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Chapter 8

Insight Change in Psychosis: Relationship with Neurocognition, Social Cognition, Clinical Symptoms and Phase of Illness

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ABSTRACT

Introduction Impaired insight is an important and prevalent symptom of psychosis. It remains unclear whether cognitive disturbances hamper improvements in insight. We investigated the neurocognitive, social cognitive, and clinical correlates of changes in insight. Methods One-hundred fifty-four patients with a psychotic disorder were assessed at baseline (T0) and after three years (T3) with the Birchwood Insight Scale (BIS), the Positive And Negative Syndrome Scale (PANSS), measures of neurocognition and social cognition. Linear regression analyses were conducted to examine to what extend neurocognition, social cognition, clinical symptoms, and phase of illness could uniquely predict insight change. Subsequently, changes in these factors were related to insight change. Results Better neurocognitive performance and fewer clinical symptoms at baseline explained insight improvements. Social cognition and phase of illness could not predict insight change. Changes in clinical symptoms, but not changes in neurocognitive performance were associated with insight change. Discussion Neurocognitive abilities may predict, in part, the development of insight in psychosis.
1. INTRODUCTION

Impairments in insight, or unawareness of illness, is a highly prevalent symptom of patients with a psychotic disorder (Amador and Gorman, 1998). Insight is typically considered a multi-dimensional concept, that includes the following aspects: (i) awareness of illness, (ii) need for treatment, and (iii) relabeling of symptoms (David, 1990). Impaired insight has adverse consequences on outcomes of the disease, including functional outcome, treatment adherence, and re-admissions (Drake et al., 2007). Multiple factors have been associated with reduced insight, including neurocognitive impairment, social cognition, and clinical symptoms (Aleman et al., 2006; Mintz et al., 2003). However, the majority of the studies investigating insight applied a cross-sectional design, leaving the question whether the above factors contribute to the course of insight over time unanswered. This may be particularly relevant information for clinicians to be able to develop treatment strategies to improve insight.

In schizophrenia, opposed to other psychotic disorders, impairments in multiple domains of neurocognition (i.e. verbal learning and memory, attention/vigilance) have been related to insight (Aleman et al., 2006). Only a few studies have investigated the course of insight longitudinally. Parellada et al. (2011) demonstrated that cognitive impairments predicted several aspects of insight after two years. However, their assessment did not include all of the neurocognitive domains defined (Nuechterlein et al., 2004). A second study failed to find a significant effect of neurocognition on future insight (Cuesta et al., 2006). In a third study, patients with improved insight were found to have better cognitive performance after six months on some tasks, but not all (Cuesta et al., 2011). However, these findings may have been the result of their inclusion of medication-naïve patients with a first psychotic episode at baseline. Therefore, although it has been suggested that cognitive impairments limit the response to psycho-social treatment (Lysaker et al., 2002), this hypothesis has not been addressed adequately with respect to insight improvement.

Previously we demonstrated that social cognition and clinical symptoms are both uniquely related to level of insight, irrespective of neurocognitive functioning; interestingly, phase of illness moderated this effect (Quee et al., 2011). Taking these findings into account, it is interesting to study whether these factors are also predictive of changes in insight. In addition, it is not known whether changes in these factors fluctuate with changes in insight change. Increases in severity of clinical symptoms have been found to be associated with decreases in insight, but only in patients with recent onset psychosis (Buchy et al., 2012).

In the current study we investigated factors associated with change in insight over time in a longitudinal design. We expected that neurocognition and social cognition would explain changes in insight over time. We also investigated whether changes in neurocognition, social cognition, clinical symptoms, and phase of illness were associated with changes in insight.
2. METHODS

2.1 Participants
Two hundred and seventy patients with psychotic disorders were assessed with the Birchwood Insight Scale at baseline (see paragraph 2.2.1). This was a subsample of the patient population participating in the GROUP project (Korver et al., 2012). The GROUP project is a large-scale multi-center study that investigates the vulnerability and protective factors for (1) the development of a psychotic disorder, and (2) the variation of the course of illness. Two out of four centers participated in the insight study (Amsterdam and Utrecht). Diagnoses were confirmed using the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992). The procedure of recruitment, informed consent, assessment instruments, approval by an accredited Medical Ethics Review Committee and population characteristics have been described in a previous report on the project (Korver et al., 2012).

