Chapter 7

Insight in psychosis: relationship with neurocognition, social cognition and clinical symptoms depends on phase of Illness

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ABSTRACT

Introduction Reduced insight has been reported in a majority of patients with a psychotic disorder. Most studies have focused on associations with neurocognition, neglecting relations with social cognition. Methods 270 schizophrenia patients participated in this study, which was part of the GROUP (Genetic Risk and Outcome of Psychosis)-project. Linear regression analyses were performed to investigate the predictive value of composite measures of neurocognition, social cognition and clinical symptoms. The moderating effect of phase of illness was also investigated. Insight was measured with a composite measure, based on the insight item on the Positive And Negative Syndrome Scale (PANSS) and the Birchwood Insight Scale (BIS). Results Insight on the BIS and the PANSS correlated significantly ($r = .406$). All independent variables correlated with the insight composite measure. The additional effect of social cognition and clinical symptoms were both significant. Phase of illness was a moderating variable: in patients with recent onset psychosis, none of the independent variables explained variance. In patients with multiple episode or chronic psychosis, both social cognition and clinical symptoms had additional effects and explained insight, along with neurocognition, together explaining 20% of the variance. Discussion These findings indicate that multiple factors are associated with insight in psychosis. Specifically, associations of insight with social cognitive and clinical symptom measures were observed, over and above a contribution of neurocognition. This supports theories that imply a role for deficient emotion recognition and mentalizing in reduced insight. Further studies need to investigate insight in recent onset psychosis into more detail.
1. INTRODUCTION

Reduced insight (or unawareness of illness) has been reported in a majority of patients with a non-affective psychotic disorder (Amador and Gorman, 1998). Insight can be studied as a set of descriptive beliefs and as a personal narrative (Roe and Kravets, 2003). Most studies investigating the neurocognitive correlates of insight treat the concept as a set of descriptive beliefs, mostly to formalize the concept of insight and thus enabling the subject for quantitative research. Even though studying insight as a personal narrative is of great importance to understand the individual differences with regard to insight, this approach is of a highly subjective nature, making it very hard to study the concept in a quantitative manner. In the current study, consistent with previous studies that investigated insight in psychosis and cognitive function, we focused on insight as a set of descriptive beliefs for which three distinct dimensions have been proposed: (1) the recognition that one has a mental illness, (2) the recognition of the need for treatment, and (3) the ability to re-label unusual mental events (delusions and hallucinations) as pathological (David, 1990). The concept of insight is clinically relevant, because poor insight is associated with psychosocial dysfunction and poorer treatment adherence, in addition to an increase in the number of re-hospitalizations (Amador and David, 2004). Therefore, investigating which factors are specifically related to poor insight is of crucial importance for understanding psychotic disorders and for further development of treatment strategies.

Over the past decades, a considerable number of studies have investigated the association between neurocognition and insight. A meta-analysis of these studies found that, although there was a significant relationship, the predictive value of neurocognition was rather modest (Aleman et al., 2006). Furthermore, in schizophrenia, all neurocognitive domains (i.e. reasoning and problem solving, verbal learning and memory) were found to predict reduced insight to a similar degree. Thus, employing a composite measure of several neurocognitive domains may be adequate and may enhance reliability (Keshavan et al., 2004). It is also possible that other neuropsychological aspects are associated with insight. Indeed, in recent years there is increasing interest in the concept of social cognitive impairments in psychosis. Social cognition has been referred to as “the ability to construct representations of the relations between oneself and others, and to use those representations flexibly to guide social behaviour” (Adolphs, 2001). Studies of social cognition in psychosis have mainly focussed on emotion perception and theory-of-mind processing (Pinkham et al., 2003). The combination of impaired social cognition and poor insight has been reported in other populations with brain abnormalities (Bach and David, 2006; Kipps and Hodges, 2006). In addition, some studies have reported a relationship between social cognition and insight in psychosis as well (Bora et al., 2007; Lysaker et al., 2005) whereas others have not (Drake and Lewis, 2003). When investigating factors associated with insight, it should be taken into account that social cognition and neurocognition are partially overlapping concepts (Sergi et al., 2007). However, most of the studies to date have investigated whether social
cognition or neurocognition is more related to insight, not whether one of these factors is of additional value in explaining insight.

