Do patients with high-functioning autism have similar social cognitive deficits as patients with a chronic cause of schizophrenia?

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Abstract

Objective: There is substantial evidence that both patients with schizophrenia and patients with autism spectrum disorders (ASD) have impaired social cognition including theory of mind (ToM) deficits. However, it remains unclear if both verbal (explicit) and non-verbal (implicit) ToM as well as social perception are similarly affected in both disorders.

Methods: Twenty-one patients diagnosed with schizophrenia and eleven patients diagnosed with ASD were matched one-to-one to healthy controls based on gender, age, and educational level. Social functioning was measured by PSP (Personal and Social Performance Scale). Neurocognition was measured using BACS-DK (Brief Assessment of Cognition in Schizophrenia), and four subtests from WAIS-IV (Wechsler Adult Intelligence Scale) were applied to estimate IQ. The Animated Triangles Task was used to measure implicit ToM, while explicit ToM and social perception were measured by TASIT (The Awareness and Social Inference Test).

Results: Patients with schizophrenia had deficits in implicit ToM and complex social perception compared to their matched controls, but no problems with explicit ToM. Surprisingly, patients with ASD solely had deficits with regard to complex social perception compared to their matched controls. The two patient groups were similar regarding estimated IQ, social functioning and years of education, but differed in age and neurocognition. When adjusting the p-values for age and neurocognitive deficits, both patients groups had similar social cognitive deficits.

Conclusions: Results imply that we compared schizophrenia patients with substantial neurocognitive deficits to a group of high-functioning patients with ASD. However, these two subgroups may have the same level of social cognitive deficits.

Key words: social cognition, theory of mind, social perception, implicit, explicit

1. Introduction

Alterations and impairments in social cognition is a common feature of many psychiatric disorders and conditions [1, 2, 3, 4]. For instance, schizophrenia and autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by marked impairments in social cognition, including theory of mind (ToM) deficits, i.e. impairment in the ability to infer and attribute independent mental states to oneself and others in order to explain and predict behavior [5]. Whereas ToM deficits have long been recognized as a primary abnormality in ASD [6], interest in ToM deficits in schizophrenia has evolved due to an increasing focus social cognitive impairments in this mental disorder [7].

Results from various meta-analyses have revealed that there is now substantial evidence showing that patients with schizophrenia likewise are characterized by marked ToM deficits [8, 9, 10]. This indicates some overlap between social cognition in schizophrenia and ASD [11]. An increasing interest in examining and comparing possible brain mechanisms or abberations underlying social cognitive deficits in the two disorders has emerged in recent years [12, 13, 14]. Similarities in the neural correlates of ToM in the two disorders have been identified [15]. However, this contemplation of social cognitive concordance is not novel as schizophrenia and ASD have a long history of diagnostic conflation stemming from apparent overlaps in certain areas of social dysfunction [16]. In spite of this, much research has focused on the ToM deficits appearing in the two disorders separately, whereas limited empirical work has targeted at directly comparing these two clinical groups. Research regarding direct comparisons is sparse, and findings from existing studies comparing ToM in ASD and schizophrenia show mixed results. Some report comparable ToM deficits in both disorders [17, 18, 19], whereas results from other studies indicate that patients with ASD have significantly more severe ToM deficits compared to patients with schizophrenia [20, 21], or that the opposite is occurring [22, 23].

A recent meta-analysis examining ToM abilities in ASD and schizophrenia found statistically large effect sizes at a similar level in both disorders [24]. Results from this meta-analysis further revealed that patients with schizophrenia tend to have larger impairments on verbal mentalizing tasks compared to nonverbal mentalizing tasks, whereas patients with ASD had similar deficits in both types of tasks. This indicates that the two patient groups may perform differently on distinct ToM tasks. This proposition was supported by results from a recent meta-analysis examining schizophrenia and ASD patients' performance on the Animated Triangles Task [25]. Results

showed that patients with ASD seem to make more inaccurate descriptions of interactions involving ToM compared to patients with schizophrenia, although no difference was found between the two patient groups regarding detection of intentionality.

