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Self-monitoring as a familial vulnerability marker for psychosis: an analysis of patients, unaffected siblings and healthy controls

J. Hommes¹, L. Krabbendam², D. Versmissen³, T. Kircher⁴, J. van Os^{1,5} and R. van Winkel^{1,6*}

¹ Department of Psychiatry and Psychology, School of Mental Health and Neuroscience, Maastricht University Medical Centre, The Netherlands

² Department of Psychology and Education, VU University of Amsterdam, The Netherlands

³ Foundation for Equal Opportunities, University of Antwerp, Belgium

⁴ Department of Psychiatry and Psychotherapy, University of Marburg, Germany

⁵ King's College London, King's Health Partners, Department of Psychosis Studies, Institute of Psychiatry, London, UK

⁶ University Psychiatric Centre Catholic University Leuven, Campus Kortenberg, Belgium

Background. Alterations in self-monitoring have been reported in patients with psychotic disorders, but it remains unclear to what degree they represent true indicators of familial vulnerability for psychosis.

Method. An error-correction action-monitoring task was used to examine self-monitoring in 42 patients with schizophrenia, 32 of their unaffected siblings and 41 healthy controls.

Results. Significant between-group differences in self-monitoring accuracy were found ($\chi^2=29.3$, $p<0.0001$), patients performing worst and unaffected siblings performing at an intermediate level compared to controls (all between-group differences $p<0.05$). In the combined group of healthy controls and unaffected siblings, detection accuracy was associated with positive schizotypy as measured by the Structured Interview for Schizotypy – Revised (SIS-R) ($\beta=-0.16$, s.e.=0.07, $p=0.026$), but not with negative schizotypy ($\beta=-0.05$, s.e.=0.12, $p=0.694$). In patients, psychotic symptoms were not robustly associated with detection accuracy ($\beta=-0.01$, s.e.=0.01, $p=0.094$), although stratified analysis revealed suggestive evidence for association in patients not currently using antipsychotic medication ($\beta=-0.03$, s.e.=0.01, $p=0.052$), whereas no association was found in patients on antipsychotic medication ($\beta=-0.01$, s.e.=0.01, $p=0.426$). A similar pattern of associations was found for negative symptoms.

Conclusions. Alterations in self-monitoring may be associated with familial risk and expression of psychosis. The association between psychotic symptoms and self-monitoring in patients may be affected by antipsychotic medication, which may explain previous inconsistencies in the literature.

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Key words: Psychosis, schizophrenia, self-monitoring.

Introduction

Self-monitoring is a specific type of source monitoring (Johnson *et al.* 1993; Brebion *et al.* 2007; Versmissen *et al.* 2007b) that enables the person to distinguish self-generated actions from those elicited by external stimuli (Frith, 1987; Knoblich *et al.* 2004). It has been proposed that the internal monitoring of speech generation and inner thoughts is analogous to the monitoring of motor actions (Frith, 1987, 1992, 1996; Blakemore *et al.* 2000; Seal *et al.* 2004; Fu *et al.* 2006; Jones & Fernyhough, 2007). According to this model,

‘thinking’ is operationalized as an action with a clear intention, thus providing a sense of agency for thoughts (Frith, 1992; Frith *et al.* 1998, 2000; Gallagher, 2004). Misattributions of self-generated thoughts as voices coming from the outside could provide a plausible mechanism underlying the hallucinatory process in psychosis (Shergill *et al.* 2000). A deficit in the process of self-monitoring thoughts may therefore result in thought insertion and auditory hallucinations (Frith, 1992; Brebion *et al.* 1998, 2005; Ditman & Kuperberg, 2005). Several studies in patients with schizophrenia have indeed provided evidence that a deficit in self-monitoring of one’s own cognitive actions is associated with psychotic symptoms e.g. (Harvey, 1985; Bentall *et al.* 1991; Daprati *et al.* 1997; Blakemore *et al.* 2000; Keefe *et al.* 2002; Brunelin *et al.* 2006; Johns *et al.* 2006; Costafreda *et al.* 2008), although

* Address for correspondence: Dr R. van Winkel, M.D., Ph.D., School of Mental Health and Neuroscience (MHeNS), Maastricht University Medical Centre, Vijverdalseweg 1, Concorde Building (SN2), 6200 MD Maastricht, The Netherlands.

(Email: ruud.vanwinkel@maastrichtuniversity.nl)

not all studies were able to find an association between psychotic symptoms and alterations in self-monitoring (Vinogradov et al. 1997; Fourmeret et al. 2001; Li et al. 2002; Versmissen et al. 2007a).

Importantly, studies suggesting that alterations in self-monitoring are associated with psychotic disorder were unable to consistently address the question of whether self-monitoring alterations are a vulnerability marker for psychotic disorder or merely a state marker of acute psychotic symptoms. Johns et al. (2006) found a self-monitoring deficit in patients currently experiencing hallucinations but not in patients who previously experienced hallucinations. Franck et al. (2000) found worse detection accuracy in patients experiencing hallucinations during the experiment compared to non-hallucinating patients. Several studies have used functional neuroimaging paradigms to detect abnormal regional activation in hallucination-prone patients when performing tasks engaging the verbal self-monitoring system, compared to non-hallucination prone patients with schizophrenia and healthy controls, focusing on various regions such as the Broca area, the anterior cingulate, the left temporal cortex and the supplementary motor area (SMA) (McGuire et al. 1995, 1996; Schnell et al. 2008). These studies reported both under- and overactivation associated with self-monitoring alterations (Shergill et al. 2000; Schnell et al. 2008; Raij et al. 2009), and these findings were hypothesized to result from a pathological increase in microstructural elements supporting excitatory neurotransmission, leading to instability (for a detailed discussion, see Bates et al. 2002).

Some studies in healthy control subjects have found evidence suggesting that alterations in self-monitoring may be associated with vulnerability for psychosis rather than acute psychosis *per se*. For example, several studies have found that healthy individuals who experienced hallucinations displayed more reality or action-monitoring errors compared to normal subjects who had not experienced hallucinations (Bentall & Slade, 1985; Rankin & O'Carroll, 1995; Laroit et al. 2004; Debbané et al. 2009). An additional argument that alterations in self-monitoring are not merely epiphenomena of acute psychosis is that some studies have also reported an inverse association between self-monitoring and negative symptoms (Brebion et al. 1999, 2002, 2005). Negative symptoms are thought to be stable over time (Pfohl & Winokur, 1982; Pogue-Geile & Harrow, 1985; Katsanis et al. 1990; Keefe et al. 1991; Rey et al. 1994; Dollfus & Petit, 1995) and to index genetic liability to psychotic disorder better than positive symptoms (Tsuang et al. 1991; Fanous et al. 2001; Schurhoff et al. 2003).

