Trait and State Attributes of Insight in First Episodes of Early-Onset Schizophrenia and Other Psychoses: A 2-Year Longitudinal Study

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Background: Increasing evidence supports the important role of illness state and individual characteristics in insight. *Methods*: Insight, as measured with the Scale to Assess Unawareness of Mental Disorder, over the first 2 years of early-onset first-episode psychosis and its correlations with clinical, socio-demographic, cognitive, and structural brain variables are studied. *Results*: (1) insight at 2 years is poorer in schizophrenia spectrum disorders (SSDs) than in subjects with other psychoses; (2) the more severe the psychosis, the worse the insight. In SSD, depressive symptoms, poorer baseline executive functioning, lower IQ, longer duration of untreated psychosis (DUP), and poorer premorbid infancy adjustment are associated with poorer insight; frontal and parietal gray matter (GM) reductions at baseline correlate with worse insight into having psychotic symptoms at 2 years; (3) insight into having a mental disorder (Scale to Assess Unawareness of Mental Disorder [SUMD]1) at 1 year, DUP, and baseline IQ are the most consistent variables explaining different aspects of insight at 2 years in SSD patients. IQ and SUMD1 at 1 year, together with left frontal and parietal GM volumes, explain 80% of the variance of insight into having specific psychotic symptoms in SSD patients (adjusted $R^2 = 0.795$, $F = 15.576$, $P < .001$). *Conclusion*: Insight is a complex phenomenon that depends both on severity of psychopathology and also on disease and subject characteristics, such as past adjustment, IQ, DUP, cognitive functioning, frontal and parietal GM volumes, and age, gender, and ethnicity.

Introduction

Lack of insight (usually referring to impaired awareness of having an illness) is a well-recognized and common clinical characteristic of both affective and nonaffective psychosis.[1–3] Insight is a complex concept, associated with symptom severity, cognitive impairment, and neurobiological dysfunction.[4–10] The most commonly and systematically used definition of insight comprises a multidimensional concept that includes,[1,2,8,11] (1) awareness of having a mental disorder, (2) awareness of the need of treatment, (3) understanding the social consequences of the disorder, (4) awareness of specific signs and symptoms of the disorder, and (5) attribution of symptoms to the disorder.[11,12]

Although few clinicians would dispute the relevance of insight, there is no a general agreement on its clinical meaning and biological substrate. Lack of insight has been considered a core symptom of schizophrenia,[13,14] a psychological coping mechanism aimed at preserving emotional well-being,[15,16] a result of some cognitive or psychological dysfunction,[9,17] a kind of neurological mechanism similar to anosognosia,[18–20] or a combination of the above.[5]

Most, but not all studies that have assessed insight in patients with psychosis report a relationship between

poor insight and diagnosis of schizophrenia,[1,6,21–23] more severe psychotic psychopathology,[5,6,21,22,24–26] lower cognitive functioning (with some specificity to executive functioning),[10,26–30] lower gray matter (GM) volumes in the temporal, frontal and/or parietal regions,[9,31] and poor outcome.[13,32–35] Very recently, poor insight has been associated with long duration of untreated psychosis.[36] In addition, poor insight has been generally related to less severe depressive symptomatology and fewer suicide attempts after a first episode of psychosis (FEP).[7,22,25,28,37,38] A meta-analysis by Mintz and colleagues[22] showed that, as positive, negative, and general symptoms increased, the degree of insight decreased, and as the degree of insight increased, depressive symptoms increased.[22] In addition, a meta-analysis by Aleman and colleagues[8] found that in patients with schizophrenia and other psychoses, although there was a significant relationship, the predictive value of neurocognition was rather modest.

Total brain, gray, and white matter volumes have been studied in relation to insight, with contradictory results.[25,39] Associations between lower gray-matter volumes in prefrontal, temporal, and parietal lobes and dimensions of insight have been observed in stable schizophrenia patients,[4,10,37,40] although some studies have found no association between structural data and insight.[38] For a review, see Gilleen et al.[20]

Taken together, these findings argue in favor of insight being partially dependent on the mental status of the patient but also having some trait value, related to the diagnosis of schizophrenia.[6] The study of insight in FEP patients entails crucial advantages. Indeed, clinical and neuropsychological correlates with insight in FEP are somewhat different than those reported for established schizophrenia.[26,28] First, insight is not a static condition and it may be influenced by neurobiological, clinical, therapeutic, and social circumstances. Furthermore, insight tends to be better in at risk mental state for psychosis than during the FEP,[41] it tends to improve after first episode,[6,25] and patients with FEP are less aware of having a mental illness than multiple-episode patients.[42] Second, FEP constitutes a heterogeneous group that includes different psychosis categories, the boundaries of which are now a subject of lively debate.[40]

Although the average age of onset of schizophrenia has been calculated as 18 in men and 25 in women,[43] very little research has been conducted to assess the effect on insight of having a FEP in adolescence, before personality and neurobiological maturation are completed. An adolescent sample as the one studied in the present investigation may give valuable information about the effect of age on the different domains of insight and also lacks the effects of chronicity, multiple episodes, or medication. In a prior publication,[6] we found that in adolescents with first-episode early onset psychosis (EOP), insight into having a mental disorder, its consequences, and

the need for treatment improved over the early phases of treatment. Poorer insight was associated with more severe positive, negative, and overall psychotic symptoms, and with poorer global functioning, at both baseline and 6-month follow-up.[6] After 6 months, poor insight correlated with final diagnosis of schizophrenia at the 1-year follow-up.

The aim of the present study was to explore prospectively the relationship between insight and depressive symptomatology, neurocognitive performance, and GM volumes. In addition, we wanted to extend our previous study[6] by examining the course of insight over the first 2 years after a first episode of EOP. We analyze all these aspects splitting the whole sample into schizophrenia spectrum disorders (SSDs) and non-SSD. To our knowledge, this is the first study that prospectively assesses the relationship of insight with depressive symptoms and neuropsychological and neurobiological markers in an early onset FEP cohort. Based on our previous studies and those by other groups reviewed in this introduction, our hypotheses were that: (1) insight improves over the first 2 years after a first episode of EOP, (2) insight is poorer in schizophrenia patients than in patients with non-SSD psychoses 2 years after the psychosis onset, (3) more severe positive or negative symptoms are associated with poorer insight throughout the course of illness, (4) better insight is associated with the presence of more depressive symptomatology over the course of EOP, and (5) poorer prefrontal cognitive functioning and/or lower prefrontal volumes are associated with poorer insight irrespective of specific diagnosis (SSD or non-SSD).

