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Social cognitive impairments in individuals with schizophrenia vary in severity

Michal Hajdúk^{a,b}, Philip D. Harvey^{c,d}, David L. Penn^{e,f}, Amy E. Pinkham^{g,h,*}

^a Department of Psychology, Faculty of Arts, Comenius University, Bratislava, Slovak Republic

^b Department of Psychiatry, Faculty of Medicine, Comenius University, Bratislava, Slovak Republic

^c Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL, USA

^d Research Service, Miami VA Healthcare System, USA

^e Department of Psychology, University of North Carolina, Chapel Hill, NC, USA

^f School of Psychology, Australian Catholic University, Melbourne, VIC, Australia

^g School of Behavioral and Brain Sciences, The University of Texas at Dallas, Richardson, TX, USA

^h Department of Psychiatry, University of Texas Southwestern Medical School, Dallas, TX, USA

ABSTRACT

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Social cognitive deficits are a hallmark feature of schizophrenia and have been confirmed by several metaanalyses; however, the uniformity of these impairments across individuals remains unknown. The present study evaluated the heterogeneity of social cognitive impairment. A secondary aim was to identify a subset of measures to quickly identify those individuals who are most in need of remediation. Two independent samples of people with schizophrenia (n = 176; n = 178) and their respective healthy control groups (n = 104; n = 154) were selected from two phases of the Social Cognition Psychometric Evaluation (SCOPE) project, which assessed multiple domains of social cognition. Latent profile analysis was utilized to identify sub-clusters of performance within each patient sample. Receiver operator curve and discriminant analysis were implemented to identify tasks suitable as screening tools. Three clusters were identified in each sample that differed primarily in severity of impairment. The first showed no social cognitive impairment ($\sim 25\%$ of patients). The second consisted of patients with mild impairment (~40% of each sample), and the third showed severe SC impairment (~32%). Patients in the severe cluster were older, less educated, more neurocognitively impaired, and lower functioning. Using the Bell Lysaker Emotion Recognition Task (BLERT) for screening provided sensitivity of 80.15% and specificity 89.13%. Combining BLERT with the Reading the Mind in the Eyes task yielded sensitivity of 91.60% and specificity 75.00% for identifying impaired individuals. These results illustrate the existence of distinct degrees of social cognitive impairment in schizophrenia and indicate that remediation efforts may not be necessary for all individuals.

1. Introduction

Social cognition (SC) is broadly defined as the automatic and volitional mental processes which form the foundation for successful social interaction (Adolphs, 2001; Green et al., 2008). Based on the consensus of experts in the field of schizophrenia, SC is considered a multidimensional construct which consists of four broad domains: theory of mind/mentalizing, emotion processing, social perception, and attributional style (Pinkham et al., 2014). Empirical studies have supported its importance as a predictor of functional outcome in patients with schizophrenia (Fett et al., 2011), and despite associations with neurocognition, SC is a distinct construct (Mehta et al., 2013) that mediates the relationship between neurocognition and functional outcome (Green

and Nuechterlein, 1999; Schmidt et al., 2011).

SC deficits in patients with schizophrenia have been confirmed via meta-analysis (Savla et al., 2013) with effect sizes ranging from 0.88 to 1.04, and several interventions have been developed to remediate these deficits (Grant et al., 2017; Kurtz et al., 2016; Kurtz and Richardson, 2012). However, simply comparing the means of patient and healthy control groups may obscure important inter-individual differences. For instance, heterogeneity of neurocognitive deficit in patients with schizophrenia has been established in several studies (Lewandowski et al., 2014; Rheenen et al., 2017). Using cluster analysis or similar statistical techniques, this work has identified three distinct groups of patients: those with very severe global neurocognitive impairment (i.e., a generalized deficit), those with milder impairment (i.e., specific

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^{*} Corresponding author. School of Behavioral and Brain Sciences, The University of Texas at Dallas, 800 West Campbell Road, GR 41, Richardson, TX, 75080, USA. *E-mail address:* amy.pinkham@utdallas.edu (A.E. Pinkham).

impairments), and those without neurocognitive deficit. It is possible that similar heterogeneity is present in social cognitive abilities; however, only a few studies have used cluster analytic approaches to evaluate this possibility, and those that have are limited by smaller sample sizes and/or restricted social cognitive batteries (Lee et al., 2017).

