A Meta-Analysis Taxonomizing Empathy in Schizophrenia

Sumayyah Varachhia*, Eamonn Ferguson and Gillian A Doody
School of Medicine, Division of Psychiatry and Applied Psychology, University of Nottingham, Nottingham, UK

Abstract

Background

Trait empathy is integral to relationship development and maintenance. Therefore, impairment in this ability can have an adverse effect on many domains of life including social, sexual, and marital. Previous reviews show in schizophrenia, this ability to be impaired but with a high amount of heterogeneity that is yet to be explored more thoroughly.

Aim and method

Considering this, we aim to synthesise the extent literature using a meta-analytic approach and examine the source of the heterogeneity observed in previous reviews and develop taxonomy of empathy deficits in schizophrenia. Hedges’ g was calculated for cognitive and affective empathy using random effects models. Meta-regression models of key cognitive, clinical and demographic risk and protective factors were run. These included: Impact year of publication, age, gender, ethnicity, education, general IQ, verbal/pre-morbid IQ, global neuro-cognition, positive, negative and general symptoms of schizophrenia, age at schizophrenia diagnosis, duration of illness and medication has on cognitive and affective empathy.

Results

A literature search revealed 39 independent studies examining empathy in schizophrenia. Healthy controls scored higher than people with a diagnosis of schizophrenia, with a small effect size for affective empathy (Hedges’ g = 0.29) and a medium effect size for cognitive empathy (Hedges’ g = 0.53). Both components were heterogeneous. Analyses using meta-regression models found age at diagnosis and the duration of illness moderated the difference in effect size for cognitive empathy, such that those with an earlier diagnosis or a more chronic course exhibit greater difficulty in cognitive empathy compared to healthy controls.

Conclusion

We find a longer duration of illness and younger age at clinical diagnosis enhances impairments in cognitive empathy in severe and enduring schizophrenia. For affective empathy, we conclude, compared to healthy controls, some patients report having a deficit [i.e. experience lower affective empathy], others report comparable levels, and the remaining report to be experiencing higher emotional arousal. As an earlier diagnosis, prolonged illness course and dysfunctional emotional reactions are significant risk factors of poorer empathic interactions, it will be important to address the underlying mechanisms of this deficit in future work.

Keywords: Affective empathy; Cognitive empathy; Meta-Analysis; Schizophrenia

Introduction

Empathy is a critical interpersonal social skill that is necessary for everyday social communication. It helps us participate in groups, socialise, develop and maintain close relationships [1] and is a potential determinant of pro-social behaviours [2,3] including altruism [4]. Therefore, an impairment in this ability can have a significant impact on an individual’s mental health and well-being, and as such, understanding its structure, purpose and mechanism is of clinical and public health relevance [5]. Psychopathy [6] and related clinical disorders (e.g., antisocial personality disorder, conduct disorder, acquired sociopathy [7] and disorders of the autistic spectrum [6,8]), have often been characterised by low or absent empathy for others. Prior work has also suggested a potential connection between the clinical characteristics of autism and schizophrenia (e.g., see Bleuler’s [9] four A’s of schizophrenia) and as such, a body of literature has now accrued investigating empathy in people with a diagnosis of schizophrenia [10-12].

Measuring and defining empathy in schizophrenia disorders

Historically, references to empathic deficits in schizophrenia dates back to Bleuler [13] and Kraepelin [14], but only over the last 11 years have researchers carried out studies comparing people with a diagnosis of schizophrenia and related disorders to controls without mental health difficulties (recruited from the general population), on measures purported to assess empathy. Commonly, studies have used the Interpersonal Reactivity Index (IRI) [15], a self-report questionnaire using four sub-scales: Fantasy, perspective-taking, personal
distress and empathic concern. Scholars do not universally accept this four-component empathic conceptualisation [4,5,16-18], instead, suggesting empathy is better represented and measured as two independent domains: Cognitive and affective [5]. The cognitive domain involves understanding and measuring the internal states of others, such as thoughts, intentions, and emotions [19] and the affective domain involves being “sensitive to and vicariously experiencing the feelings of others” (p. 85 [5]).

What is known in relation to empathy and schizophrenia

Several meta-analyses have been beneficial in quantifying empathy deficits in people with schizophrenia [10-12]. Of these reviews, Bonfils and colleagues [11,12] demonstrated the importance of using self-report and performance-based empathy measures during analysis and the need to explore additional clinical characteristics (such as symptom severity, age at illness onset and medication) to further this field of research. As such, in this study, we discuss and examine for the first time, the moderating effect of these, and demographic (age, gender, education, and year of publication) and neuro-cognitive variables (i.e. global neuro-cognition, verbal/pre-morbid and general IQ), with the aim of assessing the sources of heterogeneity (i.e. variability) observed in previous reviews [11,12]. In doing this, we seek to develop an evidence-based taxonomy of empathy deficits in schizophrenia.

Empathy and Clinical Characteristics of Schizophrenia

Clinical symptoms and empathy

Due to clinical heterogeneity, symptoms of schizophrenia have historically been understood in a variety of ways (for a review see Harrington, et al., [20]). However, reflecting the amendments made to the latest diagnostic manual, the DSM-5 (APA, [21]), which did away with sub-type specifications (i.e. paranoid, disorganised, catatonic and undifferentiated) for the schizophrenia diagnosis, symptom severity is now examined. Although a variety of symptom assessment tools are available, the Scales for the Assessment of Negative/Positive Symptoms (SANS/SAPS) [20,21] and the Positive and Negative Syndrome Scale (PANSS) [22] have been commonly used to assess positive symptoms (e.g., symptoms of delusions, hallucinations and disorganisation), negative symptoms (e.g., anhedonia, avolition, apathy, asociality, flattened affect and alogia) and general symptoms (e.g., anxiety, depression, and psychomotor symptoms) in schizophrenia.

In studies of empathy, the primary focus of some studies was not on examining symptom severity in schizophrenia [23-33]. For other studies, however, examining symptom severity in schizophrenia patients was included as part of secondary analyses, with mixed findings reported across individual studies. For example, Montag and colleagues [34] found in patients, the IRI Empathic Concern related negatively to PANSS negative and general symptoms, Thirionx, et al., [35] found, using the same sub-scales, only negative symptoms associated negatively with the IRI Perspective-Taking sub-scale. Lam, et al., [36] found a negative relationship between PANSS general symptoms and overall empathy score, and Sharan-Theyory and colleagues [37] reported the degree of impaired empathy (total IRI score) depended on how severe negative symptoms were. However, several studies reported no significant relationship between SANS and IRI sub-scales [38-43] and performance-based measures of cognitive and affective empathy [44,45]. These discrepancies further extend to the SANS and SAPS symptom measurements [46-48]. Critically, these inconsistencies have prevented the field from gaining a more nuanced understanding of how core symptoms of schizophrenia (i.e. positive, negative and general) relate to self-reported empathy. By examining this relationship in a meta-analytic framework, we can further our understanding of the mechanisms underlying empathy deficits in schizophrenia and develop, in a systematic manner, relevant clinical profiles.

Medication

In the UK, for people diagnosed with a schizophrenia disorder, medication is recommended as the first line of treatment (National institute for health and social care [49]). The rationale behind this is, if prescribed at the correct dosage, medication can help manage acute symptoms, prevent relapse, and optimise level of functioning. However, whether medication also benefits interpersonal skills such as empathy remains unclear. Like symptom severity, the association between medication dosage and empathy (Chlorpromazine equivalent, mg/day) has either not been examined [26,28,34,35,38,41,50,51] or has shown not to correlate with components of empathy [29,32,44,47]. These variations may have contributed to the heterogeneity observed for empathy deficits in previous reviews [11,12]. Therefore, it is important that this moderator is included and examined for its effect on empathy further.

Individual Differences in Empathy

Demographic variables and empathy in schizophrenia and related disorders

Empathy can vary as a function of inherent psychological similarities and differences between individuals, referred to in the Psychology literature as individual differences [15]. In schizophrenia, several protective factors have been reported to be of benefit when re-adjusting socially post-illness. These include shorter illness duration, later age at illness onset and female gender. Schizophrenia females have shown to have a better prognosis [52] and pre-morbid adjustments in domains of life which are integral to empathy. These include: Social, sexual and marital domains. Thus, females are thought to have better outcomes and social re-integration post-illness onset than their male counterpart [53-57]. As most studies in the literature have included predominantly male schizophrenia samples [10,24,27-33,37,39,46-48,51,58,59], included wide age ranges [10,38,61-64] with patients often reporting fewer years in education compared to healthy control groups [23,27,41,46,50,51,58,60,65-69] and studies making a note of key variables such as ethnicity in patients but not necessarily examining its effect on empathy [25,27,32,36,43,44,50,51,58,66,70]. The current findings make it unclear as to whether demographic risk factors exacerbate deficits in empathy and consequently, in part, explain some of the heterogeneity observed in previous reviews [11,12].

Empathy and neuro-cognition in schizophrenia and related disorders

Neuro-cognition is central to empathy, as empathy involves making inferences in which observation, memory, reasoning and cognitive flexibility/inhibitory control are all important [28,36,37,47]. Broadly, neuro-cognition refers to the mental operations or processes used to acquire knowledge, meaning and understanding [71] of a
specific task or context. Experts in this field formed the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS)-as commissioned by the national institute of mental health. This group identified six neuro-cognitive domains: Attention, working memory (verbal and non-verbal), speed of processing, reasoning and problem solving, visual learning and verbal learning as important areas for further research in schizophrenia that are to be assessed using the MATRICS Consensus Cognitive Battery (MCCB) [72,73].

In the current literature, we found only two studies to have used the MATRICS developed Consensus Cognitive Battery (MCCB) to assess all six neuro-cognitive domains [23,38]. More specifically, amongst the identified studies, authors have commonly produced a global/composite neuro-cognitive score, and examined its relation with empathy, with several studies finding no relationship between global cognition (i.e. the six neuro-cognitive abilities) and self-reported empathy in schizophrenia [23,27,38]. Other studies however, reported a positive correlation between affective empathy and global neuro-cognitive scores [67]. Two studies also reported having assessed neuro-cognitive domains proposed by the MATRICS panel (i.e. working memory (verbal and non-verbal) and attention) using measures closely aligning to the MCCB battery [31,74]. However, as neuro-cognition was not the focus of these studies, this ability was not examined in relation to empathy. Since very few studies have examined all six of the neuro-cognitive domains proposed, examining each domain separately may not be possible. However, we can gather studies which have assessed anyone, or more of the neuro cognitive domains identified by the MATRICS panel into a global neuro-cognitive score and assess its impact on cognitive and affective empathy. In this way, we would have sufficient studies to make provisional inferences relating to heterogeneity and taxonomize the role of neuro-cognition on empathy in schizophrenia.

As well as neuro cognition, findings relating to Intelligent Quotient (IQ) and empathy are also unclear. Two types of IQ’s have been measured in studies of empathy in schizophrenia: Verbal or pre-morbid IQ, and general IQ. Some studies have reported subtle impairments in pre-morbid/verbal IQ [29,30,50,66,74], while others have reported a more pronounced impairment in general IQ [36,59,67,68,75]. Since previous studies have found significant negative relationships between measures of IQ and empathetic responding in schizophrenia [23,68], it will be important to include this variable for the purposes of heterogeneity assessment and taxonomy development.

The goal of current research

Inconsistent findings have been reported for clinical, demographic and cognitive variables across studies, thereby making the understanding of the observed heterogeneity for empathy in previous reviews unclear [11,12]. As such, a synthesis of the current evidence is timely and necessary. We, therefore, aimed to undertake a meta-analysis of the available evidence to address the heterogeneity detailed above. In doing this, we went beyond the basic associations detailed in the literature and developed an evidence-based taxonomy of empathy deficits in schizophrenia.

A meta-analytic framework was chosen as it enabled us to gather data systematically and provide us with a large schizophrenia sample, which to some extent helped us in overcoming some of the problems associated with small sample sizes (a common issue in this area of research). This meta-analysis aimed to: (1) Synthesise the extant literature on self-reported cognitive and affective empathy in schizophrenia using a meta-analytic approach. (2) Examine in detail the heterogeneity observed in previous reviews by examining for the first time, the moderating effect of several important variables to create taxonomy. These included: Severity of positive, negative, and general symptoms, duration of illness, age at diagnosis, medication dosages, age, gender, ethnicity, education, global neuro-cognition, verbal/ pre-morbid IQ, general IQ and year of publication on the difference in performance on self-reported empathy between schizophrenia patients and healthy controls. Consistent with Bonfils and colleagues reviews [11,12] we hypothesised that healthy controls would report higher levels of cognitive and affective empathy than people with a diagnosis of schizophrenia. Due to mixed findings in the literature for clinical, demographic and cognitive variables, these moderators were examined in an exploratory manner.

Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [76] checklist and literature flow chart was used to carry out and report findings for this study.

Database search

The following databases were searched electronically: Psych Info, Psych Article, Embase, Web of Science Core Collection and PubMed using the keywords (with an English language filter applied, when possible): Empathy, empathising, empathising, empath* appearing with either schizophrenia, schizoaffective, or schizo* were searched up until the 1st week of February 2018. References of relevant meta-analyses [10-12] were also searched. In cases where a study reported to have assessed empathy and met the eligibility criteria, but no data was provided, the corresponding author of the study was contacted (via email) for additional data.

