# Experiential but not expressive negative symptoms are associated with social cognition and functioning in schizophrenia –findings of a preliminary study with rehabilitation inpatients

***and***

***Clinical Research Portfolio***

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# Chapter One: Systematic Review

# A systematic review of the relationship between social cognitive abilities and functional outcomes in individuals at ultra-high risk for schizophrenia

*Prepared in accordance with the requirements for submission to Psychosis (see appendix 1.1)*

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# Abstract

***Background:*** Functioning is impaired in individuals at ultra-high-risk (UHR) for schizophrenia. Social cognition is a significant predictor of functioning in those with schizophrenia, and while social cognition is impaired in UHR individuals it is unclear whether social cognitive deficits are associated with poor functioning in the UHR population. Understanding this could improve early intervention efforts.

***Methods:*** Psycinfo, Medline and CINAHL databases were searched on 14th May 2019 using keywords related to ultra-high risk, schizophrenia, functioning and social cognition. Eligible studies examined an association between functioning and social cognition in UHR participants.

***Results:*** Eleven eligible studies were identified, with overlapping samples in six of these. Methodological quality was average to good. Emotion recognition and Theory of Mind were the most studied domains. Better and faster recognition of negative emotions was associated with better functioning with small to moderate effect sizes. There was limited evidence theory of mind was associated with functioning, but this may reflect differences in IQ or cognition. Findings regarding attribution bias were mixed and interpretation was limited by poor quality measurement.

***Conclusions:*** Social cognition deficits, in particular emotion recognition appear to be associated with poor functioning in UHR individuals but there remains a relatively small number of studies in this area with varying methodological quality. Further research with independent samples and longitudinal designs and consideration of key mediator and moderator variables can extend these findings.



Keywords: psychosis; emotion recognition; functioning; at-risk mental state

# Introduction

Social cognitive deficits are a key determinant of functioning in schizophrenia and are thought to be impaired prior to the onset of active psychosis. It is not understood how this is associated with functioning in individuals at high-risk of developing schizophrenia. Improving our understanding of this relationship is crucial for improving early intervention efforts and enhancing our understanding of how social cognitive deficits contribute to illness development and progression.

## Social Cognition in Schizophrenia

The term social cognition describes cognitive processes facilitating flexible social behaviour such as detecting intentions and emotions in others and knowledge of social rules (Adolphs, 1999). It comprises of a number of inter-related but independent domains of processing and an expert panel identified four domains thought relevant in schizophrenia, alongside recommended measures of each (Pinkham et al., 2015).

- Emotion Recognition (ER) - identify and discriminate expression of emotions
- Theory of Mind (ToM) – interpret and represent the mental states of others
- Social Perception (SP) – interpreting social cues including social knowledge of rules.
- Attribution Bias (AB) – how someone makes sense, or explains causes, of social events.

Social cognitive deficits in schizophrenia have been well established with meta-analyses finding large effect sizes for impairments in ToM, SP and ER abilities (Savla et al., 2012). These deficits remain stable throughout the illness, being present in both first episode and remitted patients (Mehta et al., 2013, Healey et al., 2016) and are thought to represent a trait rather than a state dependent deficit.

Individual differences in social cognitive ability is an important determinant of *psychosocial functioning* - broadly defined as the extent to which an individual performs different social roles including work, interpersonal relationships, activities of

daily living and recreation, as well as their functional capacity and subjective wellbeing or quality of life (Priebe, 2007). Functioning is an important target for recovery given the long-term disability associated with schizophrenia which is not consistently alleviated by pharmacological interventions (Brissos et al., 2011). Social cognitive ability accounts for a quarter of variance in functional outcomes in schizophrenia, and this has been shown to be partially independent of non-social cognitive processes such as memory and attention (Fett et al., 2011). As a result, interventions have been developed to remediate or recover social cognitive ability to improve functioning. These interventions have been shown to improve underlying social cognitive abilities, such as the ability to correctly identify emotions, but less consistently improve psychosocial functioning (Tan et al., 2018).

**Ultra-High-Risk Concept**

Intervening during a prodromal phase of schizophrenia may improve outcomes, with length of untreated illness thought to significantly contribute to poorer outcomes (Fusar-Poli et al., 2009, Keshavan et al., 2003). This necessitates detecting individuals prior to onset, which has led to development of criteria and screening tools to identify those at ultra-high risk (UHR; See table 1) (Yung et al., 2005, Miller et al., 2002, Schultze-Lutter et al., 2007). However, these criteria identify a relative heterogenous group, with only 22-36% converting to psychosis within three years (Fusar-Poli et al., 2012).

**Social Cognition and Functioning in UHR**

Both social cognition and functioning are impaired in UHR individuals, regardless of later transition to schizophrenia (van Donkersgoed et al., 2015, Lee et al., 2015). Two meta-analyses examining social cognitive deficits in UHR individuals found moderate effect sizes for impaired ER and ToM with the evidence for AB being more equivocal due to a lack of research and inconsistencies in the definition of AB.

It is important to determine whether social cognitive abilities are related to psychosocial functioning prior to onset of psychosis. Firstly, given the promise of social cognition interventions for improving functioning in individuals with schizophrenia, understanding how these factors interact in the UHR state may provide

indications for prodromal phase interventions to improve functioning. Secondly, the neurodevelopmental model posits that schizophrenia is the end result of a series of biological and environmental risk factors leading to impaired cognition and functioning which result in illness (Murray and Lewis, 1987, Murray et al., 2017), and poor premorbid functioning is predictive of illness onset and outcome (Cannon-Spoor et al., 1982). Understanding the relationship between social cognition and functioning prior to illness onset will improve our understanding of how social processing abilities might contribute to psychosis development and outcomes.

Table 1: UHR Criteria

| Subgroup | Criteria |
|---|---|
| Attenuated Psychotic Symptoms (APS) | Subthreshold, positive APS during the past year. |
| Brief limited intermittent psychotic symptom (BLIPS) | Episodes of frank psychotic symptoms not lasting longer than a week which spontaneously abated without treatment |
| Trait and State Risk Factor | First-degree relative with a psychotic disorder or schizotypal personality disorder (SPD) *and* significant decrease in functioning or chronic low functioning during the previous year. |
| Basic Symptoms | Subjective abnormalities in the realms of cognition, attention, perception, and movement. |

A systematic review of 72 studies examining factors associated with poor functioning in the UHR group concluded that neurocognitive deficits and negative and disorganised symptoms predicted functional outcomes (Cotter et al., 2014). Only three of the included studies examined the association between social cognition and functioning with mixed support for an association. Initial searches of the literature indicated that since 2014, there has been a significant increase in research looking at social cognition

and functioning. Given the lack of conclusions which could be drawn from the previous review and a significant body of further literature this area warrants further review.

### Aims

The aim of the current review is to summarise the research that examines the relationship between social cognition and functioning in individuals who meet ultra-high-risk criteria for developing schizophrenia.

## Method

This review was conducted in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (Moher et al., 2009). A Prospero search revealed no similar ongoing reviews.

### Search Strategy

On 14th May 2019 an electronic database search was performed on: Psycinfo (EBSCO), CINAHL (EBSCO) and Medline (Ovid). Keywords and subject headings related to schizophrenia, UHR, functioning and social cognition were combined and adapted according to database. See Appendix 1.2 for full search strategy. No limiters were applied.

Duplicates were removed and title and abstracts screened. Full texts of papers not clearly excluded were examined to determine eligibility. To identify articles not returned by the electronic search, the journal Schizophrenia Research and the reference list of eligible studies were hand-searched.

### Eligibility Criteria

Included papers reported original research published in peer reviewed journals which examined an association between functioning and social cognition in individuals who met criteria for UHR based on a validated screening tool. For the purpose of this review, relevant domains of social cognition are those identified in the SCOPE review

(Pinkham et al., 2013): (1) ToM (2) ER (3) SP (4) AB. Functional outcome was defined on the basis of previous reviews – community functioning, social behaviour in the milieu, social problem solving and social skills (Green et al., 2000, Couture et al., 2006).

Studies which defined "risk" solely as familial or genetic risk or where UHR participants were not reported independently were excluded. Book chapters, dissertations, systematic reviews or meta-analyses, study protocols, poster abstracts, conference proceedings and studies published in a language other than English were excluded.

**Data Extraction and Synthesis**

A data extraction form was developed to collate study data (see Appendix 1.3). Due to the variability in the measurement of functioning and social cognition, a narrative synthesis approach was used. Results are described according to the domain of social cognition examined due to the finding from previous research that different social cognitive domains are differentially associated with functioning (Couture et al., 2006). Correlation coefficients will be used to describe the estimated effect size of the association between social cognition and functioning. For regression analysis, r will be calculated from the relevant *t* statistic using the following equation: $\sqrt{t2 / (t2 + DF)}$ and the following cut off conventions used: 0.1 (small), 0.3 (medium) and 0.5 (large) (Cohen, 1992).

**Quality Assessment**

The Crowe Critical Appraisal Tool v1.04 (CCAT; Crowe and Sheppard, 2011) was used to assess methodological quality. Eight domains consisting of 22 quality items are rated on a 5-point scale depending on the evidence presented. Total scores are converted to a percentage to allow comparison across studies. Total scores should be interpreted with caution as domains are not equivalent in their importance. An independent researcher co-rated 50% of included studies. Discussion was had to resolve discrepancies and reach consensus. See Appendix 1.4 for quality ratings for domains and overall percentage rating.

# Results

Following the removal of duplicates, 175 articles were screened. 124 articles were excluded from title and abstracts, with full text of the remaining 51 articles screened against inclusion criteria. 41 articles were excluded and two further papers identified from reference lists leading 12 papers meeting all inclusion criteria.

Papers were then examined for overlapping samples. Von Elm et al.'s (2004) guidance on types of sample overlap in published research was used to identify the type of overlap present in the papers and to guide decisions on inclusion or exclusion of papers. Of the 12 initially identified articles, eight papers were found to have samples derived from four cohorts.

Two papers (Thomson et al. 2011 and Cotter et al. 2017) fit pattern 1 of the classification and were found to have identical study samples. In addition to this, the outcomes reported in the Thomson et al. paper were re-reported in the Cotter et al. paper alongside additional outcomes. As such, the Thomson et al. paper was excluded from the review, with all findings from it being discussed under the Cotter et al. paper.

Six further papers were identified as fitting pattern four of Von Elm's classification – non-identical samples and non-identical study outcomes. As such, all six studies were included in the review and their results are discussed independently. See Table 2 for an overview of the cohorts and papers with overlapping samples. See Figure 1 for Prisma flowchart of paper identification.

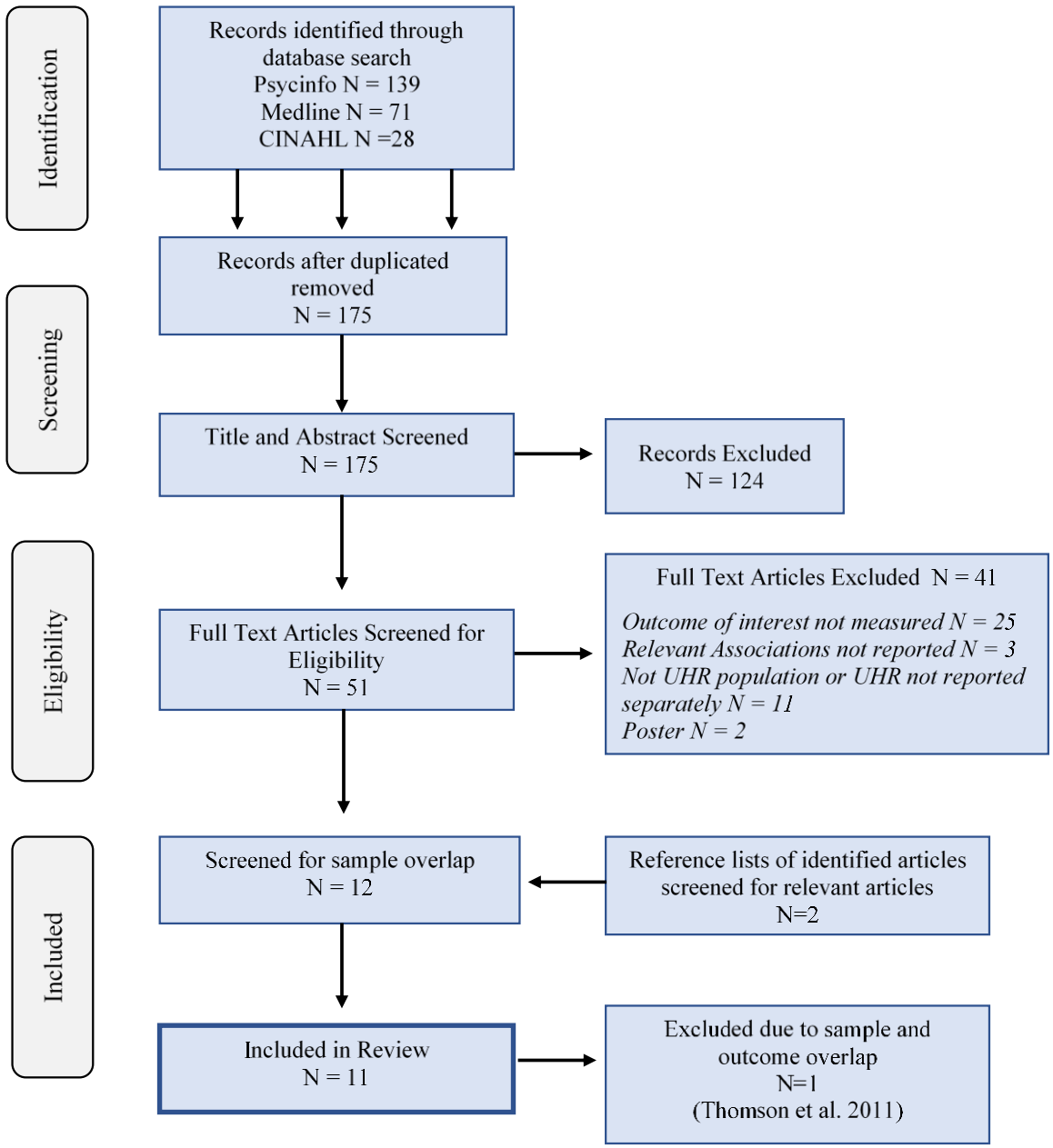
For the purpose of demographic calculations, for papers with overlapping samples, the cohort sample size will be used to calculate number of UHR participants included in the review. For papers with overlapping samples, the cohort mean ages will be extracted from the paper with the largest sample size.

*Table 2 Summary of Sample Cohorts*

| Cohort | Cohort N and description | Papers | Paper N | Description of Sample overlap | Description of outcome overlaps | Included or Excluded? |
|---|---|---|---|---|---|---|
| **Cotter** | N = 30<br>Subsample of larger study | Thomson et al. 2013 | 30 | Samples in these two papers overlap completely | Stanford et al. report on AB and functioning. Cotter et al. report on AB, ToM, ER and SP and re-report Stanford et al. results. | Excluded |
| | | Cotter et al. 2013 | 30 | | | Included |
| **Amminger** | N= 79<br>Total sample recruited for RCT | Amminger et al. 2013 | 79 | Bartholomeusz et al. report on sub-sample of overall cohort | Bartholomeusz et al. report on MRI findings not reported in Amminger et al. | Included |
| | | Bartholomeusz et al. 2014 | 39 | | | Included |
| **Stanford** | N= 63<br>Sample recruited for longitudinal study | Standford et al. 2011 | 63 | DeVylder et al. report on subsection of overall cohort. | Stanford et al. report on ToM and Functioning outcomes while DeVylder et al. report on AB and functioning | Included |
| | | DeVylder et al. 2013 | 33 | | | Included |
| **Glenthoj** | N=146 | Glenthoj et al. 2016 | 65 | Glenthoj et al. 2016 report on | | Included |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Total sample recruited for RCT | Glenthoj et al. 2018 | 146 | data collected between 2014-2016 while Glenthoj et al. 2018 report on the complete cohort. | Glenthoj et al. 2016 report on Theory of Mind, Emotion Recognition accuracy and Attribution Bias.<br>Glenthoj et al. 2018 report on emotion recognition latency. | Included |

***Figure 1: Prisma Flowchart***



## Study Characteristics

Included cohorts reported on 642 (334 female) individual UHR participants with mean ages from 16.45-24.59. Four papers included a control group. All papers reported cross-sectional data, with 8 papers reporting baseline data from a randomised control trial or longitudinal study, while two studies reported data from a sample drawn from a larger study. See table 3 for an overview of study characteristics and key findings.

## Study Quality

The percentage CCAT ratings ranged from 65-95% with a mean percentage of 72.2, indicating studies were of average to good quality with some very high quality. Common limitations were inadequate description of sample recruitment (N = 6), overlapping samples (N=8), inadequate description of the administration of functioning measurements e.g. who provided ratings (N= 6) and publication of baseline data from RCT or longitudinal study without description of sample selection (N= 8). Two studies used self-report measures of functioning, which have been shown to lack reliability (Harvey, 2013) and four studies used the GAF as their only objective rating of functioning which has been criticised for conflating symptoms with functioning.

