TITLE: THE ASSOCIATION OF LIFETIME INSIGHT AND COGNITION IN PSYCHOSIS

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ABSTRACT

Poor insight has been related to poor course in psychosis. However, the role of cognition in insight remains unclear.

The aim of this study was to examine the influence of cognition and lifetime psychopathological dimensions on insight in psychosis. We followed-up 42 patients with psychotic disorders over 10 years. Lifetime psychopathological dimensions and cognitive performance were assessed. Patients were divided into two groups by lifetime patterns of insight and compared with 42 healthy volunteers.

Lower IQ and poorer social cognition were associated with higher risks of poorer lifetime insight of feeling ill and global insight respectively. Lifetime negative symptoms were associated with a higher risk of poorer lifetime insight into symptoms.

Lifetime lack of insight is independent of cognitive impairment in specific domains, except for social cognition. Higher IQ may contribute to better lifetime awareness of illness, while better ability to manage emotions is involved in lifetime global insight.

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INTRODUCTION

Patients with psychotic disorders often exhibit lack of awareness of their illness, commonly known as lack of insight. David (1990) differentiated three components of insight into psychosis: recognition that one has an illness, the ability to recognize the symptoms of the illness and the compliance with treatment.

Poor insight is associated with psychosocial dysfunction, as well as poor treatment adherence and more rehospitalizations (Amador and David, 2004). Hence, an understanding of the mechanisms of insight is necessary for improving outcomes in psychotic disorders.

Among the various different aetiological models for lack of insight in psychosis, the neuropsychological model has generated extensive research in recent years. Studies investigating lack of insight and cognition have obtained inconsistent findings. On the one hand, lack of insight has been found to have a small but significant association with cognitive functioning, especially executive functioning, memory and global cognition (Aleman et al., 2006; Nair et al., 2014), while on the other, some authors observed a non-specific relationship with general cognitive deficits (Morgan et al., 2010) or no relationship at all (Mintz et al., 2004). Most of the research on this topic has focused on executive functioning, in many cases assessed by the Wisconsin Card Sorting Test (Keshavan et al., 2004; Rossell et al., 2003; Saeedi et al., 2007), based on the idea that a failure to change cognitive set and to monitor errors may lead to impaired insight. Again, results have been inconclusive.

The purpose of this study was to examine the relationship between cognitive performance and lifetime patterns of insight over 10 years in a sample of outpatients with a diagnosis of a psychotic disorder, controlling for the lifetime psychopathological dimensions. We hypothesized that the evolution of lifetime patterns of insight would be independent of current cognitive performance.

METHODS

Sample

The sample was part of a family cohort recruited between 1999 and 2001, which included 89 nuclear families. Patients who were affected by DSM-IV schizophrenia spectrum disorders (APA, 1994) were recruited from consecutive admissions to the Psychiatric Unit of Virgen del Camino Hospital in Pamplona, Spain; the admissions were due to psychotic exacerbations. The original sample has been described elsewhere (Rosa et al., 2005; Rosa et al., 2004).

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For the present study, we selected data from the patients who agreed to participate in a second evaluation in 2009. At the follow-up evaluations, the sample population consisted of 42 patients. The reasons for patients being lost to follow-up were as follows: 7 died; 1 had traumatic brain injury; 11 moved or were not contactable; and 28 declined to participate.

As this was a naturalistic study, patients were followed-up after hospitalization in their respective mental health settings. None of them were institutionalized or followed any specific program focused on awareness of illness.

In addition, 42 healthy volunteers were included as a control group, according to the following inclusion criteria: an absence of major psychiatric disorders and drug dependence disorder, of first-degree relatives with major psychiatric illnesses, and of any current pharmacological treatments. The healthy control group was mainly recruited in a hospital located outside of Pamplona, in the trauma and neurologic rehabilitation department. Some of the controls were staff and relatives of patients. We also recruited controls through fliers in health care centers of Pamplona, at the university and word-of-mouth. Controls received a compensation of 50 euros for their participation.

All subjects provided written informed consent for participation in the study, and the local ethics committee approved the study.