In research, a distinction between implicit and explicit ToM is often made as these abilities are suggested to work in different ways [26]. The implicit mentalizing system involves automatic and cognitive efficient ToM abilities, which is thus limited and inflexible. The explicit mentalizing system refers to a culturally inherited skill involving mental flexibility to reason about beliefs, which is a process that highly rely on language and executive functions [26, 27]. It has been suggested that patients with schizophrenia have intact implicit ToM, but impaired explicit ToM [28]. Contrary to this, patients with ASD are known to have impaired implicit ToM, whereas some patients with higher verbal ability can pass explicit ToM tasks [29, 30], presumably due to compensatory strategies [31].

However, in both schizophrenia and ASD other social cognitive areas are also identified to involve pivotal deficits. In schizophrenia, five distinct social cognitive domains have been specified to be particular affected; 1) ToM, 2) social perception, 3) social knowledge, 4) attributional bias, and 5) emotional processing [7]. Results from a recent meta-analysis revealed that ToM and social perception were the domains most severely affected in schizophrenia [9]. For this reason, we added a complex social perceptual task in order to broaden the comparison of social cognitive deficits in schizophrenia and ASD. To our knowledge, no other study has compared these two patients groups regarding social perception, which involves the ability to attend to and interpret the whole combination of complex information from different social phenomena including body language, verbal messages, paralinguistic cues as well as non-verbal behaviors [32]. As such, social perception is a very complex domain concerning the ability to 'read between the lines'.

The main aim of the present study was to compare implicit and explicit ToM as well as social perception in schizophrenia and ASD. Furthermore, we also aimed to compare the two patient groups regarding IQ and neurocognition because both mental disorders have been found to be characterized by impairments in neurocognition [28, 33, 34], and because ASD often is associated with low IQ level or even mental retardation [35, 36]. We hypothesized that patients with ASD would have more comprehensive deficits in both social cognition as well as neurocognition compared to patients with schizophrenia, but that both patient groups would be significantly impaired relative to healthy controls.

2. Materials and methods

2.1 Subjects

2.1.1 Recruited patients

The thirty-two included patients were recruited from the Neuropsychiatric unit at the Psychosis department, Aarhus University Hospital Risskov. This unit is specialized in diagnosing patients with complex psychotic disorders (e.g. suspicion of an organic mental disorder). All patients referred to the clinic were recruited and tested from March 2013 until October 2015 by an experienced neuropsychologist (HLP), and diagnoses were validated by an experienced psychiatrist. In the present study we only included those patients who met the ICD-10 (International Classification of Disease 10th edition) criteria for either schizophrenia or ASD and had no diagnosis of drug- or alcohol dependency according to ICD-10 [37]. Patients were excluded if they did not understand spoken Danish sufficiently to comprehend the testing procedures.

2.1.2 Healthy control subjects

The healthy control subjects were matched one-to-one to the patients based on gender and age. Notably, it was not possible to match perfectly one-to-one regarding age but the patients and their matched controls did not differ more than two years, and on group level no difference occurred. We also intended to match on total years of education and current occupation. However, many of the included patients were on pension or sick leave and had fewer years of education as could be expected according to their age. This strongly suggests that a group of controls matched on years of education would not constitute a representative sample. Instead, we aimed at recruiting healthy controls with different employments and educational levels. The thirty-two included controls had no history of mental illness and neither had their first-degree relatives. In addition, they did not report a history of neurological illness or any drug- or alcohol dependency according to ICD-10 criteria. The healthy controls were recruited through an advertisement in a local newspaper and through flyers posted in the local community. All healthy controls received a voucher for participating.

2.2 Social cognitive measures

2.2.1. Theory of mind

The Animated Triangles Task (AT) was applied to assess implicit ToM. This task was chosen due to its validity as a culturally independent task assessing implicit and nonverbal aspects of ToM. AT

consists of short movie clips with two animated triangles, which either move in a random or an intentional way [38, 39]. There are four clips of each type of animation lasting 38-41 seconds, and the different types of animations were shown in a random order. After each animation the participants were asked to describe what they thought was happening. The answers were rated regarding intentionality, that is, the degree of appreciation of mental states (ranging 0-5, where a score of 4 or 5 refers to mental state attribution) and appropriateness, that is how well the underlying script was captured (ranging 0-3, where 3 refers to a perfect description).

