Research Article

Investigating the contribution of decision making, cognitive insight and Theory of Mind in insight in schizophrenia. A cross-sectional study.

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Abstract

Introduction:

Insight in schizophrenia spectrum disorders (SSD) is associated with outcomes. Although the neurocognitive basis of insight is widely-accepted, the specific contribution of decision making (Jumping to Conclusions (JTC)), Cognitive Insight (CI) and Theory of Mind (ToM) to insight remains unclear.

Methods:

Sample: N=77 SSD outpatients age 18-64 years from a randomised controlled trial of metacognitive training. Assessments: JTC-Beads Task, CI-Beck Cognitive Insight Scale; ToM-Hinting Task and the Emotions Recognition Test Faces. Statistics: Hierarchical multivariable linear regression models tested their contribution to total insight (TI) and three insight dimensions - illness recognition (IR), symptom relabelling (SR) and treatment compliance (TC) - measured with the Schedule for the Assessment of Insight–Expanded version, whilst adjusting for potential confounders.

Results:

Bivariate analyses: CI was associated with TI (R^2 change = 0.214; $P < .001$), IR (R^2 change = 0.154; $P = .003$) and SR (R^2 change = 0.168; $P = .003$), while JTC predicted IR (R^2 change = 0.790; $P = .020$). Multivariable regression models: CI predicted TI (R^2 change = 0.116; $P = .036$) and SR (R^2 change = 0.166, $P = .011$), whereas JTC was linked with IR (R^2 change = 0.710; $P = 0.026$). ToM was not linked with any insight score. No cognitive variable was associated with treatment compliance.

Discussion:

Results supported the (meta)cognitive model of insight in SSD. JTC and CI emerged as the main (meta)cognitive processes underlying insight. Metacognitive interventions may therefore improve insight in SSD, although these therapies alone may fail to address treatment compliance.

Introduction

Schizophrenia spectrum disorders (SSD) are common, with a recently estimated incidence of approximately 21.4/100,000 person-years in Europe [1]. SSD remain associated with significant disability, worse quality of life and higher mortality rates compared with the general population [2].

In 1934 Aubrey Lewis defined (clinical) *insight* as *'a correct attitude to morbid change in oneself'* [3], but insight in SSD has become an area of growing research interest since the multidimensional model of insight was proposed by David in 1990 [4]. Clinical insight (thereafter, insight) encompasses awareness of illness, the capacity to relabel psychotic experiences as abnormal, and awareness of the need for treatment (hereinafter 'treatment compliance'), and this multidimensional model of insight, in which cognitive insight (explained below) is not included, has been supported by research [5]. Of relevance, impaired insight, which can affect up to 45% of subjects 3 years after first presentation with psychosis [6], has been consistently linked with poor clinical outcomes [7], including functional outcome in early psychosis [8]. However, there is no evidence-based treatment for impaired insight [9,10], which is discussed further below, which is likely to contribute to the low rates of recovery in psychosis [11]. Hence, this is a matter of major relevance to patients and clinicians. More specifically, tailoring interventions for improving insight in SSD is likely to require a better understanding of what underlies poor insight, which forms the context for this study. Thus, a previous systematic review [10] and a meta-analysis [9] reported small effect sizes of treatments on insight changes in SSD and a reanalysis of data from the European First-Episode Schizophrenia Trial (EUFEST) [12] showed that, although all trialled antipsychotics - haloperidol, amisulpride, olanzapine, quetiapine and ziprasidone- improved insight at a similar effect size except quetiapine, this effect was significantly more pronounced at 3 months. Twelve randomised controlled trials testing metacognitive interventions, which were meta-analysed, revealed more positive results [13], consistent with the proposed *metacognitive* basis of insight [5,14,15]. Hence, a better understanding of the specific determinants of insight in SSD may lead to potential treatment targets for enhancing insight.

Thus, impaired insight in SSD was first viewed as a denial mechanism, that is, being protective and preserving self-esteem [16]. Other groups, however, considered poor insight as a primary symptom of the disorder [17]. Two later meta-analyses supported the neurocognitive theory of insight in schizophrenia [18] and also, in other psychoses [15], although the associations of insight with measures of *general* cognition in both meta-analyses were relatively weak. Alternatively, insight in SSD may be more strongly linked with

more *specific* cognitive tests/tasks, particularly those evaluating reasoning, probabilistic inference and *metacognitive* skills.

In keeping with this, *Jumping to Conclusions* (JTC), i.e., drawing a conclusion on the basis of incomplete evidence, a style of decision making, was reported to be more frequent in patients with psychotic disorders than in healthy controls [19–21]. JTC was associated with delusion severity and neuropsychological functioning in first-episode psychosis (FEP) [19], including the persistence of delusions at one-year follow-up [22]. Although it is intuitive to consider that JTC deficits may be associated with impaired insight in psychosis, to our knowledge no previous studies have examined this.