Procedures

Clinical assessments

The demographic and clinical variables were assessed according to the lifetime version of the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992) at baseline and at the follow-up evaluations.

The assessment of insight was made by means of three insight items from the Manual for the Assessment and Documentation in Psychopathology (the AMDP system) (Guy and Ban, 1979). These items were lack of feeling ill (the patient denies that he/she feels ill), lack of insight (the patient is unable to recognize as morbid experiences that the doctor has judged to be due to the disease) and refusal of treatment (resistance to or refusal of various therapeutic measures). Responses were scored according to the CASH guidelines for lifetime scoring of symptoms. Lifetime insight was defined as the dominant pattern of insight over the course of illness, taking into account the course of insight in each insight dimension. Insight symptoms were surveyed to assess the current level and dominant pattern over the course of the illness at both assessments by asking whether the patient had ever experienced the symptom and, if so, ascertaining its frequency and severity. Thus, insight symptoms were endorsed for the lifetime frame at the first assessment and for the inter-evaluation period at the second one. A

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global insight score for the whole lifetime period was built by averaging the score on the three dimensions.

Clinical assessments were performed by experienced psychiatrists blind to participants' cognitive status. Both assessments were carried out when patients were clinically stabilized.

Neuropsychological assessments

A wide neuropsychological battery was applied to all patients at follow-up. The tests selected are listed in Table 1.

To normalise the different scales of measurements used for the neuropsychological tests, we calculated z-scores based on the means and standard deviations of the control group. Composite scores for cognitive domains that were represented by more than one measure (attention, processing speed, verbal memory, working memory and executive functioning) were calculated by taking the mean of all the z-scores included in each cognitive domain. Cronbach's alpha was calculated to assess the internal consistency of the composite scores.

Cognitive assessments were performed by an experienced neuropsychologist (AMS) who was blinded to the subjects' clinical status.

Data analysis

Patients were divided into two groups according to their insight lifetime profile. The demographic characteristics of these two groups were compared using t-tests and chi-squared tests. Analyses of variance (ANOVAs) were then used to compare cognitive performance at follow-up in the two groups.

Patients were also grouped according to their lifetime patterns in each insight dimension to explore the differences in cognitive performance. Bonferroni's correction for multiple comparisons was applied.

Logistic linear regression using the stepwise entry method was performed to better characterise the relationship between insight dimensions, psychopathological dimensions and cognitive performance. The selection of the psychopathological and cognitive variables to include in the regressions was made according the results of the ANOVAS, setting the threshold level at 0.05.

All analyses were conducted using the IBM SPSS Statistics for Windows version 20.0 (IBM Corp., 2011)

RESULTS

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There were no significant differences between patients who agreed (n=42) and patients who declined to participate (n=47) (Supplementary table 1). From here on the results refer to those subjects who participated in the re-evaluation in 2009 (42 patients).

The means and standard deviations of insight dimensions for the inter-evaluation period of the patients who continued in the study were as follows: 2.90±1.12 for the lack of feeling of illness dimension, 1.71±2.03 for the lack of insight dimension and 2.05±1.4 for the refusal of treatment dimension. Patients were distributed into two groups according their global insight scores. The cut-off point for separating patients by level of global insight was established at 1. Accordingly, the "no or worsened insight" (NI) group was composed of those patients who showed scores >1 in one or more of the insight dimensions, since illness onset. The "good or improved insight" (GI) group was composed of those patients who scored 0 or 1 in each insight dimension either since illness onset, or only in the inter-evaluation period, showing an improvement in their insight over time. The final composition of the groups was n=24 for the NI group and n=18 for the GI group. There were no significant differences between the socio-demographic, clinical and illness course characteristics of the two groups, except for a higher presence of negative symptoms in the NI group (Table 2).

The same procedure was used for distributing patients into each of the insight dimensions separately. The final composition of the NI and GI groups was: 36 and 6 patients respectively for the lack of feeling of illness insight dimension, 18 and 24 for the lack of insight dimension and 25 and 17 for the refusal of treatment dimension. Differences between groups in the psychopathological dimensions of the CASH are shown in Table 3.