A third group of factors that have been found to be related to insight are clinical symptoms (Mintz et al., 2003). Relationships with positive symptoms, negative symptoms and disorganization have been found (Mintz et al., 2003). Some researchers claim that symptoms have more predictive value on insight, as compared to neurocognition (Buchy et al., 2009; de Hert et al., 2009; Keshavan et al., 2004; Simon et al., 2009;) whereas others suggest that these factors may not be mutually exclusive (Osatuke et al., 2008). As with social cognition, no studies have been done to determine whether clinical symptoms really have additional predictive value.

Insight is a complex and multi-dimensional concept, and may be related to neuropsychological aspects as well as severity of psychopathology. Thereby, insight may be influenced by so called ‘trait’ and ‘state’ features of psychosis, in which neurocognition has traditionally been associated with the former, and positive symptoms with the latter, whereas the influence of social cognition is not unequivocal (de Gracia Dominguez et al., 2009; Koelkebeck et al., 2010; Pousa et al., 2008; Sprong et al., 2007). The phase of illness could be differentially related to various insight related factors. Tranulis et al. studied insight in patients in recent onset psychosis and found that self-report and interview based insight scales were not correlated with one another in this population, which was attributed to the nature of their relatively unstable and evolving period (Tranulis et al., 2008).

The current study was part of the large-scale Genetic Risk and OUtcome of Psychosis (GROUP) study (Korver et al., 2012). Data were obtained from a sample of relatively young patients, including those with recent onset psychosis. A neuropsychological assessment was administered in line with the cognitive dimensions used in Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) (Nuechterlein et al., 2004), including social cognition. Composite measures were created for insight, neurocognition, social cognition and clinical symptoms. The insight composite measure was based on an interview and a self-report questionnaire. It was expected that insight would be better explained by a model that included neurocognition as well as social cognition, as compared to a model that only encompassed neurocognition (Birchwood et al., 1994; Osatuke et al., 2008). Similarly, clinical symptoms, social cognition, and neurocognition were expected to predict insight better, particularly when as compared to a model that included social cognition and neurocognition only.

2. METHODS

2.1 Participants

270 Patients with psychotic disorders were included in this study. This was a subsample of the patient population participating in the GROUP project. Two out of four centers participated in the insight project (Amsterdam and Utrecht). The GROUP project is a large-
scale multicenter study that investigates the vulnerability and protective factors for i) the
development of a psychotic disorder, and ii) the variation in the course of illness. Diagnoses
were confirmed using the Comprehensive Assessment of Symptoms and History (Andreasen
et al., 1992). The procedure of recruitment, criteria of inclusion and exclusion, informed
consent, assessment instruments, approval by the accredited Medical Ethics Review
Committee (METC), and population characteristics have been described in a previous report
on the GROUP-study (Korver et al., 2012).

Eligible patients had to fulfill the following criteria: (1) age: between 18 and 50 (extremes
included), (2) meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
(DSM-IV) criteria for a non-affective psychotic disorder (schizophrenia, schizophreniform
disorder, schizoaffective disorder, delusional disorder, psychotic disorder NOS) (3) fluent in
Dutch, (4) able and willing to give written informed consent, and (5) the willingness of at
least one family member to participate in the project.

Table 1 shows the demographic and clinical data for the patient group. Educational
degree was adapted from Verhage (Verhage, 1964). Global Assessment of Functioning
(GAF) scores, adapted from the DSM-IV, were obtained to measure global symptoms and
disability (American Psychiatric Association, 1994). Level of intelligence was estimated with
the WAIS III short form (Blyler et al., 2000; Stinissen et al., 1970). Recent onset psychosis
(ROP) was defined as follows: one psychotic episode in the year prior to the assessment. The
other patients had an illness duration of longer than one year, or had experienced multiple
psychotic episodes and were therefore characterized as having ‘multiple episode or chronic
psychosis’ (MECP).