Metacognition was first defined by Flavell as *'knowledge and cognition about cognitive phenomena'* [23]. Compared with healthy controls, those suffering from SSD were demonstrated to have poorer metacognitive performance [24,25]. In particular, two core metacognitive domains should be considered, namely Cognitive Insight and mentalizing, also known as Theory of Mind. C*ognitive insight* refers to the person's ability to evaluate and correct his/her own distorted beliefs and misinterpretations (self-reflectiveness) and the tendency to overconfidence in one's conclusions (self-certainty) [24]. Of note, the relationship between clinical and cognitive insight seems to be weaker than previously thought [26], which is intriguing. Moreover, two earlier FEP cohort studies from our group showed cognitive, but not clinical, insight to be associated with more severe psychopathology at 1- [27] and at 4-year follow-up [8]. Interestingly, neither clinical nor cognitive insight predicted functional outcome at 1- [27] or 4-year follow-up [8]. *Theory of Mind* (ToM) can be defined as 'the ability to attribute mental states — beliefs, intents, desires, emotions and knowledge — primarily to others' [28], was reported to be impaired in patients with psychosis from first presentation [29]. Although the influence of broadly-defined metacognition on insight is well-accepted [14], the potential link between quantifiable ToM deficits and lack of insight in SSD remains to be established.

We aimed to investigate the specific contribution of JTC, Cognitive Insight and ToM to clinical insight, that is, global insight and three insight dimensions (illness awareness, symptom relabelling and treatment compliance), in a sample of outpatients with SSD, whilst adjusting for potential confounders, including measures of general cognition. In particular, two hypotheses were to be tested: i) that JTC, Cognitive Insight and ToM will be linked with all insight dimensions (unadjusted analyses); and ii) that (based on observational follow-up studies) after controlling for confounders, the strength of the association between Cognitive Insight and Insight dimensions will be stronger than that of JTC or ToM with Insight scores, i.e., Cognitive Insight will explain the highest percentage of the variance on insight scores in

the regression models. Hence, this study was not exploratory in nature since previous extensive research on 'insight and (meta)cognition' detailed above led us to formulation of these hypotheses, which, as a result, were not preregistered.

Materials and Methods

Sample

Participants came from an ongoing randomised controlled trial (RCT) of metacognitive training (MCT) [30], which has been carried out at the Hospital Universitario Fundación Jiménez Díaz (Madrid, Spain) since June 2019. Recruitment therefore began at the same time as MCT was first delivered in the hospital. However, it is worth noting that the therapists who run MCT sessions (VGRR and ASEM) had received training from one of the co-authors of the Spanish version of the MCT manual (http://www.uke.de/mkt) (MLB), who was also involved in this research project [30]. Hence, MCT was not novel to staff or researchers at the study inception.

Briefly, those outpatients (age 18-64 years) with a confirmed diagnosis of SSD based on the Mini International Neuropsychiatric Interview, 5th Edition (MINI) [31], were invited to participate in the RCT. Specifically, ICD-10 [32] SSD diagnoses included Schizophrenia (F20), Schizotypal Disorder (F21), Delusional Disorder (F22), Brief Psychotic Disorder (F23), Schizoaffective Disorder (F25), Other Psychotic Disorder (F28) and Psychotic Disorder Not Otherwise Specified (F29). Recruitment began on the 06/17/2019 and had to be stopped on the 03/11/2020 due to the COVID-19 outbreak in Spain. Exclusion criteria were: i) IQ≤70, which was assessed with the short form of the Wechsler Adults Intelligence Scale (WAIS)-IV [33], ii) a history of head injury and/or a neurological condition; iii) having received a metacognitive intervention within the previous year; iv) low level of Spanish; v) lack of cooperativeness for participating in the intervention groups detailed below, as judged by the treating consultant psychiatrist or psychologist. Participants provided written informed consent as approved by the Local Research Ethics Committee of Instituto de Investigacinoes Sanitarias Fundación Jiménez Díaz (Madrid, Spain) (EC044-19_FJD-HRJC) in accordance with the 1964 World Medical Association Declaration of Helsinki (and further amendments). The RCT is registered at ClinicalTrials.gov (NCT04104347).

Although patients were assessed at three timepoints over the trial period, for this study we only considered baseline data collected at first assessment. Of note, we did not intend to examine insight changes over time related to MCT and what factors predicted this response, which, although of major relevance, is a different research question, that is, a different study. Rather, we aimed to better understand the extent to which JTC, CI and ToM

may contribute to insight in real-world patients with SSD, i.e., in naturalistic conditions, which is what really matters for clinicians.

Variables

Outcome measures - Insight

Insight (i.e., clinical insight) was the main outcome measure and evaluated by a research psychiatrist with the Spanish version [34] of the *Schedule for Assessment of Insight* (SAI-E) [35]. The SAI-E provides scores on three insight dimensions - illness recognition, symptoms relabelling and treatment compliance - which can be summed up to create a total insight score. Higher scores indicate greater insight. Good to excellent inter-rater reliability was reported, with total insight scores intra-class correlations coefficients ranging from 0.92 to 0.98 ($p<0.001$) [36].

