THE ROLE OF SOCIAL COGNITION AND NEUROCOGNITION IN FUNCTIONAL OUTCOMES IN INDIVIDUALS WITH FIRST EPISODE PSYCHOSIS.

by
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Abstract

Impaired cognition and poor functioning are closely linked in psychosis; findings from studies of individuals with first episode psychosis (FEP), where intervention may be most effective, are less conclusive. This thesis sought to clarify the contributing role of social cognition (SC) and neurocognition (NC), relative to symptoms, in understanding functional outcome in FEP.

Results showed that whilst individuals with poor functioning in FEP have greater SC and NC impairments, negative symptoms is the most robust predictor of later social and role outcomes, with SC and NC having a subordinate role. Exploratory analyses suggest that cognition directly impacts on negative symptoms which in turn may influence functional outcome, highlighting the importance of delineating this relationship.

When examining the predictors of treatment response (i.e. improved functioning) following a psychosocial intervention targeting social disability, individuals with 'good' SC were more likely to respond to the intervention. Functional magnetic resonance imaging also provided preliminary evidence of an underlying SC neural network that might be implicated in improved functioning following the intervention.

Overall findings show that cognition plays a key role in functional outcomes in FEP. Targeting impaired SC could improve the reach and impact of intervention, to reduce the chances of social disability becoming entrenched.

Dedication

I would like to dedicate this work to my wonderful daughter,

Seren Hâf, our little star.

Acknowledgement

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ACC	Anterior Cingulate Cortex
ACORN	A classification of Residential Neighbourhoods
AIHQ	Ambiguous Intentions Hostility Questionnaire
ANOVA	Analysis of Variance
APA	American Psychiatric Association
AS	Attribution Style
BL	Baseline
BME	Black and Minority Ethnic
BOLD	Blood-Oxygen-Level-Dependant
CBT	Cognitive Behavioural Therapy
CET	Cognitive Enhancement Therapy
CI	Communicative Intentions
DSM	Diagnostic and Statistical Manual
DUP	Duration of untreated psychosis
EIS	Early Intervention Service
EP	Emotion Perception
FEP	First Episode Psychosis
fMRI	Functional Magnetic Resonance Imaging
FU	Follow-Up
FWE	Family-Wise Error
GFS	Global Functioning Scales
ICD-10	International Classification of Diseases
IPS	Individual Placement Support
IPT	Integrative Psychological Therapy
K-S	Kolmogorov-Smirnov
M	Mean
MANOVA	Multivariate Analysis of Variance
MATRICS	Measurement and Treatment to Improve Cognition in Schizophrenia
MINI	Mini-International Neuropsychiatric Interview
MNI	Montreal Neurological Institute
mPFC	Medial Prefrontal Cortex
MSCEIT	Mayer-Salovey-Caruso Emotional Intelligence Test
NC	Neurocognition
NEET	Not in Education, Employment or Training
NICE	National Institute of Clinical Excellence
NIHR	National Institute of Health Research
NIMH	National Institute of Mental Health
OPCRIT	Operational Criteria Checklist
PANSS	Positive and Negative Syndrome Scale
PAS	Premorbid Assessment Scale
PFC	Prefrontal Cortex
PhC	Physical Causality
REC	Research Ethics Committee
ROI	Region of Interest

SC	Social Cognition
SCIT	Social Cognitive Interaction Training
SD	Standard Deviation
SK	Social Knowledge
SKQ	Social Knowledge Questionnaire
SPM	Statistical Parametric Mapping
SPSS	Statistical Package for the Social Sciences
SRCBT	Social Recovery Cognitive Behavioural Therapy
STS	Superior Temporal Sulcus
SUPEREDEN	Sustaining and Enhancing Positive Engagement and Recovery - Evaluation of Early Intervention for Psychosis Services
TAU	Treatment as usual
ToM	Theory of Mind
TPJ	Temporo-Parietal Junction
TR	Time of Repetition
TUS	Time Use Survey
UHR	Ultra-High Risk
VIF	Variance Inflation Factor
WAIS	Wechsler Adult Intelligence Scale
WMS	Wechsler Memory Scale

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1.0. CHAPTER 1

1.1. Introduction

In working age adults, psychosis is the most common cause of poor functioning, with an estimated cost of £3.4 billion owing to unemployment, loss of productivity and absence from work (Hafner & an der Heiden, 1999; Mangalore & Knapp, 2007). Poor functioning emerges early in the prodromal phase of illness, reaching a peak at the onset of psychosis, and then plateaus thereafter (Agerbo *et al.*, 2004). A recent publication showed that young people with early psychosis were spending as little as 25 hours a week in structured activity (e.g. work, education, childcare, house chores and leisure activities) compared with 60 + hours in an age matched comparison group (Hodgekins, French, Birchwood, *et al.*, 2015). Furthermore, 53.6% of the early psychosis group were not in education, employment and training (NEET), compared to 10.7% in the non-clinical group (Hodgekins, French, Birchwood, *et al.*, 2015).

These findings highlight the need to intervene at an early stage of illness before poor functioning becomes entrenched. Identification of the early predictors of poor functioning could provide treatment targets to prevent further decline. Whilst a number of studies have found that impaired cognition is closely linked to poor functioning, these findings are primarily based on chronic schizophrenia samples, and findings from studies of individuals with first episode psychosis (FEP), where intervention may be most effective, are less conclusive (Allott, Liu, Proffitt & Killackey, 2011a). As such, the aim of this thesis was to clarify the role of social cognition (SC) and neurocognition (NC) on poor functional outcome in FEP.

The purpose of this chapter will be to review the current literature on the predictors of poor functioning in psychosis. The chapter will begin with a brief overview of the psychoses, introducing the concept, diagnosis, epidemiology, phases of psychosis and the critical period for intervention (Section 1.0.). This will be followed by discussions on the limitations around defining and measuring the concept of functioning, the trajectory of poor functional outcome, and the commonly identified predictors of outcome in psychosis (Section 1.2.). The association between cognitive impairment and functioning in psychosis will then be discussed (Section 1.3.). The chapter will conclude with a summary of the limitations in the current literature on predicting functional outcome (Section 1.4.), and finally, the aims of the thesis will be set out (Section 1.5.).

1.2. The Psychoses

Psychosis is potentially a severe and disabling mental health problem, which can cause considerable distress and devastation not only to the individual experiencing it, but also to those closest to them (Birchwood, 2003; Hafner & an der Heiden, 1999). The term psychosis is used to describe a cluster of different diagnoses and is characterized by significant changes to a person's perceptions, thoughts and behaviours (National Institute of Clinical Excellence - *NICE* guidelines, 2014).

1.2.1. Definition and symptoms

Typically, the symptoms of psychosis manifest as hallucinations (perception in the absence of external stimuli) and delusions (fixed beliefs that are unfounded; NICE guidelines, 2014).

These symptoms are described as the 'positive symptoms' of psychosis (characteristics that are considered as an addition to an individual's persona). Speech and communication impairments, for example, derailed and incoherent speech, are also referred to as positive symptomatology. Other symptoms of psychosis can include apathy, poverty of speech, social and emotional withdrawal; these are described as the negative symptoms of psychosis (characteristics which are considered blunted or lacking in an individual; NICE guidelines, 2014).

The diagnosis of a psychotic illness is informed by the duration of the psychotic experience and the underlying factors which contribute to the onset of psychosis. For example, for a diagnosis of Schizophrenia to be met, *The Diagnostic and Statistical Manual – fifth edition* (DSM-5; American Psychiatric Association; APA, 2013) specifies that there should be evidence of psychotic disturbance for at least a six-month period. If the psychotic episode lasts for less than six months, a diagnosis of Schizophreniform disorder will be made (APA, 2013).

1.2.2. Epidemiology: Who is likely to be affected by psychosis?

A systematic review of incidence rates in England over a 60-year period (Kirkbride *et al*., 2012) reported a pooled incidence of 37.1 per 100,000 for psychosis, for which schizophrenia was the most common diagnosis (15 / 100,000). The incidence rates tend to decline with age, with 80 percent of individuals experiencing their first episode between the ages of 16-30 years (Cheng *et al*., 2011; Kirkbride *et al*., 2006; Kirkbride *et al*., 2012; Orygen Youth Health. 2012; Shiers & Lester, 2005; van Os & Kapur, 2009).

A number of biological (Fetemi & Folsom, 2009) and environmental (van Os, Kenis & Rutten, 2010) risk factors for developing psychosis have been identified. For example, rates of childhood trauma in psychosis are reported to be high compared to healthy samples (McCabe, Maloney, Stain, Loughlan & Carr, 2012; Stain *et al.*, 2013); with a meta-analysis showing those experiencing childhood traumas are 2.8 times more likely to develop psychosis in adulthood (Varese *et al.*, 2012). Higher incidence rates of psychosis have also been reported in younger males, black and minority ethnic (BME) migrant groups and those living in urban areas (Kirkbride *et al.*, 2006; Kirkbride *et al.*, 2012; Van Os *et al.*, 2010). Other environmental risk factors include cannabis use, pre- and perinatal complications and winter birth (Tandon, Keshavan, & Nasrallah, 2008; Van Os *et al.*, 2010). Whilst a number of structural chromosomal abnormalities and genes have been associated with the development of schizophrenia, no single gene variant has been consistently identified, and it remains debated how the expression of frank disorder is influenced by gene x environment interactions (Tandon *et al.*, 2008).

1.2.3. The course of psychosis: from prodrome to recovery

The initial onset of psychosis is typically preceded by some gradual, non-specific changes in a person's thoughts, behaviour and functioning; this is known as the prodromal period and individuals in this phase of illness are often termed ultra-high-risk (UHR; Yung & McGorry, 1996). A person may also experience some attenuated or subclinical positive symptoms during this time (Yung *et al.*, 2003). The duration of the prodromal period can vary vastly, as with the type of symptoms a person may experience, and it is difficult to determine which individuals develop psychosis; as such, it is not included in the DSM-5 diagnostic criteria (Yung, Nelson, Thompson, & Wood, 2010). If a person makes the transition to psychosis, the prodromal period

will be followed by an acute phase of illness, which is marked by frank psychotic symptoms such as hallucinations, delusions or thought disorder (Yung *et al.*, 2003).

The initial onset of psychosis is often labelled 'first-episode psychosis' (FEP; Kirch, Lieberman, & Matthews, 1992). The experience of a psychotic episode, particularly in the early phase of illness, can be traumatic and highly distressing for the individual experiencing symptoms, and co-morbidity is common (Birchwood *et al.*, 2000; Birchwood, 2003; Jackson, Knott, Skeate & Birchwood, 2004; Michail & Birchwood, 2014).

The course of psychosis is very heterogeneous, and outcomes vary vastly, particularly in the early stages of illness (Birchwood & Jackson, 2001). For example, 20-25 % of individuals will experience one episode of psychosis and have full clinical remission with minimal social impairment, whilst 30% will have the poorest outcome (Birchwood & Jackson, 2001).

1.2.4. The 'critical' period of psychosis: Implications for intervention

It is now established that long delays between the first onset of psychosis and the initiation of treatment, defined as the 'duration of untreated psychosis' (DUP), is associated with poor outcome (Marshall *et al.*, 2005). Birchwood and colleagues (1998) have proposed that the early phase of illness, including the period of untreated psychosis, represents a 'critical period' in which there is potential for a rapid period of illness progression, which plateaus within three to five years of illness onset. Birchwood and colleagues argue that intervention during this 'critical period' is an opportunity to prevent further decline (Birchwood, Todd & Jackson, 1998). This

has paved the way for the introduction of Early Intervention Services (EIS), which enables the provision of specialised, assertive outreach model of care for young people between the ages of 16 - 35 years, at the earliest signs of psychosis (Birchwood, McGorry & Jackson, 1997; Birchwood, Fowler & Jackson, 2001).

A number of studies have reported on the improved clinical, social and vocational outcomes of individuals who have received specialised care under EIS (Craig *et al*., 2004; Garety *et al*., 2006; Petersen *et al*., 2005). Specifically, when compared with generic care, EIS has shown to significantly reduce the number of inpatient stays, reduce the risk of a second relapse and is more cost effective (Bertelsen *et al*., 2008; McCrone, Craig, Power & Garety, 2010).

Whilst EIS has shown to have substantive benefits in terms of vocational and educational outcomes (Fowler *et al*, 2009), in a recent publication by Hodgekins, Birchwood, Christopher *et al*. (2015), around 66% of young people with FEP were displaying high levels of social disability even after twelve months of service provision within an EIS. This is compared with a 50% rate for symptomatic recovery under EIS (Wunderink, Sytema, Nienhuis & Wiersma, *et al*., 2009).

As the first episode usually occurs in adolescence - a critical time for identity formation, strengthening and developing of social networks, and the beginnings of future vocational prospects - disruptions to an individual's peer relationships and work and school performance at this time could have a profound negative impact on their future (Hafner & an der Heiden,

1999; McGorry, Killackey & Yung, 2008; ORYGEN Youth, 2012). Indeed, prospective studies investigating the long-term predictors of outcome in psychosis demonstrate that poor functioning at illness onset is associated with poor outcome years later (Alvarez-Jimenez *et al*., 2012; Tandberg *et al*., 2012). Interventions which target poor functioning in the early stages of psychosis could therefore prove fruitful at preventing long-term social disability (Hodgekins, Birchwood, Christopher, *et al*., 2015; Hodgekins, French, Birchwood, *et al*., 2015).

The next sections will review the literature on functioning in psychosis, focusing on the trajectories and predictors of poor functional outcome, with the aim of identifying potential treatment targets for those experiencing social and role impairments in FEP.

1.3. Literature Review: Predictors of functional outcome in psychosis

A number of studies have sought to delineate the trajectories of poor functional outcome, whilst trying to identify the factors that may underlie it (Couture, Penn & Roberts, 2006). Identification of potentially 'modifiable' predictors of poor outcome may provide the basis for the development of targeted interventions to improve and potentially prevent decline in functioning for young people experiencing psychosis.

1.3.1. Defining "functional outcome" in psychosis: Problems with the concept and measurement

A major challenge in research seeking to address poor functioning in psychosis is the lack of consensus on the appropriate terminology and measurement used to conceptualise and quantify 'functional outcome' (Figueira & Brissos, 2011; Harvey & Bellack, 2009). Historically, 'outcome' or 'recovery' has been associated with symptomatic improvement, however more recently it also encompasses the functional aspects of the illness (Bartholomeusz, Killackey, Thompson & Wood, 2011). 'Functioning' or 'functional outcome' has been defined as "the performance of daily activities which are required for self-maintenance (e.g. earning an income and maintaining a residence) as well as social activities" (Harvey & Bellack, 2009). Similar concepts which are often used interchangeably in the literature are 'social recovery' (defined as involvement in work or education, independent living, and regular engagement in activities with friends; Liberman, Glynn, Blair, Ross & Marder, 2002) and 'social disability' (difficulties engaging in meaningful activities and relationships; Hodgekins, French, Birchwood, *et al*., 2015). Please refer to Table 1 for a summary of the definitions of functioning.

Beyond the general term of functioning, separate domains of functioning can also be considered: 'social functioning' typically refers to interpersonal relations, independent living and social competence, whilst 'role functioning' refers to performance and time spent in work, education or in other roles such as a homemaker (Bartholomeusz *et al*., 2011; Cornblatt *et al*., 2007). Terms such as 'functional outcome' or 'social recovery' may therefore not be helpful, as each separate domain of functioning (social and role) could be potentially explained by

different factors (Allott, Liu, Proffitt, & Killackey, 2011; Fett *et al*, 2011; Lin, Wood & Yung, 2013).

There are no 'gold standard' measures to assess functioning in psychosis, and because the definition of functional outcome remains elusive, this has led to differing approaches to measure the construct (Bartholomeusz *et al*., 2011; Brissos, Molodynski, Dias & Figueira, 2011; Figueira & Brissos, 2011). Without reliable measures, it is difficult to replicate findings, and objectively assess one's progress (Figueira & Brissos, 2011). Current measures are confounded by limited psychometric properties, which are not standardised appropriately with age and phase of illness, and some simultaneously assess symptoms and / or different areas of functioning which do not always co-vary (Cornblatt *et al*., 2007; Dickerson, 1997; Harvey & Bellack, 2009; Niendam, Jalbrzikowski & Bearde, 2009). External factors which are not controllable may also hamper the objective assessment of functioning, such as unemployment rates and the job market. Interpretations of what constitutes 'good functional outcome' can also be subjective and influenced by cultural factors, and as such, trying to conceptualise 'normal functioning' is difficult (Lin, Wood &Yung, 2013).

There is a need for the development of scales which are able to assess functioning independent of symptoms, are validated on psychosis populations, and are sensitive to age and phase of illness (Burns & Patrick, 2007, Harvey & Bellack, 2009). Improved assessment will allow for greater understanding of the factors underlying poor functioning in psychosis and allow for appropriate intervention to be developed (Yager *& Ehmann, 2006).

Table 1. Definitions encompassing 'functional outcome'

Key Term	Definition
Functioning / Functional Outcome	"The performance of daily activities which are required for self-maintenance (e.g. earning an income and maintaining a residence) as well as social activities" (Harvey & Bellack, 2009).
Social Recovery	Involvement in work or education, independent living, and regular engagement in activities with friends (Liberman *et al*., 2002).
Social Disability	Difficulties engaging in meaningful activities and relationships (Hodgekins, Birchwood, Christopher *et al*., 2015).
Social Functioning	Interpersonal relations, independent living and social competence (Bartholomeusz *et al*., 2011).
Role Functioning	Performance and time spent in work, education or in other roles such as a homemaker (Cornblatt *et al*., 2007).

1.3.2. Effectiveness of standard treatments for psychosis on functional outcome: are symptoms and functioning symbiotic?

Standard interventions primarily aimed at reducing symptoms in psychosis seem to have little impact on improving functional outcome (Bartholomeusz *et al*., 2011). This includes community-based treatments, drug treatments with atypical antipsychotics, and standard Cognitive Behavioural Therapy (CBT); all of which, despite having a significant impact on symptoms, have shown little or mixed evidence that these benefits also extend to improvements in functioning (Garety *et al*., 1997; Harvey & Bellack, 2009; Kuipers *et al*., 1997; McEvoy *et al*., 2007; Potkin *et al*., 2009; Tarrier *et al*., 1993; Ventura, Hellemann, Thames, Koellner & Neuchterlein, 2009).

This is unsurprising as research has shown that symptoms and functioning in psychosis often have distinct illness trajectories which are likely to be independent of one and another (Bellack, Morrison, Wixted & Mueser, 1990; Brekke & Long, 2000; Penn, Roberts, Combs & Sterne, 2007). To illustrate this, in a sample of young people with FEP who had been receiving treatment for 12 months, 22% made a symptomatic recovery, whilst only 7% made a functional recovery (Ventura, Wood, & Hellemann, 2011). The study found no association between symptoms and functioning, and when symptomatic and functional recovery was considered together, only 1% of the sample met criteria for 'full' recovery (Ventura *et al*., 2011). These findings also demonstrate that symptomatic remission is much higher than functional recovery in psychosis and that specific interventions targeting functioning are likely to be more effective than standard treatments. This has led to efforts to identify other factors which are likely to be theoretically associated with functional outcome.

1.3.3. Trajectories of functioning in psychosis: Identifying the markers of poor functioning

Poor social and role functioning is shown to predate the onset of frank psychosis. In ultra-high-risk samples, poor functioning is commonly reported (Cornblatt *et al*., 2007; Lin *et al*., 2011), and is associated with transition to psychosis (Cornblatt *et al*., 2012; Fusar-Poli *et al*., 2010; Velthorst *et al*., 2010). Moreover, social and role impairments are shown to be independent of clinical symptoms and remain stable from the start of the prodrome through to the first episode (Cornblatt *et al*., 2012). This suggests that social and role impairments could be a longstanding risk factor for the development of psychosis (Cornblatt *et al*., 2012). Indeed, there is evidence of such impairments emerging before the onset of illness (Addington & Addington, 1993).

Functioning prior to the onset of illness is often referred to as 'premorbid functioning' (Addington & Addington, 2005). Those who experience poor premorbid functioning are more likely to be male and have an earlier age of onset; both factors which are also associated with poor functional outcomes in psychosis (Hafner & an der Heiden, 1999). Hafner and colleagues (1999) proposed that the amount of social developmental milestones achieved prior to the onset of illness will determine the long term functional outcomes through social stagnation. Supporting this notion, Addington & Addington (2005) demonstrated that poor functioning which emerges in childhood and continues a declining course was the best predictor of functional outcome not only at illness onset, but 2 years after the initiation of treatment. Studies have also shown an association between poor premorbid adjustment and later functional impairments (Christopher *et al*., 2015; Hodgekins, Birchwood; Jeppesen *et al*., 2008; Lucas *et al*., 2008; Tandberg *et al*., 2012).

As with the concept of 'untreated psychosis', the duration of 'untreated functioning' seems to have a deleterious effect on illness course and outcome (Hodgekins, Birchwood, Christopher *et al*., 2015). Interestingly, despite the abundance of studies reporting on DUP and clinical outcomes, the findings are mixed with regards to the link between DUP and functional outcomes (Albert *et al*., 2011; Jeppesen *et al*., 2008; Marshall *et al*., 2005; Pena *et al*., 2012; Santesteban-Echarri *et al*., 2017). This is perhaps unsurprising as DUP is defined by onset of positive symptoms which are often not associated with functioning, and do not account for negative symptoms (Lin, Wood, Yung, 2013). It is well established that there is a 'symptom-disability' gap in psychosis, where social disability emerges early in the prodromal phase of illness, reaching a peak at the onset of psychosis, and then plateaus; whilst the symptom trajectory often differs in that symptoms peak at illness onset, and typically resolve after the

initiation of treatment (Agerbo *et al.*, 2004; McGorry, n.d.). It is now widely understood that anti-psychotic medication has relatively little impact on improving social disability (McGorry *et al.*, 2008).

Many studies have emphasised the role of negative symptoms in predicting poor functioning both in the early phase of illness and in chronic samples (Brier *et al.*, 1991; Ho *et al.*, 1998; Lysakar & Davis, 2003; Malla *et al.*, 2004). A long-term follow-up study of 301 FEP cases showed that apathy predicted poorer functional outcome and quality of life 10 years after the initial episode (Evensen *et al.* 2012). Other findings show that those who present with elevated negative symptoms at the onset of their illness are at greatest risk of later poorer outcomes, regardless of whether their symptoms remit or not (Gee *et al.*, 2016; Hodgekins, Birchwood, Christopher *et al.*, 2015; Rammou *et al.*, 2017). The above findings indicate that negative symptoms may be a 'trait' indicator of long term poor functioning in individuals with psychosis (Lin, Wood, Yung, 2013). This association seems to be longstanding as not only is there evidence of persistent negative symptoms in UHR groups, baseline negative symptoms in the prodrome have also been associated with psychosis conversion and poorer functioning at follow-up (Addington *et al.*, 2015; Cornblatt *et al.*, 2012; Lin *et al.*, 2011; Piskulic *et al.*, 2012).

The concept that negative symptoms may be a 'trait' manifestation of psychosis is consistent with the concept of the 'deficit' syndrome of schizophrenia (Kirkpatrick, Buchanan, Ross & Carpenter, 2001; Lin, Wood, Yung, 2013). Indeed, there appears to be a subgroup of individuals who continue to experience severe and persistent negative symptoms; this has been reported in the prodrome, in first episode samples and in those with chronic illness (Addington *et al.*, 2001; Blanchard *et al.*, 2005; Gee *et al.*, 2015). This subgroup is likely to be more neurologically

impaired and is at greater risk of poor functional outcome (Fenton & McGlashan, 1994; Kirkpatrick *et al*., 2001).

Finally, recent research has demonstrated that negative symptoms in the early course of illness may be a more predictive marker of later functioning than other known predictors of outcome such as cognition (Cacciotti-Saija Langdon, Ward, Hickie, & Guastella 2016; Langdon *et al*., 2014; Sullivan *et al*., 2016). However, previous research has shown that negative symptoms and cognition are closely linked (Addington *et al*., 2015; Lysaker *et al*., 2013; Lysaker *et al*., 2015; Ventura *et al*., 2009), and share variance in the prediction of functional outcome in psychosis (Addington *et al*., 2015; Ventura *et al*., 2009). For example, social cognitive deficits have been associated with individual negative symptoms such as social avoidance, social withdrawal, difficulty in abstract thinking, blunted affect, lack of spontaneity and stereotyped thinking (Harvey, Bartholomeusz & Penn, 2016).

In studies which have examined linkages between social cognition and anhedonia in psychosis, it is argued that the inability to form mental representations of self and others is a barrier to one seeking and anticipating pleasure, irrespective of one's affective state (Buck *et al*., 2014). The complex relationship between these variables highlights the need to examine their relative contribution to functional outcomes in order to provide appropriate intervention, but many studies have failed to consider the impact of potentially contributing or mediating variables in relation to functional outcomes in psychosis (Allott, Liu, Proffitt, & Killackey, 2011). Nonetheless, a plethora of studies have provided compelling evidence of the contributing role

of the different domains of cognitive impairment on poor functioning in psychosis. This research will now be reviewed in the following sections.

1.3.4. Cognitive impairment in psychosis and its association with functional outcome.

The coming paragraphs will provide an overview of the different domains of cognitive impairment evident in psychosis, and how cognitive deficits are associated with poor functional outcome.

(a) Neurocognition in psychosis

The term 'neurocognition' (NC) describes a group of non-social cognitive functions which are associated with specific brain regions or neural pathways. According to the National Institute of Mental Health Research (NIMH) - Measurement and Treatment to Improve Cognition in Schizophrenia (MATRICS) consensus, the main neurocognitive domains which are reported to be impaired in psychosis are: Speed of Processing, Attention/Vigilance, Working Memory, Verbal Learning and Memory, Visual Learning and Memory, Reasoning and Problem Solving, and Verbal Comprehension (Green *et al*., 2004; Green *et al*., 2008; Nuechterlein *et al*., 2004). NC deficits occur early in the course of the illness and remain relatively stable over time, likely suggesting a possible trait marker of illness rather than a consequence of illness progression (Allott, Liu, Proffitt, & Killackey, 2011).

In a large quantitative review of 204 studies assessing cognitive impairment in psychosis, Heinrichs and Zakzanis (1998) showed that all NC domains yielded at least moderate to large

effect sizes, however, the magnitude of impairment varied across studies. Verbal memory was most consistently reported as being impaired, with 78% of individuals scoring below the median compared to controls. Despite the majority of studies providing evidence of a general cognitive impairment in psychosis, there is considerable heterogeneity between individuals, with a subgroup having intact cognitive function (Heinrichs & Zakzanis, 1998).

(b) The association between impaired neurocognition and poor functional outcome in psychosis

Impairments in a number of neurocognitive abilities have been associated with poor functioning, with research showing that NC may account for 20 - 60% of variance in functional outcome (Green *et al*., 2000). However, it is worth noting that in a number of these studies, variance estimates which exceeded 40% were an exception, leaving a lot of variance in functional outcome un-accounted for (Couture *et al*., 2006). In a meta-analysis of cross-sectional studies, Fett and colleagues (2011) demonstrated that different neurocognitive abilities are differentially related to separate domains of functional outcome; for example, verbal fluency followed by verbal learning and memory, were most strongly related to community functioning (Fett *et al*., 2011). This highlights the need to use measures that examine functional domains separately as this may enhance understanding of the factors underlying functioning (Yager *&* Ehmann, 2006).

In early psychosis, a review examining baseline cognitive function as a predictor of longitudinal functional outcome found that at least one cognitive domain predicted outcome; however, when cognitive domains were examined separately, more null than significant associations were

revealed (Allott, Liu, Proffitt, & Killackey, 2011; Santesteban-Echarri *et al*., 2017). Verbal language skills were most frequently predictive of functional outcome, but this association was not always significant. Allot *et al*. (2011a) concluded that due to methodological variability (e.g. differences in defining and measuring functional outcome), no firm conclusion could be drawn with regards to cognition and functional outcome in early psychosis, and that further research is necessary to explore other predictors of outcome, such as social cognition (SC).

Whilst processing social information may require a level of NC function (e.g. memory and attention), evidence from studies of brain damaged patients and of individuals with neurodevelopmental disorders show a disassociation between NC and SC impairments (i.e. it possible to have SC impairments whilst having intact NC and vice versa), implying that SC and NC may be distinct constructs (Fett *et al*., 2011; Pinkham *et al*., 2003). Indeed, evidence suggests that impairments in SC are also associated with functioning in psychosis, with some studies showing that SC contributes unique variance to functional outcome above that accounted for by NC (Fett *et al*., 2011). The role of SC will be explored below.

1.3.5. Social cognitive deficits in psychosis: Domains of impairment and associations with poor functional outcome

Social Cognition (SC) is a multifaceted construct, referred to as the mental operations underlying social interaction, such as interpreting the intentions and emotions of others (Adolphs, 2009).

Although research into SC is not as advanced as NC, there is evidence of widespread impairments in psychosis, with deficits identified in chronic groups, first-episode samples (Addington, Saeedi & Addington, 2006), UHR groups (Chung, Kang, Shin, Yoo & Kwon, 2008; Lee *et al*., 2015; Thompson *et al*., 2012) and in first-degree relatives of individuals with schizophrenia (Janssen, Krabbendam & van Os, 2003). These deficits tend to remain stable over time and are comparable to deficits in those with chronic schizophrenia (Addington *et al*., 2006; Healey *et al*, 2016; Horan *et al*., 2012). The main abilities most frequently identified as being impaired in psychosis are emotion perception (EP), social perception (SP) or social knowledge (SK), theory of mind (ToM) and attributional style (AS; Couture *et al*., 2006; Pinkham *et al*., 2014). Please see Table 2 (page 19) for definitions of the main domains of SC.

Understanding that others have beliefs or intentions that may differ from our own is important for engaging in successful social interaction (Brothers, 1990; Brothers, 2002) and failures in this ability can result in social impairments (Fett *et al*., 2011). Research suggests that SC impairments are associated with poor functioning in psychosis. The associations between functioning and each of the SC impairments in psychosis will now be reviewed.

Table 2. Definitions of the main domains of Social Cognition.

Key Term	Definition
Social Cognition (SC)	Mental operations underlying social interaction, such as interpreting the intentions and emotions of others (Adolphs, 2009).
Emotion Perception (EP)	Identification of emotional information from facial expressions, vocal nuances or biological motion (body movement; Couture *et al*., 2006).
Social Knowledge (SK)	Understanding of how others act in social situations (Cutting & Murphy, 1990). Closely linked to social perception.
Attribution Style (AS)	A person's tendencies in explaining the cause of events (Combs, Wicher, & Waldheter, 2007).
Theory of Mind (ToM)	One's ability to infer the thoughts, emotions, and intentions of others, allowing one to predict the behaviour of others and adapt actions accordingly (Baron-Cohen, 1995; Frith, 2004). Also referred to as 'mentalising'.

(a) Emotion Perception

Emotion Perception (EP) refers to the identification of emotional information from facial expressions, vocal nuances or biological motion (i.e. body movement; Couture *et al*., 2006). In tasks of EP where one is required to recognize the emotion depicted in faces, individuals with schizophrenia show significant impairments which have been likened to that of right-brain-damaged patients (Borod *et al*., 1993), with meta-analyses reporting large effect sizes (Savla *et al*., 2013). In tasks of affective prosody recognition, individuals with schizophrenia are also significantly impaired relative to controls (Hoekert, Kahn, Pijnenborg, & Aleman., 2007). Furthermore, substantial impairments in emotional identification impairment have also been

found in individuals at the onset of their illness and in UHR groups (Addington *et al.*, 2006a; Barkl *et al.*, 2014; Pinkham *et al.*, 2007), with specific deficits in the recognition of negative emotions (Healey *et al.*, 2016).

In studies which have looked at the relationship between EP and functional outcome, EP has been linked to community functioning, social behaviour in the milieu, interpersonal relations and independent living in individuals with schizophrenia (Bartholomeusz *et al.*, 2011; Brekke *et al.*, 2005; Couture *et al.*, 2006). Cross-sectional relationships have also been reported between impaired facial affect recognition and social functioning in FEP (Addington *et al.*, 2006).

(b) Social Knowledge

Social Knowledge (SK) represents a person's understanding of how others act in social situations (Cutting & Murphy, 1990). A related construct is Social Perception (SP – a person's ability to infer social cues from their social environment). When SK was assessed using questions about how people tend to act in social situations, individuals with schizophrenia are significantly impaired relative to controls and individuals with bipolar and depressive disorders (Cutting & Murphy, 1990). SP is often assessed using non-verbal cues to make social judgments. SP impairments have been found in individuals with schizophrenia with a large effect size (Kohler *et al.*, 2010; Savla *et al.*, 2013). Impairments are also reported in FEP and UHR groups and in relatives of individuals with schizophrenia (Addington *et al.*, 2006; Bartholomeusz *et al.*, 2011; Couture *et al.*, 2006; Healey *et al.*, 2016). Whilst findings to date

show support for SP impairment in FEP, there are a limited number of studies which have assessed this construct. This might be owing to the lack of psychometrically sound measures available to assess the construct, but there is also considerable overlap between other SC domains (e.g. ToM), which pose a number of challenges in reliably measuring the SP domain (Healey *et al*., 2016).

A number of studies have found an association between SP and functioning in psychosis; specifically, there are significant associations between SP and community functioning, social behaviour in the milieu and social problem solving (Bartholomeusz *et al*., 2011; Couture *et al*., 2006; Penn *et al*., 2001). When all domains of cognition were considered in a meta-analysis, Fett and colleagues (2011) demonstrated that SK and SP had the strongest relationships with community functioning closely behind ToM. Cross-sectional relationships with SP, SK and functioning (quality of life), have also been found in FEP (Addington *et al*., 2006).

(c) Attribution Style

Attribution Style (AS) refers to how a person tends to explain the cause of events (Combs, Wicher, & Waldheter, 2007). Research has shown that individuals with persecutory delusions have a specific AS style, known as a personalizing bias or attribution bias, where they attribute the cause of negative events to others, particularly in ambiguous situations (Combs, Wicher, & Waldheter, 2007; Couture *et al*., 2006; Kaney & Bentall, 1989). Attribution Bias (AB) has been reported in chronic schizophrenia relative to controls and depressive patients (Combs, Wicher, & Waldheter, 2007) but others have failed to find a significant difference between individuals with schizophrenia relative to controls, with a recent meta-analysis reporting a negligible effect

size (Lee *et al*., 2015; Savla *et al*., 2013). Although not as pronounced, a biased attribution style has also been found in FEP groups (An *et al*., 2010; Krstev, Jackson & Maude, 1999), however generally, findings within FEP are mixed (Healey *et al*., 2016).

In recent meta-analyses of SC impairments in UHR samples, the largest effect size across the SC domains was found for AB; however, those who converted to psychosis at follow-up were less impaired relative to the non-converters, suggesting that AB impairment may not be unique to psychosis (Lee *et al*., 2015). Furthermore, others have argued that AS is associated with personality traits rather than performance-based skills and is a separable construct to other SC domains (Buck, Healey, Gagen, Roberts & Penn, 2015; Healey *et al*., 2016).

In terms of an association with functioning in psychosis, a 'hostile' AS has shown to be predictive of aggressive behaviour in in-patients with schizophrenia (Waldheter, Jones, Johnson, & Penn, 2005), whilst 'stable' attributions were shown to be linked to community functioning (Lysaker *et al*., 2004). Further work is needed before firm conclusions can be drawn with regard to AS and its relationship with poor functioning in psychosis, particularly in early psychosis.

(d) Theory of Mind

ToM (or mentalising) refers to one's ability to infer the thoughts, emotions, and intentions of others, allowing one to predict the behaviour of others and adapt actions accordingly (Baron-Cohen, 1995; Frith, 2004). A number of tasks have been developed to assess ToM, for example,

understanding false beliefs (Wimmer, 1983), detection of sarcasm (Happe, 1994), recognising *'faux pas'* (Baron-Cohen *et al*., 1999)*,* and detecting mental states by reading information from people's eyes (Baron-Cohen *et al*., 1997). Using these tasks, three meta-analyses (Bora *et al.,* 2009; Sprong *et al.,* 2007) and two systematic reviews (Brune, 2005; Harrington *et al*., 2005) have provided compelling evidence of ToM impairments in schizophrenia, with meta-analyses reporting large effect sizes (d=0.90-1.25; $g = 0.96$). Impaired ToM has also been shown to be a significant predictor of psychosis conversion (Bora & Pantelis, 2013; Lee *et al*., 2015). Interestingly, these studies also provided evidence for ToM impairments in remitted patients with schizophrenia, and although the effect was not as large as the non-remitted group, it was significant (Bora *et al.,* 2009; Sprong *et al.,* 2007). Whilst it appears that acute psychosis has a 'moderating' influence on ToM performance, the fact that ToM impairments remain in the remitted phase suggests that these impairments might be an endophenotype of the illness (Bora *et al*., 2009).

ToM impairments are present in individuals with FEP, and in some cases, the level of impairment is comparable to individuals with chronic schizophrenia (Bertrand, Sutton, Achim, Malla & Lepage, 2007; Bora *et al*., 2009; Healey *et al*., 2016). Findings from a recent review demonstrated that ToM deficits in FEP are most pronounced in tasks that assess verbal ToM; studies which have assessed non-verbal ToM are less conclusive (Healey *et al*., 2016). There is also evidence for ToM impairments in UHR groups (Chung *et al*., 2008), and in first-degree relatives of individuals with schizophrenia (Janssen, *et al*., 2003); again, this suggests that ToM impairments are a trait-like characteristic of the illness.

In a meta-analysis conducted by Fett and colleagues (2011), it was reported that ToM was more strongly related to community functioning (i.e. interpersonal relationships, work functioning) than any other domain of cognition (social and non-social cognition), suggesting that ToM explains unique variance in functional outcome above that accounted for by NC (Brekke *et al*, 2005; Harrington *et al*., 2005; Penn *et al*., 2007).

Whilst these findings make ToM a promising treatment target for improving social functioning in psychosis, these studies were mainly based on cross-sectional studies of chronic populations. Further evidence is needed to explore the prospective relationship between ToM deficits and social functioning in psychosis before firm conclusions can be drawn as to whether ToM may be a potential treatment target for social disability in young people with psychosis.

1.3.6. Origin of cognitive and functional impairments: The Neurodevelopmental Hypothesis of Psychosis

The cause of SC impairment in psychosis remains unclear, however the above findings may indicate a neurodevelopmental pathway to impairment (Bartholomeusz *et al*., 2011; Bartholomeusz & Allott, 2012; Lin, Wood, Yung, 2013). The social regions of the brain that are associated with SC function, namely the medial prefrontal cortex (mPFC), superior temporal sulcus (STS) and the anterior cingulate (ACC), go through protracted development during adolescence, which is also typically when psychosis manifests (Bartholomeusz *et al*., 2011; Blakemore, 2008; McGlasham & Hoffman, 2000). It therefore seems plausible that aberrations in the neurodevelopmental process may account for SC deficits observed in the disorder (Bartholomeusz *et al*., 2011; Blakemore, 2008; McGlasham & Hoffman, 2000).

Synaptic reorganization also occurs in the regions associated with executive neurocognitive functions (namely the prefrontal cortex; PFC) during this period (Bartholomeusz & Allott, 2012; Blakemore, 2008; Choudhury *et al*., 2006). Whilst social behavior during adolescence is also influenced by socio-cultural factors, disruption to peer relationship and social isolation as a result of emerging psychotic symptoms during this period may also to contribute to poor SC (Choudhury *et al.,* 2006). The extent of how social influences in the environment interact with brain changes during adolescence needs to be established.

Similarly, it can also be argued that a trajectory of poor functional outcome in psychosis may also reflect a neurodevelopmental process (Lin, Wood, Yung, 2013). Evidence that poor functioning emerges premorbidly, continues to remain stable during the prodrome, and persists through to chronic illness, supports this notion. Of the identified predictors of functional outcome - namely cognition (SC and NC) and negative symptoms – these also follow a similar trajectory, providing further evidence of a neurodevelopmental pathway. If this hypothesis is true, it would imply that there exists a subgroup of individuals who are at risk of longstanding poor functional outcome, and that brain changes in this subgroup that have persistent elevated negative symptoms and cognitive impairment may be different to those with absent negative symptomatology and intact cognition (Kirkpatrick *et al.,* 2001; Lin, Wood, Yung, 2013). This offers an opportunity to intervene in the early phase of illness where improvement in functioning is most likely to be achieved due to the neuroplasticity associated with ongoing neurodevelopment during the adolescent years (Bartholomeusz *et al*., 2011; Bartholomeusz & Allott, 2012).