Study selection criteria

The following study inclusion criteria were used to include/exclude studies: (1) Studies were required to compare people with a diagnosis of schizophrenia or a related disorder with a healthy (control) group on measures purported to assess empathy. (2) Participants had to be adults aged between 16 and 65 years. (3) Studies must have been written in the English language. (4) Studies must have measured each component of empathy (cognitive and affective) separately. (5) Studies had to provide sufficient data to calculate effect sizes and univariate relationships. If the necessary data could not be obtained through available records or contact with the author, the study was excluded.

Data extraction

First, year of publication, publication type, country (including the place where the study was conducted) and the sample size was extracted followed by mean age, education level (in years), gender and ethnicity (both in percent) for schizophrenia patients and healthy controls. For the schizophrenia samples, medication dosage mg/day (chlorpromazine equivalents) [77], duration of illness (in years) and diagnosis (schizophrenia, schizo-affective disorder or a schizophrenia-related disorder) in percent were coded. Mean severity of symptom score was also coded according to categories most frequently reported in studies: Positive, negative and general. Mean scores for
general IQ, verbal/pre-morbid IQ and individual neuro cognitive data based on the six neuro-cognitive domains (attention, speed of processing, working memory (verbal and non-verbal), visual learning, verbal learning, reasoning and problem-solving) as identified by the MATRICS consensus panel [72,73] was coded for both, schizophrenia patients and healthy controls. Also, we identified a few studies including measures assessing cognitive flexibility/inhibitory control. The measures used to assess this ability were entirely different from the neuro-cognitive measures measuring the six domains. However, considering the importance of cognitive flexibility/inhibitory control in empathy (see for example, [3,78]) we included this as an additional neuro-cognitive domain and extracted data for schizophrenia and healthy controls, before calculating a mean global neuro-cognitive score for each group.

**Effect sizes**

The effect size was computed using Hedges’g [78,79]. The mean, standard deviation and sample size for cognitive and affective empathy for each group (schizophrenia and healthy control) were extracted. In cases where this data was unavailable, but other values (e.g. independent sample t-value or Cohen’s d) were, then those were used instead. Where studies reported data for cognitive and affective empathy using more than one measure, then an average study effect size was calculated for each component to avoid multiple effect sizes per study, which would violate the assumption of independent observations for each study in a meta-analytic framework [80]. In cases where a study reported to have used two self-report measures of empathy, but data were available only for one, then the scale for which data was reported/available was included. A positive value of g signified that healthy controls scored higher than people with schizophrenia and a negative value of g signified that people with schizophrenia scored higher than healthy controls.

**Analyses**

**Preliminary analyses**

Before conducting the main analyses, descriptive statistics were derived using SPSS version 23.0. Then, one-study remove sensitivity analysis was conducted to assess if anyone study effect size unduly affected the overall effect size for cognitive and affective empathy [81]. Forest plots were produced for each domain to assess for outliers. Visually, any effect size which looked as though it might be an outlier, but when examined statistically (via sensitivity analysis), did not differ was retained. Publication bias was examined first via funnel plots, then using Duval and Tweedie’s [82] Trim and Fill random effects model. Funnel plots were created and inspected visually for asymmetry. The Trim and Fill approach was checked for biases or extreme values. If the model showed there to be no statistically significant difference (i.e. p > .05) between the included effect sizes, then we can have greater confidence that publication bias does not effect current results [81,83]. However, in cases where the Trim and Fill approach showed to be statistically significant, the Fail-Safe N was then examined to ascertain the number of non-significant studies necessary to make current findings nil.

**Main analyses**

Standardised mean differences were calculated for each component of empathy (cognitive and affective) using a Hedges’g random effects model. This model was used as it accounted for both, within and between study variability [84]. As Hedges’g is like Cohen’s d, the magnitude of the computed effect sizes was interpreted according to the guidelines provided by Cohen [85] such that: ≤0.20 were considered small, 0.50 were considered medium, and ≥0.80 were considered large effect sizes. The inverse variance was also computed to estimate the standard error for each effect size [84].

**Heterogeneity and moderator analyses**

Heterogeneity was assessed using Q-statistics and degree of heterogeneity using f-index [83]. When Q-statistics was significant (i.e. p < .05), and the f-index above 25% heterogeneity could be said to be present and therefore, an assessment of moderator analysis proper [85]. Moderators were examined using a random effects meta-regression model. A moderator was of significance if there was significant beta-weight (p < .05) and a decrease in the f-index.

Barring descriptive statistics, all other meta-analytic analyses were conducted on Comprehensive Meta-Analysis Version 2 (CMA) [86].

**Results**

In total, 39 studies assessing affective empathy and 36 assessing cognitive empathy were identified as meeting the inclusion criteria of this meta-analysis (See Figure 1 for the flowchart of the literature search).

**Study characteristics**

The meta-analysis included 1,479 participants with a schizophrenia disorder and 1,293 healthy controls. See Tables 1-3 for detailed study characteristics at the individual study level and Tables 4-7 for aggregate study, clinical, cognitive and demographic data (Tables 1-7).
## Table 1: Meta-Analysis Taxonomizing Empathy in Schizophrenia

| Citation (K = 39) | Country (City) | SSD N | HC N | % Patients in study with a Schizophrenia Diagnosis | M Age SSD | M Age HC | % Male SSD | % Male HC | M Years in Education SSD | M Years in Education HC | % Ethnicity SSD | % Ethnicity HC |
|------------------|----------------|-------|------|------------------------------------------------|-----------|----------|------------|-----------|-------------------------|------------------------|---------------|---------------|
| Achion, et al., [10] | Canada (Québec) | 31 | 31 | 74.2 | 24.9 | 25.2 | 83.9 | 83.8 |
| Andrews, et al., [87] | Australia (Victoria) | 18 | 18 | 61.1 | 44.1 | 58.4 | 61.1 | 44.4 | 13.3 | 15.6 |
| Berrada-Baby, et al., [88] | France (Versailles) | 20 | 20 | 100 | 46.3 | 41.5 | 54.0 | 54.0 | 12.2 | 12.5 |
| Brown, et al., [24] | USA (Baltimore) | 17 | 17 | 100 | 41.7 | 38.2 | 52.9 | 52.9 |
| Chiang, et al., [68] | Taiwan (Hualien County) | 70 | 35 | 100 | 44.5 | 46.0 | 47.1 | 48.0 | 10.9 | 13.0 |
| Corbina, et al., [58] | USA (New Haven) | 30 | 24 | 66.7 | 46.5 | 59.7 | 46.7 | 62.5 | 13.1 | 16.2 |
| Corbina, et al., [50] | USA (New Haven) | 21 | 26 | 100 | 32.2 | 50.1 | 61.9 | 57.7 | 14.9 | 14.9 |
| Derntl, et al., [2012a] [144] | Germany (Aachen) | 15 | 15 | 100 | 34.2 | 50.4 | 66.7 | 66.7 | 100-Caucasian | 100-Caucasian |
| Derntl, et al., [70] | Germany (Aachen) | 24 | 24 | 100 | 40.1 | 59.9 | 50 | 50.0 | 100-Caucasian | 100-Caucasian |
| Didehshahi, et al., [75] | USA (Dallas) | 19 | 21 | 63.2 | 32.4 | 27.1 | 88.5 | 12.6 | 14.6 |
| Fischer-Shotty, et al., [25] | Israel (Haifa) | 35 | 48 | 100 | 50.0 | 69.9 | 12.2 | 15.0 |
| Fujino, et al., [39] | Japan (Kyoto) | 69 | 69 | 100 | 36.6 | 24.2 | 57.9 | 57.9 | 13.9 | 14.5 |
| Fujikawa, et al [40] | Japan (Kyoto) | 24 | 20 | 100 | 37 | 54.6 | 50 | 50.0 | 13.7 | 14.3 |
| Gizewski, et al., [26] | Germany (Essen) | 12 | 12 | 100 | 37.8 | 36.6 | 100 | 100 | 9.3 | 9.8 |
| Haker, et al., [65] | Switzerland (Zurich) | 43 | 45 | 100 | 34 | 55.0 | 39.5 | 73.0 | 13 | 14.0 |
| Hooker, et al., [23] | USA (Berkeley/San Francisco) | 21 | 17 | 52 | 44.3 | 43.7 | 80.9 | 76.4 | 13.0 | 15.0 |
| Horon, et al., [51] | USA (Los Angeles) | 32 | 26 | 100 | 47.9 | 44.4 | 81.3 | 73.1 | 12.9 | 14.9 |
| Horon, et al., [27] | USA (Los Angeles and Chapel Hill) | 145 | 45 | 100 | 40.9 | 43.3 | 75 | 71.0 | 12.5 | 14.2 |
| Kaczarska-Pietras, et al., [61] | Poland (Lublin) | 100 | 50 | 100 | 31.3 | 29.6 | | | 12.8 | 13.7 |
| Lam, et al., [36] | China (Hong Kong) | 58 | 61 | 100 | 40.1 | 41.3 | 50 | 50.8 | 10.4 | 11.3 |
| Lee, et al., [28] | South Korea (Seoul) | 15 | 18 | 100 | 26.0 | 25.8 | 46.6 | 50.0 | 15.1 | 15.4 |
| Lee, et al., [69] | USA (Los Angeles) | 30 | 22 | 100 | 46.1 | 44.3 | 83.3 | 77.2 | 12.8 | 14.7 |
| Lehmann, et al., [29] | Germany (Berlin) | 55 | 55 | 100 | 39.8 | 38.9 | 58.1 | 54.5 | 14.0 | 15.0 |
| Matsumoto, et al., [36] | Japan (Kyoto) | 17 | 18 | 100 | 40.0 | 55.0 | 35.0 | 66.6 |
| McCormick, et al., [48] | USA (Iowa City) | 16 | 16 | 88 | 37.0 | 36.6 | 88 | 87.5 | 13.9 | 15.4 |
| McGuire, et al., [31] | Australia (Sydney) | 24 | 20 | 83 | 46.6 | 38.6 |
| McGuire, et al., [74] | Australia (Sydney) | 45 | 27 | 43.7 | 40.7 | 82.2 | 62.9 |
### Table 1: Individual demographic characteristics of the studies included in the meta-analysis.

**Note:** SSD = Schizophrenia-Spectrum Disorder Sample; HC = Healthy Control Sample; M = Mean. Supplemental information was provided by authors to assist in the coding of these studies.

| Study | Country (City) | M Age at Diagnosis | M Duration of Illness | M Medication (Chlorpromazine equivalents) - mg/day | M Positive Symptom Severity Score | M Negative Symptom Severity Score | M General Symptom Severity Score |
|-------|----------------|---------------------|-----------------------|--------------------------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Achim, et al., [10] | Canada (Québec) | - | 1.7 | - | - | - | - |
| Andrews, et al., [87] | Australia (Victoria) | 21.4 | 21.1 | - | - | - | - |
| Berrada-Baby, et al., [88] | France (Versailles) | - | - | 406.0 | - | - | - |
| Brown, et al., [24] | USA (Baltimore) | 30.5 | 9.3 | - | 19.1 | - | 45.4 |
| Corbera, et al., [50] | USA (New Haven) | 24.3 | 22.2 | 654.0 | 18.9 | - | 30.2 |
| Corbera, et al., [58] | USA (New Haven) | - | - | 181.3 | 15.2 | 15.2 | 29.2 |
| Dettl, et al., [44] | Germany (Aachen) | 28.8 | 7.3 | 329.9 | 12.3 | 14.6 | 24.5 |
| Dettl, et al., [70] | Germany (Aachen) | 28.9 | 11.5 | 661.4 | 14.0 | 14.2 | 28.9 |
| Didehnani, et al., [75] | USA (Dallas) | - | - | - | 18.9 | 16.5 | 37.1 |
| Fischer-Shorty, et al., [25] | Israel (Haifa) | - | 11.8 | - | 15.4 | 19.3 | 34.5 |
| Fujino, et al., [39] | Japan (Kyoto) | 24.2 | 13.1 | - | 14.2 | 15.9 | 31.4 |
| Fujiiwa, et al., [40] | Japan (Kyoto) | 26.9 | 10.4 | - | 14.3 | 13.9 | 32.7 |
| Güzewski, et al., [26] | Germany (Eisen) | 21.0 | 16.8 | 672.3 | 14.6 | 20.5 | 31.9 |
| Haker, et al., [65] | Switzerland (Zurich) | 24.0 | 11.0 | 297.0 | 12.2 | 14.6 | 26.3 |
| Hooker, et al., [23] | USA (Berkeley/San Francisco) | - | 24.5 | - | 11.7 | 16.5 | - |
| Horon, et al., [51] | USA (Los Angeles) | 20.8 | 26.8 | 282.5 | 1.5 | 1.7 | - |
| Horon, et al., [27] | USA (Los Angeles and Chapel Hill) | 21.0 | 20.0 | - | 2.5 | 2.1 | - |
| Kucharska-Pietura, et al., [68] | Poland (Lublin) | - | 8.6 | 408.1 | 39.4 | 59.8 | - |
Lam, et al., [36]  China (Hong Kong)  25.9  13.4  -  9.7  13.3  20.6
Lee, et al., [28]  South Korea (Seoul)  21.7  4.6  422.1  13.1  15.4  30.6
Lee, et al., [68]  USA (Los Angeles)  -  -  5.9  5.3  -  -
Lehmann, et al., [29]  Germany (Berlin)  29.8  10.0  407.8  13.2  15.9  -
Masumoto, et al., [30]  Japan (Kyoto)  -  15.2  -  16.1  6.6  10.6
McCormick, et al., [48]  USA (Iowa City)  20.7  15.8  -  4.6  9.2  -
McGuire, et al., [31]  Australia (Sydney)  22.5  22.7  -  1.3  2.1  -
McGuire, et al., [73]  Australia (Sydney)  21.6  21.80  -  1.7  2.1  -
Montag, et al., [42]  Germany (Berlin)  25.8  11.6  -  19.7  19.7  -
Montag, et al., [58]  Germany (Berlin)  26.5  10.4  453.8  17.0  19.4  35.6
Pijnenborg, et al., [60]  The Netherlands (Groningen)  24.2  7.0  -  12.8  15.3  29.2
Ramos-Loyo, et al., [62]  Mexico (Guadalajara)  -  23.4  200.0  16.9  17.8  28.9
Regenbogen, et al., [43]  Germany (Aachen)  27.8  9.5  -  14.2  23.1  -
Smith, et al., [47]  USA (Chicago)  -  14.4  360.9  0.6  0.6  -
Singh, et al., [32]  India (New Delhi)  23.7  9.5  389.3  8.6  12.6  -
Shamay-Tsoory, et al., [37]  Israel (Haifa)  -  -  -  16.5  21.0  -
Sparks, et al., [46]  Australia (Sydney)  -  -  300.9  38.8  39.3  -
Thirouc, et al., [35]  France (Paris)  -  11.8  664.4  21.6  32.2  -
Vistoli, et al., [59]  Canada (Québec)  -  7.6  547.7  16.0  9.6  -
Wojakiewicz, et al., [33]  France (Paris)  -  8.0  -  14.2  19.2  -

Table 2: Clinical data coded for patients with schizophrenia spectrum disorders from individual studies included in the meta-analysis.