As alluded to above, 'treatment compliance' does not refer to degree of compliance with a specific treatment, so compliance (as such) was not measured. Rather, 'treatment compliance' refers to a SAI-E score rating the extent to which subjects were aware of the need for treatment, including pharmacological and non-pharmacological interventions.

Jumping to Conclusions (JTC)

JTC was measured with a computerised version of the *Beads Task* [37]. On the basis of probability (in task 1 the probability of beads being blue:red is 85:15, while in task 2 the probability is 60:40), the individual must decide the jar to which the extracted bead belongs. JTC was rated if a decision was made after extracting one or two beads. This dichotomic measure of JTC as present/absent based on the 'two or less draw to decision threshold' was found to be most reliably associated with delusions [20] and widely used in previous early onset psychosis studies [8,19,38]. In addition, this dichotomous approach to JTC as 'absent or present' parallels routine clinical practice, in which continuous mental symptoms and behaviours tend to be classified as 'normal or abnormal'. This being said, prior studies considered JTC as a continuous variable, i.e., "draws to decision" [39,40]. Therefore, more theoretical debate and further investigation are required to elucidate this issue.

Cognitive Insight

Cognitive insight was assessed by a research psychiatrist using the *Beck Cognitive Insight Scale* (BCIS) [24], Spanish version [41]. The BCIS takes the form of a 15-item self-rated scale which yields two factors, namely self-reflectiveness (9 items) and self-certainty (6 items). An overall measure of cognitive insight - Composite Index - can be calculated by

subtracting self-certainty from self-reflectiveness. Higher self-reflectiveness, lower self-certainty and higher Composite Index scores indicate better cognitive insight. Internal consistency was reported to be acceptable (α = 0.60 - 0.68) [42].

Theory of Mind

Theory of Mind (ToM) was measured with the *Hinting Task* [43], Spanish short (i.e., scores ranging from 0 to 4) version [44], which was found to have good internal consistency (α = 0.64) [42], and the *Emotions Recognition Test Faces* activity (ERTF) [45], which is composed of 20 different photographs showing people's emotions. We used the Spanish version of the ERTF, which was reported to have good internal consistency (α = 0.75) [46]. Higher scores on each scale indicate better ToM performance.

Measures of General Cognition

- The vocabulary subtest of the Wechsler Adults Intelligence Scale (WAIS)-IV [33] estimated participants' IQ, which was found ot have good to excellent internal consistency (α = 0.80 - 0.91) [47]. The anticipated 'chronicity' of the sample, the lenghty set of assessments and the fact that IQ was not the primary outcome or the main independent variable of this study led us to shortening the general cognition assessment by only administering the WAIS-IV vocabulary subtest. In addition, it should be noted that executive dysfunction, which was more specifically measured (see below), is more commonly impaired in schizophrenia patients than in the general cognition [48].
- The Trail Making Test (TMT) [49] assessed executive function. Specifically, time to complete task A (in seconds) was subtracted from time to complete task B, thus providing an overall measure of executive function (set shifting), whilst controlling for processing speed [48].

Additional variables

Three demographic variables were recorded: age, gender and education level. We also collected data on ICD-10 diagnosis based on the MINI, previous suicidal behaviour (present/absent), illness duration and number of previous admissions.

Premorbid adjustment was retrospectively rated with the Premorbid Adjustment Scale (PAS) [50]. Specifically, the PAS provides scores on the level of adjustment over i) childhood (to age 11), ii) early adolescence (age 11 - 15) and iii) late adolescence (age 15 - 17) by inquiring about sociability and social withdrawal, peer relationships, scholastic performance, adaptation to school and ability to form socio-sexual relationships. Higher scores indicate

poorer premorbid adjustment. Specifically, the Spanish version, with a Cronbach's alpha of 0.85, hence internally consistent, was utilised [51].

The Spanish version [52] of the Positive and Negative Syndrome Scale (PANSS) [53] assessed symptoms severity. Overall, the α coefficients for the Positive and Negative Scales were 0.73 and 0.83, respectively, ($p < .001$), which indicates good to excellent internal consistency [53]. Five symptomatic dimensions, namely positive, negative, disorganization, mania and depression, were considered based on a previous consensus of PANSS factor analysis studies [54].