1.4. Limitations to the current literature

Whilst there is an abundance of studies investigating the predictors of functional outcome in chronic schizophrenia, due to factors associated with illness chronicity (such as medication and repeated relapse), findings from chronic samples may not necessarily generalize to younger individuals at the onset of their illness where social disability emerges and where intervention may be most effective (Allot *et al*., 2011; McGorry *et al*., 2008). Findings from studies exploring predictors of poor functioning of individuals at the onset of their illness remains inconclusive due to do methodological variability and study limitations such as: varying definitions and measurement of 'functional outcome', inadequate power, inclusion of only individuals with a diagnosis of schizophrenia, differences in length of follow-up, and lack of control of other predictor variables (Allot *et al*., 2011a; Ram *et al*., 1992). Some studies are further confounded by focusing on the concurrent relationship between cognition and outcome (Fett *et al*., 2011). Exploring the longitudinal relationship between predictor variables allows for greater inferences of causality to be made, and this will better inform interventions (Allott, Liu, Proffitt, & Killackey, 2011). Whilst the link between early negative symptoms and later functional outcome is more established, the relationship between cognition (social cognition and neurocognition) and later functioning in FEP for the reasons stated above, remains inconclusive (Allott, Liu, Proffitt, & Killackey, 2011; Neuchterlein *et al*., 2011).

Further work is needed to clarify the relative contribution of social cognition, neurocognition and negative symptoms in predicting the early course of functioning in FEP, thus informing the identification of the optimal treatment targets to improve or even prevent further decline in functioning. To clarify the role of cognition on functioning in early psychosis, exploration of

changes in cognition on changes in functional outcomes following psychosocial interventions is also warranted (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011; Allott, Liu, Proffitt, & Killackey, 2011; Green *et al*., 2004; Matza *et al*., 2006). Not only will this help to clarify the relationship between cognition and functioning in FEP, but it may also allow for the prediction of which individuals will respond to intervention, and potentially identify a subgroup that may not respond and require further intervention (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011; Allott, Liu, Proffitt, & Killackey, 2011).

1.5. Thesis Aims and objectives

The overarching theme of this thesis is to explore the contribution of SC and NC to poor functioning in early psychosis. This thesis will aim to address this in three empirical studies.

The first study aims to investigate the prospective relationship between baseline cognition (SC and NC), and (poor) social and role functioning in the early course of FEP, and whether they are distinct predictors of function from negative symptoms.

In the second and third studies, data will be used from a multi-centre randomized controlled trial of an adapted from of Cognitive Behavioural Therapy (CBT) for severe social disability in FEP (The SUPEREDEN trial, Fowler *et al*., 2009; Fowler *et al*., 2017) to explore:

1. Whether any improvement in functioning following the psychosocial intervention (Social Recovery Cognitive Behavioural Therapy; SRCBT) is associated with a corresponding change

in cognitive function (SC and/or NC), and neural changes in the brain regions implicated in SC processing;

2. The efficacy of SC and NC in predicting who will respond to SRCBT.

It is hoped that this will provide understanding of SC or NC deficits that may constrain any impact of SRCBT, and hence provide a means of identifying those whose disability can potentially be further improved through targeting of NC or SC deficits alongside the psychosocial intervention.

2.0. CHAPTER 2

OVERVIEW OF EMPIRICAL STUDIES

This chapter will provide an overview of the methodological, practical and ethical issues relating to each study in this thesis. The general sample characteristics will be described, along with timelines and data collection procedures for the three empirical studies. The ethical considerations of recruiting a vulnerable group of young people are also discussed, with focus on the wellbeing of the participants.

2.1. Study 1: A prospective 12-month follow-up study examining baseline social cognition and neurocognition as predictors of social and role functioning in first episode psychosis (Chapter 3).

2.1.1. Aims: The aim of this study was to test prospectively the relative contribution of social cognition (SC), neurocognition (NC) and negative symptoms, in predicting 12 month social and role outcomes in first episode psychosis, and to benchmark these cognitive dimensions against a healthy matched community sample.

2.1.2. Inclusion criteria for the psychosis group: (a) Aged between 16 – 35 years old with a first episode psychosis (FEP); (b) sufficient command of the English language; (c) absence of any neurological disorders, for example, epilepsy; (c) no documented history of a learning

disability; (d) no history of severe head injury (more than 5 minutes' loss of consciousness, or an overnight hospital stay).

2.1.3. Inclusion criteria for the healthy control group: (a) Sufficient command of the English language; (b) No evidence of personal history or family history of mental health problems; (c) Absence of any neurological disorders, for example, epilepsy; (c) No documented history of a learning disability.

2.1.4. Design: This was a prospective follow-up study where participants were assessed within the first year of care under an Early Intervention Service (EIS), and then twelve months after being consented to the study. Several clinical, cognitive (social cognition and neurocognition), demographic (e.g. gender, age, years in education and socio-economic status) and premorbid variables were assessed at baseline (i.e. within a year of diagnosis). The clinical variables assessed were psychopathology (negative, positive and general symptoms, measured by the Positive and Negative Syndrome Scale; Kay, Fiszbein, & Opler, 1987) and duration of untreated psychosis (delay between the onset of psychotic symptoms and initiation of criterion treatment; Larsen, McGlashan & Moe, 1996). Four social cognitive domains were assessed: Theory of Mind (Picture sequencing task; Langdon & Coltheart, 1999), social knowledge (Social Knowledge Questionnaire, SKQ; Cutting & Murphy, 1988 & 1990), emotion perception (Mayer-Salovey-Caruso Emotional Intelligence Test – Perceiving Emotions, MSCEIT; Mayer, Salovey, & Caruso, 2002) and attribution bias (Ambiguous Intentions Hostility Questionnaire, AIHQ; Combs, Penn, Wicher, & Waldheter, 2007a). In addition, three neurocognitive domains were assessed: verbal comprehension (Wechsler Adult Intelligence Scale - WAIS-IV; Wechsler, 1981); verbal learning and memory (Logical Memory subtest; Wechsler Memory

Scale Revised – IV, WMS; Wechsler, 1987), and reasoning and problem solving (Block Design subtest, WAIS, Wechsler, 1981). Finally, social functioning (relationships) and role functioning (work/study) were assessed separately at baseline and 12-month follow-up using the Global Functioning Scales (Cornblatt *et al.*, 2007).

2.1.5. Study logistics and Timeline: Recruitment for Study 1 was conducted within the Early Intervention Service (EIS) in Birmingham, UK. Participants who had been receiving care within EIS for up to 12 months were invited to take part in the research. Recruitment commenced for Study 1 in the autumn of the first year, with the follow-up assessments commencing in the autumn of year two. As the recruitment target (n=100) was not met by the third year of the PhD, it was decided that recruitment would be extended by 12 months. Recruitment for Study 1 finally concluded in the fourth year of the PhD, with the last follow-up assessment taking place in March 2015 (Year 5).

The healthy control participants were recruited via an online advert posted on a local community website (Gumtree.com Limited). Friends and acquaintances of service users consented to the present research were also invited to take part in the study with the service user's permission. Recruitment of the healthy control participants took place between November 2013 and October 2014 (Year 3 and 4).

2.1.6. Data collection procedure for Study 1: Participants first completed a consent form, which was followed by a cognitive assessment battery, and assessments of symptoms and functioning. The assessment of symptoms and functioning was repeated at 12-month follow-up. The assessments were either completed in the participant's own home or in a safe location such as

a community mental health centre. As the duration of the assessment was lengthy, the

assessments were completed over several sessions to ease participant burden. Healthy control

participants were seen for a one-off assessment, lasting approximately 1.5 hours, and were

asked to complete the same cognitive battery and assessment of functioning as the service users.

2.2. Study 2: The relationship between cognition and functional improvement in the context of a psychosocial intervention targeting social disability in first episode psychosis (Chapter 4).

2.2.1. Aims: Data were drawn from a multi-centre randomized controlled trial of an adapted

from of Cognitive Behavioural Therapy (CBT) for severe social disability in FEP (The

SUPEREDEN trial, Fowler *et al*, 2009; Fowler *et al*., 2013; Fowler *et al*., 2017). Further data

were collected to test:

1. Whether any improvement in functioning following the psychosocial intervention (Social Recovery Cognitive Behavioural Therapy; SRCBT) is associated with a corresponding change in social cognitive and neurocognitive function;

2. Whether social cognition (SC) and/or neurocognition (NC) can predict who will respond to SRCBT.

2.2.2. Inclusion criteria for the psychosis group: (a) aged between 16-35 years old with a FEP;

(b) presenting with a low level of structured activity after at least one year of treatment within

EIS (defined as 30 hours or less per week on the Time Use Survey); (c) sufficient command of

the English language; (d) absence of any neurological disorders, for example, epilepsy; (e) no

documented history of a learning disability; (f) no history of severe head injury (more than 5 minutes loss of consciousness, or an overnight hospital stay).

2.2.3. Inclusion Criteria for the Healthy Control Group: (a) Sufficient command of the English language; (b) No evidence of personal history or family history of mental health problems; (c) Absence of any neurological disorders, for example, epilepsy; (c) No documented history of a learning disability.

2.2.4. Design: This study of cognition ran alongside the multi-site NIHR SUPEREDEN trial. The trial is a single-blind, proof-of-principle trial, comparing SRCBT plus EIS care, against standard care from EIS alone (referred to as the Treatment as Usual – TAU - group). The primary outcome for the trial was time spent in structured activity measured by the Time Use Survey (TUS; Short, 2006). Cognition was assessed at baseline (pre-therapy) and at 9-month follow-up (post-intervention). The assessment of cognition included four social cognitive domains: Theory of Mind (Picture sequencing task), social knowledge (SKQ), emotion perception (MSCEIT) and attribution bias (AB; AIHQ). Three neurocognitive domains were also assessed: verbal comprehension (Vocabulary subtest, WAIS-IV); verbal learning and memory (Logical Memory subtest; WMS-IV), and reasoning and problem solving (Block Design subtest, WAIS-IV), described in section *3.4.3.* (Chapter 3).

2.2.5. Study Logistics and Timelines:

Service users from EIS centres in Birmingham, Sussex, Norwich and Lancashire were invited to take part in the SUPEREDEN trial. The research team worked closely with EIS to identify

suitable referrals. All researchers conducting the assessments were blind to group allocation, and in cases where the mask was broken, another researcher who remained masked, completed the assessments at the remaining time points. In addition to the trial assessments, participants were also asked to complete cognitive assessments.

Data collection for Study 2 commenced at the end of year two of the PhD once the SRCBT trial was underway. Recruitment concluded in the fourth year and all the follow-up assessments were completed by summer of 2015 (year 5).

2.2.6. Data Collection Procedure for Study 2:

An initial screening interview took place to assess for trial eligibility (30 hours or less of structured activity a week on the Time Use Survey, TUS; Short, 2006). If the study criteria were met and consent was obtained, participants were asked to complete the trial assessments which included psychopathology (e.g. Positive and Negative Syndrome Scale, PANSS; Kay, 1987) and functioning (structured activity; TUS), and if participants consented, the battery of cognitive assessments (four social cognitive domains and three neurocognitive domains (described in section *3.4.3., Chapter 3)* was also completed. Participants were then randomly allocated to either the treatment group (SRCBT) or TAU (standard EIS care). Participants who were allocated to the treatment group received the SRCBT over a 9-month period in addition to receiving care from EIS. Participants who were allocated to the TAU continued to receive standard care under the early intervention team. The trial assessments were repeated at 9-month follow-up, along with the follow-up assessments of cognition for those consenting to these further measures.

2.3. Study 3: A functional magnetic resonance imaging study exploring the neural correlates of theory of mind in young people with first episode psychosis receiving a psychosocial intervention aimed at improving structured activity (Chapter 5).

2.3.1. Aims: This functional Magnetic Resonance Imaging (fMRI) study ran in parallel to the SRBCT trial described above (The SUPEREDEN trial, Fowler *et al*., 2009; Fowler *et al*., 2013; Fowler *et al*., 2017). Using fMRI task designed to activate the ToM network, this study aimed to explore:

(i) Neural correlates of ToM in a group of young people with FEP presenting with severe social disability.

(ii) Changes in brain function in the ToM regions pre- and post- SRCBT.

(iii) Whether changes in brain function following SRCBT is associated with structured activity at 9-month follow-up

2.3.2. Inclusion criteria: In addition to the inclusion criteria outlined in Study 2 (page, 32), participants were screened for conditions for which fMRI might represent a health risk (see Appendix B-16 for screening form) and excluded if any contraindications were present.

2.3.3. Study logistics and timelines:

The imaging was carried out at the Birmingham University Imaging Centre by an authorised scan operator. For the convenience of the participants, and to ensure engagement, a taxi was arranged by the research team to take the participant to the imaging centre and return them home following the scan; the cost was reimbursed by the research team. Data collection for

Study 3 commenced at the end of year two once the SRCBT trial was underway. Recruitment concluded in the fourth year and the follow-up assessments were completed by the summer of 2015 (year 5).

2.3.4. Data Collection Procedures: Participants who were allocated to the treatment arm of the SUPEREDEN trial (i.e. receiving SRCBT & EIS for 9 months) were also invited to participate in the present study. This involved fMRI scanning (whilst completing the fMRI paradigm) at baseline (prior to the intervention), and at the end of the intervention (9 months). Prior to scanning, written informed consent was obtained. Participants were fully briefed on the scanning procedure and were given detailed instructions on how to perform the task prior to entering the scanner. Participants also completed two practice trials prior to scanning to ensure they had full understanding of the task.

2.4. Ethical Considerations

Careful consideration was given to the study design to ensure that a high standard of ethical practice was adhered to. All three studies were given full approval by the Black Country NHS research ethics committee (REC reference: 12/WM/009; See Appendix A-1).

2.4.1. Risk and wellbeing of participants

As vulnerable young people were taking part in the research, it was ensured that there was plenty of opportunity for participants and their carers (where applicable), to gain an understanding of the purpose of the research and any potential consequences. Written

information as well as verbal information was provided, and participants were given ample opportunity to ask questions prior to obtaining informed consent. All participants were informed that their participation is voluntary, and that they have the right to withdraw at any time without it affecting their level of care.

Again, due to the vulnerable nature of the group, the research team ensured that they liaised closely with the young person's care team prior to making contact with the service users. This was to check if the young person is well enough to participate in research, but also, to be informed of any risk issues prior to making contact. In cases where the young person was deemed too unwell, or where there was significant risk, the young person was not approached by the researcher until it was appropriate. Prior to commencing the assessments, the researcher briefed the client on the confidentiality of the research. In cases where there was reason to be concerned about their safety or the safety of others, participants were informed that confidentiality would be broken. Where risk was reported during the assessment, the care team was informed immediately, and the risk was documented in the young person's medical notes. If the participant became distressed during the assessment, the meeting was postponed, and the participant was reminded of their option of withdrawing from the research.

For Study 3, each participant was fully briefed on the scanning procedure and was made aware of the risks associated with fMRI, following the prescribed standards of the University of Birmingham Imaging Centre (BUIC). An MRI safety check was also conducted to ensure that there were no contraindications present. During the scanning, the researcher spoke to the participants regularly via an intercom, and the participant was given a buzzer which they could sound in case they became distressed or wanted to communicate with the researcher. If the

participant became distressed during the scanning, they were removed immediately and reminded of their right to withdraw from the research.

In relation to the healthy control participants, if low level symptoms were reported, the young person was encouraged to visit their general practitioner and they were also given the contact details of the Samaritans.

2.4.2. Researcher Safety

Researcher safety was also of paramount importance during the conduct of the research. A 'buddy system' was employed during participant visits, whereby the researcher gave the details of the visit (client name, address, contact details, details of the care team and duration of the visit) to another member of the research team in case of an emergency. A risk assessment was also conducted prior to each visit. Where significant risk was present, the service user was not approached until it was appropriate. In cases where there was some risk present, visits would be conducted in pairs or at a neutral venue such as a mental health community centre.

2.4.3. Data protection

In line with NHS Research Ethics Committee approval, all assessments were kept in a locked filing cabinet in a secure location. Participant names and contact details were kept separately to ensure that the assessments were not identifiable. All databases and electronic forms were encrypted and when they needed to be transferred to another computer, this was done via an encrypted USB stick.

2.5 Author contribution to the design, conceptualisation and implementation of each of the three studies.

The author (Sian L Griffiths; SLG) was responsible for the conceptualisation of the three empirical studies under the academic supervision of Professor Stephen Wood and Professor Max Birchwood. SLG designed the studies around the NIHR SUPEREDEN trial (Trial registration: ISRCTN61621571; Fowler *et al*., 2017), and was responsible for the selection of measures and design of the study protocol (for Studies 1, 2 & 3). The studies were later included as add-on studies to the SUPEREDEN trial, and the cognitive assessments and global functioning scales were embedded as part of the trial assessments. Study 1 recruited a separate sample to the SUPEREDEN trial and was adopted as a NIHR portfolio study; SLG was appointed as chief investigator. SLG was responsible for the recruitment of Study 1 and conducted the baseline and 12-month follow-up assessments; the clinical research network (CRN) assisted with recruitment and completed approximately 20% of the baseline assessments. For Study 2, SLG contributed to the recruitment of the trial at the Birmingham site, and collected trial baseline assessments (including the cognitive test battery), but due to being un-blind for the fMRI study, SLG was unable to complete the 9-month follow-up assessments for the trial. SUPEREDEN research associates in Birmingham, Lancashire, Norwich and Sussex also contributed to the data collection for Study 2. SLG was responsible for all of the recruitment and data collection for Study 3. The fMRI task was piloted by Cherine Akkari as part of a joint MSc with the University of Birmingham and University of Marseille under the supervision of Dr Renate Reniers and Professor Stephen Wood. The piloted version of the task was used in Study 3. SLG was responsible for the data analysis and write up of the three empirical studies.

3.0. CHAPTER 3

EMPIRICAL STUDY 1

3.1. A PROSPECIVE 12-MONTH FOLLOW-UP STUDY EXAMINING SOCIAL COGNITION AND NEUROCOGNITION AS PREDICTORS OF SOCIAL AND ROLE OUTCOME IN FIRST EPISODE PSYCHOSIS.

3.2. Abstract

Poor social and role functioning is commonly associated with psychosis; finding potentially treatable predictors of poor functioning has become a focus in research in recent years. Among other established predictors such as negative symptoms, deficits in neurocognition (NC) and social cognition (SC) are closely linked to impairments in functioning. However, the majority of research to-date has focused on chronic populations, often cross-sectional, where long-term illness effects may confound the findings, and may not apply to a heterogeneous group of young people early in the course of their illness where intervention may be most effective (Allott, Liu, Proffitt, & Killackey, 2011).

Design: This study is a prospective 12-month follow-up study which aims to investigate the predictive values of baseline NC and SC on poor social and role functioning in individuals with a first episode psychosis (FEP), within the context of other clinical variables.

Method:

98 individuals with FEP (mean age = 24; male = 77) were assessed within the first year of diagnosis on measures of functioning (social and role functioning), cognition (social cognition and neurocognition) and symptoms (positive, negative and general symptoms), and were followed up at 12 months for a further assessment of their current level of functioning.

Results:

When the cognitive variables were considered alone in the regression model, results showed that social knowledge predicted poor 12-month social functioning (N = 40), and verbal memory predicted poor 12-month role functioning (N= 52). However, when symptoms were added to the regression model, negative symptoms was the only significant predictor of later poor social and role functioning in FEP, explaining a greater proportion of variance than the cognitive variables alone. Exploratory analyses showed that the NC and SC variables were moderately linked to negative symptoms; explaining 20% variance to negative symptoms cross-sectionally and prospectively.

Outcome:

The findings suggest SC and NC play less of a direct role in functioning in early psychosis, and that negative symptoms may be more of a useful prognosis marker of later social and role functioning in individuals with FEP. Exploratory analyses suggest that SC and NC impact on negative symptoms, and that further analyses are needed to clarify if there is a reciprocal relationship between cognition, negative symptoms and functioning, which could potentially inform targeted interventions to improve functional outcome in young people with psychosis.

3.3. Introduction

Psychosis is one of the most socially disabling illnesses worldwide (Hafner & an der Heiden, 1999), and despite symptomatic recovery, poor functioning often remains (Bellack *et al*., 1990; Brekke & Long, 2000; Penn *et al*., 2007; Ventura *et al*., 2011). This has resulted in attempts to find potentially 'treatable' predictors of poorer functional outcome (Fett *et al*., 2011; Holthausen *et al*., 2007), with identified predictors including: duration of untreated psychosis, negative symptoms, age of onset, gender, premorbid adjustment, diagnosis of schizophrenia, cognitive function, and family history of schizophrenia (Kay & Lindenmayer, 1987; Simonsen *et al*., 2010). However, the majority of these studies have focused on chronic populations, often cross-sectionally (Lucas *et al*., 2008). Thus, prospective studies on individuals at the onset of their illness (i.e. first episode) may provide more informative data regarding predictors of poor functional outcome trajectories in psychosis (Malla & Payne, 2005). In research that has focused on individuals with FEP, demographic, premorbid and clinical variables have been consistently reported as predictors of poor outcome. These include poor adolescent premorbid adjustment, early appearance of negative symptoms, DUP, early age of onset of psychosis, and male gender (Ayesa-Arriola *et al*., 2013; Lucas *et al*., 2008; Malla & Payne, 2005; Rammou *et al*., 2017; Santesteban-Echarri *et al.,* 2017). However, there remains inconsistency in the results reported, possibly due to small sample sizes from single-sites, inclusion of only individuals with a diagnosis of schizophrenia, differences in length of follow-up and varying definitions of 'outcome' (Ram *et al*., 1992).

A number of studies have also identified neurocognition (NC) and social cognition (SC) as strong predictors of poor social and role functioning (Fett *et al*., 2011; Santesteban-Echarri *et al.,* 2017).

Stable neurocognitive impairments are evident throughout the course of the illness and account for a proportion of explained variance in poor functional outcome (Allott, Liu, Proffitt, & Killackey, 2011; Green *et al*., 2000). Green and colleagues conducted a review into the relationship between cognition and functional outcome in schizophrenia and showed that the effect sizes of these relationships fell within the medium range (r = 0.30 or d=.50; Green *et al*., 2000; Green *et al*., 2004). A recent longitudinal study in FEP looking at the trajectories of social and role functioning showed that those with greater cognitive impairment present at onset of the disorder, were less likely to improve their level of social functioning over a four-year period (Fu, Czajkpwski, Rund & Torgalsboen, 2017).

Furthermore, two systematic and meta-analytic reviews have provided evidence that at least one cognitive domain is associated with long-term functioning in early psychosis (Allott, Liu, Proffitt, & Killackey, 2011; Santesteban-Echarri *et al.,* 2017*)*. Verbal language skills are most consistently associated with impairments in functioning (Allott, Liu, Proffitt, & Killackey, 2011; Fett *et al*., 2011; Green *et al*., 2004; Heinrichs & Zakzanis, 1998). Problem-solving and general cognition are also consistently associated with functional outcome in FEP (Allott, Liu, Proffitt, & Killackey, 2011; Santesteban-Echarri *et al*., 2017). Although these reviews provide tentative evidence indicating that neurocognition predicts later functional outcome, there were more null than significant associations across the separate domains of neurocognition. The authors concluded that the inconsistent findings in the literature were due to methodological

variability and study limitations such as differences in the measurement of cognition and outcome, length of follow-up, inadequate power, and lack of control over other predictor variables (Allott, Liu, Proffitt, & Killackey, 2011). With regards to the latter point, the authors further highlighted the need to consider other potential predictors of outcome (such as symptoms) in multivariate analyses, to enhance the predictive power of the studies. Interestingly, studies where symptoms (especially negative symptoms) were controlled for, cognition made no significant independent contribution to predicting functional outcome (Addington, Saeedi & Addington, 2005; Siegel *et al*., 2006). Finally, social cognition was not considered in these reviews.

Social cognition (SC), defined as the mental operations underlying social interaction (Adolphs, 2009), is also impaired in psychosis and is arguably a trait marker of the illness (Bartholomeusz *et al*., 2011). Deficits are identified in FEP groups (Addington, Saeedi & Addington, 2006; Healey *et al*., 2016), UHR groups (Chung *et al*., 2008), and in first-degree relatives of individuals with schizophrenia (Janssen *et al*., 2003). The main abilities most frequently identified as being impaired in psychosis are emotion perception (EP), social knowledge (SK) / social perception (SP), theory of mind (ToM) and attributional style (AS; Couture *et al.,* 2006). Please see Table 2 (page 19) for definitions of the main domains of SC. A recent review of cognitive deficits in FEP showed that whilst there was some evidence for cognitive impairments across each of the SC domains, deficits were most pronounced for EP (especially recognition of negative affect), verbal ToM, and SP (Healey *et al*., 2016). Findings were mixed with regards to attribution style and non-verbal ToM. Furthermore, studies assessing SP impairments were limited in number (N=5). Further research is needed using appropriate healthy comparison

groups and psychometrically sound measures to fully elucidate the spectrum of SC impairment in early psychosis.

In studies which have investigated the relationship between cognition and functional outcome, SC has been shown to be a stronger predictor of social functioning than NC (Fett *et al*., 2011). A range of SC abilities have been shown to be significantly related to a number of domains of functional outcome; EP, SP and ToM have been associated with community functioning, social behaviour in milieu, social problem solving and social skills (Couture *et al*, 2006). Furthermore, ToM has been shown to explain 24% of variance in social behavioural abnormalities (Brune, 2005).

However, most of these studies have focused on individuals with established illness, and whilst some studies have examined the cross-sectional relationship between SC and functional outcome in FEP (Addington *et al*, 2006; Williams *et al*., 2008), research examining the prospective relationship between baseline SC and follow-up functioning is limited. Horan and colleagues (2012) found some evidence that baseline SC was related to 12-month work outcomes, independent living and social functioning in a FEP, however, when symptoms were controlled for, predictive relationships for independent living and social functioning were diminished.

3.3.1. The wider picture of functioning

Whilst the degree of overlap between SC and NC is unclear, it is important to establish the differential association between SC and NC with functional outcome, in order to identify

possible treatment targets (Fett *et al*., 2011). Furthermore, whilst NC and SC significantly contribute to the prediction of functional outcome, a bulk of the variance in outcome is unexplained (Fett *et al*., 2011). Future studies of cognitive predictors should be weighed against other potential predictors such as the clinical factors discussed previously (Allott, Liu, Proffitt, & Killackey, 2011). Looking at the contribution of a wide range of predictor variables may provide optimal treatment targets which could lead to a more meaningful and sustained functional recovery.

In FEP studies where NC and SC were considered together with other predictor variables, results are again somewhat inconsistent. Cacciotti-Saija *et al*. (2016) found that negative symptoms and social anxiety predicted outcome in early psychosis, whilst SC and NC failed to significantly contribute to the prediction of outcome. However, this finding is limited by the cross -sectional nature of the study. A recent 3-year follow-up study by Simons and colleagues (2016) found no associations between NC and SC and social functioning, but negative symptoms and general symptomatology significantly contributed to the prediction of follow-up functioning. Adding to this, Sullivan *et al*., (2014) failed to find a relationship between ToM and social functioning longitudinally (at 6 and 12 months), but neither did they find a relationship between psychosis symptoms and later social outcome. In contrast to these findings, when 12-month predictors of functional outcome were explored, Stouten, Veling, Laan, van der Helm & van der Gaag (2014) found that ToM significantly predicted one functional domain – problems with relationships – at follow-up. Negative symptoms and general symptoms predicted problems with work and study at 12 months. Although other NC and SC domains were assessed in this study, the majority of final regression models did not

contain any other cognitive predictor. Again, these inconsistent findings highlight the methodological variability between studies.

A possible explanation for these inconsistent findings is that only one of these studies looked at the separate domains of functioning. Social and role functioning have been shown to have distinct trajectories, and thus, each may be explained by different predictor variables; this highlights the need to measure functional domains separately (Cornblatt *et al*., 2007). Whilst each of these studies examined the contribution of cognition and symptoms in the prediction of outcome, only a brief cognitive assessment battery was used in two of these studies. A comprehensive assessment of cognition will allow for a further understanding of the relative contribution of each of the cognitive variables in the prediction of outcome and will likely lead to better informed interventions. Two of these studies also included participants with an older age range (Simons *et al*., 2016; Sullivan *et al*., 2014). As poor functioning often emerges in the premorbid phase during adolescence, interventions that are delivered as early as possible in one's functional trajectory are more likely to be successful due to the neuroplasticity associated with ongoing neurodevelopment during the adolescent years (Bartholomeusz *et al*., 2011; Bartholomeusz & Allott, 2012). As such, identification of the predictors of outcome soon after illness onset in younger samples may be most effective for targeting of interventions. A final consideration is a lack of appropriate comparison groups to determine the extent of cognitive impairment. Only one of these studies used a healthy comparison group, but they were not matched appropriately to the patient groups. This a general limitation particularly within the social cognitive literature, where non-clinical controls have often included undergraduate students who generally tend to be 'high functioning' and are likely to be highly motivated to complete the tasks (Combs, Wicher, & Waldheter, 2007; Couture *et al*., 2006; Gilbert, Pelham

& Krull, 1988). Careful consideration needs to be given to the selection of non-clinical comparison groups so that potential confounding factors such as level of education and socio-economic status are controlled for.

To address these limitations, the present study will explore SC, NC and functioning prospectively in FEP and will seek to address the limitations of previous studies by: 1) exploring the early predictors (i.e. soon after diagnosis) of functional outcome in a young psychosis sample; 2) comprehensively assess SC and NC and their relative contribution to symptoms in the prediction of outcome; 3) examine the predictors of social and role functioning separately; and 4) benchmark cognitive task performance with a healthy comparison group matched on age, level of education and socio-economic status.

3.3.2. The Present Study

The present study aimed to test prospectively the relative contribution of social cognition (SC), neurocognition (NC) and psychosis symptoms, in predicting 12 month social and role outcomes in FEP, and to benchmark these cognitive dimensions against a healthy matched community sample.

The research questions in this study were as follows:

(1) What are the cognitive, clinical, demographic and premorbid characteristics of the poor social and role outcome groups in FEP?

(2) Are the poor social and role outcome groups impaired on the social cognitive and neurocognitive tasks compared to the healthy control group and good outcome groups?

(3) What is the predictive efficacy of neurocognition and social cognition relative to negative symptoms in predicting 12 month social and role outcomes in FEP?

3.4. Method

3.4.1. Design

This was a prospective follow-up study where participants were assessed near to the onset of the first episode of psychosis, and at twelve months' follow-up.

3.4.2. Sampling

Service users entering the EIS in the Birmingham and Solihull Mental Health Foundation Trust were invited to take part in the study if they conformed to the following criteria:

(a) aged between 16 – 35 years old; and (b) had a schizophrenia spectrum disorder. Potential participants were initially screened for eligibility and were excluded based on the following: (a) insufficient command of the English language; (b) presence of any neurological disorders, for example, epilepsy; (c) documented history of a learning disability; and (d) history of severe head injury (more than 5 minutes' loss of consciousness, or an overnight hospital stay).

Diagnosis was confirmed using the Operational Criteria Checklist (OPCRIT) method that used International Classification of Diseases (ICD-10) criteria. Participants received £20.00 in respect of their time upon completion of the assessments. The study was approved by the Black Country NHS research ethics committee (REC reference: 12/WM/009; Appendix A-1).

Healthy Control Sample

To compare cognitive abilities of individuals with FEP to healthy age-peers, a group of matched young people between the ages of 16 – 35 years old were also recruited to the study. To control for possible confounding effects between the groups, the sample was matched on age, gender, ethnicity, level of education and socio-economic status using ACORN (a classification of

residential neighborhoods) postcode classification (please see method section, page 59 for further details on ACORN).

Participants were recruited via an online advert posted on a local community website (Gumtree.com Limited) and were initially screened via telephone for study eligibility prior to meeting the researcher. Affiliates of service users consented to the present research were also invited to take part in the study with the service user's permission. Participants were excluded based on the following: (a) insufficient command of the English language; (b) personal history or family history of mental health problems; (c) presence of any neurological disorders, for example, epilepsy; and (d) documented history of a learning disability. The Mini International Neuropsychiatric Interview (M.I.N.I; Sheehan, Janavas, Baker *et al*., 1992.) was used to rule out any current or past mental health problems using the Diagnostic and Statistical Manual (DSM-IV; APA, 2000) classification. Participants received £20.00 for their time upon completion of assessments.

3.4.3. Measures

(a) Functional Outcome:

Assessments of social and role functioning in psychosis have been standardised on chronic populations. This is problematic as they may not be sensitive in differentiating the full range of functioning that is likely to occur earlier in the course of the illness. Furthermore, the scales are often confounded by combining functioning with psychiatric symptoms and often do not distinguish between different forms of functioning (i.e. social and role functioning); all of which have been shown to have somewhat distinct trajectories (Harvey & Belack, 2009).

The Global Functioning: Social (GF: Social; Auther, Smith, & Cornblatt, 2006) and Global

Functioning: Role (GF: Role; Niendam, Bearden, Johnson, & Cannon, 2006).

The Global Functioning Scales are clinician-rated scales which provide parallel (one focusing on social, and the other targeting role functioning) scales that take age and phase of illness into account (Appendix B-1).

The GF: Social scale focuses on age-appropriate relationships outside of the family, the quantity and quality of the relationships, and the level of social withdrawal from family and friends. The GF: Role is rated based on performance in work, education or as a homemaker. The scales assess how demanding the role is, and the level of independence within that role.

Scores range from 1 to 10 (10 indicates superior functioning and 1 represents extreme dysfunction). The scales have detailed anchor points to increase reliability of the ratings (Cornblatt *et al.*, 2007). 'Current' functioning was rated for the past month, and this information was collected by a trained interviewer at baseline and at 12-month follow-up.

The scales were originally designed to assess functioning in the prodromal phase of illness and were shown to have acceptable construct validity (i.e. the scales were measuring what they were supposed to be measuring), and high inter-rater reliability (Cornblatt *et al.*, 2007). The reliability coefficients (α- levels) for current social and role

functioning respectively were 0.85 and 0.93 (Cornblatt *et al*., 2007). Furthermore, Piskulic, Addington, Auther *et al*. (2011) have provided evidence of good construct validity in a first episode sample using the GF: Social and GF: Role scales.

(b) Psychopathology:

(i) *Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987).* This widely used scale is a 30-item-scale which assesses the severity of positive and negative symptoms of schizophrenia as well as general psychopathology (Appendix B-2). There are seven rating points for each item with detailed anchor points, which represent increasing psychopathology (1 = absent to 7 = extreme). Of the 30 items, 7 items represent positive symptoms (score range of 7 to 49), 7 items represent negative symptoms (score range of 7 to 49), and 16 items represent general psychopathology (score range of 16 to 105). Scores were summated for each of these separate components.

 The PANSS has good inter-rater, test-retest and internal reliability, and established internal, external and construct validity (Kay *et al.*, 1987). The PANSS was administered at baseline and at 12-month follow-up by a trained interviewer.

(c) Diagnosis:

The Operational Criteria Checklist (OPCRIT; McGuffin, Farmer & Harvey, 1991). OPCRIT is a widely-used computer programme which generates an objective diagnosis of psychotic and affective disorders based on a 90-item electronic checklist. In this study, information on the service user's first episode was collected from online medical

notes to inform the diagnosis. The diagnosis was confirmed based on ICD-10 (World

Health Organisation, WHO; 1992) criteria. OPCRIT has been shown to have good inter-

rater reliability using ICD-10 (kappa = 0.70) in a research setting (Williams, Farmer,

Ackenheil, Kaufmann & McGuffin, 1996).

(d) Clinical and Premorbid variables:

Clinical and premorbid measures include any factors that are 'predetermined' in the sample on

presentation, which include:

(i)   Duration of Untreated Psychosis (DUP; Larsen, McGlashan & Moe, 1996).

         DUP is defined as the delay between onset of psychosis and onset of criteria

         treatment (Larsen, McGlashan & Moe, 1996). The onset of psychosis was

         defined by the presence of one psychotic symptom rating above a level 4 on the

         PANSS positive scale, or a cluster of positive symptoms scoring above a level

         7 on the PANSS negative scale, with a duration of 2 weeks or more. This

         information was collected retrospectively from online medical notes and

         participant interviews in a standardised method described by Larsen and

         colleagues (1996). As a small number of individuals in the sample had long

         DUPs, the median DUP was calculated to avoid skew of the data.

(ii)   Premorbid Social Adjustment: The Premorbid Social Adjustment Scale (PAS;

         Cannon, Jones, Gilvarry, Rifkin, *et al*., 1997) is a 26-item interview-based

         measure that retrospectively assesses social functioning from Childhood (up to

         11 years), early adolescence (12-15 years) and late adolescence (16-18 years)

(Appendix B-3). It assesses social isolation, peer relationships, school functioning and the ability to function outside of the family. The capacity to form socio-sexual relationships is also assessed from age 12 onwards. Functioning is rated on a 7-point scale which ranges from 0 (healthiest adjustment) to 6 (worst adjustment). The PAS has good predictive and concurrent validity and is widely used in first episode psychosis research (Brill, Reichenberg, Weiser & Rabinowitz, 2008). PAS was collected at 12-month follow-up due to time constraints when collecting baseline data.

(f) Neurocognitive assessments

The neurocognitive measures were selected to represent three separate cognitive domains that have been linked to impairment in early psychosis: Verbal comprehension, perceptual reasoning, and verbal learning and memory (Allot *et al*., 2011). Whilst a number of studies have comprehensively assessed NC and its relationship with functional outcome in FEP, fewer studies have explored the role of SC on functioning in FEP (Allott, Liu, Proffitt, & Killackey, 2011). As such, a decision was made to not include a full neurocognitive battery in this study due the high number of predictor variables.

(i) Logical Memory subtest - Wechsler Memory Scale Revised – IV (WMS-IV; Wechsler, 1987). This is a measure of verbal learning and memory. A participant is read two short stories; immediately after each one is read, they are asked to repeat the story as close to verbatim as possible (Appendix B-4). The WMS has

good construct validity as a measure of verbal learning and memory (Larabee, Kane & Schuck, 1983).

(ii) Vocabulary subtest Wechsler Adult Intelligence Scale - IV (WAIS-IV; Wechsler, 1981). This is a measure of verbal comprehension and production in which participants are asked to define several words and pictures (Appendix B-5). The subtest has 30 items, which includes 3 picture items and 27 verbal items. It is also a measure of the participant's crystallized intelligence, long-term memory and learning ability (Wechsler, 2008).

(iii) Block Design subtest Wechsler Adult Intelligence Scale - IV (Wechsler, 1981). Block Design measures perceptual reasoning, problem-solving skills and visuospatial ability (Wechsler, 2008). Participants are presented with several geometric designs, which they should reproduce by arranging red and white blocks accordingly within a set time frame. The subtest has 14 items in total. It is scored by the number of correctly reproduced patterns (Appendix B-6).

Raw scores for each of the neurocognitive subtests were calculated and converted into age standardised scores with a range from 1-19, a mean of 10 and a standard deviation of 3.

The Wechsler scales have strong psychometric properties: there is strong evidence of validity based on the scales' internal structure (the degree of relationship between test items and the construct being measured; Wechsler,

1981, 1987, 2008), content validity (the degree to which the test items relate to the construct being measured), and finally, it is highly correlated with other measures of cognitive ability, thus demonstrating the WAIS' construct validity (Wechsler, 2008). There is also strong evidence to support the internal consistency and test-retest stability, overall demonstrating the reliability of the Wechsler scales (Wechsler, 2008).

(g) Social Cognitive Assessments

Four SC measures were selected to assess each of the four most commonly impaired domains in psychosis: emotion perception (EP), social perception or social knowledge (SK), theory of mind (ToM) and attributional style (AS; Couture *et al*., 2006).

(i) Picture sequencing task (Langdon & Coltheart, 1999).

This non-verbal task assesses Theory of Mind (ToM) in the context of understanding false beliefs (Appendix B-7 & 8). The task was originally designed to investigate ToM deficits in autism. The task has since been adapted to demonstrate selective ToM deficits (independent of low IQ, poor logical reasoning, or executive dysfunction) in individuals with psychosis (Langdon, Ward & Coltheart, 2010; Langdon *et al*., 2014).

The task requires participants to correctly sequence four types of stories: mechanical (cause and effect reasoning), social script (basic social reasoning), false-belief (infer a character's mistaken belief), and capture (inhibition of a

misleading cue). The stories are depicted in a 4-card picture sequence, presented in a *pseudo*-random order, with each picture sequence scored out of six. There are two practice sequences, and a further four sequences for each story type. The mean score is averaged for each story type, along with response times for correctly ordered sequences. The average score of the false-belief stories were entered into the final regression model.

(ii) Mayer-Salovey-Caruso Emotional Intelligence Test – Perceiving Emotions (MSCEIT; Mayer, Salovey, & Caruso, 2002).