*Table 3- Study Characteristics and Main Findings*

| Cohort | Paper | Sample N (Male) | Mean Age | Other Control group | Study Type | FO | SC Domain | SC Measure | Main Findings |
|---|---|---|---|---|---|---|---|---|---|
| **Cotter** | **Cotter (2017)** | 30 (14) | 19.1 | - | Cross sectional data from a larger study | GFS-S, GFS-R SOFAS | ER | DANVA-2 | No correlation between facial or prosodic ER and GF-R, GF-S and OSFAS. |
| | | | | | | | ToM | Hinting Task, Visual Jokes | ToM correlated with global functioning (SOFAS; r=0.54) and role functioning (GF-R; r= 0.42). ToM predicted global functioning after controlling for negative symptoms and depression (SOFAS; r = 0.47) but no longer predicted GF-R after controlling for negative symptoms. |
| | | | | | | | AB | ANSIE | No correlation between AB (ANSIE) and global, social and role functioning |
| | | | | | | | SP | MSCEIT | Trend level association between SP (MSCEIT) and global functioning (SOFAS; r= 0.36, p=0.051). No correlation between SP and role or social functioning. |
| **Amminger** | **Amminger (2013)** | 79 (26) | 16.5 | - | Baseline data | GAF | ER | FELT, AP | Facial emotion recognition not correlated with GAF |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | from RCT | | | | Prosody correlated with GAF (r=0.25) after controlling for SANS and MADRS<br>Model including AP and symptoms accounted for 65% of variance with AP contributing 3% unique variance |
| **Amminger** | **Bartholomeusz (2014)** | 39 (14) | 16.45 | - | Baseline data from RCT | GAF | ER | FELT, AP | Larger left amygdala volume mediated better sadness recognition and worse GAF in females<br>Amygdala volume mediated better sadness recognition and worse depression, negative and positive symptoms. |
| **Stanford** | **Stanford (2011)** | 63 (50) | 19.6 | HC Youth N=24<br>SCZ N=13<br>HC Adult N=14 | Baseline data from longitudinal study | SAS-SR | ToM | RME<br>FBT<br>Strange Stories | ToM performance similar to age matched controls, better than schizophrenia control group and worse than older control group.<br>ToM performance correlated to IQ and group differences in performance no longer significant after controlling for IQ<br>ToM not related to self-reported social functioning (SAS-SR) |
| **Stanford** | **DeVylder (2013)** | 33 (27) | 18.7 | HC N=15 | Baseline data from longitu | GAF | AB | IPSAQ | No correlation between AB (IPSAQ) and modified global functioning (mGAF)<br>No difference in AB between UHR and HC |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | dinal study | | | | |
| **Glenthoj** | **Glenthoj (2016)** | 65 (26) | 24.59 | HC N=30 | Baseline data from RCT | GF-S, GF-R, SOFAS, PSP, AQoL18, HiSoC, SRS-A | ER | CANTAB-ER | Facial Disgust accuracy negatively correlated with GF-R after controlling for negative symptoms (r=0.36). Disgust and negative symptoms together predicted 35.7% of variance in GF-R<br>Facial Sadness accuracy negatively correlated with AQoL after controlling for negative and positive symptoms (r = 0.25). Sadness and symptoms together accounted for 23.1% of variance in AQoL<br>Facial Anger accuracy correlated with HiSoC (r=0.31), and sadness accuracy correlated with HiSoC (r=0.27) after controlling for anger. Together predicted 22.4% of HiSoC variance.<br>UHR had worse emotion recognition than HC. |
| **Glenthoj** | **Glenthoj 2018** | 146 (66) | 24 | - | Baseline data from RCT | GF-S, GF-R SOFAS, PSP, AQoL18 | ER | CANTAB-ER | Overall latency of correct facial ER associated with PSP (r= 0.22), SOFAS (r=0.18) and GF-S (r=0.18)<br>After controlling for cognitive processing speed, only PSP associated with overall latency (r=018) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | PSP associated with sadness (r=0.25) and anger (r=0.19) latency<br>SOFAS associated with sadness latency (r=0.18)<br>GF-S associated with happy (r=0.19), disgust (r=0.18) surprise (r=0.17) and sad (r=0.2) latency<br>AQoL associated with sadness latency (r=0.17)<br>Accuracy was not associated with any measure of functioning |
| | **Barbato (2013)** | 137 (81) | 19.96 | - | Baseline data from longitudinal study | SFS | ER | FEIT, FEDT, AP | FEIT significantly correlated with SFS (r = 0.25)<br>AP and FEDT did not correlate with SFS |
| | | | | | | | ToM | RME | ToM correlated with self-report social functioning (SFS; r=0.18)<br>ToM correlated with composite cognitive factor score (r=0.63) |
| | **Clayson (2019)** | 43 (31) | 18.8 | - | Cross sectional study | GF-S, GF-R | ER | FEIT | No correlation between pre/ post FEIT score, gain scores and functioning.<br>Significant correlation between learner categorical classification and GF-R (Kendall's Tau B = 0.26) |
| | **Haining (2019)** | 108 (26) | 21.85 | CHR Neg N = 42<br>HC N= 55 | Baseline data from | GF-S, GF-R | ER | Penn CNB ER | Facial emotion recognition and latency together predicted 11% of variance in role functioning (r=0.33) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Longitudinal study | | | | Fear latency predicted 4% of variance in GAF scores (r = 0.2) and 10% of variance in GF-S (r= 0.31). Fear and anger together predicted 12% of variance in GF-R (r=0.35).<br>Cognitive processing speed predicted 5% of variance in GF-R (r=0.22)<br>UHR participants had worse emotion recognition response time but not accuracy than HC. |
| | **Ohmuro (2016)** | 36 (14) | 20.9 | FEP N=40<br>HC N=25 | Cross sectional | GAF, SFS | ToM | Picture Stories Task | ToM did not correlate with global functioning (GAF) or self -reported social functioning (SFS)<br>UHR and FEP performed worse on ToM tasks than healthy controls, and trend-level difference between UHR and FEP.<br>After controlling for premorbid IQ, difference in performance between ARMS and HC no longer significant. |

**SC = Social cognition, ER = emotion recognition, ToM = Theory of mind, AB = Attribution Bias, SP = social perception, FO = Functional outcome measures:, GAF=global functioning scale, GFS-S/R =global functioning scale social/role, SOFAS=social and occupational functioning scale, SFS=social functioning scale, AQoL18=Assessment of Quality of Life, PSP=personal and social performance scale, HiSoC=High Risk Social Challenge, SRS-A=social responsiveness scale – adult, SAS-SR=social adjustment scale self-report, *SC Measures*: FELT = facial emotion labelling task, FEIT=facial emotion identification task, FEDT=facial emotion discrimination task, AP=Affective prosody, FBT=false belief tasks, RME=Mind in the eyes, TASIT = Task of Social Inference Test, ANSIE= Adult Nowicki Strickland Internal External LOC, IPSAQ= Internal, Personal and Situational Attributions Questionnaire, SCSQ= social cognition screening questionnaire *Other:* HC=healthy control, FEP=first episode psychosis, SCZ=Schizophrenia, CHR-N= clinical high-risk negative**

## Social Cognition and Functioning Domains

Ten different measures of functioning were used, which were classified according to previously identified domains (Couture et al., 2006). Nine were measures of community functioning of which four were self-report measures and one of social skill. Five studies used one measure of functioning and the remaining six studies used between two and seven measures of functioning. See Appendix 1.5 for a summary of functioning measures.

Eight papers examined one domain of social cognition, while the remaining three studies examined between two and four domains. ER was measured in eight of the studies, ToM in five, AB in three, and SP in one study. Two studies also looked at a composite social cognitive variable (comprising four domains).

## Emotion Recognition

Seven papers directly examined facial ER and functioning, of which three looked at recognition from tone of voice in addition to facial expression. Only one paper found no association between facial or vocal ER and functioning (Cotter et al., 2017). It should be noted this paper had a small sample (N=30) and used a measure of ER which has been criticised for poor reliability.

Five of eight papers found an association between functioning and accuracy of facial emotion recognition (Barbato et al., 2013, Glenthoj et al., 2016, Haining et al., 2019), speed of emotion recognition (Glenthoj et al., 2018, Haining et al., 2019) and ability to learn on a test-retest ER paradigm (Clayson et al., 2019). Two of these papers (Glenthoj et al. 2016, Haining et al. 2019) found that negative rather than positive emotions were associated with functioning. Haining et al. (2019) found that better ER of negative emotions was associated with better functioning, while Glenthoj et al. found the opposite of this.

Haining et al. (2019) and Glenthoj et al. (2018) found that speed of facial ER was associated with functioning. Haining et al. (2019) found that latency in addition to accuracy significantly predicted 11% of role functioning variance. Glenthoj et al. (2018) found that latency predicted global, social and interpersonal and role

functioning but that accuracy no longer predicted functioning, in contrast to their earlier paper (Glenthoj et al. 2016). Glenthoj et al. (2018) found that after controlling for cognitive processing speed, ER latency was only associated with social functioning. Haining et al. (2019) found that cognitive processing speed predicted 5% of the variance in role functioning but did not control for its effect on ER latency.

Clayson et al. (2019) found that patients' categorisation as learner or non-learner in a test-retest paradigm correlated with role functioning. However, they did not find an association between any other measures of ER and functioning including pre or post training scores or gains scores. Given the association between role functioning and cognitive processing in other studies, this association with learners and non-learners may also be influenced by this.

Three papers looked at ER from tone of voice. Amminger et al (2013) found that after controlling for negative and depressive symptoms, worse vocal ER contributed 3% of unique variance to global functioning. Two papers found no association between vocal ER and functioning (Cotter et al., 2017, Barbato et al., 2013). Limitations with Cotter et al. are discussed above, and Barbato et al. relied solely on self-reported functioning which has limitations in reliability.

Additionally, in a subsection of the sample described in Amminger et al., Bartholomeusz et al. (2014) found that larger left amygdala volume in females mediated a relationship between better sadness recognition and worse functioning. But, given that the measure used (GAF) conflates symptoms with functioning, this relationship could represent a more general relationship with overall psychopathology than functioning per se. This is supported by the fact that in the same sample, symptoms accounted for 62% of variance in GAF scores, and amygdala volume also mediated a relationship between sadness recognition and symptoms.

**Theory of Mind**

Three studies found an association between ToM ability and functioning (Glenthoj et al., 2016, Cotter et al., 2017, Barbato et al., 2013), however in two studies (Glenthoj et al. 2016, Barbato et al. 2013) this was with a self-report measure, one of which was a measure of social responsiveness design to detect autism traits. Glenthoj et al. (2016)

reported non-signification associations with 4 observer-rated measures of functioning. Two studies found no association between ToM (Stanford et al., 2011, Ohmuro et al., 2016), both of which were highest rated on the CCAT, although Ohmuro et al. (2016) only had 36 participants.

**Attribution Bias**

One study found as association between AB and functioning (Glenthoj et al., 2016) however AB appears to be conflated with ToM based on the scoring description provided. DeVylder et al. (2013) and Cotter et al. (2017) found that AB did not correlate with functioning, although these studies may have lacked power due to sample size. Overall, the AB measures used had poor psychometric properties.

**Social Perception**

Cotter et al. (2017) found that SP was not significantly correlated with functioning although there was a trend association between MSCEIT and SOFAS. Given the small sample size the study may have lacked power.

**Composite Social Cognition Variable**

Barbato et al. (2013) found that overall social cognition was associated with functioning but that this was no longer significant after neurocognition entered the model, with social cognition and neurocognition becoming more strongly associated. Cotter et al. (2017) found no associated between a composite social cognition variable and functioning.

**Comparison with Controls**

Five studies included a control group with mixed findings. Haining et al. (2019) found that ER latency but not accuracy was impaired relative to healthy controls. Glenthoj et al. (2016) found that the UHR group had worse accuracy than healthy controls. Two studies found that ToM was impaired relative to a control group (Ohmuro et al., 2016, Stanford et al., 2011) but that this difference was no longer significant after controlling for IQ while a third study found that ToM was impaired relative to controls but did not

control for IQ (Glenthoj et al. 2016). Interestingly, Stanford et al. found that ToM performance was impaired relative to an older control group, better than a schizophrenia control group, but that performance was comparable to an age matched younger control group. Finally, one study found that AB was impaired relative to controls (Glenthoj et al. 2016) while another found no difference (DeVylder et al., 2013).

## Discussion

This review is an update of the findings presented by Cotter et al. (2014) on the relationship between social cognition and functioning in UHR individuals, including an additional nine studies. Although 11 papers were identified, eight of these had overlapping samples and were drawn from RCT or longitudinal studies. There was an overall lack of description of how subsections or sub-samples were selected or the extent to which analyses were *a priori*. This could increase the risk of both sample selection and publication bias, although a number of these studies did report non-significant findings. More studies from independent research groups are needed to improve generalisability of these findings, with the description and publishing of *a priori* analysis plans for baseline data being routine.

### Is social cognition associated with functioning?

The strongest evidence was for the association between ER and functioning, with accurate and faster identification of negative facial emotions leading to better functioning with small to medium effects sizes (r=0.17-0.36). This is in keeping with the association between ER and functioning in schizophrenia (Fett et al., 2011; estimated average correlation r=0.31). Although in schizophrenia patients cognition and social cognition have been demonstrated to be partially independent (Schmidt et al., 2011), processing speed seems to be an important mediating factor between ER and functioning in these studies. It may be that the ability to process information quickly is important for successful real-world functioning, and it may be that this is particularly important when processing social information as interactions often occur quickly (Glenthoj et al., 2018).

Interestingly, one study found that worse identification was associated with better functioning, but this was in relation to self-reported quality of life. Narvaez et al. (2008) suggests that better neuropsychological functioning may lead to decreased self-reported wellbeing and it may be that better social cognitive abilities allows for greater social comparison and decreased quality of life. Harvey et al. (2013) reported that self and observer reported functioning do not correlate with one another, and that self-reported functioning may not be a reliable estimate of functioning. Studies could improve their findings by reporting on a combination of functioning measures.

There was limited evidence that ToM was associated with functioning in these UHR samples, with two high quality studies finding no association, and a further study finding an association with an autism screening tool but not with other functioning measures. The evidence also does not support an association between either AB or SP and functioning. This conclusion is limited by the small number of studies looking at these domains and known issues with AB measurement - an expert panel recently concluded that no existing measures of AB were psychometrically satisfactory (Pinkham et al., 2015).

Pathways to poor functioning are thought to be multi-faceted, and the amount of variance explained by social cognition in these studies suggests unaccounted factors. In both the present studies and previous 2014 review, negative symptoms and processing speed significantly predicted functioning. However, many studies in the present review did not measure or control for these variables. In schizophrenia, there is evidence to suggest that social cognition mediates a relationship between cognition and functioning and while one study in the present review did not find support for this relationship, there were methodological limitations which warrant further investigation (Barbato et al., 2013, Schmidt et al., 2011).

A lack of evidence for an association between ToM, AB and SP and functioning contradicts findings in patients with schizophrenia. It may be that the limited number of studies and methodological limitations prevented detection of this association. It could also be due to the lack specificity in the UHR criteria. A large percentage of individuals go on to develop another axis one disorder, and symptoms in at risk states are hypothesised to represent more general psychopathology (van Os, 2013). Given the hypothesised relevance of social cognitive processing in the development of psychotic

disorders (Frith, 1992), it may be that social cognitive deficits are more marked and more associated with functioning in those individuals who go on to develop schizophrenia spectrum disorders.

**The case for early intervention**

In individuals with schizophrenia, social-cognitive interventions have been shown to be effective in addressing both social cognitive deficits and difficulties with real-world functioning (Bordon et al., 2017). An association between social cognition and functioning in UHR individuals would indicate that such interventions could also be effective for this population. This review indicates that there is some preliminary evidence that there is an association between ER and functioning, however this is based on a limited number of studies which are cross-sectional by design. Longitudinal research is required to address causality and the direction of this association, to aid our understanding as to whether social cognitive interventions could be of benefit in improving functioning in UHR populations. A causal link between social cognitive abilities such as ER and functioning would also be in keeping with findings that emotion recognition abilities have been shown to predict later conversion to psychosis (Allot et al. 2014). The neurodevelopmental model of schizophrenia suggests illness is in part the result of abnormal development of e.g. cognitive processes (Murray and Lewis, 1987) and longitudinal studies could also seek to address the role of both social cognitive difficulties and functioning in potential pathways to developing schizophrenia spectrum illnesses.

Additionally, Pantelis et al. (2015) theorised that neurodevelopmental deficits may occur in early adulthood as well as childhood, and early interventions should differentiate between remediating existing deficits and preserving areas of unaffected ability. It appears that differences in ToM ability between UHR and healthy controls in these samples was mediated by both age and IQ. It is theorised that ToM develops in a hierarchical fashion with more advanced abilities developing later with these being more likely to be impaired in schizophrenia (Harrington et al., 2005). The lack of association between ToM and functioning could be due to the age of the UHR samples, with ToM abilities not yet sufficiently impaired so as to be associated with functioning. Longitudinal studies could address at what stage ToM becomes impaired with functional consequences and explore whether interventions to preserve ToM abilities could also be beneficial.

## Limitations

Variability in measurement and statistical analysis precluded the use of meta-analytic techniques which would have allowed for an estimation of effect size across studies. As such a narrative approach was utilised which has merit in comparing findings from heterogenous studies. Additionally, it was out with the scope of this review to compare findings across types of functioning measurement or to fully consider the effect of mediator or moderator variables such as gender, IQ, symptoms and cognition on the association between social cognition and functioning.

## Future Directions

Future studies could improve the comparability and reliability of findings by employing expert recommended measures of social cognition. Functioning measurement could be improved with the use of both self and observer rated functioning which avoid conflation of symptoms with functioning. Longitudinal studies could clarify at what stage social cognitive deficits begin to impact on functioning and address issues of causality. This could help to disentangle relationship between social cognition and other key predictors such as cognition and symptoms and pathways to poor functioning. Finally, social cognitive interventions may be beneficial in preventing or remediating social cognitive deficits and thus improve functioning but this remains to be determined.

## Conclusions

UHR individuals are a group at risk of significant social adversity and functional disability regardless of transition to schizophrenia. This review clarifies the relationship between social cognition and functioning based on the available evidence, with some clear evidence emerging regarding the relationship between functioning and ER.

# References


Adolphs, R. 1999. Social cognition and the human brain. *Trends in Cognitive Sciences,* 3**,** 469-479 doi:https://doi.org/10.1016/S1364-6613(99)01399-6

Allott, K. A., Schäfer, M. R., Thompson, A., Nelson, B., Bendall, S., Bartholomeusz, C. F., Yuen, H. P., Mcgorry, P. D., Schlögelhofer, M., Bechdolf, A. & Amminger, G. P. 2014. Emotion recognition as a predictor of transition to a psychotic disorder in ultra-high risk participants. *Schizophrenia Research,* 153**,** 25-31 doi:https://doi.org/10.1016/j.schres.2014.01.037

Amminger, G. P., Allott, K., Schlögelhofer, M., Thompson, A., Bechdolf, A., Nelson, B., Mossaheb, N. & Schäfer, M. R. 2013. Affect recognition and functioning in putatively prodromal individuals. *Schizophrenia Research,* 147**,** 404-405 doi:https://doi.org/10.1016/j.schres.2013.04.008

Barbato, M., Liu, L., Penn, D. L., Keefe, R. S., Perkins, D. O., Woods, S. W. & Addington, J. 2013. Social cognition as a mediator between neurocognition and functional outcome in individuals at clinical high risk for psychosis. *Schizophrenia Research,* 150**,** 542-6 doi:https://dx.doi.org/10.1016/j.schres.2013.08.015

Bartholomeusz, C. F., Whittle, S. L., Pilioussis, E., Allott, K., Rice, S., Schäfer, M. R., Pantelis, C. & Amminger, G. P. 2014. Relationship between amygdala volume and emotion recognition in adolescents at ultra-high risk for psychosis. *Psychiatry Research: Neuroimaging,* 224**,** 159-167 doi:10.1016/j.pscychresns.2014.10.005

Bordon, N., O'rourke, S. & Hutton, P. 2017. The feasibility and clinical benefits of improving facial affect recognition impairments in schizophrenia: Systematic review and meta-analysis. *Schizophrenia Research,* 188**,** 3-12 doi:https://doi.org/10.1016/j.schres.2017.01.014

Brissos, S., Molodynski, A., Dias, V. V. & Figueira, M. L. 2011. The importance of measuring psychosocial functioning in schizophrenia. *Ann Gen Psychiatry,* 10**,** 18 doi:10.1186/1744-859x-10-18

Cannon-Spoor, H. E., Potkin, S. G. & Wyatt, R. J. 1982. Measurement of Premorbid Adjustment in Chronic Schizophrenia. *Schizophrenia Bulletin,* 8**,** 470-484 doi:10.1093/schbul/8.3.470

Clayson, P. E., Kern, R. S., Nuechterlein, K. H., Knowlton, B. J., Bearden, C. E., Cannon, T. D., Fiske, A. P., Ghermezi, L., Hayata, J. N., Hellemann, G. S., Horan, W. P., Kee, K., Lee, J., Subotnik, K. L., Sugar, C. A., Ventura, J., Yee, C. M. & Green, M. F. 2019. Social vs. non-social measures of learning potential for predicting community functioning across phase of illness in schizophrenia. *Schizophrenia Research,* 204**,** 104-110 doi:https://dx.doi.org/10.1016/j.schres.2018.07.046

Cohen, J. 1992. A power primer. *Psychol Bull,* 112**,** 155-9

Combs, D. R., Adams, S. D., Penn, D. L., Roberts, D., Tiegreen, J. & Stem, P. 2007. Social Cognition and Interaction Training (SCIT) for inpatients with schizophrenia spectrum disorders: Preliminary findings. *Schizophrenia Research,* 91**,** 112-116 doi:https://doi.org/10.1016/j.schres.2006.12.010

Cotter, J., Bartholomeusz, C., Papas, A., Allott, K., Nelson, B., Yung, A. R. & Thompson, A. 2017. Examining the association between social cognition and functioning in individuals at ultra-high risk for psychosis. *Australian & New Zealand Journal of Psychiatry,* 51**,** 83-92 doi:10.1177/0004867415622691

Cotter, J., Drake, R. J., Bucci, S., Firth, J., Edge, D. & Yung, A. R. 2014. What drives poor functioning in the at-risk mental state? A systematic review. *Schizophrenia Research,* 159**,** 267-277 doi:https://doi.org/10.1016/j.schres.2014.09.012

Crowe, M. & Sheppard, L. 2011. A general critical appraisal tool: An evaluation of construct validity. *International Journal of Nursing Studies,* 48**,** 1505-1516 doi:https://doi.org/10.1016/j.ijnurstu.2011.06.004

Devylder, J. E., Ben-David, S., Kimhy, D. & Corcoran, C. M. 2013. Attributional Style among Youth at Clinical Risk for Psychosis. *Early Interv Psychiatry,* 7**,** 84-8 doi:10.1111/j.1751-7893.2012.00347.x

Fett, A. K. J., Viechtbauer, W., Dominguez, M. D., Penn, D. L., Van Os, J. & Krabbendam, L. 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis. *Neuroscience and Biobehavioral Reviews,* 35**,** 573-588 doi:10.1016/j.neubiorev.2010.07.001

Frith, C. D. 1992. *The cognitive neuropsychology of schizophrenia,* Hillsdale, NJ, US, Lawrence Erlbaum Associates, Inc.