2.2 Assessments

2.2.1 Insight
Insight was assessed using two measures. From the Positive And Negative Syndrome Scale (PANSS) (Kay et al., 1987), a semi-structured interview consisting of 30 items, we used item G12 (Poor Judgment and Insight). Scores on the PANSS range from 1 (absent) to 7 (extremely severe). Secondly, we used the Birchwood Insight Scale (BIS) (16). The BIS is a short self-rating questionnaire that consists of eight questions addressing the three components of insight in psychosis (Awareness of Illness, Need for Treatment, and Relabeling of Symptoms). The BIS total score ranges from 0 to 12, with higher scores indicating better insight. For insight, as well as neurocognition, social cognition, and clinical symptoms, composite measures were created (see paragraph 2.3). For insight, the composite measure consisted of the PANSS item G12, and the BIS.

2.2.2 Neurocognition
The neurocognitive measures used in the GROUP-study have been described in detail elsewhere (Meijer et al., 2011). The following tasks were administered: Continuous Performance Test – HQ (CPT-HQ) (attention/vigilance), Response Set-shifting Task (RST) (reasoning and problem solving), short form of the Wechsler Adult Intelligence Scale – III (WAIS-III) containing the subtests Block Design (reasoning and problem solving), Digit Symbol (processing speed), Arithmetic (working memory), and Information (verbal comprehension) (Blyler et al., 2000), Word Learning Task (WLT) immediate recall and delayed recall (verbal learning and memory) (Brand and Jolles, 1985). Educational degree was assessed using 9 categories, 0 being the lowest (no education) and 8 being the highest (academic degree) (Verhage, 1964). The parameters used for neurocognition were similar as in our previous
study (Quee et al., 2011), with a few exceptions. For the CPT-HQ, two parameters were created: CPT variance and CPT performance index. For CPT variance, or intra-individual variability (20), the standard deviation of the subject’s mean response time on the hit trials was used. CPT performance index consisted of an efficiency score ((accuracy/reaction time) x 1000), in which accuracy was measured as the total number of hits (range 0-28) minus the total number of errors (range 0-28), divided by 28. The RST parameter was based on the subjects’ accuracy during the experimental condition, during which the subject has to find the alternated response rule. For all neurocognitive tests, higher scores indicated better performances, except for CPT variance.

2.2.3 Social Cognition

For social cognition, the Degraded Facial Affect Recognition task (DFAR) (emotion perception) (Van ‘t Wout et al., 2004) and the Hinting Task (Theory of Mind) (Corcoran et al., 1995) were used. Higher scores on the measures of social cognition reflected better performances. The Hinting Task was measured at baseline only.

2.2.4 Clinical Symptoms

Current symptom severity was measured with the PANSS. Items on the PANSS incorporate the behavioural effect of the symptoms, as well as their severity. As in our earlier study (Quee et al., 2011) we calculated a mean score of the subject’s ratings on the 8 remission items (Andreasen et al., 2005). These items include: delusions (P1), conceptual disorganization (P2), hallucinatory behaviour (P3), blunted affect (N1), social withdrawal (N4), and lack of spontaneity (N6), mannerisms/posturing (G5), and unusual thought content (G9).

2.2.5 Phase of Illness

Phase of illness was divided into recent onset psychosis and multiple or chronic psychosis. Recent onset psychosis was defined as follows: a first psychotic episode during the year prior to the baseline assessment. All other patients were characterized as having ‘multiple episode or chronic psychosis’.

2.3 Statistical Analysis

Normality was checked for all variables. If necessary, variables were transformed to approximate normality using logarithmic or square root transformation. Subsequently, a composite measure was created for the insight measures at baseline and follow-up. As in our previous study, the scores on the G12 and BIS were transformed into z-scores, based on the mean and standard deviation of the baseline assessment (Quee et al., 2011). Insight change was computed by subtracting the insight composite score at baseline from the insight composite score at follow-up. Thus, higher scores at insight change reflect more
insight improvement. A paired t-test was used to investigate differences between baseline and follow-up insight.