Note: M = Mean; CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day. Supplemental data was provided by authors. M = Mean. In this table, only that study for which data was available is included.

| M General IQ Score in SSD | M General IQ Score in HC | M Pre-morbid/Verbal IQ Score in SSD | M Pre-morbid/Verbal IQ Score in HC | M Global Neuro-cognition Score in SSD | M Global Neuro-cognition Score in HC |
|---------------------------|--------------------------|------------------------------------|------------------------------------|--------------------------------------|--------------------------------------|
| Achim, et al., [10]       | 100.4                    | 101.8                              | -                                  | -                                    | -                                    |
| Berrada-Baby, et al., [87]| -                        | -                                  | 26.5                               | 28.9                                 | -                                    |
| Chiang, et al., [68]      | 83.9                     | 100.4                              | -                                  | -                                    | -                                    |
| Corbera, et al., [58]     | -                        | -                                  | -                                  | 39.6                                 | 52.0                                 |
| Corbera, et al., [50]     | 89.5                     | -                                  | -                                  | -                                    | 32.1                                 |
| Demet, et al., [44]       | -                        | 114.2                              | 30.2                               | 32.0                                 | -                                    |
| Dierl, et al., [70]       | -                        | -                                  | 107.7                              | 111.3                                | -                                    |
| Didehnani, et al., [75]   | 102.2                    | 112.1                              | -                                  | -                                    | -                                    |
| Fujino, et al., [39]      | -                        | -                                  | 103.1                              | 105.3                                | -                                    |
| Fujisawa, et al., [40]    | 104.0                    | 109.0                              | 104.0                              | 107.0                                | -                                    |
| Gizewski, et al., [26]    | -                        | -                                  | 102.2                              | 109.8                                | -                                    |
| Haker, et al., [65]       | -                        | -                                  | 24.4                               | 33.1                                 | 16.8                                 |
| Hooker, et al., [23]      | 101.1                    | -                                  | -                                  | -0.32                                | 0.4                                   |
| Kucharska-Pietura, et al., [61]| -                        | -                                  | -                                  | 24.4                                 | 37.4                                 |
| Lam, et al., [36]         | 34.9                     | 49.8                               | -                                  | 16.6                                 | 20.4                                 |
| Lee, et al., [28]         | -                        | -                                  | 11.4                               | 12.7                                 | 14.5                                 |
| Lehmann, et al., [29]     | -                        | -                                  | 108.5                              | 118.8                                | 25.0                                 |
| Matsumoto, et al., [30]   | -                        | -                                  | 101.7                              | 107.9                                | -                                    |
| McGuire, et al., [31]     | -                        | -                                  | 105.6                              | 107.7                                | 35.1                                 |
| McGuire, et al., [74]     | -                        | -                                  | 103.0                              | 109.5                                | 27.9                                 |
| Montag, et al., [42]      | -                        | -                                  | 25.8                               | 29.6                                 | -                                    |
| Montag, et al., [58]      | -                        | -                                  | 103.9                              | 108.9                                | -                                    |
| Pijnenborg, et al., [60]  | 90.2                     | 103.4                              | 41.9                               | 52.1                                 | 36.3                                 |

Citation: Varachhia S, Ferguson E, Doody GA (2018) A Meta-Analysis Taxonomizing Empathy in Schizophrenia. J Psychiatry Depress Anxiety 4: 016.
Table 3: Mean general IQ, pre-morbid/verbal IQ and global neuro cognitive scores for schizophrenia spectrum disorders and healthy controls coded from individual studies included in the meta-analysis.

Note: M = Mean; CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day. Supplemental data was provided by authors. M = Mean. In this table, only that study for which data was available is included.

| Study | General IQ, Healthy Controls | General IQ, Schizophrenia Spectrum Disorder | Verbal/Pre-morbid IQ, Healthy Controls | Verbal/Pre-morbid IQ, Schizophrenia Spectrum Disorder | Global Neuro-cognition, Healthy Controls | Global Neuro-cognition, Schizophrenia Spectrum Disorder |
|-------|-------------------------------|-------------------------------------------|----------------------------------------|-----------------------------------------------------|------------------------------------------|--------------------------------------------------------|
| Regenbogen, et al., [43] | 71.4 (20.3) | 57.6 (19.4) | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |
| Smith, et al., [47] | 71.4 | - | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |
| Sparks, et al., [46] | 71.4 | - | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |
| Thiroux, et al., [55] | 71.4 | - | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |
| Viatri, et al., [59] | 71.4 | - | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |
| Wojakiewicz, et al., [53] | 71.4 | - | 79.9 (40.7) | 74.9 (39.7) | 22.3 (12.6) | 0.32 |

Table 4: Study characteristics of included studies in the meta-analysis.

Note: Standard Deviation; K = Number of studies included; SPD = Schizophrenia Spectrum Disorders; HC = Healthy Control.

| Sample Type | Mean (SD)/Mean Percent (SD) | Range | K |
|-------------|-----------------------------|-------|---|
| Published Article | 94.9 | - | 37 |
| Poster (data from authors) | 5.1 | - | 2 |
| Year | 2012 | 2007-2017 | 39 |
| SPD Sample Size | 37.9 (31.4) | 10-145 | 39 |
| HC Sample Size | 33.2 (23.9) | 10-145 | 39 |
| Location | Europe | 53.3 | - | 13 |
| United States | 53.3 | - | 13 |
| Asia | 23.2 | - | 9 |
| Oceania | 10.3 | - | 4 |

Table 4: Study characteristics of included studies in the meta-analysis.

Note: Standard Deviation; K = Number of studies included; SPD = Schizophrenia Spectrum Disorders; HC = Healthy Control.

| Diagnosis | Mean (SD)/Mean Percent (SD) | Range | K |
|-----------|-----------------------------|-------|---|
| Schizophrenia | 93.2 (13.6) | 52.4-100 | 38 |
| Shizo-affective | 4.65 (15.6) | 2.7-42.9 | 10 |
| Other Psychoses | 1.86 (9.2) | 6.19-3.3 | 2 |
| Age at Diagnosis | 24.6 (3.1) | 20.7-30.5 | 22 |
| Duration of Schizophrenia | 13.5 (6.3) | 1.7-26.8 | 32 |
| Symptom Severity | Positive Symptoms | 13.9 (8.4) | 0.61-39.4 | 36 |
| Negative Symptoms | 16.6 (10.9) | 0.66-59.8 | 36 |
| General Symptoms | 31.0 (3.3) | 20.6-45.4 | 18 |
| Medication Dosage (Chlorpromazine equivalents) - mg/day | 414.3 (38.02) | 162.1-642.3 | 18 |

Table 5: Clinical characteristics of samples included in the meta-analysis.

Note: SD = Standard Deviation; K = Number of studies included.

| Demographic variables | Mean (SD)/Mean Percent (SD) | Range | K |
|-----------------------|-----------------------------|-------|---|
| Age, Healthy Controls | 35.2 (5.9) | 24-46 | 59 |
| Age, Schizophrenia Spectrum Disorders | 37.8 (6.1) | 25-48 | 38 |
| Education, Healthy Controls | 14.0 (1.7) | 9.8-16.7 | 27 |
| Education, Schizophrenia Spectrum Disorders | 12.5 (1.3) | 9.2-15.1 | 28 |
| Male, Healthy Controls | 63.9 (15.2) | 40-100 | 36 |
| Male, Schizophrenia Spectrum Disorder | 67.5 (15.2) | 47-100 | 36 |
| Ethnicity, Healthy Controls | Caucasian-69.1 (28.6) | 31-100 | 8 |
| Non-Caucasian-31.3 (28.1) | 24-100 | 7 |
| Ethnicity, Schizophrenia Spectrum Disorder | Caucasian-67.0 (27.6) | 43.3-100 | 8 |
| Non-Caucasian-33.0 (24.8) | 47-100 | 8 |

Table 7: Demographic characteristic of samples included in the meta-analysis.

Note: SD = Standard Deviation; K = Number of studies included.
Empathy measures

The Interpersonal Reactivity Index (IRI) [19] was used in 87.2% (k = 34) of included studies. Besides this, five studies [37,60,61,63,75] used the Empathy Quotient [89], Balanced Emotional Empathy Scale [89], Questionnaire Measure of Emotional Empathy [90] and Social Context Emotional Recognition Task [62] respectively (Supplementary Table S1 for a description of the empathy measures included).

Symptom assessment

Symptoms of schizophrenia was assessed in 92.3% (k = 36) of included studies. Assessment tools included the PANS [22]; SAPS [91]; SANS [92] and the Brief Psychiatric Rating Scale (BPRS) [93] (Supplementary Table S2).

Assessment of neuro-cognition

Broadly, data for neuro-cognition was available for k = 13 studies. We identified several studies assessing neuro-cognition [37,44,51,70] for which we could not gather the required data within our data collection timeframe.

One study [58] measured all six neuro-cognitive domains (i.e. attention, speed of processing, working memory (verbal and non-verbal), visual learning, verbal learning, reasoning and problem solving) using the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB) [94]). Barring the attention domain, Hooker, et al., [23] also measured the above-mentioned domains using the MCCB. Although Smith and colleagues [47] reported not to have used the MCCB battery, nonetheless assessed the six neuro-cognitive domains using approximate measures representing the MCCB assessment battery [94]. Across the remaining ten studies [29,31,36,43,51,60,61,65,69,74] few, but not all six neuro-cognitive domains were assessed using tests that differed from but comparable to the MCCB. For example, Lam, et al., [36] assessed the reasoning and problem solving, and visual learning domain, whereas other studies (see for example, [61]), assessed the attention and working memory (non-verbal) domain. We also found few studies [31,51,65,68] to have examined cognitive flexibility, which we additionally included within the global neuro-cognitive moderator (Supplementary Table S3 for a description of the neuro-cognitive measures used in individual studies and the corresponding neurocognitive domain examined).

In total, 15 studies measured pre-morbid/verbal IQ. Pre-morbid/verbal IQ was measured in 13 of these studies using either the Multiple-choice vocabulary test (German version) (MCVT) [95] or National Adult Reading Test (NART; [96]). MCVT was included by seven studies [26,29,42-44,58,70] and NART by six studies [30,31,39,46,73,74,88]. The remaining two studies [28,40] used the verbal sub-set from the Wechsler’s Adult Intelligence Scale - III [97] (Supplementary Table S4 for a short description of each of the verbal task used by the included studies).

Data for general IQ was available for ten of the included studies. Eight of these studies [10,23,33,40,50,59,68,75] used several versions of the Wechsler’s Adult Intelligence Scales (e.g. [97]). The remaining two studies [36,60] used the Raven’s Progressive Matrices Test (120) and Groninger Intelligence Test [98] respectively (Supplementary Table S5 for a description of the general IQ measures used by the included studies).

Sensitivity analysis

For cognitive empathy, a medium effect size (k =36, Hedges’ g = 0.53, 95% CI [0.43, 0.64], p<0.001) was found, such that the healthy control group reported to have better perspective-taking ability than the schizophrenia group (Figure 2). The Q-statistic was significant (Q-statistics = 52.88, df = 35, p = .02) with an I² index of 33.82%.

For affective empathy, a small effect size was found (k = 39, Hedges’ g = 0.29, 95% CI [0.16, 0.42], p<0.001) (Figure 3). This indicated the healthy control group had better affective empathic ability than the schizophrenia group. The Q-statistic was significant (Q-statistics = 98.21, df = 38, p<0.001) with an I² index of 61.31%.

Meta-analyses examining impact of co-morbid psychiatric condition on empathy

We ran additional meta-analyses, excluding studies including schizo-affective patients. For cognitive empathy, the effect size remained medium (k = 26, Hedges’ g = 0.51, 95% CI [0.39,0.63], p<0.05) and for affective empathy, it remained small (k = 29, Hedges’ g = 0.24, 95% CI [0.12,0.30], p<0.05). Thus, all samples were retained for subsequent analyses.