2.2 Assessment of Insight

Insight was assessed by means of a semi-structured interview, the Positive And Negative
Syndrome Scale (PANSS) (Kay et al., 1987), as well as a self-report scale, the Birchwood
Insight Scale (BIS) (Birchwood et al., 1994). The PANSS provides a single item on insight
(G12), based on the patient’s ability to describe and acknowledge symptoms and their
psychiatric disorder, the ability to recognize the necessity of treatment, and the ability to
describe future plans. Researchers were not always blind to the other outcome measures
(e.g. cognitive task performance): it has been suggested that this did not influence their
knowledge of the patients’ cognitive functioning while judging insight. The BIS is a short
questionnaire that consists of eight questions addressing the three components of insight
( Need for Treatment, Awareness of Illness and Relabeling of Symptoms). Each of these
components is rated on a scale of zero to four: a higher score implies better insight. A
composite measure was created, based on both the patients’ z-score on the BIS and PANSS,
with the latter being negatively recoded. Higher scores on the composite measure indicated
better insight. The procedure for translation of all raw scores into z-scores is described under
paragraph 2.6 (statistical analysis).
Table 1. Demographical and clinical data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (N=270)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.7</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Gender (N), male / female</td>
<td>222 / 48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Educational degree (score), Verhage</td>
<td>4.2</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Ethnicity (N), Dutch / other / unknown</td>
<td>209 / 52 / 9</td>
<td></td>
<td></td>
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<tr>
<td>WAIS-III estimated IQ (short form)(^a)</td>
<td>95.1</td>
<td>16.1</td>
<td></td>
</tr>
<tr>
<td>Duration of illness (years)</td>
<td>4.7</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>Psychotic episodes (number)</td>
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<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Age of Onset Psychosis (years)</td>
<td>22.5</td>
<td>6.2</td>
<td></td>
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<td>Diagnostic (N), Schizophrenia, paranoid type</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Schizo-affective disorder</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic Disorder NOS</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia, undifferentiated</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia, disorganized</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase of illness (N)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Recent Onset Psychosis</td>
<td>57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic or Multi Episode Psychosis</td>
<td>210</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations (number)</td>
<td>2.2</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Global Assessment of Functioning, Symptoms</td>
<td>53.5</td>
<td>15.6</td>
<td></td>
</tr>
<tr>
<td>Disability</td>
<td>51.7</td>
<td>15.1</td>
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</tr>
<tr>
<td>PANSS (score),(^a)</td>
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<td></td>
</tr>
<tr>
<td>Positive</td>
<td>1.9</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>2.2</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>1.8</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Insight (score),(^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interview Based (G12)(^c)</td>
<td>2.3</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Self Report (BIS)(^d)</td>
<td>8.8</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) WAIS-III: Wechsler Adult Intelligence Scale – III; \(^b\) PANSS: Positive And Negative Syndrome Scale; \(^c\) G12: PANSS Item 12 ‘Poor Judgment and Insight’; BIS: \(^d\) Birchwood Insight Scale.

2.3 Neurocognition

All patients were assessed with a neurocognitive task battery containing the following 6 tasks (intended neurocognitive domains of focus are placed between brackets): WAIS-III Digit Symbol (processing speed), CPT-HQ (attention/vigilance), Word Learning Task (verbal learning and memory) (Brand and Jolles, 1985), WAIS-III Arithmetic (working memory), WAIS-III Block Design (reasoning and problem solving), Response Set Shifting (set-shifting), WAIS-III Information (verbal comprehension), and educational degree (Verhage, 1964).
Z-scores were calculated for each domain, with $d'$ indicating a final score for attention/vigilance (Davies, 1982). For verbal learning & memory, the final z-score was based on the mean value of two distinct z-scores: immediate recall and delayed recall. For set-shifting, the z-score was based on the decrement in accuracy performance from an imitation response condition to reversal response, using the RST, a modified version of the Competing Programs Task (Bilder et al., 1992). Due to its high correlations with neurocognition, a z-score for educational degree was also created (Le Carret et al., 2003). A final composite measure of neurocognition was based on the mean of the z-scores from the 7 outcome variables, while allowing for 4 missing values.