Methods

Data were collected as part of a 2-year longitudinal study of FEP with onset in adolescence. The study population consisted of 110 consecutively treated FEP with early and recent onset of psychosis, recruited as part of a national longitudinal multicenter study.[44] Inclusion criteria for patients included an onset of positive psychosis symptoms less than 6 months prior to baseline assessment and age between 9 and 17 years. Exclusion criteria were presence of a concomitant Axis I disorder at the time of evaluation that might account for the psychotic symptoms (such as substance abuse or dependence), mental retardation (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [DSM-IV] criteria), neurological disorders, history of head trauma with loss of consciousness, and pregnancy or breast feeding. Detailed information on the characteristics of the sample and methods of the study is reported elsewhere.[44,45] The study was approved by the IRBs of all participating clinical centers. All parents or legal guardians gave written informed consent before the study, and patients agreed to participate.

Clinical Assessment

Diagnosis was made according to the DSM-IV criteria[46] (at baseline, 6 months, 1 year, and 2 years), using the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL) Spanish adaptation at baseline, and 2 years.[47,48] Socioeconomic status (SES) was estimated using parental years of formal education. Psychopathology was assessed with the Spanish adaptation of the Positive and Negative Symptom Scale (PANSS).[49] Depressive symptomatology was assessed with the Hamilton Rating Scale for Depression (HRSD).[50] The questionnaire rates the severity of symptoms observed in depression, such as low mood, insomnia, agitation, anxiety, and weight loss. Each question has 3–5 possible responses, which increase in severity. Seventeen questions contribute to the total score (HRSD-17). Presence of suicidal thoughts or behaviors was assessed by means of the Likert Clinical Global Impressions–Severity of Suicide scale.[51]

Premorbid adjustment was assessed with the childhood subscale of the Premorbid Adjustment Scale (PAS).[52]

The Children's Global Assessment of Functioning (C-GAF) Scale,[53] which measures the severity of symptoms and the level of functioning on a scale from 1 to 100, was used for assessing general functioning.

Duration of untreated psychosis (DUP) was calculated as the time elapsed between the first positive, negative, or disorganization symptom recalled and the baseline assessment, in days.

Insight Assessment. Insight was measured by the abbreviated version of the Scale to Assess Unawareness of Mental Disorder (SUMD).[2] The SUMD has been widely used to assess insight in schizophrenia and its relationship to psychopathology[11] and takes into account the aforesaid multidimensional approach. It gives more information than the G12 item of the PANSS in this population.[6] The patients were interviewed at baseline when they were in condition to cooperate with a clinical interview (those patients acutely psychotic or too disorganized were interviewed after the improvement of symptoms allowed for a clinical interview in which the SUMD could be assessed). The SUMD was completed by the clinician in the context of an interview and using all the information from the complete history, mental state examination, and chart. The first 3 items assess, in turn, the subject's general insight into having a mental disorder (SUMD1), the effects of medication on the disorder (SUMD2), and general understanding of the consequences of the disorder (SUMD3). These 3 items were completed for all subjects, and their level of insight was rated on a 5-point Likert scale (1 = full insight and 5 = no insight). Items 4–9 pertain to specific symptoms and are asked only if it has been established that the patient experienced any of these symptoms (score of 3 or more on the PANSS for that symptom). The same 5-point Likert scale was used. If the subject showed insight into a symptom, defined as a score between 1 (full insight) and 3 (partial insight), the subject's attribution of the symptom to the psychotic illness was assessed and rated on a 5-point Likert scale (1 = correct attribution and 5 = incorrect attribution). Along with SUMD items 1–3, insight and attribution of symptoms (SUMDTot1 and SUMDTot2, respectively) can be considered the 5 dimensions of insight. In all items, there was the option to score 0 = nonrelevant, which was not counted in subsequent analyses.

Neuropsychological Measures. For the purpose of the present study, we selected those measures considered to be related to executive function (EF) and dorsolateral prefrontal cortex (DLPC) functioning[54,55] because of their possible relationship with insight.[56] EF was measured by a composite score formed by a group of measures from different tests that were previously transformed into *z*-scores. That is to say, we used the total errors, perseverative errors, and conceptual-level responses from the Wisconsin Card Sorting Test (WCST),[57] the interference score of the Stroop test,[58,59] number of correct words from the verbal fluency test (Controlled Verbal Fluency Task),[60] and the time to complete the task and the number of mistakes committed from the Trail Making Test-B[61,62] to calculate an arithmetic mean index for the EF domain.[63,64]

The index measure related to DLPC functioning was calculated as a composite score grouping different results of the following tasks that have been related to the corresponding cognitive functions as follows: attention (measured using reaction time and correct responses from the Continuous Performance Test, CPT-II[65]; Digit Span Forward, Trail Making Test A[61]; words, and colors parts of the Stroop test[58,59]), working memory (Digit Span Backward and Letter–Number Sequencing from the Wechsler Adult Intelligence Scale),[66] and adding the composite score for EF itself. All tests were administered and scored according to standardized published instructions by 6 previously trained research psychologists. Interrater reliability for some scales (eg, WCST) was determined by interclass correlation coefficient, which was between 0.95 and 0.99. All subjects performed the same battery of tests in a fixed order. To estimate general intellectual functioning, we used one of the most widely used short forms from the full Wechsler Intelligence Scale, selecting 2 specific subtests: block design and vocabulary.