Figure 2: Forest plot of studies included in the cognitive empathy meta-analysis (k = 36).
Moderator analyses

The clinical characteristics: Duration of illness (in years), age at diagnosis (in years) mean symptom severity score (positive, negative and general), and medication dosage (mg/day) (chlorpromazine equivalents). Neuro-cognition: Mean general, verbal/pre-morbid and global neuro-cognition score, and demographic variables: Mean age of schizophrenia patients (in years), gender (higher percent of schizophrenia male samples), education (lower educational attainment in schizophrenia) (in years), ethnicity (higher percent of non-Caucasian compared to Caucasian schizophrenia patient) and year of study publication were examined as continuous moderators for each domain of empathy.

Cognitive empathy

Meta-regression found the duration of illness significantly moderated the difference between samples (i.e., schizophrenia vs healthy controls) on measures of cognitive empathy. Such that for every one-year increase in duration of illness, the standardised mean difference in performance between schizophrenia and healthy controls increased by 0.012. This significant finding was accompanied by a decrease in the $I^2$ index to 3.27%. Thus, the duration of illness explained 30.55% of the initially observed $I^2$ index. Age at diagnosis was also found to negatively moderate the difference in performance between patients and controls, such that as the age of symptom onset decreased, differences in performance between the two groups increased by -0.06 points. This effect was accompanied by a decrease in the $I^2$ index by 5.12%, thus explaining 28.70% of the initially observed $I^2$ index (Table 8). Besides this, none of the other moderators reached statistical significance (Table S6-S8).

Affective empathy

Meta-regression analyses found none of the clinical, cognitive and demographic moderators reached statistical significance (Table S9-S11).

Publication bias

For affective empathy, the Trim and Fill approach [81] identified four missing studies, with the effect size increasing to Hedges’ $g = 0.37$ ($p<0.05$). However, the classic fail-safe $N$ identified that we would need 409 missing studies to bring the $p$-value of the current observed effect size to non-significance. For cognitive empathy, nine studies were identified as missing, with the effect size reducing to Hedges’ $g = 0.41$ ($p < 0.05$). Here the fail-safe $N$ identified 1,367 non-significant studies necessary to bring the current effect size to nil (see Figures 4 and 5 for the funnel plots with imputed studies).

Discussion

As well as synthesising the extant literature on empathy in schizophrenia, this study considerably expanded past work by examining the moderating effect of clinical (positive, negative, general, medication effect, age at diagnosis and duration of illness), demographic (age, gender, education, ethnicity and year of publication) and...
cognitive (verbal/pre-morbid IQ, general IQ and global neuro-cognition) variables on cognitive and affective empathy. In doing this, we went beyond examining basic associations observed in the literature and developed an evidence-based taxonomy of empathy in schizophrenia. Consistent with our hypotheses, we found, healthy controls reported higher levels of affective empathy than schizophrenia patients (a small effect size). For cognitive empathy, the difference in reporting between the two groups was of a medium effect, with healthy controls reporting higher perspective-taking ability then the patient group. Amongst the variables studied, duration of illness and age at illness onset significantly moderated the difference in performance between patients and controls on measures of cognitive empathy. Besides these, none of the other moderators reached statistical significance. The effect sizes reported in this study are in line with previous reviews on this topic [11, 12].

Moderating Effect of Clinical variables on Empathy

Duration of illness and empathy

For the moderating effect of duration of illness, we found, for every one-year increase in illness duration, the difference in perspective-taking ability between patients and healthy controls increased by 0.012 points. This observation is consistent with a previous meta-analysis on this topic [12]. Adding further, we found this effect to be independent of any age-related decline in schizophrenia. Cross-sectional studies are the norm rather than the exception in this field of research. However, as the current evidence points to a progressive decline in self-reported cognitive empathy, our findings can be said to provide indirect, longitudinal evidence of deterioration over time. This can be explained by several reasons. For example, the distress caused by psychotic thinking, perhaps due to poorer clinical insight can make people with a diagnosis of schizophrenia mistrustful of others, which in turn could lead to social withdrawal [99] or a restriction in their social network [100]. Over time, this can lead to patients having fewer opportunities to socialise and hone their empathic skills, thus increasing the probability of empathic atrophy over time. Besides this, long-term residual symptom experiences, medication side-effects, sensitivity to stress, and substance misuse may also affect key cortical regions associated with empathy [23, 32, 39]. High level of stigma associated with schizophrenia [101], as well as a loss of morale and self-esteem over time can also lead to a loss of hope, confidence and motivation in people with schizophrenia [102], all of which can negatively impede a patient’s ability to engage confidently or communicate effectively in an empathetic manner.

Age at clinical diagnosis also had a moderating effect on cognitive empathy. As the age at diagnosis decreased, the difference in performance between patients and controls on self-reported cognitive empathy increased. This means that those with an earlier diagnosis-reported having greater difficulties in perspective-taking than those whose symptom onset was at a later age. Duration of illness and age at diagnosis are related. Both are reliable indicators of severity of illness in schizophrenia (i.e. the earlier the onset, the worse it is regarding functional outcome, and the longer it persists without remission, the less likely you are to improve) [103]. Therefore, it will be important to address the underlying mechanisms of this deficit in future work.

Clinical symptoms and empathy

We found none of the schizophrenia symptoms (i.e., positive, negative and general symptoms) moderated the effect sizes for cognitive or affective empathy. Amongst the included studies (k = 39), only a few studies reported a significant association between severity of clinical symptoms and empathy [37, 46, 47, 51, 58, 61, 62], with several studies not finding any statistically significant relationship between either one of the core schizophrenia symptoms and self-reported empathy [10, 23, 29, 32, 36, 39, 40, 47, 42, 43, 58, 65, 70, 88]. A closer inspection of the clinical profile of the schizophrenia group we were analysing indicated that this group was on a stable dosage of antipsychotics at the time of testing and were, therefore, only really experiencing symptoms residually (Table 5). Therefore, a restricted range in the symptom severity score or the fact that most patients were not experiencing symptoms acutely could explain the lack of relationship with empathy.

We found no moderating effect of chlorpromazine equivalents (mg/day) on self-reported cognitive and affective empathy. These findings are consistent with studies that directly compared the effects of chlorpromazine equivalent on self-reported empathy [29, 32, 44, 46, 47]. These findings also extend to haloperidol equivalents [32, 39, 40]. Singh, et al. [32] also reported having found no effect of duration of antipsychotic drug taken on any of the IRI scores in an enduring schizophrenia sample. Also, in one of the largest sample study comparing patients treated on conventional versus atypical antipsychotic drugs on social cognitive abilities, Kucharska-Pietura and colleagues [61] found no clear advantage of atypical antipsychotics over typical antipsychotics on emotional functioning in patients with schizophrenia. Results from several longitudinal studies [104] have also indicated no significant effect of antipsychotic drug treatment on several other related social-cognitive domains (e.g. facial affect perception). Thus, it appears that while antipsychotic drugs are useful in treating core symptoms of schizophrenia, deficits in empathy may perhaps be resistant to pharmacological intervention.

Demographic variables and empathy

This study included many studies which provided us with a large sample to examine several demographic variables more thoroughly. These included; the impact of age-related decline, a higher proportion of male patients (compared to female patients), ethnicity (higher proportion of non-Caucasian schizophrenia patients compared to Caucasian patients), and lower educational attainment in the schizophrenia group (compared to the healthy group), on self-reported cognitive and affective empathy. None of these demographic variables directly moderated the difference in performance between patients and controls on self-reported measures of empathy, which is consistent with several independent studies in the literature. In relation to age, several studies included this variable as a covariate and consistent with the current findings, found schizophrenia patients and controls continued to differ on empathic abilities [46, 75]. Similarly, a direct examination of gender-related effects in schizophrenia patients, on measures of cognitive and affective empathy, also revealed no significant interaction [39, 40, 58, 105] or any impact of lower education attainment on empathy [36, 46, 61, 68]. Collectively, these findings suggest other risk factors not observed here may have superseded current demographic risk factors in patients with schizophrenia.

Neuro-cognition and empathy

Several neuro-cognitive variables were examined in relation to empathy. These included: Verbal/pre-morbid IQ, general IQ and global
neuro-cognition. Regarding general and pre-morbid/verbal IQ, neither variable moderated the differences in performance between patients and controls. This finding is consistent with several studies in which differences on measures of empathy remained between groups of interest after controlling for these initial differences [40,42,75]. Together these findings indicate, that while impairments in general and verbal/pre-morbid IQ remain apparent in patients with more severe and enduring schizophrenia [29,30,36,38,58,59,60,68,74,75] they do not adequately account for the heterogeneity observed in empathy in this or previous reviews [12].

In this study, instead of examining individual neuro-cognitive domains, we examined what we termed ‘global neuro-cognitive abilities’ by including studies that assessed all, few or one of the six neuro-cognitive domains defined and recommended by the MATRICS panel [72,73] as well as an additional, cognitive flexibility/inhibitory control domain. Overall, we did not find any impact of this variable on cognitive or affective empathy which is consistent with several of the published studies in the field [23,27,58]. However, as it is well established that like IQ, neuro-cognitive deficits do exist in patients with more severe and enduring schizophrenia [106] and is an essential component of empathy [31,36,47,51,74]. Therefore, the lack of association is somewhat surprising. It may be that this moderator was somewhat underpowered, or there was a lack of dispersion in the neuro cognitive scores. Alternatively, it may have been that for neuro-cognitive abilities to relate to empathy; tasks need tapping into specific cognitive abilities. In other words, specific executive function tasks (e.g. emotion-regulation) relating to empathy [78,101] is perhaps necessary to find a significant effect.

Affective empathy and heterogeneity

For affective empathy, we found, healthy controls reported higher affective empathy than schizophrenia patients, with a small effect size (Hedges’ $g = 0.29$) with significant heterogeneity ($F = 61.31\%$), both findings are consistent with previous reviews in the field [11,12]. However, none of the moderators we examined explained the observed heterogeneity. This may be due to variability in the affective responses by the included patients. Across individual studies, we found, three affective responses: (1) Some patients reported to have deficits in affective empathy (i.e. lower levels than healthy controls) [26-29,31-33,36,37,47,51,58,68,69,74], (2) Other studies reported comparable levels of affective empathy in schizophrenia patients and healthy controls [10,24,39,59,60,62] and (3) the remaining, reported higher levels of affective empathy in patients than in controls [27,29,30,35,43,50,88]. Thus, under the rubric of schizophrenia, several affective responses may have been present, which could explain both, the small effect size and lack of moderator influence found in this study.

Limitations

Publication bias

We found an interesting effect of publication bias on current findings. For affective empathy, we found that the missing studies increased the overall effect size from the observed Hedges’ $g = 0.29$ to Hedges’ $g = 0.37$. In the studies we included, we found, patients were medically stable at the time of testing (symptom severity score; Table 5). The nature of some symptoms, especially negative symptoms means social withdrawal and anhedonia are common, and as such, patients with these experiences are unlikely to participate in research studies. Therefore, for affective empathy, the publication bias is perhaps reflective of missing studies of patients with predominantly negative symptoms where deficits in affective empathy are likely to be more pronounced.

For cognitive empathy the opposite held. In total, nine studies were identified as missing (Figure 5) and including them would have reduced the effect size from Hedges’ $g = 0.53$ to Hedges’ $g = 0.41$. This observation is consistent with a previous meta-analysis in the field [12] and together highlight two important issues: (1) The need to also publish nil findings and (2) where possible, include schizophrenia samples at different stages of the illness course, particularly at the earlier phase, where deficits in perspective-taking are likely to be less pronounced then in the more severe and enduring phase.

Measures of empathy: Self-report

Our findings for empathy are reported from self-report measures. Thus, they must be interpreted as showing how patients perceive their abilities as opposed to their actual abilities, which may differ [11]. We did not include performance-based measures since few studies have been published and a lack of psychometric properties was available for those measures [33]. Moreover, self-reported measures are more acceptable to patients, and since they tap into a wide range of situations, they are more apt in providing broader estimates of empathy levels than other measures (e.g. performance-based) which evaluate responses to specific circumstances.

Impact of additional variables

The impact substance misuse (drugs and alcohol), co-morbid medical illness, and family history of psychiatric illness has on self-reported empathy was not be examined as no or insufficient data was available for these variables. Nonetheless, these are important variables commonly found to affect patients with a diagnosis of schizophrenia [23,26,32,39] and may have therefore conflated current findings. Thus, it is important that readers take this into account when interpreting current results and report on these additional variables in future work.

Generalisability of current findings

We did not find any impact of year of publication on reported effect sizes. This means, over the years, there have been no significant changes in the methodology and samples recruited. We found schizophrenia samples in this, and previous reviews [10-12], can be classified as ‘stereotypical schizophrenia samples’. This includes a predominantly chronic, male sample, on medication, with core schizophrenia symptoms stable, with minimum (if any) negative symptoms. Since schizophrenia is a heterogenous syndromic disorder, care must be taken in term of the extent to which we generalise current findings to other phases or schizophrenia samples.