Statistics

First, exploratory analyses investigated the association of insight scores with socio-demographic, premorbid adjustment, clinical, general cognition measures, psychopathological and the aforementioned cognitive tests of interest: JTC, Cognitive Insight and ToM. Correction for multiple-testing was not applied since these analyses formed the basis for 'multivariable' regression models, thus adjusting for a potential Type I Error. Second, we conducted two series of four multivariable linear regression models to test the influence of the above three variables of interest - JTC, Cognitive Insight and ToM - on total insight and three insight dimensions. JTC, Cognitive Insight and ToM were entered into the first series of models as independent blocks, thus testing hypothesis i. Then, in order to test hypothesis ii all the potential confounders, including two measures of general cognition (IQ and executive function, i.e., TMT B-A) were added to the hierarchical multivariable linear regression models as blocks (enter method) as follows: 1) Socio-demographic variables (age, gender, education level); 2) premorbid adjustment (Childhood, early adolescence and late adolescence scores); 3) clinical variables (diagnosis, suicidal behaviour, illness duration, previous admissions); 4) psychopathological symptoms (PANSS factors: positive, negative, disorganisation, mania and depression); 5) neurocognition (IQ and TMT B-A); 6) JTC (JTC_85:15 and JTC_60:40); 7) Cognitive Insight (BCIS-self-reflectiveness and BCIS-self-certainty); and 8) ToM (Hinting Task and ERTF scores). JTC, Cognitive Insight and ToM were entered into the model as independent blocks (6, 7 and 8) in order to precisely measure the strength of the association between each of them and insight scores, which were normally distributed, so linear regression was deemed acceptable. The assumptions of normality, linearity and multi-collinearity were not violated.

The percentage of the variance on insight scores explained by each model and the contribution of each independent block to the model were investigated, with a significance level set at $\alpha = 5\%$ (two-tailed). All the analyses were performed using the Statistical Package for Social Science version 25.0 (SPSS Inc., Chicago, IL, USA).

Results

Sample characteristics

The socio-demographic and clinical characteristics of the sample (N = 77), including psychopathological, insight-related, general cognition measures, JTC, Cognitive Insight and ToM scores, are shown in Table 1.

Insert Table 1 here

Bivariate relationships between insight and tested variables

Table 2 presents the relationship between insight scores and all the aforementioned variables. Total insight scores means (14.38 vs. 16.97; $P < 0.05$) and illness recognition scores means (4.62 vs. 6.24; $P < .01$) were lower in those with JTC than in those without JTC. BCIS-SR and BCIS-CI correlated with total insight ($r = 0.476$ and $r = 0.456$, respectively), illness recognition ($r = 0.445$ and $r = 0.414$, respectively) and symptoms relabelling ($r = 0.376$ and $r = 0.345$, respectively), all of which reached significance at $P < .01$. ToM was not significantly associated with global insight or any insight dimension. Further associations of insight scores with other cognitive variables are detailed in Table 2.

Insert Table 2 here

Contribution of JTC, Cognitive Insight and ToM to insight

Table 3, below, shows the first series of multivariable regression models, i.e., only JTC, Cognitive Insight and ToM were included as independent variables, while Table 4 summarises the hierarchical multivariable regression models by adding all the tested variables to such models.

Insert Table 3 here

Insert Table 4 here

Total insight

JTC (R^2 change = 0.049; $P = .069$), Cognitive Insight (R^2 change = 0.214; $P < .001$) and ToM (R^2 change = 0.061; $P = .069$) contributed to total insight and this model accounted for 32.4% of the variance ($P < .001$) on total insight (Table 3). When adding all the potential confounders (Table 4), the model, although statistically non-significant ($P = .249$), explained 20.0% of the variance on total insight. Only the association of total insight with Cognitive Insight reached significance (R^2 change = 0.116; $P = .036$).

Illness Recognition

JTC (R^2 change = 0.079; *P* = .020), Cognitive Insight (R^2 change = 0.154; *P* = .003) and ToM (R^2 change = 0.039; *P* = .669) were related to illness recognition and this model explained 23.3% of the variance on illness recognition (*P* = .001) (Table 3). When entering potential confounders, the model (Table 4) was significant (*P* = .043) and accounted for 43.3% of the variance on illness recognition, although JTC was the only significant predictor of illness recognition (R^2 change = 0.071, *P* = .026).

Symptoms Relabelling

JTC (R^2 change = 0.006; *P* = .545), cognitive insight (R^2 change = 0.168; *P* = .003) and ToM (R^2 change = 0.049, *P* =.150) explained 16.8% of the variance on symptom relabelling (*P* = .007) (Table 3). The hierarchical multivariable linear regression model (Table 4), including all the potential confounders, accounted for 16.6% of the variance on symptoms relabelling (*P* = .271). Cognitive Insight (R^2 change = 0.166, *P* = .011) was the only significant predictor of symptoms relabelling.

Compliance

No variable, including the general cognitive tests, was significantly associated with treatment compliance (see Table 3) other than the symptom of mania (Table 2) (*r* = -0.28, *P* < .05).