Further evidence suggesting that self-monitoring alterations are associated with vulnerability for

psychosis may be derived from studies investigating groups at risk for psychotic disorder such as first-degree relatives of patients with schizophrenia (Johns & van Os, 2001; Hanssen et al. 2006) or individuals with psychometric risk states. To our knowledge, only two studies have used this approach. Johns et al. (2009) found a significant difference in self-monitoring in persons with an at-risk mental state (ARMS) compared to healthy controls, and Versmissen et al. (2007b) found evidence for self-monitoring alterations in three psychometrically and genetically defined at-risk groups compared to controls.

Of note is that the use of verbal recognition or signal detection tasks, as applied in previous research (Bentall & Slade, 1985; Rankin & O'Carroll, 1995; Morrison & Haddock, 1997; Brebion et al. 1998, 2000, 2005; Ragland et al. 2003; Heinrichs & Vaz, 2004; Johns et al. 2009), may yield biased results because performance on these tasks is strongly associated with cognitive performance in general and could thus be influenced by characteristics such as verbal intelligence, time elapsed between acquisition and recognition, memory dysfunction and executive dysfunction (Johnson et al. 1993; Seal et al. 1997). Therefore, in the present study we used an action-monitoring task, which may be less biased by cognitive performance, in patients with schizophrenia, their unaffected siblings and healthy controls. We hypothesized that: (1) patients with a non-affective psychotic disorder would show worse self-monitoring compared to healthy controls; (2) the unaffected siblings would show intermediate accuracy, supporting the notion of self-monitoring alterations as a vulnerability marker for psychosis; (3) self-monitoring accuracy would be inversely related to psychotic symptoms at the level of subclinical positive schizotypy in unaffected groups as well as at the level of psychotic symptoms in the patients; and (4) self-monitoring alterations would also be associated with negative symptoms in both patients and in non-affected groups.

Furthermore, it was hypothesized that patients do not automatically change their own movements to compensate for the action change by the computer compared to healthy controls or their first-degree relatives, as reported consistently in previous research (for an overview, see Jeannerod, 2009).

Method

Sample

The study sample consisted of 42 patients with a non-affective psychotic disorder according to DSM-IV-TR, 32 unaffected siblings of the patients and 49 control

subjects. Written informed consent conforming to the local ethics committee guidelines was obtained from all subjects. Inclusion criteria were: fluency in Dutch; aged 16–55 years; and, for patients, first contact with mental health facilities within the past 10 years. For the controls, the occurrence of a psychotic disorder in either the control or a first-degree family member was considered an exclusion criterion.

Patients were recruited through the Community Mental Health Centres and the Psychiatric Hospitals of the catchment area (South Limburg, The Netherlands). All unaffected siblings were sampled through participating patients. Twenty-two families contributed one unaffected sibling and one patient, two families contributed two siblings and one patient, one family contributed two patients, seven unaffected siblings participated without their patient sibling and 16 patients participated without an unaffected sibling. Control subjects were recruited through random mailings in nearby municipalities and through advertisements.

The 42 patients had DSM-IV-TR diagnoses of schizophrenia ($n=32$), schizo-affective disorder ($n=4$), brief psychotic disorder ($n=5$) and psychotic disorder not otherwise specified (NOS) ($n=1$). Five siblings and five healthy controls had had one episode of major depressive disorder (MDD), in full remission at the time of testing, and two controls had had one episode of MDD, in partial remission at the time of testing. The remaining siblings and controls had no DSM-IV diagnosis.

Procedures

To study the hypothesis that symptoms are associated with problems in the central monitoring of action (Frith & Done, 1989), studies on error correction can be used to test the source-monitoring system. These studies test the central monitoring system because the error correction is too rapid to use exteroceptive feedback. In this study, an error correction task was used as described previously (Knoblich & Kircher, 2004; Knoblich *et al.* 2004).

Seated in front of a computer screen, at a distance of about 60 cm, subjects were exposed to the image of a full circle (see Fig. 1a). A covered writing pad was located between the subject and the computer screen. By covering the writing pad we could ensure that the subjects could not observe their own hand movements while they were drawing with a pen.

The computer screen was an Apple Vision (Apple, USA) 17-inch monitor with a horizontal resolution of 800 pixels and a vertical resolution of 600 pixels. The vertical sync frequency was 75 Hz. The movement of the pen tip was recorded using a pressure-sensitive

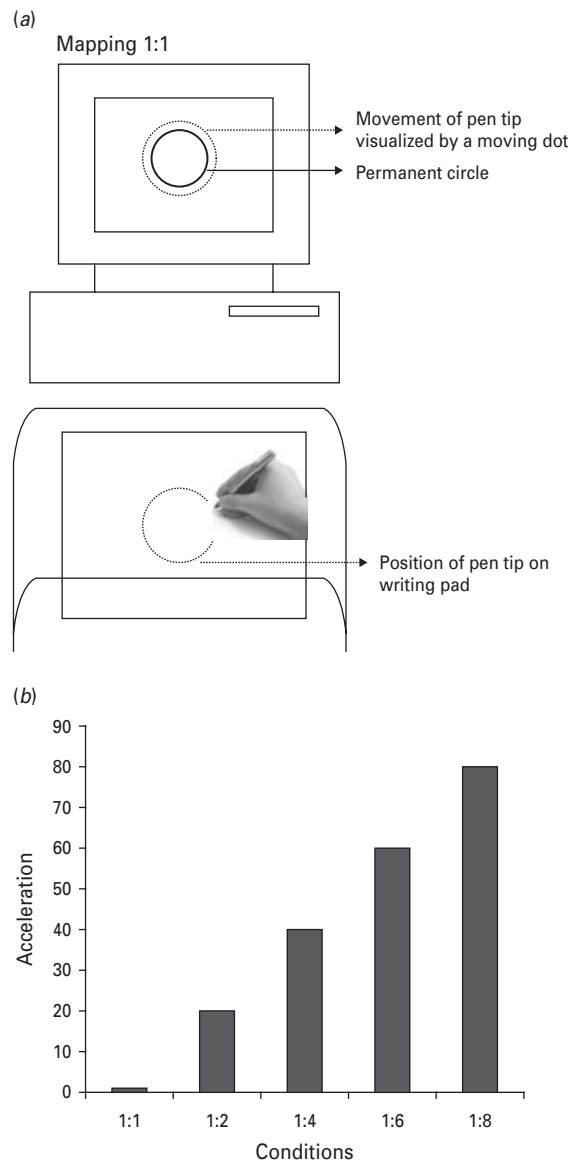


Fig. 1. (a) Visual representation of the task. Each separate trial consisted of drawing five circles around the full, permanent circle that remained on the screen during the whole trial. Participants were instructed to interrupt the test by lifting their pen from the drawing map as soon as they noticed a difference between the actual movement they made on the drawing map and the representation they saw on the computer screen. (b) The different conditions used in the error correction task. In the interval between the sixth and the eighth second, the movement of the dot on the screen was accelerated relative to the movement of the pen tip on the drawing map by 20, 40, 60 or 80%.