Neuroimaging Assessment. Magnetic resonance imaging (MRI) scans were acquired at baseline, less than 3 months after the onset of psychotic symptoms. MRIs were performed with 5 different scanners: 2 Siemens Symphony, 2 General Electric Signa, and one Philips ACS Gyroscan, all 1.5T. Data were collected from each center and processed at one site. Sequences were acquired in

axial orientation for each subject, a T_1-weighted 3D gradient echo (voxel size 1 × 1 × 1.5 mm) and a T_2-weighted Turbo-Spin-Echo (voxel size 1 × 1 × 3.5 mm). MRI images were processed using locally developed software incorporating a variety of image processing and quantification tools.[67,68] To obtain volume measurements of the main brain lobes, a method for semiautomated segmentation of the brain based on the Talairach proportional grid system was used.[59,60] The regions of interest included in the analysis were the frontal, parietal, and temporal lobes.[59] Volume of whole brain GM and that of frontal, parietal, temporal, and occipital lobes were obtained for each hemisphere. These areas were included due to the extensive deficits in GM observed in studies in first episodes of early-onset psychoses.[44,69] Full details on the neuroimaging methodology are reported elsewhere.[70]

Baseline Assessment. The patients in this study had their first lifetime acute psychotic episode when recruited. The majority of the patients (83%) were admitted to the hospital at the time of first evaluation. A baseline assessment was performed shortly after admission (either in the inpatient unit or outpatient clinic) or at the time of first assessment for those not hospitalized, except for the SUMD scale and the neuropsychological assessment, which were administered prior to discharge or at the time of best mental state during the episode.

Longitudinal Assessment. Six months, 1 year, and 2 years after the baseline visit, the clinical, insight, and functional outcome assessments were repeated. The type of psychosis was determined after the 2-year administration of the K-SADS. Taking into account the last reliable diagnosis available, the sample was divided into a group of SSDs (including schizophrenia and schizophreniform disorders)[71] and a group of non-SSDs.

Statistical Analysis

We performed repeated measures tests to analyze change in insight and other clinical variables in each of the diagnostic groups (SSD and non-SSD). We then cross-sectionally compared both groups. A Kolmogorov–Smirnov test was used to test for the normality of variables. Age, DUP, CGI, and SUMD subscales did not follow a normal distribution (except for insight into having psychosis symptoms). The rest of the variables were normally distributed. Therefore, nonparametric association tests were used to examine the relationship between insight dimensions and sociodemographic variables, premorbid adjustment, and psychopathology. Mann–Whitney tests were used to evaluate the differences in insight measurements between the diagnostic groups (24-month diagnosis). Repeated-measures *t*-tests (for the PANSS and Hamilton) and Wilcoxon rank tests (for the SUMD) were used to assess the changes in variables over time. Spearman correlations were used to assess the relationship between insight and psychopathological, neurocognitive, and neuroimaging scores.

A series of analyses (stepwise linear regression) were performed to assess which state or trait characteristics predicted the different domains of insight over the long term. The variables included in the models were those expected from the literature to predict the assessed dependent variable or those that had correlations with the dependent variable in the univariate analysis with a significance level of $P < .25$.[72] Thus, the dependent variables were the different domains of insight at 2 years and their independent variables were: diagnosis of SSD, gender, baseline executive functioning (devised *z*-score based composite index), estimated IQ, age, premorbid adjustment in infancy (infancy subscale of the PAS scale), DUP, general functioning and SUMD at 1 year, and negative symptoms (negative subscale of the PANSS) and depressive symptoms (HRSD) at 6 months (due to the fact that, in this sample, insight was very dependent on acute symptomatology at baseline and that after 6 months, the symptomatology did not further improve).[6] We included the measure of insight into having a disorder at 1 year because insight improved over the first year (see later in the text and table 2). Baseline left and right frontal and parietal GM were also included in the models.

Results

Sample

The sample consisted of 110 adolescents, 9–17 years of age, with a first episode of nontoxic psychosis. Table 1 presents socio-demographic and clinical characteristics of the sample at baseline. The attrition rate was 24.55% at 2 years. We compared the group that completed the follow up visits as established with those unavailable at 2 years, and there were no differences in baseline socio-demographic or clinical characteristics between them with the exception that the group lost for follow up had a slight better executive functioning than the other group ($P = 0 < .01$). At least some of the variables were available for 110 patients at baseline, 99 at 6 months, 92 at 1 year, and 83 at 2 years. The diagnosis used was the last one available.

Within the SSD (total of 53 patients), 44 had a diagnosis of schizophrenia and 9 of schizophreniform disorder. The non-SSD group was a heterogeneous group composed of 57 patients, including 22 patients with bipolar disorder, 16 patients with Psychosis-NOS, 9 patients with a depressive disorder with psychotic symptoms, 3 patients with a brief psychotic disorder, and 7 patients with schizoaffective disorder.

Extended demographic data are reported elsewhere.[45] The 2 groups were similar in their socio-demographic characteristics, their baseline cognitive functioning, and the severity of their psychopathology (for details, see table 1). Only depressive symptomatology was significantly

Table 1. Subject Sociodemographic, Clinical, and Brain Volumes Baseline Characteristics

$N = 110$	SSD, ($n = 53$)	Non-SSD, ($n = 57$)	Test	P
Gender (male/female)	39/14	35/22	$\chi^2 = 1.85$	.12
Race (caucasian/others)	46/7	47/10	$\chi^2 = 2.51$	.35
	Mean (SD)	Mean (SD)		
Age (years)	15.43 (1.95)	15.61 (1.58)	$U = 1498.5$	.94
DUP (days)	66.75 (54.654)	63.82 (49.98)	$U = 1505.7$	.98
Parental studies (years)	11.92 (4.15)	11.02 (3.81)	$t = 0.17$	.25
Estimated IQ	80.89 (16.95)	80.70 (18.16)	$t = -0.05$	.96
DLPC	−0.72 (0.95)	−0.58 (0.77)	$t = -0.87$	.38
Executive functioning	0.865 (0.82)	−0.85 (0.78)	$t = -0.13$	.96
PAS infancy (0–24)	7.81 (4.84)	6.74 (4.75)	$t = 1.17$	.24
GAF (0–100)	33.25 (15.82)	33.72 (13.99)	$t = -0.17$	.87
CGI (1–7)	5.62 (1.04)	5.54 (1.01)	$U = 1428.5$	.72
PANSS positive (7–49)	23.47 (5.76)	24.28 (7.15)	$t = -0.650$	.52
PANSS negative (7–49)	20.96 (8.58)	19.14 (9.03)	$t = 1.083$	.28
PANSS total score (30–210)	88.26 (17.46)	89.67 (22.28)	$t = -0.36$	.71
Hamilton (0–65)	15.77 (7)	20.75 (9.57)	$t = -3.097$	<.01
CGI-S (1–4)	1.22 (0.60)	1.35 (0.79)	$U = 1416.5$	.4
ICV (cc)	1521.6 (155.8)	1490.70 (152.86)	$t = 0.95$	.34
LFGM (cc)	78.8 (8.1)	78.52 (8.13)	$t = 0.16$	.87
RFGM (cc)	81.3 (8.3)	80.60 (8.37)	$t = 0.41$	.68
LPGM (cc)	65.3 (7.6)	65.07 (7.91)	$t = 0.13$	.89
RPGM (cc)	65.5 (7.6)	65.18 (7.95)	$t = 0.20$	.84
LTGM (cc)	84.2 (10.2)	80.80 (9.12)	$t = 1.67$	.09
RTGM (cc)	83.1 (10.0)	80.57 (9.48)	$t = 1.22$	.23
OGM (cc)	97.1 (14.8)	94.22 (14.29)	$t = 0.94$	.35

