laboratory or because they had recently taken part in other measurements. Out of the 13 pairs who agreed, 2 failed to attend.

<table>
<thead>
<tr>
<th>Twin-pair</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Zygosity</th>
<th>Medication</th>
<th>Diagnosis (DSM-III-R code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>M</td>
<td>DZ</td>
<td>0</td>
<td>Undifferentiated type (295.9C)</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>M</td>
<td>DZ</td>
<td>20</td>
<td>Schizoaffective disorder (295.7A)</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>M</td>
<td>DZ</td>
<td>30</td>
<td>Undifferentiated type (295.9C)</td>
</tr>
<tr>
<td>4</td>
<td>53</td>
<td>M</td>
<td>MZ</td>
<td>50</td>
<td>Paranoid type (295.3C)</td>
</tr>
<tr>
<td>5</td>
<td>48</td>
<td>F</td>
<td>MZ</td>
<td>200</td>
<td>Paranoid type (295.3C)</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>F</td>
<td>DZ</td>
<td>10</td>
<td>Catatonic type (295.2C)</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>M</td>
<td>MZ</td>
<td>35</td>
<td>Paranoid type (295.3C)</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>F</td>
<td>DZ</td>
<td>300</td>
<td>Paranoid type (295.3F)</td>
</tr>
<tr>
<td>9</td>
<td>59</td>
<td>M</td>
<td>DZ</td>
<td>500</td>
<td>Residual type (295.6C)</td>
</tr>
<tr>
<td>10</td>
<td>58</td>
<td>M</td>
<td>MZ</td>
<td>200</td>
<td>Undifferentiated type (295.9C)</td>
</tr>
<tr>
<td>11</td>
<td>64</td>
<td>M</td>
<td>MZ</td>
<td>380</td>
<td>Paranoid type (295.3E)</td>
</tr>
</tbody>
</table>

CPZeq, Chlorpromazine equivalent; DZ, dizygotic; F, female; M, male; MZ, monozygotic.
Manifest disease and motor cortex reactivity in twins discordant for schizophrenia
MARTIN SCHÜRKMANN, JUHA JÄRVELÄINEN, SARI AVIKAINEN, TYRONE D. CANNON, JOUKO LÖNNQVIST, MATTI HUTTUNEN and RIITTA HARI
Access the most recent version at DOI: 10.1192/bjp.bp.106.024604

Supplementary Material
Supplementary material can be found at:
http://bjp.rcpsych.org/content/suppl/2007/08/02/191.2.178.DC1.html

References
This article cites 9 articles, 1 of which you can access for free at:
http://bjp.rcpsych.org/content/191/2/178#BIBL

Reprints/permissions
To obtain reprints or permission to reproduce material from this paper, please write to permissions@rcpsych.ac.uk

You can respond to this article at
/letters/submit/bjprcpsych;191/2/178

Downloaded from
http://bjp.rcpsych.org/ on October 6, 2016
Published by The Royal College of Psychiatrists

To subscribe to The British Journal of Psychiatry go to:
http://bjp.rcpsych.org/site/subscriptions/