Wacom writing pad (Wacom Europe GmbH, Germany) with a sampling rate of 75 Hz, a horizontal resolution of 15000 dots and a vertical resolution of 11250 dots. An Apple Power PC controlled these devices. The sampling rate of the writing pad was

synchronized with the screen refresh rate. Hence, the constant delay between the visual effect and the movement of the pen tip was about 13 ms.

The experiment was made up of four tasks, which were presented in the following order.

Tracking task

The objective of the first task (20 trials) was to assess the subject's tracking performance. In each trial the subject tracked a circular target, which moved with constant velocity, using the pen and the writing pad. The location of the pen tip was indicated by a solid circular dot. Neither the circular target nor the dot left a trace on the screen. In this task the mapping between the computer screen and the writing pad was 1:1, that is a similarity of 100% between the drawing made by the subject and the visual consequence shown on the computer screen. In each trial the circular target completed five circles around the full, permanent circle, which remained on the screen during the whole trial, with a velocity of 2 s per circle and an eccentricity of 9° visually for the full circle. Crossing the 12 o'clock position of the target was indicated by a short beep (200 ms, 1000 Hz).

Training task

In this task 10 trials with mapping changes (from 1:1 to 1:2) were introduced to the subjects, similar to the main experiment.

Colour change detection task

In this condition we could assess whether there were difficulties lifting the pen during a movement. Therefore, the subject had to lift the pen as rapidly as possible when the solid circular dot changed colour. This colour change occurred while in the fourth circle.

Main experiment

Each trial (120 in total) of the experiment started by successfully crossing a small quadratic box, located above the 12 o'clock position of the circle, accompanied by a short beep. Each separate trial was composed of drawing five circles around the full, permanent circle that remained on the screen during the whole trial. Whenever the dot that represented the pen tip passed the 12 o'clock point (after 2, 4, 6, 8 and 10 s), the same beep was heard.

Participants were instructed to interrupt the test by lifting their pen from the drawing map as soon as they noticed a difference between the actual movement they made on the drawing map and the representation they saw on the computer screen. A trial could come to an end by the lifting of the pen or automatically after 11 s if no pen lift occurred.

The position of the pen tip's coordinates were recorded at the time of each beep to determine to what extent the mapping change was compensated for in the movement. This position reflects the distance between the centre of the drawn circle and the pen position on the writing pad. Therefore, the position of the pen tip at each beep represents the radius of the circle the subject was ending at the time of the beep.

Five different conditions (20% of the trials each) were possible (see Fig. 1b). The first 6 s, the mapping between the writing pad and the screen was 1:1. In the interval between the sixth and the eighth second, the movement of the dot on the screen was accelerated relative to the movement of the pen tip on the drawing map by 20, 40, 60 or 80%. In 20% of the trials, no acceleration occurred.

Instruments

For all participating patients, the Operational Criteria Checklist for Psychotic Illness (OCCPI; McGuffin *et al.* 1991) was completed, based on case-note material, and also the Positive and Negative Syndrome Scale (PANSS) interview (Kay *et al.* 1987). Where necessary, additional information was derived from ward staff or case managers. Using the information in the OCCPI, the computerized program OPCRIT (McGuffin *et al.* 1991) yielded DSM-IV diagnoses.

The Structured Interview for Schizotypy – Revised (SIS-R) was used to measure the positive, negative and disorganization dimensions of the subclinical psychosis or 'schizotypy' phenotype (Vollema & Ormel, 2000; Pfeifer *et al.* 2009). Items are scored on a four-point scale ranging from absent (score 0) to severe (score 3). Positive schizotypy covers the items referential thinking, magical ideation, illusions and suspiciousness. Negative schizotypy contains the items social isolation, social anxiety, introversion, restricted affect, referential thinking and suspiciousness. Disorganization schizotypy encompasses the items goal directness of thinking, loosening of associations, and oddness.

Finally, two verbal subtests, Information and Arithmetic, and two performance subtests, Block Design and Symbol Search, of the Wechsler Adult Intelligence Scale III (WAIS-III; Wechsler, 1997) were used to obtain a measure of intelligence quotient (IQ; Blyler *et al.* 2000).

Analysis

Associations between psychosis risk and self-monitoring ability

A three-level ordinal group variable was constructed reflecting the risk for psychosis, with a value of 2 for

patients, 1 for relatives and 0 for controls. The number of correct pen lifts in the five conditions, representing a certain extent of mapping change (hereafter 'detection accuracy'), were saved as average values over all trials for each subject. Pen lifts in the baseline conditions are errors in self-monitoring (no transformation occurs), whereas pen lifts in the other conditions are indicative of adequate self-monitoring. Therefore, to create a measure of the individual's overall detection accuracy, four observations were created for each subject, reflecting the four velocity transformation conditions where transformation occurred (1:2, 1:4, 1:6, 1:8). To account for hierarchical clustering of detection accuracies across different conditions (1:2, 1:4, 1:6, 1:8), nested in individual participants, between-group differences in the pattern of detection accuracy were modelled using multilevel linear regression analysis using the XTREG routine in STATA version 11.0 (StataCorp, 2008), with detection accuracy as the dependent variable and 'group' and 'condition', and also their interaction term, as the independent variables. This analysis investigates the increase in detection accuracy with increasing acceleration (i.e. over the different conditions), as indicated by the 'group \times condition interaction'. This approach allows for the combined analysis of all self-monitoring data, which is a better solution than analysing the conditions separately. Age, sex and IQ were included as possible *a priori* confounders. To determine whether differences between individual groups were statistically significant, *post-hoc* Wald tests based on the group \times condition interaction model were used. Effect sizes were obtained by examining the appropriate linear combinations using the LINCOM routine.

Associations between psychotic symptoms and self-monitoring ability

To examine the hypothesis that higher levels of positive and negative symptoms are associated with worse action-monitoring in patients, multilevel linear regression analysis was applied, with detection accuracy as the dependent variable and psychotic symptoms, condition and their interaction term as independent variables. A similar analysis was conducted with SIS-R subclinical symptoms in controls and unaffected siblings. For this analysis, the controls and the unaffected siblings were combined to increase the sample size and variability, resulting in greater statistical power.