The MSCEIT is a paper and pencil test which involves two separate tasks: The Faces task and Picture task (Appendix B-9 & 10). The Faces task involves identifying facial affect, and the Picture task involves identification of emotion conveyed by pictures of designs. Participants were asked to rate on a Likert scale (0-5), how much emotion is conveyed by a person's face or a picture. The emotions that the participants were asked to rate were: happiness, sadness, fear, surprise, disgust, anger and excitement. In total, there were four faces and six pictures, with five emotions to rate for each one. An age standardised 'Branch Score' was calculated for the MSCEIT, which combined the total score for the Faces and Picture Task. The MSCEIT has been shown to have excellent reliability in a non-clinical sample for branch and total test scores (Mayer, Salovey, Caruso & Sitarenios, 2003).

(iii) Ambiguous Intentions Hostility Questionnaire (AIHQ; Combs, Wicher, & Waldheter, 2007).

The AIHQ specifically targets hostile social cognitive bias in psychosis. It has 15-items consisting of short vignettes, which reflect varying negative outcomes that vary in intentionality: intentional, accidental, and ambiguous intentions. For each vignette, participants were asked why they thought the person acted in that way (hostility index). The participant then rated, on Likert scales, if they thought the person acted on purpose (1 "definitely no" to 6 "definitely yes"), felt angry (1 "not at all angry" to 5 "very angry"), and blamed the person (1 "not at all angry" to 5 "very much"). An average of these scores was calculated to form a 'blame score'. Finally, the participant had to state how they would react to that that situation (aggression index). Responses for the hostility and aggression questions were coded by the researcher on a scale that ranged from 1 "not at all hostile / aggressive" to 5 "very hostile / aggressive". Scores were then averaged for the intentional, accidental, and ambiguous items (Appendix B11 & 12).

The AIHQ has been shown to have good levels of reliability and validity in a non-clinical sample (Combs, Wicher, & Waldheter, 2007), is predictive of aggressive behaviour (Waldheter, Jones, Johnson, & Penn, 2005), and was shown to be a sensitive outcome measure in a psychosocial intervention trial in inpatients with schizophrenia (Penn *et al.*, 2007).

Previous research has shown that the self-rated blame scores for ambiguous situations has the most consistent relationship with paranoia and hostility than

responses to intentional and accidental situations (Combs, Wicher, & Waldheter, 2007). A recent psychometric evaluation of the AIHQ in a FEP sample showed that the blame score (BS) subscale had the strongest psychometric properties (Ludwig, Pinkham, Harvey, Kelsven & Pinkham, 2017). Therefore, due the high number for variables in the analysis, only the blame score for ambiguous situations were included in the final analysis as they are the most likely to demonstrate a SC bias.

(iv) The Social Knowledge Questionnaire (SKQ; Cutting & Murphy, 1988 & 1990). This is a 9-item multiple-choice questionnaire that assesses a participant's understanding of how others act in social situations. A score of '1' is given for correct items, and a score of '0' for incorrect items (Appendix B-13).

(h) Socio-demographic assessment of the Control Sample

To compare the socio- demographic profiles between the FEP sample and age-matched controls, ACORN (A classification of Residential Neighbourhoods; CACI, 2003) classification was used. ACORN is a geo-demographic segmentation of the UK's population, which segments postcodes into number of categories (e.g. Wealthy Achievers to Hard Pressed). The ACORN postcode group was used as a proxy for socioeconomic status.

(i) Screening tool for past and present mental health problems in the control sample

The Mini International Neuropsychiatric Interview (Sheehan *et al*., 1998; MINI). The MINI is a widely used, brief structured diagnostic interview for a spectrum of DSM-IV

psychiatric disorders (Appendix B-14). The MINI has been shown to generate reliable and valid DSM diagnoses in adults (Sheehan *et al*., 1998). The MINI was conducted with the healthy control participants during a screening process to check for study eligibility. Participants were excluded if they had current (past month) or historic mental health problems or substance misuse.

3.4.4. Procedure

All new referrals to EIS in Birmingham between 2012 and 2014 were screened for study eligibility using online case notes. Once potential participants had been identified, care coordinators were approached by the study team to discuss the appropriateness of the service user's involvement in research, and to check any concerns with regards to risk. If appropriate, the study team contacted the service user directly to invite them to participate in the research. Prior to obtaining consent (Appendix A-3), participants were given verbal and written information about the study and had the opportunity to ask questions about their involvement in the research (Appendix A-2). Once consent was obtained, participants were asked to complete a battery of assessments, which included measures of: (a) psychopathology (psychosis symptoms); (b) functioning (social and role); (c) four social cognitive sub-domains; (d) three neurocognitive sub-domains; and (e) demographic information. Participants were then reassessed after 12 months to complete follow-up measures of symptoms and functioning. Healthy matched control participants were recruited between 2013 and 2014, and if eligible and consented (Appendix A-4 & 5) completed the same battery of cognitive measures and functioning in a one-off assessment with the researcher. All participants received £20 for their time upon completion of the assessments.

3.4.5. Statistical Analyses

Twelve-month follow-up scores for GF: Social and GF: Role were analysed separately to explore social and role outcome trajectories (Figure 1). To identify subgroups of individuals based on functional outcome, clinical cut-off scores were used from the Global Functional Scales (GFS; Cornblatt *et al*., 2007). Scores of 7 and above on the GFS are indicative of mild impairment to superior functioning and represent functioning in the normal range (Cornblatt *et al*., 2007). Scores of 6 and below represent impaired functioning, with the lowest scores indicating the most extreme dysfunction (Cornblatt *et al*., 2007). Therefore, a 'good' outcome was defined by a score between 7 and 10, and a 'poor' outcome was defined by a score in the range of 1 and 6 on the GF: Social and GF: Role at 12-month follow-up.

Examination of the Q-Q plots indicated that the data for the FEP and Healthy Control group was reasonably normally distributed for most the variables. Results of a 1-sample Kolmogorov-Smirnov (K-S) test indicated that there were violations to the assumption of normality (with K-S Z values ranging from 0.061 to 0.289 and *p* values ranging from 0.00 to 0.20), however, this is not an uncommon finding in larger samples (Pallant, 2011).To explore group differences in functional outcome ('good' vs 'poor' outcome), an independent samples t-test was used as it is robust to violations of normality, particularly with a large sample size (e.g. 30 +); it also benefits from having more power over non-parametric statistics (Gravetter & Wallnau, 2000; Pallant, 2001). A logarithmic transformation was conducted for the DUP variable due to its non-normal, skewed distribution. The transformed variable – log_DUP – was therefore used in the analysis to correct the violation of normality.

An independent samples t-test was conducted using the following variables: premorbid / demographic (PAS, Age, Years in Education), log_DUP, symptoms (PANSS Positive, Negative and General Symptoms), NC (Verbal learning and memory, Verbal comprehension, Non-verbal problem solving), and SC (Theory of Mind, Social Knowledge, Attribution of blame bias, and emotion perception). A Chi-square test was used for the following binary variables: socio-economic status and gender.

The final step of the analysis was to test if baseline SC and NC can predict functional outcome group at 12-month follow-up (Figure 1). A logistic regression was employed in order to predict the categorical dichotomy (i.e. the predicted probability of belonging to one 'outcome' group over the other). Two outcome groups ('poor' and 'good') were defined using the clinical cut off scores of the Global Functioning Scales (Cornblatt *et al*., 2007). As such, those with 'poor outcome' at follow-up were given a code of '1', whilst those with a 'good outcome' at follow-up were given a code of '0'. This meant that the regression would estimate the change in the odds of membership to the 'poor outcome group' over the 'good outcome group' for a one-unit increase in the predictor variables (Burns & Burns, 2008; Meyers, Gamst & Guarino, 2017).

Despite the results of the K-S indicating departures of normality, the independent variables in a logistic regression do not need to be normally distributed (Burns & Burns, 2008). Separate logistic regression models were built for social and role functioning, with 'poor' and 'good' functioning groups as the dependent variables. Categorical variables were selected over continuous variables as it was felt that being able to 'classify' individuals with poor functioning using a cut-off score had greater clinical applicability and validity, and identification of the predictors of the poor outcome group could lead to potential targets for intervention.

In the first regression analysis, cognitive variables were explored in a separate model initially to investigate any univariate cognitive predictors of poor outcome. In a second stage of the regression analysis, negative symptoms were included in the regression model. This was done by adding a block for 'symptoms', followed by the cognitive variables in a second block.

A backward method was selected to find the most parsimonious predictors of outcome. The Nagelkerke pseudo R^2 (R^2_N) statistic was reported as an approximate measure of the proportion of explained variation of the final models (Nagelkerke, 1991).

Group comparisons between the healthy control and FEP samples (poor and good social and role outcome groups) on demographics, functioning and cognition were explored using a one-way between-groups analysis of variance (ANOVA), and a Chi-square test for binary variables. An ANOVA was selected over a non-parametric test as it is tolerant of violations of normality with a sample size of 30 or more (Pallant, 2001). Effect sizes for cognitive variables were calculated using a formula for Eta Squared (Pallant, 2011):

$$\frac{t^2}{t^2 + n - 1}$$

Eta Squared values were interpreted by the guidelines set out by Cohen (1988) (small effect = .01; moderate effect = .06; large effect = .14). Data was analysed using SPSS software, Version 22.
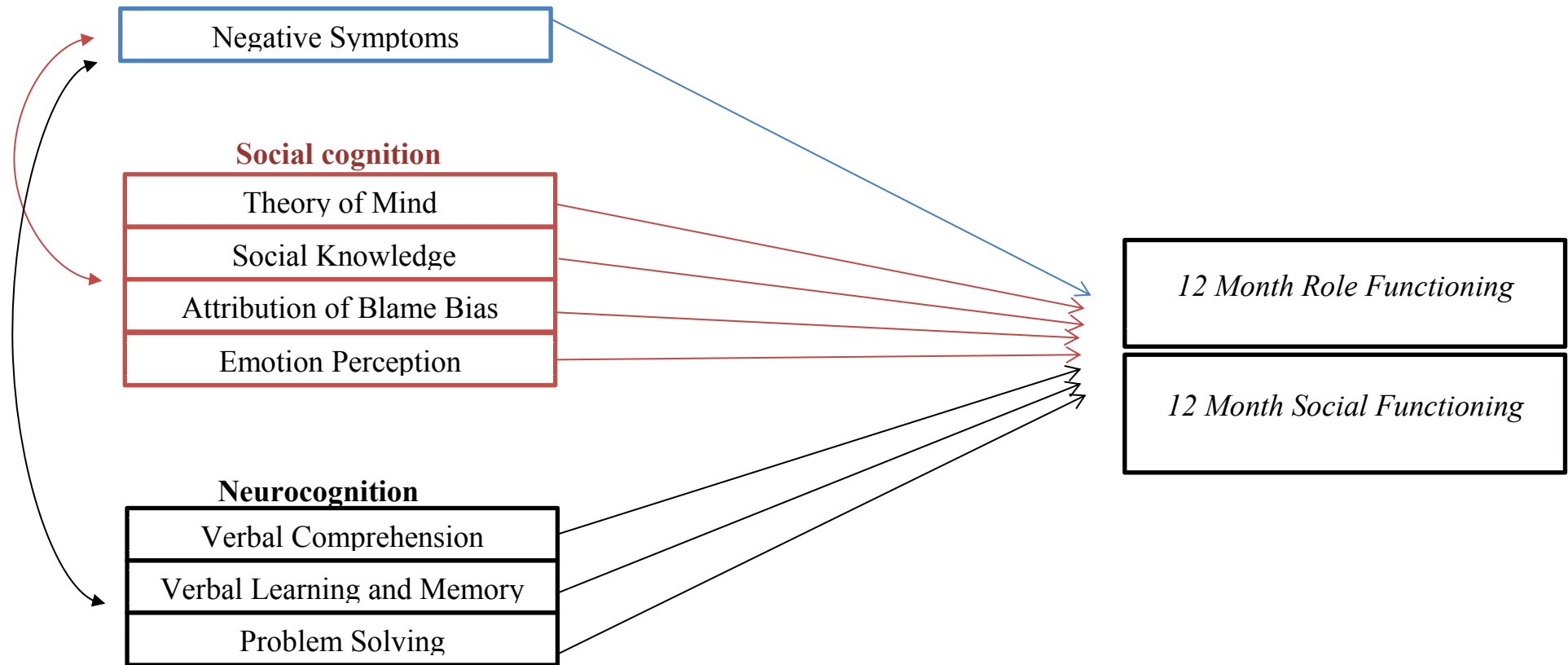
Figure 1: Visual representation of the social cognitive, neurocognitive and symptom variables examined in this study.

3.5. Results

3.5.1. The Sample

     (i)   FEP group

In total, 147 service users satisfied study criteria and were approached by the research team. One-hundred service users consented to take part in the study, 40 service users refused consent, and 7 were unable to be contacted. One participant withdrew from the study at baseline and another participant became ineligible due to having an autoimmune disorder affecting the brain (Lupus erythematosus), leaving a final sample of 98 consented participants (Mean time spent in EI service = 7 months; Median DUP = 8.4 weeks). Table 3 provides a breakdown of the sample characteristics at baseline. 76 participants (77.6%) completed a follow-up assessment after 12 months. Of those participants who did not return for follow-up: 6 were unable to be captured due to lack of engagement or change of contact details; 8 refused to be seen for a follow-up assessment but did not withdraw from the study, and finally, 8 moved out of area. Where there was sufficient information, follow-up data on current level of social and role functioning (over the past month) was rated from the participant's online medical notes. To increase the reliability of the rating, two members of the research team rated the level of functioning based on the information collected from the online medical notes. The ratings were compared for concordance. Thus, at 12-month follow-up, data on the primary outcome (Global Functioning Scales, Cornblatt *et al.*, 2007) was available for 89 (90.8%) participants.

     (ii)   Healthy Control Group

In total, 30 controls were recruited to the study. Although there were no significant differences between the control sample and FEP sample in terms of age, gender, ethnicity and level of

education / qualifications, the groups did significantly differ on socio-economic status (Table 3). Seventy-seven percent of the FEP sample were living in areas of socio-economic deprivation, in contrast to 53% of the healthy control group, according to the ACORN classification of postcodes (see method section, page 59).

Table 3. Demographic and clinical characteristics of the psychosis group and healthy control group at baseline

	FEP (N= 98)	Healthy Controls (N = 30)	Statistical Significance
Mean Age (years; mean / SD)	23.6 (4.7)	22 (4.7)	NS [a]
Males (n; %)	77; 79	15; 50	NS [b]
Years in Education (mean / SD)	12.40 (2.4)	12.7 (2.18)	NS [a]
Qualifications (%)			
No qualifications	9.2	3.3	
School Qualifications	36.7	40	NS [b]
Further education	36.7	36.7	
Higher Education	17.3	20	
Employment Status (%)			
Unemployed	60.2	6.7	<0.001[b]
Ethnicity (%)			
Caucasian	45	40	
Asian	35	33.3	NS [b]
Black	14	10	
Other	6	16.7	
OPCRIT ICD-10 Diagnosis			
Non-affective psychosis (%)	90	n/a	n/a
Affective psychosis (%)	10	n/a	
ACORN Classification			
Living in areas of socio-economic deprivation (%)	77	53	.016 [b]

[a] Independent samples t-test. [b] Chi-Square test. NS = Non-significant.

(iii) Defining 'poor' and 'good' functioning groups at 12-month follow-up

Using the clinical cut-off scores of GFS (Cornblatt *et al*., 2007), 52 participants were classified as having a 'poor' role functioning at follow-up, and 37 with 'good' role functioning at 12-month follow-up. Using the GFS social functioning, 40 participants were classified as having 'poor' social functioning at follow-up, and 49 as 'good' social functioning at follow-up. Forty-

nine percent of individuals met criteria for both poor role and social functioning, whereas 21%

had functional impairment on only one of the scales (10% had poor social outcome with good

role outcome, and 11% had poor role outcome with good social outcome) at 12-month follow-

up.

An *a priori* power analysis using GPower (Faul & Erdfelder, 1996) showed that with power (1

– β) set at 0.90, a total sample size of N = 68 (N= 34 per group) is needed in order for group

differences to achieve statistical significance at the 0.05 alpha level with a large effect size

(0.8). The sample used in this study therefore had power to detect a large effect between the

outcome groups.

3.5.2. Data Analysis 1 (Research Question 1): Do the 'poor' social and role outcome groups

differ from the 'good' outcome groups on cognition, symptoms, and on demographic and

premorbid characteristics?

      (i)   Demographic and premorbid characteristics of the 'poor' and 'good' outcome

            groups for Social and Role functioning.

Independent t-test comparisons of demographic and premorbid characteristics between the poor

and good social and role outcome groups are presented in Table 4. For social and role outcome,

the poor and good outcome groups did not differ significantly on demographic characteristics

including gender, age, years in education and socio-economic status.

Individuals with poor role outcomes at 12 months had poorer role functioning at baseline and poorer premorbid: scholastic performance, social withdrawal, and peer relationships in late adolescence, compared to those with good role outcomes.

Individuals with poor social outcomes had poor social functioning at baseline, poorer premorbid socio-sexual relationships, poorer adaption to school in late adolescence and were more socially withdrawn in early and late adolescence compared to those with good social outcomes.

The groups did not significantly differ on clinical characteristics such as age at onset of psychosis, DUP, or positive symptoms (Table 5). However as expected, the poor social and role outcome groups did have significantly higher levels of negative symptoms and general symptomatology at baseline (Table 5).

Table 4. Comparison of the demographic characteristics and premorbid functioning of the FEP 'poor' and 'good' social and role outcomes.

	Poor Role Outcome (N = 52)	Good Role Outcome (N = 37)			Poor Social Outcome (N = 40)	Good Social Outcome (N = 49)		
	M±SD	M±SD	T	p – value	M±SD	M±SD	t	p - value
Premorbid variables								
Childhood Scholastic Performance	2.63; 1.67	1.53; 1.93	2.42	**0.02**	2.64; 1.76	1.96;1.71	1.77	0.08
Early Adolescence Scholastic Performance	3.29; 1.66	2.30; 1.66	2.73	**0.01**	3.28; 1.85	2.59; 1.62	1.82	0.07
Late Adolescence Scholastic Performance	2.35; 1.90	2.28; 1.87	2.15	**0.04**	3.09; 1.77	2.59; 1.67	1.24	0.22
Early Adolescence Socio-Sexual Relationships	1.34; 1.63	1.38; 1.67	-0.11	0.92	2.17; 1.71	0.86; 1.40	3.75 [a]	**<0.01**
Early Adolescence Sociability and Withdrawal	1.60; 1.44	1.11; 1.58	1.48	.144	2.17; 1.71	0.86; 1.40	2.37 [a]	**0.02**
Late Adolescence	1.68; 1.51	0.87; 1.31	2.35	**0.02**	1.81; 1.58	0.90; 1.25	2.73	**0.01**

	M; SD	M; SD	t	p-value	M; SD	M; SD	t	p-value
Sociability and Withdrawal								
Late Adolescence Adaption to School	2.15; 1.59	1.59; 1.90	1.34	.185	2.44; 1.87	1.59; 1.65	2.03	**0.05**
Late Adolescence Socio-Sexual Relationships	1.88; 1.91	1.55; 2.10	0.68	.502	2.66; 2.10	0.95; 1.50	3.85 [a]	**<0.01**
Late Adolescence Peer Relationships	2.05; 1.28	1.27; 1.36	2.47	**0.02**	2.00; 1.32	1.48; 1.36	1.65	0.10
Demographic variables								
Age (years)	24.06; 5.00	22.68; 4.09	1.38	0.17	23.90; 4.67	23.18; 4.65	0.72	0.47
Years in Education	12.23; 2.53	12.54; 2.04	-0.62	0.54	11.93; 2.66	12.71; 1.97	-1.56 [a]	0.12
			χ^2	p – value			χ^2	p - value
Socio-economic status	———	———	.000 [b]	1.000	———	———	2.92 [b]	5.89
Gender	——	——	.281 [b]	0.60	——	——	1.22 [b]	0.73

[a] M= Mean. SD = Standard Deviation. Violation of the assumption of equal variance (Levene's Test for Equality of Variances $p = <.05$). Compensatory t-value reported. [b] Yates' Correction for Continuity statistic was reported as it compensates for the overestimation of the chi-square value in 2x2 design.

(ii) Baseline social cognitive and neurocognitive comparisons between 'poor' and 'good' outcome groups.

Parametric group comparisons of SC and NC variables showed that individuals with poor role outcomes performed significantly worse at baseline on tasks of verbal learning and memory (eta squared = 0.07) and verbal comprehension (eta squared = 0.05) compared to the good role outcome group (Table 5). There were no significant group differences for non-verbal problem solving, social knowledge, emotion perception, attribution bias and theory of mind (Table 5).

For social outcomes, parametric comparisons revealed there were no significant group differences on SC and NC task performance at baseline, except for one SC domain (social knowledge), where individuals with poor social outcomes performed significantly worse at baseline compared to those with good social outcomes (Table 5). The magnitude of difference between the groups was moderate (eta squared = 0.05).

Table 5. Comparison of baseline symptoms and cognition for FEP 'poor' vs 'good' social and role outcomes

	Poor Role Outcome (N = 52)	Good Role Outcome (N = 37)			Poor Social Outcome (N = 40)	Good Social Outcome (N = 49)		
	M±SD	M±SD	t	p – value	M±SD	M±SD	t	p - value
Baseline Clinical Variables								
PANSS Negative Symptoms	16.61; 6.47	11.50; 5.27	4.05 [a]	**<0.001**	17.18; 7.43	12.52; 5.17	-3.32 [a]	**.001**
PANSS Positive Symptoms	12.92; 5.28	11.58; 4.70	1.22	0.23	13.18; 5.74	11.56; 4.14	-1.47 [a]	0.15
PANSS General Symptoms	30.51; 8.13	25.33; 8.25	2.91	**0.01**[**]	30.85; 8.99	26.67; 8.27	-2.24	**.027**
Delay of Untreated Psychosis	1.73; 0.85	1.67; 0.67	0.33	0.74	1.76; .84	1.67; .75	0.54	0.59
Age of onset of psychosis (years)	22.77; 4.97	21.59; 4.21	1.17	0.25	22.45; 4.72	22.14; 4.70	0.31	0.76
Baseline Cognitive variables								
Verbal learning and memory	5.96; 2.33	7.40; 3.07	-2.48	**0.02**	6.00; 2.78	7.02; 2.62	-1.77	0.08
Verbal Comprehension	7.06; 2.67	8.28; 2.88	-2.03	**0.05**	7.44; 3.03	7.63; 2.66	-0.04	0.76

Non-verbal Problem Solving	7.69; 2.39	8.43; 2.93	-1.32	0.19	8.08; 2.84	7.92; 2.50	0.28	0.78
Theory of Mind	3.53; 1.62	4.11; 1.47	-1.72	0.09	3.69; 1.77	3.76; 1.43	-0.21[a]	0.83
Social Knowledge	6.44; 1.72	6.89; 1.60	-1.25	0.21	6.20; 1.79	6.92; 1.57	-2.02	**0.05**
Attribution bias	2.76; 0.72	2.69; 0.91	0.36	0.72	2.69; 0.74	2.71; 0.76	-0.12	0.90
Emotion perception	90.42; 17.79	94.83; 16.83	-1.18	0.24	92.86;19.22	92.02;16.70	0.48	0.63

[a] Violation of the assumption of equal variance (Levene's Test for Equality of Variances $p = <.05$). Compensatory t-value reported.

3.5.3. Data Analysis 2 (Research Question 2): Are the poor and good outcome groups impaired on the social cognitive and neurocognitive tasks?

(i) *Comparing performance on the cognitive tasks between the Healthy Control Group versus FEP Poor and Good Role Outcome Groups*

A one-way between group analysis of variance (ANOVA) was conducted to explore any differences between the healthy control group and the FEP poor and good role outcome groups. There was a statistically significant difference between the 3 groups for verbal learning and memory, vocabulary comprehension, ToM and social knowledge (Table 6).

Post-hoc comparisons using a Tukey HSD test indicated that the FEP poor role outcome group performed significantly worse than the healthy control group on 2 neurocognitive domains (verbal learning and memory and verbal comprehension), and 2 social cognitive domains (social knowledge and ToM).

There were no significant differences between the healthy and FEP good role outcome groups on any of the social cognition tasks, however, there was a significant difference on 1 neurocognitive domain (verbal learning and memory), where the FEP good outcome group also performed worse than the healthy controls (Table 6).

(ii)   Comparing performance on the cognitive tasks between the healthy control group

versus FEP poor and good social outcome groups

Results of a one-way ANOVA between the healthy control group and the poor and good social outcome groups showed that verbal learning and memory, verbal comprehension and social knowledge were significantly different between the groups (Table 6).

Post-hoc comparisons using Tukey HSD indicated that both the poor and good social outcome groups performed significantly worse on 2 neurocognitive tasks (verbal learning and memory, and verbal comprehension) compared to the healthy control group. The 'poor' social outcome group had significantly poorer performance on a social cognitive task (social knowledge) when compared to the healthy control group (Table 3); the good social outcome group was not significantly poorer than the healthy control group on social knowledge.

In summary, results of the comparisons between the FEP outcome groups and the healthy controls show that whilst some NC impairments were found across the poor and good FEP outcome groups, SC impairments by contrast were *only* evident in the poor functional outcome groups.

To further illustrate the extent of cognitive impairment in the FEP social and role outcome groups, an indicative exploratory analysis was carried out on the cognitive domains that were significantly different from the healthy controls. Table 7 shows the percentage of individuals in the FEP poor and good outcome groups falling below the healthy controls' range (using the 95% confidence interval, i.e. 'normal range', on the cognitive tasks). There was greater

cognitive impairment in the poor social and role outcome groups, evidenced by a higher percentage of individuals in the poor outcome groups scoring below the normal range. There was 9% greater impairment in the poor role groups on social knowledge, 21% greater impairment in verbal learning and memory, 28% greater impairment in verbal comprehension, and finally, 21% greater impairment in ToM compared to those with good role outcomes. For the social outcome groups, there was 15% greater impairment for social knowledge, 16% greater impairment on verbal learning and memory, and 12% greater impairment in verbal comprehension for individuals in the poor social outcome group (Table 7).

Table 6. Comparisons of cognitive scores between the healthy control group with the FEP 'poor' and 'good' social and role outcome groups.

	Poor Role Outcome (N = 52)	Good Role Outcome (N = 37)	Healthy control Group (N = 30)			Poor Social Outcome (N = 40)	Good Social Outcome (N = 49)	Healthy control Group (N = 30)		
	M±SD	M±SD	M±SD	*F*	*P*	M±SD	M±SD	M±SD	*F*	*p*
Baseline Cognitive variables										
Verbal learning and memory	5.96; 2.33	7.39; 3.07	9.83; 3.68	16.39	**<0.01**	6.00; 2.78	7.02; 2.62	9.83; 3.68	14.86	**<0.01**
Verbal Comprehension	7.06; 2.67	8.28; 2.88	9.70; 2.69	8.87	**<0.01**	7.44; 3.03	7.63; 2.66	9.70; 2.69	6.69	**<0.01**
Non-verbal Problem Solving	7.69; 2.39	8.43; 2.93	9.13; 2.75	2.87	0.06	8.08; 2.84	7.92; 2.50	9.13; 2.75	2.07	0.13
Theory of Mind	3.53; 1.62	4.11; 1.47	4.34; 1.12	7.21	**0.04**	3.69; 1.77	3.76; 1.43	4.34; 1.12	1.94	0.15

Social Knowledge	6.44; 1.72	6.89; 1.60	7.43; 1.57	9.44	**0.03**	6.20; 1.79	6.92; 1.57	7.43; 1.57	5.02	**0.01**
Attribution bias	2.75; 0.72	2.69; 0.91	2.69; 0.67	0.10	0.90	2.69; 0.74	2.71; 0.76	2.69; 0.67	0.01	0.99
Emotion perception	90.42; 17.79	94.83; 16.83	97.99; 13.81	2.11	0.11	92.86; 19.21	91.02; 16.70	97.99; 13.81	1.61	0.21

M = Mean. SD = Standard Deviation.

Table 7. Indicative exploratory analysis showing the percentage of individuals performing below the healthy control range on the cognitive tasks in the 'poor' and 'good' social and role outcome groups.

Cognitive Variable	Poor Role Outcome Group	Good Role Outcome Group	Poor Social Outcome Group	Good Social Outcome Group
Social Knowledge	44%	35%	50%	35%
Theory of Mind	60%	32%	-----	-----
Verbal Learning and Memory	83%	62%	83%	67%
Verbal Comprehension	39%	11%	35%	23%

NB: Table showing % of individuals below the 95% confidence interval for healthy controls' cognitive task performance.
Exploratory analyses were only carried out on the cognitive variables where the FEP outcome groups showed significantly poorer performance relative to healthy controls (Analysis 2, *i)*.

3.5.4. Data Analysis 3 (Research Question 3): Does social cognition and neurocognition predict 12-month social and role outcomes when accounting for negative symptoms?

The univariate analyses showed that the following baseline variables differentiated between the social outcome groups at 12 months follow-up: negative symptoms, general symptoms and social knowledge (Table 5). For role outcome at 12 months, the following baseline variables differentiated between the poor and good role outcome groups: negative symptoms, general symptoms, verbal comprehension and verbal learning and memory (Table 5).

In the following analyses, the significant terms (above) were entered into the equation to test the relative predictive efficacy of these variables in predicting social and role outcome at 12 months. First, all the cognitive variables were entered into a separate regression model to assess their independent contribution to functional outcome. In a second analysis, symptoms were added in a separate block in the regression model to see if cognition could contribute additional variance beyond symptoms. In this analysis, due to the high number of predictor variables, only the significant terms (described above) were entered into the regression to avoid saturating the model.

(i)   *Role Outcome*

Results of a binary logistic regression showed that when the SC and NC variables were considered alone in predicting role outcome, verbal learning and memory significantly predicted group membership at 12 months ($r = -.184$, $p = .033$, $R^2_{N} = .076$). Those with better verbal memory are less likely to have poor functioning (OR = 0.83). This

association was no longer significant once symptoms were included in the full model. The final logistic regression model for role outcome can be seen in Table 8.

A backward regression reduced the full regression model leaving negative symptoms as the sole significant predictor of (poor) role outcome (x^2= 13.82; p = <.001), explaining 20% (R^2 $_N$ = .202) of variance in role outcome. In other words, having more negative symptoms at baseline increased the likelihood of poor role outcome at 12-month follow-up (Table 8).

(ii)   Social Outcome

In the initial regression model which included the SC and NC variables alone, results demonstrated that baseline social knowledge significantly predicted social functioning at 12-month follow-up (*r* =-.275*, p* = .049*, R²* $_{N\ =}$ .064). Those with better social knowledge at baseline were less likely to be in the poor functioning groups at follow-up (OR = .76). However, in a full regression model, which included the symptom variables, this effect was no longer significant (Table 9).

Again, in the final model, baseline negative symptoms was the only independent significant predictor of social outcome (x^2= 11.02; p = .001), accounting for 15.9% (R^2 $_N$ = 0.159) of the overall variance. Participants with more negative symptoms at baseline had greater odds of being in the poor social outcome group (Table 9).

Table 8. Final logistic regression model predicting binary role outcome

Predictors	Beta	Wald χ^2	$p-value$	Odds Ratio
Negative Symptoms	1.146	10.86	**.001**	1.157

Table 9. Final logistic regression model predicting binary social outcome

Predictors	Beta	Wald χ^2	$p-value$	Odds Ratio
Negative Symptoms	.115	9.593	**.002**	1.122

3.5.5. Exploratory Analyses

Based on the results of the regression analyses, exploratory analyses were carried out to test whether the cognitive variables share variance with negative symptoms, and thus potentially indirectly influence functioning via negative symptoms. Previous research has demonstrated a close relationship between these constructs (Addington *et al*., 2015; Lysaker *et al*., 2013; Lysaker *et al*., 2015; Ventura *et al*., 2009). To explore this in the present study, two analyses were carried out. Firstly, a Pearson correlation analysis showed that each of the cognitive variables, apart from block design, were significantly associated with negative symptoms, with a small to medium strength (Table 10). Secondly, a regression analysis tested whether baseline cognitive variables contribute variance in negative symptoms concurrently (negative symptoms at baseline) and prospectively (negative symptoms at 12-month follow-up). Multiple correlation coefficients from these analyses indicated a moderate positive linear association between negative symptoms and the combined NC and SC cognitive variables at baseline (R = .45; p = .008; R^2 = .200), and at 12-month follow-up (R = .45; p = .041; R^2 = .200).

Table 10. Pearson Correlations between baseline cognitive variables and negative symptoms

Measure	PANSS Negative Symptoms
WMS Logical Memory	**-.316**[**]
WAIS Block Design	-.166
WAIS Vocabulary	**-.300**[**]
Social Knowledge	**-.255**[*]
False Belief Story	**-.235**[*]
Attribution of Blame Bias	**.230**[*]
MSCEIT	**-.214**[*]

* $p < 0.05$. ** $p < 0.01$.

3.6. Discussion

This was the first study to comprehensively assess early cognitive predictors (social cognition and neurocognition) in understanding variability in the early trajectory of social and role functioning in FEP and benchmark these cognitive dimensions against a healthy matched community sample. The principal findings of this prospective study were as follows:

First, the 'poor' social and role outcome groups were characterized by widespread impairments in their premorbid functioning, suggesting that these early trajectories are a continuation of those in adolescence and are likely to be an enduring trait.

Secondly, the sub-groups of individuals who had poor social and role outcomes differed from those who had good outcomes in terms of greater negative and general symptoms at baseline, and more severe cognitive impairments. In the cognitive domains that were significantly impaired, a higher percentage of individuals in the poor outcome groups scored below the average range of the healthy control group. Around half of those individuals with poor social and role outcomes had low scores on social knowledge, and 60% of those with poor role outcomes scored below the average range on Theory of Mind (ToM). Most notably, 80% of individuals in the poor social and role outcome groups scored below the 'normal range' on logical memory.

Third, results also showed that the trajectories of social and role functioning are somewhat distinct from one-another. Poor *social* functioning was characterized by significant impairments in interpersonal problems during adolescence, and the social cognitive domain –

social knowledge – was the best cognitive predictor of social outcome at 12 months. Those with poor *role* functioning had significant academic impairments during childhood and adolescence, and when the cognitive variables were considered in a regression model, role outcome at 12-months was predicted by the NC domain – logical memory. These findings seem internally congruent, namely that individuals who have poor understanding of their social world appear to struggle with their interpersonal relationships, and that those who have a poorer verbal memory seem to struggle to maintain performance in main roles such as work or education.

Despite this, when negative symptoms were included in the regression model, neither SC nor NC contributed additional variance in functional outcome: negative symptoms at baseline were predictive of 12 month social and role outcomes in individuals with FEP.

3.6.1. Exploring the relationships between cognition, negative symptoms, and social and role outcome

The finding that the cognitive predictors of social and role outcomes became non-significant after the addition of negative symptoms in the regression model was investigated in further analyses. Indicative exploratory analyses showed that the NC and SC variables were moderately linked to negative symptoms, such that NC and SC contributed 20% variance to negative symptoms cross-sectionally and prospectively. These findings show that a moderate relationship exists between negative symptoms and cognition.

It is not clear if poor cognition plays a role in the formation of negative symptoms, if for example, the 'concept' of negative symptoms is simply a summary of impaired cognitive

dimensions (e.g. memory), or if they are indeed independent constructs. However, findings from this study and previous studies show that these two constructs are interwoven (Healey *et al*., 2016; Piskulic *et al*., 2011). For example, it is argued that the inability to form mental representations of self and others (i.e. Theory of Mind) leads to difficulties in building rapport and can become a barrier to seeking and anticipating pleasure and pursue goal-directed behavior, potentially resulting in social withdrawal – a major negative symptom (Buck *et al*., 2014; Lysaker & Dimaggio, 2014).

In established psychosis, previous studies have shown that the effect of cognition (SC and NC) on functioning was mediated by negative symptoms (Madeira *et al*., 2016; Mehta, Bhagyavathi & Thrithalli, 2014; Ventura *et al*., 2009); with motivational deficits playing a key role in mediating this relationship (Gard, Fisher, Garett, Genevsky & Vinogradov, 2009; Meyer *et al*., 2014). Furthermore, in studies which have targeted cognitive impairment as means of improving functioning in individuals with psychosis, cognitive improvements were reported in addition to improvements in negative symptoms and functioning (Roder *et al*., 2006; Roder *et al*., 2011), suggesting that negative symptoms and cognition are phenomenologically related. Delineating this relationship in early psychosis has important implications for intervention, as targeting impaired cognition could have a direct impact on negative symptoms, and in turn, improve functional outcome (Gard *et al*., 2009).

3.6.2. Comparison with findings from previous literature

Nevertheless, the findings of this study are in line with other studies which have shown that negative symptoms are an important determinant of poor functional outcome in early psychosis

(Gee *et al*., 2016; Rammou *et al*., 2017).The findings are further corroborated by several recent publications that found that when negative symptoms were compared to SC and NC variables in the prediction of functional outcome in FEP, negative symptoms significantly contributed to the prediction of outcome, whilst SC and NC did not (Cacciotti-Saija *et al*., 2016; Horan *et al*., 2012; Langdon *et al*., 2014; Simons *et al*., 2016). Only one of these studies (Simons *et al*., 2016) used a prospective design as in this present study. Exploring the prospective relationship between functioning and cognition allows for greater inferences of causality to be made, and thus, the findings from this study, together with that of Simons and colleagues (2016) suggests that the presence of negative symptoms early in the course of psychosis is a useful marker of later social and role functioning.

In contrast to these findings, a similar study by Stouten and colleagues (2014) found that ToM significantly predicted problems with relationships at 12-month follow-up, whilst negative symptoms and general symptoms predicted problems with work and study at follow-up. However, despite comprehensively assessing SC and NC, most final regression models in Stouten and colleagues' study did not contain any other cognitive predictor, which again is in line with other studies showing that cognition alone is of modest importance in explaining functional outcome in FEP (Allott, Liu, Proffitt, & Killackey, 2011; Stouten *et al*., 2014).

3.6.3. Cognitive impairment and social and role outcome in early psychosis – comparisons with findings from previous literature in chronic schizophrenia

Alongside the evidence from other longitudinal studies in FEP, it appears that SC and NC play a more subordinate role in predicting early functional outcome in early psychosis; this is in

contrast to chronic samples, where findings may be influenced by effects associated with long term-illness, such as multiple episodes and anti-psychotic treatment (Allot *et al*., 2011). It also indicates that the association between cognition and poor functioning is stronger in individuals with an established illness (Simons *et al*., 2016). This is in line with the proposed notion of clinical staging in psychosis, where each stage of illness is impacted by different factors (Allott, Liu, Proffitt, & Killackey, 2011; McGorry *et al*., 2007).

Another possible explanation for the differences in findings between this study and chronic psychosis may be the level of intensive support offered by EIS teams after a first episode. During this early phase of illness where outcomes are heterogeneous, some individuals may learn to enhance their level of functioning whilst finding compensatory mechanisms to overcome cognitive deficits. Or, it may be the case that cognition could indirectly improve because of psychosocial interventions which are applied more consistently in early intervention services (Simons *et al*., 2016). Cognition was only assessed at baseline in this study, and therefore it may be of interest for future studies to explore whether any change in cognition during this time also corresponds with changes in functioning. This possibility is explored in Chapter 4 where changes in functioning linked to a trial psychosocial intervention are examined against any co-occurring changes in cognition.

It is particularly interesting that SC impairment, specifically impairments in ToM and social knowledge, were only evident in the poor outcome groups; suggesting that SC impairments only effect a subgroup of individuals with FEP. In contrast, the FEP groups *as a whole* were impaired on verbal learning and memory; this is consistent with previous findings highlighting a marked impairment in verbal learning in psychosis (Green *et al*., 2000). However, when the

exploratory analyses were conducted using the benchmark of the healthy control group, it showed that 80% of individuals in the poor outcome groups had verbal learning and memory impairments compared to 60% in the good outcome groups, highlighting that NC impairment was indeed greater in the poor outcome groups.

It is important to note that several SC (emotion perception, attribution of blame bias) and NC (visual-spatial processing) domains were not significantly different in the psychosis groups compared to the controls (despite a trend for poorer performance in poor outcome groups). Other studies have also found that cognitive deficits in early psychosis samples are not uniform and some individuals are likely to have intact cognitive function (Ludwig *et al*., 2017; Simons *et al*., 2016), highlighting that deficits in the early course of illness are less widespread compared to chronic samples.

The findings in this study may reflect the heterogeneous profiles of those presenting with FEP. There is evidence that SC impairments are sensitive to the heterogeneity in symptom expression in psychosis; for example, ToM impairments are most pronounced in those with negative symptoms, and individuals with paranoid features are believed to 'hyper-mentalise' (i.e. over-attribute other people's intentions, as opposed to 'hypo-mentalise'; Abu-Akel & Bailey, 2000; Walter *et al*., 2009). In contrast, there is some evidence that those with paranoid subtypes show less impairments with facial affect perception than those with non-paranoid sub-types (Davis & Gibson, 2000), and finally, those with persecutory delusions are more likely to have an attribution bias to negative events compared to those without persecutory delusions (Bentall, Corcoran, Howard, Blackwood & Kinderman, 2001; Pinkham *et al*., 2003).