For example, using data from only facial and facial affect recognition tests (n = 100), Nelson et al. (2007) found two clusters of patients with different levels of impairment. Both groups were impaired relative to normative data, but the cluster with more pronounced impairment had also higher severity of thought disorder. Likewise, using data from social perception and emotion processing tasks (n = 77). Bell et al. (2013) identified both low and high social cognition subgroups of patients. Finally, Rocca et al. (2016) analyzed emotion processing and mentalizing performance in a sample of 809 outpatients and identified three clusters: unimpaired (42%), impaired (50%), and very impaired (8%). Those patients classified as unimpaired were significantly younger and better educated, with higher psychosocial functioning, better cognitive abilities, and lower levels of positive and negative symptoms. Collectively, these studies suggest substantial variability in SC abilities among patients that are likely relevant for determining who would be likely to benefit from treatment. Further, across all of these studies, the clusters that have been found represent groupings based on the levels of severity of the social cognitive impairment (i.e., quantitative differences) and not groups with differential profiles of impaired and unimpaired performance across tasks (i.e., qualitative differences).

To our knowledge, no study has yet used a comprehensive battery of tasks spanning the broad array of SC domains to assess distinct impairment patterns. It is possible that a broader assessment of social cognition will reveal previously undiscovered qualitative differences. Here, we utilized latent profile analysis to examine data from the Social Cognition Psychometric Evaluation (SCOPE) project to: 1) investigate subgroups of impairment, 2) examine whether identified subgroups differ only on quantitative degree of impairment severity or if differences are qualitative (i.e., distinct profiles across domains/tasks), 3) test the replicability of identified subgroupings using different batteries of tasks and samples, 4) analyze whether identified groups differ in demographic, clinical, and outcome variables, and 5) identify a subgroup of measures that can be used to identify those individuals who are most in need of remediation.

2. Methods

2.1. Participants

Two independent samples of participants were drawn from the SCOPE project database. Sample 1 (n = 176 patients and n = 104 demographically matched healthy controls) consisted of individuals who took part in the initial psychometric study (Pinkham et al., 2016). Sample 2 (n = 178 patients and n = 154 demographically matched healthy controls) consisted of participants in the final validation study (Pinkham et al., 2018). Participants from Sample 1 who also participated in the validation study (n = 35) were omitted from Sample 2, resulting in smaller size for Sample 2 than previously reported.

Clinical participants were stable outpatients with diagnoses of schizophrenia or schizoaffective disorder, confirmed by Mini International Neuropsychiatric Interview (Sheehan et al., 1998) and Structured Clinical Interview for DSM Disorders Psychosis Module (First et al., 2012). Patients could not have been hospitalized within the last 2 months and had to be on a stable medication regimen for a minimum of 6 weeks with no dose changes for a minimum of 2 weeks. Healthy controls were screened to ensure the absence of psychopathology. Exclusion criteria for both patients and controls were: (i) presence or history of pervasive developmental disorder or mental retardation (defined as IQ < 70) by DSM-IV criteria, (ii) presence or history of medical or neurological disorders that may affect brain

function (e.g., seizures, central nervous system tumors, or loss of consciousness for 15 min or more), (iii) presence of sensory limitation including visual (e.g., blindness, glaucoma, vision uncorrectable to 20/40) or hearing impairments that interfere with assessment, (iv) no proficiency in English, (v) presence of substance abuse in the past month, and (vi) presence of substance dependence not in remission for the past 6 months.