Given the known overlap between positive and negative symptoms, the multilevel regression analysis investigating the association between positive symptoms and self-monitoring was controlled for the presence of negative symptoms, as in a previous study (Brebion *et al.* 1999), and *vice versa*. In addition, age, sex

Table 1. Demographics

	Controls	First-degree relatives	Patients	<i>p</i> value
No. of participants	49	32	42	
Male (%)	32.7	36.4	66.7	0.003
Age (years)	34.81	30.84	33.48	0.293
IQ	114.18	100.59	95.63	<0.001

and IQ were included as possible *a priori* confounders. The role of antipsychotic use was also considered as potentially relevant because antipsychotics exert a direct effect on symptomatology and it may be that they also influence the ability to monitor one's motor actions given the effects on nigrostriatal dopaminergic neurotransmission. Therefore, the analysis in patients was additionally controlled for use of antipsychotic medication (yes/no) and subanalyses also investigated the association between detection accuracy and symptomatology in patients stratified for current use of antipsychotic medication. Two-way interactions between condition and symptoms stratified for antipsychotic use were derived from the three-way condition \times symptoms \times antipsychotic use interaction model.

Compensation of mapping change

The radial components, reflecting the radius of the pen tip at the time of each beep, were transcribed for each beep (five beeps per trial), with separate values for the various mapping change conditions. Because the velocity transformation occurred after radius 3, the compensation movement per velocity transformation was calculated by subtracting the mean radial component before the velocity transformation from the mean radial component after the velocity transformation. Similar to the detection accuracy, the mean compensation movements per velocity transformation per subject were reshaped into five observations per subject based on the latter five velocity transformation conditions. Between-group differences were assessed, with 'mean compensation' as the dependent variable and 'group' and 'condition' and also their interaction term as the independent variables.

Results

Sample characteristics

The error-correction task was carried out by 124 subjects: 42 patients with psychosis, 32 siblings and 49 healthy controls. Significant between-group differences were found for intelligence and sex (see Table 1).

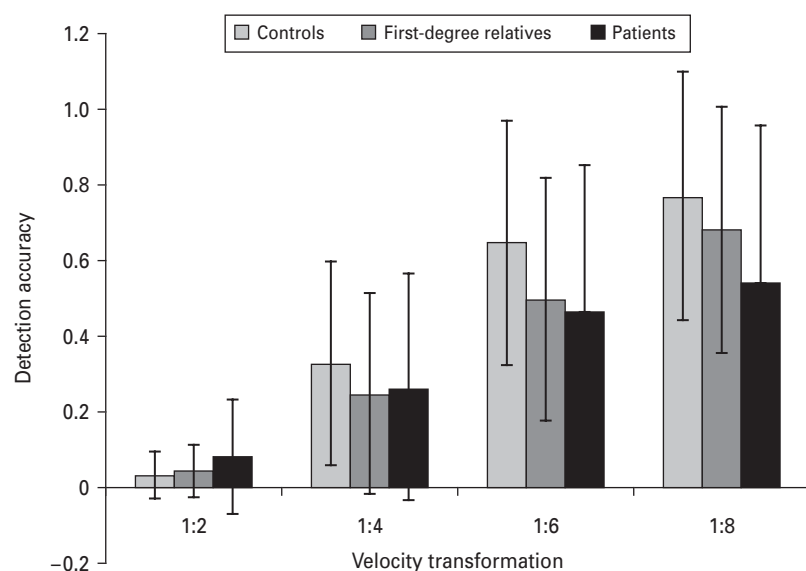


Fig. 2. Patterns of detection accuracy in different conditions across groups.

Twenty-nine patients with psychosis were currently using antipsychotic medication, 10 patients were not, and no information on antipsychotic use was available for three patients. There were no large or significant differences between patients with or without current antipsychotic treatment in positive ($t = -0.28$, $p = 0.778$) or negative symptoms ($t = -0.90$, $p = 0.374$).

Self-monitoring ability and psychosis

The detection accuracy increased significantly in all groups as the transformations became larger ($p < 0.001$ for all). Performance on the action-monitoring task was modestly associated with IQ in the patient group ($\beta = 0.02$, $s.e. = 0.01$, $p = 0.033$) but not in the siblings ($\beta = 0.004$, $s.e. = 0.01$, $p = 0.61$) or healthy controls ($\beta = 0.01$, $s.e. = 0.01$, $p = 0.14$). Significant differences between groups were found in detection accuracy over the different conditions when covarying for age, sex and IQ [group \times condition interaction $\chi^2(2) = 29.3$, $p < 0.0001$], as depicted in Fig. 2 and Table 2. Patients showed the worst detection accuracy ($\beta = 0.41$, $s.e. = 0.04$), controls had the best ($\beta = 0.68$, $s.e. = 0.03$) and the siblings performed at a level that was intermediate between the other groups ($\beta = 0.56$, $s.e. = 0.04$). Differences between controls and patients were statistically significant [$\chi^2(1) = 29.8$, $p < 0.0001$], as were differences between controls and siblings [$\chi^2(1) = 5.8$, $p = 0.016$] and patients and siblings [$\chi^2(1) = 7.0$, $p = 0.008$]. Because psychomotor slowing, as measured by the Symbol-Digit Substitution task, was observed in both patients ($\beta = -18.0$, $s.e. = 1.57$, $p < 0.01$) and unaffected siblings compared to the controls ($\beta = -4.26$, $s.e. = 1.69$, $p = 0.012$), a sensitivity

analysis investigated action monitoring while covarying for psychomotor performance (in addition to the *a priori* confounders age, sex and IQ). This did not alter the results, indicating that the observed associations are not due to psychomotor slowing in the siblings and patients. Patients did not perceive changes significantly more often than their unaffected siblings or the controls in the 1:1 condition in which there was no acceleration (siblings: $\beta = 0.02$, $s.e. = 0.02$, $p = 0.30$; controls: $\beta = 0.02$, $s.e. = 0.02$, $p = 0.13$).

Self-monitoring ability and symptoms (Fig. 3)

In the non-patient groups (i.e. the combined group of healthy controls and the unaffected siblings), detection accuracy over the different conditions was associated with positive schizotypy as measured by the SIS-R ($\beta = -0.16$, $s.e. = 0.07$, $p = 0.026$). This was not the case for negative schizotypy ($\beta = -0.05$, $s.e. = 0.12$, $p = 0.694$).

In patients, the level of positive psychotic symptomatology was not robustly associated with detection accuracy over the different conditions ($\beta = -0.01$, $s.e. = 0.01$, $p = 0.094$). Although the overall three-way condition \times symptoms \times antipsychotic use interaction was not statistically significant [interaction $\chi^2(1) = 1.4$, $p = 0.232$], probably because of limited power, further stratification revealed a borderline significant association in patients not using antipsychotic medication ($\beta = -0.03$, $s.e. = 0.01$, $p = 0.052$), whereas no association was apparent in patients on antipsychotic medication ($\beta = -0.01$, $s.e. = 0.01$, $p = 0.407$). A similar pattern of associations was found for negative symptoms. There was a suggestion of an association

Table 2. Differences in self-monitoring in the five conditions between the genetic risk groups

Condition	Controls	First-degree relatives			Patients		
		β	95% CI	p	β	95% CI	p
1:1	N.A.	0.02	−0.01 to 0.04	0.216	0.03	0.01 to 0.06	0.018
1:2	N.A.	0.01	−0.03 to 0.06	0.660	0.05	0.01 to 0.06	0.027
1:4	N.A.	−0.08	−0.20 to 0.04	0.196	−0.06	−0.18 to 0.05	0.277
1:6	N.A.	−0.15	−0.30 to 0.00	0.051	−0.18	−0.33 to −0.43	0.010
1:8	N.A.	−0.09	−0.25 to 0.06	0.249	−0.23	−0.37 to −0.08	0.002

CI, Confidence interval; N.A., not applicable.