Discussion/Conclusion

Principal Findings

We investigated the specific contribution of decision making (Jumping to Conclusions (JTC)), Cognitive Insight and Theory of Mind (ToM), to global insight and three insight dimensions - illness recognition, symptoms relabelling and treatment compliance - in a sample of SSD patients, whilst adjusting for potential confounders, including psychopathology and measures of general cognition. In line with our first hypothesis, those individuals who had a tendency to JTC had lower levels of illness recognition, although no further relevant associations of JTC with insight dimensions were revealed by the analyses, and Cognitive Insight was associated with total insight and symptoms relabelling - higher Cognitive Insight levels, better clinical insight. However, ToM was not linked with any insight dimension and no cognitive test contributed to treatment compliance, which partially conflicted with hypothesis i. Consistent with hypothesis ii, not only was Cognitive Insight significantly associated with global insight and symptoms relabelling, but also Cognitive Insight explained a higher percentage of the variance on these two insight scores (11.6%

and 16.6%, respectively) than the other tested cognitive variables, hence making a stronger contribution to overall insight, particularly to symptoms relabelling.

Jumping to Conclusions cognitive bias was associated with illness recognition

Patients with SSD tend to reach conclusions despite having limited evidence to do so, which is known as *Jumping To Conclusions (JTC)* [20], a cognitive bias leading to delusional ideas [19]. Of relevance, JTC at baseline predicted functional outcome assessed with the Global Assessment of Functioning [55] in the GAP FEP cohort at 4-year follow-up [8]. However, JTC may be modified through so-called metacognitive training (MCT) [56] in early-onset psychosis patients [38], cognitive-behavioural therapy for psychosis [57] and Metacognition Reflection and Insight Therapy [58].

As alluded to above, to our knowledge the relationship between JTC and insight has been seldom researched. Therefore, our novel results, which revealed an association of JTC with illness awareness, should encourage more work in this area, including intervention studies. However, the percentage of the variance on illness recognition explained by JTC, although statistically significant, was low (7.1%). In other words, JTC cognitive bias appears to play a small part in poor insight in patients with SSD, which may make this finding of little value from a clinical point of view. Hence, no large effect sizes of interventions targeting only JTC on insight changes should be expected since other variables, such as premorbid personality [17,59] and premorbid adjustment [60–62], which may be less prone to this type of interventions, appear to contribute to gaining awareness of having a mental illness.

Relationship between cognitive and clinical insight

As noted above, our results replicated the relationship between *cognitive* and *clinical insight* [14,15]. In particular, both total (clinical) insight score and symptom relabelling were linked with Cognitive Insight, which remained significant after controlling for confounders (Table 4). However, the relationship between the two may be weaker than previously thought [26]. More recently, a systematic review and meta-analysis of twelve RCTs found evidence of the positive effect of metacognitive interventions on both clinical and Cognitive Insight [13], consistent with this study results which showed Cognitive Insight to be the strongest contributor to clinical insight.

With regard to metacognitive interventions and Cognitive Insight, while metacognitive interventions were particularly demonstrated to increase self-reflectiveness levels, self-certainty appeared to be less prone to these interventions [13]. Given the role of Cognitive Insight in global insight and symptom relabelling, as highlighted by our results, Cognitive Insight may become the main treatment target for *insight improving interventions*. Future

trials should elucidate whether interventions addressing Cognitive Insight, such as MCT, can not only result in greater clinical insight levels, but also in better clinical outcomes, which is what really matters for patients. More specifically, there are grounds to consider that patients may gain the ability to recall previous psychotic experiences as pathological following MCT sessions, although *maintenance* MCT sessions are likely to be required to sustain these effects in the longer-term [13]. The MCT-based smartphone application (https://clinical-neuropsychology.de/app_en) may be useful in achieving this, which already showed promising results in terms of feasibility and efficacy for depressive symptoms [63], particularly during the ongoing COVID-19 pandemic.

Theory of Mind was not linked with clinical Insight

Over two decades ago deficits in metacognition about other minds known as *Theory of Mind (ToM)* were linked with paranoid delusions in schizophrenia [64], which was later replicated by an independent study [65], which also showed ToM to be a state-dependent feature (rather than a trait) of schizophrenia. Other groups reported ToM impairment to be associated with negative symptoms [66–68] and disorganisation [69].

Interestingly, ToM deficits were also related to impaired insight in a case-control study of schizophrenia patients, independently of neurocognitive deficits and severity of symptoms [70]. Additionally, a systematic review [26] found ToM to affect clinical insight, while no association between ToM and Cognitive Insight was observed. ToM may therefore contribute to clinical insight independently of the relationship between cognitive and clinical insight, consistently with the aforementioned report [70]. Hence, two explanations may have contributed to the lack of association of between ToM deficits and impaired insight in our sample. First, we used two ToM instruments, such as the Hinting Task short version and the ERTF, which may have not captured those ToM features more strongly associated with insight. Second, Cognitive Insight, which was the main predictor of clinical insight in our sample of SSD outpatients, may have acted as mediator/confounder in the relationship between ToM and insight. Future studies in this area should therefore address these methodological issues.