Fusar-Poli, P., Bonoldi, I., Yung, A. R., Borgwardt, S., Kempton, M. J., Valmaggia, L., Barale, F., Caverzasi, E. & Mcguire, P. 2012. Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Arch Gen Psychiatry,* 69**,** 220-9 doi:10.1001/archgenpsychiatry.2011.1472

Fusar-Poli, P., Meneghelli, A., Valmaggia, L., Allen, P., Galvan, F., Mcguire, P. & Cocchi, A. 2009. Duration of untreated prodromal symptoms and 12-month functional outcome of individuals at risk of psychosis. *British Journal of Psychiatry,* 194**,** 181-182 doi:10.1192/bjp.bp.107.047951

Glenthoj, L. B., Albert, N., Fagerlund, B., Kristensen, T. D., Wenneberg, C., Hjorthoj, C., Nordentoft, M. & Jepsen, J. R. M. 2018. Emotion recognition latency, but not accuracy, relates to real life functioning in individuals at ultra-high risk for psychosis. *Schizophrenia Research,* 28**,** 28 doi:https://dx.doi.org/10.1016/j.schres.2018.12.038

Glenthoj, L. B., Fagerlund, B., Hjorthoj, C., Jepsen, J. R. M., Bak, N., Kristensen, T. D., Wenneberg, C., Krakauer, K., Roberts, D. L. & Nordentoft, M. 2016. Social cognition in patients at ultra-high risk for psychosis: What is the relation to social skills and functioning? *Schizophrenia research. Cognition,* 5**,** 21-27 doi:https://dx.doi.org/10.1016/j.scog.2016.06.004

Haining, K., Matrunola, C., Mitchell, L., Gajwani, R., Gross, J., Gumley, A. I., Lawrie, S. M., Schwannauer, M., Schultze-Lutter, F. & Uhlhaas, P. J. 2019. Neuropsychological deficits in participants at clinical high risk for psychosis recruited from the community: Relationships to functioning and clinical symptoms. *Psychological Medicine,* doi:10.1017/s0033291718003975

Harrington, L., Siegert, R. & Mcclure, J. 2005. Theory of mind in schizophrenia: A critical review. *Cognitive Neuropsychiatry,* 10**,** 249-286 doi:10.1080/13546800444000056

Harvey, P. D. 2013. Assessment of everyday functioning in schizophrenia: implications for treatments aimed at negative symptoms. *Schizophrenia research,* 150**,** 353-355 doi:10.1016/j.schres.2013.04.022

Healey, K. M., Bartholomeusz, C. F. & Penn, D. L. 2016. Deficits in social cognition in first episode psychosis: A review of the literature. *Clinical Psychology Review,* 50**,** 108-137 doi:https://doi.org/10.1016/j.cpr.2016.10.001

Keshavan, M. S., Haas, G., Miewald, J., Montrose, D. M., Reddy, R., Schooler, N. R. & Sweeney, J. A. 2003. Prolonged Untreated Illness Duration From Prodromal Onset Predicts Outcome in First Episode Psychoses. *Schizophrenia Bulletin,* 29**,** 757-769 doi:10.1093/oxfordjournals.schbul.a007045

Lee, T. Y., Hong, S. B., Shin, N. Y. & Kwon, J. S. 2015. Social cognitive functioning in prodromal psychosis: A meta-analysis. *Schizophrenia Research,* 164**,** 28-34 doi:10.1016/j.schres.2015.02.008

Mehta, U. M., Thirthalli, J., Naveen Kumar, C., Keshav Kumar, J., Keshavan, M. S. & Gangadhar, B. N. 2013. Schizophrenia patients experience substantial social cognition deficits across multiple domains in remission. *Asian Journal of Psychiatry,* 6**,** 324-329 doi:https://doi.org/10.1016/j.ajp.2013.02.001

Miller, T. J., Mcglashan, T. H., Rosen, J. L., Somjee, L., Markovich, P. J., Stein, K. & Woods, S. W. 2002. Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. *Am J Psychiatry,* 159**,** 863-5 doi:10.1176/appi.ajp.159.5.863

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. & And The, P. G. 2009. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA

StatementThe PRISMA Statement. *Annals of Internal Medicine,* 151**,** 264-269 doi:10.7326/0003-4819-151-4-200908180-00135

Murray, R. M., Bhavsar, V., Tripoli, G. & Howes, O. 2017. 30 Years on: How the Neurodevelopmental Hypothesis of Schizophrenia Morphed Into the Developmental Risk Factor Model of Psychosis. *Schizophrenia Bulletin,* 43**,** 1190-1196 doi:10.1093/schbul/sbx121

Murray, R. M. & Lewis, S. W. 1987. Is schizophrenia a neurodevelopmental disorder? *British medical journal (Clinical research ed.),* 295**,** 681-682 doi:10.1136/bmj.295.6600.681

Narvaez, J. M., Twamley, E. W., Mckibbin, C. L., Heaton, R. K. & Patterson, T. L. 2008. Subjective and objective quality of life in schizophrenia. *Schizophrenia Research,* 98**,** 201-208 doi:https://doi.org/10.1016/j.schres.2007.09.001

Ohmuro, N., Katsura, M., Obara, C., Kikuchi, T., Sakuma, A., Iizuka, K., Hamaie, Y., Ito, F., Matsuoka, H. & Matsumoto, K. 2016. Deficits of cognitive theory of mind and its relationship with functioning in individuals with an at-risk mental state and first-episode psychosis. *Psychiatry Research,* 243**,** 318-25 doi:https://dx.doi.org/10.1016/j.psychres.2016.06.051

Pantelis, C., Wannan, C., Bartholomeusz, C. F., Allott, K. & Mcgorry, P. D. 2015. Cognitive intervention in early psychosis — preserving abilities versus remediating deficits. *Current Opinion in Behavioral Sciences,* 4**,** 63-72 doi:https://doi.org/10.1016/j.cobeha.2015.02.008

Pinkham, A. E., Penn, D. L., Green, M. F. & Harvey, P. D. 2015. Social Cognition Psychometric Evaluation: Results of the Initial Psychometric Study. *Schizophrenia Bulletin,* 42**,** 494-504 doi:10.1093/schbul/sbv056

Priebe, S. 2007. Social outcomes in schizophrenia. *British Journal of Psychiatry,* 191**,** s15-s20 doi:10.1192/bjp.191.50.s15

Savla, G. N., Vella, L., Armstrong, C. C., Penn, D. L. & Twamley, E. W. 2012. Deficits in Domains of Social Cognition in Schizophrenia: A Meta-Analysis of the Empirical Evidence. *Schizophrenia Bulletin,* 39**,** 979-992 doi:10.1093/schbul/sbs080

Schmidt, S. J., Mueller, D. R. & Roder, V. 2011. Social Cognition as a Mediator Variable Between Neurocognition and Functional Outcome in Schizophrenia: Empirical Review and New Results by Structural Equation Modeling. *Schizophrenia Bulletin,* 37**,** S41-S54 doi:10.1093/schbul/sbr079

Schultze-Lutter, F., Addington, J., Ruhrmann, S. & Klosterkötter, J. 2007. Schizophrenia proneness instrument, adult version (SPI-A). *Rome: Giovanni Fioriti,* Stanford, A. D., Messinger, J., Malaspina, D., Corcoran, C. M., Stanford, A. D., Messinger, J., Malaspina, D. & Corcoran, C. M. 2011. Theory of Mind in patients at clinical high risk for psychosis. *Schizophrenia Research,* 131**,** 11-17 doi:10.1016/j.schres.2011.06.005

Tan, B. L., Lee, S. A. & Lee, J. 2018. Social cognitive interventions for people with schizophrenia: A systematic review. *Asian J Psychiatr,* 35**,** 115-131 doi:10.1016/j.ajp.2016.06.013

Thompson, A. D., Bartholomeusz, C. & Yung, A. R. 2011. Social cognition deficits and the 'ultra high risk' for psychosis population: A review of literature. *Early Intervention in Psychiatry,* 5**,** 192-202 doi:10.1111/j.1751-7893.2011.00275.x

Van Donkersgoed, R. J. M., Wunderink, L., Nieboer, R., Aleman, A. & Pijnenborg, G. H. M. 2015. Social Cognition in Individuals at Ultra-High Risk for Psychosis: A Meta-Analysis. *PLOS ONE,* 10**,** e0141075 doi:10.1371/journal.pone.0141075

Van O, J. 2013. The dynamics of subthreshold psychopathology: implications for diagnosis and treatment. Am J Psychiatry. United States.

Von Elm, E., Poglia, G., Walder, B. & Tramèr, M. R. 2004. Different Patterns of Duplicate Publication: An Analysis of Articles Used in Systematic Reviews. JAMA, 291, 974-980 doi:10.1001/jama.291.8.974

Yung, A. R., Yuen, H. P., Mcgorry, P. D., Phillips, L. J., Kelly, D., Dell'olio, M., Francey, S. M., Cosgrave, E. M., Killackey, E., Stanford, C., Godfrey, K. & Buckby, J. 2005. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *Aust N Z J Psychiatry,* 39**,** 964-71 doi:10.1080/j.1440-1614.2005.01714.x

# Chapter Two: Major Research Project

# Experiential but not expressive negative symptoms are associated with social cognition and functioning in schizophrenia –findings of a preliminary study with rehabilitation inpatients

*Prepared in accordance with submission guidelines for the journal Psychosis (see appendix 1.1)*

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# Plain English Summary

**Background:** People with schizophrenia spectrum illnesses are known to have difficulties with their everyday functioning, including in their work and social lives. This is likely to affect those individuals who are in inpatient rehabilitation services to a greater extent. We know from previous research that social cognitive ability – that is our ability to understand what others and thinking and feeling and interpret social rules – determines how well someone is able to function. This study was interested in understanding how this social cognitive ability is related to another important predictor of functioning – negative symptoms which are deficits in experiences such as motivation and enjoyment, and reduced expression of emotion. We hoped to understand whether social cognition and functioning are more closely related to experience rather than expression negative symptoms. This could help us to understand whether people with difficulties in processing social information are more likely to have poor motivation, and understand how this impacts on their functioning and overall recovery.

**Methods:** 11 patients with a diagnosis of schizophrenia or schizoaffective disorder were recruited from Greater Glasgow and Clyde Rehabilitation Services. Participants were asked to complete a one-off testing session lasting between 90-120 minutes in which they completed a series of cognitive and social cognitive tasks and an interview about negative symptoms. Their named nurse was interviewed to obtain a rating of their functioning.

**Results:** Due to the number of people who participated we were not able to test all of our hypotheses. We found that there was a trend for people with higher levels of experiential negative symptoms to have worse social cognitive ability and worse functioning. There did not seem to be an association between these factors and expressive negative symptoms. Because of the significant difficulties with recruitment we decided to include an additional aim of looking at feasible it was to recruit from the rehabilitation wards. We found 33% of eligible patients decided to participate. Data on new admissions to the wards was obtained which indicated that an estimated 14 eligible people would be admitted in a year and if 33% of those decided to participate, 4 additional people could be recruited a year.

**Discussion and Implications:** . Although our sample was small and findings should be interpreted with caution as they may not generalise, we found patterns in the data which suggests that different types of negative symptoms are associated with other key

predictors of functioning, and functional ability itself. This has important implications for understanding how poor functioning might occur. This may indicate that motivation and how good we are at processing social information are importantly related to how well we perform day to day.. We found that recruiting from a rehabilitation population was challenging, and to recruit enough participants to test some of our hypothesis would likely require a significant amount of time and resources. Making the testing session shorter and improving how we frame research to patients might enhance recruitment rates. This study provides important information about patterns in the data which would be important to replicate and extend in a larger inpatient sample and we provide information on the resources which might be needed to do this. Furthering our understanding of this in a larger inpatient sample could help us to understand how to develop more effective psychosocial interventions and improve the day to day functioning of people who require the most complex care.

# Abstract

**Background:** Functional disability represents a significant barrier to recovery in people with schizophrenia, often impacting those in in-patient rehabilitation to the greatest extent. There is evidence that social cognition is an important predictor of functional outcomes but the relationship between social cognition and functioning and other key variables such as symptoms remain unclear. Previous research has examined negative symptoms as a unitary construct. This study aims to clarify whether there is a differential association between experiential and expressive symptoms, functioning and social cognition, and whether experiential negative symptoms mediate a relationship between social cognition and functioning.

**Methods:** 11 participants with schizophrenia or schizoaffective disorder were recruited. Participants were administered a battery of cognitive, social cognition and symptoms measures and an observer rated measure of functioning was completed with a named nurse.

**Results:**. Due to the sample size obtained, data was visually examined and Spearman's Rho correlations used to estimate effect sizes of linear relationships.. Higher levels of experiential but not expressive negative symptoms appeared to be associated with poorer social cognitive ability and worse functioning.. Due to recruitment challenges, post-hoc exploration of recruitment feasibility was conducted which demonstrated that recruitment figures were poor with only 33% of eligible patients participating. Ward turnover rates were low and indicate long recruitment periods to be necessary to recruit adequate samples

**Discussion and conclusion:** The small sample reflects the difficulty of testing predictors of functioning in people who, by definition, do not readily engage in everyday roles. With acknowledgement of the limited generalisability, these preliminary data suggest a differential association between experiential and expressive negative symptoms and their relationship to functioning and social cognition. This highlights the importance of motivational constructs in determining functioning and may be a potential pathway from social cognition to functioning. Suggestions are made to address the low recruitment rates and increase participation.



***Key Words: psychosis, theory of mind, feasibility, negative symptoms***

# Introduction

Improving understanding of the pathways to poor functioning in schizophrenia is vital for developing effective psychological interventions to promote recovery, especially in those individuals requiring the most expensive and complex care. There is a growing recognition of the role of negative symptoms and how these might relate to other known predictors of functioning.

## The Functional Deficit in Schizophrenia

Psychosocial functioning is significantly impaired in many people diagnosed with schizophrenia and is an increasingly important target within mental health services, with clinicians recognising the need to direct efforts beyond alleviating positive symptoms (Brissos et al., 2011). Positive symptoms are often those which bring people to the attention of services and to an inpatient admission, but poor psychosocial functioning often leads to poorer recovery from these episodes and, for some people, admission to psychiatric rehabilitation services. Functioning is defined as an individual's ability to perform the activities of daily living in key areas of life such as social and interpersonal functioning, recreation, occupation and self-care, as well as their perceived level of satisfaction or quality of life (Priebe, 2007). Around 10% of individuals with schizophrenia have poor long-term functioning and complex care needs which account for an estimated 25-50% of mental health spending in the UK (Department of Health, 2012). This type of care requiring intensive input with admissions of more than 18 months (Joint Commission Panel for Mental Health, 2016). There is a clear need for improved interventions to support recovery of functioning which has directed research efforts towards (1) understanding the predictors of functioning; (2) understanding the potential mechanisms leading to poor functioning.

## Predictors of functioning

Two of the most consistently reported predictors of functioning in schizophrenia are cognition and social cognition (Green, 1996, Green et al., 2000, Fett et al., 2011). Cognition refers to our ability to think and reason such a memory, processing speed, attention. Social cognition refers to processes which specifically underly complex social

interactions (Adolphs, 2001) Cognition domains including secondary verbal memory, immediate memory, executive functioning and vigilance accounts for 20-60% of variance in functioning (Green et al., 2000). Similarly, there is strong evidence that *social* cognition significantly contributes to functional outcomes. A narrative review by Couture et al. (2006) identified social perception (SP) and emotion recognition (ER) to be significantly associated with functioning. Fett et al. (2011) quantified these findings in a meta-analysis of 52 studies, demonstrating mean correlations between domains of social cognition and functioning ranged from 0.2 to 0.4 with the largest effect size found between community functioning and Theory of Mind (ToM). Further research has concluded that social cognition has effects on functioning that are independent of the effects of cognition alone (Allen et al., 2007, Sergi et al., 2007, van Hooren et al., 2008). A meta-analysis by Schmidt et al. (2011) of 15 studies found that 25% of variance in functioning is explained by a model whereby social cognition mediates the relationship between neurocognition and functioning.

These findings have begun to shed light on the potential pathways to poor functioning, with important implications for interventions such as the development of cognitive and social cognitive remediation programmes. However, it remains the case that relatively small amounts of variance are accounted for by these factors (~25%) and intervention programmes do not always generalise to real world functioning with improvements often not sustained beyond the intervention (Wykes et al., 2011, Tan et al., 2018). This suggests that other important factors need to be examined in understanding the pathway to poor functioning such as understanding causal relationships in order to improve future interventions.