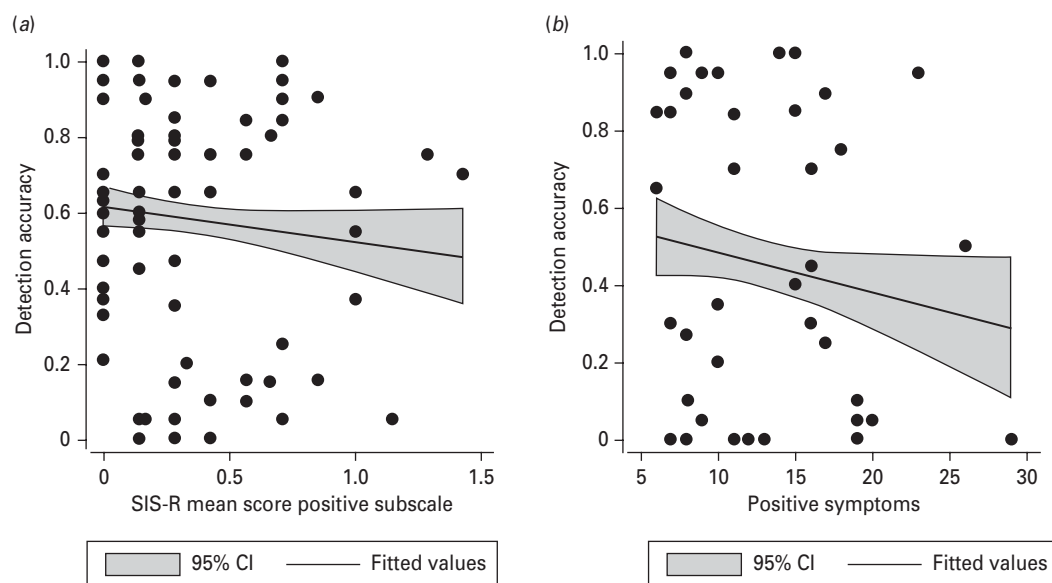


Fig. 3. Scatter plots of the detection-symptoms relationship in the most discriminative condition (1:6, see Table 2) in (a) unaffected participants and (b) patients with psychotic disorder. SIS-R, Structured Interview for Schizotypy – Revised; CI, confidence interval.

between negative symptoms and detection accuracy ($\beta = -0.01$, $s.e. = 0.01$, $p = 0.064$), which was much larger in patients not using antipsychotic medication ($\beta = -0.04$, $s.e. = 0.02$, $p = 0.052$), and which was absent in patients on antipsychotic treatment ($\beta = -0.01$, $s.e. = 0.01$, $p = 0.167$), whereas the overall three-way interaction was non-significant [interaction $\chi^2(1) = 2.2$, $p = 0.135$]. Covarying for indicators of severity of illness, that is the number of psychotic episodes and age at first onset, did not alter the results (data not shown).

Compensation for mapping change

The distance of the compensation movements increased with the acceleration in all three groups. Multilevel regression analysis revealed no significant differences in compensation among groups over all

mapping changes [group \times condition interaction: $\chi^2(2) = 1.66$, $p = 0.44$].

Discussion

This study assessed the relationship between self-monitoring in healthy controls, patients with psychosis and their unaffected siblings using an action-monitoring task. Several findings emerged. Detection accuracy increased if the mapping change was more obvious in all three groups, but this pattern was more pronounced in the healthy controls than in the patients. Detection accuracy of the unaffected siblings was at an intermediate level between patients and controls. In addition, associations between detection accuracy and symptoms were found. In the combined unaffected groups, an association between detection accuracy and positive schizotypy,

but not negative schizotypy, was shown. In patients, associations between detection accuracy and symptoms were less convincing, although there was suggestive evidence that this association may only be detectable in patients off antipsychotic medication.

The finding that self-monitoring in patients with psychosis was significantly worse than in healthy controls is in line with a large body of work (McGuire *et al.* 1995; Rankin & O'Carroll, 1995; Stirling *et al.* 1998, 2001; Keefe *et al.* 1999, 2002; Bocker *et al.* 2000; Frith *et al.* 2000; Franck *et al.* 2001; Ditman & Kuperberg, 2005; Woodward *et al.* 2007). The finding that unaffected siblings also show worse self-monitoring than healthy controls, but better than their affected brother or sister, is in agreement with two studies that have assessed self-monitoring in groups at increased risk for psychotic disorder (Versmissen *et al.* 2007b; Johns *et al.* 2009). Johns *et al.* (2009) found a significant difference in self-monitoring in persons with an ARMS compared to healthy controls whereas Versmissen *et al.* (2007b) found evidence for self-monitoring alterations in three psychometrically and genetically defined at-risk groups, in a comparison with well controls. These findings may thus suggest that self-monitoring alterations are not merely epiphenomena of acute psychosis in patients. The hypothesis that alterations in the process of the monitoring of one's motor actions may have relevance for the aetiology of psychotic disorder carries the implicit assumption that action-monitoring alterations are associated with psychological processes relevant for the development of psychotic symptoms. Following this reasoning, a global rather than a modality-specific self-monitoring deficit (i.e. limited to the monitoring of one's motor actions) is most likely to increase the risk for psychotic disorder. Future work should address this hypothesis empirically.

In addition, the finding that self-monitoring may be associated with positive symptoms at the level of the disorder and also at the level of subclinical expression suggests that alterations in self-monitoring may have aetiological relevance, as suggested by previous experimental and neuroimaging studies (see Allen *et al.* 2007 for an overview). Nevertheless, the present results do not entirely support previous claims of alterations in self-monitoring as a so-called 'endophenotype' or 'intermediate phenotype' for psychosis (Versmissen *et al.* 2007b), given the possible moderating role of antipsychotic use in the association between self-monitoring and expression of psychosis, which is not in agreement with the notion that endophenotypes are characterized by stability over time and independence of phase of the illness and treatment (Gottesman & Gould, 2003). However, the three-way condition \times symptoms \times antipsychotic use interaction was not

significant, because of limited power, indicating that any suggestion of moderation by antipsychotics should be interpreted with caution. If replicated, however, it may be one reason for the non-replication of the association between symptoms and self-monitoring in several previous studies (Vinogradov *et al.* 1997; King, 1998; Fournier *et al.* 2001; Li *et al.* 2002; Moller, 2003; Erhart *et al.* 2006; Versmissen *et al.* 2007a). A similar pattern of results was found for negative symptoms in patients, but this association was not found in the unaffected groups, suggesting that the association with psychotic symptoms may be primary, especially given the known overlap between positive and negative symptoms in patients, which is difficult to account for statistically (Kay, 1990).