Treatment compliance does not appear to have a neuro-metacognitive basis

Contrary to our expectations, our study did not link the tested cognitive variables, namely JTC, Cognitive Insight and ToM, with *treatment compliance*, which may have been due to the chronicity of most participants. Alternatively, from a more conceptual point of view, it is worth noting that *'awareness is not the same as acceptance'* [71]. Indeed, some previous FEP studies linked a range of *external* variables such as negative attitude toward medication,

quality of life, use of substances and unemployment with compliance [72,73], which were not evaluated in our investigation. Moreover, psychosocial interventions addressing treatment compliance and availability of Long-Acting Injectable Antipsychotics (LAIA) are thought to improve compliance [72] and social stigma may affect adherence in psychosis [6,14]. It therefore seems that external factors, such as receiving outpatient care under restriction, receiving social support and benefits subject to compliance and cultural issues, and the conceptualization of mental illness across ethnic minorities, may underlie variations in treatment compliance. Future social psychiatry-based studies are needed to elucidate what determines treatment compliance both in early psychosis and in more chronic samples [74].

Other contributors to insight

One may intuitively think that more severe psychotic symptoms go with worse insight in schizophrenia. While this association was supported by a 2003 meta-analysis of 40 studies, the effect size was relatively small [75]. Interestingly, insight has been consistently linked with mood - greater insight, lower mood - [76], which led to speculation that insight may increase risk of suicidal behaviour in psychosis, although three independent FEP cohorts did not confirm this [77,78]. Bivariate analyses from the present study found an inverse association of a psychosis dimension, namely disorganization, with total insight and illness recognition. Also, mania was the only variable significantly associated with treatment compliance: higher manic levels, worse insight. However, these relationships did not survive the multivariable regression models, in line with the above meta-analysis [75].

Although previous SSD studies revealed an association of previous suicidal behaviour [79] and premorbid adjustment [60,62] with insight, we failed to replicate both of them, which may have been due to insufficient power to examine these relationships which were not the primary outcome of this study.

Also, a more prolonged duration of untreated psychosis (DUP) [17,79] and premorbid sociopathic and schizoid personality traits [59] were linked with impaired insight. Regretfully, we did not collect data on these variables.

Strengths and Limitations

To the best of our knowledge, this is the first study in analysing the specific influence of JTC, Cognitive Insight and ToM on multiple insight dimensions in a representative sample of SSD outpatients, whilst controlling for a set of potential confounders. While this piece of work makes a novel contribution to the field with implications on treatment, which are discussed below, replication studies are warranted.

However, several limitations should be borne in mind when interpreting the study results. First, the sample was comprised of outpatients with SSD receiving mental healthcare and living in an inner-city area, such as Madrid (Spain). Hence, these findings may not apply to those SSD patients residing in rural areas and/or those who receive treatment in primary care. Second, other non-tested variables, such as premorbid personality [17,59] and neuroanatomical correlates [80], may affect insight, particularly taking into account the low percentage of the variance on insight scores explained by the models. Third, the researcher (JDLM) who administered the SAI-E was not blind to other scales such as the PANSS, which may have affected the insight assessment. Fourth, insight changes over time [6] could not be captured by our cross-sectional design. Predictors of state-insight may change over the course of the psychotic illness, which requires further cohort studies from prodromal stages. Fifth, the relatively small sample size (N = 77) may have lacked sufficient power to investigate some associations of insight dimensions, although this was unlikely to significantly alter the main findings from the study. Finally, individuals with poor insight may have refused to participate in this RCT, which may limit the generalisability of our results.

Clinical implications and directions for future research

Cognitive Insight and JTC emerged as the main cognitive domains underlying insight, thus becoming potential treatment targets for changing insight. Based on our results, while these interventions may succeed in helping patients to gain illness recognition and symptoms relabelling ability, addressing treatment compliance, which does not seem to have such a cognitive basis, may be more challenging, which is of concern. Most importantly, whether this insight improvement has an impact on long-term clinical outcomes is yet to be demonstrated.

In particular, it seems that making SSD patients aware of having a mental illness, including improving their ability to relabel previous psychotic experiences as pathological, requires a change in their thinking style, that is, cognitive insight or how they reach conclusions, including the possibility of being wrong. Can we achieve this? As noted above, metacognitive interventions have been demonstrated to successfully address cognitive and clinical insight [13]. However, this insight improvement (at least, in the short-term) may lead to depression and increased risk of suicidal behaviour. Hence, delivering insight improving interventions should be combined with measures to improve mastery and retrieve low mood. This noted, tackling cognitive insight, and to a lesser degree JTC, through metacognitive interventions is not the whole story. In this regard, we have demonstrated that these two (meta)cognitive variables only explain a relatively low percentage of the variance on insight scores. Most importantly, ‘awareness of the need for treatment’ (which has been referred to as ‘treatment compliance’) was not showed to have a metacognitive basis, from which three

conclusions can be drawn. First, ‘awareness is not the same as compliance’ [71]. Second, these metacognitive interventions may have a small effect on compliance. Third, enhancing compliance through compulsory treatment (e.g. Long-Acting Antipsychotics Injections) may not improve long-term clinical and social outcomes, as demonstrated by decades of clinical practice. The question therefore arises: What can we do? In brief, not only ‘further research is needed’ but also, comprehensive integrative treatment plans should be formulated by high quality multidisciplinary teams working collaboratively from a multi-agency approach [9].