Next, composite scores were created for baseline neurocognition, cognition, and clinical symptoms. The composite score included all test scores of each of the abovementioned factors (see paragraph 2.2.2, 2.2.3, and 2.2.4). For neurocognition and social cognition, this was done by transforming all the raw scores into z-scores, using the mean and standard deviations from the patient population included at baseline (N=270). For neurocognition, the composite score consisted of 8 measures: CPT-HQ (average performance index and variance, the latter being negatively transformed), RST, WAIS-III Digit Symbol, Block Design, Arithmetic, and Information, WLT (average immediate and delayed recall), and educational degree. For clinical symptoms, a mean score was created, based on the 8 PANSS items.

Hierarchical regression analyses investigated the predictive value of neurocognition, social cognition, clinical symptoms, and phase of illness at baseline. These variables were entered block-wise, which enabled us to investigate the explained variance of neurocognition, as well as the additional explained variance of social cognition, clinical symptoms, and phase of illness. Age at baseline and sex were entered in the first block, as covariates. Scatterplots were used to evaluate the direction of the effects. Changes ≥ 1 SD were considered insight improvement, whereas changes ≤ -1 SD were considered insight decrease.

Next, we analyzed whether changes in neurocognition, social cognition, clinical symptoms and phase of illness were related to insight change. This was done by subtracting the score at baseline from the score at follow-up. These change scores were then transformed into z-scores to create a composite measure for neurocognition. Thus, for neurocognition change as well as social cognition, higher change scores indicated improved performance; for clinical symptoms change, higher scores indicated more symptoms. Variables were entered block-wise in a new regression analysis, again with the covariates age and sex in the first block.

All analyses were performed with 2-tailed hypothesis testing, with $\alpha = .05$. For the evaluation of the scaled scores, and composite measures, we allowed for 30% of missing values. Statistical analyses were performed using SPSS 18.0. For descriptive purposes, correlations between all variables are displayed in Supplementary Table S1.

3. RESULTS

3.1 Descriptives
Out of the 270 patients assessed with the assessment of insight at baseline, 154 were assessed in GROUP at follow-up. Dropout in Utrecht and Amsterdam was relatively similar (45% and 55%, respectively). These patients (n=116) received a questionnaire to investigate reasons for dropout; however none of these patients responded to this request. Insight at baseline of the remaining patients differed significantly from the dropout patients ($F(1,272)=12.649$,
with the former having higher levels of insight \((z=.16, z=-.19\), respectively). The effect size is this difference was small \((d=.46)\), suggesting that the sample is still relatively reliable. Differences were also significant for education \((F(1,272)=7.605, p=.006)\), but not for neurocognition, social cognition, clinical symptoms, phase of illness, age, and sex. Table 1 shows the demographic and clinical data for the included 154 patients of the current study. At baseline, 21\% of the patients included had a recent onset psychosis.

**Table 1. Baseline characteristics of the patients \((n=154)\)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline ((T_{0\text{years}}))</th>
<th>Follow-up ((T_{3\text{years}}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>28 (7)</td>
<td>31 (7)</td>
</tr>
<tr>
<td>Gender, male %</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Education(^a)</td>
<td>4.6 (2.1)</td>
<td>4.9 (1.9)</td>
</tr>
<tr>
<td>Duration of illness, years</td>
<td>5 (5)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Diagnostic, Schizophrenia, %</td>
<td>103</td>
<td>102</td>
</tr>
<tr>
<td>Schizo-affective, %</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td>Psychosis NOS, %</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Anti-psychotics, Olanzapine, %</td>
<td>32</td>
<td>20</td>
</tr>
<tr>
<td>Risperidone, %</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>Clozapine, %</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Aripiprazol, %</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Quetiapine, %</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Other, %</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>No anti-psychotics, %</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>PANSS,(^c)</td>
<td>1.9 (0.8)</td>
<td>1.6 (0.6)</td>
</tr>
<tr>
<td>Positive</td>
<td>2.2 (0.8)</td>
<td>1.7 (0.7)</td>
</tr>
<tr>
<td>Negative</td>
<td>1.8 (0.5)</td>
<td>1.5 (0.4)</td>
</tr>
<tr>
<td>General</td>
<td>1.9 (1.3)</td>
<td>1.7 (1.2)</td>
</tr>
<tr>
<td>BIS(^b)</td>
<td>9.3 (2.5)</td>
<td>8.9 (2.7)</td>
</tr>
</tbody>
</table>