Reports were recorded and transcribed. Two raters (LV and HLP), blind to diagnosis, independently scored each transcribed description after having been trained to use the published set of scoring criteria by VB [39, 40], and their scores were averaged for data analysis. Inter-rater agreements were fair to substantial (Random animations: Intentionality κ=0.74, Z=8.14, P<0.0001, Appropriateness κ=0.58, Z=9.47, P<0.0001; ToM animations: Intentionality κ=0.54, Z=8.55, P<0.0001, Appropriateness κ=0.35, Z=7.58, P<0.0001).

2.2.2 Social perception

The Danish version of The Awareness of Social Inference Test, Part 2A (TASIT) was used to assess explicit ToM and social perception [41]. This test was chosen due to its substantial ecological validity as a real life measure of social perception and ToM abilities requiring a combination of visual and verbal information. TASIT consists of small video clips lasting 16-53 seconds, where professional actors perform small everyday interactions [32, 42]. TASIT contains three different types of video clips: 1) sincere clips, where congruence exists between what the persons are literally saying and the paralinguistic and facial cues, 2) simple sarcastic clips, where one of the persons is being sarcastic and no congruence exists between the spoken word and the paralinguistic and facial cues, 3) paradoxical sarcastic clips, which only make sense if the participant is able to detect the sarcasm being used in the dialogue. After each video clip, the participants were asked to answer four questions concerning different aspects of the communicative intentions of the persons (what they were doing, saying, thinking, and feeling). Scoring of each type of video clip range from 0-20, which corresponds to a maximum score of 60.

2.3 Neurocognitive measures

2.3.1 Neurocognition

The Danish version of the Brief Assessment of Cognition in Schizophrenia (BACS) was used to measure verbal memory, working memory, motor speed, verbal fluency, executive functions, attention, and speed of processing [43, 44].

2.3.2. Intelligence

Intelligence was estimated using four subtests from WAIS-IV (Wechsler Adult Intelligence Scale, Fourth version): Vocabulary, Similarities, Block Design, and Matrix Reasoning. These subtests were chosen due to their high correlation with the total WAIS-IV IQ-score [45].

2.4 Psychopathology and social functioning

All patients had attended an extensive interdisciplinary diagnostic program based on ICD-10 criteria. Diagnoses were based on clinical psychiatric interviews and neuropsychological tests combined with interviews of relatives. All subjects were interviewed with the Personal and Social Performance Scale (PSP), which is a tool to measure social functioning in schizophrenia [46]. The healthy controls were interviewed with the Present State Examination interview (PSE, ICD-10).

2.5 Ethics

All participants received written and verbal information about the project and a written informed consent was obtained and signed before participation. The study was approved by the Danish Data Protection Agency (Ref: 2007-58-0010), and the project complied with the Helsinki-II declaration.

2.6 Data-analysis

Statistical analyses were performed with Stata IC 14.2 software. All data were examined for distribution and outliers. Continuous variables were examined by Wilcoxon rank-sum test (Mann-Whitney) and effect sizes were reported in terms of Harrell's C (HC). Categorical variables were examined by Fisher's exact test (if $N<5$ in a cell) or Chi^2 and reported with the counts and proportions of the group total. Composite scores for BACS were calculated as the weighted mean of z-scores, separately computed for each subtest relative to the mean and standard deviation of the

healthy control sample (mean=0, SD=1). Regression analyses were calculated for the social cognitive scores and p-values were adjusted with age and composite BACS scores as covariates.

3. Results

3.1 Demographics and social functioning

Demographics and social functioning of the patients and their matched controls are summarized in Table 1 and Table 2. Both patient groups and their matched controls did not differ in gender and age. However, the two patient groups differed markedly in age with the schizophrenia sample being older than the ASD sample (Z=3.42, p=0.0006). As expected, educational level and current occupation of both patient groups were significantly lower compared to their matched controls. Likewise, the social functioning of both patient groups was significantly lower compared to their matched controls. The patient groups did not differ regarding years of education (Z=1.07, p=0.29) or social functioning (Z=-1.13, p=0.26).