2.2. Measures

2.2.1. Social cognition measures

SC batteries differed between the two samples/studies and were dictated by the larger SCOPE project. In both samples, the tasks covered four broad SC domains: Theory of Mind/Mentalizing (ToM), Emotion processing (EP), Social perception (SP) and Attributional Style (AS). The following tasks were administered to both samples: Hinting Task (ToM), Reading Mind in the Eyes Test - Eyes (ToM), The Awareness of Social Inferences Test, Part III - TASIT (ToM), Penn Emotion Recognition Test - ER-40 (EP), Bell – Lysaker Emotion Recognition Task - BLERT (EP). Sample 1 also completed the Ambiguous Intentions and Hostility Questionnaire - AIHQ (AS), Relationships Across Domains - RAD (SP), and Trustworthiness Task (Trust). Sample 2 completed the Mini Profile of Nonverbal Sensitivity - MiniPONS (SP), The Social Attribution Task - Multiple Choice - SAT-MC (SP), and Intentional Bias Task - IBT (AS). All tasks were administered at baseline and retest, which occurred 2–4 weeks after the initial assessment.

2.2.2. Neurocognition

An abbreviated version of the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008; Kern et al., 2008) was administered that included the Brief Assessment of Cognition – Schizophrenia – Symbol Coding (BACS-SC), Trail Making Test – Part A (Trails A), Animal Fluency, Letter – Number Span (LNS), and Hopkins Verbal Learning Test (HVLT).

2.2.3. Psychopathology

Current levels of psychopathology were assessed with Positive and Negative Syndrome Scale (Kay et al., 1987). Mean scores for positive, negative and general psychopathology were used. Level of depressive symptomatology was assessed by Beck Depression Inventory II (Beck et al., 1996).

2.2.4. Functional capacity and functional outcomes

The UCSD Performance-Based Skills Assessment, Brief (UPSA-B) (Patterson et al., 2001a) was used as a measure of functional capacity. Social Competence was evaluated using the Social Skills Performance Assessment (SSPA) (Patterson et al., 2001b). Real world functioning was assessed using informant reports on the Specific Level of Functioning Scale (SLOF) (Schneider and Struening, 1983). Informants were high contact clinicians, family members, or close friends identified by the participants. Further details regarding the tasks are available in (Pinkham et al., 2016, 2018).

2.2.5. Statistical analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences), and R software (Version 3.2.5). For each sample, SC variables were first transformed to Z-scores using the respective healthy control group as normative data (Pinkham et al., 2016, 2018). Presented Z-scores are therefore interpreted in terms of difference from healthy control performance. Patients with missing data on SC variables were omitted from the analysis, which resulted in the exclusion of 3 participants from Sample 1 due to missing data on Hinting and RAD.

MClust package (Fraley et al., 2007) in R software was then used to conduct Latent Profile Analysis (LPA) within each sample. LPA is a model-based clustering method that aims to identify hidden groups from observed data and that allows for examination of both quantitative and qualitative differences (Oberski, 2016). An optimal number of clusters (best-fitting model) in LPA were selected according to Bayesian information criterion (BIC), and participants in each identified cluster had similar SC response profiles. Consistency between samples in the magnitude of SC impairment for each cluster was then evaluated with Cohen's d. Smaller differences between samples were considered evidence for consistency. Mean consistency was calculated for each task and each cluster.

Next, demographic, clinical, cognitive, and social functioning differences between the identified clusters were evaluated using one-way ANOVA or Chi-Square tests (x^2) as appropriate. To constrain type I error, a reduced alpha level of p < 0.01 was utilized to determine significance in ANOVA post – hoc tests.

Samples were then combined, and ROC analysis was used to evaluate the discriminatory power of our tasks in detecting SC impairment. The area under the curve (AUC) was calculated for each measure that was shared between samples. Discriminant analysis was also used to determine the best linear combination of tasks for identification of patients with SC impairment. Sensitivity, specificity, and positive and negative predictive values were calculated.