Contrary to these findings, a recent review showed evidence of consistent SC deficits in FEP, which were comparable to deficits in individuals with chronic schizophrenia (Healey *et al*., 2016). These deficits were most consistent for EP, verbal ToM, and social perception (SP). Results were mixed with regards to attribution style in FEP compared with healthy controls, and findings were less conclusive for non-verbal ToM. As non-verbal ToM was assessed in this study, it might explain why there was no consistent ToM deficit. Verbal ToM is considered a more complex and later-developing ability and given the extent of verbal impairments observed in FEP, assessing verbal ToM may have yielded a specific ToM deficit in this group (Brune, 2005). Whilst this study failed to show EP deficits, the review by Healey and colleagues (2016) demonstrated that this impairment is more pronounced when individuals interpret negative emotions. As a global score of affect recognition was used in this study, again, this might be an explanation for the lack of EP impairment observed. Finally, given the lack of support of an attribution style impairment in this study and previous studies, this likely indicates that individuals with FEP have un-impaired attribution style.

3.6.4. Early trajectories of social and role outcome

The finding that the poor outcome groups had widespread impairments in premorbid functioning is supported by previous research demonstrating that functional impairments emerge long before the onset of psychosis (Agerbo *et al*., 2004; Hodgekins, Birchwood, Christopher *et al*., 2015). The results also showed continuity within the domains of functioning, that is, those with poor social functioning were impaired on adolescent interpersonal functioning, whilst those with poor role functioning were predominantly impaired in academic performance in adolescence; suggesting that these deficits are enduring and domain-specific.

These findings may also suggest that functional deficits are already in place before psychosis formally manifests, and intervention in this premorbid phase of illness may be most effective to prevent long-term disability. This is likely to prove challenging as often these individuals will not come to the attention of clinical services until they have transitioned to psychosis. The focus of this thesis however is on the trajectory of functional outcome following the onset of psychosis and identifying potentially 'modifiable' predictors of poor outcome that could be used as treatment targets as early as possible during the illness course.

Given that social avoidance problems seem entrenched in the poor outcome groups, one could argue that the SC impairments may be a secondary acquired problem through a lack of appropriate social exposure and modelling during their childhood and adolescence.

The importance of early childhood experience and their impact on later functional outcomes in FEP has been demonstrated in a study by Stain and colleagues (2013), where childhood trauma was associated with poorer premorbid functioning and later functioning in individuals with FEP. Trauma can disrupt attachment and impact on the development of the individual's interpersonal skills, leading to problems in social functioning (such as social isolation); these maladaptive patterns are then likely to be maintained over time (Stain *et al*., 2013). Childhood maltreatment is also associated with neurochemical brain changes and can disrupt the development of cognition (Barker *et al*., 2015). For example, lowered cognitive functioning in childhood has been associated with adversity (McCabe *et al*., 2012), with prolonged exposure to trauma linked to alterations in the brain regions associated with learning and memory (Anda *et al*., 2006). Furthermore, it is argued that mentalising ability develops within the context of a

secure attachment, and those with adverse interpersonal experiences during childhood and adolescence are likely to have decreased opportunity to develop metalizing skills, subsequently impairing one's ability to understand mental states (Barker *et al*., 2015; MacBeth, Gumley, Schwannauer & Fisher, 2011). Indeed, it has been shown that individuals with FEP who are impaired in their ability to mentalize have poorer premorbid social adjustment (MacBeth *et al*., 2014) and a dismissing attachment style (MacBeth *et al*., 2011). These findings suggest that interventions which aim to re-establish a secure attachment style (e.g. mentalisation-based therapy; Stoffers *et al*., 2012) could potentially benefit those with SC impairment in psychosis (Barker *et al*., 2015). This remains a question for future research.

3.6.5. Study strengths and limitations

The strength of this research is the prospective exploration of functional outcome, with a broad assessment of cognitive (social and non-social) and clinical variables in a large and diverse first episode sample, with a healthy comparison group. Furthermore, the FEP participants were recruited from a large, ethnically diverse urban area, making the sample highly representative. The healthy control participants were also recruited from the same urban areas so that they had a similar social-economic profile, and their level of education was also matched. All FEP participants were recruited within a year of entering an EIS, thus ruling out any confounding effects of illness chronicity. Data on the primary outcome was available for 91% of participants at follow-up, and thus the study benefitted from low attrition. Nevertheless, the limitations of this study should be considered

(i) Threats to internal validity

Firstly, the effects of medication on functioning and cognition were not controlled for and should be considered a limitation. Although, others have argued that the effect of medication at this early stage of illness is likely to be minimal (Mishara & Gouldberg 2004; Stouten *et al*., 2014), and the effect would have to be more pronounced in the poor outcome groups to be a confounder, which seems unlikely. Secondly, as this was a pragmatic study exploring functioning in individuals with FEP, individuals with non-affective and affective psychoses were included in the study. There is some evidence showing that affective symptoms may be more strongly related to social functioning than psychotic symptoms (Chudleigh *et al*., 2011); however, as 90% of the current sample had non-affective psychosis, it is unlikely that including those with affective psychoses would have impacted on the findings, particularly as general affective symptomatology failed to significantly predict poor outcomes in either of the regression models.

(ii) Threats to external validity

Another limitation to this study, and other studies in this area, is potential lack of sensitivity and ecological validity of the measures used (Green *et al*., 2008). With regards to assessing functioning, although the measures were age-appropriate and distinguished between two key areas of functioning – social and role functioning – the term functional outcome is broad and multifaceted, and thus some domains of functioning were not assessed in this study such as quality of life and functional capacity (performance of everyday skills, such as getting dressed), which might also be explained by different predictors (Niendam *et al*, 2009; Yager & Ehmann,

2006). Including additional measures (such as the Quality of Life Scale; WHO, 1991) would have provided a more comprehensive assessment of functioning. Furthermore, the global functioning scales were originally developed to assess functioning in an UHR sample, and although the scales have since been validated in a FEP sample, there may have been a floor effect for the more functionally impaired individuals, which might have compressed variance and thus reducing statistical linkage with poor outcome - in a group which may be the most at risk of developing chronic schizophrenia. Whilst SC was comprehensively assessed, fewer neurocognitive domains were assessed in this study. Seven cognitive domains are represented in the MATRICS consensus cognitive battery for clinical trials in psychosis (Green *et al*., 2004; Green *et al*., 2008); three domains - working memory, attention and vigilance, and visual learning - were not assessed in this study and should be explored in future longitudinal studies in FEP to see if they can explain additional variance beyond that of negative symptoms. Finally, there does not seem to be a 'gold standard' for assessing each of the SC domains in the literature, and there is considerable conceptual, and measurement overlap across SC domains, making it difficult to draw inferences across studies (Green *et al*., 2008; Ludwig *et al*., 2017; Pinkham *et al*., 2014).

In addition, current SC measures may not be sensitive enough to reflect the complex dynamics of everyday social interactions (Stouten *et al*., 2014). There is a need for future studies to develop more ecologically valid measures that may enhance understanding of the relationship between SC and social and role functioning in early psychosis (Green *et al*., 2008; Simons *et al*., 2016; Stouten *et al*., 2014).

Finally, although the rates of overall variance (17-20%) in social and role outcomes in the full regression models (which included negative symptoms and cognitive variables) are similar to the explained variance reported in other FEP studies (Allott, Liu, Proffitt, & Killackey, 2011; Stouten *et al.*, 2014), this shows that the bulk of variance in functional outcome remains unexplained. Strauss & Carpenter (1977) have argued that much of the variance in outcome is driven by 'normal' factors explaining variance in healthy populations (such as wider social factors including social networks, education, and opportunities). This suggests that research should also attempt to explore the more general predictors of outcome (e.g. social networks) that affect the general population, in addition to pathological factors that are relevant to specific clinical populations, to better understand the complexities of functional outcome.

3.6.6. Conclusion

This study is the first to assess both social and non-social cognition and their relative contribution to understanding the observed variability in social and role outcome in FEP, and to benchmark these cognitive capacities against a matched healthy comparison sample. The study suggests the following conclusions:

First, those individuals with poor social and role functioning in the early stage of psychosis had enduring social and role impairments stemming from their adolescence, increasing the likelihood that this group are at risk of long-term poor social outcome and chronicity.

Second, the group of individuals with poor functioning had more negative symptoms at baseline and had greater social cognitive and neurocognitive impairment. This was particularly evident for the NC domain – logical memory – where 80% of the poor outcome groups scored outside the normal range.

Third, social and role functioning in FEP appeared to have somewhat distinct and internally continuous trajectories: those with poor social functioning were likely to have more interpersonal problems during adolescence, and social outcome at 12 months was predicted by the SC domain, social knowledge. On the other hand, those with poor *role* outcome had greater academic impairment in adolescence, and was predicted by the NC domain, logical memory.

Finally, although SC and NC failed to contribute variance beyond negative symptoms in the regression, subsequent exploratory analyses suggested that cognition may contribute to functional outcomes through their impact on negative symptoms. It is also argued that some negative symptoms (e.g. poor rapport, social withdrawal) is in part a phenomenological manifestation of cognition (e.g. mental state representation). Delineating the relationship between cognition and negative symptoms could potentially inform targeted intervention to prevent decline in functioning in FEP.

4.0. CHAPTER 4

EMPIRICAL STUDY 2

4.1. THE RELATIONSHIP BETWEEN COGNITION AND FUNCTIONAL IMPROVEMENT IN THE CONTEXT OF A PSYCHOSOCIAL INTERVENTION TARGETING SOCIAL DISABILITY IN FIRST EPISODE PSYCHOSIS.

4.2. Abstract

Many young people with first episode psychosis (FEP) continue to show poor functioning even after receiving specialised care from an Early Intervention Service (EIS). This has brought about a need for the development and refinement of new psychosocial interventions to improve functioning for these young people. Examinations of cognition, pre- and post- psychosocial intervention, may provide new insights into the mechanisms of improved functioning and provide means of identifying those whose disability is more likely to be amenable to treatment; thus, guiding intervention for these individuals and potentially informing the refinement of current psychosocial interventions.

Aims:

This was an explorative study which ran in parallel to a multi-site proof of concept trial of social recovery cognitive behavioural therapy (SRCBT), for young people with FEP and severe social disability. The main aims of this explorative study were to investigate whether an improvement in social functioning following a psycho-social intervention (SRCBT), corresponded with a

change in social cognition (SC) and neurocognition (NC), and whether baseline SC and NC could predict who is more likely to respond to the SRCBT intervention.

Method:

Individuals between the ages of 16-35 years old, with First Episode Psychosis (FEP) who were participating the NIHR SUPEREDEN trial of SRCBT, were eligible to take in the study. All participants had less than 30 hours a week of structured activity before entering the trial. At baseline, 123 participants completed a battery of SC and NC assessments. Fifty-nine participants were randomly allocated to the therapy group (SRCBT), and 64 were randomly allocated to the standard care group (care from an EIS). All participants completed a follow-up assessment at 9 months on the same cognitive battery, and a further assessment of their structured activity. The assessors were blind to group allocation.

Results:

For those who received the SRCBT, there was no significant change in overall SC and NC (i.e. a composite score) at 9-month follow-up (post-intervention). Despite the SRCBT having little impact on cognition, regression analyses consistently showed that SC predicted which individuals responded to the intervention. Specifically, those who had better social knowledge at baseline were most likely to benefit from the SRCBT, with those scoring in the top quartile for social knowledge achieving an additional 11 hours on average of structured activity post-intervention.

Implications:

These findings have implications for future trials, where remediation of SC prior to therapy may improve the efficacy of the SRCBT, particularly for individuals who have poorer social knowledge.

4.3. Introduction

Impairments in social and role functioning have long been considered a defining feature of psychosis and are rooted early in development (Jones, Rodgers, Murray & Marmot, 1994; Lauronen, Miettunen, Karhu, Jones & Isohanni, 2007). Whilst EIS is the 'gold standard' treatment for young people with psychosis, in a study of over 1000 FEP cases, 66% of individuals were experiencing a high level of poor functioning, despite receiving care under EIS for a period of 12 months (Hodgekins, Birchwood, Christopher et al., 2015). In contrast, symptomatic recovery rates for individuals receiving care under EIS are reported to be around 50% (Wunderink et al., 2009). These findings highlight the need for new interventions to specifically target social and role impairments in early psychosis.

Individual placement support (IPS) is a commonly used vocational intervention offered in EIS that has been shown to be effective at helping young people with psychosis obtain competitive employment (Bartholomeusz et al., 2011; Bond, Drake & Luciano, 2014). Yet despite the evidence of IPS's effectiveness, a recent study found that 53.6% of individuals with FEP who were receiving care under EIS were 'not in education or employment' (NEET), compared to 10.7% in a non-clinical sample (Hodgekins, French, Birchwood, et al., 2015). IPS is most effective when individuals are motivated, and it may therefore not be successful in complex NEET groups (Bond et al., 2014, Fowler et al., 2017).

Furthermore, IPS specifically addresses role functioning alone, and other aspects of functioning such as returning to education, engagement in leisure activities and interpersonal relationships - which are also meaningful functional recovery markers - are not targets of the intervention

(Hodgekins, French, Birchwood, *et al*., 2015). Intervention should be focused on a broader concept of recovery and target the factors likely to be contributing to poor functioning (Fowler *et al*., 2017).

A specialised Social Recovery Cognitive Behavioural Therapy (SRCBT) has been developed which aims to address hypothesized underlying factors impeding social recovery through incorporating the IPS ethos of assertive outreach approach to motivate individuals who are ambivalent about re-engaging into a social environment, whilst also using CBT techniques to target any residual symptoms and overcome blocks to change (Fowler *et al*., 2009). SRCBT has been shown to be effective at improving structured activity in individuals with early psychosis and those with established illness, with a recent randomised control trial (NIHR SUPEREDEN trial) reporting an increase of 8.1 hours of weekly structured activity for those receiving SRCBT plus EIS compared to those receiving EIS alone (Fowler *et al*., 2009; Fowler *et al*., 2013; Fowler *et al*., 2017). Whilst these findings are encouraging, to ensure that targeted psychosocial therapies are being delivered appropriately, it is important to further understanding of the factors that contribute to functional change and identify individuals who are more likely to benefit from specialized treatments such as SRCBT (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011).

Results from the first empirical study showed that those with poor functional outcomes had more SC and NC impairment, and that cognition contributed some variance in functional outcomes in FEP. If a reciprocal relationship between impaired cognition and functioning exists in FEP, it would be expected that improvement in functioning following effective intervention might also lead to improved cognitive function. Although cognition is not addressed by the

SRCBT intervention described above, through receiving the intervention, a young person may improve their understanding of social situations, resulting in more social exposure, which then in turn may improve one's SC and NC function.

Following the same rationale, given that SC and NC have a contributing role in functional outcome in FEP, it could also be argued that those who have poorer SC and NC function at the start of therapy may benefit the least from the SRCBT. For example, if a young person is unable to make correct inferences about others in social situations, they may struggle to motivate themselves to engage in a social intervention, and they may also be less likely to adapt their cognitive strategies for social situations via therapy.

Exploration of SC and NC pre- and post-intervention will therefore be important to test underlying mechanisms of functional change and identify individuals who are more likely to benefit from the specialized SRCBT (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011). No studies to date have examined predictors of treatment response to a CBT intervention specifically targeting functional impairment in FEP.

To put these assumptions and predictions to the test, the present research ran alongside the NIHR SUPEREDEN trial (Fowler *et al*., 2017), and was designed to add value to the assessment of the effectiveness of SRCBT by addressing two main questions:

(1) Does SRCBT lead to improvements in SC and NC?

(2) Does baseline SC and NC predict those more likely to respond to the SRCBT?

4.4. Method

4.4.1. The NIHR SUPEREDEN trial

This study of cognition ran alongside the multi-site NIHR SUPEREDEN trial. The trial is a single blind, proof-of-principle trial, comparing SRCBT plus EIS care, against standard care from EIS alone (referred to as the Treatment as Usual – TAU – group). A battery of NC and SC measures were carried out at baseline (pre-SRCBT) and at the end of therapy (after 9 months).

Social Recovery Cognitive Behavioural Therapy (SRCBT)

The SRCBT draws on psychological intervention and multi-systemic assertive outreach case management to promote social recovery. The therapy is delivered by supervised and accredited CBT therapists from the EIS teams. The SRCBT is delivered in three stages. The first stage is developing a formulation. The objective is to set realistic and meaningful personal goals to promote social recovery, whilst accepting potential threats and barriers. The second stage involves preparing the young person for new activities. This may involve more general vocational management, in addition to cognitive work, such as addressing hopelessness or negative schemas. The final stage is the promotion of social activity linked to meaningful personal goals. This is achieved using behavioural experiments, and management of symptoms such as anxiety and psychotic symptoms. The therapist will adopt an assertive outreach approach in helping the young person achieve their goals. This will involve visiting the young person at home, or in the community or education settings, and working collaboratively with

the family and community activity providers to address any barriers to social recovery. Further details on the specific therapeutic approach can be found in Fowler *et al*. (2017).

Trial participants

The formal trial inclusion criteria (taken from Fowler *et al.,* 2017) were as follows: (1) males and females between the ages of 16-35 years with non-affective psychosis; (2) receiving care under an EIS in Birmingham, Lancashire, Norfolk or Sussex (individuals with psychotic symptoms of 4 or above on the PANSS meet entry criteria for EIS in the UK); (3) experiencing a low level of structured activity after at least 12 months treatment from EIS (defined as 30 hours or less per week on the Time Use Survey); (4) clients had been with EIS between 12-30 months. Participants were excluded if they were: (1) not proficient in the English language to engage in the intervention; and (2) deemed too unwell to partake in the intervention (Fowler *et al*., 2017).

One-hundred and fifty-five service users of EIS in Birmingham, Lancashire, Norwich and Sussex, consented to the SUPEREDEN trial. Of the 155 consenting, 76 participants were randomly allocated to the therapy group (SRCBT), and 79 were randomly allocated to the Treatment as usual (TAU) group (Figure 2, CONSORT diagram). There were data available for 92% of the trial sample at 9-month follow-up (Figure 2).

Primary trial outcome

The primary hypothesis of the trial was that SRCBT (plus EIS) would lead to improvements in social recovery (assessed as time spent in structured activity at 9 months). Structured activity was assessed using the following measure:

The Time Use Survey (TUS) (Short, 2006) was used to assess functioning at baseline and 9-month follow-up. The Time Use Survey is a semi-structured interview, which asks about time spent over the last month in activities such as work, education, voluntary work, socialising, leisure, sports, chores / housework and childcare (Appendix B-15). The information gathered is used to calculate average hours per week spent in 'structured activity'. According to the Office of National Statistics, a non-clinical population aged between 16-36 years spend an average of 63.5 hours per week in structured activity (Short 2006). Using the TUS in a sample of individuals with psychosis, Hodgekins, French, Birchwood, *et al*. (2015) established the following cut-off scores for assessing social disability in young people experiencing psychosis: 45 hours or more per week (*Good Social Functioning*); 30 – 45 hours per week (*At-Risk of Social Disability*); below 30 hours per week (*Social Disability*); below 15 hours per week (*Severe Social Disability*). Potential participants were screened using the TUS and considered eligible for the SRCBT trial if they met the cut-off of below 30 hours per week in structured activity (*Social Disability*).

Trial Procedure

The research team liaised closely with care coordinators to discuss appropriateness of the service user's involvement in the research, and, to check any concerns with regards to risk. If appropriate, the study team contacted the service user directly to invite them to partake in a screening interview. Once the researcher met with the service user, verbal and written information about the trial was provided and they were given opportunity to ask questions prior to consent (Appendix A-6 & 7). The service user was also screened using the TUS to check if they met study criteria (30 hours or less of structured activity a week, see above in *Trial Participants* section). If the study criteria were met and consent was obtained, participants were asked to complete a battery of assessments, which included measures of psychopathology and functioning. Participants were then randomly allocated using a computer program to either the treatment group (SRCBT + standard EIS care) or TAU (standard EIS care alone). Participants who were allocated to the treatment group received the SRCBT over a 9-month period by a clinical psychologist. Participants who were allocated to the TAU continued to receive standard care under the early intervention team. Participants completed follow-up assessments at 9 and 15 months. The assessments were administered by researchers who were blind to group allocation, and participants were reminded not to disclose their group allocation. In cases where an un-blinding occurred, the assessments were conducted by another researcher who remained blind to group allocation. The study was approved by the Black Country NHS research ethics committee (REC reference: 12/WM/009; Appendix A-1). The trial is registered (ISRCTN61621571).
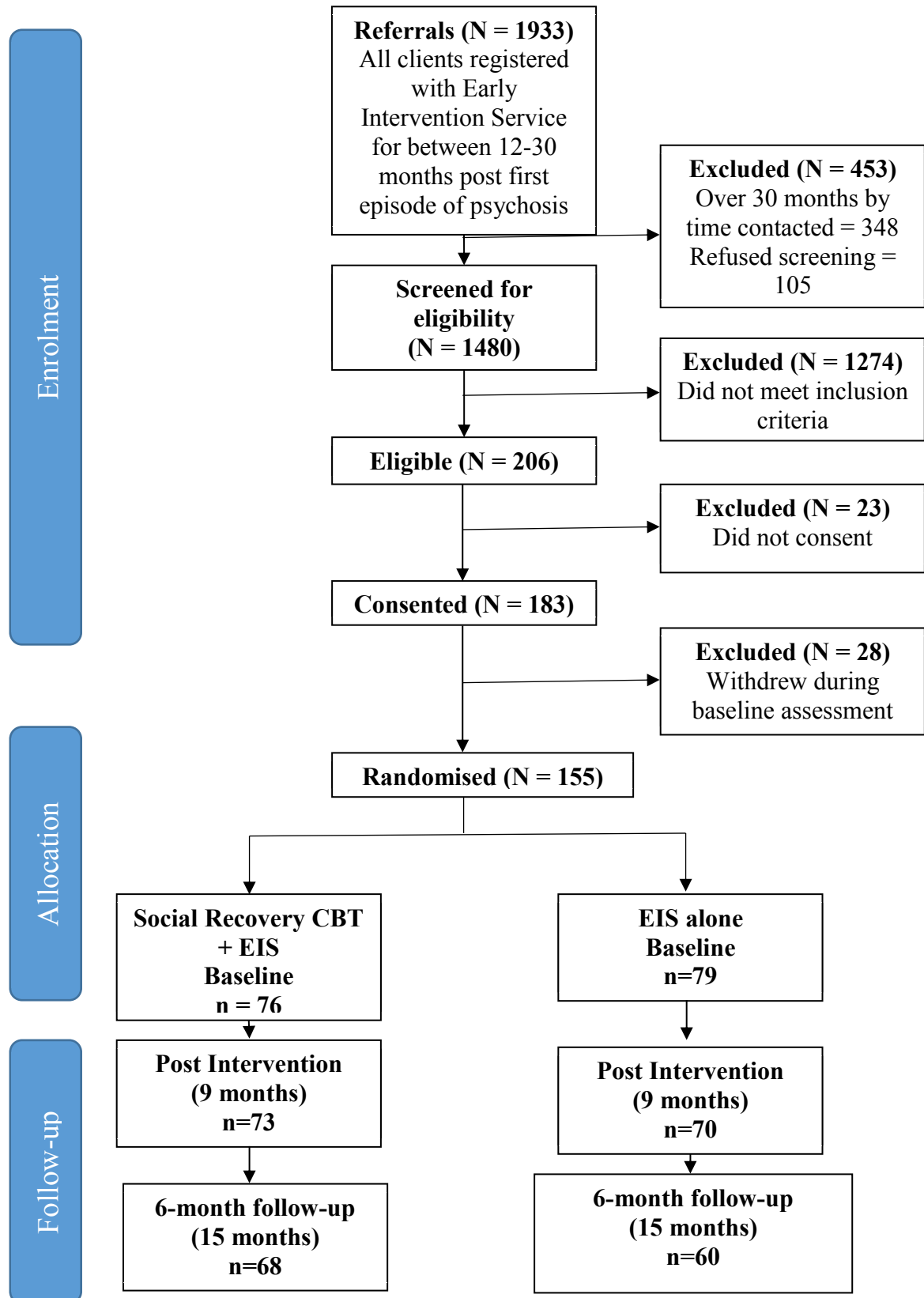
Figure 2. CONSORT diagram showing trial design and stages of recruitment up to treatment allocation for the full trial sample. Taken form Fowler *et al*., 2017 with permission from the authors.

SUPEREDEN trial – Results

An intention to treat analysis on the primary outcome (Time Use Survey) indicated that for the group receiving the SRCBT intervention, there was a large and clinically important increase of 8.1. hours a week of structured activity (95% CI 2.5 to 13.7; $p = 0.005$), compared to those in the TAU group (receiving EIS alone) at 9 months (Fowler *et al*., 2017).

4.4.2. The Present Study

Design

This was a follow-up study of cognition which was assessed as part of a single-blind, randomized controlled trial of SRCBT plus EIS, versus treatment as usual from EIS. Cognition was assessed at baseline, prior to randomisation, and at 9 months follow-up (post-intervention and primary outcome endpoint).

The sample

Inclusion criteria for this study were as follows: (1) Participants who had consented to the NIHR SUPEREDEN trial; (2) met full inclusion criteria for the SUPEREDEN trial (see *Trial Participants* section, page 106). Participants were excluded if they met the following criteria: (a) insufficient command of the English language; (b) presence of any neurological disorders, for example, epilepsy; (c) documented history of a learning disability; (d) history of severe head injury (more than 5 minutes loss of consciousness, or an overnight hospital stay).

Of the 155 individuals who consented to the trial, 122 (77%) completed the cognitive assessments at trial baseline. Of the 122 who completed cognitive assessments, the breakdown of group allocation post-randomisation were as follows: 59 participants were allocated to the SRCBT plus EIS group, and 63 participants were allocated to the TAU group (EIS alone). Table 11 provides a breakdown of the demographic and clinical characteristics of the sample (by randomisation group) at baseline.

Table 11. Demographic and clinical characteristics of the sample completing cognitive assessments at baseline.

	Social Recovery CBT Group + Standard Care (N= 59)	Treatment as Usual (N = 63)	Statistical Significance
Mean Age (years)	25.89	24.8	NS [a]
Males (n; %)	43; 72.9	54; 84.4	NS [b]
Years in Education (mean)	12.1	12.2	NS [a]
Marital Status (%)			
Single	92.7	93.7	
Married	3.6	6.3	NS [b]
Divorced / Separated	3.6	0	
Hour per week in Structured activity (Time Use Survey)	10.27	11.62	NS [a]
Ethnicity (%)			
Caucasian	88.1	62.5	
Asian	6.8	20.3	.012 [b]
Black	1.7	9.4	
Other	3.4	7.8	
Symptoms (PANSS)			
Positive	13.32	14.08	NS [a]
Negative	15.58	16.84	NS [a]
General	32.41	32.31	NS [a]
Delay of Untreated Psychosis (DUP; days)	388	270	NS [a]

[a] One-way Analysis of Variance (ANOVA). [b] Chi-Square test. NS = Non – significant.

Measures

The social cognitive and neurocognitive assessments used this study are the same as those used in empirical study 1 and were previously described in section 3.4.3. (pages 55-60).

Neurocognitive assessments

(i) Logical Memory subtest - Wechsler Memory Scale Revised – IV (WMS-IV; Wechsler, 1987). This is a measure of verbal learning and memory. A participant is read two short stories; immediately after each one is read, they are asked to repeat the story as close to verbatim as possible. The WMS has good construct validity as a measure of verbal learning and memory (Larabee, Kane, Schuck & Francis, 1985).

(ii) Vocabulary subtest Wechsler Adult Intelligence Scale - IV (WAIS-IV; Wechsler, 1981). This is a measure of verbal comprehension and production in which participants are asked to define a number of words and pictures. The subtest has 30 items, which includes 3 picture items and 27 verbal items. It is also a measure of a participant's crystallized intelligence, long-term memory and learning ability (Wechsler, 2008).

(iii) Block Design subtest Wechsler Adult Intelligence Scale - IV (Wechsler, 1981). Block Design measures perceptual reasoning, problem-solving skills and visuospatial ability (Wechsler, 2008). Participants are presented with several geometric designs, which they have to reproduce by arranging red and white blocks accordingly within a set time frame. The subtest has 14 items in total. It is scored by the number of correctly reproduced patterns. Raw scores for each of the

neurocognitive subtests were calculated and converted into age standardised scores with a range from 1-19, a mean of 10 and a standard deviation of 3.

The Wechsler scales have strong psychometric properties: there is strong evidence of validity based on the scales internal structure (the degree of relationship between test items and the construct being measured); content validity (the degree to which the test items relate to the construct being measured), and finally, it is highly correlated with other measures of cognitive ability, thus demonstrating the WAIS' construct validity (Wechsler, 1981, 1987, 2008). There is also convincing evidence to support the internal consistency and test-retest stability; overall demonstrating the reliability of the Wechsler scales (Wechsler, 2008).

(a) Social Cognitive Assessments

(i)   Picture sequencing task (Langdon & Coltheart, 1999). This task is a non-verbal task that assesses Theory of Mind (ToM) in the context of understanding false beliefs. The task was originally designed to investigate ToM deficits in autism. The task has since been adapted to demonstrate selective ToM deficits (independent of low IQ, poor logical reasoning, or executive dysfunction) in individuals with psychosis (Langdon, Ward & Coltheart, 2010; Langdon *et al*., 2014). The task requires participants to correctly sequence four types of stories: mechanical (cause and effect reasoning), social script (basic social reasoning), false-belief (infer a character's mistaken belief), and capture (inhibition of a misleading cue). The Capture stories

are a good control, since the false belief stories requires the participant to inhibit salient objective facts in order to infer the mistaken belief. Furthermore, as the capture stories were designed to be particularly difficult, group differences in false-belief scores can simply not be explained by sensitivity to increasing task difficulty (Langdon, Ward & Coltheart, 2010).

The stories are depicted in a 4-card picture sequence, presented in a *pseudo*-random order, with each picture sequence scored out of six. There are two practice sequences, and a further four sequences for each story type. The mean score is averaged for each story type, along with response times for correctly ordered sequences. The average score of the false-belief stories was entered into the final regression model. The 3 other stories were used to compare task performance between the FEP group and the healthy controls.

(ii)   Mayer-Salovey-Caruso Emotional Intelligence Test – Perceiving Emotions (MSCEIT; Mayer, Salovey, & Caruso, 2002). The MSCEIT is a paper and pencil test which involves two separate tasks: The Faces task and Picture task. The Faces task involves identifying facial affect, and the Picture task involves identification of emotion conveyed by pictures of designs. Participants were asked to rate on a Likert scale (0-5), how much emotion is conveyed by a person's face or a picture. The emotions that the participants were asked to rate were: happiness, sadness, fear, surprise, disgust, anger and excitement. In total, there were four faces and six pictures, with five emotions to rate for each one.

An age standardised 'Branch Score' was calculated for the MSCEIT, which combined the total score for the Faces and Picture Task. The MSCEIT has been shown to have excellent reliability in a non-clinical sample for branch and total test scores (Mayer, Salovey, Caruso & Sitarenios, 2003).

(iii)   Ambiguous Intentions Hostility Questionnaire (AIHQ; Combs, Wicher, & Waldheter, 2007). The AIHQ specifically targets hostile social cognitive bias in psychosis. It has 15 items consisting of short vignettes, which reflect varying negative outcomes that vary in intentionality: intentional, accidental, and ambiguous intentions. For each vignette, participants were asked why they thought the person acted in that way (hostility index). The participant then rated, on Likert scales, if they thought the person acted on purpose (1 "definitely no" to 6 "definitely yes"), felt angry (1 "not at all angry" to 5 "very angry"), and blamed the person (1 "not at all angry" to 5 "very much"). An average of these scores was calculated to form a 'blame score'. Finally, the participant had to state how they would react to that that situation (aggression index). Responses for the hostility and aggression questions were coded by the researcher on a scale that ranged from 1 "not at all hostile / aggressive" to 5 "very hostile / aggressive". Scores were then averaged for the intentional, accidental, and ambiguous items.

The AIHQ has been shown to have good levels of reliability and validity in a non-clinical sample (Combs, Wicher, & Waldheter, 2007); shown to be predictive of aggressive behaviour in in-patients with Schizophrenia (Waldheter *et al.*, 2005), and

has been shown to be a sensitive outcome measure in a psychosocial intervention trial in inpatients with Schizophrenia (Penn *et al*., 2005).

Previous research has shown that the self-rated blame scores for ambiguous situations showed the most consistent relationship with paranoia and hostility than responses to intentional and accidental situations (Combs, Wicher, & Waldheter, 2007). Therefore, due the high number of variables in the analysis, only the blame scores for ambiguous situations were included in the final analysis as they are the most likely to demonstrate a social cognitive bias.

(iv)   The Social Knowledge Questionnaire (SKQ; Cutting & Murphy, 1988 & 1990). This is a 9-item multiple-choice questionnaire that assesses a participant's understanding of how others act in social situations. A score of 1 is given for correct items, and a score of zero for incorrect items.

The selection of cognitive assessments was limited due to time constraints and because this study was as an add-on to the SRCBT trial. The above SC measures were therefore selected to represent each of the four most commonly reported SC impairments in psychosis (Couture *et al*., 2006). As verbal skills have shown to be most impaired in psychosis (Allot *et al*. 2010), two of the NC test battery included assessments of verbal language skills. The third NC test assessed non-verbal skills and was selected to provide a more balanced view of cognition.

(c) Psychopathology:

(i) Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). This widely used scale is a 30-item-scale which assesses the severity of positive and negative symptoms of schizophrenia as well as general psychopathology. There are seven rating points for each item with detailed anchor points, which represent increasing psychopathology (1 = absent to 7 = extreme). Of the 30 items, 7 items represent positive symptoms (score range of 7 to 49), 7 items represent negative symptoms (score range of 7 to 49), and 16 items represent general psychopathology (score range of 16 to 105). Scores were summated for each of these separate components.

The PANSS has good inter-rater, test-retest and internal reliability and established internal, external and construct validity (Kay *et al.,* 1987). The PANSS will be collected at baseline and at 12-month follow-up by a trained interviewer.

Procedure

Once participants were consented to the SRCBT trial and the primary outcome measures were completed, the cognitive assessments were then completed. Following completion of the assessments, participants were randomized to the SRCBT group or the TAU group (described in *Trial Procedure* page 108). After 9 months, participants repeated the full follow-up battery of cognitive assessments following completion of the trial outcome measures (e.g. TUS and PANSS). Researchers who administered the cognitive assessments were blind to group allocation (as described in the trial procedure). Participants were reminded of their right to withdraw from the study at any stage without their care being affected. Consent was obtained

on one occasion at the start of the trial assessments. The study was approved by the Black

Country NHS research ethics committee (Appendix A-1).

4.4.3. Statistical Analyses

Analysis 1: Impact of SRCBT on cognition and structured activity *(Main Research*

Question: Does SRCBT lead to improvements in SC and NC?)

   (i)   Impact of SRCBT on structured activity

The primary aim of the SUPEREDEN trial was to test the effectiveness of SRCBT at improving

structured activity. To confirm that SRCBT had an impact on structured activity in the present

sample, a mixed ANOVA was used. The between-subjects factors were SRCBT group vs. TAU

group; the within-subject factor was time (baseline and 9-month follow-up). The group x time

interaction was inspected to determine the impact of the therapy on structured activity.

   (ii) Impact of SRCBT on Social cognition and Neurocognition

To explore the impact of the SRCBT intervention on cognition (SC and NC), two mixed 2x2

Multivariate Analysis of Variance (MANOVA) were used. The between-subjects factors were

SRCBT group vs. TAU group; the within-subject was time (baseline and 9-month follow-up).

Composite scores were computed within the MANOVA model in SPSS based on a linear

combination of each of the dependent variables. Two separate composites were created: a

social cognitive composite and a neurocognitive composite. These composites were created

because, whilst SC and NC are shown to be highly related (Vauth, Rusch, Wirtz & Corrigan,

2004), research examining their factor structure have identified these concepts to be distinct

(Sergi *et al.*, 2007), and each contribute unique variance to functional outcome (Fett *et al.*,

2011). The 'social cognitive' composite consisted of a weighted linear combination of each of

the social cognitive sub-domains: ToM, social knowledge, attribution of blame bias and

emotion perception. The 'neurocognitive' composite was created based on a weighted linear

combination of the neurocognitive sub-domains: verbal learning and memory (Logical

memory), verbal comprehension (Vocabulary) and perceptual reasoning and problem solving

(Block Design).

The multivariate main effects were explored as well as a group x time interaction for a SC

composite and NC composite to investigate the overall impact of the intervention on the

cognitive variables. If the group x time interaction was significant for the composite score, the

univariate analyses were inspected. Partial Eta Squared (ηp^2) was used as a measure of effect

size, with small, medium and large effects corresponding to ηp^2 values of 01, .06, and .14,

respectively (Cohen, 1988).

A MANOVA was used in this study as it has greater power to detect an effect compared with

ANOVA, because it considers whether there are group differences along a combination of

variables (i.e. a composite), rather than across a single dimension (Field, 2005). MANOVA

also reduces the familywise error rate, which is increased when a series of univariate analyses

are conducted (Field, 2005; Pallent *et al.*, 2011); as such, MANOVA was the preferred

method.

Checking the assumptions of the Multivariate Analysis of Variance (MANOVA)

Results of a 1-sample Kolmogorov-Smirnov (K-S) test indicated that there were some violations of the assumption of normality (with K-S Z values ranging from 0.060 to 0.215 and *p* values ranging from 0.00 to .200), however, this is not an uncommon finding in larger samples (e.g. n > 30; Pallant, 2011). Furthermore, examination of the Q-Q plots indicated that the data for the SRCBT and TAU group was sufficiently normally distributed for the variables. MANOVAs are robust to modest violations of normality, particularly with a large sample size such as in the present study (Pallant, 2001). Two additional assumptions of MANOVA - multivariate normality and outliers - were explored using Mahalanobis distances. Results showed that the maximum value of the Mahalanobis distances for each of the dependent variables were less than the critical value of Chi-square (Tabachnick & Fidell, 1996), suggesting that there were no multivariate outliers. Upon further inspection of the univariate outliers identified in the box plots, there was a slight difference between the mean of the individual cognitive variables and the 5% trimmed mean, indicating that the outliers were not problematic and therefore remained in the analysis (Pallant, 2001). Inspection of the scatterplots for each of the individual cognitive variables showed no obvious evidence of non-linearity, therefore the assumption of linearity was satisfied. Finally, a Pearson correlation analysis indicated that there was no evidence of multicolinearity or singularity.

(iii) Correlation between changes in cognition and changes in structured activity post-intervention (exploratory)

To explore whether SC and NC improve in line with any changes in structured activity following SRCBT, a Pearson correlation analysis was carried out. If any cognitive variables were identified from the univariate analysis as being significantly improved post- SRCBT compared to the TAU group (please refer to previous analysis), they were selected for the correlation analysis. Change in structured activity was calculated for the TUS and correlated with any SC or NC variables that significantly changed following SRCBT.

Checking the assumptions of the bivariate correlation analysis.

Examination of the Q-Q plots indicated that the data for the SRCBT and TAU group was adequately normally distributed. Examination of the scatterplots demonstrated evidence of linearity and homoscedasticity, thus supporting the assumptions of a correlation analysis (Pallant, 2011).

(iv) Cognitive deficits in the sample at baseline (exploratory analysis)

To determine whether SC and NC are impaired in the FEP groups at baseline, an independent t-test was carried out between the healthy control group used in Study 1 (see Chapter 3, page 50) and the combined SRCBT and TAU group.

Analysis 2: Social cognition and Neurocognition as predictors of response to SRCBT

(***Main Research Question:*** *Does baseline SC and NC predict those more likely to respond to the SRCBT?*)

To explore if baseline (pre-SRCBT) SC and NC can predict response to SRCBT, linear regression and binary logistic regression analyses were employed. To ensure that treatment response is objectively measured, several approaches were explored; each will be discussed in turn in the results.

Shared variance between cognition and negative symptoms in the prediction of functional outcome has previously been reported in FEP (Addington *et al*., 2015). As such, to test if cognition contributes unique variance to the prediction of outcome (treatment response) in this study, negative symptoms will also be added into the regression model to account for any shared variance.

Checking the assumptions of regression

Inspection of the residuals in the normal probability plots indicated no departure from normality, supporting the assumption of regression analysis. The probability plots also support the assumptions of linearity and homoscedasticity. To check the assumption of multicolinearity, results of the bivariate correlation showed that there were no correlations greater than .7, indicating that there is no multicolinearity present in the data (Tabachnick & Fidell, 1996). To check the presence of outliers, Mahalanobis distances were explored. Results showed that the maximum value of the Mahalanobis distances for each of the dependent variables was less than

the critical value of Chi-square (Tabachnick & Fidell, 1996), suggesting that there were no outliers present in the data.