3.2 Pairwise comparisons of patients and matched controls

Pairwise comparisons revealed significant differences in estimated IQ, neurocognition, and complex aspects of social cognition between patients with schizophrenia and their matched controls (see Table 3). However, no differences were found regarding the sincere and the simple sarcastic TASIT film clips. Surprisingly, no differences were found in estimated IQ, neurocognition and all social cognitive domains, besides TASIT paradoxical sarcasm, when comparing patients with ASD to their matched controls (see Table 4).

3.3 Comparisons of patients with schizophrenia and patients with ASD

We found no difference in estimated IQ (Z=-0.56, p=0.58), but patients with schizophrenia had significantly more comprehensive neurocognitive deficits compared to patients with ASD (Z=-2.84, p=0.005). No differences were found between the two patient groups regarding social cognition, when p-values were adjusted for age and neurocognition (p>0.25).

4. Discussion

Surprisingly, we found no significant differences in social cognition between schizophrenia and ASD. However, patients with schizophrenia were significantly impaired in both implicit and explicit ToM as well as in social perception compared to their matched controls, whereas patients with ASD performed on a similar level as their matched controls on most social cognitive domains. As such, our results do not support the assumption that implicit ToM is intact in schizophrenia [28]. Moreover, only the patients with schizophrenia were significantly impaired in IQ and neurocognition compared to the matched controls and further, patients with schizophrenia had significantly neurocognitive deficits compared to patients with ASD.

Although the patients with schizophrenia in the present study seem to have more impaired social cognition than the patients with ASD, these differences were not significant when controlling for age and neurocognition. As such, our findings seem to differ from other studies who found that schizophrenia and ASD differ significantly with regard to ToM deficits [20, 21, 22, 23]. On the other hand, our results support the findings from studies implying that comparable social cognitive ToM deficits exists in schizophrenia and ASD [17, 18, 19]. It should be noted that we found a trend towards more social cognitive deficits in the schizophrenia patients (see table 4), but the difference was non-significant which might be due to the small sample size.

Former studies in this field have used various measures to assess social cognition, but none has used TASIT to assess explicit ToM and social perception. As suggested in the existing literature, appliance of different social cognitive tasks might be pivotal to research findings, as the two patient groups may perform differently on distinct tasks [24, 25]. Furthermore, the different tasks may in essence involve various abilities or aspects of the complexity of social cognition making it difficult to compare studies. However, in the present study, we tried to accede this issue by applying two distinct social cognitive measures, but still no differences were found between the two patients groups. Future studies should aim at continuing to compare the two patient groups with different social cognitive measures to ensure a more comprehensive insight into the potential convergence or divergence in social cognition between the two disorders.

Notably, our results imply that we have compared low-functioning patients with schizophrenia who had a chronic and longer-lasting course of illness to high-functioning patients with ASD with intact neurocognitive abilities and no mental retardation. This may contribute to the incongruence between our preliminary hypothesis and our findings. However, the results regarding ToM are in

accordance with previous research findings suggesting that patients with longer-lasting schizophrenia have more severe ToM deficits than patients with first-episodes or remitted schizophrenia [8, 25]. Moreover, recent research findings indicate that high-functioning patients with schizophrenia have preserved social perceptual abilities compared to low-functioning patients [47]. Likewise, high-functioning patients with ASD have been found to have less severe ToM deficits compared to low-functioning patients [48, 49]. In accordance to this, our results are in congruence with the hypothesis that some high-functioning patients with ASD are able to pass explicit mentalizing tasks [29, 30]. However, the fact that we did not find any significant differences regarding implicit nor explicit ToM between ASD and matched controls seems to be in conflict with the existing literature stating that ToM deficits are well-known in ASD [6]. Again, it is important to notice that the patients with ASD neither differentiated from the matched controls regarding IQ nor neurocognition, and so our ASD sample may not be completely representative.

Future research in this area should bear in mind that different subgroups exist in both disorders and that these subgroups seem to perform differently on social cognitive measures. These subgroups for instance involve level of functioning, symptom severity, duration of illness, as well as IQ and neurocognitive abilities. As such, it seems fallible to consider both patient groups as one entire group when making comparisons of social cognition in schizophrenia and ASD.