3. Results

3.1. Descriptive statistics for each sample

Descriptive statistics for each patient sample on demographic, clinical, SC, neurocognition, and functional outcome variables are shown in Table 1. Cohen's d was used for comparing patient samples from the two studies on continuous variables; Cramer's V was used for

Table 1

Descriptive statistics for demographic and clinical characteristic of each sample.

categorical variables. Mean standardized differences between the patient samples ranged from negligible to small. Effect sizes for categorical variables ranges from 0.01 to 0.21. Samples are similar in age, education, premorbid intellectual functioning, severity of symptoms, and neurocognition. The largest differences were found in social functioning (d range from -0.19 to -0.39).

3.2. Latent profile analysis

A three-cluster solution (VEI, diagonal, cluster with equal shape) was identified as best-fitting based on the BIC (BIC = -5849.335) in Sample 1. Clusters are characterized as Intact (I) (26%), Mild impairment (M) (41%) and Severe impairment (S) (33%). A three-cluster solution (VEI, diagonal, cluster with equal shape) was also identified as best fitting (BIC = -4353.88) in Sample 2. Identified clusters were very similar to those found in Sample 1 in severity and size. Accordingly, clusters were named Intact (I) (26%), Mild impairment (M) (43%), and Severe impairment (S) (31%). Profile plots for both samples are shown in Fig. 1.

Within each sample, clusters were compared using one-way ANOVAs with Bonferroni correction to examine pairwise differences between clusters. Mean scores on BLERT, ER-40, TASIT, Eyes, Hinting, RAD, SAT-MC, MINI Pons, IBT, AIHQ-HB, and AIHQ-Blame significantly differed across clusters. Except for IBT, AIHQ-HB, and AIHQ-Blame, post-hoc analyses revealed that the Intact cluster had significantly better performance than Mild impairment, and Mild impairment had better SC abilities than the Severely impaired cluster. Mean Trustworthiness judgements across clusters were not significantly different (F (2, 173) = 0.686, p = 0.505) nor were mean scores on AIHQ-

	Sample 1 (n = 176) Sample 2 (n = 178)				
	M/%	SD	M/%	SD	Cohen's d/Cramer's V
Male	66%		69%		0.03
Race					0.15
Caucasian	42%		55%		
African American	53%		38%		
Other	5%		7%		
Primary Diagnosis					0.01
Schizophrenia	54%		54%		
Schizoaffective Disorder	45%		45%		
Medication Type					0.21
Atypical only	70%		75%		
Typical only	14%		12%		
Both	2%		7%		
No antipsychotic	11%		6%		
Information unavailable	4%		0%		
Age	41.90	12.31	41.41	11.95	0.04
Estimated total years of education	12.66	2.12	13.09	2.54	-0.18
WRAT-3 Standard Score	93.72	15.88	95.48	14.65	-0.12
PANSS - Positive	16.11	5.78	15.95	5.06	0.03
PANSS - Negative	13.71	5.30	14.53	5.78	-0.15
PANSS - General	30.73	7.99	32.02	8.14	-0.16
BDI-II	16.68	12.23	14.15	12.01	0.21
Neurocognitive Functioning					
BACS - SC	42.19	11.87	43.06	11.22	-0.08
Animal Fluency	18.49	5.13	20.23	6.27	-0.30
Trails A	41.17	18.91	40.41	18.16	0.04
HVLT	20.29	5.38	21.31	5.64	-0.19
LNS	11.39	4.10	12.37	4.23	-0.24
Functional Outcome					
SSPA	4.22	0.62	4.15	0.50	0.13
UPSA-B	69.80	14.40	70.15	14.21	-0.02
SLOF - Interpersonal Relationships	3.27	0.89	3.58	0.92	-0.35
SLOF - Social Acceptability	4.33	0.56	4.48	0.56	-0.26
SLOF - Activities	4.31	0.77	4.58	0.91	-0.33
SLOF - Work Skills	3.55	0.88	3.73	0.99	-0.19
SLOF - Total	3.92	0.57	4.16	0.65	-0.39





Note: Patient data were first normed to the respective healthy control group and are thus shown as z-scores representing the distance, in standard deviation units, from the healthy control mean. AIHQ and IBT are reverse scored to assist interpretation (i.e., lower scores indicate worse performance/stronger bias).