Given the shared variance previously reported between cognition and negative symptoms in the prediction of functional outcome (Addington *et al*., 2015), colinearity diagnostics were inspected to examine the variables inter-correlations'. The tolerance value (.619) and Variance Inflation Factor – VIF (1.616) for negative symptoms was acceptable, and Pearson correlations between negative symptoms and the cognitive variables were less than .7, indicating that there was no multicolinearity present. Negative symptoms and the cognitive variables were therefore included together in the regression analysis to explore their relative contribution in predicting treatment response.

Methods of measuring and defining treatment response to SRCBT.

  (i) Absolute change score method

An 'absolute' change score was calculated by subtracting the number of hours per week in structured activity (captured by the TUS) post SRCBT, from the number of hours spent in structured activity per week at baseline (pre-intervention).

Absolute change scores from the TUS were entered as dependent variables in the linear regression, and the SC and NC scores were entered as predictor variables. A backward regression method was selected to find the most parsimonious predictors of outcome. The

adjusted R² statistic was reported as an approximate measure of the proportion of explained variance of the final models.

(ii) Social Disability cut-off score method

According to the cut-off scores for the TUS established by Hodgekins, French, Birchwood, *et al*. (2015), a score below 30 hours a week of structured activity on the TUS was classified as 'social disability'. Participants were deemed eligible for the trial if they met this criterion. It would therefore seem logical to define 'treatment response' to the SRCBT as those achieving *30 hours or above* of structured activity per week at follow-up (post SRCBT). Two groups were entered into a binary logistic regression as the dependent variable: 'treatment responders' (30 hours or more of weekly structured activity) and treatment non-responders (below 30 hours of weekly structured activity). 'Treatment responders' were coded as '1' and 'non-responders' were given a code of '0'. The predictor variables were therefore explaining the likelihood of belonging to the 'treatment response group'.

Baseline SC and NC scores were entered as predictor variables into the regression model. A backward method was selected to find the most parsimonious predictors of outcome. The Nagelkerke pseudo R² (R^2_N) statistic was reported as an approximate measure of the proportion of explained variation of the final models (Nagelkerke, 1991).

Strengths and limitations of the methods of defining 'treatment response'

Defining treatment response by identifying groups based on social disability cut-off scores provides a threshold at which individuals have moved out of the 'social disability' range. This has wider implications in clinical settings as it provides means for clinicians to easily quantify treatment response. The advantage of using absolute change on the other hand, is that it may highlight changes that, although below the cut-off, are meaningful for an individual with low functioning. A disadvantage to defining treatment response by absolute change is that it may misrepresent the magnitude of change between individuals; for example, an individual with an improvement in structured activity of 5 to 10 hours and 25 to 30 hours would have the same absolute change score of 5; arguably a change of 5 hours may mean more to an individual with a baseline of only 5 hours of activity.

As each definition of treatment response has its advantages and uses, both approaches described above were explored in the analyses in order to capture a more balanced measure of treatment response.

Analysis 3 (Exploratory) – Social cognition and Neurocognition as predictors of change in structured activity in the combined SRCBT and treatment as usual group.

The final analysis explored whether SC and NC could predict change in structured activity in the combined SRCBT and TAU sample. Each of the SC and NC variables were entered into a linear regression as predictor variables. The dependent variable was the 'absolute change' in

structured activity. Group allocation was entered as a control variable in the regression analysis to see if any of the cognitive variables explain additional variance to the change in structured activity, above what is accounted for by the therapy.

4.5. Results

4.5.1. The Sample

From the overall trial sample (155), data on the cognitive assessments were available for 122 participants and analysed in this study. After randomisation and treatment allocation, 75% of the trial sample had completed cognitive assessments in the SRCBT group at baseline, and 84% of the trial sample had completed cognitive assessments in the TAU group. Demographic and clinical comparisons between the trial sample and the sub-group completing cognitive assessments are shown in Table 12. There were no differences on demographic or clinical characteristics between the samples suggesting that the sub-group used in this study was highly representative of the full trial sample.

At 9-month follow-up (post SRCBT), there were data available for 109 of the 122 participants (89%) on the primary outcome measure, the Time Use Survey. Not all the cognitive assessments were completed by each participant who returned for a follow-up assessment for the SRCBT trial. Table 13 shows the completion rates for each of the cognitive measures (by randomisation group) at baseline and 9-month follow-up.

4.5.2. Analysis 1: Impact of SRCBT on cognition and structured activity

Research Question 1: *Does SRCBT lead to improvements in SC and NC?*

(i)   Impact of SRCBT on structured activity

Before the main research questions are addressed, the first step involves repeating the main trial analysis on the primary outcome (structured activity) for the sub-sample consenting to the present study. This was explored using a mixed ANOVA comparing the SRCBT and TAU groups over time.

Results of a mixed ANOVA showed a significant group x time interaction for TUS structured activity [$F_{(1)} = 69.20$, $p = .010$] with a medium effect ($\eta p^2 = .061$). At 9-month follow-up, the SRCBT group had increased their structured activity by 18.85 hours, whilst structured activity in the TAU group had increased by 7.21 hours, meaning that there was 11.64 hours difference in structured activity increase between the groups (please see Table 14 for means and standard deviations).

The sample consenting to this study (79% of the trial sample) therefore also showed a significant effect of SRCBT, with comparable effect size as the full trial sample.

Table 12. Comparison of demographic and clinical characteristics (by trial allocation) between the trial sample and the sub-group completing cognitive assessments.

Item	SRCBT group allocation in the sub-sample (n=59).	SRCBT group allocation in the trial sample (n=79).	Statistical significance.	TAU group allocation in the sub-sample (n=63).	TAU group allocation in the trial sample (n=75).	Statistical significance.
Mean Age (years)	25.89	24.8	.851	24.8	24.2	.750
Gender: **Male** (n; %)	43; 72.9	56; 74.67	.929[a]	54; 84.4	60; 75.95	.369[a]
Years in Education (Mean)	12.1	12	.584	12.2	12	.738
Ethnicity (%)						
Caucasian	88.1	77.3		62.5	77.2	
Asian	6.8	12.0	.981[b]	20.3	11.4	.912[b]
Black	1.7	2.7		9.4	7.6	
Other	3.4	8.0		7.8	3.8	
DUP (days)	341	240	.522	270	285	.828
Time Use Survey	10	11	.577	11.6	12	.814
Symptoms (PANSS)						
Positive	13.3	13.3	.989	14.1	14.6	.601
Negative	15.6	15.5	.940	16.8	16.6	.834
General	32.4	32.8	.790	32.3	33.7	.367

[a] Yates' Correction for continuity. [b] Pearson Chi-Square. SRCBT = Social Recovery Cognitive Behavioural Therapy. TAU = Treatment as Usual. NS = Not statistically significant ($p = >0.05$). Sub-sample = Participants from the trial who completed cognitive assessments.

Table 13. Completion rates of the cognitive measures by randomisation group at baseline and 9 Month follow-up.

Measure	SRCBT Group Baseline (N=59)	TAU Group Baseline (N=63)	SRCBT Group 9 Month FU	TAU Group 9 Month FU
WMS Logical Memory[a]	57	62	47	42
WAIS Vocabulary[b]	57	63	47	40
WAIS Block Design[c]	58	62	48	41
False Belief Stories[d]	58	57	48	41
AIHQ[e]	57	60	50	38
MSCEIT[f]	56	59	41	42
Social Knowledge Questionnaire[g]	59	60	52	43

WMS – Wechsler Memory Scale; WAIS – Wechsler Adult Intelligence Scale; ToM – Theory of Mind; AIHQ – Attribution of Intentions Questionnaire; MSCEIT – Mayer– Salovey–Caruso Emotional Intelligence Test; SRCBT – Social Recovery Cognitive Behavioural Therapy; TAU – Treatment as usual; FU – Follow-up. Neurocognitive Measures: [a] Verbal learning and memory; [b] Verbal Comprehension; [c] Non-verbal Problem Solving. Social Cognitive Measures: [d] Theory of Mind; [e] Attribution Bias; [f] Emotion Perception; [g] Social Knowledge.

Table 14. Means and standard deviations for structured activity in the SRCBT and TAU group sub-sample at baseline and 9-month follow-up.

Group Allocation	Baseline (Mean / Standard Deviation)	9 Month Follow-up (Mean / Standard Deviation)
SRCBT Group (N= 59)	$M = 10.52$, SD = 7.63	$M = 29.37$, $SD = 25.6$
TAU Group (N= 63)	$M = 11.70$, SD = 8.13	$M = 18.91$, SD = 20.71

M = Mean; SD = Standard Deviation; SRCBT – Social Recovery Cognitive Behavioural Therapy; TAU – Treatment as usual.

(ii)   Impact of SRCBT on cognition

Two group x time mixed MANOVAs were conducted. In the first, all SC variables were entered and in the second, all NC variables were entered. Results showed that the group x time interaction was non-significant, suggesting there was no significant impact of SRCBT on neurocognition (F = .794; p = .501; ηp^2 = .029), or social cognition (F = 2.138; p = .086); however, there was a large effect for social cognition (ηp^2 = .118). To examine whether the non-significant result could be due to a lack of statistical power, a post-hoc power analysis was computed. The observed power for the group x time interaction for the NC and SC composite was .601 and .214, respectively, suggesting that the sample is underpowered, especially for the SC analysis. A power calculation using GPower (Erdfelder, Faul & Buchner, 1996) showed a total sample size of N = 122 would be necessary to achieve 90% statistical power at the .05 level.

The time analyses revealed a significant main effect for time for both the SC composite (F = 4.012; p = .006) and NC composite (F = 14.949; p = .001), with a large effect size for SC (ηp^2 = .200) and NC (ηp^2 = .359).

(iii)   Correlation between changes in cognition and changes in structured activity post-intervention (exploratory)

The MANOVAs showed that there was no impact of SRCBT on SC and NC. Therefore, the planned correlation analysis was not conducted between cognition and structured activity.

(iv) Cognitive deficits in the sample at baseline.

Results of a post-hoc one-way ANOVA between the healthy control group (recruited in Study 1, page 50) and the combined SRCBT and TAU group showed that the combined FEP group performed significantly worse on verbal learning and memory, verbal comprehension and social knowledge, compared with the healthy control group (Table 15). Despite a trend for poorer performance in the combined FEP group, there were no other significant differences between the FEP and healthy control groups (Table 15). These findings replicate the findings in Study 1 where deficits were evident for social knowledge, verbal comprehension and verbal learning memory for individuals with poor social and role functioning.

Table 15. Comparisons of cognitive scores between the healthy control group and the combined SRCBT group and TAU group at Baseline.

	Combined SRCBT and TAU Group (N = 122)	Healthy control Group (N = 30)		
	M±SD	M±SD	*t*	*p*
Baseline Cognitive variables				
Verbal learning and memory	7.32; 3.53	9.83; 3.68	-3.456	**.001**
Verbal Comprehension	7.72; 3.24	9.70; 2.69	-3.093	**.002**
Non-verbal Problem Solving	8.08; 2.99	9.13; 2.75	-1.763	.080
Theory of Mind	4.30; 1.07	4.34; 1.12	-0.170	.865
Social knowledge	6.68; 1.75	7.43; 1.57	-2.146	**.034**
Attribution bias	2.86; 0.91	2.69; 0.67	0.990	.324
Emotion perception	97.16; 20.36	97.99; 13.81	-0.210	.834

TAU – Treatment as usual (Care under an Early Intervention Service). SRCBT – Social Recovery Cognitive Behavioural Therapy.

4.5.3. Data Analysis 2: Social cognition and Neurocognition as predictors of response to SRCBT.

Research Question 2: Can baseline SC and NC predict those more likely to respond to the SRCBT?

Two methods of defining treatment response were used in the analyses (please refer to 'statistical analyses' section for further information). First, results from the binary regression predicting treatment responders vs. non-responders using social disability cut-off scores from the TUS will be presented. Second, results of the linear regression predicting 'absolute change' scores from the TUS will be presented.

    (i)   Predicting treatment response to SRCBT using 'social disability' cut-off scores from the Time Use Survey (TUS).

Using the TUS social disability cut-off scores established by Hodgekins, French, Birchwood, *et al*. (2015), 16 participants had 30 hours or more of structured activity post SRCBT; for this analysis, this group was defined as 'treatment responders'. Thirty-one participants had scores below 30 hours a week of structured activity post SRCBT; this group was defined as the 'treatment non-responders'.

When the treatment responders vs. treatment non-responders were entered as a dependent variable in a backward binary regression, social knowledge was the only significant predictor of treatment response (*Wald* χ^2 = 4.073; p = .044), accounting for 16% (R^2_N = 0.162) of the overall variance. The results indicated that those who had better social knowledge at baseline were more likely to respond to the SRCBT intervention.

Given the shared variance between negative symptoms and cognition reported in other studies, the predictive impact of negative symptoms was explored. If negative symptoms significantly predicted treatment response, it was then subsequently included in the regression equation along with cognitive symptoms to explore if SC and NC were predictive of treatment response beyond any predictive impact of negative symptoms. A binary logistic regression revealed that baseline negative symptoms did not significantly predict treatment response using the TUS cut-off scores (*Wald* χ^2 = 2.551; *p* = .110). PANSS negative symptoms was therefore not entered into the regression equation with the cognitive variables.

(ii)   *Predicting absolute change in functioning following SRCBT using the Time Use Survey*

The absolute change score in TUS was entered into a backward linear regression as the dependent variable. The final model of the backward regression included social knowledge and attribution of blame bias (F (2, 44) 3.843, *p* = .029), accounting for 11% (R^2 = 0.110) of variance. However, baseline social knowledge was the only significant independent predictor of change in structured activity (*ß* = .350; *t* = 2.431; *p* = .019). Consistent with the previous finding, those with better social knowledge at baseline appear to be more likely to improve their structured activity post SRCBT (*ß* = .350; *t* = 2.431; *p* = .019).

To illustrate the magnitude of the effect of social knowledge on treatment response, individuals in the SRCBT group who scored in the top 25th percentile at baseline increased, on average, their structured activity by 11 hours more than those who scored below the 50th percentile.

Finally, to explore if social knowledge remained predictive of treatment response beyond any predictive impact of negative symptoms, a further regression was carried out. PANSS Negative symptoms did not significantly predict change in structured activity post intervention (β = -.930; t = -.178; p = .081). PANSS negative symptom score was therefore not entered into the regression equation with the cognitive variables

4.5.4. Analysis 3 (Exploratory) – Social cognition and Neurocognition as predictors of change in structured activity in the combined SRCBT and treatment as usual group.

To explore whether SC and NC account for variance in the change in structured activity beyond the variance explained by the effect of SRCBT, a linear regression was employed on the entire sample (SRCBT group and TAU group combined). Group allocation was force entered into the regression model followed then by baseline SC and NC. Absolute change scores for TUS was entered as the dependent variable. Once the group allocation was accounted for in the regression model, neither SC nor NC variables predicted a change in structured activity, thus suggesting that change in structured activity was attributable to randomisation to the SRCBT group (F (1, 87) 4.096, p = .046), and not to social or neurocognition. This is consistent with Study 1, where SC and NC were not able to contribute variance to the prediction of functional outcome when other variables were controlled.

4.6. Discussion

The SUPEREDEN trial was a proof-of-principle study comparing EIS in combination with Social Recovery CBT, plus EIS alone in a group of socially disabled young people who had not responded to treatment under EIS over a period of 12 months. The trial showed that those receiving SRCBT (augmented with EIS) over a period of 9-months made large, significant gains in structured activity compared to those receiving EIS alone (Fowler *et al*., 2017). The present study ran alongside the trial and sought to investigate whether an improvement in functioning (i.e. structured activity) arising from SRCBT also led to a change in social cognition (SC) and/or neurocognition (NC); and secondly whether baseline SC or NC would predict those more likely to respond to the SRCBT intervention.

4.6.1. Impact of SRCBT on social cognition and neurocognition

Whilst structured activity significantly increased for those who received the therapy in this sample, there was no difference in a composite SC or NC from baseline to follow-up between those who received the SRCBT and those who received TAU, suggesting that the SRCBT had no impact on cognition.

Given the established link between cognition and functioning found in previous studies of psychosis (Fett *et al*., 2011), and evidence from intervention studies showing that cognition is amenable to change (Combs, Adams, Penn, Roberts, Tiegreen, Stem, 2007; Eack *et al*., 2009), it is plausible to argue that if functioning improves, then cognition could also improve, especially in a sample selected on the basis of low baseline functioning. This reasonable hypothesis was however, was not supported in this study. This may be for several reasons.

Firstly, the intervention being studied – SRCBT – did not seek to directly address SC and NC. In previous studies where changes in cognition were observed with a corresponding change in functioning, the interventions were designed specifically to target SC and NC deficits (e.g. cognitive remediation and social interaction training; Combs, Adams, Penn, Roberts, Tiegreen, Stem, 2007; Eack *et al*., 2009; Roberts *et al*., 2014). In contrast, the SRCBT was a motivational CBT intervention for those who were underperforming and feeling demoralized and could do more in terms of their functioning and possibly within the constraints of their (impaired) cognition.

Secondly, the majority of the aforementioned studies were based on chronic schizophrenia samples and therefore may not hold among those in the early stages of their illness. Indeed, studies are emerging which suggest that SC and NC play a less important role in explaining functioning in early psychosis, compared to chronic illness (Cacciotti-Saija *et al*., 2016; Langdon *et al*., 2014; Simons *et al*., 2016; Sullivan *et al*., 2014). This notion supported in this study, as SC and NC also failed to predict the change in structured activity in the entire sample (the combined SRCBT and TAU group), beyond the variance explained by the therapy.

Unlike other FEP samples, this particular group were highly selected and presented with severe and stable social disability, spending a group total of less than 12 hours per week in structured activity (compared to 60 hours in an age-matched non-clinical sample; Hodgekins, French, Birchwood, *et al*., 2015). With such a severely disabled group, it could be that the initial improvements in functioning do not rely as much on cognition. The upper end of functional change (e.g. maintaining employment) may require relatively preserved cognitive function and might explain why there was no change observed in cognition in this study, particularly as the goal of the intervention was *not* to get individuals back into main roles such as work or

education, but to encourage engagement across a range of leisure activities. Furthermore, through making the initial changes in functioning, encouraged by the intervention, some individuals may be finding compensatory mechanisms to overcome their cognitive deficits (Simons *et al*., 2016). For the gains in functioning to be maintained in the long term, individuals may also need to improve their cognitive function. Longer term cognition and functioning was not explored in this study.

Consistent with the findings of Study 1 (Chapter 3), the combined FEP group was significantly impaired on tasks of verbal learning and memory, verbal comprehension and social knowledge. However, there were also some SC and NC domains that were not significantly impaired compared to the healthy control group, which were verbal comprehension, attribution of blame, emotion perception and Theory of Mind; again, consistent with findings in Study 1.

Despite there being SC and NC impairment present, the lack of widespread impairments might explain why SC and NC variables when considered together (i.e. as a composite score), were not significantly different between the SRCBT and TAU group post-intervention, as there would have been less scope for improvement. That said, a significant time effect for NC and SC composites were observed for both groups. Whilst this improvement might reflect a natural recovery process, improvement over time might simply reflect a practice effect. Comparisons with a healthy control group repeat tested over time will help clarify this in future research.

4.6.2. Can cognition predict those who are more likely to respond to the SRCBT intervention?

The second aim of this study was to explore whether SC and NC could predict those who are more likely to respond to the SRCBT intervention. Results of regression analyses showed that SC consistently predicted treatment response. Individuals who had better social knowledge at baseline were more likely to improve their structured activity post-SRCBT; specifically, those scoring in the top quartile on social knowledge at baseline, gained an additional 11 hours in their structured activity post intervention on average, compared to those with lower social knowledge scores at baseline.

Social knowledge assesses understanding of why and how others act in social situations. It therefore seems logical that when encouraged through therapy, those who have a better baseline understanding of the social world are going to be more motivated and more likely to engage in social activity, prescribed by SRCBT, than those who struggle to understand social situations. Furthermore, those with good social knowledge may be more likely to form a better therapeutic alliance leading to a better therapy response (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011).

4.6.3. Study Strengths and Limitations

The study benefits from being part of a large scale, multi-site, randomised controlled trial where researchers were blind to group allocation. Participants were recruited from several centres across the UK, which included urban, rural and town settings, making the sample highly diverse and representative. This study was the first to explore cognitive predictors of treatment response to a CBT intervention targeting poor functioning in FEP. It benefitted from a high rate of

consent to this study of cognition (79%), and a significant effect of SRCBT in this consenting sample with a comparable effect size to the trial sample. Nevertheless, the limitations of this study should be addressed.

The trial and the present study were exploratory to investigate the role of cognition within the context of a larger trial investigating the effectiveness of a new social recovery CBT. This meant that cognition was not routinely assessed in all trial participants. Despite a substantial proportion of the overall sample completing cognitive assessments at baseline, 20% of the trial sample did not. This may have biased the findings of the study as those with poorer cognitive function were the ones who refused to engage in the cognitive assessments. An analysis comparing those who completed the cognitive assessments with those who did not (Appendix A-10) showed however that there were no group differences on demographic and clinical characteristics apart from general symptomatology, where those who did not complete any cognitive assessment had more general symptoms. Given the lack of difference between these groups, it is unlikely that the observed effects were the result of sampling bias.

Another consideration is the high attrition at follow-up on some of the cognitive measures (Table 13). In the follow-up assessment sessions, priority was given to the completion of the primary trial outcome measures; therefore, non-completion of the cognitive measures was either due to participants disengaging or becoming fatigued. In the latter situation, the researcher would make a case-by-case decision to terminate the assessments.

Again, it is possible that those who did not complete assessments at follow-up were likely to be more cognitively and socially impaired, potentially biasing the current sample. The high attrition on some of the cognitive measures also meant that there was inadequate power to detect

a significant post-intervention effect. Interestingly, a large effect size was detected for the group x time interaction for the SC composite despite being non-significant. It is possible that if the study was adequately powered, the group x time interaction for the SC composite may have become significant.

Finally, as discussed in Chapter 3, the cognitive measures used in this study may not have completely captured the complex dynamics of everyday social interaction, and therefore there is a need to develop more ecologically sound measures of SC in order to build a wider understanding of the role that SC plays in disability in FEP (Green *et al.,* 2008; Ludwig *et al.,* 2017; see final chapter for further discussion). Nevertheless, these measures represent the current standard for studies of SC and NC.

4.6.4. Conclusion

Those who received the SRCBT significantly increased their structured activity at 9 months follow-up compared with those who received TAU. There was no significant change in SC or NC post-intervention, suggesting that the SRCBT had no impact on cognition. Although previous studies have found a close association between cognition and functioning in schizophrenia, these findings may imply that cognition may play less of a prominent role in social functioning in early psychosis than in chronic schizophrenia. However, the results may also simply reflect the nature of the intervention being studied, as cognition was not directly targeted by the intervention and the sample suffered from low power.

Despite the SRCBT having little impact on cognition, regression analyses consistently showed that SC predicted response to the SRCBT intervention. Specifically, those scoring in the top

quartile on social knowledge at baseline gained an additional 11 hours in their structured activity post-intervention on average, compared to those with lower social knowledge scores at baseline. This has implications for future trials, where we might hypothesise that remediation of SC prior to therapy may improve the efficacy of the SRCBT, particularly for individuals assessed to have poorer social knowledge.

5.0. CHAPTER 5

EMPIRICAL STUDY 3

5.1. A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY EXPLORING THE NEURAL CORRELATES OF THEORY OF MIND IN YOUNG PEOPLE WITH FIRST EPISODE PSYCHOSIS RECEIVING A PSYCHOSOCIAL INTERVENTION AIMED AT IMPROVING STRUCTURED ACTIVTY.

5.2. Abstract

Deficits in everyday functioning are a core feature of psychosis, and often begin in adolescence. The social regions of the brain, linked to social cognitive function, go through substantial changes during the adolescent years. Interventions targeting social disability might be most effective in the early phase of illness, where individuals are less removed from the neurodevelopmental trajectories (Bartholomeusz, *et al*., 2011; Wood, Yung, McGorry & Pantelis, 2011).

Social cognition (SC), especially Theory of Mind (ToM), is impaired in psychosis and is closely linked to impaired functioning. Altered brain activation in the regions associated with ToM processing are evident during (and prior to) illness onset, making it a promising endophenotype.

Research should clarify to what extent abnormal brain function in the social brain regions (e.g. ToM) are associated with deficits in everyday functioning, and whether intervention,

particularly where social disability is targeted early in the course of illness, could improve brain function in the SC regions.

Design:

This was a 9-month follow-up Functional Magnetic Resonance Imaging (fMRI) study, exploring the neural changes in the ToM regions in a sample of young people with FEP who were receiving a psychosocial intervention targeting their poor functioning. The study ran in parallel to the multi-site NIHR SUPEREDEN trial, which is a single-blind, proof-of-principle trial, comparing Social Recovery-Oriented Cognitive Behavioural Therapy (SRCBT) plus treatment as usual (TAU) from an Early Intervention Service (EIS), against TAU alone.

Method:

Six participants who were allocated to the treatment arm of the SRCBT trial underwent fMRI scanning (whilst completing a cartoon ToM task) at baseline (prior to the SRCBT intervention), and at the end of the therapy (after 9 months).

Results:

Results showed increased activation post-intervention in the temporal, parietal and frontal regions. Activations become more refined and localised in the ToM regions, namely the temporo-parietal Junction (TPJ), and there were also significantly more bilateral activations by 9 months follow-up. This was evidenced both at the individual and group level. Further inspection of the change in activation in TPJ from pre- to post-intervention showed a trend for increased activation which was associated with more hours of structured activity at 9 follow-up.

Implications:

Although tentative, this study has provided preliminary insights into the mechanisms underlying social recovery and the brain networks that might be implicated in functional change. This may allow for the refinement of the SRCBT, or may lead to the development of new interventions, particularly for those who do not respond to therapy.

5.3. Introduction

Impairments in everyday functioning are a common feature of psychosis. These deficits are shown to stem from adolescence, which is a critical stage for brain maturation, particularly in the social brain regions (Pantelis & Bartholomeusz, 2014).

The social regions of the brain which are associated with social cognitive (SC) function – namely the medial prefrontal cortex (mPFC), superior temporal sulcus (STS) and the anterior cingulate (ACC) – go through protracted development during adolescence, which is also typically when psychosis manifests (Bartholomeusz *et al*., 2011; Blakemore, 2008; McGlasham & Hoffman, 2000). It seems plausible that aberrations in the neurodevelopmental process may be associated with SC deficits observed in the disorder (Bartholomeusz *et al*., 2011; Blakemore, 2008; McGlasham & Hoffman, 2000).

Social cognitive impairments are closely linked to deficits in everyday functioning in psychosis (Couture *et al*., 2006; Fett *et al*., 2011; Stouten *et al*., 2014). Most notably of these SC impairments, Theory of Mind (ToM) – defined as the ability to make mental state inferences about others – has shown to contribute unique variance to functional outcomes above general cognition and symptoms in psychosis, making it a promising treatment target (Baron-Cohen, 1995; Brune, 2005; Fett *et al*., 2011).

Using functional magnetic resonance imaging (fMRI), a consensus of studies in psychosis have shown differences in functional activation in the ToM network compared to activation in healthy control participants (Bosia, Riccaboni, Poletti, 2012). Differential activation has been shown in the key regions associated with ToM processing, which include: the medial prefrontal cortex (MPFC), temporal parietal junction (TPJ) and superior temporal sulcus (STS; Bosia *et*

al., 2012; Gallagher & Frith 2003; Walter *et al.,* 2004). This network of regions has now been defined as the ToM or mentalising network (Abu-Akel & Shamay-Tsoory, 2011).

Interestingly, these differences have not only been found in individuals with chronic schizophrenia, but also in individuals with FEP, those at ultra-high risk (UHR) of developing psychosis, and in healthy controls who have a genetic risk for schizophrenia (Brunet, Surfati, Hardy-Bayle & Decety, 2003; Lee *et al*., 2006; Walter *et al*., 2009; Walter *et al.,* 2011). This suggests that aberrant functioning in these regions may be a promising endophenotype, and likely reflect a neurodevelopmental pathway to impairment.

Similarly, poor functioning emerges premorbidly, continues to remain stable during the prodrome, and persists through to chronic illness, suggesting that these deficits are enduring and neurodevelopmental in nature (Lin, Wood, Yung, 2013; Wiersma *et al*., 2000). There may be a subgroup of individuals with psychosis whose poor functioning and social cognitive impairment are underpinned by aberrant functioning in the social brain regions, stemming from adolescence. Research should clarify to what extent abnormal brain function in the social brain regions are associated with functional impairments, and whether intervention, particularly where social disability is targeted, could improve brain function in these regions.

One such intervention that has been specifically developed to target social disability in individuals with early psychosis is Social Recovery Cognitive Behavioral Therapy (SRCBT), introduced in Study 2 (Chapter 3). SRCBT has already been shown to be effective at improving structured activity in individuals with persistent social disability in established psychosis and in first episode psychosis (FEP; Fowler *et al*., 2009; Fowler *et al*., 2013; Fowler *et al*., 2017).

It is important to investigate neuroplasticity effects of social interventions, such as SRCBT, as this may demonstrate the durability of the intervention and long-term benefits to the individual or may lead to refinement of current interventions to produce a more sustained and improved treatment effect (Campos *et al*., 2016).

For example, through receiving the SRCBT and gaining greater social exposure, this may encourage changes in social brain activity, by presumably tapping in to the brain's neuroplasticity abilities (Campos *et al*., 2016). Fortifying the social cognitive brain regions may in turn allow for improved cognitive function and enhanced real-world social experience, leading to a cyclical relationship between social brain function and social behaviour (Dodell-Feder *et al*., 2015; Horan & Green, 2017).

In intervention studies which have specifically targeted impaired SC function, a recent systematic review has provided evidence of structural and functional improvements following SC interventions (Campos *et al*., 2016). Whilst these findings are encouraging and demonstrate that social interventions can induce neuroplasticity changes, studies have so far largely focused on individuals with chronic schizophrenia (Campos *et al.,* 2016). It is important to explore the effectiveness of interventions in the early phase of illness, where improvement in functioning is most likely to be achieved due to the neuroplasticity associated with ongoing neurodevelopment during the adolescent years (Bartholomeusz *et al*., 2011; Bartholomeusz & Allott, 2012).

Furthermore, none of the studies under review used a ToM task. Selecting an appropriate task paradigm is important for investigating SC brain changes, as certain brain regions may be distinctly activated by specific experimental paradigms (Campos *et al*., 2016).

As such, investigating the neural correlates of ToM pre- and post- SRCBT may further understanding of the brain networks associated with functional change. If the brain regions associated with SC are indeed implicated in functional change, this could lead to refinement of the current intervention, particularly for individuals who may not respond to the SRCBT.

5.3.1. Using a Theory of Mind functional imaging task to investigate the neural networks implicated in functional change in early psychosis.

fMRI is a useful, non-invasive tool used to explore the neural underpinnings of ToM deficits in psychosis (Bosia *et al*., 2012). It works by detecting changes in the local oxygenation of blood, which acts as a surrogate measure of neuronal activity (Logothetis & Wandall, 2004). It is believed that as neuronal activity increases, cells require more oxygen to metabolise, resulting in increased blood flow to that specific area. The fMRI signal detects the oversupply of oxygenated blood to an active brain region and is referred to as the blood-oxygen-level-dependent, or BOLD signal (Poldrack, Mumford, Nichols, 2011). Despite being an indirect measure, the BOLD signal has a high correlation with the brain's electrical activity (Weiskopf, *et al.,* 2004); it also has good spatial resolution and relatively good temporal resolution when compared to other methods such as positron emission tomography (PET; Poldrack *et al.,* 2011).

Using fMRI, Walter and colleagues (2009) investigated the dysfunction in the ToM regions in a homogenous group of individuals with paranoid schizophrenia. The 'attribution of intentions task' which was used by the authors, is a previously validated task (Ciaramidaro *et al*., 2007; Walter *et al*., 2004), involving cartoon picture stories varying in intentionality. The task requires participants to select the most logical ending to a set of stories, which include a control

condition involving objects (known as the 'physical causality' condition), and three 'intention' conditions, each differing in the level of social interaction. All three experimental 'intention' conditions require the inferences of an intention for either non-social goal-directed actions, or social goal-directed actions of a protagonist. The most complex condition (communicative intentions), consists of scenarios of characters interacting with each other; the participant must attribute the intention of one character communicating with the other (Figure 3). The control condition (physical causality) requires participants to attribute the cause of an event to a non-intentional factor (Figure 4).
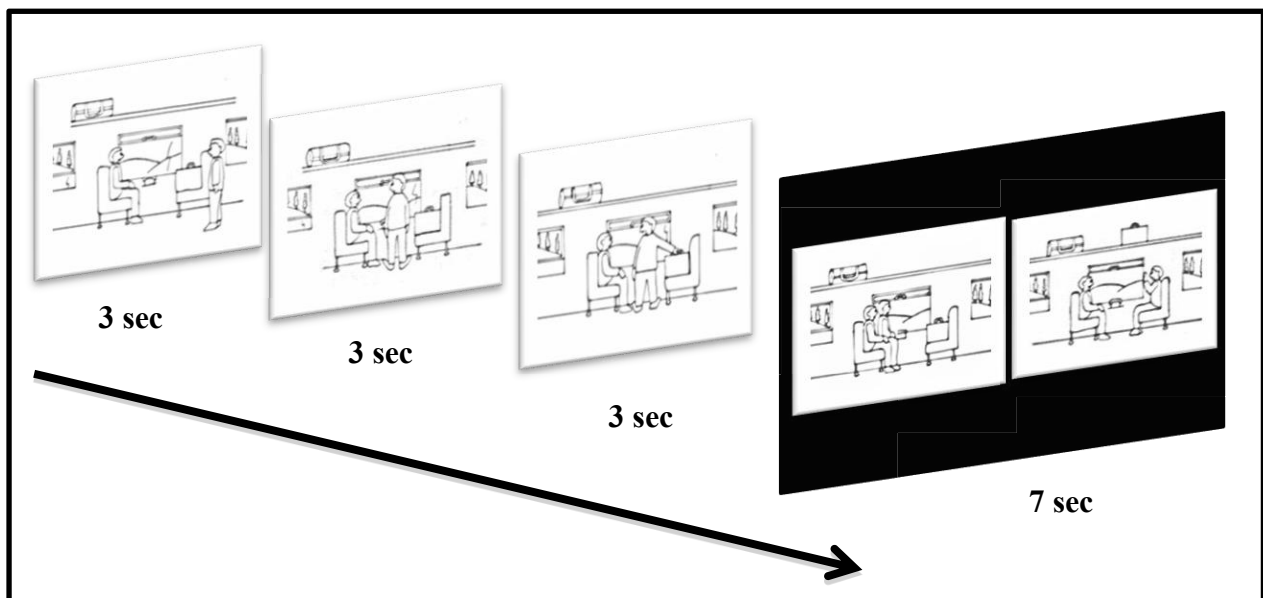
Figure 3: 'Attribution of Intentions' task paradigm. Example of a scenario presented during a trial of the Communicative Intentions (CI) condition.
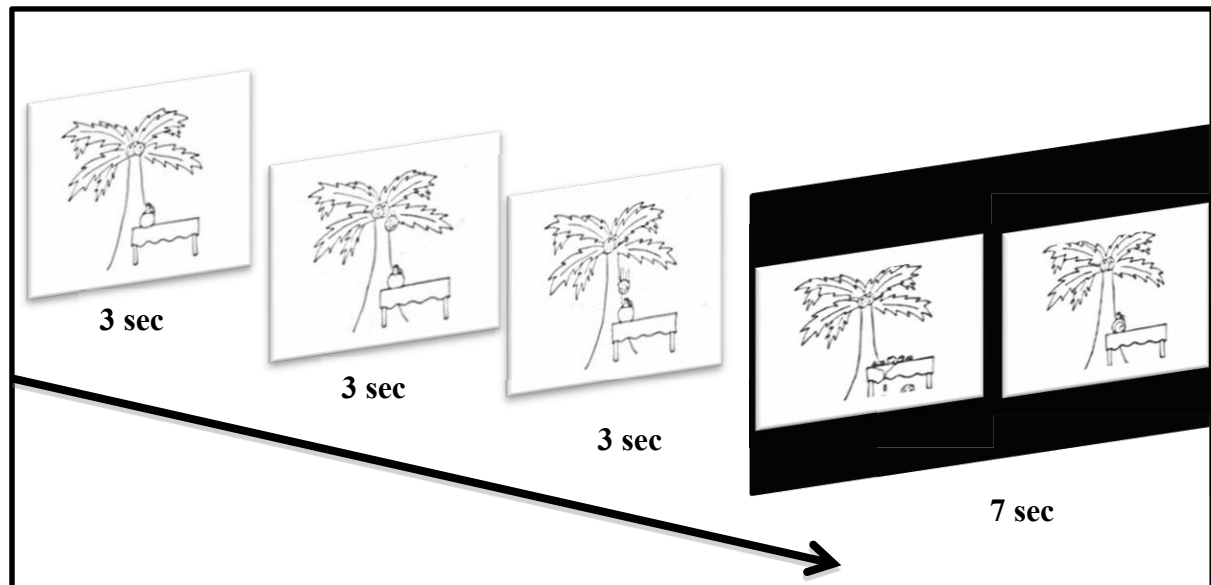
Figure 4: 'Attribution of Intentions' task paradigm. Example of a scenario presented during a trial of the Physical Causality (PhC) condition.

Using this task in a group of individuals with paranoid schizophrenia, the authors found dysfunction in the ToM network dependent on the type of intention involved. Compared to the healthy control participants, the MPFC, and left and right TPJ were less activated in the patient group for the social intention scenarios (Figure 3). There were no group differences for the non-social intention scenarios, thus showing a specific ToM impairment in psychosis. However, the findings of this study are limited as they focused on homogenous subgroups with chronic illness and may not generalise to young people experiencing a FEP. Individuals in the early stages of illness are less removed from their neurodevelopmental trajectories, and neuronal circuits may still be intact or only functionally impaired, and as such, intervention is most likely to be effective in this stage of illness (Bartholomeusz, *et al.*, 2011; Wood e*t al.*, 2011).

5.3.2. *The Present Study*

Using an adapted version of the 'attribution of intentions task' used by Walter and colleagues (2004), the present research aimed to explore the neural correlates of ToM ability in a sample of young people with FEP, before and after receiving a psychosocial intervention targeting social disability. The intervention studied was Social Recovery Oriented Cognitive Behavioural Therapy (SRCBT), which was evaluated as part of the NIHR SUPEREDEN Study (please see Chapter 4 for more information relating to the SRCBT).

The present study will examine whether improvement in functioning (i.e. structured activity) following SRCBT will correspond with improved brain function on the ToM task. It is hoped that this will add value to the assessment of the efficacy of the intervention by providing new insights into the underlying mechanisms supporting successful treatment (i.e. improvement in structured activity).

5.3.3. *Aims and Objectives*

Using an adapted version of the fMRI 'attribution of intentions' task (Walter *et al*., 2009), this study aims to explore:

(a) Neural correlates of ToM in a sample of young people with FEP who present with social disability

(b) Changes in brain function in the ToM regions pre- and post- SRCBT.

(c) Whether changes in brain function following SRCBT is associated with structured activity at 9-month follow-up

5.4. Method

5.4.1. Design

This was a 9-month follow-up study running in parallel to the multi-site NIHR SUPEREDEN trial, which is a single blind, proof-of-principle trial, comparing SRCBT plus standard care from an Early Intervention Service (EIS), against standard care from EIS alone. fMRI was carried out at baseline (pre-SRCBT) and at the end of therapy (after 9 months).

Please see Chapter 4, section *4.4.* for further information on the SRCBT and trial procedure.

5.4.2. Sampling

Service users of the EIS in Birmingham, who consented to the NIHR SUPEREDEN trial, and were randomly allocated to the SRCBT group, were invited to take part in this fMRI study. The study was approved by the Black Country NHS research ethics committee (Appendix A-1). Of the nineteen individuals who were allocated to the SRCBT group (at the Birmingham site of the NIHR SUPEREDEN trial), ten consented to the fMRI study. Exclusion criteria were as follows: (a) insufficient command of the English language; (b) presence of any neurological disorders, for example, epilepsy; (c) documented history of a learning disability; (d) history of severe head injury (more than 5 minutes loss of consciousness, or an overnight hospital stay).

Seven scans were successfully conducted at baseline. Three scanning sessions were ceased because two participants become claustrophobic during scanning, and the other participant refused to remove jewellery. One participant refused to attend for a follow-up scan, therefore, the final sample consisted of six participants who received scans both at baseline and after 9-month follow-up. Furthermore, for one participant who attended for a follow-up scan (B005),

the behavioural data was not obtained at the same time point as the scanning but was obtained at the next follow-up point (2 months after scanning).