The reliability of the neuropsychological tests was assessed by calculating Cronbach's alpha for all subscale scores, except for visual memory and social cognition (which were composed of only one measure). The Cronbach's alpha coefficients for the composite scores of the neuropsychological tests were as follows: 0.58 for the attention score, 0.49 for the processing speed score, 0.86 for the verbal memory score, 0.77 for the working memory score and 0.59 for the executive function score. All scores indicated low to moderate reliability, except for the verbal memory score.

The threshold for significance after Bonferroni's correction for multiple comparisons was set at 0.006 (0.05 divided by 8, for the 8 cognitive scores) in the ANOVAS. No differences were found between NI and GI groups in global insight in the cognitive dimensions. When analysing separately the three insight dimensions, significant differences were found in estimated IQ (p=0.005) in the lack of feeling of illness dimension, with patients with better insight outperforming those with poorer lifetime insight. Regarding the lack of insight and

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refusal of treatment dimensions, no significant differences were found between groups by level of insight (Table 4).

In addition, linear logistic regression was used to test for the predictive value of composite measures of neurocognition in the patients' lifetime insight patterns, controlling for positive, negative, disorganised, manic and depressive symptoms. P-values under 0.05 were set as the criterion for including psychopathological dimensions and cognitive domains in the regression analyses. The variables that fulfilled this criterion were: social cognition and negative symptoms for global insight; estimated IQ, executive functions and disorganised symptoms for the lack of feeling of illness dimension; and executive functions, and negative and manic symptoms for the lack of insight dimension. No cognitive domain or psychopathological dimension fulfilled the criterion to enter in the regression analyses for the refusal of treatment dimension.

The regression analysis showed that performance on the social cognition task was the only variable that increased the risk of having poor lifetime global insight in the patients (OR=2.16; 95%CI=1.17-3.98; p=0.014). Regarding insight dimensions, lower estimated IQ was related to a higher risk of having a lifetime pattern of poor insight in the lack of feeling ill dimension (OR=1.13; 95%CI=1.02-1.23; p=0.023). Finally, a higher presence of lifetime negative symptoms was related to a lower probability of having good insight in the lack of insight dimension (OR=0.48; 95%CI=0.27-0.85; p=0.011).

We recalculated Cronbach's alpha coefficients for those composite scores showing alpha values <0.6, excluding the measures that limited the internal consistency. These measures were: the CPT score for the attention domain (α=0.67), the TMT-A for the processing speed domain (α=0.88) and the TMT-B for the executive function domain (α=0.64). Then we performed all the analysis with these new domains, to assure that the internal consistency of the cognitive domains did not affect our results. Regarding the ANOVAS, patients with no/worsened insight and good/improved insight in the three insight dimensions and global insight did not show significant differences in attention and processing speed performance. Patients showed differences in the executive function domain for the lack of feeling ill (F=4.44, p=0.042) and lack of insight dimensions (F=4.21, p=0.047), that did not reach statistical significance after Bonferroni's correction. However, they were included in the logistic regression, and again the results respect of our previous analyses did not change. Therefore, as the results of the ANOVAS and the logistic regression did not change when improving the internal consistency of the attention, processing speed and executive function composite measures, we decided to report the results with the original measures, as exposed in Table 1.

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DISCUSSION

Our results showed an association between a lower IQ and a higher risk of poorer lifetime patterns in the lack of feeling ill dimension. Social cognition was found to contribute to the lifetime patterns of global insight, poorer performance in the social cognition task being related to poorer lifetime global insight. The presence of lifetime negative symptoms also played a role in lifetime insight patterns, being associated with a higher risk of having a poor ability to recognize the symptoms as pathological. None of the cognitive domains or lifetime psychopathological dimensions analysed were related to the lifetime patterns in the refusal of treatment dimension.

Lifetime patterns of insight were not associated with cognitive performance in specific domains, namely attention, processing speed, verbal and visual memory, working memory and executive functions in this sample of patients with a psychotic disorder. A trend towards significance was observed in executive functions, with patients who showed less feeling of illness and lack of insight into symptoms performing less well. However, after applying Bonferroni's correction for multiple comparisons the trend disappeared.