AB (F (2, 173) = 0.824, p = 0.441). Results from ANOVA analyses are provided in Supplemental Table 1.

3.3. Consistency of SC impairment severity across samples

BLERT, ER-40, Eyes, Hinting, and TASIT were administered to both samples. Consistency of impairment severity for these three clusters was evaluated by comparing means and standard deviations for Intact, Mild, and Severe clusters between samples. Mean standardized differences for the Intact groups were negligible on average (d = -0.12). Averaged

differences for the Mildly (d = -0.34) and Severely (d = -0.25) impaired clusters were small in terms of effect size. Details are provided in Supplemental Table 2.

3.4. Correlates of cluster membership

In both samples, the Intact cluster was younger than Mild and Severe clusters and showed higher premorbid intellectual functioning and education. Gender ratios were similar across all clusters. No differences were found for positive and general symptoms in either sample; however, in Sample 1, the Intact cluster showed significantly lower levels of negative symptoms relative to the Severe cluster (p < 0.001). Level of depressive symptoms were equal across clusters in Sample 1 (F (2, 173) = 0.214, p = 0.808) and Sample 2 (F (2, 175) = 0.533, p = 0.576).

Neurocognitive performance significantly differed between clusters in a consistent manner across samples. Overall, the Intact cluster showed better performance than Mild, and the Mild cluster performed better than the Severe cluster.

In both samples, functional capacity and social skills were significantly lower in the Severe impairment cluster, and overall levels of real world functioning were reduced (Sample 1: p < .01 for Severe compared to both Intact and Mild; Sample 2: p = .017 for Severe compared to Mild). Detailed results for all comparisons in both samples are presented in Supplemental Tables 3 and 4.

3.5. Screening for SC impairment

For those tasks that were administered to both samples (BLERT, ER-40, Eyes, Hinting, and TASIT), ROC analysis was used to evaluate the sensitivity and specificity for detecting impairment. Samples were merged, resulting in a total of 354 patients, and patients with mild and severe impairment were merged into a single group. AUC were significant for all measures: BLERT (0.912), ER-40 (0.818), Eyes (0.910), Hinting (0.746) and TASIT (0.880). Classification accuracy and proposed cut-off scores are displayed in Table 2. For single tasks, BLERT had the best psychometric properties for identifying patients with SC impairment. A cutoff of 15 or lower (Raw score) on BLERT provided sensitivity of 80.15% (CI: 74.80–84.81) and specificity of 89.13% (CI: 82.92–94.66) for classifying patients as either with or without SC impairment. Positive predictive value was 95.45% (CI: 92.10–97.42), and negative predictive value was 61.19% (CI: 55.03–67.02).

To determine whether a combination of tasks would perform better for screening, Discriminant analyses were also conducted to identify the best combination of tasks for identification of SC impairment. The following criteria were set in advance: 1) combination of tasks should be from two distinct SC domains, and 2) administration time should be as short as possible. We omitted combinations of tasks within social cognitive domains in order to more comprehensively cover the SC construct and to ensure that first-time administration of some psychometrically sound tasks could be preserved for evaluation of treatment efficacy. From these analyses, BLERT and Eyes were identified as the best combination, and both can be administered in 15 min total. The overall Chi-square test was significant (Wilks $\lambda = 0.555$, $x^2 = 206.880$, p < 0.001, Canonical correlation = 0.667). Standardized canonical coefficients were 0.593 and 0.615 for BLERT and Eves, respectively. 87.30% of patients were classified correctly. Using a leave-one-out procedure in which each patient was classified by the functions derived from all patients other than that one, 86.7% of patients were classified