\(^a\)Table presents means (SD) or numbers (in \%); \(^b\)Education (Verhage): range 0 (no education), 3-5 (school diploma) to 8 (academic degree); \(^c\)PANSS: Positive And Negative Syndrome Scale; \(^d\)G12: PANSS item G12 ‘Judgment and Insight’; \(^e\)BIS: Birchwood Insight Scale.

**3.2 Insight change: relationship with baseline insight**

The difference between insight at baseline and follow-up was not statistically significant \((p=.388)\). The relationship between insight at baseline and insight at follow-up was significant \((r=.415, p<.001)\). Furthermore, baseline insight was significantly related to insight change \((r=.515, p<.001)\), with better insight at baseline being associated with more insight improvement.
3.3 Insight change: relationships with baseline neurocognition, social cognition, clinical symptoms, and phase of illness

Insight change was significantly related to baseline neurocognition ($r=.231$, $p=.005$), and clinical symptoms ($r=-.215$, $p=.009$). Better baseline neurocognitive performances were related to improvements in insight after 3 years (Figure 1). Patients with more symptoms at baseline had decreased insight (Figure 2). The relationship with social cognition and phase of illness was non-significant. When neurocognition and clinical symptoms were entered in the regression analysis consecutively, with age and sex as covariates, the additional explained variance of clinical symptoms was significant. Together, these factors explained insight improvement for 10% (Table 2).

3.4 Insight change: relationships with changes in neurocognition, social cognition, and clinical symptoms

Insight change was significantly related to change in clinical symptoms ($r=-.223$, $p=.008$). Decreases in clinical symptoms over time were related to increases in insight. The relationships with change in neurocognition, social cognition, and phase of illness were non-significant. When change in clinical symptoms was entered in the regression analysis, with age and sex as covariates, the explained variance of the model was 12%, with the contribution of clinical symptoms being significant ($\beta=-.324$, $p<.001$) (Table 3).

Figure 1. Insight change as a function of baseline neurocognition
Figure 2. Insight change as a function of baseline clinical symptoms

![Graph showing insight change as a function of baseline clinical symptoms.](image)

Table 2. Relationships of baseline neurocognition and clinical symptoms with insight change for patients with non-affective psychosis

<table>
<thead>
<tr>
<th>Model</th>
<th>df</th>
<th>$\beta_{\text{Cognition}}$</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>Neurocognition</td>
<td>3,137</td>
<td>.259&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
<td>.018</td>
<td>3.450</td>
<td>.265</td>
<td>.070</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>+ Clinical Symptoms</td>
<td>4,136</td>
<td>.200&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-.176&lt;sup&gt;a&lt;/sup&gt;</td>
<td>.007</td>
<td>3.660</td>
<td>.312</td>
<td>.097</td>
<td>.046</td>
<td>4.061</td>
<td>.027</td>
</tr>
</tbody>
</table>

Note: $\beta$ = standardized beta coefficient; $P_{\text{Change}}, F_{\text{Change}}, R_{\text{Change}},$ and $R^2_{\text{Change}}$ refer to the statistical significance of the model as compared with its preceding model. <sup>a</sup>Correlation significant at the .05 level; <sup>b</sup>Correlation significant at the .01 level. Included covariates are age and sex.