The relationship between cognitive impairment and insight has been examined in two meta-analyses, finding small but significant associations between lack of insight and general cognitive impairments and especially in the case of memory (Nair et al., 2014) and executive functions (Aleman et al., 2006). Aleman et al (2006) pointed out that, although the relationship between insight and cognition was significant, the predictive value of neurocognition was rather modest. Poor insight has also been related to working memory (Mutsatsa et al., 2006) and memory impairments (Keshavan et al., 2004; Wiffen et al., 2012). Some studies did not find relationships between lack of insight and specific cognitive domains (Mintz et al., 2004), while others found an association with general cognitive performance (McEvoy et al., 2006; Wiffen et al., 2012). However, it has been argued that this relationship may be a reflection of patients' difficulties in expressing insight, rather than the deficit leading directly to lack of awareness of their illness (Morgan and David, 2004).

Our results are in agreement with previous findings of our group that lack of insight and cognitive performance in specific domains were not associated in patients with psychosis (Cuesta et al., 2006). However, considering that there was no association with specific cognitive domains, we found a striking association between lower IQ and poorer lifetime patterns in the lack of feeling ill dimension. Green et al (2000) proposed that high cognitive ability leads to good insight, although it is not a sufficient condition. They argued that some aspects of insight, particularly in terms of relabelling of symptoms, seem to require a certain

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level of neuropsychological functioning. A possible explanation for the association of higher IQ and better insight may be provided by the cognitive reserve hypothesis, which proposes that those with higher premorbid intellectual function are more able to cope with the impact of neural insult, either because of higher brain structural reserve or because of better functional capacity to use compensatory forms of neural processing (Stern, 2002). Here we assessed current, not premorbid, estimated IQ; however, we assume that a current high IQ is also an indicator of a high premorbid IQ. Barnett et al (2006) have proposed that in schizophrenia, better cognitive reserve may moderate the impact of psychosis in patients' lives. It is related to fewer psychotic symptoms because of superior reasoning skills or the ability to inhibit the abnormal neural processing that mediates psychotic symptoms. Thus, higher cognitive reserve may lead to better acceptance and understanding of the illness due to a greater ability to discern between normal and pathological phenomena. However, these results should be interpreted with caution, given the unbalanced sample distribution in the lack of feeling ill dimension.

Even though social cognition and neurocognition are partially overlapped constructs, we found an independent contribution of social cognition to insight in our patient sample. Indeed, this finding is consistent with the idea that social cognition and neurocognition are separate constructs although they are related (Sergi et al., 2007). Previous research has also found a significant association between insight and social cognition (Quee et al., 2011). Social cognition is not a unitary construct; it implies emotion processing, social perception, theory of mind and attribution bias. Our findings suggest that the ability to manage emotions plays a role in patients' appraisal of their psychiatric condition and awareness of illness. The role of social cognition in insight may be due to patients' difficulty in adopting others' mental perspectives, which may contribute to a lower awareness of illness independently of their general cognitive status (Quee et al., 2011). Since we used the "Managing emotions" part of the MSCEIT to assess social cognition, our results concerning this domain must be circumscribed to the ability to perform tasks involving emotions and solving emotional problems.

Further, the assessment of social and emotional skills is not exempt of the influence of personality traits, which may moderate the relationship with insight in our results. Indeed, previous research of our group demonstrated an association of poor insight with antisocial and schizoid personality traits (Campos et al., 2011). Regarding social cognition, a moderate positive association has been described between the managing emotions branch of the MSCEIT and agreeableness and conscientiousness personality traits, and a negative association

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with openness to experience. However, the MSCEIT has demonstrated discriminant validity in relation to well-studied personality traits (Lopes et al., 2004).

The disparity of findings in the study of insight and cognition may be partly due to the variability in the assessment methods (Cuesta et al., 2006; Chan et al., 2012; Drake and Lewis, 2003; Keshavan et al., 2004; Quee et al., 2011), the heterogeneity of patient samples (Amador et al., 1994; David et al., 1995; McEvoy et al., 2006; Parellada et al., 2009) and differences in study designs, with most studies being cross-sectional, which limits the scope of their results because of the state-dependent nature of insight. Thus, longitudinal studies are preferable for examining the associations between insight and cognition (Cuesta et al., 2011; Mintz et al., 2004; Parellada et al., 2011).