Also, over 90 percent of the studies included were conducted in developed countries (Table 1). Better outcomes have been found in many developing compared to developed countries [101]. Thus, findings from this study may not be fully general is able to those recovering in developing countries.
Conclusion

In conclusion, we found a prolonged illness course or earlier diagnosis taxonomized deficits in cognitive empathy in patients with enduring schizophrenia. For affective empathy, we conclude, some patients report a deficit; others report comparable levels to healthy controls, and the remaining report experiencing higher emotional arousal then healthy controls. As an earlier diagnosis, prolonged illness course and dysfunctional emotional reactions are significant risk factors of poorer empathic interactions; it will be important to address the underlying mechanisms of these deficits in future work.

Supplementary Material

Funding

This work was supported by the Economic and Social Research Council [grant number 1379509].

Acknowledgement

We would like to thank the many authors who provided supplementary data to help with coding their study in this review.

References

1. Cheng Y, Chena C, Decety J (2014) An EEG/ERP investigation of the development of empathy in early and middle childhood. Dev Cogn Neurosci 10: 160-169.
2. Decety J, Cowell JM (2014) The complex relation between morality and empathy. Trends Cogn Sci 18: 337-339.
3. Ferguson E (2016) Empathy “The good, the bad and the ugly”. In: Wood A, et al., (Eds.) Posi clinic psychol: An integrative approach to studying and improving well-being. Wiley-Blackwell, Chichester, UK. Pg no: 103-124.
4. Batson CD (1991) The altruism question: Towards a social-psychological answer. Lawrence Erlbaum Associates, Inc, Routledge, Hillsdale, New Jersey, USA, Pg no: 268.
5. Reniers RL, Corcoran R, Drake R, Shryane NM, Völlm BA (2011) The QCAE: A questionnaire of cognitive and affective empathy. J Personali Asses 93: 84-95.
6. Blair RJ (2005) Responding to the emotions of others: Dissociating forms of empathy through the study of typical and psychiatric populations. Conscious Cogn 14: 698-718.
7. Spinella M (2005) Prefrontal substrates of empathy: Psychometric evidence in a community sample. Send to Biol Psychol 70: 175-181.
8. Lee KH, Farrow TF, Spence SA, Woodruff PW (2004) Social cognition, brain networks and schizophrenia. Psychol Med 34: 391-400.
9. Bleuler E (1950) Dementia Praecox or the Group of Schizophrenias. International Universities Press, Madison, Connecticut, USA.
10. Achim AM, Ouellet R, Roy MA, Jackson PL (2011) Assessment of empathy in first-episode psychosis and meta-analytic comparison with previous studies in schizophrenia. Psychiatry Res 190: 3-8.
11. Bonfils KA, Lysaker PH, Minor KS, Salyers MP (2016) Affective empathy in schizophrenia: A meta-analysis. Schizophr Res 175: 109-117.
12. Bonfils KA, Lysaker PH, Minor KS, Salyers MP (2017) Empathy in schizophrenia: A meta-analysis of the Interpersonal Reactivity Index. Psychiatry Res 249: 293-303.
13. Bleuler E (1911) Dementia Praecox: Or the Group of Schizophrenias. International Universities Press, New York, USA.
14. Kraepelin E (1919) Dementia praecox and paranoia. Chicago Medical Book Co, Chicago, USA.
15. Davis MH (1983) Measuring individual differences in empathy: Evidence for a multidimensional approach. J Pers Soc Psychol 44: 113-126.
16. Decety J (2011) The neuroevolution of empathy. Ann NY Acad Sci 1231: 35-45.
17. Eisenberg N, Strayer J (1987) Critical issues in the study of empathy. In: Eisenberg N, et al. (Eds.) Empath and its Develop, Cambridge University Press, Cambridge, UK, Pg no: 13.
18. Jolliffe D, Farrington DP (2004) Empathy and offending: A systematic review and meta-analysis. Aggress Violent Behav 9: 441-476.
19. Davis MH (1990) A multidimensional approach to individual difference in empathy. American Psychological Association Massachusetts, USA.
20. Harrington L, Siegert RJ, Mcclure J (2005) Theory of mind in schizophrenia: a critical review. Cogn Neuropsychiatry 10: 249-286.
21. American Psychiatric Association (2013) Diagnostic and Statistical Manual of Mental Disorders, (5th edn), APA, Washington, DC, USA.
22. Kay SR, Fisbein A, Opler LA (1987) The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 13: 261-276.
23. Hooker CI, Bruce L, Lincoln SH, Fisher M, Vinogradov S (2011) Theory of mind skills are related to gray matter volume in the ventromedial prefrontal cortex in schizophrenia. Biol Psychiatry 70: 1169-1178.
24. Brown EC, Gonzalez-Liencres C, Tan C, Brune M (2016) Reward modulates the mirror neuron system in schizophrenia: A study into the mu rhythm suppression, empathy, and mental state attribution. Soc Neurosci 11: 175-186.
25. Fischer-Shofty M, Brüne M, Ebert A, Shefet D, Levkovitz Y, et al. (2013) Improving social perception in schizophrenia: The role of oxytocin. Schizophr Res 146: 357-362.
26. Gизewski ER, Müller BW, Scherbaum N, Lieb B, Forsting M, et al. (2013) The impact of alcohol dependence on social brain function. Addict Biol 18: 109-120.
27. Horan WP, Reise SP, Kern RS, Lee J, Penn DL, et al. (2015) Structure and correlates of self-reported empathy in schizophrenia. J Psychiatr Res 66-67: 60-66.
28. Lee SJ, Kang DH, Kim CW, Gu BM, Park JY, et al. (2010) Multilevel comparison of empathy in schizophrenia: an fMRI study of a cartoon task. Psychiatry Res 181: 121-129.
29. Lehmann A, Bahcesular K, Brockmann EM, Biederbick, SE, Dziobek I, et al. (2014) Subjective experience of emotions and emotional empathy in paranoid schizophrenia. Psychiatry Res 220: 825-833.
30. Matsumoto Y, Takahashi H, Murai T, Takahashi H (2015) Visual processing and social cognition in schizophrenia: Relationships among eye movements, biological motion perception, and empathy. Neurosci Res 90: 95-100.
31. McGuire J, Barbanel L, Brüne M, Langdon R (2015) Re-examining Kohlberg’s conception of morality in schizophrenia. Cogn Neuropsychiatry 20: 377-381.
32. Singh S, Modi S, Goyal S, Kaur P, Singh N, et al. (2015) Functional and structural abnormalities associated with empathy in patients with schizophrenia: An fMRI and VBM study. J Biosci 40: 355-364.
33. Wojakiewicz A, Januel D, Braha S, Prkachin K, Danziger N, et al. (2013) Alteration of pain recognition in schizophrenia. Eur J Pain 17: 1385-1392.
34. Montag C, Brockmann EM, Lehmann A, Müller DJ, Rujescu D, et al. (2012) Association between oxytocin receptor gene polymorphisms and self-rated ‘empathic concern’ in schizophrenia. PLoS One 7: 51882.

35. Thirious B, Tandonnet L, Jaaflari N, Berthoz A (2014) Disturbances of spontaneous empathic processing relate with the severity of the negative symptoms in patients with schizophrenia: A behavioural pilot-study using virtual reality technology. Brain Cogn 90: 87-99.

36. Lam BY, Raine A, Lee TM (2014) The relationship between neurocognition and symptomatology in people with schizophrenia: Social cognition as the mediator. BMC Psychiatry 14: 138.

37. Shamay-Tsoory SG, Shur S, Harari H, Levkovitz Y (2007) Neurocognitive basis of impaired empathy in schizophrenia. Neuropsychology 21: 431-438.

38. Corbella S, Wexler BE, Ikezawa S, Bell MD (2013) Factor structure of social cognition in schizophrenia: Is empathy preserved? Schizophrenia Research and Treatment 1-13.

39. Fujino J, Takahashi H, Miyata J, Sugihara G, Kubota M, et al. (2014) Impaired empathic abilities and reduced white matter integrity in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 48: 117-123.

40. Fujiwara H, Shimizu M, Hiroko K, Miyata J, Namiki C, et al. (2008) Female specific anterior cingulate abnormality and its association with empathic disability in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 32: 1726-1734.

41. Haker H, Rössler W (2009) Empathy in schizophrenia: Impaired resonance. Eur Arch Psychiatry Clin Neurosci 259: 352-361.

42. Montag C, Heinz A, Kunz D, Gallinat J (2007) Self-reported empathic abilities in schizophrenia. Schizophr Res 92: 85-89.

43. Regenbogen C, Kellermann T, Seubert J, Schneider DA, Gur RE, et al. (2015) Neural responses to dynamic multimodal stimuli and pathology-specific impairments of social cognition in schizophrenia and depression. Br J Psychiatry 206: 198-205.

44. Derntl B, Finkelmeyer A, Voss B, Eickhoff SB, Kellermann T, et al. (2012) Neural correlates of the core facets of empathy in schizophrenia. Schizophr Res 142: 58-64.

45. Sparks A, McDonald S, Lino B, O’Donnell M, Green MJ (2010) Social cognition, empathy and functional outcome in schizophrenia. Schizophr Res 122: 172-178.

46. Smith MJ, Horan WP, Cobia DJ, Karpouzian TM, Fox JM, et al. (2014) Performance-based empathy mediates the influence of working memory on social competence in schizophrenia. Schizophr Bull 40: 824-834.

47. McCormick LM, Brumm MC, Beadle JN, Paradiso S, Yamada T, et al. (2012) Mirror neuron function, psychosis, and empathy in schizophrenia. Psychiatry Res 201: 233-239.

48. National Institute for Health and Care Excellence (NICE) (2014) Psychosis and schizophrenia in adults: Prevention and management. Clinical guideline, London.

49. Corbella S, Cook K, Brocke S, Dunn S, Wexler BE, et al. (2014) The relationship between functional deficits and empathy for emotional pain in schizophrenia. Biol Psychiatry 75: 200.

50. Horan WP, Pineda IA, Wynn JK, Jacoboni M, Green MF (2014) Some markers of mirroring appear intact in schizophrenia: Evidence from mu suppression. Cogn Affect Behav Neurosci 14: 1049-1060.

51. Bardenstein KK, McGlashan TH (1990) Gender differences in affective, schizoaffective, and schizophrenic disorders: A review. Schizophr Res 3: 159-172.

52. Cernovsky ZZ, Landmark JA, O’Reilly RL (1997) Symptom patterns in schizophrenia for men and women. Psychol Rep 80: 1267-1271.

53. Meltzer HY, Rabinowitz J, Lee MA, Cola PA, Ranjan R, et al. (1997) Age at onset and gender of schizophrenic patients in relation to neuroleptic resistance. Am J Psychiatry 154: 475-482.

54. Halari R, Kumari V, Mehtrotra R, Wheeler M, Hines M, et al. (2004) The relationship of sex hormones and cortisol with cognitive functioning in schizophrenia. J Psychopharmacol 18: 366-374.

55. Lindamer LA, Bailey A, Hawthorne W, Folsom DP, Gilmer TP, et al. (2003) Gender differences in characteristics and service use of public mental health patients with schizophrenia. Psychiatr Serv 54: 1407-1409.

56. Goldstein JM, Link BG (1988) Gender and the expression of Schizophrenia. J Psychiatr Res 22: 141-155.

57. Montag C, Brockmann EM, Lehmann A, Muller DJ, Rujescu D, et al. (2012) Association between oxytocin receptor gene polymorphisms and self-rated ‘empathic concern’ in schizophrenia. PLoS One 7: 51882.

58. Vistoli D, Lovioce, MA, Sutliff S, Jackson PL, Achim AM (2017) Functional MRI examination of empathy for pain in people with schizophrenia reveals abnormal activation related to cognitive perspective-taking but typical activation linked to affective sharing. J Psychiatry Neurosci 42: 263-272.

59. Pijnenborg GH, Spikman JM, Jerominus BF, Alemann A (2013) Insight in schizophrenia: associations with empathy. Eur Arch Psychiatry Clin Neurosci 26: 299-307.

60. Kucharska-Pietura K, Tylec A, Czemikiewicz A, Mortimer A (2012) Attentional and emotional functioning in schizophrenia patients treated with conventional and atypical antipsychotic drugs. Med Sci Monit 18: 44-49.

61. Ramos Loyo J, Mora Reynoso L, Sanchez Loyo LM, Medina Hernandez V (2012) Sex differences in facial, prosodic and social context emotional recognition in early-onset schizophrenia. Schizophrenia Research and Treatment 1-12.

62. Sparks A, McDonald S, Lino B, O’Donnell M, Green MJ (2010) Social cognition, empathy and functional outcome in schizophrenia. Schizophrenia Res 122: 172-178.

63. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I (2001) The “Reading the Mind in the Eyes” test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. J Child Psychol Psychiatry 42: 241-251.

64. Haker H, Rössler W (2009) Empathy in schizophrenia: Impaired resonance. Eur Arch Psychiatry Clin Neurosci 259: 352-361.

65. Montag C, Brockmann EM, Lehmann A, Muller DJ, Rujescu D, et al. (2012) Association between oxytocin receptor gene polymorphisms and self-rated ‘empathic concern’ in schizophrenia. PLoS One 7: 51882.

66. Pijnenborg GH, Spikman JM, Jerominus BF, Alemann A (2013) Insight in schizophrenia: associations with empathy. Eur Arch Psychiatry Clin Neurosci 26: 299-307.

67. Chiang SK, Hua MS, Tam WCC, Chao JK, Shiah YJ (2014) Developing an alternative chinese version of the interpersonal reactivity index for normal population and patients with schizophrenia in taiwan. Brian Impairment 15: 10-131.

68. Lee J, Zaki J, Harvey PO, Ochsner K, Green MF (2011) Schizophrenia patients are impaired in empathic accuracy. Psychol Med 41: 2297-2304.