Note: Chi-square test for categorical variables; *t*-test for normally distributed continuous variables, and Mann–Whitney *U* for nonnormal continuous variables. Possible ranges in parentheses after the variable name. SSD, schizophrenia spectrum disorder; non-SSD, nonschizophrenia spectrum disorder; DLPC, dorsolateral prefrontal cortex; IQ, intelligence quotient; PAS, premorbid adjustment scale; GAF, global assessment functioning; CGI, clinical general impression; PANSS, Positive and Negative Syndrome Scale; ICV, intracranial volume; LFGM, left frontal gray matter; RFGM, right frontal gray matter; LPGM, left parietal gray matter; RPGM, right parietal gray matter; LTGM, left temporal gray matter; RTGM, right temporal gray matter; OGM, occipital gray matter; DUP, duration of untreated psychosis.

less severe in the SSD group in comparison with the non-SSD group.

Of the baseline socio-demographic variables, age, gender, and ethnicity correlated with some aspects of insight at 2 years. Parental education did not. In the whole group of patients, the older the patient, the better the insight into having a disorder, into the consequences of the disorder, into having psychotic symptoms, and their correct attribution (Spearman rho SUMD1 = −0.263, $P = .02$; SUMD2 rho = −0.211, $P = .08$; SUMD3 rho = −0.270, $P = .02$; SUMD Tot1 rho = −0.341, $P = .04$; SUMD Tot2 rho = −0.420, $P = .05$). Females had better insight into having psychotic symptoms, only in the non-SSD group (Mann–Whitney $U = 7.5$, $P = .02$), and Caucasians had better attribution of the origin of the symptoms in the whole group ($U = 9.00$, $P = .03$).

Course of Insight Over the First 2 Years of Psychosis

In the SSD group, insight into having a disorder, the need for treatment, the consequences of the disorder, and insight into psychotic symptoms all improved over the first year after the first episode (see table 2 and figure 1) with deterioration in the 2 first subscales between the first and second year. In the non-SSD group, insight into having a disorder, the need for treatment, and the consequences of the disorder also improved during the first year. After that, no further significant change was observed (see figure 2).

Long-term Insight and Socio-Demographic, Cognitive, and Clinical Correlates

At 2 years, insight into having a disorder and the consequences of the disorder were worse in the group of schizophrenia patients compared with the non-SSD patients ($U = 435.5$, $P < .01$ and $U = 449.5$, $P < .01$, respectively).

Between the first and second year of illness, no change was found in the severity of psychotic symptoms (measured by the PANSS) in any of the groups. No change was observed in general functioning. Changes in

Table 2. Insight Means Over Time

		Baseline	6 Months	1 Year	2 Years	Baseline–1 Year, Z, P	1 Year–2 Years, Z, P
SSD	SUMD1	3.38 ± 1.51 (52)	2.74 ± 1.36 (50)	2.57 ± 1.45 (46)	2.80 ± 1.48 (40)	−2.999, <.001	−2.269, .02
	SUMD2	3.23 ± 1.51 (52)	2.42 ± 1.30 (48)	2.16 ± 1.36 (43)	2.36 ± 1.51 (39)	−3.578, <.001	−1.936, .05
	SUMD3	3.52 ± 1.50 (52)	3.16 ± 1.41 (49)	2.67 ± 1.47 (45)	2.80 ± 1.50 (40)	−3.052, <.01	
	TOT1	3.26 ± 1.46 (52)	3.34 ± 1.27 (38)	3.06 ± 1.25 (29)	3.54 ± 1.02 (22)	−1.939, .05	
	TOT2	1.98 ± 1.73 (52)	2.92 ± 0.87 (26)	2.67 ± 0.75 (19)	3.13 ± 0.85 (12)		
Non-SSD	SUMD1	3.31 ± 1.54 (54)	2.00 ± 1.38 (48)	1.89 ± 1.28 (44)	1.91 ± 1.40 (34)	−3.741, <.001	
	SUMD2	2.91 ± 1.62 (54)	2.20 ± 1.45 (49)	1.90 ± 1.26 (42)	1.82 ± 1.33 (33)	−2.438, .01	
	SUMD3	3.37 ± 1.40 (54)	2.33 ± 1.42 (49)	2.16 ± 1.31 (44)	1.97 ± 1.35 (34)	−3.671, <.001	
	TOT1	2.3 ± 1.66 (54)	3.11 ± 1.50 (31)	2.41 ± 1.10 (22)	2.91 ± 1.38 (14)		
	TOT2	1.40 ± 1.39 (54)	2.43 ± 1.31 (19)	2.62 ± 1.13 (20)	2.64 ± 1.12 (11)	−2.833, <.01	

Note: Results are presented as means and SDs. Wilcoxon rank tests. Sample size in parentheses. Results < 0.1 are shown. SUMD1, general awareness of a mental disorder; SUMD2, the effects of medication on the disorder; SUMD3, general understanding of the consequences of the disorder (SUMD3); TOT1, awareness of specific psychotic symptoms; SUMD Tot2, attribution of symptoms. Abbreviations are explained in the first footnote to table 1.

psychopathological symptoms over the first year of the disorder are reported elsewhere.[6]

Table 3 shows the correlations between insight at 2 years and concurrent and 1-year psychopathological and global functioning and insight at 2 years and baseline psychopathological and individual characteristics (age, IQ, cognitive functioning, and premorbid adjustment) by group.