Our current results add evidence to the view that lack of insight is an independent manifestation of psychotic illness, and not a consequence of impaired cognitive functioning in specific domains. To our knowledge, this is the first study that assesses lifetime patterns of insight and their relationship with cognitive performance with such a long follow-up period (nearly 10 years). This particularity of our study may explain the differences between our results and those of cross-sectional studies (Aleman et al., 2006) and longitudinal studies with shorter follow-up periods (Parellada et al., 2011). Insight is a dynamic phenomenon which can change over time and is state-related, while cognitive impairment has been shown to be present before illness onset and to remain stable after illness onset (Rodriguez-Sanchez et al., 2013). Thus, the relationships between cognition and insight may be confounded if the assessment is made in the early phases or even in the first years of the psychotic illness. Nevertheless, it could be argued that the time interval between the two assessments was too long, meaning that insight between assessments could have followed different trajectories, and not necessarily a continuous one. However, we assessed insight retrospectively to obtain the lifetime predominant patterns of insight, appealing to the trait-like properties of insight and not only the awareness of illness at the current moment.

Limitations

The lengthy follow-up period resulted in high attrition rates, which limited the sample size and therefore the significance of our results. The heterogeneity in the diagnosis of the sample, due to the naturalistic recruitment at baseline, also represents a limitation.

Lifetime estimates of insight covered between 15 and 20 years of the illness but not the whole process of the illness, since our patients had a mean age of less than 40 years. However, most symptomatic changes in psychotic illness occur in the first decades after onset and usually symptom changes and degree of severity gradually decrease or stabilise over the long term (Lang et al., 2013).

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Here we report an association between impaired social cognition and lack of insight. Caution is warranted when interpreting our results concerning social cognition, because the assessment of social cognition was not made by means of objective performance tests, unlike other cognitive domains such as attention or processing speed. The MSCEIT is a self-report questionnaire that intends to assess emotional skills through the evaluation of possible actions in interpersonal situations. Therefore, it is a performance-based measure but the responses may be mediated by personality traits or social knowledge. In fact, there may be differences between what patients' think is the best action in a hypothetical situation and the way they act in a real situation. In addition, we only assessed the managing emotion branch, which implies the ability to regulate emotions in oneself and in others. Thus, further investigation is needed in other areas of social cognition, such as metacognition and emotion processing.

Although in this work we focused on cognitive performance and psychotic symptoms, there are other factors, such as personality traits, that have demonstrated an association with the trait features of insight (Campos et al., 2011) and may play a role in the course of illness. Indeed, our group reported that better premorbid adjustment, fewer personality disturbances, shorter DUP, fewer psychotic symptoms and better cognitive performance were related to insight improvement at 6-months follow-up after a first episode of psychosis (Cuesta et al., 2011).

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Conflict of interests

None.

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Contributors

Manuel J. Cuesta and Victor Peralta designed the study and supervised the draft completion. Ana M. Sánchez-Torres and Amalia Zarzuela collected the cognitive data, managed the literature searches and contributed to data analysis. Ana Sánchez-Torres wrote the first draft of the manuscript. All authors contributed to and approved the final draft of the paper.

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Table(s)

Table 1. Neuropsychological tests.