2.4 Social Cognition

In addition to the neurocognitive battery, patients were assessed with two social cognitive tasks, concerning emotion perception and theory of mind. The degraded facial affect recognition task (DFAR) was used as a measure of emotion perception (van ‘t Wout et al., 2004). Sixty-four trials were presented, consisting of 16 face presentations in each of four conditions: angry, happy, fearful and neutral. Patients were asked to label each expression with the appropriate emotion. Theory of mind (or mentalizing) was assessed using the Hinting Task (Corcoran et al., 1995). This task tests the ability of subjects to infer the real intentions behind indirect speech utterances. The task comprises 10 short passages presenting an interaction between two characters. All passages end with one of the characters dropping a hint. For instance: following a long and exhausting journey, Peter enters the Ann’s office. Ann immediately starts to update him on a number of business developments. Peter interrupts Ann by saying “Gosh, that really was a long, exhausting journey”. The participant is asked to describe what he thinks Peter is implying with this comment. A composite measure for social cognition was based on the z-score on both tasks, allowing for 1 missing value.

2.5 Clinical Symptoms

In the GROUP-project, current symptom severity was measured with the PANSS, which consists of 30 items (Kay et al., 1987). Each item is scored on a scale ranging from 1 (absent) to 7 (extreme), with item rating incorporating the behavioural effect of symptoms as well as their severity. Originally, three domains or factors were described for the PANSS. Later, a 5-factor structure was developed (Lançon et al., 2000). A more universally used method is that of remission, for which a number of items (measuring either positive, negative or disorganization symptoms) on the PANSS have been selected that also appear in other symptom rating scales. For remission, a score of 3 or lower for a period of 6 months on the following items is required (PANSS items are placed between brackets): delusions (P1), unusual thought content (G9), hallucinatory behaviour (P3), conceptual disorganization (P2), mannerisms/posturing (G5), blunted affect (N1), social withdrawal (N4) and lack of spontaneity (N6) (Andreasen et al., 2005). Since the current study did not emphasize
symptom dimensions but rather the concept of clinical symptoms in relation to insight, we decided to calculate the mean (cross-sectional) score of the z-transformed remission items, allowing for 3 missing values.

2.6 Statistical analysis

Subject scores exceeding 2 standard deviations (SD) from the mean patient group score were replaced by the recalculated mean group score ± 2 SD. All variables measuring insight (PANSS G12 and BIS), neurocognition, social cognition and clinical symptoms (see paragraph 2.2 to 2.5) were checked for normal distribution of residuals from regression analysis (Field, 2005) and transformed into z-scores using the mean and SD of the patient group. Otherwise, test scores were transformed to approximate normality by logarithmic, square root or reciprocal transformations. Higher scores on the neurocognitive and social cognitive domains indicated better performance, whereas higher scores on the clinical symptom dimension indicated more severe symptomatology. Missing values were replaced by the average z-score, which is zero (BIS and PANSS-G12: both 11 cases; neurocognition and social cognition: both 6 cases; clinical symptoms: 11 cases).

First, bivariate correlation analyses were performed to separately investigate relations between insight and neurocognition, social cognition and clinical symptoms. Second, we investigated the additional explained variance using multiple regression analysis. Neurocognition, social cognition and clinical symptoms were entered block-wise. This enabled us to investigate the explained variance of each factor in one model, as well as the additional explained variance of social cognition as well as the additional explained variance of clinical symptoms. Age, gender and phase of illness (recent onset / multiple episode or chronic psychosis) were entered as co-variates into the first block.

Next, we investigated the moderating role of phase of illness. This was done by repeating the first regression analyses, but with the addition of three interaction terms: neurocognition x recent onset yes/no, social cognition x recent onset yes/no, and clinical variables x recent onset yes/no.

Finally, two separate regression analyses were performed for ROP and MECP with only those predictors that showed a significant interaction with recent onset yes/no in the previous regression analysis. All analyses were performed with one-tailed hypothesis testing with $\alpha = 0.05$. Statistical analyses were performed using SPSS 16.0. For descriptive purposes, correlations between all variables are displayed in table S1 as supplementary material.