In SSD, concurrent severity of psychotic symptomatology positively correlated with long-term (2 year) insight (the more severe the psychotic symptoms, the worse the insight). Both concurrent and 1-year better global functioning correlated with better insight into having a mental disorder and its consequences. As in the whole group of patients, the younger the patient at baseline, the worse the insight at 2 years. Poorer baseline executive function-

ing, lower IQ, and poorer premorbid infancy adjustment correlated with poorer insight into having a disorder and its consequences, at the 2-year follow-up. Regarding insight into having symptoms of a psychotic disorder (SUMD Tot1), SSD patients had poorer insight if they had more severe concurrent total or negative psychopathology and lower baseline IQ. No correlations were found between correct attribution of symptoms and any of the variables measured.

Within the non-SSD group, some insight domains at 2 years correlated with concurrent positive and total psychopathology, better concurrent and 1-year global functioning, and better DLPC functioning (both baseline and at 2 years). Non-SSD patients had poorer insight into having symptoms of a psychotic disorder if they had poorer baseline or 2-year prefrontal cognitive functioning (DLPC
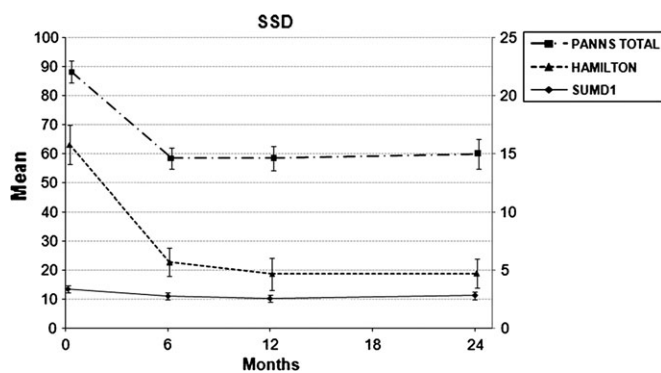

Fig. 1. Insight into Having a Disorder (Scale to Assess Unawareness of Mental Disorder [SUMD]1), Depressive Symptomatology (Hamilton Score), and Total Psychopathology (Total Positive and Negative Symptom Scale [PANSS] Score), in Schizophrenia Spectrum Disorder Patients. Mean and SE represented. Axis to the left represents the score in the PANSS. Axis to the right represents score in SUMD1 and Hamilton.
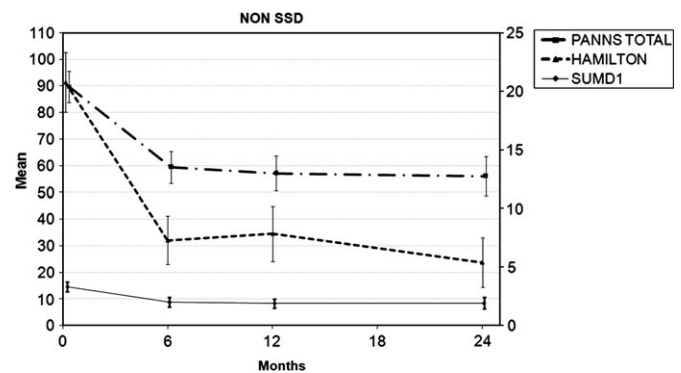

Fig. 2. Insight into Having a Disorder (Scale to Assess Unawareness of Mental Disorder [SUMD]1), Depressive Symptomatology (Hamilton Score), and Total Psychopathology (Total Positive and Negative Symptom Scale [PANSS] Score), in Non-Schizophrenia Spectrum Disorder Patients. Mean and SE represented. Axis to the left represents the score in the PANSS. Axis to the right represents score in SUMD1 and Hamilton.

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Table 3. Long-term Insight Correlations with Concurrent Psychopathology and Baseline Individual Characteristics and Psychopathology

		SSD 2 Year					Non-SSD 2 Year				
		SUMD 1	SUMD 2	SUMD 3	TOT 1	TOT 2	SUMD 1	SUMD 2	SUMD 3	TOT 1	TOT 2
2 Years	PANSS positive	0.445**	0.422**	0.544**	0.373	−0.157	0.574**	0.509**	0.530**	0.423	0.320
	PANSS negative	0.413**	0.342*	0.460**	0.528*	0.507	0.067	0.078	0.114	−0.012	0.465
	PANSS total	0.559**	0.450**	0.601**	0.668**	0.38	0.500**	0.482**	0.410*	0.352	0.444
	DLPC	0.065	0.114	−0.015	0.587*	−0.183	−0.383*	−0.483**	−0.479**	−0.792**	−0.473
	GAF	−0.433**	−0.281	−0.571**	−0.399	−0.205	−0.484**	−0.634**	−0.458**	−0.343	−0.429
1 year	PANSS positive	0.365*	0.293	0.390*	0.118	−0.015	0.328	0.236	0.224	0.175	0.440
	PANSS negative	0.388*	0.274	0.440**	0.224	−0.215	0.204	0.180	0.123	0.354	0.480
	PANSS total	0.538**	0.409*	0.595**	0.378	−0.035	0.299	0.241	0.192	0.114	0.438
	GAF	−0.386*	−0.174	−0.561**	−0.297	−0.191	−0.568**	−0.659**	−0.442**	−0.321	−0.730*
Baseline	AGE	−0.490**	−0.332*	−0.460**	−0.385	−0.165	0.072	−0.032	−0.038	−0.325	−0.723*
	DLPC	0.087	0.187	−0.018	−0.019	−0.492	−0.272	−0.364*	−0.283	−0.679**	−0.563
	Executive function	−0.383*	−0.272	−0.313*	−0.391	0.088	−0.003	−0.074	−0.051	−0.529	−0.105
	PAS infancy	0.345*	0.164	0.392*	−0.002	−0.094	0.041	0.071	0.012	0.369	0.641*
	DUP	0.411**	0.413**	0.379**	0.516**	0.374	0.296	0.354*	0.340*	−0.181	0.456
	IQ	−0.455**	−0.237	−0.467**	−0.497*	0.27	−0.095	0.002	−0.186	−0.109	−0.130

Note: Spearman correlations. *$P < .05$; **$P < .01$. SUMD, Scale to Assess Unawareness of Mental Disorder. Abbreviations are explained in the first footnote to table 1 and table 2.

measure). No correlations were found between correct attribution of symptoms and any of the variables measured.