Cognitive domain	Type of test	Measures used for domain summary scores
Attention	Continuous Performance Test-Identical Pairs (CPT-IP) (Cornblatt et al., 1988; Nuechterlein, 2006)	Mean response sensitivity (D-prime).
	Digit Span Test –Forward (Wechsler Adult Intelligence Scale-III) (Wechsler, 1999)	Total number of series correctly repeated.
	Spatial Span-Forward (Wechsler Memory Scale-III) (Wechsler, 1998)	Total number of series correctly performed.
Processing Speed	Digit Symbol Coding (WAIS-III)	Total scale score of the coding part of the test.
	Symbol Search (WAIS-III)	Total scale score
	Trail Making Test (Form A) (Reitan and Wolfson, 1993)	Time to complete form A
Verbal Memory	California Verbal Learning Test, Spanish version (TAVEC) (Benedet and Alejandre, 1998)	Total number of words recalled at immediate, delayed and recognition trials.
Visual Memory	Brief Visual Memory Test-Revised (BVMT-R) (Benedict, 1997)	Total T score
Working Memory	Digit Span Test-Backward (WAIS-III)	Total backward score
	Spatial Span Test-Backward (WMS-III)	Total backward score
	Letter-Number Sequencing (WAIS-III)	Total scale score
	N-Back task (Braver et al., 1997)	Total number of errors
Executive Functions	Wisconsin Card Sorting Test, (WCST-128-CV) (Heaton, 1993)	Number of completed categories, total correct responses and perseverative errors.
	Iowa Gambling Task (Bechara, 1992)	Total T score
	Tower of Hanoi test (four discs)	Number of movements to complete the task
	Semantic fluency (Peña-Casanova, 1990)	Number of animal names produced in 1 minute
	Phonological fluency (Peña-Casanova, 1990)	Number of words beginning with “P” produced in 1 minute
	Hayling Sentence Completion test (Burgess and Shallice, 1997)	Total score
	Trail Making Test (form B) (Reitan and Wolfson, 1993)	Time to complete form B
	Similarities subtest (WAIS-III)	Total scale score
Social cognition	Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) (Mayer et al., 2009): Managing emotions branch, which is composed of the “Emotion management” and “Social management” tasks	Total T score of the “Managing emotions” branch
Estimated IQ	Vocabulary, Block design and Similarities (WAIS-III), based on the proposal of Sattler (Sattler, 2001).	

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Table 2. Socio-demographic and clinical characteristics of patients according their insight lifetime patterns.

	No/worsened lifetime insight n=24	**Good/Improved lifetime insight n=18**	**Sig.**
Age: mean (s.d.)	37.25(5.27)	36.72 (5.48)	t=0.32 (p=0.754)
Years of education: mean (s.d.)	11.83 (4.59)	12.22 (2.8)	t=-0.32 (p=0.753)
Gender (male/female)	20/4	10/8	z=-1.95 (p=0.051)
Estimated IQ	100 (11.53)	99.11 (14.16)	t= 0.22 (0.824)
Age at illness onset	23 (5.4)	20.61 (5.64)	t=1.39 (p=0.171)
Years since illness onset	14.33 (5.08)	16.06 (5.95)	t=-1.01 (p=0.318)
Hospitalizations	8.75 (12.29)	5.50 (4.48)	t=1.07 (p=0.292)
Course of illness: n (%)			
Episodic with total remission	3 (12.5)	3 (16.7)	X^2=3.1 (p=0.377)
Episodic with stable impairment	11 (45.8)	7 (38.9)	
Episodic with gradual decline	9 (41.7)	6 (33.3)	
Chronic	0	2 (11.1)	
DSM-IV Diagnoses: n (%)			
Schizophrenia	15 (62.5%)	8 (44.4%)	z=-1.53 (p=0.125)
Schizoaffective disorder	7(29.2%)	4 (22.2%)	
Psychotic mood disorder	2 (8.4%)	5 (27.8%)	
Brief psychotic disorder	0 (0%)	1 (5.6%)	
Lifetime psychotic symptoms (CASH)			
Positive	2.68 (1.27)	2.44 (0.97)	F= 0.46 (p=0.502)
Negative	2.77 (1.4)	1.88 (1.26)	**F=4.58 (p=0.039)***
Disorganised	1.45 (0.97)	1.51 (0.92)	F=0.05 (p=0.824)
Mania	0.75 (1.19)	1.44 (1.25)	F=3.37 (p=0.074)
Depression	2.08 (1.61)	2.28 (1.18)	F=0.19 (p=0.668)

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Table 3. Lifetime psychopathological dimensions scores in the three insight dimensions.