**The Functional Importance of Negative Symptoms**

Negative symptoms have been recognised as a hallmark feature of schizophrenia since its initial conceptualisation (Kraeplin, 1919) and the NIMH-MATRICS Consensus Statement on Negative Symptoms affirmed their importance important as a treatment target (Kirkpatrick et al., 2006). Negative symptoms refer to absence of behaviours and experiences including alogia, blunted affect, apathy, avolition and anhedonia which were originally characterised as a unitary domain. Recent factor analysis research points towards a two-factor conceptualisation of negative symptoms: *expressive* deficits

including blunted affect and alogia, and *experiential* deficits, including apathy, avolition and anhedonia (Blanchard and Cohen, 2005).

Negative symptoms are an important predictor of psychosocial outcomes with a meta-analysis of 52 studies reporting a mean correlation of 0.4 between negative symptoms and functioning. Additionally, there is strong evidence to suggest that negative symptoms act as a mediator between cognition and functioning (Ventura et al., 2009). Foussias et al. (2011) found that motivation accounted for between 72 -74% of functional outcome at baseline and 6-month follow up. Additionally, Leifker et al.(2009) found that apathy was related to real-world behaviour independent of functional capacity (i.e. necessary skills). Hence it is possible that deficits in cognitive abilities lead to failures in performance which reduce the motivation to pursue similar goals in the future, regardless of functional capacity to do so, thus leading to the observable functional deficits. Defeatists performance beliefs such as *"If you cannot do something well, there is little point in doing it at all"* have been found to mediate a relationship between cognition and both functioning and negative symptoms (Grant and Beck, 2008, Weissman, 1979). This points to a potential mechanism between cognitive deficits, negative symptoms and functioning, consistent with theories of motivation in human behaviour regarding expectation of success (Grant and Beck, 2008). This may mean that even when someone relearns a skill (e.g. through cognitive remediation) this may not translate to everyday behaviour without the relevant beliefs and motivation to support this.

**Negative Symptoms and Social Cognition**

There has been relatively little research into the relationship between negative symptoms and social cognition. Theoretically this relationship is likely to be a complex one, as lowered motivation could partially disrupt the development or display of social cognitive abilities, but social cognitive deficits could also contribute to lowered motivation to engage in social interactions (Marder and Galderisi, 2017). There is some limited evidence to suggest that social cognition and negative symptoms are related to one another. Lincoln et al. (2011) found that social cognition including ToM, empathy, and attribution bias accounting for 54% of variance in negative symptoms in individuals with low self-esteem. Sergi et al. (2007) also found evidence for a small correlation between emotion recognition and negative symptoms. Two studies to date have looked at whether negative symptoms mediate a relationship between social cognition and negative

symptoms with Lin et al. (2013) finding support for this hypothesis while Couture et al. (2011) did not. Social skills training programmes have been shown to improve negative symptoms and functioning with small to medium effect sizes and this is thought to be mediated by defeatist performance beliefs (Granholm et al., 2017, Turner et al., 2014).

In understanding how social cognitive abilities relate to negative symptoms and how this might guide further interventions efforts, we need to understand whether different domains of negative symptoms relate differently to social cognitive abilities. Previous studies of this relationship have measured negative symptoms as a unitary construct or examined amotivation in isolation without comparison to expressive deficits. Theoretically, it may be that avolition and apathy are more associated with social cognition than expressive deficits based on the relevance of social cognitive abilities for motivated social behaviour. This is supported by the finding that social skills training improved experiential but not expressive negative symptoms (Granholm et al. 2014). However, appropriate social signalling is also thought to be important for overcoming negative symptoms (Elis et al., 2013). Understanding whether there is a differential relationship between different types of negative symptoms, social cognition and functioning and whether negative symptoms act as a mediator will provide important information regarding potential pathways to poor functioning and could inform the development of psychosocial interventions.

**Aims**

We wish to clarify the relationship between social cognition, functioning and two distinct domains of negative symptoms – experiential and expressive, and to determine whether negative symptoms mediate a relationship between social cognition and functioning. We aim to explore the relative predictive contribution of these variables to functioning through testing a regression model.

We hypothesise that:

1. Social cognitive ability will be positively correlated with functioning.
2. Greater levels of *experiential* but not *expressive* negative symptoms will be negatively correlated with functioning.

3. Greater levels of *experiential* but not *expressive* negative symptoms will be negatively correlated with social cognition.
4. Experiential negative symptoms will mediate a relationship between social cognition and functioning.

In addition to these specific hypotheses we aim to explore the relative contributions of executive functioning, social cognition and negative symptoms to functioning through testing of a regression model.

# Methods

## Participants

Participants were eligible to participate if they (a) had a diagnosis of schizophrenia or schizoaffective disorder, (b) aged between 18-65 years, (c) no medication changes for past 4 weeks, (d) ability to provide informed consent, (e) fluent in English. Participants were excluded who (a) had a history of significant head injury, (b) intoxication at time of testing, (c) IQ below 75 or established learning disability, (d) other diagnoses that affect cognition (e.g. dementia).

## Recruitment

Recruitment took place between April and June 2019 from Greater Glasgow and Clyde Rehabilitation Wards. Screening was carried out by named nurses who provided eligible participants with verbal information about the study and invited them to be approached by the primary researcher. Participants agreeing to an initial approach met with the researcher on the ward and were given an information sheet (Appendix 2.1). The researcher verified the patient's capacity to give informed consent. Participants were given a minimum of 24 hours before being asked to provide written informed consent. Those who declined an initial approach were offered the opportunity to meet with the researcher at a future ward visit unless they expressly declined future approaches. The rationale for this was to account for variability in patients' mental states between ward visits.

## Measures

### Clinical Information and Symptomology

Consultant Psychiatrists provided verification of the diagnosis. Duration of illness, length of admission and prescribed medication were obtained from medical records.

Negative symptoms were assessed using the Clinical Assessment Inventory of Negative Symptoms (CAINS; Kring et al., 2013), a 13-item semi-structured interview yielding two domains– motivation and pleasure (MAP) and expressive symptoms (EXP). The CAINS was administered by the researcher and audio recorded for retrospective scoring. Amotivation and anhedonia were measured using self-report questionnaires. The Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS; Gooding and Pflum, 2014), a 17-item questionnaire with higher scores indicating greater capacity to anticipate and enjoy interpersonal interactions. The Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2006), an18-item questionnaire with higher scores denoting greater capacity to gain pleasure from experiences in the moment and in the future.

The Depression Stress and Anxiety Scale (DASS-21; Lovibond and Lovibond, 1995) (Lovibond and Lovibond, 1995; DASS-21), a 21-item self-report questionnaire with higher scores indicate more severe symptoms in each domain.

### Social Cognition

Social cognitive domains were selected on the basis of previous literature (Sergi et al., 2007, Lincoln et al., 2011), with measures selected on the basis of psychometric properties (Pinkham et al., 2015). ToM was assessed using The Hinting Task (Corcoran et al., 1995). Participants were read ten vignettes wherein one character drops a “hint” to another with participants asked to identify the true meaning. A correct response scores two points; incorrect responses are followed up with an additional hint with correct responses following this scoring one point. Emotion recognition was assessed using the Bell Lysaker Emotion Recognition Task (BLERT; Bryson et al., 1997). 21 ten-second video clips of an actor talking are shown to participants who select the emotion the actor is feeling from a response card with 7 possible emotions – happiness, sadness, anger, surprise, disgust, fear or no emotion. One point for each correct answer.

**Neurocognition**

Executive functioning measures were selected on the basis of previous study addressing similar research questions (Konstantakopoulos et al., 2011). The Trail Making Task Part B (TMT-B) requires participants to connect letters and numbers in ascending and alternating order. Performance is measured by completion time (seconds) with faster time indicating better performance. Phonemic fluency (Benton and Hamsher, 1983) requires participants to produce words beginning with the letters F, A and S in one minute. More words indicate better performance.

**Psychosocial Functioning**

Functioning was assessed using the Personal and Social Performance Scale (PSP) (Morosini et al., 2000) which provides an overall measure of observer rated functioning based on four domains: (a) socially useful activities, (b) personal and social relationships, (c) self-care, (d) disturbing and aggressive behaviours. The reference period was the previous four weeks. The UCLA loneliness scale (Russell et al., 1980), is a 20 item self-report questionnaire with lower scores indicating greater subjective loneliness.

**Procedures**

All procedures were approved by the East of Scotland Research Ethics Service (Appendix 2.2 and 2.3). All participants provided written informed consent. A single test session was conducted at the ward lasting between 90-120 minutes. All measures were administered by the primary researcher. The participants named nurse was interviewed within two weeks to obtain a rating of functioning using the PSP.

**Statistical Analysis**

All data were analysed using SPSS Version 26. Demographic characteristics were described using mean and standard deviation. Associations between key variables were examined visually using scatterplots. As variables were not normally distributed and the sample size small, non-parametric tests were used. Two-tailed Spearman's Rho correlations were calculated between key variables of social cognition, negative symptoms and functioning for estimations of effect sizes.

# Results

## Sample Characteristics

Sample characteristics are shown in Table 1. Eleven participants (7 male) with schizophrenia (N=9, 82%) or schizoaffective disorder (N=2, 18%) with an average illness duration of 16 years participated. All were white British with the exception of one white Polish participant. Rehabilitation admission was on average 14.5 months, and the total duration of inpatient admission, including prior acute, continuing care or forensic admission was 4.1 years. In addition to antipsychotic medication, five participants took an antidepressant and 6 participants were prescribed mood stabilisers. The neurocognitive and symptom characteristics are shown in Table 2.

*Table 1: Sample Demographics*

| | | Mean | SD |
|---|---|---|---|
| **Participants (N)** | | 11 | - |
| **Male (%)** | | 7 (64) | - |
| **Schizophrenia (%)** | | 9 (82) | - |
| **Age (Years)** | | 39.36 | 7.7 |
| **Illness Duration (Years)** | | 16.1 | 9.5 |
| **Rehabilitation Admission (Months)** | | 14.5 | 17.2 |
| **Total inpatient admission (Months)** | | 50.2 | 80.8 |
| **Atypical Antipsychotic (N)** | | | |
| | Clozapine | 9 | - |
| | Paliperidone | 1 | - |
| **Typical Antipsychotic (N)** | | | |
| | Zuclopenthixol | 1 | - |
| **Adjunctive Antipsychotic (N)** | | | |
| | Amisulpiride | 2 | - |
| | Risperidone | 1 | - |
| | Aripiprazole | 1 | - |

*Table 2 Neurocognitive and Clinical Characteristics*

| Variable | Mean | SD | Possible Range |
|---|---|---|---|
| **Negative Symptoms** | | | |
| CAINS Total | 21.77 | 2.89 | 0-52 |
| CIANS MAP | 16.09 | 7.45 | 0-36 |
| CAINS EXP | 5.64 | 4.13 | 0-16 |
| ACIPS | 85.55 | 11.44 | 17-102 |
| TEPS Total | 85.36 | 14.86 | 18-108 |
| **Other Symptoms** | | | |
| DASS 21 – Total | 24.73 | 20.96 | 0-63 |
| Depression | 7.82 | 2.40 | 0-21 |
| Anxiety | 7.45 | 2.17 | 0-21 |
| Stress | 9.45 | 2.32 | 0-21 |
| **Psychosocial Functioning** | | | |
| PSP (Total) | 43.73 | 18.54 | 0-100 |
| PSP – socially useful | 2.82 | 0.87 | 0-5 |
| PSP – Personal and social | 2.64 | 1.03 | 0-5 |
| PSP - Self care | 1.64 | 1.36 | 0-5 |
| PSP – Disturbing and aggressive | 1.36 | 1.12 | 0-5 |
| UCLA Loneliness Scale | 41.70 | 7.70 | 20-80 |
| **Neurocognition** | | | |
| TMT-B (seconds) | 167.82 | 123.21 | - |
| TMT-B Z-score | 7.06 | - | - |
| Phonemic Fluency – N correct | 31.91 | 12.55 | - |
| Phonemic Fluency Z score | -0.92 | - | - |
| **Social Cognition** | | | |
| Hinting Task Total | 10.55 | 6.73 | 0-20 |
| BLERT Total Correct | 12 | 4.47 | 0-21 |
| BLERT Positive Correct | 4 | 1.61 | 0-5 |
| BLERT Negative Correct | 3.91 | 1.76 | 0-5 |

**Relationship between Social Cognition, Negative Symptoms and Functioning**

***Hypothesis 1: Social cognitive ability will be positively correlated with functioning***

We hypothesised that Theory of Mind and Emotion Recognition abilities would be positively correlated with functioning. Scatterplots of these relationship are shown in Figure 1. These show a moderate positive linear relationship between performance on social cognitive measures and PSP ratings of functioning. Better functioning appears to be associated with better performance on social cognitive tasks. This relationship is stronger for performance on the Hinting Task, than for the BLERT. There were two outliers for BLERT and functioning – with one participant scoring higher than would be expected based on functioning performance, and one scoring lower than would be expected. There were no significant outliers for the hinting task and functioning variables.

Spearman's Rho correlations showed that the correlation coefficient between the Hinting Task and functioning was r= 0.87 and the correlation coefficient between BLERT and functioning was r=0.65.

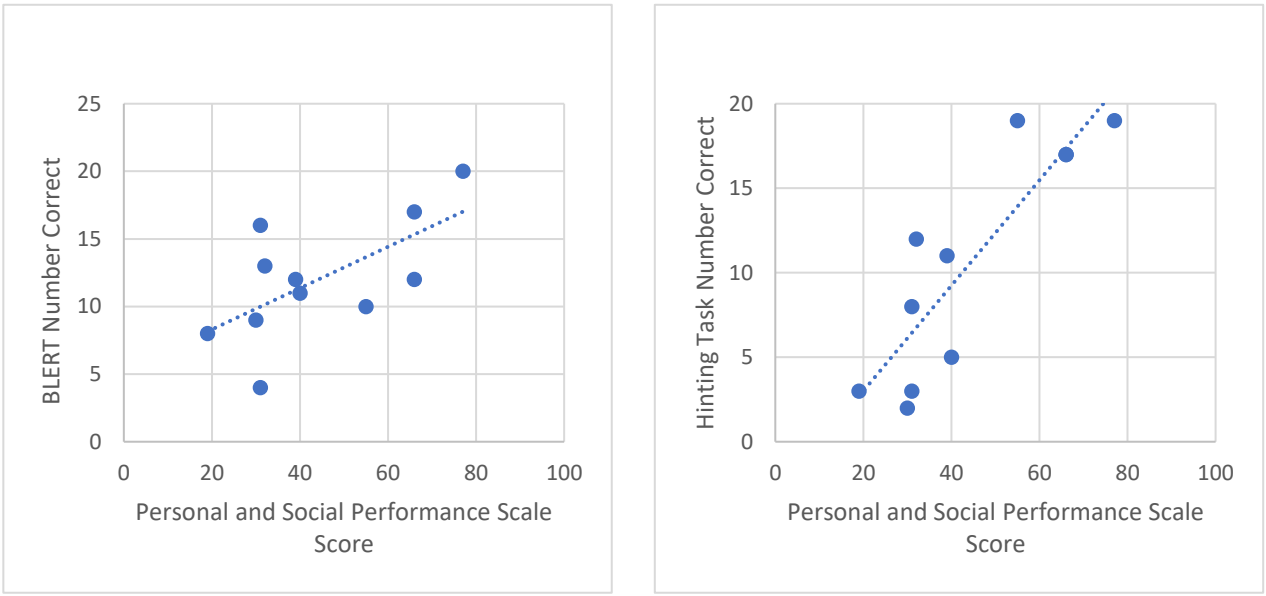


*Figure 1: Scatterplot of social cognition and functioning variables*

***Hypothesis 2: Experiential but not expressive negative symptoms will be negatively correlated with functioning***

Figure 2 shows scatterplots of the relationship between experiential and expressive negative symptoms and functioning. Higher scores on the CAINS MAP and CAINS EXP indicate worse negative symptoms. The scatterplots suggest that in this sample there is a strong, negative linear relationship between experiential negative symptoms and functioning, but there appears to be no relationship between expressive negative symptoms and functioning. There was one outlier who had low experiential negative symptoms but also scored low on functioning.

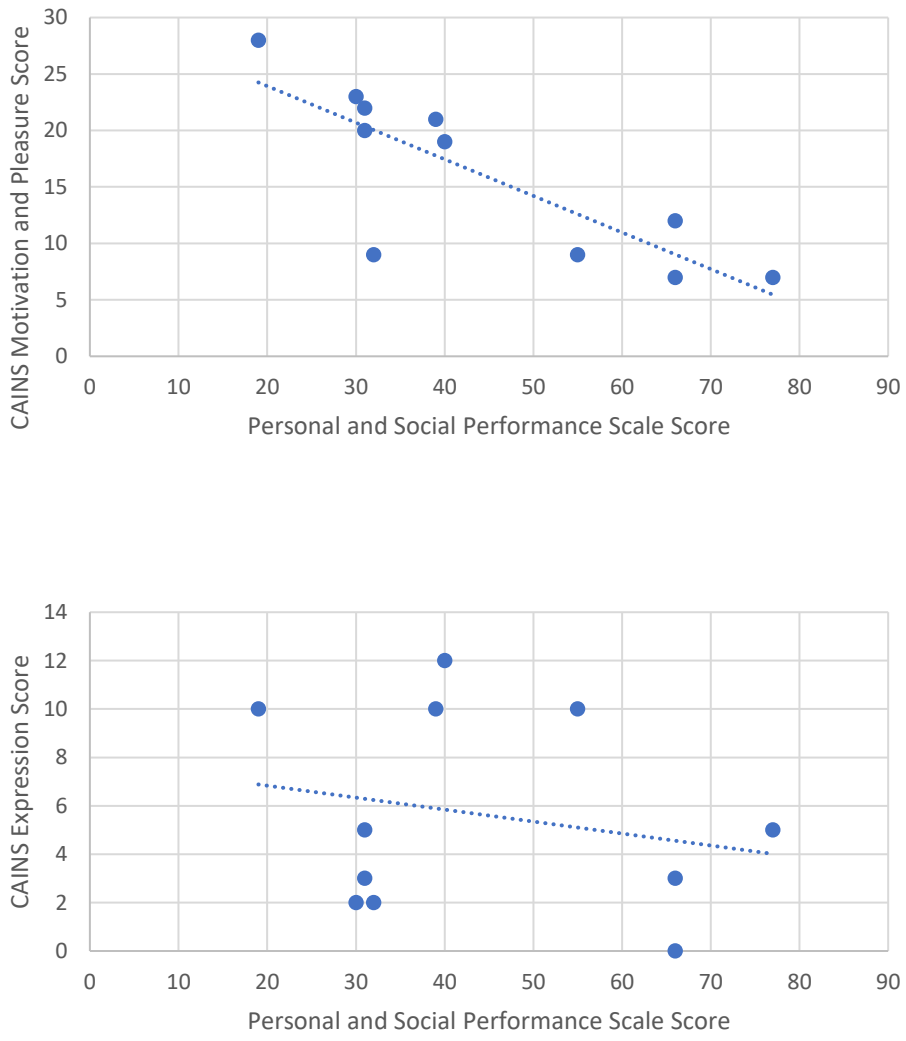


*Figure 2: Scatterplot between Negative Symptoms and Functioning*

Spearman's Rho correlations showed that the association between experiential negative symptoms and functioning was r= -.87 while the association between expressive negative symptoms was r= -.04. In this small sample there appears to be a differential association between functioning and experiential and expressive negative symptoms.