Insight and Depression

Depressive symptoms, as measured by the Hamilton scale, improved over the first 6 months after the first episode in both groups of patients ($t = 9.83$, $P < .001$ in SSD and $t = 7.543$, $P < .001$ in non-SSD) and did not change thereafter (see figures 1 and 2). There were positive correlations between depressive symptoms and negative symptoms, in SSD at 1 and 2 years (Pearson rho = 0.463, $P = .001$ and 0.626, $P < .001$, respectively) and in non-SSD at baseline, 1 year, and 2 years (Pearson rho = 0.273, $P = .04$ and 0.598, $P < .001$ and 0.369, $P = .02$, respectively).

In SSD patients, depressive symptoms correlated with some aspects of insight at 6 months and 1 year but not at 2 years (see table 4); the higher the patient's depression score, the worse the insight. These correlations did not occur in the group of non-SSD patients. Figures 1 and 2 show the course of insight into having a mental disorder and depressive symptomatology (together with the PANSS total score) over time in the SSD and non-SSD groups.

Neuroimaging and Insight

Brain images were available for 91 patients. No significant relationship between volumetric variables and insight measures (any of the 5 domains studied) were found considering the whole group of patients. However, in SSD patients, significant partial Spearman correlations, removing the effect of age on insight and brain volumes, were observed in the GM volume of frontal and parietal lobes, bilaterally (left frontal Spearman rho = −0.575, $P < .01$; right frontal Spearman rho = −0.611, $P < .01$; left parietal Spearman rho = −0.495, $P = .03$; and right parietal Spearman rho = −0.46, $P = .04$).

Table 4. Correlations of Insight and Depressive Symptoms at Each Point in Time

	SSD					Non-SSD				
	SUMD 1	SUMD 2	SUMD 3	TOT 1	TOT 2	SUMD 1	SUMD 2	SUMD 3	TOT 1	TOT 2
Baseline Hamilton	0.164	0.341*	0.114	0.087	−0.161	0.305*	0.433**	0.219	0.147	0.028
6-month Hamilton	0.305*	0.433**	0.219	0.147	0.028	0.075	0.223	0.016	−0.311	0.075
1-year Hamilton	0.334*	0.373*	0.456**	0.336	−0.217	0.238	0.343	0.099	0.303	0.591
2-year Hamilton	0.261	0.206	0.303	0.171	0.261	0.292	0.264	0.028	−0.259	0.647

Note: Spearman correlations. *$P < .05$; **$P < .01$. Abbreviations are explained in the first footnote to table 1 and table 2.
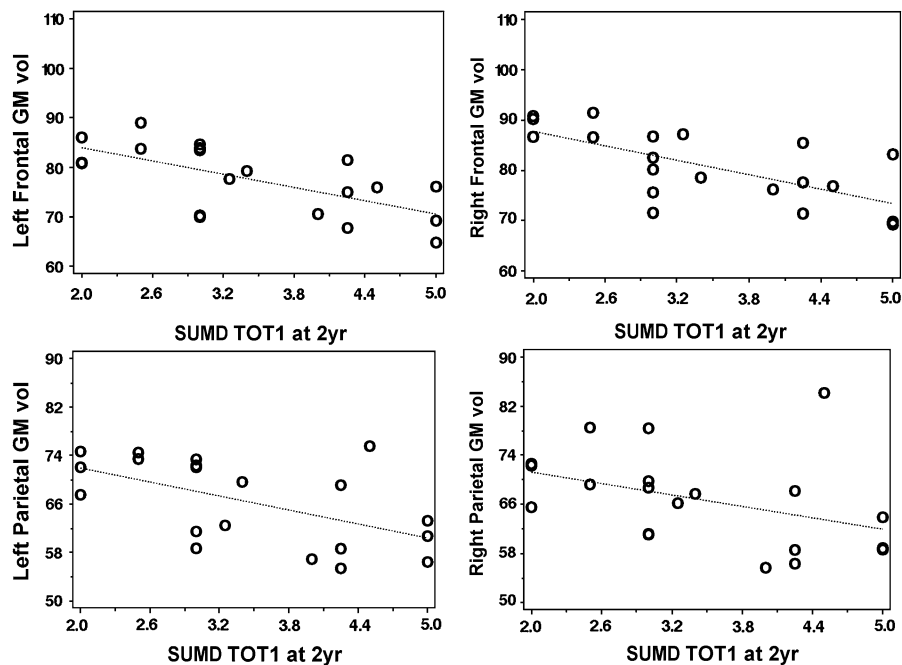
44

Fig. 3. Spearman Partial Correlations between Baseline Frontal and Parietal (Left and Right) Gray Matter (GM) and Insight into Having Psychosis Symptoms at 2 Years (SUMDTOT1).

Thus, more frontal and parietal GM at baseline was correlated with better insight into having psychotic symptoms at 2 years (see figure 3). No other aspects of insight correlated with the structural measurements.

Multivariate Analysis

Table 5 shows the explanatory variables for the different models that used different insight domains at 2 years as dependent variables.

Insight into having a mental disorder at 1 year, DUP, and IQ emerged as the most significant contributors to explain insight domains at 2 years in SSD patients. In addition, left and right parietal GM added some explanatory effect on the SUMD3 and left frontal and parietal GM on SUMDT1. In SSD patients, IQ, DUP, and SUMD1 at 1 year explained 60% of the variance of having a mental illness; these variables, together with the right and left parietal GM volume, explained 70% of the variance of insight into the consequences of illness and IQ, SUMD1 at 1 year, together with left frontal and left parietal GM volumes, explained 80% of the variance of insight into having specific psychotic symptoms. Only DUP entered in the model to explain insight into the need of treatment (17% of the variance) and only gender in the model of the correct attribution of symptoms (44% of the variance).

In non-SSD, GAF at 1 year explained part of the main insight domains. Gender explained 44% of the variance of insight into psychotic symptoms and together with PAS, and the negative score of the PANSS at 6 months explained 93% of correct attribution of symptoms. Tak-

ing the whole group of patients together, diagnosis did not contribute to explain insight at 2 years.