Table 2

Screening	accuracy	of	SC	tasks
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Task (cutoff score)	% of correct classification	Sensitivity	Specificity	PPV	NPV
BLERT (15)	82	80.15	89.13	95.45	61.19
ER-40 (32)	73	71.76	77.17	85.92	48.97
Hinting (15)	69	74.43	54.35	82.28	42.74
Eyes (23)	82	82.44	80.43	92.31	61.67
TASIT (48)	80	82.44	72.83	89.63	59.29
BLERT + Hinting	87	93.51	69.57	87.74	79.01
BLERT + Eyes	87	91.60	75.00	91.25	75.82
BLERT + TASIT	89	94.66	79.91	91.18	82.93
ER-40 + Hinting	79	91.98	42.39	81.97	65.00
ER-40 + Eyes	86	91.98	68.48	89.26	75.00
ER-40 + TASIT	84	92.75	57.61	86.17	73.61

Abbreviations: PPV - Positive predictive value; NPV - Negative predictive value.

correctly. The combination of BLERT and Eyes has adequate sensitivity of 91.60% (CI: 87.56–94.66) and specificity 75.00% (CI: 64.89–83.45). Positive predictive value was 91.25% (CI: 87.97–93.71), and negative predictive value was 75.82% (CI: 67.39–82.64). The combination of BLERT and TASIT showed slightly better diagnostic accuracy but had a significantly longer administration time (approximately 25 min), which renders this combination less practical as a screening tool. Results of diagnostic accuracy for all possible task combinations based on the proposed criteria are presented in Table 2.

To facilitate clinical use of BLERT and Eyes as screening measures, Canonical Discriminant Function Coefficients can be used for prediction of social cognitive impairment. For utilization at the level of the individual, the following equation from discriminant analysis can be used:

D = -5.414 + 0.185BLERT + 0.140Eyes

The cut-off value was set to 0.490 based on groups centroids. Values lower than this cut-off indicate SC impairment. A calculator for D scores is provided in Supplemental Material and can be used by entering raw scores from BLERT and Eyes.

4. Discussion

The present study is the first to identify variable levels of SC impairment in patients with schizophrenia using a comprehensive battery of tasks spanning all SC domains and to provide a within-study replication using different participants and tasks. LPA analyses on both samples identified three clusters with very similar impairment patterns and distributions of individuals. Replication of similar cluster solutions on the two independent samples provides strong evidence in favor of three distinct levels of social cognitive performance. Approximately 25% of all patients had social cognitive abilities comparable to healthy subjects. About 40% of both samples consisted of patients with mild impairment, and approximately 33% of patients showed severe SC impairment. These results qualify the findings of meta-analyses reporting significant SC difficulties in schizophrenia by demonstrating that a substantial portion of patients do not show impairment.

Validation of an intact SC group has important clinical implications. First, it appears that SC remediation may not be necessary for all individuals with schizophrenia. Instead, resources should be directed to those individuals who may be most likely to benefit (Horan and Green, 2017). To this end, we suggest two possible options for screening for SC impairment: 1) The BLERT alone provides adequate sensitivity and specificity and can be completed in 7 min on average, or 2) the combination of the BLERT and Eyes task yields even greater sensitivity and retains adequate specificity, with an administration time of approximately 15 min. One potential pitfall of this combination is the strong association of Eyes with verbal abilities; however, it does enable evaluation of more than one domain of social cognition and improves sensitivity. Both screening options could therefore allow providers to quickly evaluate levels of impairment in individual patients.

Second, our findings are also highly relevant for clinical trials attempting to improve social cognition. Including participants with average SC abilities could possibly lead to null findings due to ceiling effects on the outcome measures. Based on this analysis, about 25% of patients score within the normative range or higher across SC tasks. Thus, in future clinical trials, we recommend that investigators screen for SC impairment before randomization of patients.