4.1 Limitations

The sample size was small. For this reason replication in larger cohorts (with more statistical power) is needed. Moreover, the sample sizes in the two patient groups were not the same, and the age difference between the two clinical groups was high. But, each patient was closely matched one-to-one to a healthy control subject and all patients were recruited from the same mental health clinic. We investigated two different patient groups and the patients who were referred to the Neuropsychiatric unit were not necessarily optimal medicated. This made it impossible for us to control for medication in our analyses. We cannot rule out, that medication may have had an impact on cognition. No symptom scales were used. However, all patients were tested by the same experienced neuropsychologist and the exact diagnoses were carefully made on the basis of a comprehensive and profound psychiatric interview program involving both the patient and their relatives.

4.2 Conclusion

The results from the present study imply that different subgroups in both schizophrenia and ASD are characterized by differences in severity of ToM deficits and social perceptual abilities. This seems to be a critical issue in the research of possible overlaps and diversities in social cognition between these two mental disorders. Moreover, an important methodological question regarding measurement of social cognition are emphasized. More specific, the results indicate that we might have compared low-functioning patients with schizophrenia to a group of high-functioning patients with ASD.

As such, low-functioning patients with schizophrenia may be more severely impaired in both neurocognition and social cognition than high-functioning patients with ASD. Prospective research should aim at comparing different subgroups in both disorders in order to clarify the exact convergence and divergence in social cognition between these two patient groups. This should be done by using different social cognitive measures, and with an awareness of the diversity of particular tasks.

Author disclosure

None

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Table 1. Pairwise comparisons of patients with schizophrenia and their matched controls on demographics and social functioning. Continous variables were examined by Wilcoxon rank-sum test (Mann-Whitney) and reported with mean (95% CI) and effect size in terms of Harrell's C (95% CI). Categorical variables were examined by Fisher's exact test (if N<5 in a cell) or Chi^2 and reported with the counts and proportions of group total N (percentage).

Measure	Schizophrenia (N=21)	Matched controls (N=21)	Harrell's C	P value
Age[a]	40.48 (34.84;46.11)	25.45 (21.30;29.61)	0.49 (0.31;0.68)	0.95
Females	11 (52.4)	11 (52.4)	-	1.00
Years of education	12.57 (11.31;13.83)	15.98 (14.69;17.26)	0.80 (0.65;0.94)	**0.001**
PSP[b] scores	48.24 (42.57;53.91)	85.67 (82.66;88.68)	0.99 (0.98;1.01)	**<0.0001**
Current occupation			-	**<0.001**
Work	1 (4.8)	14 (66.7)		
Student	2 (9.5)	4 (19.0)		
Sick leave	13 (61.9)	2 (9.5)		
Pension	5 (23.8)	1 (4.8)		

Note: [a]Matched on group level, [b] Personal and Social Performance Scale.

Table 2. Pairwise comparisons of patients with autism spectrum disorders (ASD) and their matched controls on demographics and social functioning. Continous variables were examined by Wilcoxon rank-sum test (Mann-Whitney) and reported with mean (95% CI) and effect size in terms of Harrell's C (95% CI). Categorical variables were examined by Fisher's exact test (if N<5 in a cell) or Chi^2 and reported with the counts and proportions of group total N (percentage).

Measure	ASD (N=11)	Matched controls (N=11)	Harrell's C	P value
Age[a]	25.09 (20.77;29.41)	25.45 (21.30;29.61)	0.52 (0.24;0.80)	0.89
Females	7 (63.6)	7(63.6)	-	1.00
Years of education	11.73 (9.82;13.63)	15.45 (14.12;16.79)	0.90 (0.72;1.09)	**0.001**
PSP[b] scores	52.45 (44.41;60.50)	87.73 (84.48;90.98)	1.00	**0.0001**
Current occupation				**<0.001**
Unemployed	2 (18.2)	0	-	
Work	0	4 (36.4)		
Student	1 (9.1)	7 (63.4)		
Sick leave	1 (9.1)	0		
Pension	7 (63.6)	0		

Note: [a]Matched on group level, [b] Personal and Social Performance Scale.