The six participants were male, aged between 16-35 years, and were right-handed (see table 16 for socio-demographic information). All participants presented with a low level of structured activity after at least one year of treatment within EIS (defined as 30 hours or less per week on the Time Use Survey), thus meeting eligibility criteria for the SUPEREDEN trial (see Chapter 4). Table 16 provides a summary of the demographic and clinical characteristics of the study sample at baseline. The clinical characteristics that were explored were psychopathology, which was rated by the Positive and Negative Syndrome Scale (PANSS; Kay *et al.,* 1987), delay of untreated psychosis (Larsen *et al*., 1996) and structured activity (assessed using the time use survey; Short, 2006). Please refer to Chapters 3 and 4 for full description of these measures.

All six participants were screened for conditions for which fMRI would represent a health risk (Appendix B-16) and would have been excluded if any contraindications were present.

Table 16. Demographic and clinical characteristics of the fMRI group at baseline

	FEP participants (*n = 6*)
Age (years; M±SD)	22.83 (5.15)
Gender (*Male; n*)	6
Ethnicity (*n*)	
Black	1
Asian	4
Mixed	1
Education (years; M±SD)	11.67 (4.08)
Positive and Negative Syndrome Scale	
Positive (M±SD)	9.00 (2.45)
Negative (M±SD)	16.17 (5.57)
General Psychopathology (M±SD)	27.83 (8.77)
Level of functioning at study entry (Time Use Survey)	
Hours per week spent in structured activity (M±SD)	17.08 (6.44)
DUP (days; M±SD**)**	79.67 (120.69)

DUP = Delay of Untreated Psychosis. M = Mean. SD = Standard Deviation.

5.4.3. Materials

(a) Functional Magnetic Resonance Imaging (fMRI) Paradigm

An adapted version of the 'attribution of intentions' task was used to investigate the neural correlates of ToM. The task was based on the original work of Walter and colleagues (2004) who demonstrated that the task robustly activated the ToM network in healthy controls and in individuals with paranoid schizophrenia (Walter *et al*., 2004; Walter *et al*., 2009; Walter *et al*., 2011).

During the task, participants were asked to look at picture stories and then decide on the most logical ending to the story. The adapted version of the task comprised of two conditions:

communicative intention (CI) and physical causality (PhC). The CI condition involves a scenario where two characters are interacting with each other; the participant must attribute the intention of one character communicating with the other. For example, Person A is looking for a seat on a train and indicates to Person B to move their luggage, so they can take a seat (Figure 3). This condition was selected as it involves the most complex social intention where two people interact. To interpret this scenario would require ToM ability. Walter and colleagues (2009) demonstrated that group differences between individuals with schizophrenia and healthy controls were most pronounced for the CI condition, compared to the simpler conditions in which a single protagonist was acting in isolation towards a social goal.
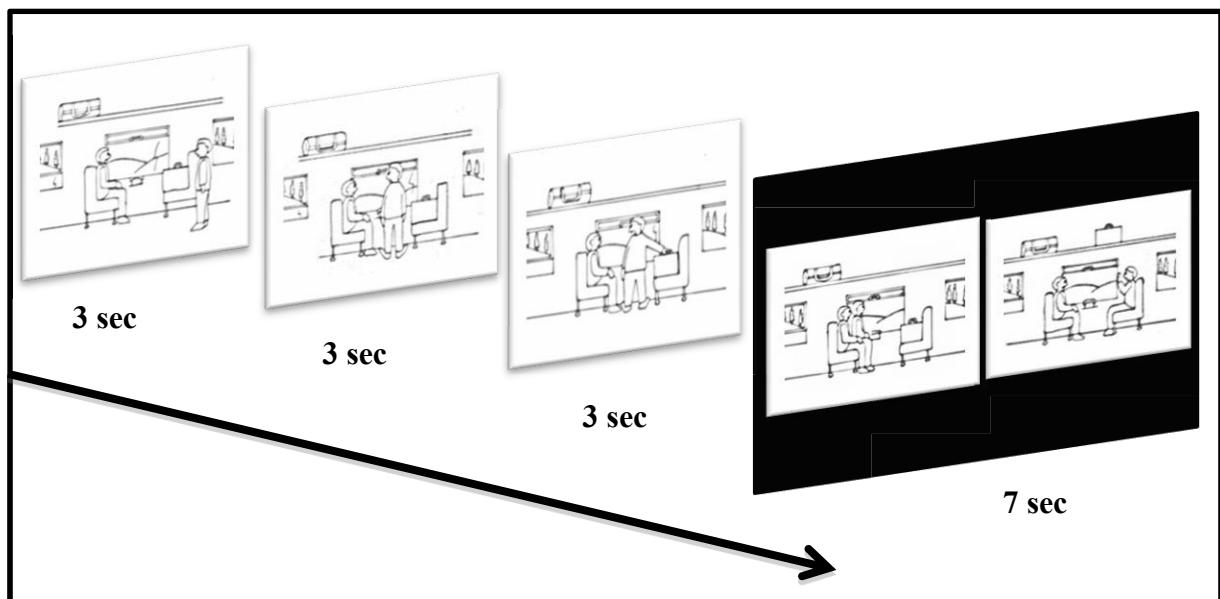
Figure 3: 'Attribution of Intentions' task paradigm. Example of a scenario presented during a trial of the Communicative Intentions (CI) condition.

For the PhC condition, participants are required to attribute the cause of an event to a non-intentional factor. For example, a coconut falls from a tree and smashes a glass bottle placed on

a table underneath the tree (Figure 4). To clarify, unlike the CI condition, there was no social content depicted in these pictures.

The CI condition and PhC condition consisted of cartoon stories presented in three consecutive pictures (presented for 3 seconds each). Participants were required to select the most logical ending to the story from two options presented simultaneously for 7 seconds (response phase); one picture was correct, and the other picture was highly improbable. Participants were required to respond using a button box. In the original version of the task (Walter *et al.*, 2009), a third-choice picture was presented, which composed of elements of pictures from previous scenes. This was removed from the adapted version of the task, as it was highly unlikely that participants would select this option. Presenting only two choices would decrease the time needed for participants to look at the images before making a choice, thus reducing the weight of information presented to participants and minimising the likelihood of concentration diminishing during the task. All pictures were presented in black and white (Figure 3 and Figure 4). Each trial lasted for 16 seconds (story plus response phase), followed by a 16-second rest period between trials. A decision was made to include the 'rest' condition, firstly as way of reducing the information given to participants, and secondly to allow for the BOLD signal to resolve to a baseline level.

Eleven stories were presented for each of the conditions in a pseudo-randomised order. In total, there were 22 trial blocks, separated into two scanning sessions, five minutes apart. This was to reduce to likelihood of the participants' concentration diminishing. The first block of trials (fMRI session 1) lasted approximately 7 minutes, and the second block of trials (fMRI session 2) lasted approximately five minutes. The order of the fMRI trial blocks was counterbalanced across participants and across baseline and follow-up, in order to rule out any order effects. As

the focus of the task was to explore the process of ToM, a block design was used so that comparisons could be made between activation during the ToM condition (CI) vs. the non-social condition (PhC). Stimuli were presented using Presentation® Software (Neurobehavioural Systems, Davis, CA). Participants' response accuracy and reaction times were recorded during scanning.
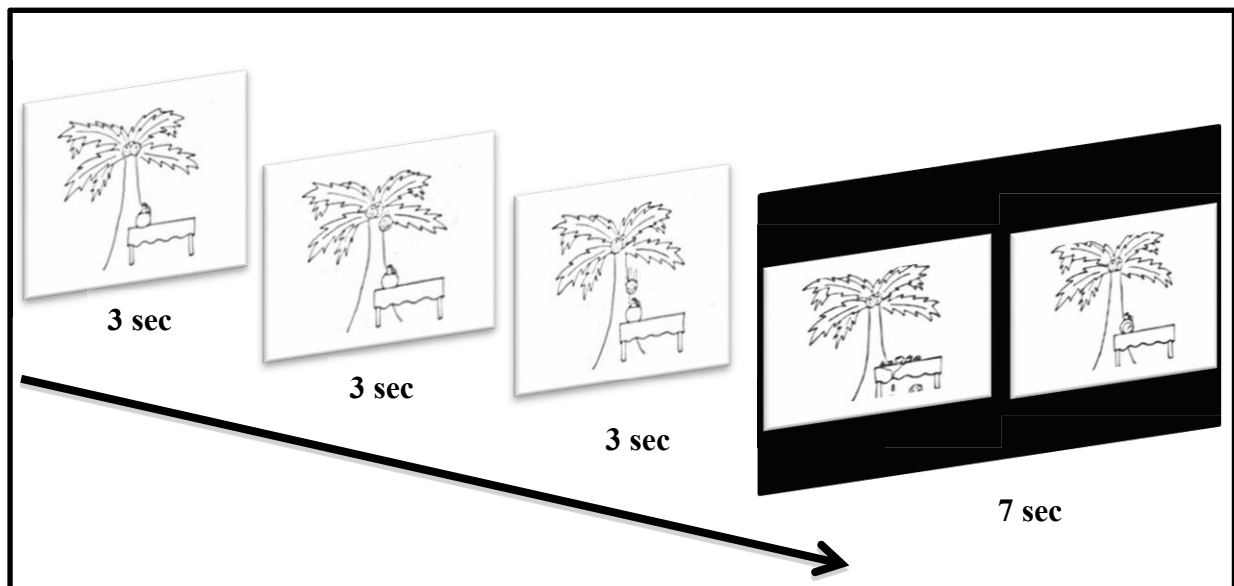
Figure 4: 'Attribution of Intentions' task paradigm. Example of a scenario presented during a trial of the Physical Causality (PhC) condition.

(b) Piloting the adapted version of the attribution of intentions task: Results

In a pilot study of five healthy control participants conducted as part of a Master's thesis at the Aix-Marseille University, France (Akkari, 2012), the adapted version of the attribution of intentions task (described above) was used. The results showed the primary areas of the ToM network were more involved in the CI condition compared to the neutral PhC condition, consistent with Walter and colleagues' findings (Walter *et al.*, 2009). The main activations were spread from the temporo-parietal junction along the superior temporal sulcus (Akkari, 2012).

The results support the efficacy of the adapted version of the attribution of intentions task in exploring the neural correlates of ToM.

5.4.4. Measures

(a) Functioning

The Time Use Survey (TUS; Short, 2006) was used to assess functioning at baseline and at 9 months follow-up. The Time Use Survey is a semi-structured interview, which asks about time spent over the last month in activities such as work, education, voluntary work, socialising, leisure, sports, chores / housework and childcare. The information gathered is used to calculate average hours per week spent in 'structured activity'. According to the Office of National Statistics, a non-clinical population aged between 16-36 years spend an average of 63.5 hours per week in structured activity (Short 2006). Using the TUS in a sample of individuals with psychosis, Hodgekins, French, Birchwood, *et al.* (2015) established the following cut-off scores for assessing social disability in young people experiencing psychosis: 45 hours or more per week (*Good Social Functioning*); 30 – 45 hours per week (*At-Risk of Social Disability*); below 30 hours per week (*Social Disability*); below 15 hours per week (*Severe Social Disability*). Potential participants were screened using the TUS and considered eligible for the SRCBT trial if they met the cut-off of below 30 hours per week in structured activity (*Social Disability*).

(b) Clinical Assessments

(i)   *Positive and Negative Syndrome Scale* (PANSS; Kay *et al.,* 1987). This is a 30-item scale which assesses the severity of the positive and negative symptoms of schizophrenia as well as general psychopathology. The PANSS has good inter-

rater, test-retest and internal reliability and established internal, external and construct validity (Kay *et al*., 1987). The PANSS was conducted by trained interviewers.

(ii) Duration of untreated psychosis (DUP; Larsen, McGlashan & Moe, 1996). DUP is defined as the delay between onset of psychosis and onset of criteria treatment (Larsen, McGlashan & Moe, 1996). The onset of psychosis was defined by the presence of one psychotic symptom rating above a level 4 on the PANSS positive scale, or cluster of positive symptoms scoring above a level 7 on the PANSS, with a duration of 2 weeks or more. This information was collected retrospectively from online medical notes and participant interview in a standardised method described by Larsen and colleagues (1996).

5.4.5. Procedure

Individuals with FEP who consented to the SUPEREDEN trial were randomly assigned to either the intervention group (SRCBT & standard care from EIS) or the Treatment as Usual Group (TAU), where individuals received standard care from EIS alone. Participants who were assigned to the intervention group were invited to participate in the present study, for which they underwent fMRI scanning (whilst completing the aforementioned fMRI paradigm) at baseline (prior to the intervention), and at the end of the intervention (9 months). Information on functioning, demographic (Appendix B-18) and clinical variables were collected at baseline and at 9 months follow-up by researchers who were blind to group allocation. The imaging was carried out at the Birmingham University Imaging Centre (BUIC) by an authorised scan operator. Prior to scanning, written informed consent was obtained (Appendix A-8, A-9). Each session lasted approximately 45 minutes, and participants received £20 in recognition of their

time and expenses. Before performing the ToM task in the scanner, participants were fully briefed on the scanning procedure and were given detailed instructions on how to perform the task (Appendix B-17). Participants also completed two practice trials prior to scanning to ensure they had full understanding of the task.

5.4.6. fMRI data acquisition

fMRI images were acquired using a 3.0 Tesla Philips Achieva MRI scanner (Philips Medical Systems, Eindhoven, the Netherlands). The scanner was equipped a with a 32-channel head volume coil. T2-weighted functional images were acquired in a sagittal planning, with whole brain coverage (excluding the cerebellum). A pencil beam (PB) volume shimming technique was also applied. One brain volume consisted of 36 slices; each slice was 3mm in thickness with no gap between the slices. The time of repetition (TR) was 2.2 seconds and the echo time was 35 milliseconds. Voxel size was 2.5x2.5x3mm. The first fMRI session contained 196 volumes, and the second session contained 160 volumes.

5.4.7. Analysis of behavioural data

Results of a 1-sample Kolmogorov-Smirnov (K-S) test indicated that the data were parametric (with K-S Z values ranging from 0.183 to 1.60 and p values ranging from 0.047 to 0.200), therefore repeated-measures t-tests were used to explore group change (N=6) from baseline (pre-SRCBT) to follow-up (post SRCBT) for psychopathology, functioning (i.e. structured activity) and fMRI task performance. Graphical examination of the QQ plots also indicated no departure from normality, which is one of the key assumptions of a t-test. Separate repeated measures t-tests were performed on the following clinical variables: negative symptoms (PANSS), positive symptoms (PANSS), general psychopathology (PANSS) and structured

activity (assessed by the TUS). Behavioural fMRI task performance was also explored for group mean reaction times (in seconds; incorrect and correct responses included) and task response accuracy (maximum number of correct response = 21).

Given the small sample size of this study, in addition to reporting significance at the $p = 0.05$ level, effect sizes were calculated using a formula for Eta Squared (Pallant, 2011):

$$\frac{t^2}{t^2 + n - 1}$$

Eta Squared values were interpreted by the guidelines set out by Cohen (1988) (small effect = .01; moderate effect = .06; large effect = .14). Statistical analyses were carried out using SPSS 22 for Windows.

5.4.8. fMRI data analysis

   (a) fMRI data pre-processing

To increase the robustness of the statistical analysis, a series of pre-processing steps were conducted to remove acquisition–specific artefacts from the data. Data pre-processing and statistical analysis were conducted using Statistical Parametric Mapping (SPM 8; Wellcome Institute of Cognitive Neurology, London, UK) and MATLAB 7.4 (MathWork, Natick, London, UK). Prior to the pre-processing, images were obtained from the Phillips scanner in PARREC format which was converted into SPM- ANALYZE format using MRIcro software (Rorden & Brett, 2000). The anatomical image and functional images were then re-oriented and repositioned using the extremity of the genu of the corpus callosum as a reference point. The first step in the pre-processing involved realigning the functional images to correct for

participant motion. This was done using a 6-parameter spatial transformation (3 translations and 3 rotations), producing a graph indicating the direction and amplitude of head movement. Excessive movement (defined as data rotation exceeding 2 degrees or translation exceeding 1 voxel size) was corrected using Artrepair (N=2). In cases where there was excessive movement in more than one-third of the data, volumes with excessive movement were excluded from the analysis (N=1). Before Artrepair was applied, to improve its accuracy, the realigned images for these participants were smoothed with a kernel Full-Width Half Maximum of 4mm. Once the images were realigned (and corrected for excessive movement), they were then slice-time corrected. The purpose of this was to correct for the time difference in the acquisition of the slice images between the two scanning sessions (ensure that each slice corresponds with the same point in time). The mean functional image created by the realignment step above was then co-registered to the structural image so that both images were in the same space. The structural image comprising of different tissues (e.g. grey matter, white matter and cerebral spinal fluid) was defined using a segmentation procedure. This produced a grey matter segmented image which was then used to normalise the structural image into a standard stereotactic space using an SPM template. The functional images were spatially normalised using the same normalisation matrix from the segmentation procedure. The structural and functional images were then in the same stereotactic space allowing for inter-subject comparisons (group analysis). In the final step of the spatial preprocessing, functional images were smoothed with a Gaussian kernel to facilitate averaging of data points across subjects. The Full-Width Half Maximum of Gaussian kernel was twice the voxel size (5x5x6). It was decided that a smaller kernel was to be used to minimise the likelihood that effects within small structures would not be smoothed out. For images that were corrected for excess movement using Artrepair (previously smoothed with a kernel Full-Width Half Maximum of 4mm), in the final stage of

the preprocessing, these images were smoothed with a 3x3x4.5mm Gaussian kernel to ensure that the overall smoothing was equal.

(b) First-Level Analysis

Once the pre-processing was complete, a first-level analysis was conducted on each subject individually to detect BOLD signal changes that fit the desired model. The model employs a block design based on the two conditions in the experiment: Communicative Intentions (CI) and Physical Causality (PhC). It was decided that a rest condition would not be included in the model due to the overlap of social cognitive regions activated as part of the default mode network during resting state. Inferences were made based on the variances in each voxel's signal over time. Before proceeding with the analysis, the onset times and exact durations of each of the blocks (CI and PhC) were calculated using Microsoft Excel. A high-pass filter was then calculated to remove slow signal drifts caused by noise in the fMRI time series. This was calculated based on the largest difference between the onset blocks for the both conditions, multiplied by 2. Once the model was specified, SPM applied a high pass filter (calculated prior to the analysis) and global normalisation to remove any unnecessary signal changes in the model. For the case study analysis, where data were interpreted on the individual level, serial correlations were applied to the model to account for any autocorrelations in the data. A design matrix was then produced, and the model was estimated, producing beta images showing how the model fits each voxel for each of the conditions. Contrast weights were then defined in order to determine how well each voxel in the brain fits the specified model (for each condition).

As the main focus of the analysis was to determine which regions are more activated during the ToM condition (CI) compared to the non-theory of mind condition (PhC), the t-contrast was

defined as 'CI>PhC' (weight added to the CI condition). A t-test is run within SPM by subtracting the beta images from one another. This produced images on a glass brain highlighting the areas that were significantly more activated in the CI condition compared to the PhC condition. Due to the small sample size of this study and the interpretation of the findings at the individual level, Family-Wise Error (FWE), the most stringent height threshold control, was applied, reducing the likelihood of a Type 1 error. The first level analysis was run separately for each participant and baseline and then at follow-up.

(c) Second-Level Analysis

Once the analysis was conducted at the individual level, a second level analysis was conducted to determine BOLD signal changes between the conditions (CI and PhC) across participants. This was done using several exploratory analyses. Firstly, a one-sample t-test was run in SPM to investigate which brain regions showed more activation in the CI condition compared to the PhC condition across participants. Two separate one-sample t-tests were applied for baseline and follow-up. Once specified, the model was then estimated, and the same t-contrast was applied (CI>PhC) as in the first level analysis.

The second analysis conducted was a two-sample t-test to explore the change in the BOLD signal between baseline and follow-up across subjects for the t-contrast of 'CI>PhC' (defined in the first level analysis). The t-contrasts were defined to explore which areas were more activated at baseline compared to follow-up, defined as 'BL>FU'. For regions that are more activated for follow-up compared to baseline, the contrast was defined as 'FU>BL'. The t-contrasts were calculated by subtracting the beta images from the design matrix, and inference

was made on how well each voxel fitted the model based on the type of condition (areas more active for the CI condition compared to PhC condition).

Due to the small number of participants (N=6), an uncorrected threshold of activation was defined as $p = 0.01$, and an extent threshold of 10 voxels was applied for each of the analyses. Images were then produced on a glass brain and overlaid on a standard Montreal Neurological Institute (MNI) brain template. Coordinates were also reported based on the MNI atlas showing the most significant activation (peaks) within each cluster.

(d) Region of Interest Analysis

Given the hypothesized role of the posterior temporoparietal junction (TPJ) region in mentalising (Mars *et al.,* 2012) this area was selected as the region of interest (RoI), to explore the relationship between the change in signal intensity (between baseline and follow-up) and changes in structured activity post SRCBT.

The RoI (TPJ) was defined using MARSBAR software (http://marsbar.sourceforge.net). A sphere was built based on the coordinates proposed by Brett, Anton, Valabregue, & Poline (2002) as being the centre of gravity of the posterior cluster of the TPJ (Mars *et al*., 2012). Thus, the coordinates for the centre of the sphere in this study were 54, -55, 26, and the sphere radius was set at 10mm (See Figure 5).
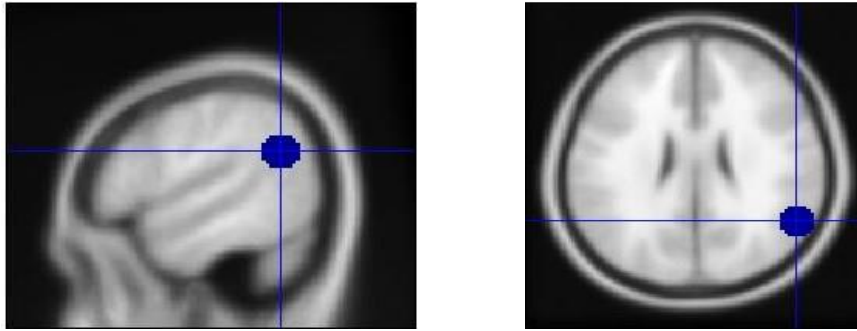
Figure 5: Posterior temporoparietal junction used for the region of interest analysis, displayed on MNI brain. The coordinates of the centre of the sphere in MNI space were 54, -55, 26. Sphere radius 10mm.

MARSBAR software was then used to extract the average signal intensity within the RoI for each subject at baseline and follow-up for the contrast of CI>PhC (see *Second Level Analysis*, page 165). The average follow-up intensities for each participant were subtracted from the average baseline intensities to compute an average 'change in signal intensity' value.

Analyses conducted within SPM explore the peak activation of clusters across the whole brain. The peak activations are more susceptible to inter-subject variance, particularly within a small sample size. In contrast, MARSBAR analysis extracts the average activation within a specific region of interest. This also reduces the issues with multiple comparisons when comparing many voxels across the brain, thus increasing the overall power of a region of interest analysis.

Once the average change in signal intensity was calculated for each participant, correlation analysis was conducted in SPSS 22 to explore the relationship between the change in signal intensity (from baseline to follow-up) within the posterior TPJ, and functioning scores at follow-up (i.e. hours per week spent in structured activity). A 1-sample Kolmogorov-Smirnov test indicated that the data were parametric, therefore a Pearson Correlation was used (with K-S Z values ranging from .130 to .195 and all p values = .200). Significance was assessed at the $p = 0.05$ level. The strength of the correlation was assessed by the size of the value of Pearson

correlation (r), interpreted by the guidelines set out by Cohen, 1988 (Small: r = .10 to .29; Moderate: r = .30 to .49; Large: r = .50 to 1.0).

5.5. Results

The results will be divided into two sections: (a) exploratory group analyses, and (b) individual case studies. It was decided to present a selection of case studies due to the small sample size of this study; it is hoped that this will provide a more in-depth illustration of the changes in brain functioning in relation to the change in structured activity, post SRCBT.

5.5.1. Exploratory group analysis

(i)   Psychopathology and Functioning

A group analysis was carried out to explore changes in structured activity between baseline (pre - SRCBT) and 9 months follow-up (post - SRCBT). There was an increase in the hours per week spent in structured activity from baseline (*M* = 17.08, *SD* = 6.44) to follow-up (*M* = 46.07, *SD* = 26.98); this difference was statistically significant [*t*(5) = -2.77; *p* = .039]. The magnitude of the difference in the means was very large (eta squared = 0.61). According to the cut off scores set out by Hodgekins, French, Birchwood, *et al*. (2015), 46.07 hours per week of structured activity is indicative of good social functioning.

There were no significant differences for positive symptoms [*t*(5) = 1.90, *p* = .116], negative symptoms [*t*(5) = -2.01, *p* = .101], and general psychopathology [*t*(5) = .611, *p* = .568] from baseline to follow-up (Table 17).

(ii)   Behavioural Results – Attribution of Intentions task

There was a trend for quicker reaction times at follow-up ($M = 1.30$, $SD = .07$), compared to baseline ($M = 1.63$, $SD = .37$). The eta squared statistic (0.21) indicated a large effect size, although the difference between the means was non-significant [$t(5) = 2.32$, $p = .068$]. A similar trend emerged for task response accuracy (number of correct responses), where, on average, participants made more accurate responses at 9-month follow-up ($M = 18.17$, $SD = 4.83$) compared to baseline ($M = 16.50$, $SD = 4.04$); this difference was non-significant [$t(5) = -1.15$, $p = .303$]. The eta squared statistic again indicated a large effect (0.52). Please see Table 17 for mean response accuracy and reaction times for the CI and PhC conditions.

Table 17. Information on functioning, psychopathology and fMRI task performance (accuracy and reaction times) for each participant at baseline and follow-up.

Participants	Hours of Structured Activity per week		Task Accuracy (%)		Task Reaction Times (s)		PANSS Positive Symptoms		PANSS Negative Symptoms		PANSS General Psychopathology	
	BL	FU	BL	FU	BL	FU	BL	FU	BL	FU	BL	FU
B005	11.22	68.55	68.18	100	1.96	1.41	8	12	11	9	20	25
B017	9.5	41.46	95.45	100	1.32	1.09	13	14	25	21	34	30
B021	15.19	20.69	54.54	54.54	1.55	1.50	7	10	12	13	26	22
B026	17.91	12.06	63.63	54.54	1.96	1.41	11	17	17	18	32	36
B030	22.50	51.86	100	95.45	1.08	1.25	8	7	12	8	16	21
B032	26.14	81.82	68.18	90.90	1.89	1.14	7	7	20	12	39	18

BL – Baseline (pre-SRCBT); FU – Follow-up (post-SRCBT). PANSS – Positive and Negative Syndrome Scale.

(iii)   Explorative group neuroimaging findings

         (a) Exploring the change in brain activation pre-and post SRCBT

Firstly, one-sample t-tests were conducted to explore group neural activation at baseline and then at follow-up for the comparison between the CI condition (experimental ToM condition) and PhC condition (control condition). For baseline and follow-up, activation was noted in the key ToM regions, which spread from the temporo-parietal area along the superior temporal sulcus during the CI condition. Compared to the activation seen at baseline, there was additional activation seen in a number of regions at follow-up; there was significantly more bilateral activation noted within the areas associated with ToM, such as: bilateral superior temporal gyrus, bilateral middle temporal gyrus and bilateral preceunus. There was no significant bilateral activation in these regions at baseline. Figure 6 illustrates these changes.

Figure 6 (a) Baseline
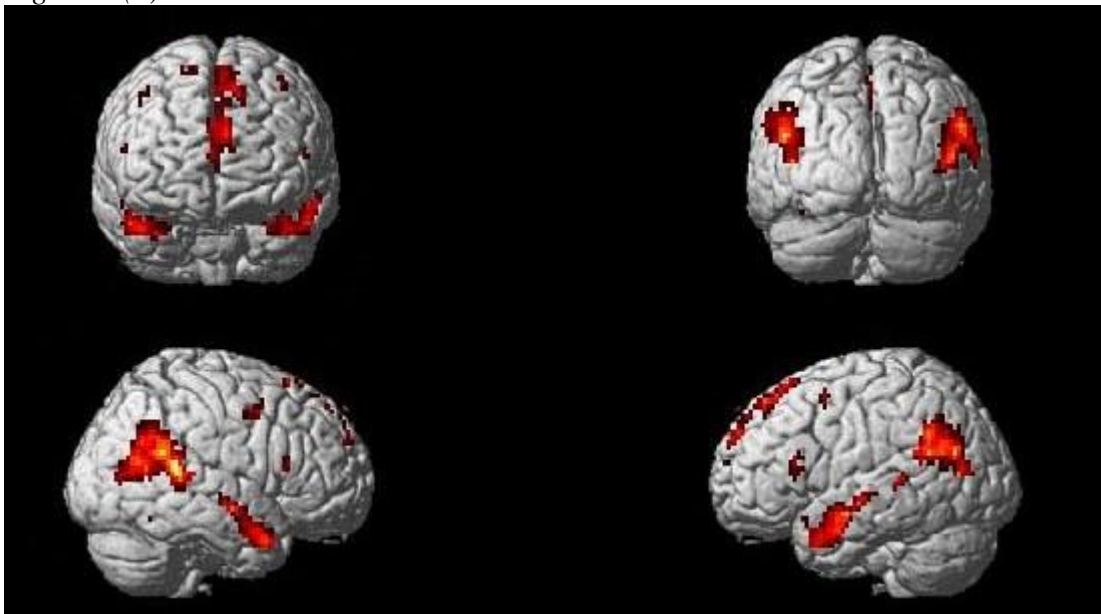
Figure 6 (b) Follow-up
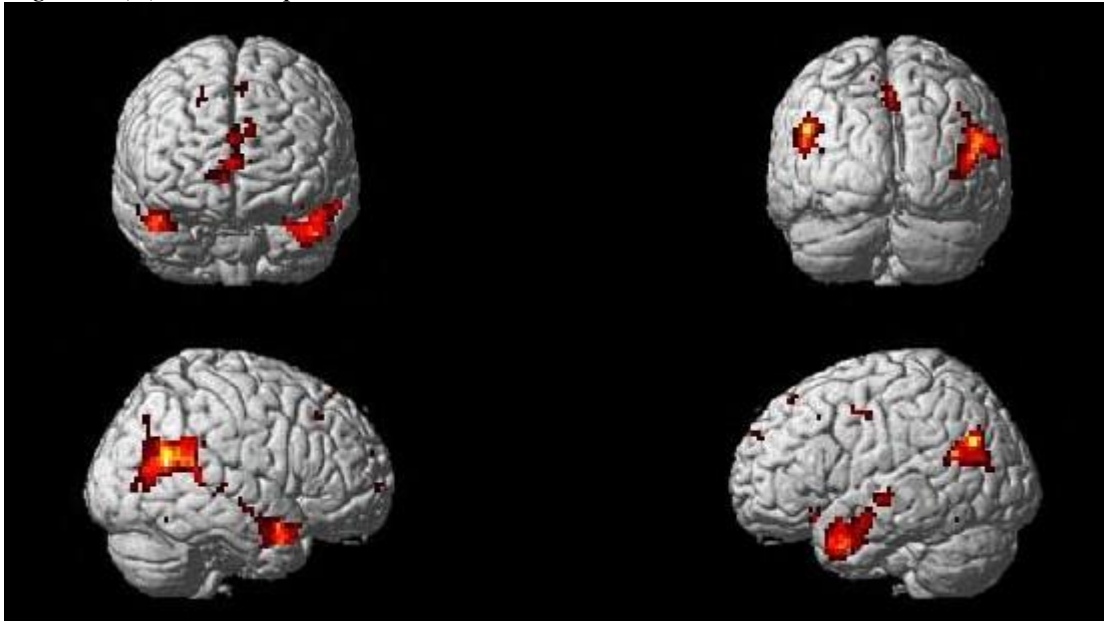
Figure 6. One sample t-test showing neural activations at baseline (Figure 6, a) and follow-up (Figure 6, b). NB: $p = 0.01$, uncorrected, extent threshold = 10. Images are shown within the MNI template. The lighter the colour of the activation suggests the areas are more significantly activated.

To further demonstrate the change in brain activation, a two-sample t-test was conducted to explore the change in the BOLD signal between baseline and follow-up across participants. Results showed that for the CI condition there was increased neural activation at baseline compared to follow-up (Baseline > Follow-up) in the bilateral superior temporal lobe, right inferior parietal lobule, left supramarginal gyrus (parietal lobe) and the occipital lobe.

There was increased activation at follow-up compared to baseline (Follow-up > Baseline) for the CI>PhC contrast in the following regions: Right precuneus, sub-gyral temporal lobe (left), left posterior cingulate, right anterior cingulate, thalamus, left insula, right inferior frontal gyrus, right superior frontal gyrus and extra nuclei. Figure 7 illustrates the change in activation across the two time points.

Figure 7 (a) Baseline compared to Follow-up   *Figure 7 (b)* Follow-up compared to
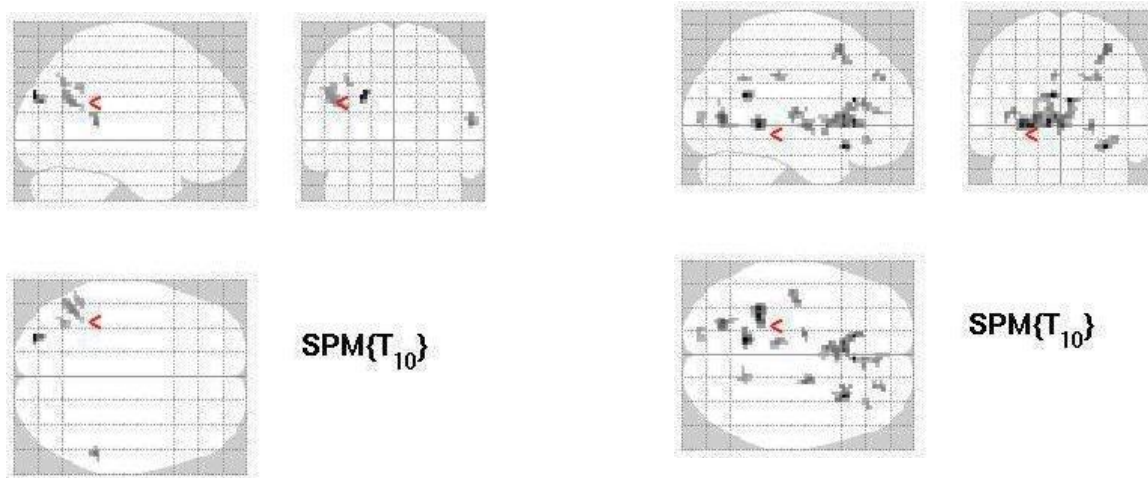
baseline.

Figure 7. Two sample t-test showing neural activations for the Baseline > Follow-up comparison (Figure 7, a) and Follow-up > Baseline comparison (Figure 7, b). NB: Second level t-test, $p = 0.01$, uncorrected, extent threshold $= 10$.

(b) Correlation between the change in signal intensity in the posterior temporoparietal junction area, and structured activity post- SRCBT: Region of Interest Analysis.

Once the average change in signal intensity was calculated for the temporoparietal area (please refer to Method section, page 166, for further information on the region of interest analysis), a correlation analysis was conducted to explore the relationship with structured activity at follow-up. Although not statistically significant, the correlation coefficient implies a moderate, positive relationship ($r = .455$; $p = .365$), suggesting that greater brain signal intensity changes (from baseline to follow-up), was associated with higher scores of structured activity at 9 month follow-up.

5.5.2. Case studies

Case Study 1 - Participant B017

    (a) Socio-demographic information and background

Participant B017 is a 19-year-old black British male, with a history of psychosis and Obsessive-Compulsive Disorder (OCD). He has a duration of untreated psychosis (DUP) of 316 days and has spent approximately 14 years in education. At baseline he was living with his family, was unemployed and spent very little time engaging in activities outside the family home. He spent fewer than 9.5 hours per week in structured activity (indicative of severe social disability; Hodgekins, French, Birchwood, *et al*., 2015). His main activities were drawing and occasionally socialising with friends.

Participant B017 had good engagement in the SRCBT therapy and attended 9 sessions in total. His engagement reduced once he started university. The main problems addressed by the therapy were his self-esteem and shyness due to a fear of negative evaluation. This resulted in an avoidance cycle of not engaging or initiating conversation with others. Through receiving SRCBT, he was learning to be more forgiving and compassionate towards himself. After therapy, he was no longer avoiding certain social situations, had started attending university, and made lots of friends. He stated that he felt less anxious during social interactions.

    (b) Functioning, psychopathology and task performance

Baseline functioning increased from 9.5 hours per week spent in structured activity, to 41.46 hours at follow-up (post- SRCBT), falling in the category of 'at risk of social disability' at follow-up (Hodegkins *et al*., 2015). There was an improvement in task accuracy from 95.45% at baseline to 100% at follow-up, and the participant was also on average .13 seconds quicker

at making task responses at follow-up. There was little change in positive symptoms, however there was a slight decrease in negative symptoms and general psychopathology post-intervention (Table 17).

(c) Neuroimaging findings

The contrast of the CI and PhC conditions at baseline revealed a significantly greater increase in signal during the CI condition, compared to the PhC condition in the following regions: left middle temporal gyrus, right superior temporal gyrus, right precuneus, bilateral superior frontal and middle frontal gyrus, left medial frontal gyrus, right inferior frontal gyrus, fusiform gyrus and the occipital lobe.

At 9-month follow-up, there was additional activation in the inferior temporal gyrus, middle temporal gyrus (bilaterally), right anterior cingulate, cerebellum, and bilateral inferior frontal gyrus. There was no significant activation in the precuneus or medial frontal gyrus at follow-up.

Figure 8 suggests a signal increase from baseline to follow-up in the temporo-parietal area along the superior temporal sulcus; key areas that are implicated in the ToM network. Activation at follow-up resembles activation usually seen in healthy controls. Increase in activation in the frontal regions at follow-up is also evident (Figure 8, b).

Figure 8 (a)   *Figure 8 (b)*

Figure 8. Neural activations are shown for the experimental CI condition versus PhC control condition (CI>PhC) at baseline (Figure 8, a) and at follow-up (Figure 8, b) for participant B017. NB: First level t-test, $p = 0.05$, Family-wise error (FWE) corrected p - value, uncorrected at the cluster level. For location within the Montreal Neurological Institute (MNI) template, please refer to the bottom images; the lighter the colour of the activation suggests the areas are more significantly activated.

Case Study 2 – Participant B032

   (a) Socio-demographic information and background

Participant B032 is a 16-year-old British Asian male, with a history of psychosis. He has a DUP of 75 days and has spent approximately 10 years in education. At baseline he was living with his family and attending school for approximately 17 hours per week. He was studying for two GCSEs (General Certificate of Secondary Education); however, he found this to be a highly

challenging process. He occasionally socialised with friends outside of school to play football but spent the majority of his time at home.

Participant B032 had good engagement with the SRCBT and received thirteen sessions in total. The main problems addressed in therapy were motivation and lack of energy, social anxiety and confidence in engaging in activities with friends. To challenge this, a series of behavioural experiments were carried out, and by the end of the therapy, he was feeling more confident being around his friends, and he was no longer experiencing social anxiety. He stated that he was 80% back to his premorbid self.

At follow-up, he was studying full-time for a college diploma. He was now also spending around 50 hours per week socialising and engaging in a number of leisure and sporting activities.

(b) Functioning, psychopathology and task performance

Baseline functioning increased from 26.14 hours per week spent in structured activity, to 81.82 hours at follow-up (post SRCBT), indicating good social functioning (Hodegkins *et al.*, 2015). There was an improvement in task accuracy from 68.18% at baseline to 90.90% at follow-up, and the participant was also on average .75 seconds quicker at making task responses at follow-up. There was no positive symptomatology present pre- or post-therapy, however from observation of symptom scores on the PANSS, negative symptoms and general psychopathology had substantially decreased by follow-up (Table 17).

(c) Neuroimaging findings

The contrast of 'CI and PhC' condition at baseline revealed a significantly greater increase in activation during the CI condition (compared to PhC condition) in the following areas: bilateral superior temporal gyrus, right middle temporal gyrus, supramarginal gyrus, right middle frontal gyrus, left medial frontal gyrus and right inferior frontal gyrus. In addition to the increased activation seen at baseline for the bilateral superior temporal gyrus and right inferior frontal gyrus, there was additional activation at follow-up in the bilateral middle temporal gyrus, right inferior temporal gyrus, right precuneus, right inferior frontal gyrus, left fusiform, and the occipital lobe. It is evident from the examination of Figure 9 that there is an increase in bilateral activation in the temporal regions at follow-up; in addition, activation becomes more refined and localised within the temporo-parietal region post SRCBT.