In summary, this study revealed the relevant role of two cognitive processes, namely JTC and Cognitive Insight, in clinical insight in psychosis. Future functional neuroimaging studies are warranted to link neuropsychological findings with neuroanatomical correlates, which may shed some light on the putative neural circuits involved in the complex metacognitive processes underlying clinical and cognitive *insight*. This may pave the way towards more targeted interventions, such as MCT, for enhancing insight. In particular, future RCTs using large sample sizes over prolonged follow-up periods are needed to establish whether these interventions may improve long-term insight and clinical and psychosocial outcomes.

Statements

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Statement of Ethics

This study is part of a randomised controlled trial (RCT) which obtained ethical approval from the Local Research Ethics Committee (Instituto de Investigaciones Sanitarias Fundación Jiménez Díaz, Madrid, Spain. EC044-19_FJD-HRJC) in accordance with the World Medical Association 1964 Declaration of Helsinki and further amendments. The RCT is registered at ClinicalTrials.gov (NCT04104347).

Participants, who were informed of the study procedures and their right to decline to participate in the study and/or to drop out of the trial at any time without implications on care provision, provided written informed consent.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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The funders had no role in hypothesis generation, study design, decision to publish or the manuscript writing. No funder has a conflict of interest in relation to the study's results and findings.

Author Contributions

JDLM is the Principal Investigator of this randomised controlled trial, of which this study is part. JDLM, PJEA, ASEM, VGRR, SSA, LMI, LML, EBG and ASD contributed in the process of protocol design, hypothesis generation, manuscript preparation and fulfilled the criteria for authorship. JDLM wrote the first draft. EBG and ASD conceived of the study, participated in its design, implemented the project and contributed to the interpretation of results. All the authors read and approved the final manuscript.

Table 1. Sample characteristics (n=77)

Socio-demographic variables	
Age (years)	47.69 ± 9.76
Gender (males)	41 (53.2%)
Education level (primary)	13 (16.9%)
Premorbid Adjustment (PAS)	
Childhood	5.80 ± 3.79
Early adolescence	7.64 ± 4.64
Late adolescence	7.69 ± 4.90
Clinical variables	
Diagnosis	
Schizophrenia	48 (62.3%)
Schizotypal Disorder	
Delusional Disorder	
Brief Psychotic Disorder	
Schizoaffective Disorder	
Other Psychotic Disorder	
Psychotic Disorder NOS	
Previous suicidal behaviour	31 (40.3%)
Duration of illness (>5years)	69 (89.6%)
Previous admissions	3.46 ± 3.99
Psychopathology (PANSS)	
Positive	8.44 ± 3.67
Negative	14.91 ± 5.89
Disorganisation	6.05 ± 2.61
Depression	6.25 ± 1.86
Mania	6.94 ± 2.70
Insight (SAI-E)	
Total Insight	15.55 ± 2.29
Illness Recognition	5.36 ± 2.68
Symptoms relabelling	5.87 ± 2.81
Treatment Compliance	4.31 ± 1.57
Neurocognition	
IQ	104.61 ± 11.72
TMT B-A	68.91 ± 43.65
Jumping to Conclusions (JTC)	
JTC_85:15	42 (56.0%)
JTC_60:40	38 (51.4%)
Cognitive Insight	
BCIS-Self-Reflectiveness	15.43 ± 5.11
BCIS-Señf-Certainty	7.67 ± 3.42
BCIS-Composite Index	7.74 ± 6.66
Theory of Mind (ToM)	
ToM - Hinting Task	2.25 ± 1.33
ToM - ERTF	16.86 ± 2.16

PAS: Premorbid Adjustment Scale. (Cannon-Spoor et al., 1982). NOS: Not Otherwise Specified. PANSS: Positive and Negative Syndrome Scale for Schizophrenia (Kay et al., 1987). SAI-E: Schedule for Assessment of Insight, Expanded Version (Kemp & David, n.d.). TMT: Trail making Test (Reitan, 1958). BCIS: Beck Cognitive Insight Scale (Beck et al., 2004). ERTF: Emotions Recognition Test Faces (Baron-Cohen et al., 1997).