***Hypothesis 3: Greater levels of experiential but not expressive negative symptoms will be negatively correlated with social cognition***

We hypothesised that higher levels of experiential negative symptoms would be negatively correlated with social cognitive performance, but that this association would not be present with expressive negative symptoms. Figure 3 and 4 show scatterplots of the association between Theory of Mind and emotion recognition performance and negative symptoms. For Theory of Mind, there is evidence for a negative, liner association with experiential negative symptoms with better performance on the hinting task being associated with lower CAINS MAP scores.. There is no apparent relationship with expressive negative symptoms.

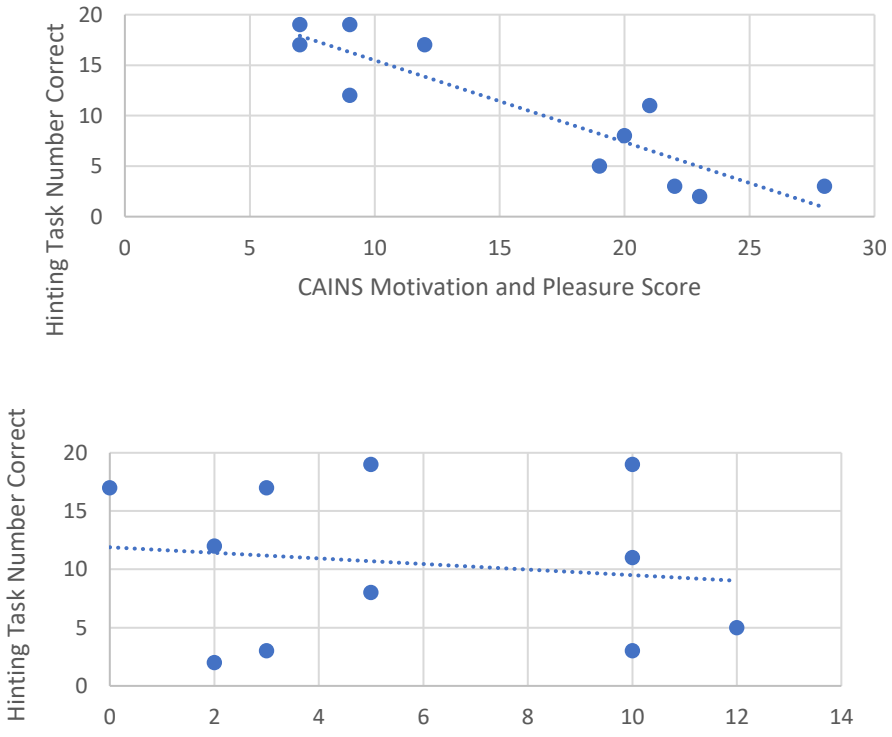


*Figure 3 Scatterplot of Hinting Task and Negative Symptoms*

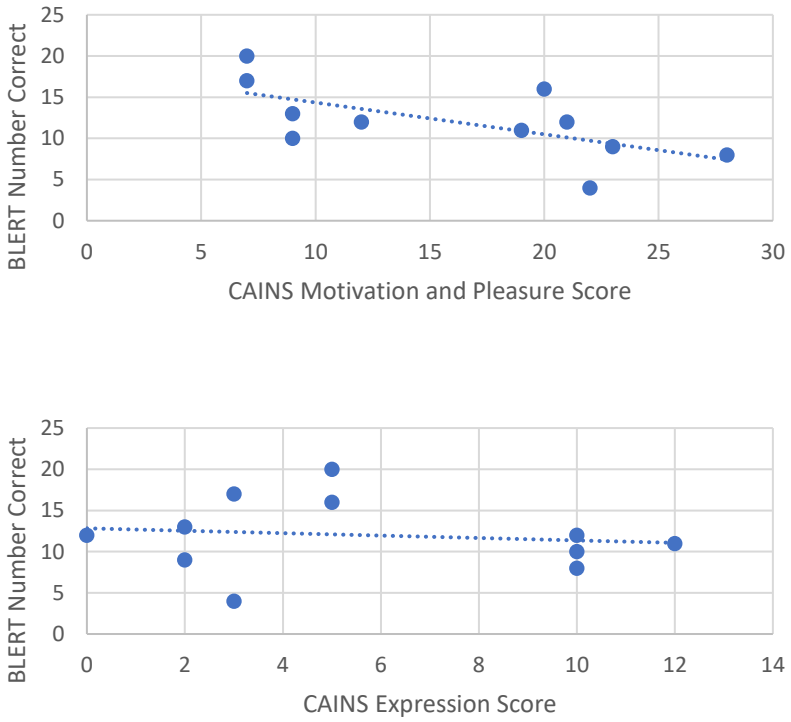


*Figure 4 Scatterplot of Emotion Recognition and Negative Symptoms*

Regarding emotion recognition, there does not appear to be a linear relationship with expressive negative symptoms. There appears to be a moderate negative linear association with experiential negative symptoms, with better performance on the BLERT being associated with lower levels on the CAINS motivation and pleasure scale. The relationship between emotion recognition and experiential negative symptoms appears weaker than the relationship with hinting task performance.

Spearman's Rho correlations between social cognitive task performance and negative symptoms are shown in Table 3. This also suggests that in this small sample there is an indication of a differential association between social cognitive task performance and different domains of negative symptoms, with better performance on social cognitive tasks being associated with lower levels of experiential negative symptoms.

*Table 3 Spearman's Rho Correlations between social cognitive task performance and negative symptoms*

| Social Cognitive Task | CAINS MAP Score | CAINS EXP Score |
|---|---|---|
| **Hinting Task** | r=-0.89 | r=-0.02 |
| **Emotion Recognition** | r=-0.77 | r=-0.12 |

### *Additional Hypothesis and Aims*

Due to the small sample size obtained, we were unable to test our hypothesis that negative symptoms would mediate a relationship between social cognition and functioning. We were additionally unable to construct a regression model to test the relative predictive contribution of these variables to functioning.

### Post-Hoc Analysis of Recruitment Feasibility

Due to challenges with recruitment which led to the small sample size obtained for the current study, an additional post-hoc exploration of recruitment feasibility was carried out. Figure 5 shows a flowchart of participant recruitment. A total of 69 patients were inpatient in Glasgow City rehabilitation services between April and June 2019. Thirty patients were ineligible after screening with a further 6 deemed ineligible by the researcher, leaving 33 eligible participants (48%). Nineteen (57%) eligible patients agreed to an approach by the researcher and 11 (33% of eligible patients) participated. This represented 16% of the in-patient population within the recruitment period.

Additional data was sought from the wards regarding patient turnover to determine the feasibility of increased recruiting figures with an extended recruitment period. Two of the five wards responded; the North West sector reported an average annual turnover from two wards as 7 per year which reflects a 35% annual turnover.

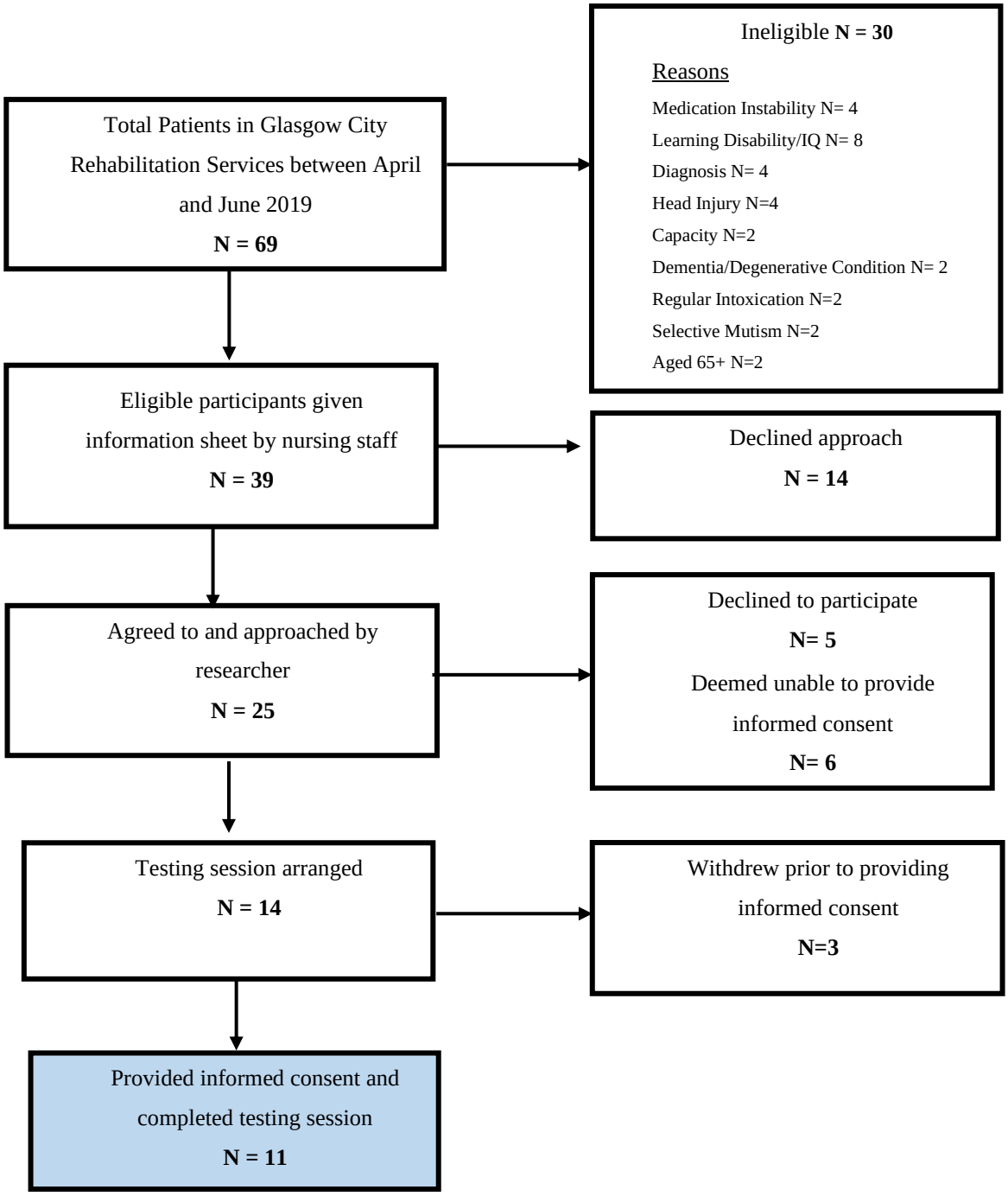


*Figure 5. Recruitment and Participation Flowchart*

# Discussion

The current study demonstrated that there may be a differential association in the relationship between two negative symptoms domains, social cognitive ability and functioning. Due to the small sample size obtained these associations were explored using descriptive rather than inferential statistical methods but, taken together with the additional information gathered regarding recruitment feasibility, the results provide important information for future research within this population.

### *The Importance of a two-factor model of negative symptoms*

Firstly, we found that both social cognition and negative symptoms appeared to be associated with functioning. This is consistent with previous research which has shown that social cognitive ability accounts for around 25% of variance in functioning, with theory of mind showing the largest effect sizes (Fett et al., 2011). Examination of the data in this small inpatient sample suggested that ToM may have been more strongly associated with functioning that emotion recognition ability. Additionally, negative symptoms seemed to show an association with functioning, but there was a differential association between domains of negative symptoms. Previous research has shown that higher levels of negative symptoms are associated with poor functioning, but these studies have typically looked at negative symptoms as a unitary construct combining both expressive and experiential negative symptoms (Ventura et al., 2009). Other studies have examined apathy or motivation in relation to functioning but have not directly compared this with expressive negative symptoms (e.g. Foussias et al., 2011). This study is one of the first (to our knowledge) to suggest that experiential but not expressive negative symptoms are associated with functioning. This is supported by a recently published study of 135 outpatients which found that experiential negative symptoms correlated significantly with interpersonal functioning, while expressive negative symptoms did not (Harvey et al., 2019). Understanding the predictors and pathways to poor functioning has been of growing interest in schizophrenia research since the mid 2000's, and the present study extends knowledge of this issue to suggest that when examining the role of negative symptoms in functional disability, we should examine negative symptoms domains separately from one another. Future studies could seek to extend and replicate these findings in a larger in-patient sample.

Secondly, our findings indicate that there may also be a differential association between social cognition and negative symptom domains. Specifically, the data are suggestive of an association between Theory of Mind ability and experiential negative symptoms, but not expressive negative symptoms. Although there did appear to be a pattern in the data for a relationship with emotion recognition, this appeared to be weaker that with ToM with more outliers present. Social cognitive abilities such as the ability to understand and recognise emotions and others mental state could be hypothesised to be associated with reduced expression of emotion and speech production in social situations (Elis et al., 2013). However, these findings suggest that this may not always be the case. Expressive deficits such as alogia have been found to be related to retrieval from verbal memory, and blunted affect has been shown to be related to a motor production difficulty (Alpert et al., 2000, Fervaha et al., 2016). Taken together with our initial findings, this suggests that expressive deficits are less related to difficulty in the interpretation of social information but more strongly linked to cognitive or motor functions, and that different neurocognitive processes may underly the expression of different symptoms domains.

Social cognitive ability appears to be related to the motivation and pleasure constructs of negative symptoms which are expressed in the marked lack of drive to engage in meaningful activity and establish and maintain interpersonal relationship. ToM and the ability to represent another's mental state has been theorised to play a key role in the development of positive symptoms through deficits in self and other monitoring (Frith, 1992). What has been less fully explored is how social cognitive ability may contribute to negative symptom development. Previous research has suggested that defeatist performance beliefs may mediate a relationship between cognitive ability and negative symptoms and it may be that a similar relationship exists between social cognition and negative symptoms (Grant & Beck, 2008). One could hypothesise that poor social cognitive ability may contribute to similar defeatist beliefs regarding one's ability to engage in successful social interactions, leading to the marked amotivation and apathy that is so common among individuals with schizophrenia. It may then be that these motivational deficits reduce the ability to perform key interpersonal and societal roles leading to poor functional ability. Two previous studies have found conflicting evidence as to whether negative symptoms mediate a relationship between functioning and social cognition (Lin et al., 2013, Couture et al., 2011). However, both of these

studies looked at negative symptoms as a unitary construct. Given these domains may be differentially related to social cognitive domains, examining them as unitary construct may have impacted on the ability to detect a mediated relationship between social cognition, negative symptoms and functioning.

These propositions remain speculative as the present study did not obtain a large enough sample size to be able to test whether there was a mediated relationship between social cognition, experiential negative symptoms and functioning, and the experimental design cannot address questions of causality. However, there is evidence that social cognitive ability is impaired and associated with poor functioning prior to a first episode of active psychosis and poorer premorbid social adjustment predicts worse negative symptoms in later illness (Bora & Pantelis., 2013, Kelley et al., 1992). Additionally, social cognitive interventions have been shown to reduce experiential but not expressive negative symptoms, and a reduction in defeatist beliefs has been identified as one mechanism by which this occurred (Granholm et al., 2014, Granholm et al., 2017). The findings presented here could be replicated and extended in a larger inpatient sample which would allow some of these hypotheses to be more fully explored.

**Recruitment Feasibility**

A post-hoc aim of exploring recruitment feasibility was included following the identification of significant recruitment difficulties. We found that conversion rates were low, even when a sufficient number of eligible participants were approached. A low ward turnover of 35% presents challenges to the recruitment of a sufficient sample in a limited timeframe. We could cautiously assume that with full occupancy of 80 beds and annual turnover of 35%, over one year of recruitment, 28 new patients would be admitted, of which 14 (48%) could be eligible and 4.8 (33%) could be expected to participate based on our recruitment rates. This could be slightly higher if we assume that all participants would meet medication stability in the course of a year's recruitment. Our initial sample size calculation indicated a required sample size of 40 participants. Based on our recruitment figures, this would require a baseline population of 250 patients, or an additional 5-6 years of recruitment from the wards included in this study based on estimated turnover rates. It should be noted that these rates are based on one sector and may not be representative of other sectors. However, this is in

keeping with average inpatient admissions in rehabilitation wards and reflects the slow-stream nature of this work. This provides an indication of the resources which would be required to recruit a sufficient sample to extend the preliminary findings discussed above. Future studies could seek to include additional sites (e.g. across Scotland), widen the inclusion and exclusion criteria or extend the available recruitment period.

High refusal rates could in part be due to the marked negative symptoms which could reduce motivation to participate, and recruitment could be improved in a number of ways. Our protocol length may have deterred patients and researchers should aim to balance completeness of measures to test hypotheses and participant burden. We found that self-reported negative symptoms did not appear to be associated with any other measures, including the CAINS, which contrasts with findings from out-patient samples (Kring et al., 2013). This may have been due to the sample size, but Harvey et al. (2013) has suggested that self-report measures in schizophrenia may not be as reliable as observer ratings, and in more impaired inpatient populations self-report measures may be less useful and could be excluded.

Additionally, future studies could seek to understand how to engage relevant stakeholders to improve recruitment rates. Anecdotal evidence from this study suggests that staff framing the initial approach positively or negatively influenced whether patients agreed to meet the researcher. Of eligible participants agreeing to meet the researcher, 58% completed the test session. Nursing staff are often a key contributor to recruitment into mental health research studies and a number of factors may contribute to how they view and engage with research These will need to be more fully understood to improve recruitment. Previous research has identified potential barriers to recruitment from mental health services including staff feeling that research is not relevant to them and their patients, clinical workloads impacting the prioritisation of research activity (Borschmann et al., 2014) and staff's understanding of research aims and eligibility criteria (Howard et al., 2009). Additionally, a common theme emerges around staff feeling responsible for balancing potential harms and benefits and seeking to protect patients (Adams et al., 2015). Future studies should endeavour to address these barriers in collaboration with those who are being asked to support recruitment. An alternative approach to improving recruitment which reduces the burden on frontline staff was proposed by Callard et al. (2014). They tested a model of "consent to contact" allowing direct approach by researchers which improved participation rates.

While innovative ideas are clearly required in order to advance research with hard-to-reach populations, there are significant legal and ethical issues which would need to be taken into consideration, particularly within in-patient contexts.
Despite these challenges, continuing research efforts in these populations is an important endeavour, as research often occurs with easier-to-recruit outpatient samples, but these findings may not generalise to the inpatient population who may have more marked difficulties, and tend to be the recipients of the social cognitive interventions which are subsequently developed.