Table 3. Pairwise comparisons of schizophrenia patients and their matched controls regarding IQ, neurocognition, and social cognition. Variables were examined by Wilcoxon rank-sum test (Mann-Whitney) and reported with mean (95% CI) and effect size by terms of Harrell's C (95% CI).

Measure	Schizophrenia (N=21)	Matched controls (N=21)	Harrell's C	P value
Estimated IQ [a]	98.14 (88.83;107.46)	110.52 (103.66;117.39)	0.68 (050;0.85)	**0.048**
BACS composite score [b]	-2.31 (-3.01;-1.61)	0.06 (-0.41;0.54)	0.90 (0.81;1.00)	**<0.0001**
TASIT [c]				
Sincere	16.05 (14.70;17.39)	17.48 (16.32;18.63)	0.64 (0.47;0.82)	0.11
Simple sarcasm	14.67 (12.27;17.06)	16.95 (15.61;18.29)	0.63 (0.45;0.81)	0.14
Paradoxical sarcasm	15.95 (14.19;17.71)	19.52 (18.92;20.13)	0.87 (0.76;0.99)	**<0.0001**
Animated Triangles				
Appropriateness ToM	6.37 (5.56;7.18)[d]	8.14 (7.34;8.94)	0.78 (0.63;0.93)	**0.003**
Appropriateness Random	11.47 (10.98;11.97)[d]	10.40 (9.63;11.18)	0.29 (0.13:0.45)	**0.016**
Intentionality Random	0.66 (0.02;1.30)[d]	1.48 (0.77;2.18)	0.69 (0.52;0.85)	**0.033**
Intentionality ToM	9.84 (8.15;11.54)[d]	14.64 (13.48;15.81)	0.86 (0.74;0.98)	**0.0001**

Note: aWechsler Adult Intelligence Scale-IV (Vocabulary, Similarities, Block Design, and Matrix Reasoning), [b]BACS, Brief Assessment of Cognition in Schizophrenia, [c]The Awareness and Social Inference Test, Part 2A, [d]N=19.

Table 4. Pairwise comparisons of patients with autism spectrum disorders (ASD) and their matched controls regarding IQ, neurocognition, and social cognition. Variables were examined by Wilcoxon rank-sum test (Mann-Whitney) and reported with mean (95% CI) and effect size by terms of Harrell's C (95% CI).

Measure	ASD (N=11)	Matched controls (N=11)	Harrell's C	P value
Estimated IQ [a]	104.55 (89.11;119.98)	108.09 (99.58;116.60)	0.56 (0.31;0.88)	0.45
BACS composite score [b]	-0.92 (-1.73;-0.12)	-0.12 (-0.75;0.52)	0.66 (0.40;0.92)	0.20
TASIT [c]				
Sincere	17 (15.30;18.70)	17.27 (15.93;18.62)	0.52 (0.24;0.80)	0.87
Simple sarcasm	15.27 (12.65;17.89)	17.45 (16.10;18.81)	0.66 (0.39;0.93)	0.20
Paradoxical sarcasm	16.91 (15.31;18.51)	19.36 (18.82;19.91)	0.84 (0.66;1.02)	**0.0056**
Animated Triangles				
Appropriateness ToM	7.61 (6.20;9.02)[d]	8 (6.91;9.09)	0.57 (0.28;0.87)	0.59
Appropriateness Random	10.94 (9.92;11.97)[d]	10.41 (8.92;11.89)	0.45 (0.17;0.74)	0.72
Intentionality Random	0.94 (0.12;1.77)[d]	1.64 (0.13;3.15)	0.54 (0.25;0.83)	0.75
Intentionality ToM	12.78 (10.46;15.09)[d]	13.73 (11.73;15.72)	0.63 (0.34;0.92)	0.34

Note: aWechsler Adult Intelligence Scale-IV (Vocabulary, Similarities, Block Design, and Matrix Reasoning), [b]BACS, Brief Assessment of Cognition in Schizophrenia, [c]The Awareness and Social Inference Test, Part 2A, [d]N=9.