Table 2. Relationship between insight dimensions and other variables

	TOTAL	RECOGNITION	RELABELING	COMPLIANCE
Binary variables				
Gender (m / f)	15.49 / 15.61	5.17 / 5.58	6.00 / 5.72	4.32 / 4.31
Education (low / high)	17.23 / 15.20	5.54 / 5.33	6.77 / 5.69	4.92 / 4.19
Diagnosis (F20 / non-F20)	15.25 / 16.03	5.27 / 5.52	5.73 / 6.10	4.25 / 4.41
Duration (>5y. / <5y.)	15.41 / 16.75	5.20 / 6.75	5.88 / 5.75	4.32 / 4.25
JTC (present / absent)	14.38 / 16.97 *	4.62 / 6.24 **	5.74 / 6.12	4.02 / 4.61
Continuous variables (r=)				
Age	-0.028	-0.074	-0.094	0.200
PAS Child	-0.039	-0.028	-0.078	0.055
PAS early	-0.104	-0.214	-0.031	0.068
PAS late	-0.105	-0.329**	0.075	0.091
PANSS-Positive	-0.162	-0.021	-0.163	-0.220
PANSS-Negative	-0.139	-0.216	-0.034	-0.037
PANSS-Disorganization	-0.239*	-0.343**	-0.099	-0.042
PANSS-Mania	-0.193	-0.158	-0.052	-0.287*
PANSS-Depression	0.113	0.192	-0.041	0.126
IQ	0.062	0.082	-0.036	0.131
TMT_B-A	-0.015	-0.083	0.051	0.003
BCIS-Self-Reflectiveness	0.476**	0.445**	0.376**	0.168
BCIS-Self-Certainty	-0.154	-0.113	-0.097	-0.152
BCIS-Composite Index	0.456**	0.414**	0.345**	0.216
Hinting Task	0.136	0.211	-0.071	0.118
ERTF	0.040	0.137	-0.070	-0.103

JTC: Jumping to Conclusions. PAS: Premorbid Adjustment Scale. (Cannon-Spoor et al., 1982). PANSS: Positive and Negative Syndrome Scale for Schizophrenia (Kay et al., 1987). SAI-E: Schedule for Assessment of Insight, Expanded Version (Kemp & David, n.d.). TMT: Trail making Test (Reitan, 1958). BCIS: Beck Cognitive Insight Scale (Beck et al., 2004). ERTF: Emotions Recognition Test Faces (Baron-Cohen et al., 1997).

Table 3. Linear regression models on insight scores with only metacognitive variables as predictors

	TOTAL INSIGHT			RECOGNITION			RELABELING			COMPLIANCE		
	R^2 change	***F change***	***p***	***R^2 change***	***F change***	***p***	***R^2 change***	***F change***	***p***	***R^2 change***	***F change***	***p***
JTC	0.049	3.424	0.069	0.079	5.642	0.020	0.006	0.370	0.545	0.020	1.346	0.250
CI	0.214	9.285	<0.001	0.154	6.446	0.003	0.168	6.505	0.003	0.033	2.108	0.337
ToM	0.061	2.789	0.069	0.039	1.669	0.669	0.049	1.954	0.150	0.073	2.570	0.085
	0.324		<0.001	0.233		0.001	0.168		0.007	0.126		0.131

JTC: Jumping to Conclusions. CI: Cognitive Insight. ToM: Theory of Mind.

Table 4. Multivariable linear regression models on insight scores

	TOTAL INSIGHT			RECOGNITION			RELABELING	
	R^2 *change*	*F change*	*P*	R^2 *change*	*F change*	*P*	R^2 *change*	*F change*
Block 1- Demographic variables:	0.031	0.569	0.638	0.030	0.557	0.646	0.062	1.181
Age, gender and education level								
Block 2 – Premorbid Adjustment:	0.034	0.615	0.608	0.157	3.294	0.028	0.041	0.776
Childhood, early and late adolescence PAS scores								
Block 3 – Clinical variables:	0.029	0.376	0.824	0.090	1.465	0.228	0.027	0.371
Diagnosis, SB, illness duration, admissions								
Block 4 – Psychopathological dimensions:	0.084	0.862	0.515	0.115	1.598	0.182	0.048	0.487
PANSS factors								
Block 5 – Neurocognition:	0.049	1.269	0.292	0.018	0.605	0.551	0.036	0.928
IQ (WAIS vocabulary), TMT B-A								
Block 6 – JTC:	0.067	3.684	0.062	0.071	5.350	0.026	0.013	0.675
Beads Task (JTC present)								
Block 7 – Cognitive Insight	0.116	3.649	0.036	0.057	2.271	0.117	0.166	5.065
BCIS-SR, BCIS-SC								
Block 8 – Theory of Mind	0.036	1.154	0.327	0.006	0.245	0.784	0.047	1.457
Hinting Task, ERTF								
	0.200		0.249	0.433		0.043	0.166	

PAS: Premorbid Adjustment Scale. (Cannon-Spoor et al., 1982). SB: Suicidal behaviour (previous). PANSS: Positive and Negative Syndrome Scale for Schizophrenia (Kay et al., 1987). TMT: Trail making Test (Reitan, 1958). BCIS: Beck Cognitive Insight Scale (Beck et al., 2004). SR: Self-Reflectiveness. SC: Self-Confidence. ERTF: Emotions Recognition Test Faces (Baron-Cohen et al., 1997).

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