Although the detection accuracy of non-self-generated actions was impaired among patients with psychotic disorder and their unaffected siblings, the groups were not impaired in their ability to automatically compensate for the mismatch between self-generated action and their consequences. This was expected and is in accordance with previous work (Kircher & Leube, 2003; Knoblich *et al.* 2004). This finding confirms the literature showing that automatic processes are usually left intact in patients with psychotic disorder, even though conscious cognitive processes are known to be affected (see Jeannerod, 1999 for an overview).

Previous work has claimed that impaired verbal memory, guessing biases or generalized cognitive impairment, rather than alterations in self-monitoring *per se*, may underlie the observation of worse self-monitoring performance in psychosis (Keefe *et al.* 2002). In addition, the use of signal detection tasks using detection of distorted feedback of the patients' speech, which has been applied in previous research (Johns & McGuire, 1999; Johns *et al.* 2001; Fu *et al.* 2006), has also been criticized because these tasks may pick up problems with the appraisal of distorted stimuli instead of problems related to the self-monitoring of the intention to generate (verbal) material (Levelt, 1983). This is supported by the observation of patients with auditory verbal hallucinations and also non-clinical subjects making misattributions of their own voice while passively hearing recorded tapes (Allen *et al.* 2004, 2006). An action-monitoring task, as applied in the present study, is less prone to these possible sources of bias, which is a strength of the study, as is the use of a genetic at-risk group (the unaffected siblings). An important limitation of the study is the small number of patients with psychosis who were not on current antipsychotic treatment. A further limitation is the significant difference in IQ between the three groups tested. Although differences in IQ were present, it is

unlikely that this explains the present results because we controlled statistically for IQ *a priori*, and IQ was only moderately associated with self-monitoring accuracy in the patients but not in the controls or unaffected siblings. To a degree, cognitive alterations such as attention deficits or psychomotor slowing present in families affected with psychotic disorder could explain the observed between-group differences in self-monitoring. Although we did not observe this effect with regard to psychomotor slowing, attention was not specifically assessed in this sample. In addition, environmental factors that are associated with both psychotic disorder and attention deficits, such as cannabis use, could be a source of unmeasured confounding.

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Declaration of Interest

None.

References

- Allen P, Aleman A, McGuire PK (2007). Inner speech models of auditory verbal hallucinations: evidence from behavioural and neuroimaging studies. *International Review of Psychiatry* **19**, 407–415.
- Allen P, Freeman D, Johns L, McGuire P (2006). Misattribution of self-generated speech in relation to hallucinatory proneness and delusional ideation in healthy volunteers. *Schizophrenia Research* **84**, 281–288.
- Allen PP, Johns LC, Fu CH, Broome MR, Vythelingum GN, McGuire PK (2004). Misattribution of external speech in patients with hallucinations and delusions. *Schizophrenia Research* **69**, 277–287.
- Bates AT, Kiehl KA, Laurens KR, Liddle PF (2002). Error-related negativity and correct response negativity in schizophrenia. *Clinical Neurophysiology* **113**, 1454–1463.
- Bentall RP, Baker GA, Havers S (1991). Reality monitoring and psychotic hallucinations. *British Journal of Clinical Psychology* **30**, 213–222.
- Bentall RP, Slade PD (1985). Reality testing and auditory hallucinations: a signal detection analysis. *British Journal of Clinical Psychology* **24**, 159–169.
- Blakemore SJ, Smith J, Steel R, Johnstone CE, Frith CD (2000). The perception of self-produced sensory stimuli in patients with auditory hallucinations and passivity experiences: evidence for a breakdown in self-monitoring. *Psychological Medicine* **30**, 1131–1139.
- Blyler CR, Gold JM, Iannone VN, Buchanan RW (2000). Short form of the WAIS-III for use with patients with schizophrenia. *Schizophrenia Research* **46**, 209–215.
- Bocker KB, Hijman R, Kahn RS, De Haan EH (2000). Perception, mental imagery and reality discrimination in hallucinating and non-hallucinating schizophrenic patients. *British Journal of Clinical Psychology* **39**, 397–406.
- Brebion G, Amador X, David A, Malaspina D, Sharif Z, Gorman JM (2000). Positive symptomatology and source-monitoring failure in schizophrenia – an analysis of symptom-specific effects. *Psychiatry Research* **95**, 119–131.
- Brebion G, Amador X, Smith MJ, Malaspina D, Sharif Z, Gorman JM (1999). Opposite links of positive and negative symptomatology with memory errors in schizophrenia. *Psychiatry Research* **88**, 15–24.
- Brebion G, David AS, Jones H, Pilowsky LS (2005). Hallucinations, negative symptoms, and response bias in a verbal recognition task in schizophrenia. *Neuropsychology* **19**, 612–617.
- Brebion G, David AS, Ohlsen R, Jones HM, Pilowsky LS (2007). Visual memory errors in schizophrenic patients with auditory and visual hallucinations. *Journal of the International Neuropsychological Society* **13**, 832–838.
- Brebion G, Gorman JM, Amador X, Malaspina D, Sharif Z (2002). Source monitoring impairments in schizophrenia: characterisation and associations with positive and negative symptomatology. *Psychiatry Research* **112**, 27–39.
- Brebion G, Smith MJ, Amador X, Malaspina D, Gorman JM (1998). Word recognition, discrimination accuracy, and decision bias in schizophrenia: association with positive symptomatology and depressive symptomatology. *Journal of Nervous and Mental Disease* **186**, 604–609.
- Brunelin J, Combris M, Poulet E, Kallel L, D'Amato T, Dalery J, Saoud M (2006). Source monitoring deficits in hallucinating compared to non-hallucinating patients with schizophrenia. *European Psychiatry* **21**, 259–261.
- Costafreda SG, Brebion G, Allen P, McGuire PK, Fu CH (2008). Affective modulation of external misattribution bias in source monitoring in schizophrenia. *Psychological Medicine* **38**, 821–824.
- Daprati E, Franck N, Georgieff N, Proust J, Pacherie E, Dalery J, Jeannerod M (1997). Looking for the agent: an investigation into consciousness of action and self-consciousness in schizophrenic patients. *Cognition* **65**, 71–86.
- Debbané M, Van der Linden M, Gex-Fabry M, Eliez S (2009). Cognitive and emotional associations to positive schizotypy during adolescence. *Journal of Child Psychology and Psychiatry, and Allied Disciplines* **50**, 326–334.
- Ditman T, Kuperberg GR (2005). A source-monitoring account of auditory verbal hallucinations in patients with schizophrenia. *Harvard Review of Psychiatry* **13**, 280–299.
- Dollfus S, Petit M (1995). Negative symptoms in schizophrenia: their evolution during an acute phase. *Schizophrenia Research* **17**, 187–194.
- Erhart SM, Marder SR, Carpenter WT (2006). Treatment of schizophrenia negative symptoms: future prospects. *Schizophrenia Bulletin* **32**, 234–237.
- Fanous A, Gardner C, Walsh D, Kendler KS (2001). Relationship between positive and negative symptoms of schizophrenia and schizotypal symptoms in nonpsychotic relatives. *Archives of General Psychiatry* **58**, 669–673.