Discussion

In this 2-year longitudinal study of insight after a FEP occurring in adolescents, we have shown that: (1) Older age is associated with better insight at 2 years; (2) Insight at 2 years is poorer in adolescents with SDD than in subjects with non-SSD psychoses; (3) The improvement of most aspects of insight found in the initial stages of the disorder does not continue after 1 year. In fact, insight into having a mental disorder and into the need for treatment deteriorates between years 1 and 2 in SSD patients; (4) Different correlates of long-term insight were found in SSD and non-SSD patients. The more severe the psychotic symptomatology, the poorer the insight in both groups. Worse depressive symptoms were associated with poorer insight at baseline in both groups. However, depressive symptoms were associated with poorer insight after baseline only in SSD subjects (at 6 months and 1 year). In addition, age, IQ, executive functioning, and premorbid adjustment were associated with insight only in SSD group; (5) Insight at 1 year, DUP and IQ explain a moderate amount of the variance in different aspects of insight at 2 years, in SSD patients. Frontal and parietal GM volumes also contributed to explain part of the long-term insight in this group. Different clinical aspects explained part of the insight at 2 years in non-SSD, general functioning at 1 year being the most pervasive across different domains. Gender explained

Table 5. Explanatory Models in SSD and Non-SSD Patients, With Insight Domains at 2 Years as Dependent Variables

SSD	Adjusted		Standardized		Non-SSD	Adjusted		Standardized	
	R^2	F (df)	Beta	P		R^2	F	Beta	P
Insight into having a mental illness	0.598	16.894 (32)		<.001	Insight into having a mental illness	0.268	8.690 (21)		<.01
1-year SUMD1			0.608	<.001	1-year GAF			−0.550	<.01
IQ			−0.316	<.01					
DUP			−0.265	.03					
Insight into the need of treatment	0.167	7.208 (31)		.01	Insight into the need of treatment	0.501	11.041 (20)		<.01
DUP			0.440	.01	1-year GAF			−0.527	<.01
					1-year SUMD1			0.431	.01
Insight into the consequences of illness	0.694	15.540 (32)		<.001	Insight into the consequences of illness	0.415	8.458 (21)		<.01
1-year SUMD1			0.609	<.001	1-year GAF			−0.757	<.01
IQ			−0.350	<.01	6-month Hamilton			−0.434	.03
RPGM			0.594	<.01					
DUP			0.286	<.01					
LPGM			−0.376	.04					
Insight into having psychotic symptoms	0.795	15.576 (15)		<.001	Insight into having psychotic symptoms	.436	7.970 (9)		.02
IQ			−0.658	<.001	Gender			0.706	.02
1-year SUMD1			0.738	<.001					
LFGM			0.406	<.01					
LPGM			0.402	.01					
Attribution of psychotic symptoms	0.436	7.970 (9)		.02	Attribution of psychotic symptoms	0.930	31.953 (7)		<.01
Gender			0.706	.02	PAS infancy			0.769	<.01
					6-month PANSS negative			0.612	<.01
					Gender			0.385	.03

Note: Stepwise linear regression analysis. Abbreviations are explained in the first footnote to table 1 and table 2.

part of the insight into psychotic symptoms in non-SSD patients and their correct attribution in both groups.

Trait and State Attributes of Insight

The age range of the patients in the present study coincides with a stage in life important for the construction of personal identity. The impact of a psychotic episode on the attribution of mental states to others and oneself at this stage is largely unknown.[73,74] Older age, female gender, and white ethnicity were also shown to be associated with more insight in a sample of more than 250 patients experiencing their FEP.[25] In regards to gender, typically girls have been shown to have better mentalizing ability than boys[75,76] and many studies have shown the better performance of women and/or girls in phenomena, such as autobiographical memory,[77,78] which is associated with concepts like self-awareness or theory of mind, also shown to explain a substantial amount of var-

iance of insight in some studies.[79] The result that insight is poorer in SSD patients than in non-SSD patients is in agreement with the literature.[1,6,21,22,26,80] We had previously shown that insight improved over the early phases of the illness, in parallel with psychopathological improvement and that schizophrenia patients had poorer insight than patients with bipolar disorder at 6 and 12 months but not at baseline.[6] Contrary to our hypothesis, insight worsens after 1 year in the case of SSD patients. How the intensity of follow-up, presence of psychoeducational interventions, chronicity, medication, treatment adherence, and methodological issues related to the studies, such as attrition, influence the course of insight need further exploration. In any event, the fact that insight improves during the first year after the FEP, and the predictive value of insight at 1 year for insight at 2 years suggests that the first year is crucial for improving later insight and possibly general functioning (as insight correlates with general functioning at 2 years).

As shown in many other studies,[6,25,36] multiple factors contribute to insight. Positive psychotic psychopathology is a major contributor to insight, irrespective of the diagnosis. This relationship has been shown in many studies[22]. In addition, in SSD patients, insight is poorer when baseline cognitive function is worse, negative symptoms are more severe, and in patients with poorer premorbid adjustment and longer DUP. The relationship between insight and neurocognitive functioning and with negative symptoms has also been shown in adults with schizophrenia.[9,17,28,81,82] Also, better premorbid adjustment has previously been associated with better insight.[6,26,82] Poor premorbid adjustment, negative symptoms, and poor neurocognitive functioning have been classically considered intrinsic to schizophrenia and probably form part of the disorder itself. In fact, the prediction analysis shows that cognitive functioning is a better predictor of long-term insight than the diagnosis itself. The cumulative effect of moderators of poor insight in SSD patients (such as poor premorbid adjustment and negative symptoms) may explain why younger age is associated with poorer insight only in SSD patients. In addition, some of the negative results in the non-SSD group could be due to the heterogeneity of the patients included in the latter.