Table 3. Relationships of changes in clinical symptoms with insight change for patients with non-affective psychosis

<table>
<thead>
<tr>
<th>Model</th>
<th>df</th>
<th>$\beta_{\text{Clinical Symptoms}}$</th>
<th>$P$</th>
<th>$F$</th>
<th>$R$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in clinical symptoms</td>
<td>3,138</td>
<td>-.343&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.001</td>
<td>6.087</td>
<td>.342</td>
<td>.117</td>
</tr>
</tbody>
</table>

Note: $\beta$ = standardized beta coefficient; <sup>a</sup>Correlation significant at the .05 level; <sup>b</sup>Correlation significant at the .01 level. Included covariates are age and sex.
4. DISCUSSION

The current study investigated factors associated with insight change in non-affective psychosis. Results can be summarized as follows. Most importantly we found that, though the mean group-level of insight was relatively stable over time, improvement of insight within patients was positively related to baseline neurocognitive performances, and negatively related to baseline symptom severity. In addition, changes in insight were found to fluctuate with changes in symptom severity, but not with changes in neurocognition, between baseline and follow-up.

The course of insight was stable in the majority of this relatively young population. This is in line with findings that interventions to date had only limited success in improving insight over time (Pijnenborg et al., 2012; unpublished data). It therefore becomes relevant to study the underlying factors of this insight stability. Longitudinal studies focusing on insight have provided mixed results (Cuesta et al., 2006; Cuesta et al., 2011; Parellada et al., 2011;). Rather than predicting the future level of insight, our study focused on factors contributing to changes in insight. The advantage of this approach is that by using a difference score as the outcome measure, both the level of insight at baseline, as well as insight at follow-up are taken into account.

In line with the hypotheses, baseline neurocognition substantially contributed to insight change, together with clinical symptoms. This shows that neurocognition has a rate-limiting effect on the development of insight. Baseline symptom severity and decreases in symptoms over time were associated with an increase in insight as well. This may indicate that treatment of symptoms may be partly beneficial to improve insight in psychosis. In a subsequent analysis, we found that some of the neurocognitive abilities and clinical symptoms may be particularly responsible for this (Supplementary Table S1). The relationship between these significant variables should be tested in a new sample to confirm their predictive value on insight change.

In contrast to our expectations, phase of illness and social cognition were not related to insight change. Therefore, insight change may not differ between recent onset patients and other patients. On the other hand, it cannot be ruled out that the correlates of insight change would differ in a study covering a longer period of time. In an earlier study, we found social cognition to be of additional value for insight as well (Quee et al., 2011). Social cognition has been found to mediate the relationship between neurocognition and functional outcome (Andreasen et al., 2005). Neurocognitive impairments may thereby underlie the deficits in emotion perception and theory of mind, and this may also apply to the enduring impairments in insight.

The current study may have clinical implications. It has been suggested that patients with more severe neurocognitive impairments are less able to profit from psycho-social interventions (Schmidt et al., 2011). This may also explain why they only minimally improve
insight. Such interventions may need to be provided with a high level of structure, and more rehearsal, in order to improve insight. We did not find a relationship between neurocognitive change and insight change. Still, this does not rule out a role of cognitive remediation here. Enhanced cognition, together with decreased symptoms may give the patients more possibilities to increase their awareness of illness over time.

Strengths of the current study were its longitudinal design, the assessment of several cognitive domains, and the methodology used. Some limitations should also be considered. First, a substantial subgroup did not participate in the GROUP study at follow-up. Although effect sizes were small, patients who did not participate at follow-up study had poorer insight at baseline. Reasons for dropout were unknown. Second, our assessment of social cognition was limited. We did not include a measure of metacognition, which may be more closely related to insight (Lysaker and Buck, 2007). Third, stigma and depressive symptoms were not assessed in the current study (Koren et al., 2004; Pruβ et al., 2012). Fourth, the assessment of insight may have been more comprehensive would we have used the Structured Assessment of Insight – Expanded (SAI-E) (Kemp and David, 1996). Due to these limitations our results should be interpreted cautiously.

In conclusion, the current study highlights the role of neurocognition and clinical symptoms for insight improvement. Therefore, it may be necessary to develop treatment strategies that incorporate these aspects, among others such as stigma, metacognition, and depressive symptoms (e.g., Pijnenborg et al., 2011).