**Strengths and Limitations**

Firstly, our small sample size reduces the generalisability of the findings and may have introduced bias into the sample by the participants who did choose to take part. This also limited our ability to conduct an inferential exploration of our hypotheses or to model relationships between relevant predictors of functioning. However examining the feasibility of recruiting from this hard-to-reach populations in combination with patterns present in the data has provided valuable information for the development of future research protocols. Secondly, due to lack of response, our turnover data is based solely on North-West sector and may not generalise to other sectors. Thirdly, diagnoses provided by the clinical team were not independently verified by the researchers and errors in diagnosis could have been present. However, all of the included sample were in-patient in long term rehabilitation services and prescribed an atypical antipsychotic, indicating that the sample was representative of the target population regardless of any diagnostic issues. Finally, social cognition is a multifaceted construct and we only included two domains of social cognition; however, this was in consideration of the length of the protocol.

Strengths of this study were the use of objective measurements of functioning and negative symptoms which have both been designed to reduce overlap which has been a criticism of previous research. In particular, the CAINS has been designed to specifically assess internal motivation as well as external behaviours and so does not just reflect behaviour. A further strength is the use of social cognitive measures which have demonstrated high psychometric properties and have been recommended by an expert panel for use in schizophrenia research.

## Future Directions

Future studies could seek to replicate and extend the preliminary findings presented here in a larger sample of in-patients to map out the relationship between social cognition, negative symptoms and functioning using a two-construct model of negative symptoms and include additional domains of social cognition. Longitudinal studies could seek to clarify the nature of causal relationships, as long-term hospitalisation could also atrophy social cognitive abilities and this may be more marked in people with prominent negative symptoms. Intervention studies could examine the contribution of baseline experiential negative symptoms in determining outcomes in social cognitive remediation programmes. Given that different negative symptoms may be related to different underling constructs, assessing negative symptoms as a unitary construct may mask effects on one domain and intervention studies should take this into consideration.

## Conclusion

We provide preliminary data on a potential differential association between two domains of negative symptoms, social cognition and functioning as well as important information on the feasibility of recruiting from hard-to-reach in-patient populations who are under-researched. Our findings are limited by our small sample and future studies should seek to extend these findings in a larger sample and address practical issues to recruitment.

# References


Adams, M., Caffrey, L. & Mckevitt, C. 2015. Barriers and opportunities for enhancing patient recruitment and retention in clinical research: findings from an interview study in an NHS academic health science centre. Health research policy and systems, 13, 8-8 doi:10.1186/1478-4505-13-8

Adolphs, R. 2001. The neurobiology of social cognition. *Curr Opin Neurobiol,* 11**,** 231-9

Allen, D. N., Strauss, G. P., Donohue, B. & Van Kammen, D. P. 2007. Factor analytic support for social cognition as a separable cognitive domain in schizophrenia. *Schizophrenia research,* 93**,** 325-333

Alpert, M., Rosenberg, S. D., Pouget, E. R. & Shaw, R. J. 2000. Prosody and lexical accuracy in flat affect schizophrenia. *Psychiatry research,* 97**,** 107-118 doi:https://doi.org/10.1016/S0165-1781(00)00231-6

Benton, A. L. & Hamsher, K. D. 1983. *Multilingual aphasia examination : manual of instructions,* [Iowa City], Dept. of Neurology and Psychology, University of Iowa.

Blanchard, J. J. & Cohen, A. S. 2005. The Structure of Negative Symptoms Within Schizophrenia: Implications for Assessment. *Schizophrenia Bulletin,* 32**,** 238-245 doi:10.1093/schbul/sbj013

Bora, E. & Pantelis, C. 2013. Theory of mind impairments in first-episode psychosis, individuals at ultra-high risk for psychosis and in first-degree relatives of schizophrenia: Systematic review and meta-analysis. *Schizophrenia research,* 144**,** 31-36 doi:https://doi.org/10.1016/j.schres.2012.12.013

Borschmann, R., Patterson, S., Poovendran, D., Wilson, D. & Weaver, T. 2014. Influences on recruitment to randomised controlled trials in mental health settings in England: a national cross-sectional survey of researchers working for the Mental Health Research Network. BMC medical research methodology, 14, 23-23 doi:10.1186/1471-2288-14-23

Brissos, S., Molodynski, A., Dias, V. V. & Figueira, M. L. 2011. The importance of measuring psychosocial functioning in schizophrenia. *Ann Gen Psychiatry,* 10**,** 18 doi:10.1186/1744-859x-10-18

Bryson, G., Bell, M. & Lysaker, P. 1997. Affect recognition in schizophrenia: a function of global impairment or a specific cognitive deficit. *Psychiatry Res,* 71**,** 105-13

Callard, F., Broadbent, M., Denis, M., Hotopf, M., Soncul, M., Wykes, T., Lovestone, S. & Stewart, R. 2014. Developing a new model for patient recruitment in mental health services: a cohort study using Electronic Health Records. *BMJ Open,* 4**,** e005654 doi:10.1136/bmjopen-2014-005654

Cohen, J. 1992. A power primer. *Psychol Bull,* 112**,** 155-9

Corcoran, R., Mercer, G. & Frith, C. D. 1995. Schizophrenia, symptomatology and social inference: investigating "theory of mind" in people with schizophrenia. *Schizophrenia research,* 17**,** 5-13

Department of Health – Mental Health Strategies. (2012). 2011/12 National Survey of Investment in Adult Mental Health Services. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/140098/FinMap2012-NatReportAdult-0308212.pdf

Elis, O., Caponigro, J. M. & Kring, A. M. 2013. Psychosocial treatments for negative symptoms in schizophrenia: Current practices and future directions. *Clinical Psychology Review,* 33**,** 914-928 doi:https://doi.org/10.1016/j.cpr.2013.07.001

Fervaha, G., Takeuchi, H., Foussias, G., Agid, O. & Remington, G. 2016. Using poverty of speech as a case study to explore the overlap between negative symptoms and cognitive dysfunction. *Schizophrenia research,* 176**,** 411-416

Fett, A. K. J., Viechtbauer, W., Dominguez, M. D., Penn, D. L., Van Os, J. & Krabbendam, L. 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis. *Neuroscience and Biobehavioral Reviews,* 35**,** 573-588 doi:10.1016/j.neubiorev.2010.07.001

Foussias, G., Mann, S., Zakzanis, K. K., Van Reekum, R., Agid, O. & Remington, G. 2011. Prediction of longitudinal functional outcomes in schizophrenia: The impact of

baseline motivational deficits. *Schizophrenia research,* 132**,** 24-27 doi:https://doi.org/10.1016/j.schres.2011.06.026

Frith, C. D. 1992. *The cognitive neuropsychology of schizophrenia,* Hillsdale, NJ, US, Lawrence Erlbaum Associates, Inc.

Gard, D. E., Gard, M. G., Kring, A. M. & John, O. P. 2006. Anticipatory and consummatory components of the experience of pleasure: a scale development study. *Journal of research in personality,* 40**,** 1086-1102

Gooding, D. C. & Pflum, M. J. 2014. The assessment of interpersonal pleasure: introduction of the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS) and preliminary findings. *Psychiatry research,* 215**,** 237-243

Granholm, E., Holden, J., Link, P. C. & Mcquaid, J. R. 2014. Randomized clinical trial of cognitive behavioral social skills training for schizophrenia: improvement in functioning and experiential negative symptoms. *Journal of consulting and clinical psychology,* 82**,** 1173-1185 doi:10.1037/a0037098

Granholm, E., Holden, J. & Worley, M. 2017. Improvement in Negative Symptoms and Functioning in Cognitive-Behavioral Social Skills Training for Schizophrenia: Mediation by Defeatist Performance Attitudes and Asocial Beliefs. *Schizophrenia Bulletin,* 44**,** 653-661 doi:10.1093/schbul/sbx099

Grant, P. M. & Beck, A. T. 2008. Defeatist Beliefs as a Mediator of Cognitive Impairment, Negative Symptoms, and Functioning in Schizophrenia. *Schizophrenia Bulletin,* 35**,** 798-806 doi:10.1093/schbul/sbn008

Green, M. F. 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry,* 153**,** 321-330

Green, M. F., Kern, R. S., Braff, D. L. & Mintz, J. 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? *Schizophr Bull,* 26**,** 119-36 doi:10.1093/oxfordjournals.schbul.a033430

Harvey, P. D. 2013. Assessment of everyday functioning in schizophrenia: implications for treatments aimed at negative symptoms. *Schizophrenia research,* 150**,** 353-355 doi:10.1016/j.schres.2013.04.022

Harvey, P. D., Deckler, E., Jones, M. T., Jarskog, L. F., Penn, D. L. & Pinkham, A. E. 2019. Depression and reduced emotional experience in schizophrenia: Correlations with self-reported and informant-rated everyday social functioning. *Journal of Experimental Psychopathology,* 10**,** 2043808719829313 doi:10.1177/2043808719829313

Hickey, G. & Kipping, C. 1998. Exploring the concept of user involvement in mental health through a participation continuum. *Journal of Clinical Nursing,* 7**,** 83-88 doi:10.1046/j.1365-2702.1998.00122.x

Howard, L., De Salis, I., Tomlin, Z., Thornicroft, G. & Donovan, J. 2009. Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness. Contemporary Clinical Trials, 30, 40-46 doi:10.1016/j.cct.2008.07.007

Joint Commissioning Panel for Mental Health. (2016). Guidance for commissioners of rehabilitation services for people with complex mental health needs. Available at https://www.jcpmh.info/resource/guidance-for-commissioners-of-rehabilitation-services-for-people-with-complex-mental-health-needs/

Kirkpatrick, B., Fenton, W. S., Carpenter, W. T., Jr. & Marder, S. R. 2006. The NIMH-MATRICS Consensus Statement on Negative Symptoms. *Schizophrenia Bulletin,* 32**,** 214-219 doi:10.1093/schbul/sbj053

Konstantakopoulos, G., Ploumpidis, D., Oulis, P., Patrikelis, P., Soumani, A., Papadimitriou, G. N. & Politis, A. M. 2011. Apathy, cognitive deficits and functional impairment in schizophrenia. *Schizophr Res,* 133**,** 193-8 doi:10.1016/j.schres.2011.07.003

Kraeplin, E. 1919. *Dementia Praecox and Paraphenia,* New York, Robert E Krieger Publishing Co.

Kring, A. M., Gur, R. E., Blanchard, J. J., Horan, W. P. & Reise, S. P. 2013. The Clinical Assessment Interview for Negative Symptoms (CAINS): Final Development and Validation. *American Journal of Psychiatry,* 170**,** 165-172 doi:10.1176/appi.ajp.2012.12010109

Leifker, F. R., Bowie, C. R. & Harvey, P. D. 2009. Determinants of everyday outcomes in schizophrenia: the influences of cognitive impairment, functional capacity, and symptoms. *Schizophrenia research,* 115**,** 82-87

Lim, J., Lee, S. A., Lam, M., Rapisarda, A., Kraus, M., Keefe, R. S. E. & Lee, J. 2016. The relationship between negative symptom subdomains and cognition. *Psychological Medicine,* 46**,** 2169-2177

Lincoln, T. M., Mehl, S., Kesting, M.-L. & Rief, W. 2011. Negative Symptoms and Social Cognition: Identifying Targets for Psychological Interventions. *Schizophrenia Bulletin,* 37**,** S23-S32 doi:10.1093/schbul/sbr066

Lovibond, S. H. & Lovibond, P. F. 1995. *Manual for the depression anxiety stress scales,* Sydney, Psychology Foundation of Australia.

Marder, S. R. & Galderisi, S. 2017. The current conceptualization of negative symptoms in schizophrenia. *World psychiatry : official journal of the World Psychiatric Association (WPA),* 16**,** 14-24 doi:10.1002/wps.20385

Morosini, P. L., Magliano, L., Brambilla, L., Ugolini, S. & Pioli, R. 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr Scand,* 101**,** 323-9

Pinkham, A. E., Harvey, P. D. & Penn, D. L. 2017. Social Cognition Psychometric Evaluation: Results of the Final Validation Study. *Schizophrenia Bulletin,* 44**,** 737-748 doi:10.1093/schbul/sbx117

Pinkham, A. E., Penn, D. L., Green, M. F. & Harvey, P. D. 2015. Social Cognition Psychometric Evaluation: Results of the Initial Psychometric Study. *Schizophrenia Bulletin,* 42**,** 494-504 doi:10.1093/schbul/sbv056

Priebe, S. 2007. Social outcomes in schizophrenia. *British Journal of Psychiatry,* 191**,** s15-s20 doi:10.1192/bjp.191.50.s15

Russell, D., Peplau, L. A. & Cutrona, C. E. 1980. The revised UCLA Loneliness Scale: concurrent and discriminant validity evidence. *J Pers Soc Psychol,* 39**,** 472-80

Sergi, M. J., Rassovsky, Y., Widmark, C., Reist, C., Erhart, S., Braff, D. L., Marder, S. R. & Green, M. F. 2007. Social cognition in schizophrenia: relationships with neurocognition and negative symptoms. *Schizophrenia research,* 90**,** 316-324

Turner, D. T., Van Der Gaag, M., Karyotaki, E. & Cuijpers, P. 2014. Psychological Interventions for Psychosis: A Meta-Analysis of Comparative Outcome Studies. *American Journal of Psychiatry,* 171**,** 523-538 doi:10.1176/appi.ajp.2013.13081159

Van Hooren, S., Versmissen, D., Janssen, I., Myin-Germeys, I., À Campo, J., Mengelers, R., Van Os, J. & Krabbendam, L. 2008. Social cognition and neurocognition as independent domains in psychosis. *Schizophrenia research,* 103**,** 257-265 doi:https://doi.org/10.1016/j.schres.2008.02.022

Ventura, J., Hellemann, G. S., Thames, A. D., Koellner, V. & Nuechterlein, K. H. 2009. Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: A meta-analysis. *Schizophrenia research,* 113**,** 189-199 doi:https://doi.org/10.1016/j.schres.2009.03.035

Weissman, A. N. 1979. The dysfunctional attitude scale: A validation study.

# Chapter 1 Appendices

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*Updated 18-05-2018*

## Appendix 1.2 Full Search Strategy: Ovid Medline

1. psychotic disorders/ or schizophrenia/
2. (schizophrenia or schizophrenic or psychos?s or psychotic or schizoaffective).ti,ab,kw
3. 1 or 2
4. prodromal symptoms/
5. (Attenuated adj1 (psychos*s or symptoms or psychotic)).ti,ab,kw.
6. ((High risk or at risk) adj1 (mental state or population or patient or person or group or individual)).ti,ab,kw.
7. (ultra high risk or clinical* high risk or psychosis risk or at risk for psychosis or prodrom*).ti,ab,kw.
8. 4 or 5 or 6 or 7
9. "Quality of Life"/ or "Activities of Daily Living"/ or Community Participation/
10. ((work or vocation* or occupation* or functional or psychosocial or community or social or prosocial or adaptive or interpersonal or global or role) adj1 (function* or adjust* or behavio?r* or outcome* or satisfaction)).ti,ab,kw.
11. (quality of life or activit* of daily living or independent living skills or social skills).ti,ab,kw.
12. 9 or 10 or 11
13. "theory of mind"/ or social perception/ or facial recognition/ or facial expression/
14. (theory of mind or false belief or tom or mentali?ing or mentali?ation or attribution* or social perception or social cog*).ti,ab,kw.
15. ((Emotion or social or affect or facial) adj1 (recognition or perception)).ti,ab,kw.
16. 13 or 14 or 15
17. 3 and 8 and 12 and 16

**Appendix 1.3 - Data Extraction Form**

1. General Information

| | |
|---|---|
| Date data extracted | |
| Name of person extracting data | |
| Title of study, authors and date | |

2. Inclusion Criteria

| **Criteria** | **Location in text (e.g. Page #)** |
|---|---|
| Original research paper | |
| Measured social cognition – ToM, ER, AB, SP | |
| Measured Functioning | |
| Examined association between functioning and social cognition | |
| Population – UHR? | |
| Validated UHR screening tool used? | |

3. Study Characteristics

| | |
|---|---|
| Number of Participants UHR (N) | |
| Control or other comparison group included (N) | |
| Study design | |
| Study Aims | |

4. Demographics (UHR Sample)

| | |
|---|---|
| Gender (% Male) | |
| Age | |
| Education | |
| UHR Criteria used | |

*for age and education Mean and SD

5. Measures

| | |
|---|---|
| Measures of social cognition used | |
| Measures of functional outcome used | |

6. Results

| Measures | Statistical test | Statistical result |
|---|---|---|
| | | |
| | | |

7. Comparison with control group (if relevant)?

| |
|---|
| |

**Appendix 1.4: CCAT Rating for Included Studies**

| **Paper** | Preliminaries | Introduction | Design | Sampling | Data Collection | Ethical Matters | Results | Discussion | Total Score (%) |
|---|---|---|---|---|---|---|---|---|---|
| Amminger et al. 2013 | 3 | 1 | 4 | 3 | 5 | 5 | 4 | 4 | 29 (73) |
| Barbato et al. 2013 | 4 | 5 | 3 | 2 | 1 | 4 | 5 | 5 | 29 (73) |
| Bartholomeus z et al. 2014 | 5 | 5 | 5 | 2 | 5 | 4 | 5 | 5 | 36 (90) |
| Clayson et al. 2019 | 5 | 5 | 3 | 2 | 3 | 5 | 5 | 5 | 33 (83) |
| Cotter et al. 2017 | 5 | 5 | 4 | 3 | 4 | 5 | 4 | 5 | 36 (90) |
| DeVylder et al 2013 | 4 | 3 | 3 | 2 | 3 | 4 | 3 | 4 | 26 (65) |
| Glenthoj et al. 2018 | 5 | 5 | 5 | 3 | 4 | 5 | 5 | 5 | 37 (93) |
| Glenthoj et al. 2016 | 4 | 5 | 3 | 3 | 2 | 4 | 3 | 4 | 28 (70) |
| Haining et al. 2019 | 4 | 4 | 4 | 4 | 4 | 2 | 5 | 5 | 32 (80) |
| Ohmuro et al. 2016 | 5 | 5 | 5 | 4 | 4 | 5 | 5 | 5 | 38 (95) |
| Stanford et al. 2011 | 5 | 4 | 5 | 4 | 4 | 5 | 5 | 5 | 37 (93) |

## Appendix 1.5 Description of Functioning Measures in Included Studies

| Measure Name | Domains Included/Measure Description |
|---|---|
| **Community Functioning: Observer or Informant Rating** | |
| Social and Occupational Functioning Assessment Scale [1] | Global rating of functioning scored from 0-100 |
| Global Assessment of Functioning [2] | Global rating of functioning including symptoms severity– single score from 0-100 |
| Global Functioning Scale – Social[3] | Engagement in social activity and interpersonal relationships |
| Global Functioning Scale – Role[3] | Educational and Vocational Engagement and performance |
| Personal and Social Performance Scale[4] | Functioning in four areas– socially useful activities, personal and social relationships, self-care tasks and disturbing and aggressive behaviours – rated on four anchor points to obtain overall rating of personal and social performance. |
| **Community Functioning - Self-Report Measures** | |
| Social Functioning Scale – Self report[5] | Social engagement, interpersonal communication, independence performance, independence competence, recreation, prosocial, employment |
| Social Responsiveness Scale[6] | Total score representing overall social deficits and 5 sub-scores: Social Awareness Social Cognition, Social Communication, Social Motivation, Restricted Interests and Repetitive Behaviour |
| Assessment of Quality of Life[7] | 5 dimensions: illness, independent living, social relationships, physical senses and psychological wellbeing |
| Social Adjustment Scale[8] | Self report of individuals satisfaction with social situation |
| **Social Skills Performance** | |
| High Risk Social Challenge Task[9] | Videotaped speech challenge coded for social functioning |

References


**1.** Rybarczyk B. Social and Occupational Functioning Assessment Scale (SOFAS). In: Kreutzer JS, DeLuca J, Caplan B, eds. *Encyclopedia of Clinical Neuropsychology*. New York, NY: Springer New York; 2011:2313-2313.