3. RESULTS

3.1 Self-reported insight and interview based insight

Self-reported insight was significantly correlated with interview based insight ($r = .406$, $p < .001$). Score on the PANSS and BIS correlated significantly with the composite measure of
insight ($r=-.837, \ p<.001$; $r=.846, \ p<.001$, respectively), as with the BIS subscales Relabeling of symptoms ($r=.615, \ p<.001$), Awareness of Illness ($r=.672, \ p<.001$) and Need for Treatment ($r=.682, \ p<.001$). On the raw PANSS G12 scores, 43.1% of the patients ($n=132$) had no impairment of insight, 17.0% had ‘minimal’ impairment, 15.7% had mild impairment ($n=48$), 11.8% had moderate impairment ($n=35$), 5.1% had moderately severe impairment ($n=15$), 4.1% had severe impairment ($n=12$), and 0.7% had extreme impairment ($n=2$). On the raw BIS scores, 50.7% had a score in the ‘no-mild impairment’ range (9.1-12; $n=103$), 30.3% had a score in the ‘mild-moderate impairment’ range (6.1-9; $n=93$), 14.1% had a score in the ‘moderate-severe impairment’ range (3.1-6; $n=43$), and 4.9% had a score in the ‘severe-extreme impairment’ range (0-3; $n=15$).

3.2 Relationships with insight

Bivariate correlation analyses revealed that all independent factors significantly correlated with insight (neurocognition: $r = .249; \ p<.001$; social cognition: $r = .248, \ p<.001$; clinical symptoms: $r = -.290, \ p < .001$). In addition, neurocognition was significantly correlated with social cognition ($r = .454, \ p<.001$), and both neurocognition and social cognition were inversely correlated with clinical symptoms ($r = -.341, \ p<.001$; $r = -.228, \ p<.001$). Results of the multiple regression analysis are displayed in Table 2. Neurocognition significantly predicted insight scores. Social cognition, as an additional predictor variable, significantly increased the explained variance ($R^2_{\text{change}} = .020; \ p_{\text{change}} = .018$). The contribution of both neurocognition and social cognition were significant. Finally, clinical symptoms showed a significant additional increase in the explained variance. More specifically, clinical symptoms explained insight significantly, while the explained variance of neurocognition was non-significant.

The next step was to determine whether the phase of illness moderated the effect of the independent factors on insight. When scores of the groups Recent Onset Psychosis (ROP) and Multiple Episode or Chronic Psychosis (MECP) were compared, these did not differ with respect to insight ($p = .228$), neurocognition ($p = .308$), social cognition ($p = .655$), nor clinical symptoms ($p = .105$). However, when the interaction term neurocognition was added to a regression model containing neurocognition and the covariates (age, gender and phase of illness), the interaction term was significant ($\beta = .549, \ p = .037$). The same moderating effect of phase of illness was found in regression analyses that included social cognition ($\beta = .483, \ p = .052$) and clinical symptoms ($\beta = -.582, \ p = .025$). These results indicated that separate analyses for ROP and MECP groups were justified.
Table 2. Relationships with insight for patients overall, patients with recent onset psychosis (ROP) and patients with multiple episode psychosis (MECP)