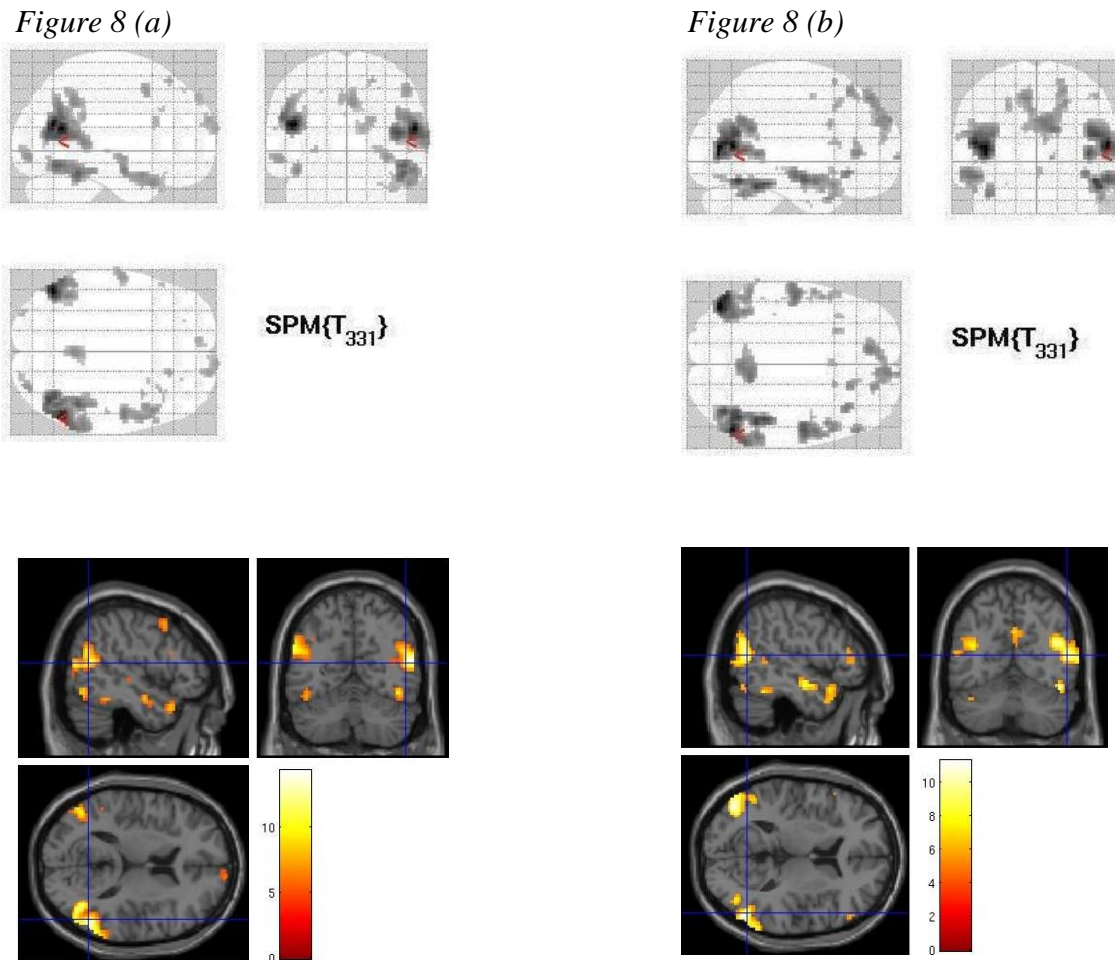*Figure 9 (a) Baseline*   *Figure 9 (b) Follow-up*
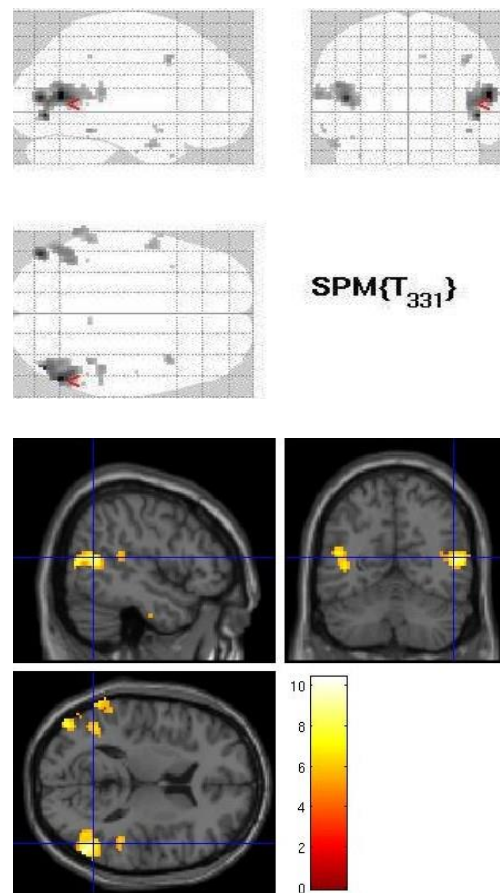
Figure 9. Neural activations shown for the experimental CI condition compared with the PhC control condition (CI>PhC) at baseline (Figure 9, a) and at follow-up (Figure 9, b) for participant B032. First level t-test, $p = 0.05$, FWE corrected, uncorrected at the cluster level. For location within the MNI-template, please refer to the bottom images: the lighter the colour of the activation suggest the areas are more significantly activated.

Case Study 3 - Participant B005

(a) Socio-demographic information and background

Participant B005 is a 28-year-old British Asian male, with a history of psychosis. He has a DUP of 73 days and has spent approximately 11 years in education. At baseline he was living with his family and spending approximately 6 hours per week studying for an accountancy course at

college. He was not engaging in any leisure activities and spent around 2 hours a week socialising with others.

Initially he engaged in three face-to-face sessions with the SRCBT therapist, however, after this, his main contact with the therapist was via telephone conversations. His reduced engagement was partly due to exams and coursework. The main concern discussed in the therapy sessions was feelings of guilt over past behaviours. Feelings of self-criticism, shame and low mood were also discussed. He stated that therapy helped him to talk with others about his behaviours and feelings of guilt; he found great benefit from this.

At follow-up, he was spending around 12 hours per week socialising with others and was engaging in a number of leisure and sporting activities. He was now in a romantic relationship and living independently, and he spent an increased amount of time doing housework and chores. Since completing his therapy, he had obtained a full-time job and completed his accountancy course; however, he was no longer in work at the time of the research follow-up.

(b) Functioning, psychopathology and task performance

Baseline functioning increased from 11.22 hours per week spent in structured activity, to 68.55 hours at follow-up, suggesting good social functioning (Hodgekins, French, Birchwood, *et al*., 2015). There was an improvement in task accuracy from 68.18% at baseline to 100% at follow-up, and the participant was also on average .55 seconds quicker at making task responses at follow-up (Table 17). From observing the PANSS scores, there was an increase in positive symptoms and general psychopathology at follow-up, and a slight decrease in negative symptoms (Table 17).

(c) Neuroimaging findings

The contrast of 'CI and PhC' condition at baseline revealed a significantly greater increase in activation during the CI condition (compared to the PhC condition) in the following regions: bilateral middle temporal gyrus, right superior temporal gyrus, sub-gyral (temporal lobe), right precuneus, supramarginal gyrus, bilateral middle frontal gyrus, right superior and inferior frontal gyrus and occipital lobe. At follow-up, the areas which showed greater activation in the CI condition were the bilateral middle temporal gyrus, bilateral precuneus, right middle frontal gyrus and occipital lobe. Examination of Figure 10 not only reveals increased activation from baseline to follow-up in the temporo-parietal region, it also shows that activation within this region becomes more refined post SRCBT.
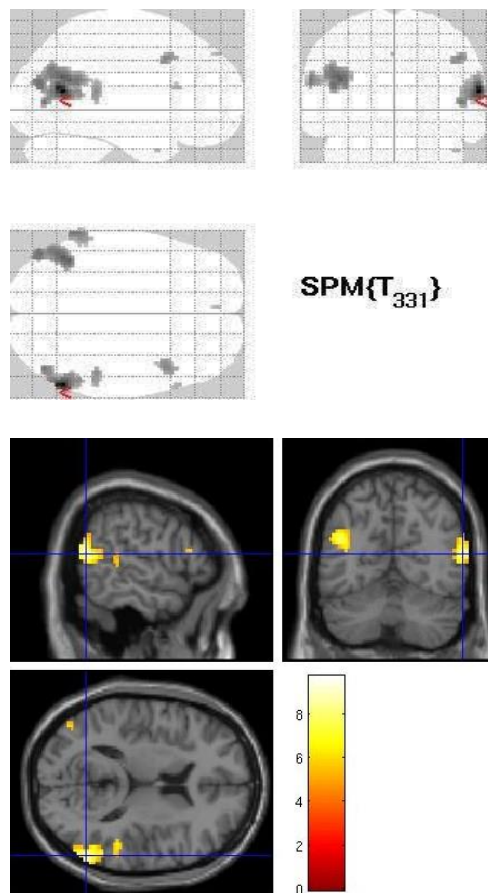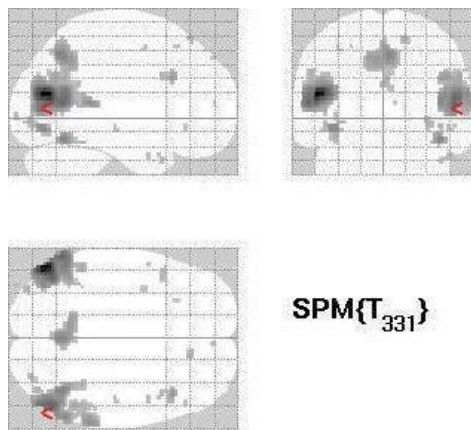
Figure 10 (a)   *Figure 10 (b)*
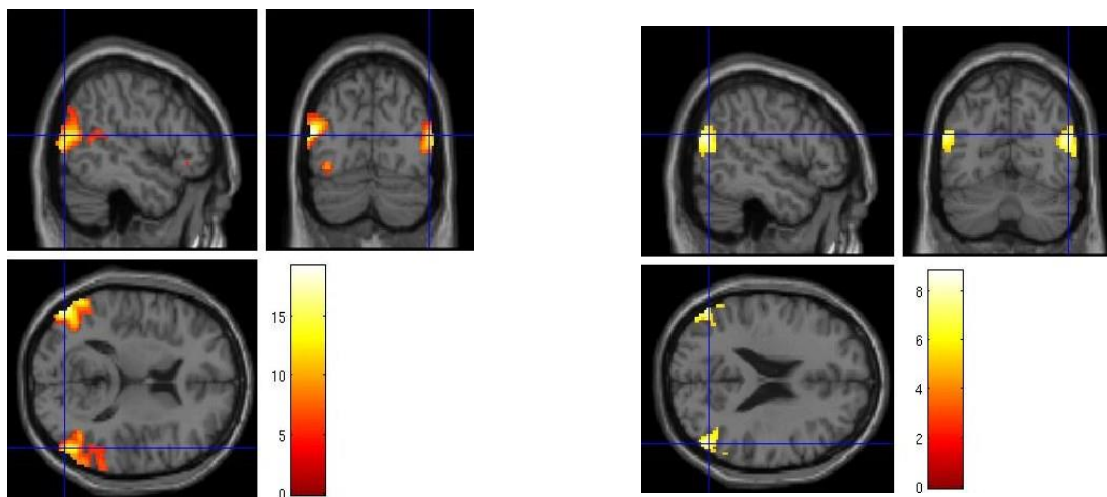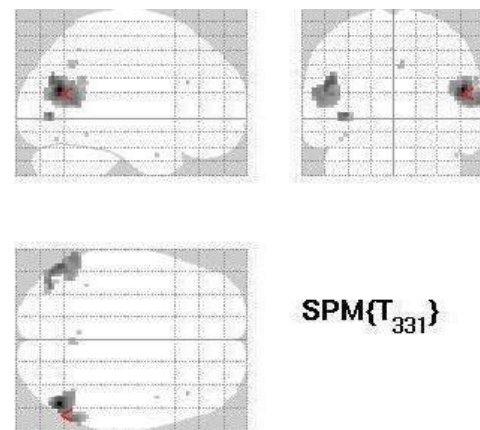
Figure 10. Neural activations shown for the experimental CI condition compared with the PhC control condition (CI>PhC) at baseline (Figure 10, a) and at follow-up (Figure 10, b) for participant B005. First level t-test, p = 0.05, FWE corrected, uncorrected at the cluster level. For location within the MNI-template, please refer to the bottom images: the lighter the colour of the activation suggests that the areas are more significantly activated.

Case Study 4 - Participant B021

   (a) Socio-demographic information and background

Participant B021 is a 28-year-old Asian male, born in Pakistan. He has a history of psychosis, with a short DUP of 8 days. At baseline, he was living with his wife and spending approximately

5 hours a week learning English as a second language. He was attending the gym regularly but spent very little time (approximately 1 hour a week) socialising.

He engaged in approximately 7 face-to-face meetings with the SRCBT therapist. During the initial meeting with the therapist, he was unable to identify a purpose for engaging in the therapy, explaining that he had made subsequent progress in his social functioning since being assessed for the trial. He did however agree that it would be useful to have the therapy as a 'backup' and that he would be seen by the therapist for monitoring purposes. He attributed his improvement in functioning to a reduction in paranoid thinking and had also made a number of life changes (such as losing weight and stopping smoking), which had helped him feel more motivated and committed to obtaining his goal of improving his functioning.

At follow-up, participant B021 was living with his wife and spending approximately 9 hours a week studying for an English language course. He occasionally engaged in leisure activities and spent around 3 hours a week socialising. He was also spending time on housework and chores.

(b) Functioning, psychopathology and task performance

At baseline, Participant B021 was spending approximately 15.19 hours per week in structured activity, and 20.69 hours a week at follow-up, suggesting he still had social disability. There was no change in task accuracy from baseline to follow-up (54.54%), and little change in reaction times (Table 17). Positive and negative symptoms were present at both follow-up points with very little change pre- and post- SRCBT (Table 17).

(c) Neuroimaging findings

The contrast of CI and PhC condition at baseline revealed a significantly greater increase in activation during the CI condition, compared to the PhC in the following regions: Bilateral middle temporal lobe, bilateral superior temporal lobe, Precuneus parietal lobe, left sub-gyral temporal lobe (Figure 11). In addition to these areas, the Para-hippocampal gyrus and occipital gyrus were significantly activated at follow-up (Figure 11).

Figure 11 (a)
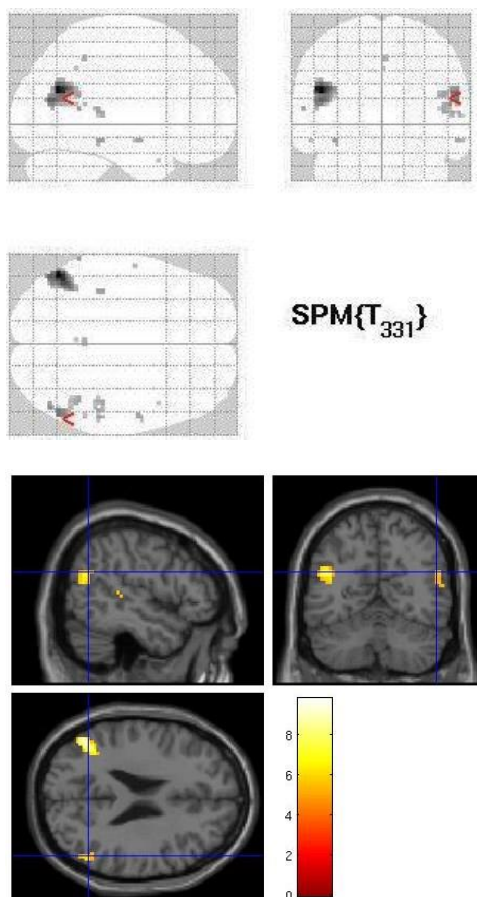
Figure 11 (b)
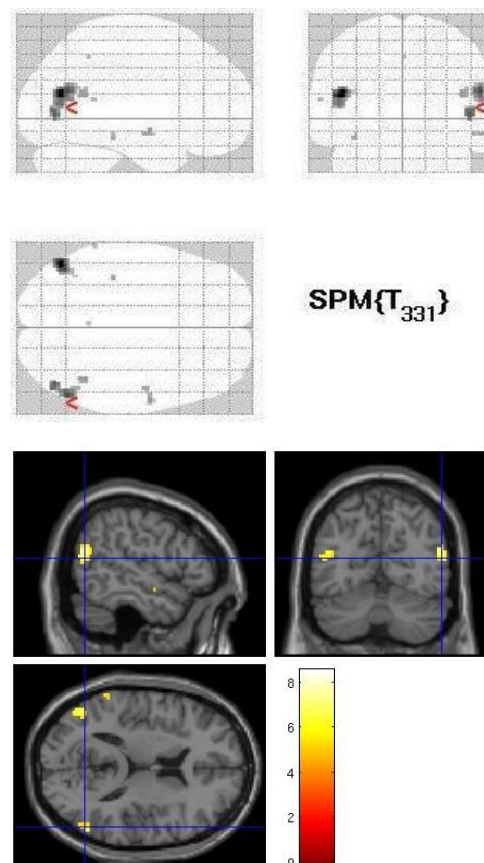
Figure 11. Neural activations shown for the experimental CI condition compared with the PhC control condition (CI>PhC) at baseline (Figure 11, a) and at follow-up (Figure 11, b) for participant B021. First level t-test, p = 0.05, FWE corrected, uncorrected at the cluster level. For location within the MNI-template, please refer to the bottom images: the lighter the colour of the activation suggests the areas are more significantly activated.

Case Study 5 - Participant B030

(a) *Socio-demographic information and background*

Participant B030 is a 26-year-old mixed-ethnicity male who had expereicned a first episode of psychosis. He has completed 17 years of education and has a postdgraduate univeristy degree. At baseline, participant B030 was working part-time (7 hours a week) as a tennis coach. He was also engaged in some leisure and sporting activities at baseline but spent less than an hour a week socialising with others.

B030 was very engaged in the SRCBT therapy and recevied fourteen sessions in total with the SRCBT therapist. His main concerns addressed in therapy were motivation, inflexible thinking patterns and the need for perfectionism. The aim of therapy was to work on developing self-compassion and challenging inner critical thoughts that may be impeding his social recovery.

At follow-up, participant B030 remained in employment and was now working 23 hours per week in two separate jobs. He was spending more time engaging in leisure and sporting activities and spent around 10 hours a week socialising. He was also spending more time on housework and chores.

(b) *Functioning, psychopathology and task performance*

At baseline, participant B030 was spending approximately 22.50 hours per week in structured activity, and 51.86 hours a week at follow-up, suggesting good social functioning (Hodegkins *et al*., 2015). There was little change in task accuracy due to a possible ceiling effect at baseline, and he was 0.17 seconds quicker at performing the task at baseline (Table 17). There were no

positive symptoms present at baseline and there was no longer any negative symptoms present at follow up. The PANSS scores indicated that general psychopathology increased by follow-up (Table 17).

(c) Neuroimaging findings

The contrast of 'CI and PhC' condition at baseline revealed a significantly greater increase in activation during the CI condition (compared to the PhC condition) in the following regions: bilateral middle temporal gyrus, bilateral syb-gyral temporal lobe, right para-hippocampal gyrus, right inferior parietal lobule, bilateral paracentral lobule, supramarginal gyrus (parietal lobe), bilateral inferior frontal gyrus, right superior frontal gyrus, bilateral middle frontal and left occipital lobe.

The areas which showed greater activation in the CI condition compared to PhC condition by follow-up were: bilateral middle temporal gyrus, bilateral superior temporal gyrus, right fusiform gyrus, left subgyral temporal lobe, bilateral preceunus, left supramarignal gyrus (parietal lobe), left inferior parietal lobule, right middle frontal gyrus, right inferior frontal gyrus and occipital gyrus. More activation within the temporal regions is evident at follow-up compared to baseline (Figure 12). Less activation is seen in the frontal regions by follow-up (Figure 12).

Figure 12 (a)
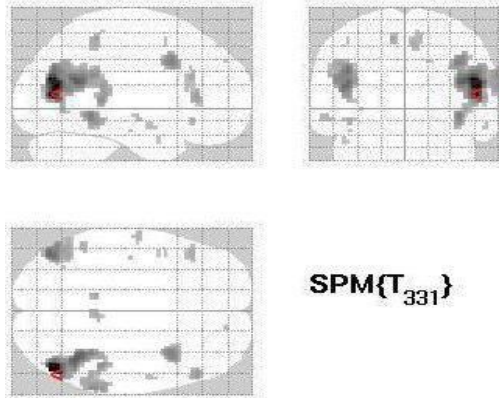
Figure 12 (b)
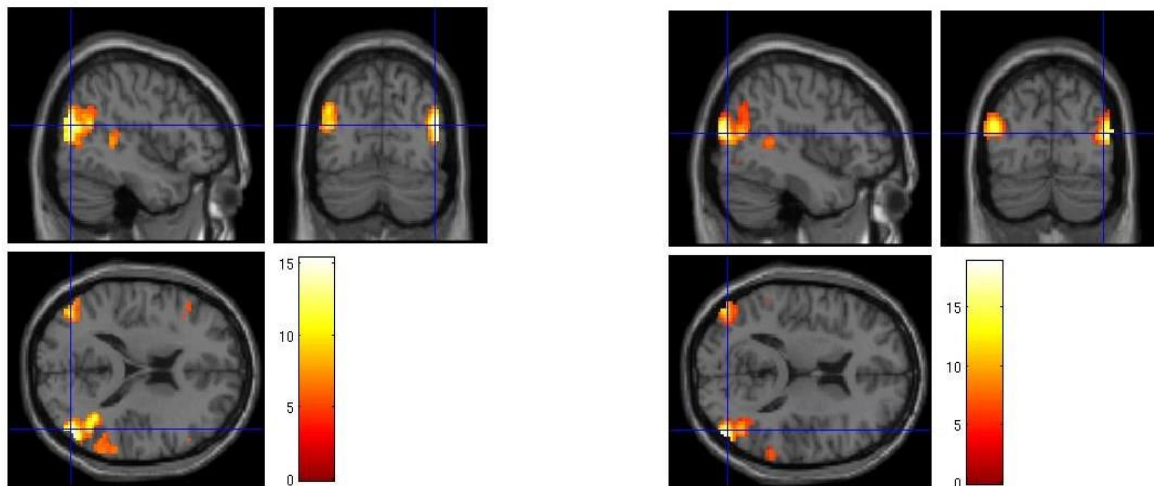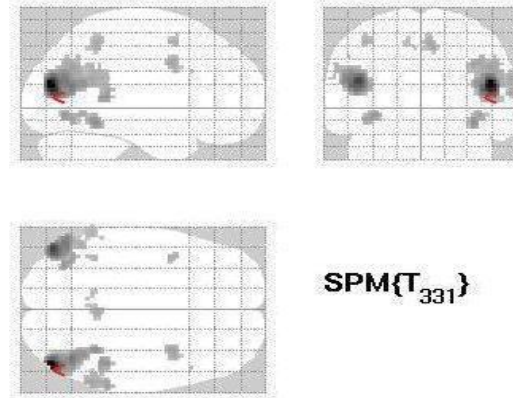
Figure 12. Neural activations shown for the experimental CI condition compared with the PhC control condition (CI>PhC) at baseline (Figure 12, a) and at follow-up (Figure 12, b) for participant B030. First level t-test, p = 0.05, FWE corrected, uncorrected at the cluster level. For location within the MNI-template, please refer to the bottom images; the lighter the colour of the activation suggests the areas are more significantly activated.

Case Study 6 - Participant B026

   (a) Socio-demographic information and background

Participant B026 is 20-year-old single Asian male, born in Afghanistan. He has a low level of education (total of 5 years) and his second language is English. He has a history of psychosis, with a short DUP of 6 days. He smokes cannabis daily.

At baseline, participant B026 was living in supported accommodation. He was not in education or paid work, but he was spending around 6 hours a week in voluntary labouring work. He occasionally engaged in leisure and sports activities (e.g. football and pub games) and spent two hours a week socialising with others. He also engaged in around 9 hours a week of housework and chores.

He engaged in nine sessions with the SRCBT therapist. The main concerns addressed in therapy that were influencing his social functioning were: 1) malevolent voices that would make derogatory remarks when he was around others; 2) thought broadcast and paranoid ideation which further maintained his avoidance of social situations; and 3) daily cannabis use to manage his social anxiety. He was encouraged to use techniques such as attention switching behavioural experiments when he was in public places and around others. On a few occasions, he did not attend his sessions with the therapist or he was unable to participate in the sessions due to his excessive cannabis use.

At follow-up, Participant B026 was still living in supported accommodation, but he was no longer in work. On two occasions over the course of 9 months, he obtained part-time work, lasting several weeks. There was little change from baseline to follow-up in terms of his engagement with leisure and sports activities and he continued to spend around 2 hours a week socialising. He also spent fewer hours doing housework and chores.

(b) Functioning, psychopathology and task performance

At baseline, Participant B026 was spending approximately 17.91 hours per week in structured activity, and 12.06 hours a week at follow-up, indicating severe social disability (Hodgekins, French, Birchwood, *et al*., 2015). There was a decrease in task accuracy and the participant was

0.55 seconds quicker at performing the task at follow-up (Table 17). There was a worsening of positive symptoms by follow-up, but there was little change in negative symptoms and general psychopathology (Table 17).

(c) Neuroimaging findings

The contrast of CI and PhC condition at baseline revealed a significantly greater increase in activation during the CI condition, compared to the PhC in the following regions: right middle temporal lobe, right inferior temporal lobe, right superior temporal gyrus, left transverse temporal gyrus, left sub-gyral temporal lobe, left Angular gyrus (parietal lobe), extra nuclear, bilateral sub-gyral frontal lobe, cerebellum and occipital lobe.

At follow-up, the areas which showed greater activation in the CI condition, compared to PhC condition were: bilateral middle temporal gyrus, left sub-gyral temporal lobe, left supramarginal gyrus (parietal lobe), left preceunus, right inferior parietal lobule, left medial frontal gyrus and right inferior frontal gyrus. Figure 13 demonstrates that at follow-up, the increase in activation is more concentrated around the temporoparietal region.
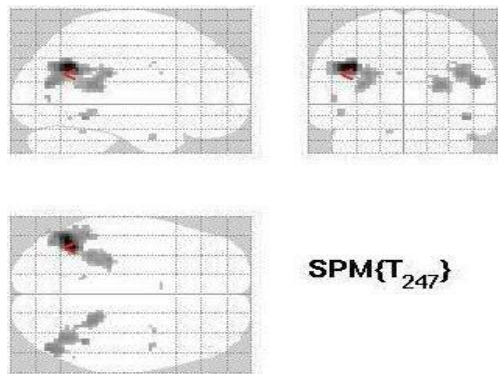
Figure 13 (a)   *Figure 13 (b)*
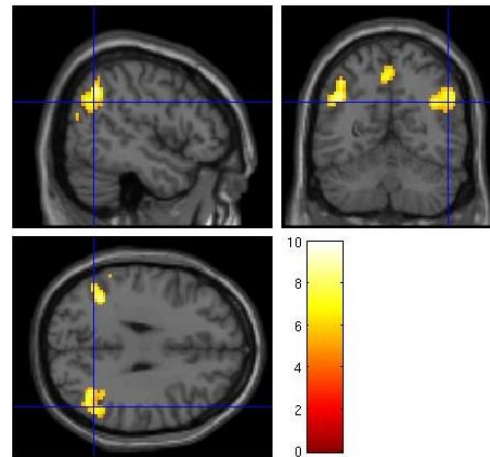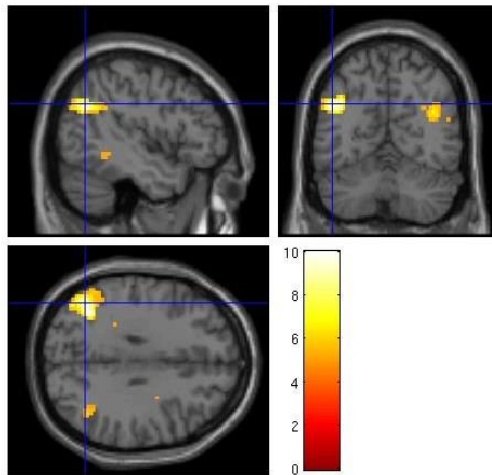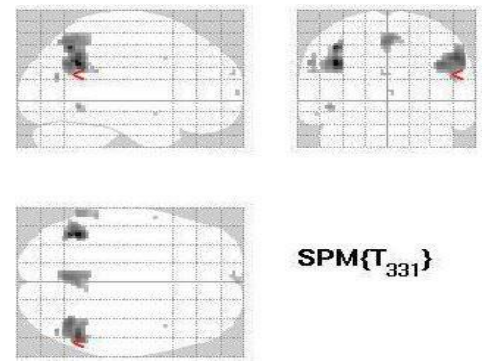
Figure 13. Neural activations shown for the experimental CI condition compared with the PhC control condition (CI>PhC) at baseline (Figure 13, a) and at follow-up (Figure 13, b) for participant B026. First level t-test, p = 0.05, FWE corrected, uncorrected at the cluster level. For location within the MNI-template, please refer to the bottom images; the lighter the colour of the activation suggests that the areas are more significantly activated.

5.6. Discussion

This was an exploratory study which aimed to investigate the neural changes in the ToM brain regions in a sample of young people with FEP who were receiving SRCBT to target their social disability. The work also investigated whether brain changes in the ToM regions during an fMRI 'attribution of intentions task' was associated higher scores of structured activity at 9-month follow-up.

The lack of statistical power in this study meant that findings are preliminary, and generalizability is limited. Several challenges were encountered during the recruitment phase which likely reflects the complex nature of this group, and which subsequently led to the low power of this study. The challenges and feasibility of conducting a study of this kind will be discussed, in addition to the preliminary findings of this study and implications for further work.

5.6.1. Exploratory Group Changes

    (a) Behavioural Data

There were a number of group changes from pre- to post-SRCBT. Firstly, there was significant improvement in functioning (i.e. structured activity) at follow-up, with the group achieving a level of functioning that was indicative of 'good social functioning' (Hodgekins, French, Birchwood, *et al.*, 2015). Interestingly, there was no significant change in symptomatology. By follow-up, participants had faster reaction times and made more accurate responses. Although this was not significant, there was a large effect size, possibly indicating that with a larger sample, this difference may have become significant.

(b) Neuroimaging data

Exploratory group analyses of the neuroimaging data revealed that there were differences in neural activation at follow-up compared to baseline. When inspecting the activations in the key ToM regions at follow-up, it appeared that there was significant bilateral activation in the superior temporal gyrus, middle temporal gyrus and bilateral precuneus. There was no significant bilateral activation in these regions at baseline. There was significantly more activation seen at follow-up in number of other regions, such as the precuneus, temporal lobe, posterior and anterior cingulate, insula cortex, and frontal regions. These areas have previously been implicated in ToM processing (Abu-Akel, 2003; Koster-Hale & Saxe, 2013; Walter *et al*., 2009).

Conversely, there was significantly more activation in one of the key ToM regions – the superior temporal lobe – at baseline compared to follow-up. Inspection of the individual findings demonstrated that activation in these key regions was more refined (and localised) at follow-up, and thus, when comparing the average group differences at baseline and follow-up, more widespread (and less localised) activations in the key ToM regions at baseline may have accounted for this.

Indeed, it is also important to keep in mind the small sample size of the group analysis, which impacts on the reliability of the findings. In addition, the *p.* value threshold was not corrected during the analysis, and it may be possible that some areas could appear to be implicated in the task when this may not be accurate.

Focusing on the TPJ – a region believed to be uniquely involved when reasoning about the contents of mental states (Saxe, 2006) – results showed that greater increases in brain signal

intensity within the TPJ (from baseline to follow-up), was associated with more hours of structured activity at 9-month follow-up. Again, although this difference was not statistically significant, there was moderate effect, possibly suggesting that with a larger sample size, this difference may become significant. Nevertheless, these findings are encouraging and may suggest that through receiving the SRCBT, those with more structured activity post intervention were able to challenge their interpretations of social situations impeding their social recovery; this in turn may have resulted in changes in brain function in the ToM regions. A larger sample, with an adequate control group, would be necessary to confirm this hypothesis.

5.6.2. Changes in ToM and corresponding changes in structured activity at the individual level

For all participants, the main areas of activation during the experimental condition were seen mainly in the temporal and parietal areas and also in the frontal regions; this is in line with previous functional imaging studies of ToM correlates (Bosia *et al*., 2012; Gallagher & Frith 2003; Walter, *et al*., 2004; Walter *et al.,* 2009). After receiving the SRCBT, four participants were able to achieve a 'meaningful' improvement in their functioning (i.e. no longer defined as socially disabled; Hodgekins, French, Birchwood, *et al*., 2015). The remaining two participants were still defined as having a social disability at follow-up.

On observation of the neuroimaging findings, slight differences emerged between participants. The four participants who had achieved a 'meaningful improvement' in their structured activity consistently showed increased activation in the temporo-parietal regions at follow-up; more bilateral activation was also evidenced. Walter and colleagues (2009) demonstrated that there is less activation in these regions in individuals with schizophrenia compared to healthy

participants. Thus, the increase in activation seen at follow-up may suggest that participants were more able to distinguish between the ToM and control condition (i.e. more able to make inferences about intentions in the appropriate context). It could be argued that this is indicative of participants improving their ToM, evidenced by a possible 'normalisation' of brain activation in the ToM regions. However, because there was no comparison with a healthy control group, it is not possible to determine firstly if the brain activation at baseline is indeed different, but also, whether the improvement in brain activation at follow-up is comparable to that of 'healthy' individuals. More interestingly, not only was the increase in activation evident at follow-up, these activations become more refined and localised in the ToM regions, namely the TPJ. This may be the result of more finely tuned neural circuits. A similar hypothesis has been proposed by Burnett and Blakemore (2009) to explain the reasons for the neurodevelopmental differences between adults and adolescents within the social regions of the brain; that is, with age, adults have built on their social experiences to develop more effective social cognitive strategies, making these processes less effortful and more reliant on stored social knowledge.

With regards to participants in this study, it might be plausible that by follow-up, these participants were using different cognitive strategies to approach the ToM task; this could be a result of developing their comprehension of social situations through receiving the SRCBT and subsequently building on new social experiences, resulting in more efficient neural circuits. More widespread activations within the temporal and parietal regions at baseline may indicate less efficient neural circuits.

Contrastingly, the same pattern of change was not evidenced for the participants who showed no improvement in their social disability at follow-up. Although there were some differences at follow-up compared to baseline, for the one participant, these differences did not seem as

pronounced (participant B021). For the other participant with no change in social disability, there was increase in activation at follow-up, but this was mainly in the parietal regions and there was less activation in temporal cortex compared to baseline (participant B026).

Whilst some interesting trends emerged from the data, the findings were based on observations at the individual level, and thus it is not possible to determine whether these findings are representative of individuals with severe social disability at a group level.

5.6.3. Study strengths and limitations

At the time of writing, this was the first study to report on longitudinal functional brain changes in the ToM regions in a sample of socially disabled young people with FEP, and the first to report functional neural changes in a social cognitive region of the brain after participants receive a CBT to improve functioning. Whilst there is evidence from previous studies of changes in social brain networks following psychosocial interventions (e.g. social cognitive interventions; see General Discussion, Chapter 6, section *6.0*) in individuals with schizophrenia (Campos *et al*., 2016), this study extends to individuals in the early stage of illness where intervention is more likely to be effective, due to neuroplasticity associated with ongoing development in adolescence (Bartholomeusz *et al*., 2011). Furthermore, this was the first study to use a ToM paradigm and provide evidence of neural changes in the TPJ following intervention, which is a region known to be specifically involved in ToM processing (Campos *et al*., 2016; Saxe & Kanwisher, 2004). However, due to a number of limitations, it is not possible to draw any firm conclusions on whether the brain changes were a direct result of the SRCBT.

Firstly, a significant limitation to this study is the small number of participants (N=6). It is usually recommended that a minimum of twelve participants is required for valid fMRI results (Friston, Holmes & Worsley, 1999). With such a small sample, it is not possible to determine whether the changes observed in this study are representative of a larger sample, and therefore the generalisability is limited. Due to the small sample size, the group analyses lacked sufficient power and the results were visually inspected at the individual level to look for any patterns of interest that may not have been detected at the group level. Due to a high-level of inter-subject variability, again, results should be carefully interpreted, and further studies are needed with adequately powered group analyses. Nevertheless, there were some interesting trends emerging in the data and replication of this study with a larger sample size will allow for firmer conclusions to be drawn.

Secondly, without comparing the findings with participants in the control arm of the SRCBT trial, it is not possible to determine whether these changes are a direct result of receiving the SRCBT, reflect a normal recovery process, or simply a result of practice effect. Furthermore, a comparison with healthy control participants with poor functioning would firstly clarify if aberrant functioning in the ToM regions is unique to psychosis, or simply a result of poor functioning; if so, would these changes also occur in their healthy contemporaries over time?

Another limitation to consider is that each participant received a different amount of SRCBT over the 9-month period. Although most of the participants had good engagement with the therapy, two participants failed to engage after the initial sessions. One of these participants achieved good functioning at follow-up, which would suggest that the SRCBT may not have accounted for this change, or, it could be the case that this individual may have benefitted (and achieved gains) from the initial contact with the therapist.

Despite being unable to draw firm conclusions as to the effectiveness of the SRCBT on the observed changes, what seems to be apparent is that for those individuals who had better structured activity at follow-up, there were more changes evidenced both at the behavioural and neural level compared to those who continued to have a poor functioning. This again may provide some support that the neural correlates of ToM are implicated in functional change in FEP and should be further investigated.

A further limitation is the generalisability of the sample, as it consisted only of males, and also, although the sample was somewhat ethnically diverse, Caucasian participants were not represented. Furthermore, due to the limited pool of participants, handedness was not controlled for in this study. Previous studies of functional lateralization have demonstrated differences between right-handed and left-handed participants whilst performing certain tasks, such as language-related tasks (Knecht *et al*., 2000), and tasks of verbal memory (Cuzzocreo *et al.,* 2009). It possible that there were also differences in the neural localisations during the ToM tasks in the left-handed participants compared with the right-handed participants, and therefore this is something to control for in future studies with a larger sample size.

Several confounding factors were not controlled for in the analysis due to the lack of power owing to the small sample size which may have impacted on the findings. For example, individuals with FEP present with heterogeneity in terms of their symptoms and diagnosis. It has been suggested that the type of psychotic symptom impacts on the degree of ToM impairment (Abu-Akel & Bailey, 2000; Frith, 1992). Individuals presenting with passivity symptoms are often the least impaired on ToM tasks, and disorganised and paranoid patients are the most impaired (Frith, 1992; Walter *et al*., 2009). Furthermore, it is argued that

individuals who present with negative symptoms may have different neural underpinnings to those with positive symptoms (Abu-Akel, 2003). This may have accounted for some of the individual differences observed in this study. Although it appears that within this present sample, most individuals presented with negative symptoms at baseline, therefore the group was homogenous in terms of symptomatology.

Age is another factor that might explain the differences in brain activation between individuals, particularly as the age range in this study was between 16 and 28 years old. Regions which are involved in SC go through protracted development throughout adolescence, and fMRI studies have shown differences between adolescents and adults on tasks of SC (Burnett & Blakemore, 2009); this should be considered in future studies.

5.6.4. Feasibility of conducting MRI research in individuals with severe social disability

The limited sample size of this study highlights a number of methodological issues that should be considered in future studies of this kind. Firstly, the primary aim of the trial was not related to imaging which meant that recruitment to this study was not given priority. In addition, as the focus of this study was on recruiting participants from the treatment arm of the SRCBT trial, there was already a restricted pool of potential participants to recruit to the fMRI study.

During the recruitment phase, a number of problems emerged, both at the technical and participant level, and this subsequently reduced the number of potential candidates for this study. Upon reflection, consideration needs to be given to the challenges faced when recruiting this particular sub-group of participants. For example, a number of participants were initially

excluded due to not meeting the fMRI study criteria (see method section, *5.4*). In the overall sample recruited to the SUPEREDEN trial, a number of participants reported a history of learning difficulty, head trauma and a history of seizures. This is important to consider because a proportion of young people presenting with a social disability may also have co-occurring difficulties which may also be contributing to their social disability; this is something which should be explored further. Thus, as these factors were exclusion criteria to the fMRI study, these individuals were not represented in this study. Furthermore, it is established that young people who present with social disability often present with negative symptoms, lack of motivation and are socially isolated. They may also be experiencing social anxiety or positive symptoms such as delusions of persecution which may in part account for the social withdrawal. Encouraging this sub-group to participate in the additional study and undergo an fMRI scan was often challenging, and even when participants attended for their scan, some participants became anxious and claustrophobic whilst in the scanner and subsequently withdrew from the study.