**2.** Jones SH, Thornicroft G, Coffey M, Dunn G. A Brief Mental Health Outcome Scale: Reliability and Validity of the Global Assessment of Functioning (GAF). *British Journal of Psychiatry* 1995;166(5):654-659.

**3.** Cornblatt BA, Auther AM, Niendam T, Smith CW, Zinberg J, Bearden CE, Cannon TD. Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. *Schizophrenia bulletin* 2007;33(3):688-702.
**4.** Morosini PL, Magliano L, Brambilla L, Ugolini S, Pioli R. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr Scand* Apr 2000;101(4):323-329.
**5.** Birchwood M, Smith JO, Cochrane R, Wetton S, Copestake S. The social functioning scale the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *The British Journal of Psychiatry* 1990;157(6):853-859.
**6.** Constantino JN. Social Responsiveness Scale. In: Volkmar FR, ed. *Encyclopedia of Autism Spectrum Disorders*. New York, NY: Springer New York; 2013:2919-2929.
**7.** Hawthorne G, Richardson J, Osborne R. The Assessment of Quality of Life (AQoL) instrument: a psychometric measure of health-related quality of life. *Quality of Life Research* 1999;8(3):209-224.
**8.** Weissman MM, Prusoff BA, Thompson WD, Harding PS, Myers JK. Social adjustment by self-report in a community sample and in psychiatric outpatients. Vol 166. US: Lippincott Williams & Wilkins; 1978:317-326.
**9.** Gibson CM, Penn DL, Prinstein MJ, et al. Social skill and social cognition in adolescents at genetic risk for psychosis. *Schizophrenia Research* 2010;122(1-3):179-184.

# Chapter 2 Appendices

## Appendix 2.1 Ethical Approval Letter


**East of Scotland Research Ethics Service (EoSRES)**
**Research Ethics Service**

Tayside medical Science Centre
Residency Block Level 3
George Pirie Way
Ninewells Hospital and Medical School
Dundee, DD1 9SY

Professor Hamish McLeod
Professor of Clinical Psychology
University of Glasgow Gartnavel
Royal Hospital Administration
Building 1055 Great western
Road G12 0HX

Date: 26 February 2019
Your Ref:
Our Ref: LR/**19/ES/0006**
Enquiries to: Mrs Lorraine Reilly
Direct Line: 01382 383878
Email: eosres.tayside@nhs.net

Dear Professor McLeod

| | |
|---|---|
| **Study Title:** | **The relationship between social cognition, negative symptoms and interpersonal functioning in persistent psychosis** |
| **REC reference:** | **19/ES/0006** |
| **Protocol number:** | **N/A** |
| **IRAS project ID:** | **248610** |

Thank you for your letter dated 19 February 2019, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide

a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

**Conditions of the favourable opinion**

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.
*Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).*
*Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.*

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.*

*Sponsors are not required to notify the Committee of management permissions from host organisations*

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be

permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**Ethical Review of Research Sites**

**NHS Sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

**Non-NHS sites**

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| Document | Version | Date |
|---|---|---|
| Copies of advertisement materials for research participants [Staff Information sheet] | 1.04 | 14 February 2019 |
| Covering letter on headed paper [Covering Letter Response to REC Provisional Opinion] | | 19 February 2019 |
| Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of sponsor indemnity (non-NHS)] | | 06 August 2018 |
| GP/consultant information sheets or letters [Notification of Participation Letter] | 1.04 | 19 February 2019 |
| IRAS Application Form [IRAS_Form_20122018] | | 20 December |
| IRAS Checklist XML [Checklist_20122018] | | 20 December |
| IRAS Checklist XML [Checklist_21022019] | | 21 February |
| Participant consent form [Consent Form] | 1.04 | 14 February |
| Participant information sheet (PIS) [PIS] | 1.04 | 14 February |
| Referee's report or other scientific critique report [Proposal feedback and Review] | | 19 February 2018 |
| Research protocol or project proposal [Study Protocol] | 1.04 | 19 February |
| Sample diary card/patient card [Case Record Form] | 1.04 | 14 February |
| Summary CV for Chief Investigator (CI) [Hamish McLeod CI CV] | | 09 August 2018 |
| Summary CV for student [Anna Kondol CV] | | |
| Validated questionnaire [ACIPS] | | |
| Validated questionnaire [CAINS] | 1.0 | 03 May 2012 |
| Validated questionnaire [DASS-21] | | |
| Validated questionnaire [Hinting Task] | | |
| Validated questionnaire [PSP See Table 1] | | |
| Validated questionnaire [TEPS] | | |
| Validated questionnaire [UCLA Loneliness Scale] | 3 | |
| Validated questionnaire [Phonemic Fluency] | 1.01 | 30 November |
| Validated questionnaire [Trail Making Test Part B] | 1.01 | 30 November |
| Validated questionnaire [BLERT] | | |

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

**After Ethical Review**

Reporting Requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments

Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

**User Feedback**

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/qualityassurance/

**HRA Training**

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

| **19/ES/0006** | **Please quote this number on all correspondence** |
|---|---|

With the Committee's best wishes for the success of this

project. Yours sincerely

**pp.**
**Dr Robert Rea**
**Chair**

**Appendix 2.2 NHS Greater Glasgow and Clyde Research and Design Study Approval**

**Administrator: Mrs Elaine O'Neill**
**Management Office**
**Telephone Number: 0141 232 1815**
**Glasgow ACH**
**E-Mail: elaine.o'neill2@ggc.scot.nhs.uk**
**Street**
**Website: www.nhsggc.org.uk/r&d**

**w G3 8SW**

**R&D**

**West**

**Dalnair**

**Glasgo**

4 April 2019

## NHS GG&C Board Approval

Dear Dr I Kevan,

| | |
|---|---|
| **Study Title:** | **The Relationship between Social Cognition, Negative Symptoms and Interpersonal Functioning in Persistent Psychosis** |
| **Principal Investigator:** | **Dr Ian Mark Kevan** |
| **GG&C HB site** | **Gartnavel Royal Hospital** |
| **Sponsor** | **NHS Greater Glasgow and Clyde** |
| **R&D reference:** | **GN18MH640** |
| **REC reference:** | **19/ES/0006** |
| **Protocol no:** | **V1.04; 19/02/2019** |

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

**Conditions of Approval**

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004

   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan.
   a. Recruitment Numbers on a monthly basis
   b. Any change of staff named on the original SSI form
   c. Any amendments – Substantial or Non Substantial
   d. Notification of Trial/study end including final recruitment figures
   e. Final Report & Copies of Publications/Abstracts

**Please add this approval to your study file as this letter may be subject to audit and monitoring.** Your personal information will be held on a secure national web-based NHS database. I wish you every success with this research study

Yours sincerely,

Mrs Elaine O'Neill
**Senior Research Administrator**

**Cc:** Emma Jane Gault (GU)

## Appendix 2.3 Participant Information Sheet



### Participant Information Sheet

### Study Title: Understanding Interpersonal Functioning in Persistent Psychosis

**Invitation and Brief Summary**

We would like to invite you to take part in a research study. Before you decide, we would like you to understand why the research is being done and what it would involve for you. We will go through the information sheet with you and answer and questions you have before you decide whether you want to take part.

**Why are we doing this research?**

Research has shown that people with long term psychosis often have ongoing problems with their day to day functioning, including how they get on with others. This can happen even when some of their other symptoms have improved. We know that the ability to work out what other people are thinking and feeling (social cognition) can affect recovery of functioning. Recovery of functioning is also affected by "negative symptoms" such as loss of motivation. We are conducting our research to help us understand how difficulties with social cognition (the ability to understanding how other people think and feel) and negative symptoms (lack of motivation and loss of interest) might lead people to have difficulties in how they get on with other people (i.e. their interpersonal functioning). We hope that finding out more about how these different factors are related will help us to develop more effective psychological therapies.

**Why have I been invited to take part?**

You are being invited to take part because we are recruiting people aged between 18 and 65 who have experienced psychosis and are admitted to the long -term rehabilitation wards of NHS Greater Glasgow and Clyde. We are hoping to recruit 40 people to take part.

**Do I need to take part?**

No, participation is entirely voluntary. It is up to you if you want to take part. One of the research team will go through the information sheet and the study in more detail with you. If you decide to take part, you will be asked to sign a consent form. You are free to withdraw from the study at any time, without giving a reason. Choosing to participate or

not  will not affect your usual care and treatment now or in the future. If you decide to withdraw from the study at any point, we will keep any test data that we have already collected and may use this in our analysis. However, we will not collect any further data either from yourself, your records or your clinical team.

**What will happen to me if I take part?**

If you give consent to take part, you will be asked to attend a single session with the researcher. This will take place on the ward and will last between 90 minutes and two hours with time for breaks where needed. This will be arranged so that it does not interfere with any of your meal or recreation times. The test session will be administered by the researcher but you will have the option of having a member of ward staff who you know well, such as a key worker, accompany you.

The testing session will involve:

- An interview asking about your symptoms. With your consent we will voice record this to use for scoring the interview. If you do not wish to have this recorded you can still take part and we will write down your answers instead.
- Questionnaires asking about your mood, levels of motivation and loneliness.
- Tasks of social cognition – this will include watching a video and identifying emotions and listening to some short stories and answering some questions
- Tasks of cognition – this will include a paper and pencil task connecting letters and numbers, and a task coming up with lists of words.

We will also ask to speak to a member of your clinical team to get a rating of your recent levels of interpersonal functioning on the ward.

As part of the study we would also request permission to look at your medical notes to gather some demographic information such as your age, medication, diagnosis and the date of your admission to the ward.

This study does not involve any change to your normal care. We will not prescribe or change any medication, collect any blood samples or ask you to do anything differently other than what we ask you to complete during the one-off testing session.

We will write to your Psychiatrist to let them know you are taking part in the study.

**What are the possible benefits of taking part?**

There are no direct benefits to taking part in this study.  However, this research may help improve our understanding of the factors that affect personal recovery and we will use this information to develop more effective treatments.

**What are the possible disadvantages or risks of taking part?**

There are no significant risks associated with taking part in this research although that it is possible that a small number of people could find some of the questions upsetting. You may also find that the testing session is quite tiring. We will check how you are feeling regularly throughout the testing session and you can let us know if you are feeling upset or want to take a break. We will pause testing and support you with any distress you are experiencing. If you or the researcher feel that you are too distressed to continue or that it would be harmful to continue then we will stop the testing session and inform a member of your clinical team who will offer you support. You will be able to take breaks during the test session to minimise fatigue as required.

**Will my results be shared with anyone?**

With your consent, we will give a copy of your results to your clinical team to help them understand you and plan care. This information will be securely stored in your medical records and will not be kept by the research team.

**Will my information in the study be kept confidential?**

Yes – we will follow ethical and legal practices to keep your data safe and confidential. Other than sharing your results with your clinical team (if you consent), all data will be anonymous and stored securely on University of Glasgow computers and secure locked filing cabinets on NHS Greater Glasgow and Clyde premises. This data will only be accessed by members of the research team and possibly the study Sponsor, NHS GG&C, to check that the study is being carried out properly. Anonymised data will be stored for 10 years after the study finishes before being securely destroyed. The voice recording of the clinical interview will be stored securely on NHS GG&C computers until the end of the study. This will be used to score a clinical interview which will be anonymised and stored on University of Glasgow computers

**What will happen with the results?**

The study is being carried out as part of Anna Kondol's Doctorate in Clinical Psychology training. This means that the results will be written up and submitted to the university in the form of a thesis. The research will also be examined through an oral examination. We hope to publish the results in an academic journal afterwards. A summary of the results will be circulated to the wards which took part in the research. Your data and information will not be identifiable from any of the published results of the study. If you would like to receive a copy of the results, the research team will make this available to you after the study has finished.

**Who has reviewed this study?**

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from NHS Greater Glasgow and Clyde whose role is to check that research is properly conducted and the interests of those taking part are adequately protected. NHS Greater Glasgow and Clyde Research and Development Department have also reviewed this study and given it approval to proceed.

**Further information and contact details**

If you wish to find out more about this study and your participation, please contact Anna Kondol on 0141 211 0607 or a.lamont.1@research.gla.ac.uk.

If you would like to speak with someone independent who is not involved in the study, you can contact Professor Tom McMillan on 01412110354 or Thomas.McMillan@glasgow.ac.uk

**What if I want to make a complaint?**

If you wish to make a complaint about this study you can

Write to us:
Complaints Department
West Glasgow Ambulatory Care Hospital
Dalnair Street
Glasgow
G3 8SJ
Phone us: 0141 201 4500
Email us: complaints@ggc.scot.nhs.uk

**How we will use your data**

NHS Greater Glasgow and Clyde is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for monitoring that your information is being collected, used, and stored properly. NHS Greater Glasgow and Clyde may conduct audits of the research to ensure

quality and governance procedures are adhered to. Information about this study and its conduct may be kept by the study sponsor for up to 10 years after the study has finished.

Your rights to access, change or move your information is limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information here https://www.nhsinform.scot/care-support-and-rights/health-rights/confidentiality-and-data-protection/how-the-nhs-handles-your-personal-health-information .

**Thank you for reading this Information Sheet.**

Matriculation Number:

## Appendix 2.4 Major Research Project Proposal

**Name of Assessment**: MRP Proposal

**Title of Project**: The relationship between social cognition, negative symptoms and interpersonal functioning in persistent psychosis

**Matriculation Number**:

**Academic Supervisor**: Hamish McLeod

**Field Supervisor**: Ian Mark Kevan

**Submission Date**: 21-5-18

**Version Number**: 7

**Word Count**: 3582

## Abstract

**Background:** Schizophrenia is associated with significant disruption to interpersonal functioning. There has been an increasing interest in describing and understanding the factors which might contribute to an individual's everyday functioning. Neurocognition and social cognition have been identified as important predictors of functioning, with social cognition posited as more predictive of real world behaviour that neurocognition. The pathway from social cognition to interpersonal functioning remains to be tested and described to identify key areas for treatment. Negative symptoms are another important predictor of functioning and may mediate the relationship between social cognition and interpersonal functioning.

**Aims:** The aim of the current study is to explore the relationship between social cognition, negative symptoms and interpersonal functioning. We aim to explore whether social cognition and negative symptoms are correlated, and whether negative symptoms mediate the relationship between social cognition and interpersonal functioning. In addition, we aim to test a predictive model of interpersonal functioning which hypothesises that difficulty processing rapidly unfolding real-world information, difficulties in identifying and interpreting social cues, and feelings of apathy and amotivation lead to poorer interpersonal functioning and potentially loneliness.

**Method:** The present study will recruit patients with schizophrenic-spectrum illnesses from NHS Greater Glasgow and Clyde Rehabilitation Wards. Using a cross-sectional design, participants will complete a battery of measures including measures of social cognition, neurocognition, negative symptoms and measures of interpersonal functioning and loneliness.

**Applications:** This study has applications in better understanding potential pathways to poor interpersonal functioning in patients with chronic schizophrenia-spectrum conditions. By identifying the early links in the pathway from basic neuro/social cognitive deficits to poor functioning, this will allow us to identify specific targets for remediation.


## Introduction

Schizophrenia is one of the leading causes of disability globally (Whiteford et al., 2013). A core feature of schizophrenia is functional deficits, such as deficits in social and occupational functioning. In spite of advances in antipsychotic treatments and the availability of medications which are somewhat effective in treating positive symptoms such as delusions and hallucinations (Leucht et al., 2012) patients continue to experience significant difficulty in their daily lives (Brissos et al., 2011). Identifying those factors which may underlie poor psychosocial functioning in schizophrenia and developing targeted treatments has become a major focus for researchers (Juckel and Morosini, 2008).

**Psychosocial functioning in schizophrenia**

A decline in psychosocial functioning in a core feature of schizophrenia (Brissos et al., 2011) Ro and Clark (2009) define psychosocial functioning as an "individuals' performance in their environment regarding significant aspects of daily living". Many people diagnosed with schizophrenia experience impairments in social interactions, maintaining relationships and workplace performance (Brissos et al., 2011) which have a deleterious effect on their overall recovery. Operationalisation of psychosocial functioning varies but has generally focussed on activities of daily living and self-care, fulfilment of work requirements, engagement in meaningful activity etc. One aspect of psychosocial functioning which is of interest is interpersonal functioning – e.g. the ability to develop and maintain relationships. Interpersonal functioning may be particularly important to an individual's outcome in schizophrenia as it may influence other types of functioning through increased social capital (Fett et al., 2011). Indeed research suggests social connectedness is a strong predictor of overall health in the general population (Fiorillo and Sabatini, 2011). Most studies looking at functioning in schizophrenia have focussed on broader measures of psychosocial functioning. Interpersonal functioning is a potentially important treatment target to improve the long-term outcome for schizophrenic patients.

**Predictors and correlates of psychosocial functioning**

There has been a surge in research exploring what may underlie poor psychosocial functioning in schizophrenia. A review conducted by Green (1996) highlighted the

importance of neurocognitive deficit. The review included 16 studies which looked at the relationship between various domains of neurocognition and community functioning. They concluded that patients with cognitive deficits, e.g. verbal memory, had poorer community functioning. A further systematic review of 37 studies found correlations between cognition and functioning ranging between 0.2 and 0.6 (Green et al., 2000). Theoretically if an individual is cognitively compromised this could affect their ability to learn, problem solve and to carry out important tasks in an efficient manner. Understanding this relationship has been important for re-thinking treatment targets in schizophrenia, beyond positive symptoms.

However, neurocognition only accounts for between 20-60% of variance and cognitive remediation programmes suggest that improving cognitive functioning alone does not necessarily lead to improved overall functioning (Wykes et al., 2011). Clearly, there are other factors which are important for understanding psychosocial functioning, such as social cognition.

Social cognition is defined as "the ability to construct representations of the relation between oneself and others and to use those representations flexibly to guide social behaviour'' (Adolphs, 2001). Social cognitive abilites consist of various domains of functioining - 1) Theory of mind 2) emotion perception 3) Social perception and knowledge and 4) attribution style (Fett et al., 2011). Social congnition is theoretically important for social interactions as our ability to identify and interpret how others are thinking and feeling and to apply that knowledge to a particular situation determines how we perform in interpersonal situations.

A review by Couture et al. (2006) of 22 studies found small to modest effect sizes between emotion perception, theory of mind and social perception, and functional outcome such as community functioning, social behaviour, social skills and problem solving. Fett et al., (2011) conducted a meta-analysis of 21 studies and found associations between theory of mind, emotion perception and social skills and functional outcome with effect sizes ranging between 0.22 and 0.48. Though there is overlap between cognitive and social cognitive abilities, social cognition has been found to be a seperable domain in schizophrenia (Sergi et al., 2007), may

mediate the relationship between neurocognition and community functioning (Schmidt et al., 2011) and may account for more variance in functioning than neurocognition (Fett et al., 2011).