It is also noteworthy that the Intact group scored better than controls on some tasks within the battery (i.e., BLERT, ER40, and Eyes). While this may suggest superior performance rather than intact performance, this interpretation may be overly optimistic given that the patient scores are still generally falling within .5 standard deviations from the control sample mean. It is also important to consider that this pattern of better performance is not consistent across all tasks and domains. Thus, for social cognition as a whole, there does not appear to be evidence for superior abilities.

The current findings also clarify the characteristics of those patients who do show impairments. Patients with the most severe SC impairment were older, less educated, and more neurocognitively impaired. This cluster also exhibited the strongest impairments in functional capacity and real-life functioning, which is in line with findings of Rocca et al. (2016). Importantly, symptom levels were largely similar across groups, demonstrating that clusters were not merely a reflection of symptom severity but rather more indicative of overall functioning. The exception to this was negative symptoms in Sample 1, where the severely impaired cluster showed higher ratings than the intact cluster. However, as this difference was not seen in Sample 2, future work is needed to clarify this discrepancy and may benefit by including measures that better capture the multifaceted nature of negative symptoms.

In terms of generalized or specific patterns of SC impairment, our results support a generalized deficit across domains with different levels of severity across individuals. Specifically, both impaired groups showed lower performance for emotion processing, social perception, and theory of mind/mentalizing, with the severely impaired group scoring significantly lower than the mildly impaired group, who performed significantly below the intact group. The one exception was attributional style, where only the severely impaired group differed from the intact group. This distinction between domains is consistent with views that social cognitive capacity may be fundamentally different from social cognitive bias and indicates that bias is most evident in those individuals also displaying the most impaired capacity (Roberts and Pinkham, 2013; Walss-Bass et al., 2013). The current results may also suggest meaningful heterogeneity among individuals with schizophrenia that could be broadly parsed as social cognitively impaired vs. not impaired. This possibility could be explored by examining whether any genetic or biological differences exist between impaired and nonimpaired individuals that may support these discrete subgroups.

When interpreting these results, potential limitations also require consideration. Although this study is the first to utilize a broad social cognitive battery, tasks assessing social perception and attributional style tended to show poorer psychometric properties than those addressing emotion processing or mentalizing (Pinkham et al., 2016, 2018). This could call into question the clustering of groups for these domains; however, the consistency of clustering across tasks and samples suggests that similar results would be found even with more psychometrically sound measures. It is also possible that the separation of SC clusters could be secondary to neurocognitive abilities. To assess this possibility, we conducted a series of ANCOVAs to evaluate SC differences between clusters while controlling for neurocognitive performance. Differences between clusters remained significant and all results were unchanged. Utility of the tasks as screening measures would also be strengthened via cross-validation using an independent sample. Finally, due to the short test-retest interval of the SCOPE study and the practice effects that were evident at retest for the majority of measures (18, 19), we were unable to accurately assess the stability of cluster membership. Future studies with longer follow-up periods are needed as are alternative forms or new measures that lack practice effects.

These limitations notwithstanding, the current manuscript presents novel evidence for variability in social cognitive impairment in schizophrenia such that approximately one quarter of patients retain intact social cognitive abilities across multiple domains. Such results support the importance of screening for social cognitive impairment in order to provide interventions that are optimally matched to individual needs.

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5. Statement of conflicts of interest

Dr. Harvey serves as a consultant/advisory board member for Boeheringer Ingelheim, Lundbeck, Otsuka Digital Heath, Roche, Sanofi, Sunovion, and Takeda. Dr. Hajduk reports receiving a fee from Lundbeck Slovakia as a speaker at an education grant conference unrelated to the contents of the article. Drs. Penn and Pinkham report no conflicts of interest.

6. Author contributors

Dr. Hajdúk aided in study design and implementation, oversaw and completed all statistical analyses, wrote the first draft of the manuscript, and contributed substantially to all subsequent drafts of the manuscript.

Drs. Harvey, Penn, and Pinkham obtained primary funding, aided in study design and original data collection, assisted with data interpretation, and substantially edited all drafts of the manuscript.

All authors have approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx. doi.org/10.1016/j.jpsychires.2018.06.017.

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