<table>
<thead>
<tr>
<th>Patient group / model</th>
<th>df</th>
<th>( \beta_{\text{Neurocognition}} )</th>
<th>( \beta_{\text{Social Cognition}} )</th>
<th>( \beta_{\text{Clinical Symptoms}} )</th>
<th>( p )</th>
<th>( F )</th>
<th>( R )</th>
<th>( R^2 )</th>
<th>( p_{\text{change}} )</th>
<th>( F_{\text{change}} )</th>
<th>( R^2_{\text{change}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>4,262</td>
<td>.250**</td>
<td>-</td>
<td>-</td>
<td>&lt;.001</td>
<td>5.540</td>
<td>.279</td>
<td>.078</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>+ Social Cognition</td>
<td>5,261</td>
<td>.177**</td>
<td>.159*</td>
<td>-</td>
<td>&lt;.001</td>
<td>5.642</td>
<td>.312</td>
<td>.098</td>
<td>.018</td>
<td>5.655</td>
<td>.020</td>
</tr>
<tr>
<td>+ Clinical symptoms</td>
<td>6,260</td>
<td>.108</td>
<td>.140*</td>
<td>-.225**</td>
<td>&lt;.001</td>
<td>7.110</td>
<td>.375</td>
<td>.141</td>
<td>&lt;.001</td>
<td>13.141</td>
<td>.043</td>
</tr>
<tr>
<td>ROP Patients</td>
<td>3,533</td>
<td>.011</td>
<td>-</td>
<td>-</td>
<td>.942</td>
<td>.129</td>
<td>.085</td>
<td>.007</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>+ Social Cognition</td>
<td>4,521</td>
<td>.019</td>
<td>.051</td>
<td>-</td>
<td>.975</td>
<td>.118</td>
<td>.095</td>
<td>.009</td>
<td>.763</td>
<td>.092</td>
<td>.002</td>
</tr>
<tr>
<td>+ Clinical symptoms</td>
<td>5,511</td>
<td>-.038</td>
<td>.057</td>
<td>-.059</td>
<td>.986</td>
<td>.127</td>
<td>.111</td>
<td>.012</td>
<td>.684</td>
<td>.168</td>
<td>.003</td>
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<td>MECP Patients</td>
<td>3,206</td>
<td>.315**</td>
<td>-</td>
<td>-</td>
<td>&lt;.001</td>
<td>8.621</td>
<td>.334</td>
<td>.112</td>
<td>-</td>
<td>-</td>
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<tr>
<td>+ Social Cognition</td>
<td>4,205</td>
<td>.229**</td>
<td>.203**</td>
<td>-</td>
<td>&lt;.001</td>
<td>8.671</td>
<td>.380</td>
<td>.145</td>
<td>.005</td>
<td>7.950</td>
<td>.033</td>
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<tr>
<td>+ Clinical symptoms</td>
<td>5,204</td>
<td>.148*</td>
<td>.169*</td>
<td>-.258**</td>
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<td>10.216</td>
<td>.447</td>
<td>.200</td>
<td>&lt;.001</td>
<td>14.165</td>
<td>.056</td>
</tr>
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</table>

* correlation significant at the .05 level; ** correlation significant at the .01 level; \( \beta \) = Standardized Beta Coefficient, \( p_{\text{change}} \), \( F_{\text{change}} \), and \( R^2_{\text{change}} \) refer to the statistical significance of the model as compared to its preceding model. Included covariates are gender, age and phase of illness.
Therefore, final regression analyses were performed separately for ROP patients and MECP patients. In ROP patients, neither neurocognition nor the additional effect of social cognition ($R^2_{\text{change}} < .002; p_{\text{change}} = .763$) showed a significant effect. In addition, when clinical symptoms were also investigated, the explained variance was again non-significant. In MECP patients it was demonstrated that neurocognition did significantly explain insight. When social cognition was added to the equation, the explained variance increased significantly ($R^2_{\text{change}} = .033; p_{\text{change}} = .005$). Both neurocognition and social cognition significantly explained insight in MECP patients. With the addition of the variable clinical symptoms to the above mentioned equation, the explained variance increased once again significantly. Clinical symptoms explained insight significantly, as did neurocognition and social cognition. In total, the predictors explained insight for 20%.

4. DISCUSSION

The current study investigated the relation of insight in psychosis with neurocognition, social cognition and clinical symptoms. Results can be summarized as follows: when investigated separately, neurocognition, social cognition and symptom dimensions were all associated with insight. Phase of illness was found to moderate the relation between insight and the studied predictors. In patients with multiple episode or chronic psychosis (MECP), both social cognition and clinical symptoms had additional effects and explained insight, along with neurocognition. In patients with recent onset psychosis (ROP) patients, none of the factors were found to be associated with insight.