There remain unresolved issues regarding the relationship between social cognition and other important correlates of functional outcome such as negative symptoms which warrant further exploration. Negative symptoms in schizophrenia are generally understood as falling into two broad constructs – 'expressive' encompassing blunted affect and alogia, and 'experiential' including anhedonia, asociality and apathy (Marder and Galderisi, 2017). Negative symptoms, and in particular experiential symptoms, are associated with poorer functional outcome. Lysaker et al. (2004) found that fewer negative symptoms was associated with better global functioning, while Ventura et al. (2009) in a meta-analysis of 73 studies found that negative symptoms correlated significantly with functioning (r=-.42). Other studies have suggested that apathy and motivation may account for between 18 and 75% of variance in global functioning (Foussias et al., 2011, Chang et al., 2016)

It has also been suggested that experiential negative symptoms mediate the relationship between neurocognitive deficits and outcome. Using statistical modelling Thomas et al. (2017) tested a bottom-up model by which neurocognitive deficits contribute to social cognitive deficits and negative symptoms and subsequently functioning and found this to be the best fit for the data. Similar models have been supported by previous research (Green et al., 2012), and in studies examining individuals at 'ultra-high risk' of schizophrenia (Glenthoj et al., 2017).

What has been less fully explored is whether there is a potential pathway from social cognition to negative symptoms to interpersonal functioning. There is evidence that negative symptoms are associated with social cognition, for example Hofer et al. (2009) found that poor affect recognition was associated with worse negative symptoms and some studies have found evidence that negative symptoms may mediate the relationship between social cognition and functional outcome in a similar way as with neurocognition (Mehta et al., 2014, Lin et al., 2013, Ventura et

al., 2009). Some authors have suggested that the lack of distinction in the literature between experiential and expressive negative symptoms in the literature may contribute to the lack of clarity regarding the relationship between social cognition and negative symptoms. It may be that examining negative symptoms as two distinct constructs may add greater clarity.

A greater understanding of the relationships between a person's ability to understand social cues and rules, and their level of symptoms such as apathy and anhedonia and in particular whether there is a pathway from social cognition through negative symptoms to functioning would aid in the development of more targeted and specific treatment interventions to social cognitive deficits. For example, social cognitive deficits may lead individuals to find social tasks more difficult which may lead to apathy and lack of pleasure for social situations. This in turn could lead to a lack of engagement with others either through active or passive avoidance and poor interpersonal functioning. Untangling the relationship between these various factors will help to identify key treatment targets for remediation.

## Aims and Hypothesis

The present study aims to examine the relationship between social cognition, experiential and expressive negative symptoms and interpersonal functioning. We hypothesise the following.

1. Social cognitive deficits will be positively correlated with poorer interpersonal functioning
2. Greater experiential negative symptoms will be correlated with poorer interpersonal functioning
3. Social cognitive deficits will be positively correlated with greater experiential negative symptoms
4. Experiential negative symptoms will mediate the relationship between social cognition and interpersonal functioning.

In addition to these specific hypotheses, we aim to explore the relative contributions of executive functioning, social cognition and negative symptoms to interpersonal functioning. We will construct and test a regression model to determine whether these variables significantly predict interpersonal functioning.

# Plan of Investigation

## Participants

In patients with schizophrenia-spectrum illness within NHS Greater Glasgow and Clyde Rehabilitation wards.

## Criteria

Inclusion

- Diagnosis of Schizophrenia or schizoaffective disorder
- Age 18-65
- Stable medication (no changes in medication type or dose in 4 weeks)
- Able to provide informed consent

Exclusion

- History of head injury or neurological disorder
- Other Axis-1 diagnosis
- Current diagnosis of substance abuse disorder
- IQ <85
- Acute psychosis

## Recruitment Procedures

Participants who may be suitable for the study will be identified by a relevant clinician working within the rehabilitation wards who will provide the patient with written and verbal information. The participant will meet with the primary researcher who will provide further information and obtain informed consent.

## Measures

*Demographics*

- Length of illness
- Medication
- Age
- Sex

*Psychopathology*

- Depression and Anxiety Stress Scale – 2nd Edition (DASS-21) (Lovibond and Lovibond, 1995)
- Clinical Assessment Interview of Negative Symptoms (Kring et al., 2013)

*Executive Functioning*

- Phonemic Fluency from the Verbal Fluency Test (Benton and Hamsher, 1978)
- Trail Making Test Part B

*Social Cognition*

Psychometric measures and domains of social cognition have been selected based on a consensus expert panel (Pinkham et al., 2013).

- Emotion recognition – Bell Lysaker Emotion Recognition Task (Bryson et al., 1997)
- Theory of Mind –The Hinting Task (Frith and Corcoran, 1996)

*Interpersonal Functioning*

- Personal and Social Performance Scale (Morosini et al., 2000)
- Revised UCLA Loneliness Scale (Russell et al., 1980)

*Negative symptoms*

- The Temporal Experience of Pleasure Scale (Gard et al., 2006)
- Anticipatory and Consummatory Interpersonal Pleasure Scale (Gooding and Pflum, 2014)

*Design*

This study will use a cross-sectional design to allow for correlational and regression analysis between variables.

*Research Procedures*

Once participants have been identified and informed consent obtained, a further appointment will be scheduled to administer the test battery. Test sessions will be conducted in a private clinic room at the NHS Hospital where they are in-patients. Testing sessions will be conducted by the primary researcher (AK). Testing will be completed in one session lasting approximately 1 hours 20 minutes plus breaks where necessary to minimise fatigue. The PSP will be completed by a clinician who knows the patient well. See Table 1 below for details of measure administration. Interviews will be recorded to allow for validation of the reliability of ratings on semi-structured interviews.

*Data Analysis*

First order correlations will be performed between variables of social cognition, negative symptoms and interpersonal functioning/loneliness. A mediation analysis will be carried out to determine whether negative symptoms mediate the relationship between social cognition and interpersonal functioning. This will be conducted using the techniques outlined by Shrout and Bolger (2002). Finally, a multiple regression model will be used to examine the predictive validity of executive functioning, social cognition and negative symptoms on interpersonal functioning.

*Justification of sample size*

On the basis of previous studies (Fett et al., 2011, Ventura et al., 2009) we expect to find medium to large effect sizes for correlational analysis between social cognition and interpersonal functioning (r=0.48) and negative symptoms and interpersonal functioning (r=0.42). In addition, several studies (Konstantakopoulos et al., 2011, Rocca et al., 2014) have found large effect sizes for a multivariate regression model similar to that proposed by the present study ($r^2$=0.75 and $r^2$=0.54 respectively). As such we expect to find large effect sizes across our analyses. Based on a multivariate regression model with 3 predictors and large effect size would require a sample size of 40 participants. This is in keeping with sample sizes used in similar studies.

*Settings and Equipment*

Rehabilitation wards of Glasgow City - Parkhead Hospital, Leverndale, Stobhill and Gartnavel Royal. Equipment will consist of the specified measures which are administered on a laptop or paper and pencil, and a voice recorder.

*Table 4: Study Measures and Administration Times*

| Method | Measure Name | Domain | Admin Time | Description |
|---|---|---|---|---|
| **Clinician Administered** | CAINS | Psychopathology | 35 | Semi structured interview |
| | Hinting Task | Social cognition | 6 | 10 vignettes and questions |

| | | | | |
|---|---|---|---|---|
| | BLERT | Social cognition | 10 | 21 10-second video clips. Participant identifies emotion |
| | Verbal Fluency | Executive Functioning | 5 | 3 letters, participant has 1 minute to generate words |
| | Trails (Part B) | Executive Functioning | 5 | Paper and pencil task connecting letters and numbers. Total completion time recorded. Discontinue after 300 seconds |
| **Self-rated** | DASS-21 | Psychopathology | 5 | 21-item questionnaire |
| | UCLA Loneliness | Interpersonal functioning | 5 | 20-item questionnaire |
| | TEPS | Negative Symptoms | 5 | 20-item questionnaire |
| | ACIPS | Negative symptoms | 5 | 17-item questionnaire |
| **Clinician Rated** | PSP | Interpersonal functioning | Clinician rated | |
| Total Participant Time | 81 minutes (1 hour 21 minutes) | | | |

## Health and Safety Issues

The proposed study will be undertaken on various hospital sites across NHS Greater Glasgow and Clyde and as such relevant local Health and Safety policies and procedures will be adhered to.

*Researcher Safety Issues*

Participants with a diagnosis of schizophrenia will be recruited which presents a potential risk to the researcher. A psychiatrist will be asked to comment on their ability to give informed consent and suitability to participate in the study. Participants in the acute period of psychosis will not be recruited to the study. The

primary researcher will carry an alarm throughout interviews. The research will be conducted on hospital sites across NHS Greater Glasgow and Clyde and all relevant health and safety policies and procedures will be adhered to. All interviews will be conducted during working hours and a member of staff will be aware of the researcher's location and intended completion time.

*Participant Safety Issues*

A psychiatrist will be asked to comment on a patient's ability to provide informed consent to participant in the study. Participants will be advised of their ability to withdraw from the study at any time. Participants may become distressed during the interview. The researcher will monitor participants for signs of distress through the interview. At any indication of distress, the researcher will use their clinical skills to manage this. The researcher will ask the participant if they wish to continue and remind them of their ability to withdraw. Any significant distress during the interview will be relayed to the medical team on the ward.

## Ethical Issues and approval

*Ethical approval*

Following approval of the research proposal by the University of Glasgow, Mental Health and Wellbeing Research Director ethical and management approval will be sought. Management approval will be sought from NHs Greater Glasgow and Clyde Research and Development and ethical approval will be sought from West of Scotland Research Ethics Service.

*Ethical Issues to address*

1. Participants ability to provide informed consent
2. Participant fatigue and/or distress during testing

## Financial Issues

A request has been submitted for funding of £54.18 to cover the cost of stationery and photocopying.

## Timetable

It is proposed that data collection will commence in September 2018. The anticipated end date for the study is April 2019.

## Practical Applications

This study has applications in better understanding potential pathways to poor interpersonal functioning in patients with chronic schizophrenia-spectrum conditions. By identifying the early links in the pathway from basic neuro/social cognitive deficits to poor functioning, this will allow us to identify specific targets for remediation.

## References


Adolphs, R. 2001. The neurobiology of social cognition. *Current Opinion in Neurobiology,* 11**,** 231-239.

Benton, A. & Hamsher, K. 1978. *Multilingual Aphasia Examinaton Manual - Revised*, University of Iowa.

Brissos, S., Molodynski, A., Dias, V. V. & Figueira, M. L. 2011. The importance of measuring psychosocial functioning in schizophrenia. *Ann Gen Psychiatry,* 10**,** 18.

Bryson, G., Bell, M. & Lysaker, P. 1997. Affect recognition in schizophrenia: a function of global impairment or a specific cognitive deficit. *Psychiatry Res,* 71**,** 105-13.

Chang, W. C., Hui, C. L. M., Chan, S. K. W., Lee, E. H. M. & Chen, E. Y. H. 2016. Impact of avolition and cognitive impairment on functional outcome in first-

episode schizophrenia-spectrum disorder: a prospective one-year follow-up study. *Schizophrenia Research,* 170**,** 318-321.

Couture, S. M., Penn, D. L. & Roberts, D. L. 2006. The functional significance of social cognition in schizophrenia: A review. *Schizophrenia Bulletin,* 32**,** S44-S63.

Fett, A. K. J., Viechtbauer, W., Dominguez, M. D., Penn, D. L., Van Os, J. & Krabbendam, L. 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis. *Neuroscience and Biobehavioral Reviews,* 35**,** 573-588.

Fiorillo, D. & Sabatini, F. 2011. Quality and quantity: The role of social interactions in self-reported individual health. *Social Science & Medicine,* 73**,** 1644-1652.

Foussias, G., Mann, S., Zakzanis, K. K., Van Reekum, R., Agid, O. & Remington, G. 2011. Prediction of longitudinal functional outcomes in schizophrenia: The impact of baseline motivational deficits. *Schizophrenia Research,* 132**,** 24-27.

Frith, C. D. & Corcoran, R. 1996. Exploring 'theory of mind' in people with schizophrenia. *Psychological Medicine,* 26**,** 521-530.

Gard, D. E., Gard, M. G., Kring, A. M. & John, O. P. 2006. Anticipatory and consummatory components of the experience of pleasure: A scale development study. *Journal of Research in Personality,* 40**,** 1086-1102.

Glenthoj, L. B., Jepsen, J. R. M., Hjorthoj, C., Bak, N., Kristensen, T. D., Wenneberg, C., Krakauer, K., Nordentoft, M. & Fagerlund, B. 2017. Negative symptoms mediate the relationship between neurocognition and function in individuals at ultrahigh risk for psychosis. *Acta Psychiatrica Scandinavica,* 135**,** 250-258.

Gooding, D. C. & Pflum, M. J. 2014. The assessment of interpersonal pleasure: Introduction of the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS) and preliminary findings. *Psychiatry Research,* 215**,** 237-243.

Green, M., Hellemann, G., Horan, W., Lee, J. & Wynn, J. 2012. From Perception to Functional Outcome in Schizophrenia: Modeling the Role of Ability and Motivation. *Arch Gen Psychiatry,* 69**,** 1216-1224.

Green, M. F. 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry,* 153**,** 321-330.

Green, M. F., Kern, R. S., Braff, D. L. & Mintz, J. 2000. Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the "right stuff"? *Schizophrenia Bulletin,* 26**,** 119-136.

Hofer, A., Benecke, C., Edlinger, M., Huber, R., Kemmler, G., Rettenbacher, M. A., Schleich, G. & Wolfgang Fleischhacker, W. 2009. Facial emotion recognition and its relationship to symptomatic, subjective, and functional outcomes in outpatients with chronic schizophrenia. *European Psychiatry,* 24**,** 27-32.

Juckel, G. & Morosini, P. L. 2008. The new approach: psychosocial functioning as a necessary outcome criterion for therapeutic success in schizophrenia. *Current Opinion in Psychiatry,* 21**,** 630-639.

Konstantakopoulos, G., Ploumpidis, D., Oulis, P., Patrikelis, P., Soumani, A., Papadimitriou, G. N. & Politis, A. M. 2011. Apathy, cognitive deficits and functional impairment in schizophrenia. *Schizophr Res,* 133**,** 193-8.

Kring, A. M., Gur, R. E., Blanchard, J. J., Horan, W. P. & Reise, S. P. 2013. The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. *Am J Psychiatry,* 170**,** 165-72.

Leucht, S., Tardy, M., Komossa, K., Heres, S., Kissling, W. & Davis, J. M. 2012. Maintenance treatment with antipsychotic drugs for schizophrenia. *Cochrane Database of Systematic Reviews*.

Lin, C.-H., Huang, C.-L., Chang, Y.-C., Chen, P.-W., Lin, C.-Y., Tsai, G. E. & Lane, H.-Y. 2013. Clinical symptoms, mainly negative symptoms, mediate the influence of neurocognition and social cognition on functional outcome of schizophrenia. *Schizophrenia Research,* 146**,** 231-237.

Lovibond, S. H. & Lovibond, P. F. 1995. *Manual for the depression anxiety stress scales*, Psychology Foundation of Australia.

Lysaker, P. H., Lancaster, R. S., Nees, M. A. & Davis, L. W. 2004. Attributional style and symptoms as predictors of social function in schizophrenia. *Journal of Rehabilitation Research and Development,* 41**,** 225-232.

Marder, S. R. & Galderisi, S. 2017. The current conceptualization of negative symptoms in schizophrenia. *World Psychiatry,* 16**,** 14-24.

Mehta, U., Thirthalli, C., Kumar, C., Kumar, J. & Gangadhar, B. 2014. Negative symptoms mediate the influence of theory of mind on functional status in schizophrenia | SpringerLink. *Social Psychiatry and Psychiatric Epidemiology,* 49**,** 1151-1156.

Morosini, P. L., Magliano, L., Brambilla, L., Ugolini, S. & Pioli, R. 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr Scand,* 101**,** 323-9.

Pinkham, A. E., Penn, D. L., Green, M. F., Buck, B., Healey, K. & Harvey, P. D. 2013. The Social Cognition Psychometric Evaluation Study: Results of the Expert Survey and RAND Panel. *Schizophrenia Bulletin,* 40**,** 813-823.

Ro, E. & Clark, L. A. 2009. Psychosocial functioning in the context of diagnosis: Assessment and theoretical issues. *Psychological Assessment,* 21**,** 313-324.

Rocca, P., Montemagni, C., Zappia, S., Piterà, R., Sigaudo, M. & Bogetto, F. 2014. Negative symptoms and everyday functioning in schizophrenia: A cross-sectional study in a real world-setting. *Psychiatry Research,* 218**,** 284-289.

Russell, D., Peplau, L. A. & Cutrona, C. E. 1980. The revised UCLA Loneliness Scale: concurrent and discriminant validity evidence. *J Pers Soc Psychol,* 39**,** 472-80.

Schmidt, S. J., Mueller, D. R. & Roder, V. 2011. Social Cognition as a Mediator Variable Between Neurocognition and Functional Outcome in Schizophrenia:

Empirical Review and New Results by Structural Equation Modeling. *Schizophrenia Bulletin,* 37**,** S41-S54.

Sergi, M. J., Rassovsky, Y., Widmark, C., Reist, C., Erhart, S., Braff, D. L., Marder, S. R. & Green, M. F. 2007. Social cognition in schizophrenia: Relationships with neurocognition and negative symptoms. *Schizophrenia Research,* 90**,** 316-324.

Shrout, P. E. & Bolger, N. 2002. Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol Methods,* 7**,** 422-45.

Thomas, M. L., Green, M. F., Hellemann, G., Sugar, C. A., Tarasenko, M., Calkins, M. E., Greenwood, T. A., Gur, R. E., Gur, R. C., Lazzeroni, L. C., Nuechterlein, K. H., Radant, A. D., Seidman, L. J., Shiluk, A. L., Siever, L. J., Silverman, J., Sprock, J., Stone, W. S., Swerdlow, N. R., Tsuang, D. W., Tsuang, M. T., Turetsky, B. I., Braff, D. L. & Light, G. A. 2017. Modeling Deficits From Early Auditory Information Processing to Psychosocial Functioning in Schizophrenia. *Jama Psychiatry,* 74**,** 37-46.

Ventura, J., Hellman, G., Thames, A., Koellner, V. & Nuechterlein, K. 2009. Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis. *Schizophrenia research,* 113.

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., Charlson, F. J., Norman, R. E., Flaxman, A. D., Johns, N., Burstein, R., Murray, C. J. L. & Vos, T. 2013. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet,* 382**,** 1575-1586.

Wykes, T., Huddy, V., Cellard, C., Mcgurk, S. R. & Czobor, P. 2011. A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. *http://dx.doi.org/10.1176/appi.ajp.2010.10060855*