- Fourneret P, Franck N, Slachevsky A, Jeannerod M** (2001). Self-monitoring in schizophrenia revisited. *Neuroreport* **12**, 1203–1208.
- Franck N, Farrer C, Georgieff N, Marie-Cardine M, Dalery J, d'Amato T, Jeannerod M** (2001). Defective recognition of one's own actions in patients with schizophrenia. *American Journal of Psychiatry* **158**, 454–459.
- Franck N, Rouby P, Daprati E, Dalery J, Marie-Cardine M, Georgieff N** (2000). Confusion between silent and overt reading in schizophrenia. *Schizophrenia Research* **41**, 357–364.
- Frith C** (1996). Neuropsychology of schizophrenia, what are the implications of intellectual and experiential abnormalities for the neurobiology of schizophrenia? *British Medical Bulletin* **52**, 618–626.
- Frith C, Rees G, Friston K** (1998). Psychosis and the experience of self. *Annals of the New York Academy of Sciences* **843**, 170–178.
- Frith CD** (1987). The positive and negative symptoms of schizophrenia reflect impairments in the perception and initiation of action. *Psychological Medicine* **17**, 631–648.
- Frith CD** (1992). *The Cognitive Neuropsychology of Schizophrenia*. Lawrence Erlbaum Associates Ltd: East Sussex.
- Frith CD, Blakemore S, Wolpert DM** (2000). Explaining the symptoms of schizophrenia: abnormalities in the awareness of action. *Brain Research Reviews* **31**, 357–363.
- Frith CD, Done DJ** (1989). Experiences of alien control in schizophrenia reflect a disorder in the central monitoring of action. *Psychological Medicine* **19**, 359–363.
- Fu CH, Vythelingum GN, Brammer MJ, Williams SC, Amaro Jr. E, Andrew CM, Yaguez L, van Haren NE, Matsumoto K, McGuire PK** (2006). An fMRI study of verbal self-monitoring: neural correlates of auditory verbal feedback. *Cerebral Cortex* **16**, 969–977.
- Gallagher S** (2004). Neurocognitive models of schizophrenia: a neurophenomenological critique. *Psychopathology* **37**, 8–19.
- Gottesman II, Gould TD** (2003). The endophenotype concept in psychiatry: etymology and strategic intentions. *American Journal of Psychiatry* **160**, 636–645.
- Hanssen M, Krabbendam L, Vollema M, Delespaul P, van Os J** (2006). Evidence for instrument and family-specific variation of subclinical psychosis dimensions in the general population. *Journal of Abnormal Psychology* **115**, 5–14.
- Harvey PD** (1985). Reality monitoring in mania and schizophrenia. The association of thought disorder and performance. *Journal of Nervous and Mental Disease* **173**, 67–73.
- Heinrichs RW, Vaz SM** (2004). Verbal memory errors and symptoms in schizophrenia. *Cognitive and Behavioral Neurology* **17**, 98–101.
- Jeannerod M** (1999). The 25th Bartlett Lecture. To act or not to act: perspectives on the representation of actions. *Quarterly Journal of Experimental Psychology. A, Human Experimental Psychology* **52**, 1–29.
- Jeannerod M** (2009). The sense of agency and its disturbances in schizophrenia: a reappraisal. *Experimental Brain Research* **192**, 527–532.
- Johns LC, Allen P, Valli I, Winton-Brown T, Broome M, Woolley J, Tabraham P, Day F, Howes O, Wykes T, McGuire P** (2009). Impaired verbal self-monitoring in individuals at high risk of psychosis. *Psychological Medicine* **1–10**.
- Johns LC, Gregg L, Allen P, McGuire PK** (2006). Impaired verbal self-monitoring in psychosis: effects of state, trait and diagnosis. *Psychological Medicine* **36**, 465–474.
- Johns LC, McGuire PK** (1999). Verbal self-monitoring and auditory hallucinations in schizophrenia. *Lancet* **353**, 469–470.
- Johns LC, Rossell S, Frith C, Ahmad F, Hemsley D, Kuipers E, McGuire PK** (2001). Verbal self-monitoring and auditory verbal hallucinations in patients with schizophrenia. *Psychological Medicine* **31**, 705–715.
- Johns LC, van Os J** (2001). The continuity of psychotic experiences in the general population. *Clinical Psychology Review* **21**, 1125–1141.
- Johnson MK, Hashtroudi S, Lindsay DS** (1993). Source monitoring. *Psychological Bulletin* **114**, 3–28.
- Jones SR, Fernyhough C** (2007). Thought as action: inner speech, self-monitoring, and auditory verbal hallucinations. *Consciousness and Cognition* **16**, 391–399.
- Katsanis J, Iacono WG, Beiser M** (1990). Anhedonia and perceptual aberration in first-episode psychotic patients and their relatives. *Journal of Abnormal Psychology* **99**, 202–206.
- Kay SR** (1990). Significance of the positive-negative distinction in schizophrenia. *Schizophrenia Bulletin* **16**, 635–652.
- Kay SR, Fiszbein A, Opler LA** (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* **13**, 261–276.
- Keefe RS, Arnold MC, Bayen UJ, Harvey PD** (1999). Source monitoring deficits in patients with schizophrenia: a multinomial modelling analysis. *Psychological Medicine* **29**, 903–914.
- Keefe RS, Arnold MC, Bayen UJ, McEvoy JP, Wilson WH** (2002). Source-monitoring deficits for self-generated stimuli in schizophrenia: multinomial modeling of data from three sources. *Schizophrenia Research* **57**, 51–67.
- Keefe RS, Lobel DS, Mohs RC, Silverman JM, Harvey PD, Davidson M, Losonczy MF, Davis KL** (1991). Diagnostic issues in chronic schizophrenia: kraepelinian schizophrenia, undifferentiated schizophrenia, and state-independent negative symptoms. *Schizophrenia Research* **4**, 71–79.
- King DJ** (1998). Drug treatment of the negative symptoms of schizophrenia. *European Neuropsychopharmacology* **8**, 33–42.
- Kircher TT, Leube DT** (2003). Self-consciousness, self-agency, and schizophrenia. *Consciousness and Cognition* **12**, 656–669.
- Knoblich G, Kircher TT** (2004). Deceiving oneself about being in control: conscious detection of changes in visuomotor coupling. *Journal of Experimental Psychology. Human Perception and Performance* **30**, 657–666.
- Knoblich G, Stottmeister F, Kircher T** (2004). Self-monitoring in patients with schizophrenia. *Psychological Medicine* **34**, 1561–1569.