69. Derntl B, Seidel EM, Schneider F, Habel U (2012) How specific are social cognition empathic abilities in schizophrenia, bipolar and depressed patients. Schizophr Res 142: 58-64.

70. Miller EK, Wallis JD (2009) Executive Function and Higher-Order Cognition: Definition and Neural Substrates. Ene NeuroSci 4: 99-104.
72. Kern RS, Nuechterlein KH, Green MF, Baade LE, Fenton WS, et al. (2008) The MATRICS consensus cognitive battery, part 2: Co-norming and standardization. Am J Psychiatry 165: 214-220.
73. Nuechterlein KH, Green MF, Kern RS, Baade LE, Barch DM, et al. (2008) The MATRICS consensus cognitive battery, part 1: Test selection, reliability, and validity. Am J Psychiatry 165: 203-213.
74. McGuire J, Brüne M, Langdon R (2017) Judgement of moral and social transgression in schizophrenia. Compr Psychiatry 76: 160-168.
75. Didehbani N, Shad MU, Tammringa CA, Kandalaft MR, Krawczyk DC, et al. (2012) Insight and empathy in schizophrenia. Schizophr Res 142: 246-247.
76. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. PLoS Med 6: 1000097.
77. Andreasen NC, Pressler M, Nopoulos P, Miller D, Ho BC (2010) Antipsychotic dose equivalents and dose-years: A standardized method for comparing exposure to different drugs. Biol Psychiatry 67: 255-262.
78. Decety J, Jackson PL (2006) A social-neuroscience perspective on empathy. Current Directions In Psychological Science 15: 54-58.
79. Hedges LV (1981) Distribution theory for glass’s estimator of effect size and related estimators. Journal of Educ 6: 107-128.
80. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Introduction to meta-analysis. John Wiley & Sons, Chichester, UK.
81. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Introduction to Meta-Analysis. John Wiley & Sons, Ltd, Chichester, UK.
82. Duval S, Tweedie R (2000) Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 56: 455-463.
83. Card NA (2012) Applied Meta-Analysis for Social Science Research. Guilford Press, New York, USA.
84. Lipsey MW, Wilson DB (2001) Practical Meta-Analysis. SAGE Publications, California, USA.
85. Cohen J (1992) A power primer. Psychol Bull 112: 155-159.
86. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2011) Comprehensive Meta-Analysis (Version 2). Biostat, Englewood, USA.
87. Andrews SC, Enticott PG, Hoy KE, Fitzgerald PB (2013) Mirror systems and social cognition in schizophrenia. Schizophr Bull 39: 218.
88. Berrada-Baby Z, Oker A, Courageon M, Urbach M, Buzin N, et al. (2016) Patients with schizophrenia are less prone to interpret virtual others’ empathetic questioning as helpful. Psychiatry Research 242: 67-74.
89. Mehrabian A (2000) Manual for the Behavioural Emotional Empathy Scale (BEES).
90. Mehrabian A, Epstein N (1972) A measure of emotional empathy. J Pers 40: 525-543.
91. Andreasen NC (1989) Scale for the Assessment of Negative Symptoms (SANS). The British Journal of Psychiatry 155: 53-58.
92. Andreasen NC (1984) Scale for the assessment of positive symptoms: SANS/SAPS. Dept. of Psychiatry, College of Medicine, the University of Iowa, Iowa City, Iowa, USA.
93. Overall JE, Gorham DR (1962) The brief psychiatric rating scale. Psychological Reports 10: 799-812.
94. Nuechterlein KH, Green MF (2006) MATRICS Consensus Cognitive Battery Manual. MATRICS Assessment Inc, Los Angeles, USA.
95. Lehrl S, Triebig G, Fischer B (1995) Multiple choice vocabulary test MWT as a valid and short test to estimate premorbid intelligence. Acta Neurol Scand 91: 335-345.
96. Nelson HE (1982) National Adult Reading Test (NART) test manual (Part 1). NFER-Nelson, Windsor, UK.
97. Wechsler D (1997) Wechsler Adult Intelligence Scale (3rd edn). Psychological Corporation, San Antonio, USA.
98. Luteijn F, Van der Ploeg FAE (1983) Groninger Intelligenet Test. Swets and Zeitlinger, Lisse, Netherlands.
99. Watkins J (1996) Living with Schizophrenia. Hill of Content Publishing Co Pty Ltd, Victoria, Australia.
100. Horan WP, Green MF, Kring AM, Nuechterlein KH (2006) Does anhedonia in schizophrenia reflect faulty memory for subjectively experienced emotions? J Abnorm Psychol 115: 496-508.
101. Jablensky A, Sartorius N (2008) What did the WHO studies really find? Schizophr Bull 34: 253-255.
102. Leff J (2001) The unbalanced mind. Columbia University Press, New York, USA.
103. Gulati G, Lynall ME, Saunders K (2014) Schizophrenia. In Psychiatry Lecture Notes (11th Edn). Wiley Blackwell, Oxford, UK.
104. Heilbronner U, Samara M, Leucht S, Falkai P, Schulze TG (2016) The Longitudinal Course of Schizophrenia Across the Lifespan: Clinical, Cognitive, and Neurobiological Aspects. Harv Rev Psychiatry 24: 118-128.
105. Derntl B, Finkelmeyer A, Toygar TK, Hülsmann A, Schneider F, et al. (2009) Generalized deficit in all core components of empathy in schizophrenia. Schizophr Res 108: 197-206.
106. Bora E (2017) A comparative meta-analysis of neurocognition in first-degree relatives of patients with schizophrenia and bipolar disorder. Eur Psychiatry 45: 121-128.
Supplementary

| Measures of Empathy                                      | Original Article | Studies in Meta-Analysis | Description of Tasks and Scores Produced                                                                                     |
|----------------------------------------------------------|------------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Interpersonal Reactivity Index (IRI)                     | [1]              | [2-35]                  | A 28-item self-report scale including four sub-scales: Empathic Concern, Perspective-Taking, Personal Distress and Fantasy. The Empathic Concern sub-scale taps into ‘other-oriented’ feelings of sympathy and concern for unfortunate others. The Perspective-Taking sub-scale assesses the ability to see things from the others perspective or how the other person thinks. The Personal Distress sub-scale measures levels of anxiety, sorrow or emotional distress in emergency situations. The Fantasy sub-scale measures the ability to relate to fictional characters (e.g. books or movies). Items on these sub-scales are measured on a 5-point Likert scale, with responses ranging between does not describe me well, to describes me very well. |
| Empathy Quotient (EQ)                                   | [36]             | [37]                    | A 60-item self-report scale. 40 items measure empathy on the cognitive and affective dimension and the remaining are included as control items. Each response is measured on a 4-point Likert scale, with responses ranging between strongly agree-to-strongly disagree. |
| Questionnaire for Cognitive and Affective Empathy (QCACE) | [38]             | [17,39]                 | A 31-item self-report scale consisting of five sub-scales: Perspective-Taking and Online Stimulation, measuring cognitive empathy. The Perspective-Taking sub-scale measures a respondent’s ability to understand the perspective of others. The Online Stimulation sub-scale measures how well a respondent can mentally represent another’s emotional state. The Emotion Contagion taps into assessing the extent to which self-oriented emotions match the affective state of others. The Proximal Responsivity sub-scale examines a respondent’s emotional response to the moods of significant others (e.g. friends) and the Peripheral Responsivity sub-scale measures affective responsiveness to detached, or fictional social context (e.g. characters in movies, plays, books etc). Items on these subscales are measured on a 4-point Likert scale, with responses ranging between describes me very well to does not describe me well. |
| Balanced Emotional Empathy Scale (BEEES)                 | [40]             | [41]                    | A 30-item self-report scale measuring spontaneous, or vicarious emotional reactions in response to another’s emotional distress (i.e. affective/emotional empathy). Each item is rated on a 9-point extent to which you agree-disagree spectrum. |
| Questionnaire Measure of Emotional Empathy (QMEEE)       | [42]             | [43]                    | A 33-item self-report scale assessing affective role-taking empathy. In other words, this scale measures the extent to which the respondent agrees with the self-oriented emotional responses someone would typically experience in response to another’s emotional distress. Items on this scale are measured on a 4-point Likert scale, ranging between strongly agree to strongly disagree. |
| Social context emotional recognition task                | [44]             | [44]                    | In this task, participants watched short films representing a happy, sad, angry and fearful context. Participants rated their emotional reaction (affective empathy) to each film and the intensity of the emotion they felt using a rating scale. The rating scale consisted of a continuous 10 cm line on which participants had to mark: Scores to the extreme left corresponded to the lowest intensity (0 cm) and scores to the extreme right corresponded to the highest intensity. |

Table S1: List of empathy measures used by studies included in the meta-analysis.

| Symptom Assessment Measure                           | Studies in Meta-Analysis | Description of Measure                                                                                          |
|-----------------------------------------------------|--------------------------|------------------------------------------------------------------------------------------------------------------|
| Positive and Negative Syndrome Scale (PANSS)        | [2-44]                   | A 38-item semi-structured measure completed by clinicians in an interview or observation format. 7 items measure positive symptoms of schizophrenia, 7 items measure negative symptoms and 16 items measures general psychopathology. |
| Schedule for the ASSESSMENT of Positive Symptoms(SAPS) | [23-25,29,30,32,41]      | A 34-item clinician rated scale which is used to measure the following positive symptoms: Bizarre behaviour, formal thought disorder, hallucinations and delusions. |
| Schedule for the Assessment of Negative Symptoms(SANS) | [17-23, 25-29,30,32,41]  | The originally published scale consisted of 25 items. Currently, SANS comprises of 19-items, representing 5 scales: Blunted/flattened affect, alogia, avolition-apathy, anhedonia/associability and inattention. Items on this scale are rated by clinicians. |
| Brief Psychiatric Rating Scale (BPRS)-positive symptom sub-scale | [16,17,20]              | A 24-item scale assessing positive symptoms of schizophrenia via self-report and clinical observations. Each item on this scale is measured on a 7 (extremely severe) anchor points. |
| BPRS-Negative symptom subscale                      | [16,20]                  | This sub-scale consists of items assessing negative symptoms of schizophrenia and is measured in the same way as the BPRS-positive symptom sub-scale. |

Table S2: List of symptom assessments used by studies included in the meta-analysis.
| Neurocognitive Domain | Neurocognitive Measures | Description of Measure | Studies in Meta-Analysis |
|-----------------------|-------------------------|------------------------|-------------------------|
| Attention/ Vigilance (reported by three studies) | The test of everyday attention [49] | This test included three tasks: 1. Visual selective attention task. This task involved searching a map for 2 minutes. 2. Auditory selective attention task. In this task participants must count the number of times they hear a tone while ignoring a distracting tone of a higher intensity. 3. Sustained visual attention task. The Visual elevator task. In this task participants are presented with an elevator which they are told represents floors. Participants are instructed to count the number of elevator doors they pass. | [41] |
|                        | Continuous performance task-identical pairs [50] | A computerised test assessing sustained attention. A button must be pressed each time the participant sees two numbers matching onscreen. | [6,29] |
| 2. Verbal learning (reported by six studies) | Hopkins verbal learning test-revised [51] | The task administrator presents 12 words from three categories (e.g. animal, colours and numbers). Participant is assessed on how many words they can recall after each of three learning trials. | [6,7,15] |
|                        | Rey auditory verbal learning test (English version) [52] | Participants are presented with 15 words over five trials. Participants must say the words immediately. An interference trial is then presented which involved presenting new words. Participants are asked to recall words from the initial list presented. | [26,43] |
|                        | California verbal learning test-second edition [53] | Participants are presented with a list of 16 words which they recall immediately over five trials. This is followed by an interference list, in which 16 words are presented in a single trial which must be recalled immediately. 20 minutes later a recognition trial is administered. Recall can be free or category-cued. | [29] |
| 3a. Working Memory (verbal) (Reported by Five Studies) | Wechsler memory scale-third edition (WMMS-III): Letter-number span [54] | Participants are instructed to mentally re-order strings of numbers and letters and repeat them orally to the test administrator. | [6,15,24,29] |
|                        | WAIS Digit Span Forward/Backwards Subtitle [55] | Participants are instructed to repeat the numbers presented to them in the same or reverse order. Over the course of the task, the number sequence increases. | [29] |
|                        | Repeatable battery for the assessment of neuropsychological status-story memory sub-test [56] | A 12-item short story is presented visually in three separate parts over two trials. Each story is read aloud with a low reading speed. Participants recall as much of the story as they can after each presentation. A verbatum criterion is used to score participant response. | [25] |
| 3b. Working memory (non-verbal) (reported by five studies) | WAIS-Revised (R)-working memory subtest [57] | This test uses an arithmetic and digit span test. For the digit span test, participant recalls a series of numbers in a specific order (i.e., ascending, backward or same order). For the arithmetic test, participants work within a specified time limit to mentally resolve a series of mental arithmetic problems. | [28] |
|                        | WMS-III: Spatial span [54] | Participants are presented with 12 blocks on which a sequence is tapped by the administrator. Participants must tap the blocks in the order requested by the administrator (either reverse or same order). | [7,15,29] |
|                        | Short recognition memory test for faces [58] | Participants are presented with 25 grey scale faces of male actors at a rate of 1 face every 3 seconds. Participants decide (using a forced choice option) whether the image presented is pleasant or unpleasant immediately post stimulus onset. Each stimulus item is paired with a distractor item. | [41] |
| 4. Speed of processing (reported by eight studies) | Trail Making Test A (TMT A) [59] | In this test, numbers placed irregularly on a sheet of paper, which participants are instructed to join correctly? This is a timed pencil and paper test. | [6,15,28,29,43] |
|                        | Trail Making Test B (TMT B) [59] | In part B, participants are presented with numbers and letters in random order, which they connect in alternating order. | [28,43] |
|                        | Brief Assessment of Cognition in Schizophrenia (BACS): Symbol coding [60] | This is a timed test in which participants are required to write down the digit corresponding to nonsense symbols within 90 seconds. | [6,15] |
|                        | WAIS-III Digit symbol substitution sub-test [55] | Participants are presented with a series of numbers and symbols in a grid. Participants reproduce symbols corresponding to the numbers in the grid within a 120 second time limit. | [29] |
|                        | Category fluency-animal subtest [61] | In this test, participants are instructed to generate exemplars of animals within 60 seconds. The total number of true animal exemplars within the time frame is measured. | [6,15,29] |
|                        | Five-point test [62] | There are two parts to this test: Verbal and non-verbal. In the verbal test participants must make words that begin with a specific letter (e.g., “A”) within three minutes. Participants are instructed not to produce nouns or repeat words. In the non-verbal test participants are presented with four squares on a sheet of paper. Each square consists of 5 symmetrical dots. Within a 5-minute timeframe, participants must create as many designs as they can by joining the dots in each square with one or more straight lines. | [14] |
|                        | Repeatability battery for the assessment of neuropsychological status-coding sub-set [63] | A page filled with symbols is presented to participants. Each symbol corresponds to a number on top of the page. Participant must match the symbol to its corresponding number within 90 seconds. | [25] |
| 5. Cognitive flexibility (reported by Three studies) | Stroop test [64] | There are three sub-tests to this task: The colour word sub-test in which participants must read the colour of the word presented in black ink. The colour name sub-test, in which participants must name the colour of the triangle, and in the interference sub-test, participants ignore the word they see and say the colour of the word (e.g. if the word black is written in the colour red, then the correct answer would be red). | [14,16] |
|                        | Delis-kapan executive function scale-colour word interference sub-test [65] | In this test, a participant must inhibit a dominant and automatic verbal response of a word presented, and instead, name the colour of the ink for the word presented. | [24] |
6. Reasoning and problem solving (reported by six studies) | Tower of London Test [66] | Participants are presented with coloured beads arranged vertically on pegs of different heights. How they must be arranged and the number of moves allowed is determined by the experimenter, which they (the participant) must follow in order to achieve a specific arrangement | [21]