Depression and Insight

The relationship between depressive symptoms and insight is complex. Some authors[83,84] have not found an association between insight and depression, while others have shown an inverse relationship between depression and insight (more insight, less depression), as in this study in the SSD group. This was also shown at admission but not at discharge in a group of acutely ill patients with schizophrenia[85] and also, in a modest association, in a group of chronic patients.[86] Our group also showed such a relationship in the early stages of FEP.[87] Owen et al[88] argued that severe depressive symptomatology could be associated with lack of insight via irrationality. Most previous studies, however, have shown that better insight is associated with more depressive symptoms in first episodes.[1,12,21,22,24,25,28,37,38,63,82] (an explanation being that better insight would be secondary to the hyperrealism that frequently accompanies depressive symptoms). In fact, the meta-analysis by Mintz[22] showed positive associations between better insight and more depressive symptomatology (with small effect sizes), for all domains of insight. An association between more depressive symptoms and more insight into psychotic symptoms[7,87] has also been shown in a sample of adolescents. However, the subjects in that study were assessed soon after hospital admission (less than 1 month) and were therefore in the acute psychosis stage, while our study also explored insight when patients were stable (2 years after the first episode). In our sample, no difference was found in depressive symptoms between SSD and non-SSD, when subjects were in the acute psychosis stage (see table 1), although the SSD group scored higher on the Hamilton scale, probably because a significant number of patients in the non-SSD group were manic at baseline (there were 22 bipolars in this group, most of them manic). As shown in table 4, our results are consistent in showing higher Hamilton scores related to less insight (higher insight scores) in SSD patients. However, the scores for the Hamilton scale are low (mean 4.70 ± 4.95 for SSD, 5.39 ± 6.52 for non-SSD at 2 years),[89] and there is a possibility that scores were produced by symptoms more related to negative schizophrenia symptoms than to depression (such as apathy or lack of volition). However, a correlation was found between negative and depressive symptoms both in SSD and non-SSD while the association between poorer insight and depressive symptoms was found only in SSD. The more severe negative symptomatology in SSD could be one mediator. The possibility that cognitive dysfunction was also an intermediate mechanism was tested and discarded, as cognitive function did not correlate with depressive symptomatology. Given the discrepancies with the literature, we further assessed the temporal relationship between insight and depression, which is an aspect basically neglected in previous studies.[22] Cross-sectionally, depressive symptoms were more intense in poor insight patients at the 6-month and 1-year assessments (table 4). We also looked at the possible association between the change in insight into having a mental disorder with the change in depressive score, in the periods from 6 months to 1 year and from 1 to 2 years, and there was no such correlation.

The question about the relationship between depressive symptoms and insight in schizophrenia remains open. The nature of depressive symptoms in stable schizophrenia and how to assess them needs to be further assessed. Studies have used different instruments to study depressive symptoms in schizophrenia; some of them have used just an item from a general scale, such as the PANSS or the Brief Psychiatric Rating Scale. The complexity of the relationship between depressive symptoms and insight and the difficulty discriminating between depressive, negative, and other cognitive difficulties in patients with schizophrenia deserves a specifically targeted study. However, studies that have used the Calgary scale, specifically meant to measure depression in schizophrenia, both in acute and remission stages, have also yielded mixed results.[7]

Cognitive Functioning and Insight

Regarding cognitive function, general cognitive functioning (estimated IQ) and baseline prefrontal cognitive dysfunction were associated with poorer long-term insight in SSD patients but not in non-SSD patients. Other studies have shown concurrent associations between poorer

cognitive performance and insight,[10,25,65] but we looked for long-term associations, on the basis that cognitive functioning after a first episode mainly stays stable[90] and that insight during acute episodes is highly dependent on psychopathology.[6]

Early Predictors of Long-term Insight

In addition, the prediction analysis shows that, apart from previous insight, baseline general cognitive functioning and DUP are the best predictors of insight at 2 years, in SSD patients. These factors have been associated with insight in other studies.[25,28,36] Our study shows that estimated IQ is a consistent predictor of almost all domains of insight in SSD patients. More GM volume in frontal and parietal lobes also explain part of the different insight domains, although the contribution they make is weak or modest; this is in agreement with previous studies.[4,37] Anosognosia, which some consider to be a neurological analog of poor insight,[1,27] is associated with lesions in subcortical, parietal lobe, and temporal lobe structures, as well as with frontal lesions.[91] The strongest relationship found in the study by Cooke et al[4] was between the Awareness of Problems score and the volume of the left precuneus, located in the medial parietal lobe. Shad et al[10] propose a model in which the neurological underpinnings of insight would involve a neural network comprising subregions of prefrontal and parietal cortex mediating specific insight deficits into having psychotic symptoms and their attribution.[27]

The correlation analysis and the lack of predictive validity of diagnosis into insight at 2 years support the idea that the categorical classification of psychosis has important limitations regarding aspects of validity of diagnosis such as the prediction of outcome. Cognitive functioning and previous insight, but not diagnosis, predict long-term insight, which in turn is very much related with general functioning. These data support a dimensional view of psychosis, where insight adds to genetic and other neurobiological data in distributing itself across different psychotic diagnoses, with no further value when establishing nosological cutoffs.

Altogether, our neurocognitive and neuroimaging data support involvement of the frontal and parietal lobes. In agreement with our previous findings,[6] insight appears to be a complex symptom that, at least in schizophrenia, depends both on current psychopathological (state) and long-term individual characteristics, some of which are unrelated to the disease (age, gender, and ethnicity) and others probably partially dependent on the individual and the disorder itself (past adjustment, IQ, brain structure, and cognitive functioning). The fact that this sample is younger than most samples that have been used to assess the correlations of insight may explain part of the differences in the results, particularly regarding depressive symptoms and insight.

Limitations

The main limitations of the study are that: (1) we have not studied aspects of personality traits such as self-awareness, self-concept, autobiographical memory, adjustment abilities, or coping styles, which could also influence the development of insight after a FEP; (2) we had an attrition rate of 25% over 2 years (quite standard for this type of study); (3) we have not conducted our own factor analysis study of the cognitive measures to define an EF separated from the others, which would have been the ideal approach; we rather followed the literature (including our own studies) to create our cognitive indexes, due to space constraints and the fact that the focus is set on insight and not on cognition. The main advantages of the study sample are its early age and the longitudinal follow-up. Adolescence is a developmental period in which cognitive, personality, and brain development are still in progress. In addition to diagnosis and psychopathological status, we have been able to assess the impact on the course of insight of some individual characteristics, such as demographics, cognitive functioning, and brain maturation indicators.

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