- Laroi F, Van der Linden M, Marczewski P (2004). The effects of emotional salience, cognitive effort and meta-cognitive beliefs on a reality monitoring task in hallucination-prone subjects. *British Journal of Clinical Psychology* **43**, 221–233.
- Levelt WJ (1983). Monitoring and self-repair in speech. *Cognition* **14**, 41–104.
- Li CS, Chen MC, Yang YY, Chen MC, Tsay PK (2002). Altered performance of schizophrenia patients in an auditory detection and discrimination task: exploring the 'self-monitoring' model of hallucination. *Schizophrenia Research* **55**, 115–128.
- McGuffin P, Farmer A, Harvey I (1991). A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Archives of General Psychiatry* **48**, 764–770.
- McGuire PK, Silbersweig DA, Wright I, Murray RM, David AS, Frackowiak RS, Frith CD (1995). Abnormal monitoring of inner speech: a physiological basis for auditory hallucinations. *Lancet* **346**, 596–600.
- McGuire PK, Silbersweig DA, Wright I, Murray RM, Frackowiak RS, Frith CD (1996). The neural correlates of inner speech and auditory verbal imagery in schizophrenia: relationship to auditory verbal hallucinations. *British Journal of Psychiatry* **169**, 148–159.
- Moller H (2003). Management of the negative symptoms of schizophrenia. *CNS Drugs* **17**, 793–823.
- Morrison AP, Haddock G (1997). Cognitive factors in source monitoring and auditory hallucinations. *Psychological Medicine* **27**, 669–679.
- Pfeifer S, van Os J, Hanssen M, Delespaul PA, Krabbendam L (2009). Subjective experience of cognitive failures as possible risk factor for negative symptoms of psychosis in the general population. *Schizophrenia Bulletin* **35**, 766–774.
- Pfohl B, Winokur G (1982). The evolution of symptoms in institutionalized hebephrenic/catatonic schizophrenics. *British Journal of Psychiatry* **141**, 567–572.
- Pogue-Geile MF, Harrow M (1985). Negative symptoms in schizophrenia: their longitudinal course and prognostic importance. *Schizophrenia Bulletin* **11**, 427–439.
- Ragland JD, Moelter ST, McGrath C, Hill SK, Gur RE, Bilker WB, Siegel SJ, Gur RC (2003). Levels-of-processing effect on word recognition in schizophrenia. *Biological Psychiatry* **54**, 1154–1161.
- Raij RT, Valkonen-Korhonen M, Holi M, Therman S, Lehtonen J, Hari R (2009). Reality of auditory verbal hallucinations. *Brain* **132**, 2994–3001.
- Rankin PM, O'Carroll PJ (1995). Reality discrimination, reality monitoring and disposition towards hallucination. *British Journal of Clinical Psychology* **34**, 517–528.
- Rey ER, Bailer J, Brauer W, Handel M, Laubenstein D, Stein A (1994). Stability trends and longitudinal correlations of negative and positive syndromes within a three-year follow-up of initially hospitalized schizophrenics. *Acta Psychiatrica Scandinavica* **90**, 405–412.
- Schnell K, Heekeren K, Daumann J, Schnell T, Schnitker R, Moller-Hartmann W, Gouzoulis-Mayfrank E (2008). Correlation of passivity symptoms and dysfunctional visuomotor action monitoring in psychosis. *Brain* **131**, 2783–2797.
- Schurhoff F, Szoke A, Bellivier F, Turcas C, Villemur M, Tignol J, Rouillon F, Leboyer M (2003). Anhedonia in schizophrenia: a distinct familial subtype? *Schizophrenia Research* **61**, 59–66.
- Seal ML, Aleman A, McGuire PK (2004). Compelling imagery, unanticipated speech and deceptive memory: neurocognitive models of auditory verbal hallucinations in schizophrenia. *Cognitive Neuropsychiatry* **9**, 43–72.
- Seal ML, Crowe SF, Cheung P (1997). Deficits in source monitoring in subjects with auditory hallucinations may be due to differences in verbal intelligence and verbal memory. *Cognitive Neuropsychiatry* **2**, 273–290.
- Shergill SS, Bullmore E, Simmons A, Murray R, McGuire P (2000). Functional anatomy of auditory verbal imagery in schizophrenic patients with auditory hallucinations. *American Journal of Psychiatry* **157**, 1691–1693.
- StataCorp (2008). *STATA Statistical Software: Release 10.1*. Stata Corporation: College Station, TX.
- Stirling JD, Hellewell JS, Ndlovu D (2001). Self-monitoring dysfunction and the positive symptoms of schizophrenia. *Psychopathology* **34**, 198–202.
- Stirling JD, Hellewell JS, Quraishi N (1998). Self-monitoring dysfunction and the schizophrenic symptoms of alien control. *Psychological Medicine* **28**, 675–683.
- Tsuang MT, Gilbertson MW, Faraone SV (1991). The genetics of schizophrenia. Current knowledge and future directions. *Schizophrenia Research* **4**, 157–171.
- Versmissen D, Janssen I, Johns L, McGuire P, Drukker M, a Campo J, Myin-Germeys I, van Os J, Krabbendam L (2007a). Verbal self-monitoring in psychosis: a non-replication. *Psychological Medicine* **37**, 569–576.
- Versmissen D, Myin-Germeys I, Janssen I, Franck N, Georgieff N, a Campo J, Mengelers R, van Os J, Krabbendam L (2007b). Impairment of self-monitoring: part of the endophenotypic risk for psychosis. *British Journal of Psychiatry* (Suppl.) **51**, s58–s62.
- Vinogradov S, Willis-Shore J, Poole JH, Marten E, Ober BA, Shenaut GK (1997). Clinical and neurocognitive aspects of source monitoring errors in schizophrenia. *American Journal of Psychiatry* **154**, 1530–1537.
- Vollema MG, Ormel J (2000). The reliability of the Structured Interview for Schizotypy-Revised. *Schizophrenia Bulletin* **26**, 619–629.
- Wechsler D (1997). *Wechsler Adult Intelligence Scale III (WAIS-III)*. Psychological Corporation: San Antonio, TX.
- Woodward TS, Menon M, Whitman JC (2007). Source monitoring biases and auditory hallucinations. *Cognitive Neuropsychiatry* **12**, 477–494.