Neuropsychological assessment battery: Mazes sub-test [67] | Participants are presented with seven mazes, each increasing in difficulty. Participants complete each maze within a 30-second time limit | [6,15]

WAIS-III-Matrix reasoning sub-test [55] | Participants are presented with different figures. Each figure must be analysed in order to determine which figure best fits the order of the sequence presented | [29]

Wisconsin card sorting test [68] | Participants sort a series of cards by a specific rule (e.g. by colour, shape or number of shapes). Feedback on performance is provided. After ten correct sorts, the rules for sorting are changed to a new rule without warning | [18,19]

Brief visuospatial memory test-revised [69] | The instructor presents six geometric figures which participants reproduce from memory | [6,15]

The Judgement of Line Orientation test [70] | Participants are presented with two angle lines. They are instructed to match the set to a set of 11 lines by re-arranging them so that all the lines are 18 degrees apart and form a semi-circle | [21]

Table S3: List of studies included in meta-analysis measuring neurocognition in schizophrenia and healthy controls.

| Neuro-cognitive Measures | Description of Task | Studies in Meta-Analysis |
|--------------------------|---------------------|-------------------------|
| Multiple-choice vocabulary test (german version) [71] | This measure presents 37 rows of five words. From each row, participants pick the actual word and rule out the pseudo-words. The number of correctly identified words provides the test result | [8,9,13,18,26-28] |
| National adult reading test [72] | This test comprises 50 words with irregular spellings (e.g. aisle). Participants are assessed on their vocabulary comprehension rather than their ability to apply regular pronunciation rules | [11,22,24,25,32,39] |
| WAIS-III-verbal subset [55] | In this test, participants name the object in the picture or define the words presented to them | [12,19] |

Table S4: List of the studies in the meta-analysis measuring verbal comprehension in schizophrenia and healthy controls.

| Neuro-cognitive Measures | Studies in Meta-Analysis | Description of General IQ Tests |
|--------------------------|-------------------------|--------------------------------|
| Wechsler abbreviated adult intelligence scale [73] | [12,15,37] | The many versions of the Wechsler’s Adult Intelligence Scales measure a person’s ability to act purposefully, reason and deal effectively with his/her surrounding/environment [74]. This aim is fulfilled using several verbal ability and cognitive reasoning/style sub-tests (for a detailed description of each sub-test refer to Wechsler’s administration manual and scales [54,55,73,75]) |
| Wechsler Adult Intelligence Scale III [55] | [2,5,7,35] | |
| Wechsler adult intelligence scale-IV [75] | [34] | |
| Raven’s progressive matrices test [76] | [21] | This is a non-verbal group test designed to measure abstract reasoning |
| Groninger Intelligence Test [77] | [43] | This test is used in the Netherlands as a reliable alternative to the Wechsler Adult Intelligence Tests. As such, this test includes examining the same cognitive and verbal abilities as the WAIS sub-tests [55] |

Table S5: List of studies in the meta-analysis that examined general IQ.

| Cognitive Empathy | \( k \) | \( B \) | \( SE \) | \( 95\% CI \) | \( Z \) | \( P \) | \( F \) |
|-------------------|------|-----|-----|----------|------|-----|-----|
| Age at Diagnosis  | 20   | -0.06 | 0.018 | [-0.09, -0.02] | -3.35 | 0.0008 | 28.70 |
| Duration of Illness | 29 | 0.012 | 0.008 | [0.001, 0.03] | 2.11 | 0.03 | 30.55 |
| Positive symptoms | 33 | 0.008 | 0.008 | [-0.007, 0.024] | 1.004 | 0.31 | 30.73 |
| Negative Symptom severity | 33 | 0.004 | 0.007 | [-0.009, 0.01] | 0.67 | 0.50 | 30.64 |
| General Symptom Severity | 15 | 0.01 | 0.01 | [-0.01, 0.03] | 1.86 | 0.28 | 5.04 |
| CPZ-Equivalent -mg/day | 16 | -0.0005 | 0.0006 | [-0.001, 0.0008] | -0.77 | 0.43 | 13.50 |

Table S6: Moderating effect of clinical characteristics on the difference in performance between schizophrenia patients and healthy controls on cognitive empathy.

Note: \( k \) = Number of studies. \( B \) = regression coefficient. \( SE \) = standard error. 95% CI = 95% confidence interval. \( Z \) = indicates the extent of uncertainty in the regression coefficient. \( P \) = statistical significance, 2-tailed. \( F \) indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent, milligram per day.
Table S7: Moderating effect of neuro-cognitive abilities on the difference in performance between schizophrenia patients and healthy controls on cognitive empathy

Note: K = Number of studies. B = regression coefficient. SE = standard error. 95% CI = 95% confidence interval. Z = indicates the extent of uncertainty in the regression coefficient. P = statistical significance, 2-tailed. I² indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day

Table S8: Moderating effect of demographic variables on the difference in performance between schizophrenia patients and healthy controls on cognitive empathy

Note: K = Number of studies. B = regression coefficient. SE = standard error. 95% CI = 95% confidence interval. Z = indicates the extent of uncertainty in the regression coefficient. P = statistical significance, 2-tailed. I² indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day

Table S9: Moderating effect of clinical characteristics on the difference in performance between schizophrenia patients and healthy controls on affective empathy

Note: K = Number of studies. B = regression coefficient. SE = standard error. 95% CI = 95% confidence interval. Z = indicates the extent of uncertainty in the regression coefficient. P = statistical significance, 2-tailed. I² indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day

Table S10: Moderating effect of cognitive on the difference in performance between schizophrenia patients and healthy controls on affective empathy

Note: K = Number of studies. B = regression coefficient. SE = standard error. 95% CI = 95% confidence interval. Z = indicates the extent of uncertainty in the regression coefficient. P = statistical significance, 2-tailed. I² indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day
Table S11: Moderating effect of demographic variables on the difference in performance between schizophrenia patients and healthy controls on affective empathy

| Table S11 | K | B | SE | 95% CI | Z | P | F |
|-----------|---|---|----|--------|---|---|---|
| Affective Empathy | | | | | | | |
| Age, Schizophrenia | 36 | 0.01 | 0.01 | [-0.005, 0.03] | 1.43 | 0.15 | 39.60 |
| Fewer Years in Education in Schizophrenia compared to Healthy Controls | 23 | -0.04 | 0.07 | [-0.19, 0.10] | -0.55 | 0.57 | 25.46 |
| Higher Proportion of Male Schizophrenia then Female Schizophrenia | 29 | -0.001 | 0.006 | [-0.01, 0.001] | -0.30 | 0.76 | 31.43 |
| Higher Proportion of Non-Caucasian Schizophrenia compared to Caucasian Patients | 7 | 0.005 | 0.007 | [-0.009, 0.021] | 0.74 | 0.45 | 5.28 |
| Year of Study Publication | 39 | -0.04 | 0.02 | [-0.09, 0.008] | -1.65 | 0.09 | 41.16 |

Note: K = Number of studies, B = regression coefficient. SE = standard error. 95% CI = 95% confidence interval. Z = indicates the extent of uncertainty in the regression coefficient. P = statistical significance, 2-tailed. F = indicates the amount of between-study heterogeneity. CPZ-equivalent-mg/day = Chlorpromazine Equivalent in milligram per day

References

1. Davis MH (1980) A multidimensional approach to individual differences in empathy. Diss Abstr Int 40: 3480.

2. Achim AM, Ouëlett R, Roy MA, Jackson PL (2011) Assessment of empathy in first-episode psychosis and meta-analytic comparison with previous studies in schizophrenia. Psychiatry Res 190: 3-8.

3. Andrews SC, Enticott PG, Hoy KE, Fitzgerald PB (2013) Mirror systems and social cognition in schizophrenia. Schizophr Bull 39: 218.

4. Brown, EC, Gonzalez Liencres, C, Tas, C, Brune M (2016) Reward modulates the mirror neuron system in schizophrenia: A study into the mu rhythm suppression, empathy, and mental state attribution. Soc Neurosci 11: 175-186.

5. Chiang SK, Hua MS, Tam WCC, Chao JK, Shah YJ (2014) Developing an alternative Chinese version of the interpersonal reactivity index for normal population and patients with schizophrenia in Taiwan. Brain Impair 15: 120-131.

6. Corbera S, Wexler BE, Ikezawa S, Bell MD (2013) Factor structure of social cognition in schizophrenia: is empathy preserved? Schizophrenia Research and Treatment 1-13.

7. Corbera S, Cook K, Brocke S, Dunn S, Wexler BE, et al. (2014) The relationship between functional deficits and empathy for emotional pain in schizophrenia. Biol Psychiatry 75: 200.

8. Derntl B, Finkelmeyer A, Voss B, Eickhoff SB, Kellermann T, et al. (2012) Neural correlates of the core facets of empathy in schizophrenia. Schizophr Res 136: 70-81.

9. Derntl B, Seidel EM, Schneider F, Habel U (2012) How specific are emotional deficits? A comparison of empathic abilities in schizophrenia, bipolar and depressed patients. Schizophr Res 142: 58-64.

10. Fischer Shofty M, Brüne M, Ebert A, Shefet D, Levkovitz Y, et al. (2013) Improving social perception in schizophrenia: The role of oxytocin. Schizophr Res 146: 357-362.

11. Fujino J, Takahashi H, Miyata J, Sugihara G, Kubota M, et al. (2014) Impaired empathic abilities and reduced white matter integrity in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 48: 117-123.

12. Fujisawa H, Shimizu M, Hirao K, Miyata J, Namiki C, et al. (2008) Female specific anterior cingulate abnormality and its association with empathic disability in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 32: 1728-1734.

13. Gizewski ER, Müller BW, Scherbaum N, Lieb B, Forsting M, et al. (2013) The impact of alcohol dependence on social brain function. Addict Biol 18: 109-120.

14. Haker H, Rössler W (2009) Empathy in schizophrenia: Impaired resonance. Eur Arch Psychiatry Clin Neurosci 259: 352-361.

15. Hooker CI, Bruce L, Lincoln SH, Fisher M, Vinogradov S (2011) Theory of mind skills are related to gray matter volume in the ventromedial prefrontal cortex in schizophrenia. Biol Psychiatry 70: 1169-1178.

16. Horan WP, Pineda JA, Wynn JK, Iacoboni M, Green MF (2014) Some markers of mirroring appear intact in schizophrenia: Evidence from mu suppression. Cogn Affect Behav Neurosci 14: 1049-1060.

17. Horan WP, Reise SP, Kern RS, Lee J, Penn DL, et al. (2015) Structure and correlates of self-reported empathy in schizophrenia. J Psychiatr Res 66-67: 60-66.

18. Lehmann A, Bahcesular K, Brockmann EM, Biedebrock, SE, Dziobek I, et al. (2014) Subjective experience of emotions and emotional empathy in paranoid schizophrenia. Psychiatry Res 220: 825-833.