To our best knowledge, this is the first study that has investigated the unique contribution of neurocognition, social cognition and clinical symptoms in relation to insight in psychosis. To demonstrate this, not only the predictive value of each factor within one model was investigated, but also the additional predictive value of the factor. In addition, most of the studies to date have focused on sub functions of neurocognition (e.g. working memory) or social cognition (e.g. mentalizing) in relation to insight. The current study used composite measures for each factor. This implies that multiple tests have been used to measure the construct, which may represent a more reliable estimate. Furthermore, the analysis is more parsimonious as there is no large number of measures that compromises degrees of freedom. Although this approach may lead to a certain loss of the fine-grained interpretation of cognitive sub functions indexed by individual tests, the results show that each of the cognitive outcome variables are related to insight, when analyses were restricted to the MECP population (see table S1). In fact, the association of neurocognition with insight within this group ($r = .312, p<.001$) is even higher as compared to the results of a meta-analysis of the previously published literature (Aleman et al., 2006), in which mean weighted effect sizes were reported ranging from $r = 0.14$ to 0.28.
Social cognition, highly correlating with neurocognition, explained additional variance on insight. Social cognition has only been investigated in a few studies in relationship to awareness of illness in psychoses (Bora et al., 2007; Lysaker et al., 2005; Lysaker et al., 2008). Our results support previous findings of a significant association. For example, Lysaker et al. (2008) found that schizophrenia patients with “superficial” insight not only had poorer executive function but also poorer emotion recognition ability, and capacity for social relationships than a patient group with “full awareness”. With regard to mentalizing, Langdon and Ward reported an association between deficient Theory of Mind performance (measured with tasks of picture sequencing and joke appreciation) and poor insight (Langdon and Ward, 2009). Our findings go beyond such previous studies, because we show that the concept of social cognition explains additional variance, when added to a regression model that already contains a wide range of neurocognitive variables. Similar results have been found in studies that investigated the predictive value of these concepts on distinct functional outcomes, such as social behavior (Brüne, 2005), vocational outcome (Bell et al., 2009), and interpersonal skills (Pinkham and Penn, 2006). The finding that social cognition uniquely contributes to insight is supported by theories that imply a role for deficient mentalizing in reduced insight in one’s illness (David, 1999; Langdon and Ward, 2009; Lysaker et al., 2005). That there is a general difficulty in adopting other mental perspectives, i.e., with “seeing the world as others do”, may contribute to deficient awareness of illness over and above general cognitive problems and next to clinical symptoms. A limitation of the current study was that a third described social cognitive domain, namely attributional style, was not included. In addition, it is possible that the additional explained variance of social cognition represents a general capacity to think about thinking, rather than a specific ability to infer other people’s mental state. This general capacity has been referred to as ‘metacognition’, which also includes the knowledge of one’s own mental state (David, 1999; Semerari et al., 2003). Indeed, a study on metacognitive decisions in a test of mental flexibility (the Wisconsin Card Sorting Test), found this to be significantly correlated with insight in psychosis (Koren et al., 2004).

In ROP-patients, neither neurocognition nor social cognition and clinical symptoms were significantly related to insight, although their mean scores were not dissimilar from those with MECP. This is in contrast with a study by Keshavan et al., which did find a linear trend of a composite measure of neurocognition with PANSS G12 score in ROP patients (Keshavan et al., 2004). An explanation for this discrepancy may be that the correlation between the measures of insight was modest in the current population ($r = -.257, p = .032$). Tranulis et al. (2008) have suggested that, in patients with recent-onset psychosis, specific factors may contribute to the measurement of insight. Particularly, recent-onset patients find themselves in a relatively unstable and evolving period. They may be aware of their distress but not yet attribute it to a mental disorder. In addition, different perspectives
between the patient who has recently become ill and the interviewer may be responsible for discrepant findings. A recent study by Parellada et al. (2009) investigated insight in patients with ROP longitudinally using interview based measures. The authors suggested that, during the acute phase, severity of clinical symptoms may overrule the association of other factors with insight, that may become more apparent after symptom stabilization. Viewing the supplementary table, it cannot be ruled out that clinical symptoms are related to insight in ROP. Thereby, the current study seems to give some support to this rationale. Future GROUP-studies should be able to assess insight and related factors in the current ROP population longitudinally.