	Lack of feeling ill			*Lack of insight*			*Refusal of treatment*		
	No/worsened insight (n=36)	**Good/Improved insight (n=6)**	***p value***	**No/worsened insight (n=18)**	**Good/Improved insight (n=24)**	***p value***	**No/worsened insight (n=25)**	**Good/Improved insight (n=17)**	***p value***
CASH lifetime assessment									
Positive	2.63 (1.17)	2.33 (1.03)	0.569	2.97 (1.32)	2.29 (0.91)	0.055	2.66 (1.08)	2.47 (1.26)	0.604
Negative	2.54 (1.37)	1.46 (1.29)	0.579	3.01 (1.39)	1.92 (1.24)	**0.010**	2.48 (1.39)	2.25 (1.45)	0.607
Disorganised	1.6 (0.93)	0.71 (0.51)	**0.005**	1.47 (0.96)	1.48 (0.94)	0.981	1.63 (0.91)	1.25 (0.96)	0.201
Mania	1 (1.22)	1.33 (1.51)	0.551	1.22 (1.5)	1.04 (0.44)	**0.005**	1.32 (1.28)	0.65 (1.11)	0.086
Depression	2.19 (1.41)	2 (1.67)	0.762	2.17 (1.69)	2.17 (1.24)	1	2.24 (1.45)	2.06 (1.43)	0.692

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Table 4. Means and standard deviations of the z-scores in the cognitive domains. ANOVAS for global lifetime insight and the three insight dimensions.

	Global insight			***Lack of feeling ill***			***Lack of insight***			***Refusal of treatment***		
	No insight (n=24)	**Good/Improved insight (n=18)**	***p value***	**No/worsened insight (n=36)**	**Good/Improved insight (n=6)**	***p value***	**No/worsened insight (n=18)**	**Good/Improved insight (n=24)**	***p value***	**No/worsened insight (n=25)**	**Good/Improved insight (n=17)**	***p value***
Estimated IQ	100 (11.53)	99.11 (14.16)	0.824	97.47 (11.25)	112.50 (13.26)	**0.005***	97.89 (12.49)	100.92 (12.73)	0.446	98.68 (11.6)	101 (14.12)	0.563
Attention	-1.25 (1.96)	-1.46 (1.10)	0.693	-1.41 (1.7)	-0.94 (1.2)	0.522	-1.77 (1.77)	-1.02 (1.48)	0.144	-1.46 (1.72)	-1.17 (1.54)	0.585
Processing speed	-1.51(1.43)	-1.72 (1.25)	0.608	-1.72 (1.35)	-0.88 (1.17)	0.160	-1.77 (1.63)	-1.47 (1.11)	0.476	-1.78 (1.29)	-1.33 (1.42)	0.298
Verbal memory	-0.8 (1.08)	-1.06 (1.28)	0.483	-0.97 (1.12)	-0.54 (1.43)	0.405	-1.05 (1.12)	-0.8 (1.21)	0.502	-0.93 (1.06)	-0.88 (1.34)	0.910
Visual memory	-1.24 (1.51)	-1.52 (1.53)	0.552	-1.41 (1.46)	-1.08 (1.87)	0.629	-1.75 (1.64)	-1.07 (1.35)	0.144	-1.6 (1.59)	-1 (1.33)	0.208
Working memory	-0.12 (0.44)	-0.06 (0.52)	0.672	-0.15 (0.48)	0.23 (0.33)	0.069	-0.21 (0.47)	-0.01 (0.47)	0.182	-0.2 (0.49)	0.07 (0.41)	0.071
Executive functions	-1.23 (1.06)	-0.79 (0.83)	0.165	-1.16 (0.92)	-0.26 (0.98)	0.034	-1.45 (1.08)	-0.73 (0.79)	0.021	-1.22 (0.92)	-0.74 (1.01)	0.125
Social cognition	-1.21 (1.05)	-0.22 (1.24)	0.008	-0.93 (1.19)	0.05 (1.15)	0.070	-0.98 (1.06)	-0.64 (1.33)	0.380	-0.86 (1.26)	-0.68 (1.19)	0.659

* Significant after applying multiple comparisons Bonferroni correction ($p<0.006$)

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