19. Lee SJ, Kang DH, Kim CW, Gu BM, Park JY, et al. (2010) Multi-level comparison of empathy in schizophrenia: An fMRI study of a cartoon task. Psychiatry Res 181: 121-129.

20. Lee J, Zaki J, Harvey PO, Ochsner K, Green MF (2011) Schizophrenia patients are impaired in empathy accurate. Psychol Med 41: 2297-2304.

21. Lam BY, Raine A, Lee TM (2014) The relationship between neurocognition and symptomatology in people with schizophrenia: Social cognition as the mediator. BMC Psychiatry 14: 138.

22. Matsumoto Y, Takahashi H, Murai T, Takahashi H (2015) Visual processing and social cognition in schizophrenia: Relationships among eye movements, biological motion perception, and empathy. Neurosci Res 90: 95-100.

23. McCormick LM, Brumm MC, Beadle JN, Paradiso S, Yamada T, et al. (2012) Mirror neuron function, psychosis, and empathy in schizophrenia. Psychiatry Res 201: 233-239.

24. McGuire J, Barbanel L, Brüne M, Langdon R (2015) Re-examining Kohlberg’s conception of morality in schizophrenia. Cogn Neuropsychiatry 20: 377-381.

25. McGuire J, Brüne M, Langdon R (2017) Judgment of moral and social transgression in schizophrenia. Compr Psychiatry 76: 160-168.

26. Montag C, Heinz A, Kunz D, Gallinat J (2007) Self-reported empathic abilities in schizophrenia. Schizophr Res 92: 85-89.

27. Montag C, Brockmann EM, Lehmann A, Muller DJ, Rujescu D, et al. (2012) Association between oxytocin receptor gene polymorphisms and self-rated ‘empathic concern’ in schizophrenia. PLoS One 7: 51882.

28. Regenbogen C, Kellermann T, Seubert J, Schneider DA, Gur RE, et al. (2015) Neural responses to dynamic multimodal stimuli and pathology-specific impairments of social cognition in schizophrenia and depression. Br J Psychiatry 206: 198-205.

29. Smith MJ, Horan WP, Cobia DJ, Karpouzian TM, Fox JM, et al. (2014) Performance-based empathy mediates the influence of working memory on social competence in schizophrenia. Schizophr Bull 40: 824-834.
30. Singh S, Modi S, Goyal S, Kaur P, Singh N, et al. (2015) Functional and structural abnormalities associated with empathy in patients with schizophrenia: An fMRI and VBM study. J Biosci 40: 355-364.

31. Shamay-Tsoory SG, Shur S, Harari H, Levkovitz Y (2007) Neuropsychological basis of impaired empathy in schizophrenia. Neuropsychology 21: 431-438.

32. Sparks A, McDonald S, Lino B, O’Donnell M, Green MJ (2010) Social cognition, empathy and functional outcome in schizophrenia. Schizophr Res 122: 172-178.

33. Thiriaux B, Tandonnet L, Jaafari N, Berthoz A (2014) Disturbances of spontaneous empathic processing relate with the severity of the negative symptoms in patients with schizophrenia: A behavioural pilot-study using virtual reality technology. Brain Cogn 90: 87-99.

34. Vistoli D, Loviose, MA, Satliff S, Jackson PL, Achim AM (2017) Functional MRI examination of empathy for pain in people with schizophrenia reveals abnormal activation related to cognitive perspective-taking but typical activation linked to affective sharing. J Psychiatry Neurosci 42: 262-272.

35. Wojakiewicz A, Januel D, Braha S, Pkrachin K, Danziger N, et al. (2013) Alteration of pain recognition in schizophrenia. Eur J Pain 17: 1385-1392.

36. Baron-Cohen S, Wheelwright S (2004) The empathy quotient: An investigation of adults with asperger syndrome or high functioning autism, and normal sex differences. J Autism Dev Disord 34: 163-175.

37. Didehbani N, Shad MU, Tamminga CA, Kandalaft MR, Allen TT, et al. (2012) Insight and empathy in schizophrenia. Schizophr Res 142: 246-247.

38. Reniers RL, Corcoran R, Drake R, Shryane NM, Völlm BA (2011) The QCA: A questionnaire of cognitive and affective empathy. J Pers Assess 93: 84-95.

39. Berrada-Baby Z, Oker A, Courgeon M, Urbach M, Bazin N, et al. (2016) Patients with schizophrenia are less prone to interpret virtual others’ empathetic questioning as helpful. Psychiatry Res 242: 67-74.

40. Mehrabian A (2000) Manual for the Behavioural Emotional Emotion Scale (BEES). Monterey, CA, USA.

41. Kucharska-Pietura K, Tylec A, Czernikiewicz A, Mortimer A (2012) Attentional and emotional functioning in schizophrenia patients treated with conventional atypical antipsychotic drugs. Med Sci Monit 18: 44-49.

42. Mehrabian A, Epstein N (1972) A measure of emotional empathy. J Pers 40: 525-543.

43. Pijnenborg GHM, Spikman JM, Jeromineus BF, Aleman A (2013) Insight into schizophrenia: A comprehensive review. Eur Arch Psychiatry Clin Neurosci 261: 299-307.

44. Ramos-Loyo J, Mora-Reynoso L, Sanchez-Loyo LM, Medina-Hernandez V (2012) Sex differences in facial, prosodic and social context emotional recognition in early-onset schizophrenia. Schizophr Res Treatment: 1-12.

45. Kay SR, Fiskein A, Opler LA (1987) The positive and negative symptom scale (PANSS) for schizophrenia. Schizophr Bull 13: 261-276.

46. Andreasen NC (1984) Scale For The Assessment Of Positive Symptoms (SAPS). University of Iowa, Iowa, USA.

47. Andreasen NC (1983) Scale for the assessment of negative symptoms (SANS). Iowa City, Iowa, USA.

48. Overall JE, Gorham DR (1962) The brief psychiatric rating scale. Psychological Reports 10: 799-812.

49. Robertson IH (1994) The test of everyday attention. Thames Valley Test Company, England, UK.

50. Cornblatt B, Risch NJ, Fairis G, Friedman D, Erlenmeyer-Kimling L (1988) The Continuous Performance Test, Identical Pairs Version (CPT-IP): I. New findings about sustained attention in normal families. Psychiatry Res 26: 223-238.

51. Brandt J (1991) The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. Clinical Neuropsychologist 5: 125-142.

52. Heubrock D (1994) Auditiv-verbales Lernenunter standardisierten Bedingungen: Erste deutsche Normen für 16- bis26-jährige Männer und Frauen zum Auditiv-VerbalemLentest (AVLT) [Standardized auditory-verbal learning: Preliminary German Auditory-Verbal Learning Test (AVLT) norms for male and female population aged 18 to 26]. J Individ Diff 15: 65-76.

53. Delis DC, Kramer JH, Kaplan E, Ober BA (2000) California Verbal Learning Test Manual: Second edition, adult version. Pearson, London, UK.

54. Wechsler D (1997) WMS-III: Wechsler Memory Scale Administration and Scoring Manual. Psychological Corporation, San Antonio, USA.

55. Wechsler D (1997) Wechsler Adult Intelligence Scale - 3rd Edition (WAIS-III). The Psychological Corporation, San Antonio, USA.

56. Randolph C (2012). RBANS Update : Repeatable Battery for the Assessment of Neuropsychological Status. NCS Pearson, Bloomington, Indiana.

57. Wechsler D (1955) Manual for the Wechsler Adult Intelligence Scale. Psychological Corporation, New York, USA.

58. Warrington E (1996) The Camden Memory Tests: Short Recognition Memory Test for Faces (Volume 5). Psychology Press, New York, USA.

59. Reitan RM (1955) The relation of the Trail Making Test to organic brain damage. J Consult Psycho 19: 393-394.

60. Koepe RS, Goldberg TE, Harvey PD, Gold JM, Poe MP, et al. (2004) The Brief Assessment of Cognition in Schizophrenia: reliability, sensitivity, and comparison with a standard neurocognitive battery. Schizophr Res 68: 283-297.

61. Benton AL, Hamsher deS, Sivan AB (1994) Multilingual Aphasia Examination, Third Edition. Psychological Assessment Resources, Inc, Iowa, USA.

62. Regard M, Strauss E, Knapp P (1982) Children’s production on verbal and non-verbal fluency tasks. Percept Mot Skills 55: 839-844.

63. Randolph C (1999). Repeatable Battery for the Assessment of Neuropsychological Status. Psychological Corporation, Bloomington, Indiana.

64. Stroop JR (1935) Studies of interference in serial verbal reactions. Journal of Experimental Psychology 18: 643-662.

65. Delis DC, Kaplan E, Kramer J (2001) Delis–Kaplan executive function scale. The Psychological Corporation, San Antonio, USA.

66. Shalllice T (1982) Specific impairments of planning. In: Broadent DE, Weiskrantz L, (eds.). The neuropsychology of cognitive function. The Royal Society, London, UK.

67. Stern RA, White T (2003) Neuropsychological Assessment Battery. Psychological Assessment Resources Inc, Florida, USA.

68. Grant DA, Berg EA (1948) A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. J Exp Psychol 38: 404-411.

69. Benedikt RHB (1997) Contributions to neuropsychological assessment. Oxford University Press Inc, New York, USA.
71. Lehrl S, Triebig G, Fischer B (1995) Multiple choice vocabulary test 
MWT as a valid and short test to estimate premorbid intelligence. Acta 
Neurol Scand 91: 335-345.

72. Nelson HE (1991) National Adult Reading Test. NFER-Nelson, Windsor, 
UK.

73. Psychological Corporation Harcourt Brac (1999) WASI Wechsler Ab 
breviated Scale of Intelligence. The Psychological Corporation Harcourt 
Brace, New York, USA.

74. Wechsler D (1958) The measurement of adult intelligence. Baltimore: 
William & Wilkins, Literary Licensing, Maryland, USA.

75. Wechsler D (2008) WAIS-IV administration and scoring manual. Psych- 
Corp, San Antonio, USA.

76. Raven J, Raven JC, Court JH (1998) Manual for Raven’s progressive ma 
trices and vocabulary scales. Oxford Psychologists Press, Oxford, UK.

77. Luteijn F (1983) GIT Groninger Intelligent Test. Swets & Zeitlinger bv, 
California, USA.
Journal of Anesthesia & Clinical Care
Journal of Addiction & Addictive Disorders
Advances in Microbiology Research
Advances in Industrial Biotechnology
Journal of Agronomy & Agricultural Science
Journal of AIDS Clinical Research & STDs
Journal of Alcoholism, Drug Abuse & Substance Dependence
Journal of Allergy Disorders & Therapy
Journal of Alternative, Complementary & Integrative Medicine
Journal of Alzheimer’s & Neurodegenerative Diseases
Journal of Angiology & Vascular Surgery
Journal of Animal Research & Veterinary Science
Archives of Zoological Studies
Archives of Urology
Journal of Atmospheric & Earth-Sciences
Journal of Aquaculture & Fisheries
Journal of Biotech Research & Biochemistry
Journal of Brain & Neuroscience Research
Journal of Cancer Biology & Treatment
Journal of Cardiology & Neurocardiovascular Diseases
Journal of Cell Biology & Cell Metabolism
Journal of Clinical Dermatology & Therapy
Journal of Clinical Immunology & Immunotherapy
Journal of Clinical Studies & Medical Case Reports
Journal of Community Medicine & Public Health Care
Current Trends: Medical & Biological Engineering
Journal of Cytology & Tissue Biology
Journal of Dentistry: Oral Health & Cosmesis
Journal of Diabetes & Metabolic Disorders
Journal of Dairy Research & Technology
Journal of Emergency Medicine Trauma & Surgical Care
Journal of Environmental Science: Current Research
Journal of Food Science & Nutrition
Journal of Forensic, Legal & Investigative Sciences
Journal of Gastroenterology & Hepatology Research
Journal of Gerontology & Geriatric Medicine
Journal of Genetics & Genomic Sciences
Journal of Hematology, Blood Transfusion & Disorders
Journal of Human Endocrinology
Journal of Hospice & Palliative Medical Care
Journal of Internal Medicine & Primary Healthcare
Journal of Infectious & Non Infectious Diseases
Journal of Light & Laser: Current Trends
Journal of Modern Chemical Sciences
Journal of Medicine: Study & Research
Journal of Nanotechnology: Nanomedicine & Nanobiotechnology
Journal of Neonatology & Clinical Pediatrics
Journal of Nephrology & Renal Therapy
Journal of Non Invasive Vascular Investigation
Journal of Nuclear Medicine, Radiology & Radiation Therapy
Journal of Obesity & Weight Loss
Journal of Orthopedic Research & Physiotherapy
Journal of Otolaryngology, Head & Neck Surgery
Journal of Pathology Clinical & Medical Research
Journal of Pharmacology, Pharmaceutics & Pharmacovigilance
Journal of Plant Science: Current Research
Journal of Psychiatry, Depression & Anxiety
Journal of Pulmonary Medicine & Respiratory Research
Journal of Practical & Professional Nursing
Journal of Reproductive Medicine, Gynaecology & Obstetrics
Journal of Stem Cells Research, Development & Therapy
Journal of Surgery: Current Trends & Innovations
Journal of Toxicology: Current Research
Journal of Translational Science and Research
Trends in Anatomy & Physiology
Journal of Vaccines Research & Vaccination
Journal of Virology & Antivirals

Submit Your Manuscript: http://www.heraldopenaccess.us/Online-Submission.php