In line with previous findings, the current study showed medium relationships between the insight measures, and a relation of its composite score with important outcome variables such as GAF-scores and number of hospitalizations (Lincoln et al., 2007). Scores on the PANSS and BIS reflected good insight in 43% of our sample. Although one influential study showed that poor insight affected up to 81% of patients with schizophrenia (Wilson et al., 1986), the numbers in the present study are consistent with comparable studies that were published over the last decades (Birchwood et al., 1994; Jensen et al., 2004; Karow et al., 2008). Indeed, one of the largest studies to date, that included a comprehensive assessment of 412 patients found that 41% of schizophrenia patients were aware that they suffered from a mental disorder (Amador et al., 1994). Treatment factors, such as the widespread use of psycho-education in the Netherlands, might contribute to the relatively high number of unimpaired patients in our sample. Alternatively, our brief measures of insight might have overseen some insight problems. The use of more comprehensive interview-based measures such as the Schedule of Assessment of Insight-Expanded version (SAI-E) (Kemp and David, 1996) and the Scale to Assess Unawareness of Mental Disorder (SUMD) (Amador et al., 1993) could yield a higher sensitivity in that regard. Utilisation of such scales may also allow for a deeper and more comprehensive exploration of the several domains of insight described in the Introduction. In addition, it has recently been suggested that insight should not only be studied as a belief that leads to treatment adherence, or the possession of specific knowledge, but also as a facet of a larger understanding of an individual life, also referred to as an inextricable part of a personal narrative (Lysaker et al., 2002; Lysaker et al., 2008). Another drawback of the current study was the use of the PANSS for both the independent measure (clinical symptoms) and the dependent measure (insight, in part). This may well explain the decrease in explained variance of neurocognition and social cognition, when the contribution clinical symptoms was also taken into account. Another drawback of the current study was the use of the PANSS for both the independent measure (clinical symptoms) and the dependent measure (insight, in part). This may well explain the decrease in explained variance of neurocognition and social cognition, when the contribution clinical symptoms was taken into account as well. Finally, correlation does not
imply causation. Whereas neurocognitive and social cognitive abilities may partly underlie the patients’ level of insight, the direction of the effect is less straightforward for clinical symptoms, such as delusions and hallucinations. For instance, a deluded person without insight in his/her psychotic beliefs may receive higher positive symptom ratings as compared to a similar person with insight. Thus, it may not be that stronger symptoms cause poor insight but that poor insight results in higher symptom ratings.

In conclusion, the results of the current study indicate that insight in psychosis is associated with multiple factors, and that a distinction between patients in different phases of their illness may lead to a better understanding of this concept. Lack of insight in MECP patients may not only require traditional cognitive aspects (e.g. learning, attending, information processing, remembering), but also successful perception and interpretation of social-emotional information. In this, the former may be necessary to understand the world around us as an individual, whereas the latter may be more important to understand others and oneself; it should be noted that the border between these concepts is, in reality, more diffuse. In addition to neurocognition and social cognition, a certain presence of behaviour and emotion, and absence of deviant perceptions (clinical symptoms), may be requirements for full insight. It should be noted that the nature of insight is paradoxical. Patients with full insight have been found to experience more depressive symptoms and hopelessness (Buchy et al., 2010), and the stigma associated with having a schizophrenia diagnosis has been suggested to be a moderating factor (Staring et al., 2009). However, increasing insight through treatment does not lead to lasting increases in depression. Indeed, improved insight has been shown to be associated with decreased suicidality (Bourgeois et al., 2004). Indeed, interventions with positive effects on neuropsychological aspects, clinical symptoms as well as well-being and functional outcome (Roder et al., 2006) may hypothetically increase insight as a by-product, while preventing the occurrence of negative effects on depressive symptoms (Buchy et al., 2010). Such interventions should also address stigma-sensitivity, and may benefit from using a broader concept of insight, which incorporates the personal narrative. How to increase insight in ROP needs further investigation.
Supplementary Table S1. Pearson Correlations (p-value, 1 tailed) of z-scores of neurocognition, social cognition, clinical symptoms and other variables with insight.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Insight variable</th>
<th>Birchwood Insight Scale</th>
<th>PANSS Item G12 Insight and Judgment</th>
<th>Insight Composite Measure</th>
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<td>ROP</td>
<td>MECP</td>
<td>Overall</td>
<td>ROP</td>
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<td>.083’</td>
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<td>WLT Immediate Recall</td>
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<td>WLT Delayed Recall</td>
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<tr>
<td>CPT-HQ % hits</td>
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<td>.157’</td>
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<td>CPT-HQ % false positives</td>
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<td>.055’</td>
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</table>

* significant at the < .05 level; ** significant at the < .01 level; ROP = Recent Onset Psychosis; MECP = Multiple Episode or Chronic Psychosis; WAIS = Wechsler Adult Intelligence Scale; WLT = Word Learning Task; CPT-HQ = Continuous Performance Test HQ; PANSS = Positive And Negative Syndrome Scale; GAF = Global Assessment of Functioning (S = symptoms, D = disability). Higher scores on the insight variables indicate better insight.