During the course of recruitment, a small number of scans were cancelled due to factors that were out of the researcher's control, such as scanner malfunction. This subsequently led to another participant withdrawing and resulted in other participants' scans having to be re-arranged. Given the characteristics of the sample and the difficulties in the initial engagement, it is important to keep participants motivated and engaged should technical problems occur. All of the above factors contributed to the small sample size of this study and it could be argued that the final fMRI sample may have included a biased group of participants who are likely to be more motivated to improve their functioning and benefit from therapy.

Strategies were utilized by the research team to try overcome some of the challenges, which included: organizing travel from the participant's home to the imaging centre, offering monetary reimbursement for the participant's time and expenses, encouraging a carer or a member of the care team to attend the scan along with the participant, and finally, allowing adequate time before the scan so that the researcher could attempt to alleviate any concerns the participant had about going in the scanner. Participants were given the opportunity to practice the imaging task on a computer prior to their scan, and had the option of using the mock-scanner to familiarize themselves with the MRI environment.

Despite these strategies, a number of participants still did not engage with the study, and the exclusion of participants due to the presence of neurological disorders and / or health concerns which contraindicate scanning would suggest that this is common problem, which is problematic when implementing a study of this kind in young people with severe social disability. Future studies should try to address these challenges. For example, a recent randomized control trial demonstrated the effectiveness of patients watching a video about the MRI procedure prior to scanning; this significantly reduced pre-procedural MRI anxiety (Tugwell, Goulden & Mullins, 2017).

5.6.5. Conclusion

This study showed changes in brain activation in the regions associated with ToM in individuals with FEP who had received a specialized CBT targeting social disability. Specifically, greater activation was seen in the temporal, parietal and frontal regions post-intervention, and this was observed both at the individual and group level. Activations became more refined and localized in the temporo-parietal Junction (TPJ), an area known to be implicated in ToM processing.

Furthermore, there was a trend for greater changes in the TPJ over the course of the intervention which was associated with more hours of structured activity at follow-up.

Although these findings are tentative given the small sample, this study has provided preliminary insights into the mechanisms underlying social recovery and the brain networks that might be implicated in functional change. This may allow for the refinement of the SRCBT, or may lead to the development of new interventions, particularly for those who do not respond to therapy. However, in the first instance, replication of the current findings in a larger sample, with an appropriate control comparison group, is necessary. Future studies should also consider the feasibility of conducting a study of this kind in young people experiencing social disability, and the challenges will need to be addressed.

6.0. CHAPTER 6

GENERAL DISCUSSION

The overall aim of this thesis was to examine the contributing role of SC and NC on poor functional outcome in FEP. Whilst a number of cross-sectional studies have found a close relationship between SC and NC and poor functioning in chronic schizophrenia, findings from studies of individuals in the early phase of illness, where intervention may be most effective, are less clear (Allott, Liu, Proffitt, & Killackey, 2011; Brekke *et al*., 2005; Fett *et al*., 2011).

Identification of the early predictors of potentially enduring poor functioning in psychosis may provide targets for intervention to improve and prevent decline in functioning for individuals who are most at risk. The main aims of this thesis therefore were to explore: (a) the prospective relationship between cognition (SC and NC) and functional outcome in FEP; (b) whether an improvement in functioning (i.e. structured activity) following a psychosocial intervention (Social Recovery Cognitive Behavioural Therapy; SRCBT) is associated with a corresponding change in cognitive function (SC and NC), and neural changes in the brain regions implicated in SC processing; and (c) whether SC and / or NC is able to predict who will respond to SRCBT.

6.1. Summary and interpretation of the main findings

     6.1.1. Study 1

The aim of Study 1 was to investigate the predictive efficacy of baseline NC and SC on social and role outcomes in individuals with FEP when considered alongside negative symptoms and

benchmark these cognitive dimensions against a healthy comparison group. There were several key findings.

Firstly, those with poor social and role outcomes had significant impairments in their premorbid functioning, greater negative and general symptoms, and greater cognitive impairment compared to those with good outcomes at 12 months. Several cognitive domains were more impaired in the poor outcome groups: social knowledge, Theory of Mind (ToM), verbal comprehension, and finally, verbal learning and memory, where 80% of individuals in the 'poor' outcome groups scored below a normal range on this this domain.

Social and role functioning were distinct in their trajectories and there was continuity within domains: those with poor social functioning were likely to have more interpersonal problems during adolescence, and social outcome at 12 months was predicted by social knowledge. Those with poor role outcome had greater academic impairment in adolescence, and role outcome at 12 months was predicted by verbal learning and memory. These findings demonstrate that the functional deficits present in FEP groups are a continuation of their adolescent trajectories, confirming previous research demonstrating that functional impairments emerge long before the formal onset of psychosis (Hodgekins, Birchwood, Christopher *et al*., 2015), and continuity within these do suggest that SC and NC might also be enduring deficits arising in adolescence and potentially domain specific.

Finally, when negative symptoms were added to the regression model, negative symptom scores were the only significant predictor of social and role functioning in FEP at 12 months, explaining a greater proportion of variance than the cognitive variables. Further exploratory

analyses showed that cognitive variables were linked to negative symptoms and explained 20% of variance in negative symptoms cross-sectionally and prospectively.

These findings are consistent with previous research which has reported on the link between negative symptoms and cognition in psychosis, with negative symptoms mediating the relationship between SC and NC and functional outcome (Lin, Huang, Chang *et al*., 2013; Madeira *et al*., 2016; Mehta *et al*., 2014; Ventura *et al*., 2009). Further evidence of this relationship comes from intervention studies which aim to improve functioning by targeting impaired cognition; these studies showed that negative symptoms improved alongside cognition (SC and NC) and functioning (Roder *et al*., 2006; Roder *et al*., 2011). Although it was not possible to explore the mediating role of negative symptoms in the relationship between cognition and functioning due to lack of statistical power, it is likely that SC and NC in early psychosis contribute to functional outcomes through their impact on negative symptoms.

The findings of Study 1 are corroborated by several recent publications where cognition was considered alongside symptoms in the prediction of functional outcome in FEP. These studies also found no prospective relationship between SC or NC and functioning, whilst negative symptoms significantly contributed to the prediction of outcome in early psychosis (Cacciotti-Saija *et al*., 2016; Horan *et al*., 2012; Langdon *et al*., 2014; Simons *et al*., 2016; Sullivan *et al*., 2014).

These findings are in contrast to a number of previous studies which have found a strong association between cognition and functioning in psychosis (Brekke *et al*., 2005; Fett *et al*., 2011; Stouten *et al*., 2014). However, the majority of these studies have focused on individuals with chronic schizophrenia, where findings may be influenced by effects associated with long term-illness, such as multiple-episodes and treatment (Allot *et al*., 2011; Green, 2008). These

studies are further confounded by focusing on the concurrent relationship between cognition and outcome where it is less possible to make causal inferences (Fett *et al*., 2011). Furthermore, in recent-onset samples, there is significant heterogeneity in illness course and outcome, unlike those with chronic schizophrenia where there is a 'selection bias', consisting of homogeneous groups of individuals with the poorest functional prognoses, and where predictors of outcome are likely to be different (Hodgekins, Birchwood, Christopher *et al*., 2015; Stouten *et al*., 2014). The findings of the present study, along with previous findings in chronic samples, may indicate that the association between cognition and poor functioning is more explicit in individuals at the severe end of the psychosis continuum, such as individuals with an established illness (Simons *et al*., 2016). This is in line with the proposed notion of clinical staging in psychosis, where each stage of illness is impacted by different factors (Allott, Liu, Proffitt, & Killackey, 2011; McGorry *et al*., 2007).

Whilst it has been proposed that poor functioning and cognitive impairments represent trait-like-characteristics of psychosis, identification of individuals with 'trait-related' phenomena, who are potentially at risk of longstanding poor functioning, is likely to prove challenging in the early phase of illness, when the clinical picture is still emerging, and most individuals remain functionally impaired following the initial episode (Lin, Reniers, Wood, 2013; Lin, Wood, Yung, 2013). Negative symptoms in the early course of illness might therefore be a better determinant of later functioning in individuals with FEP, but consideration should be given to the contributing role of SC and NC on functional outcome via their impact on negative symptoms.

6.1.2. Study 2

The first aim of Study 2 was to investigate whether NC and SC changed in line with any changes in functioning (i.e. structured activity) following a psycho-social intervention (Social Recovery Cognitive Behavioural Therapy - SRCBT). There were sound theoretical and empirical reasons to support this hypothesis, but not substantiated in this study.

Results showed that there was no significant difference in general SC and NC (i.e. composite scores) from baseline to follow-up between those who received the SRCBT and those who received standard care alone (treatment with an Early Intervention Service). This may suggest that the intervention had no impact on cognitive function, however, despite being statistically non-significant, there was a large effect size for the group x time interaction for the social cognitive composite; this analysis has limited statistical power, and so replication with a larger sample size may lead the interaction to become significant.

Whilst functioning improved as a result of the SRCBT, the intervention had no impact on cognition. Previous research has demonstrated a close link between functioning and cognition; as such, it was hypothesized that a change in functioning following intervention would lead to changes in cognition, however, this was not supported. This might be for several reasons. Firstly, the SRCBT did not seek to address cognitive impairments. Secondly, as some cognitive domains were un-impaired, this might explain why cognition in general (i.e. as a composite score) did not improve, as any change is likely to be subtle.

Unlike previous findings in chronic populations, the sample in Study 2 represented a subgroup of individuals with FEP who were heterogeneous in their clinical profiles, categorized as having

a 'severe social disability', and likely to be a 'chronic' sample of the future. As such, the aim of the intervention was to encourage engagement with a range of leisure activities rather than a return to main roles such as work or education. The initial, more subtle changes in functioning may not rely as much on cognition and perhaps for improvements to be maintained in the long term, individuals may also need to improve their cognitive function. Cognitive function beyond nine months was not explored in this study, and therefore it was not possible to test this proposal.

A further aim of Study 2 was to investigate the cognitive predictors of treatment response to SRCBT. Results showed that better SC predicted treatment response (increased structured activity). Individuals who had better social knowledge at baseline were more likely to improve their structured activity post SRCBT. To illustrate the magnitude of this effect, those scoring in the top quartile on social knowledge at baseline increased their structured activity by an additional 11 hours on average post-intervention, compared with those who had a lower social knowledge score at baseline. This finding suggests that social knowledge may have a moderating influence on those responding to the SRCBT. For example, those who have a better understanding of the social world are more likely to be motivated to engage in social activity and a psychosocial intervention, compared to those who struggle to understand social situations. Those with better social knowledge may also be more likely to form a better therapeutic alliance leading to better therapy response (Allot, Alvarez-Jimenez, Killackey, Bendall, McGorry & Jackson, 2011). Furthermore, as part of the SRCBT, individuals might be encouraged to use more adaptive cognitive reappraisal strategies to approach social situations, however, individuals with poor social knowledge may struggle with this. For example, if a friend seems cross with you, a useful reappraisal might be to understand that the friend is having a difficult day, but if the individual is impaired in their understanding of social situations, they may not

be flexible enough to re-appraise the situation and subsequently resort to more maladaptive reappraisal strategies, thus impeding their social recovery (Rowlands *et al.*, 2013).

6.1.3. Study 3

Study 3 was an explorative functional magnetic resonance imaging (fMRI) study, which aimed to investigate the neural correlates of SC (specifically Theory of Mind; ToM) in a sample of young people with FEP, before and after receiving SRCBT. Findings from the exploratory group analysis and observations of the individual participant analyses consistently demonstrated that there was significantly greater activation in the brain regions associated with ToM, post-SRCBT. Activation in the key regions, namely the temporo-parietal regions, also became more refined and localised by follow-up. Furthermore, in a region of the brain known to be uniquely involved in processing of mental states – the temporo-parietal-junction (TPJ; Mars *et al.,* 2012) – there was a trend for greater changes in the TPJ post intervention which was associated with more hours of structured activity at follow-up.

A final observation from inspecting the individual analyses is that for the individuals who improved their functioning following the intervention, there appeared to be differences both at the behavioural and neural level, compared to those who were still considered as having a 'social disability' post-intervention. For example, those with improved functioning (those who increased their structured activity), had improved task speed and accuracy, and increased activation, which was localised to the ToM regions. In contrast, those who remained socially disabled after receiving the intervention had worse task performance and there appeared to be a less significant change in the key brain regions implicated in ToM processing.

Previous findings have shown hypo-activation in ToM regions in individuals with schizophrenia, compared to healthy controls (Walter *et al*., 2009). Increased activation post intervention may represent normalisation in the ToM regions after receiving the SRCBT. Similarly, more refined and localised activation in the ToM regions at follow-up may represent more efficient neural circuits, which again may suggest that ToM improved.

It is plausible that through receiving the SRCBT, these individuals were able to use different cognitive strategies to approach the ToM task as a result of developing their comprehension of social situations, and subsequently building on new social experiences, resulting in more efficient neural circuits. More widespread activations within the temporal and parietal regions at baseline may indicate less efficient neural circuits. Similarly, functional imaging studies in at-risk populations have proposed that over-activation is indicative of a compensatory mechanism to perform adequately on tasks requiring mental state attribution (Bosia *et al*., 2012). A similar hypothesis has also been proposed by Burnett and Blakemore (2009) to explain the reasons for the neurodevelopmental differences between adults and adolescents within the social regions of the brain.

These findings provide preliminary insights into the brain networks that are associated with improved functioning in early psychosis. However, given the small sample size, and the absence of a comparison group, replication of the findings is needed with a larger sample to confirm this finding.

Consideration should also be given to the challenges that were encountered during the recruitment phase, which likely reflects the complex nature of this group, and which subsequently led to the low power of this study. A number of participants were excluded due to the presence of neurological disorders, and for health concerns which contraindicate

scanning. This is important for future studies to consider, as a proportion of young people presenting with a social disability may also have co-occurring difficulties which could be contributing to their social disability. Exclusion of these individuals in imaging studies means that the generalizability of these findings is limited. Furthermore, many individuals in the SRCBT trial did not give consent to participate in this study, and some participants who attended for a scan subsequently withdrew after becoming anxious in the scanner.

Despite the research team putting into place some strategies to overcome these challenges, participants still did not engage with the study; the exclusion of participants is likely to be a widespread problem, which calls into question the feasibility of implementing a study of this kind in young people with severe social disability.

6.2. Main strengths and limitations of the research

A limitation to previous research in this area is that studies have generally focused on cross-sectional relationships between cognition and functioning in chronic samples, where factors such as illness chronicity impact on generalizability of the findings, and where inferences of causality are less meaningful. In studies which have focused on FEP groups, there is considerable methodological variability, numerous study limitations (such as differences in the measurement of cognition and outcome, length of follow-up, inadequate power, and lack of control over other predictor variables), and fewer studies investigating the role of SC on outcome in FEP (Allott, Liu, Proffitt, & Killackey, 2011). Furthermore, whilst the association between cognition and functioning has been explored by a number of studies, less is understood about the underlying mechanisms of functional change.

To address these limitations, the present research comprehensively assessed cognition (SC and NC), using large and representative FEP groups over time, so that the prospective relationship between cognition and functioning could be explored. The outcome measures used were not confounded by jointly assessing symptoms, were age-appropriate, and different areas of functioning were considered separately (social and role functioning; Cornblatt *et al*., 2007). Negative symptoms were also included in the analyses to see if cognition can explain additional variance above that accounted for by negative symptoms. Uniquely, a healthy comparison group which was carefully matched on age, education and demographic variables, was also recruited to benchmark cognitive function with the FEP groups.

The impact of SC and NC on a psychosocial intervention (SRCBT) was examined in a large multi-site randomized controlled trial (SUPERDEN; Fowler *et al*., 2017). To our knowledge, Study 2 was the first to investigate cognitive predictors of treatment response to a CBT intervention addressing poor social functioning in FEP. Furthermore, at the time of writing, Study 3 was the first study to report on longitudinal functional brain changes in the ToM regions in a sample of socially disabled young people with FEP, and the first to report functional neural changes in a social cognitive region of the brain after participants receive a CBT to improve functioning. Despite these strengths, there are limitations which should be considered when interpreting the findings. The limitations will now be discussed.

6.2.1. The sample

While some interesting trends emerged from the fMRI study, the small sample size dictates that results are tentative and further research is needed to clarify if the findings generalise to a larger group of individuals undergoing SRCBT. The lack of comparison with the control arm of the

trial also means that it is not possible to fully determine whether these changes are indeed a result of the therapy, reflect a general recovery process, or are simply a practice effect. They do however encourage further research.

In Study 2, despite a large proportion of the overall sample completing cognitive assessments at baseline, 20% of the sample did not. Although speculative, this may have biased the findings of the study as it is not possible to rule out that those who have poorer cognitive function were the participants who refused to engage in the cognitive assessments. To explore this further, an analysis was carried out which showed that there were no differences between the participants and refusers on demographic and clinical characteristics (apart from more general symptoms present in the refusers), making it less likely that there were any differences in cognitive function (Appendix A-10).

It is also worth noting that in each of the empirical studies there were gender differences, where most of the sample consisted of males. It could be argued that the findings do not generalise to females with FEP, however, the sample likely reflects the higher incidence of young males presenting with FEP (Kirkbride *et al*., 2006). Further, previous research has shown that a greater proportion of males with psychosis are more likely to have poor functional outcome (Hodgekins et al., 2015). Comparisons between the sample in study 2 and the full SRCBT sample (Fowler et al., 2017), showed there were no significant gender differences (A-10), demonstrating that the sample in Study 2 is likely to be representative of those who have severe social disability in FEP. It would be interesting for future work to consider why young males in particular appear to have greater problems in their everyday functioning in psychosis, and what might be the protective factors for females.

6.2.2. Measures and assessment of outcome

The cognitive measures used in the studies may not have been sensitive enough to capture the complex dynamics of everyday social interaction (Simons *et al*., 2016). The possible lack of ecological validity may also explain why Studies 1 and 2 failed to find a consistent SC impairment across the FEP groups (when compared with the healthy comparison group) where subtle impairment (which may be present   at this early phase of illness) may have not been captured. SC measures which are more ecologically sound are needed to further understand the relationship between SC and poor functioning in FEP (Pinkham *et al.,* 2014). An inherent problem in the field is the inconsistency in how SC domains are assessed; furthermore, the psychometric soundness of the measures is not well established (Davidson, Lesser, Parente, & Fizdon, 2017; Grant, Lawrence, Preti, Wykes & Cella, 2017; Pinkham *et al*., 2014).

To address this, the social cognitive psychometric evaluation (SCOPE) study was developed, bringing together an expert panel to identify a standard social cognitive test battery with sound psychometric properties that could be implemented in clinical trials in schizophrenia; eight candidate measures were identified (Pinkham *et al.,* 2014). The study has since been extended to identify candidate measures for use in early psychosis (Ludwig *et al*., 2017). Of the eight measures used in in the SCOPE study, only one measure, which assessed ToM (The Hinting Task; Corcoran, Mercer & Frith, 1995) was consistently shown to have adequate psychometric properties in chronic schizophrenia and FEP. The remaining measures were deemed inappropriate for the assessment of SC in early psychosis. These findings highlight the need for future research to develop new measures that are psychometrically sound, are appropriate for phase of illness, and will adequately capture variance in SC deficits and not error variance (Healey *et al*., 2016; Ludwig *et al*., 2017). There is also implication for the use of state-of-the-

art technology, such as virtual reality simulators, to aid in intervention and assessment of social cognition, as they could provide more of a useful opportunity for complex and dynamic social encounters which current test batteries may not provide (Horan & Green, 2017; Peyroux & Franck, 2014).

As the main outcome measure in Study 1, the Global Functioning Scales (GF; Cornblatt *et al*., 2007), was originally standardised on an ultra-high risk (UHR) sample, there may have been a possible floor effect, as UHR samples tend to be less functionally impaired (Hodgekins, French, Birchwood, *et al*., 2015). Given the heterogeneity in outcome in FEP, those with the poorest outcome (who are most likely to be at risk of longstanding functional impairment and chronic illness) may not have been distinguished from those who have more moderate or 'state-like' functional impairment (Lin, Reniers, Wood, 2013; Lin, Wood, Yung, 2013). However, further inspection of the GF scores showed that there was heterogeneity within the scales (GF role range = 9; M = 5.1; Variance = 8.89; GF: Social range = 7; M = 6.5; Variance = 2.11), and there was no evidence that the scores were truncated in the bottom quartile. Correlations between the GF scores collected as part of Study 2 and the trial primary outcome measure were explored, which showed that the TUS was significantly related to the GF scales (GF: Social: r = .311; p = 0.01; GF Role: r = .510; p = <0.01). This provides support for the GF scales' reliability and suggests that a floor effect is likely not present.

It must also be acknowledged that for Study 1, the inter-rater reliability was not formally checked for the 'observer-rated' scales, potentially impacting on the reliability of the findings. High inter-rater reliability has been established in previous research for the global functioning scales (see Cornblatt *et al*., 2007) and PANSS assessment (see Kay *et al*., 1987). The two researchers who were involved in completing the assessments received formal training on the

measures, and ratings were compared by the researchers on a small number of participants to check for concordance in the ratings. The vast majority of the assessments were conducted by the same researcher (SLG), who had more than 5 years of experience completing the PANSS assessments, and regularly completed concordance checks in line with the NIHR SUPEREDEN protocol (Fowler *et al*., 2017), increasing the likelihood that the outcome measures were rated reliably.

For Study 1, a logistic regression was employed to look at the dichotomous outcome (poor vs. good outcome) to identify the characteristics and markers of those with poor functioning at 12 months. This is important as the SRCBT targeted individuals who had proved to be 'treatment unresponsive' and had a high level of social disability despite receiving high quality EIS care over a 12-month period. As such, identifying the early markers of those who are likely to be treatment unresponsive at 12 months could potentially lead to earlier identification and earlier targeting of interventions for these individuals. A dichotomous outcome was also used in Study 2 to define treatment response, using a social disability cut-off score to demonstrate which individuals have moved out of the 'social disability' range. The reason for selecting a dichotomous outcome in this study was to test the predictive power of cognition on functional change by setting a higher threshold for 'treatment response'. This would help to determine if cognition could explain which individuals made the greatest functional gains to achieve a good social recovery, and hence would hold as a promising treatment target. However, despite having a strong conceptual reason for dichotomising outcome, it is important to highlight the limitations of this approach. For example, in Study 2, a disadvantage of using a dichotomy is that it may not accurately represent 'treatment response', as some individuals, despite making meaningful improvements in their level of functioning, may still be performing below the social-disability cut-off. To ensure that a more balanced measure of treatment response was

captured, a linear relationship was explored between cognition and increases in structured activity (using an absolute change score, see methods, Section 4.4.3, page 123) following intervention. Similarly, in Study 1, using a cut-off score makes the assumption that those scoring immediately above and below the 'cut-off' are qualitatively distinct, however, on the individual level there is not likely to be much difference in their level of functioning. An alternative approach would have been to conduct a multiple linear regression to preserve variance in the outcome measure, but this was not explored in Study 1.

6.2.3. Possible confounding variables

Substance misuse, particularly persistent cannabis use, is associated with poor functional outcome and NEET status in the general population (Rodwell et al., 2018). Whilst some studies have found no association between substance use and poor functional outcome in early psychosis (Addington & Addington, 2007; Larsen et al., 2006), a longitudinal study investigating the trajectories of social functioning in individuals FEP, demonstrated that despite receiving specialised early intervention care, individuals who used cannabis were less likely to make improvements in their social functioning, compared to their counterparts who did not use cannabis (González-Blanch et al., 2015). The sample recruited for the SRCBT trial were those whose disability was unresponsive to EIS care, and it might be that cannabis use may have contributed to their social disability. Indeed, Seddon and colleagues (2016) found that cannabis use was linked to continued social disability in FEP, and conversely, those who reduced their cannabis use improved their social disability. Within study 3, one case example of note was B026, whose marked cannabis use appeared to contribute to his poor functioning, and he also did not respond to the intervention. As substance misuse was not controlled for in the study, it

is not possible to determine to what extent cannabis use influenced his level of functioning and possibly his lack of response to treatment.

Social anxiety has also been shown to be associated with poor functioning in psychosis (Chudleigh *et al.*, 2011; Voges & Addington, 2005), with a recent study showing that negative symptoms and social anxiety were better markers of later functional outcome in early psychosis, compared to social cognition and neurocognition (Cacciotti-Saija *et al.*, 2016). It is therefore a limitation that social anxiety was not considered as a covariate in the regression models, particularly given that the Study 2 sample presented with complex comorbidities including high-levels of depression and anxiety (Fowler et al., 2017). The addition of social anxiety in the models may have explained additional variance in functional outcome, and as such, could potentially be an important treatment target to improve social disability, and should be considered in future research.

6.3. Future directions and clinical implications

This thesis showed that negative symptoms is an important prognostic marker of those with poor outcome in first episode psychosis, consistent with previous findings (Gee *et al.*, 2016; Hodgekins, Birchwood, Christopher *et al.*, 2015; Rammou *et al.*, 2017). Whilst negative symptoms have been identified as an important intervention target by the NIMH-MATRICS consensus (Kirkpatrick, Fenton, Carpenter & Marder, 2006), existing treatments such as anti-psychotic medication does little in improving negative symptoms (Goldberg *et al.*, 2007). The results of this thesis demonstrate that a complex relationship exists between negative symptoms and cognition (SC and NC), consistent with previous research showing that certain cognitions have direct impact on negative symptoms (Madeira *et al.*, 2016). Understanding the

interrelationships between cognition and negative symptoms could therefore inform interventions addressing functional outcome in early psychosis. For example, it is argued that the inability to form mental representations of self and others may be a barrier to seeking and anticipating pleasure and pursuing goal-directed behaviour (Buck *et al*., 2014; Lysaker & Dimaggio, 2014); specifically targeting mental state representation could directly improve negative symptoms and in turn lead to improvements in functioning. A further understanding of which components of cognition impact on different negative symptoms could prove fruitful at improving functioning for young people with psychosis and deserves further exploration.

The finding that baseline SC is able to predict which individuals are most likely to respond to the SRCBT intervention, together with the preliminary finding that the SC brain network might be associated with functional change, has a number of clinical implications. Firstly, the potential to identify individuals at an early stage who are less likely to respond to intervention will ensure that costly interventions (for both health service and service user) are not delivered to those who are unlikely to respond. Secondly, these findings also have the potential to guide targeted interventions for those who are less likely to respond to this psychosocial intervention; improving social cognition might improve response to SRCBT.

To confirm if those with poor social knowledge are less likely to benefit from SRCBT, a proposal for future work would be to conduct an *a priori* study comparing response to SRCBT between those with 'poor' and 'good' social knowledge. Another proposal for future work would be to refine the SRCBT intervention by incorporating a social cognitive intervention prior to the commencement of the SRCBT, to test whether this could enhance its efficacy in those with deficits in social cognition.

Penn and colleagues (2007) have demonstrated the success of a specialised SC intervention with the development of Social Cognitive Interaction Training (SCIT). SCIT consists of three distinct phases: emotion training, figuring out situations, and integration of these skills into everyday life. SCIT has been shown to significantly improve a number of social cognitive abilities, including ToM, as well as improve social relationships and social functioning in individuals with established psychosis (Combs, Adams, Penn, Roberts, Tiegreen & Stem, 2007; Roberts *et al*., 2014). A recent meta-analysis of social cognitive training in schizophrenia showed large effect sizes of training on facial affect recognition, moderate-sized effects for ToM, and small to medium effects for attribution style, in addition to moderate to large effects for community functioning (Kurtz, Gagen, Rocha, Machado & Penn, 2016). There is also preliminary data suggesting that SCIT is potentially effective at improving SC and functioning in young people with FEP (Bartholomeusz *et al*., 2013).

A proposal for future research would therefore be to deliver the SRCBT in adjunct to SCIT to maximise the output of the therapy. Indeed, there is growing evidence to suggest the most robust findings for cognitive rehabilitation programmes are demonstrated when cognitive training is integrated with other therapeutic approaches, such as social skills training and interpersonal problem solving, resulting in greater cognitive and real-world functional improvements (Horan & Green, 2017; Roder *et al*., 2011). An example of such an approach is Integrated Psychological Therapy (IPT), which is a group-based CBT programme. The programme is broken down into subdomains of therapy which have an increasing level of complexity; the underlying assumption is that basic cognitive functions influence higher order behavioural organizations such as social skills and social functioning (Roder *et al*., 2011). It is believed that each of the different components act together in synergistic manner, enhancing the durability of the therapeutic effects and improving functioning; this may be explained by the mediating

influence of SC on NC (Gard *et al*., 2009; Roder *et al*., 2011). In meta-analyses where IPT has been evaluated, results showed greater improvements in NC, SC, functioning and negative symptoms for those who received IPT compared to a control condition, and these effects were maintained over time (Roder *et al*., 2006; Roder *et al*., 2011). These findings are consistent with other integrated approaches such as Cognitive Enhancement Therapy (CET; Barlati, De Peri, Deste, Fusar-Poli & Vita, 2012; Eack *et al*., 2009; Roder *et al*., 2011), which has also been implicated as having neuro-protective and neuro-enhancing effects in early schizophrenia (Eack *et al*., 2009). Furthermore, a recent systematic review of social cognitive training programmes in schizophrenia has provided evidence of structural and functional changes associated with social cognitive processing, including: the limbic system, prefrontal and perceptual areas (Campos *et al*., 2016).

In a comparable way, the application of an integrated, multi-dimensional treatment approach combining SRCBT with a form of social cognitive intervention may produce more durable and sustained therapeutic effects for individuals with poor functioning in early psychosis. This approach would not only allow one to regain essential skills for functional improvement, but also allow for the transfer and practice of these skills in real-life situations (Roder *et al*., 2011).

Finally, replication of the fMRI findings in a larger sample is necessary to confirm that the ToM network is associated with functional change. Although Study 2 found that SRCBT had little impact on SC, when neurobiological changes occur, behaivoural changes do not always occur in parallel, and this might suggest that investigating the neurobiological markers may provide a more sensitive way of examining changes following intervention (Lin, Reniers & Wood, 2013; Fornito, Yoon, Zalesky, Bullmore & Carter, 2011). Examining the neuroplasticity effects may also provide useful information of durability and long-term benefits of social interventions

such as SRCBT, and therefore it is important to explore this further (Campos et al., 2016). Furthermore, if ToM is implicated in functional change, impaired ToM could therefore be a target for intervention which could lead to refinement of current intervention (SRCBT), potentiallyimproving its effectiveness.

A larger sample in a future study would also allow for exploration of the neurobiological predictors (using fMRI) of treatment response (i.e. improved functioning), which was not possible in the current study due to the group analysis lacking sufficient power. Although SC was not a robust predictor of 12-month outcome in FEP, investigating the neurobiological predictors (e.g. using fMRI) might be more of a sound marker of outcome. This warrants further investigation. Comparisons with appropriate control groups are also necessary to determine if changes are a result of receiving the SRCBT, reflect a general recovery process, or represent a practice effect.

6.4. Final comments and conclusion

The studies in this thesis were novel in their prospective investigation of the contributing role of social cognition and neurocognition, relative to symptoms, in understanding functional outcome in FEP. It is also the first study to report on the cognitive predictors of response to a specialised CBT intervention targeting poor functioning in FEP, and the first to provide preliminary imaging data on a social cognitive neural network supporting change in functioning following a specialized CBT for social disability

This thesis showed that young people who have poor social and role outcomes in early psychosis have greater SC and NC impairments than those with good outcomes, and that these

functional deficits form part of their prior adolescent trajectories, suggesting that these functional challenges are at high-risk of progression.

Negative symptoms were found to be the most robust predictor of later social and role outcomes in FEP, with SC and NC having a subordinate role in predicting later functional outcome. Exploratory analyses suggest that cognition directly impacts on negative symptoms which in turn may influence functional outcome. The findings highlight the need to delineate the relationship between cognition and negative symptoms, as this could potentially inform targeted intervention to prevent decline in functioning in FEP.

This research also found evidence of SC's contribution to functional change in individuals with FEP who are undergoing a psychosocial intervention targeting social disability. Together with the preliminary evidence of functional brain changes in the SC regions following intervention, these findings have implications for targeted intervention for individuals in the early phase of psychosis with poor SC, who appear to be less likely to respond to the SRCBT intervention. A proposal would be to combine and evaluate the SRCBT intervention with a social-cognitive intervention, to maximise its impact, and potentially provide more durable and sustained treatment effects, particularly for those who have not responded to the SRCBT intervention.

Overall the findings of this thesis have shown that cognition, in particular social cognition, plays an important role in functional outcomes in FEP, principally in affecting the reach and impact of SRCBT in those with high disability and unresponsive to EIS, thus potentially reducing the changes of social disability becoming entrenched.

LIST OF REFERENCES

Abu-Akel, A. (2003). The neurochemical hypothesis of "theory of mind". *Medical Hypotheses, 60*(3), 382-386. https://doi.org/10.1016/S0306-9877(02)00406-1

Abu-Akel, A., & Bailey, A. L. (2000). The possibility of different forms of theory of mind impairment in psychiatric and developmental disorders. *Psychological Medicine. 30*, 735–738 https://doi.org/10.1017/S0033291799002123

Abu-Akel, A., & Shamay-Tsoory, S. (2011) Neuroanatomical and neurochemical bases of theory of mind. *Neuropsychologia, 49*, 2971–2984.

Acorn © (2013). *ACORN - A Classification of Residential Neighborhoods postcode.* Retrieved from https://acorn.caci.co.uk/

Addington, J., & Addington, D. (1993). Premorbid functioning, cognitive functioning, symptoms and outcome in schizophrenia. *Journal of psychiatry & neuroscience, 18,* 18-23.

Addington, J., & Addington, D. (2005). Patterns of premorbid functioning in first episode psychosis: relationship to 2-year outcome. *Acta Psychiatrica Scandinavica, 112*(1), 40-46.

Addington, J., & Addington, D. (2007). Patterns, Predictors and Impact of Substance Use in Early Psychosis: A Longitudinal Study. *Acta Psychiatrica Scandinavica, 115,* 304309

Addington, J., Addington, D., Jones, B., & Ko, T. (2001). Family intervention in an early psychosis program. *Psychiatric Rehabilitation Skills*, *5*(2), 272–286. https://doi.org/10.1080/15487760108415433

Addington, J., Liu, L., Buchy, L., Cadenhead, K., Cannon, T., A Cornblatt, B., … Mcglashan, T. (2015). North American Prodrome Longitudinal Study (NAPLS 2): The prodromal symptoms. *Journal of Nervous and Mental Disease, 203*(5), 328-335. https://doi.org/10.1097/NMD.0000000000000290

Addington, J., Saeedi, H., & Addington, D. (2005). The course of cognitive functioning in first episode psychosis: Changes over time and impact on outcome. *Schizophrenia Research*, *78,* 35-43.

Addington, J., Saeedi, H., & Addington, D. (2006). Influence of social perception and social knowledge on cognitive and social functioning in early psychosis. *The British Journal of Psychiatry*, *189*(4), 373–378. https://doi.org/10.1192/bjp.bp.105.021022

Adolphs, R. (2009). The social brain: neural basis of social knowledge. *Annual Review Psychology, 60,* 693-716.

Agerbo, E., Byrne, M., Eaton W. W., & Mortensen P. B. (2004). Marital and labor market status in the long run in schizophrenia. *Archives of General Psychiatry, 61*, 28–33.

Akkari, C. (2012). Development of a functional imaging task to assess social cognition in early psychoses (unpublished Master of Science Thesis, University of Birmingham / Aix-Marseille University).

Albert, N., Bertelsen, M., Thorup, A., Petersen, L., Jeppesen, P., Quack, P. L., . . . Norden tofy, M. (2011). Predictors of Recovery from Psychosis: analyses of clinical and social factors associated with recovery among patients with first-episode psychosis after 5 years. *Schizophrenia Research, 125,* 257-266.

Allot, K., Alvarez-Jimenez, M., Killackey, E.J., Bendall, S., McGorry, P.D., & Jackson, H. J. (2011). Patient predictors of symptom and functional outcome following cognitive behavioural therapy or befriending in first-episode psychosis. *Schizophrenia Research, 132,* 125-130.

Allott, K., Liu, P., Proffitt, T-M., & Killackey, E. (2011). Cognition at illness onset as a predictor of later functional outcome in early psychosis: a systematic review and methodological critique. *Schizophrenia Research, 125,* 221-235.

Alvarez-Jimenez, M., Priede, A., Hetrick, S. E. Bendall, S., Killackey, E., Parker, A. G., . . .

    Gleeson, J. F. (2012). Risk factors for relapse following treatment for first episode

    psychosis: a systematic review and meta-analysis of longitudinal studies. *Schizophrenia*

    Research, 139, 116–128.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental*

    disorders (4th ed.). Text Revision. Washington, DC.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental*

    disorders (*5th ed.).* Washington, DC.

An, S. K., Kang, J. I., Park, J. Y., Kim, K. R., Lee, S. Y., & Lee, E. (2010). Attribution bias in

    ultra-high risk for psychosis and first-episode schizophrenia. *Schizophrenia Research*,

    118(1), 54–61. https://doi.org/10.1016/j.schres.2010.01.025

Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C., Perry, B. D., … Giles,

    W. H. (2006). The enduring effects of abuse and related adverse experiences in

    childhood: A convergence of evidence from neurobiology and epidemiology.

    European Archives of Psychiatry and Clinical Neuroscience, *256*(3), 174–186.

    https://doi.org/10.1007/s00406-005-0624-4

Auther, A., Smith, C., & Cornblatt, B. (2006). Global Functioning: Social Scale (GF: Social).

    Glen Oaks, NY: Zucker-Hillside Hospital.

Ayesa-Arriola, R., Manuel Rodríguez-Sánchez, J., Pérez-Iglesias, R., González-Blanch, C.,

    Pardo-García, G., Tabares-Seisdedos, R., … Crespo-Facorro, B. (2013). The relevance

    of cognitive, clinical and premorbid variables in predicting functional outcome for

    individuals with first-episode psychosis: A 3 year longitudinal study. *Psychiatry*

    Research, *209*(3), 302–308. https://doi.org/10.1016/j.psychres.2013.01.024

Barker, V., Gumley, A., Schwannauer, M., & Lawrie, S. M. (2015). An integrated

    biopsychosocial model of childhood maltreatment and psychosis. *The British Journal*

of Psychiatry, *206*(3), 177–180. https://doi.org/10.1192/bjp.bp.113.143578

Barkl, S., Lah, S., Harris, A., & Williams, L. (2014). Facial emotion identification in early-onset and first-episode psychosis: A systematic review with meta-analysis. *Schizophrenia Research, 159*(1), 62-69. https://doi.org/10.1016/j.schres.2014.07.049

Barlati, S., De Peri, L., Deste, G., Fusar-Poli, P., & Vita, A. (2012). Cognitive remediation in the early course of schizophrenia: A critical review. *Current Pharmaceutical Design, 18*(4), 534-541. https://doi.org/10.2174/138161212799316091

Baron-Cohen, S. (1995). *Mindblindness: an essay on autism and theory of mind.* Cambridge MA: MIR Press.

Baron-Cohen, S., Jolliffe, T., Mortimore, C., & Robertson, M. (1997). Another advanced test of theory of mind: Evidence from very high functioning adults with autism or Asperger Syndrome. *Child Psychology & Psychiatry & Allied Disciplines, 38*(7), 813-822.

Baron-Cohen, S., O'Riordan, M., Stone, V., . . . Jones, R., Plaisted, K. (1999). Recognition of faux pas by normally developing children and children with Asperger syndrome or high-functioning Autism. *Journal of Autism and Developmental Disorders. 29*(5), 407-418.

Bartholomeusz, C., & Allott, K. (2012). Neurocognitive and social cognitive approaches for improving functional outcome in early psychosis: Theoretical considerations and current state of evidence. *Schizophrenia Research and Outcome, 2012*, 1-15. https://doi.org/10.1155/2012/815315

Bartholomeusz, C., Allott, K., Killackey, E., Liu, P., Wood, S., & Thompson, A. (2013). Social cognition training as an intervention for improving functional outcome in first-episode psychosis: A feasibility study. *Early Intervention in Psychiatry, 7*(4), 421-426. https://doi.org/10.1111/eip.12036

Bartholomeusz, C.F., Killackey, E., Thompson, A., & Wood, S. J. (2011). Interventions

targeting social and vocational dysfunction in individuals with a schizophrenia spectrum

disorder. In *Handbook of Schizophrenia Spectrum Disorders.* (ed. M.S. Ritsner),

Volume III.

Bellack, A. S., Morrison, R. L., Wixted, J.T., & Mueser, K. T. (1990). An analysis of social

competence in schizophrenia. *British Journal of Psychiatry, 156*, 809-818.

Bentall, R. P., Corcoran, R., Howard, R., Blackwood, N., & Kinderman, P. (2001). Persecutory

delusions: A review and theory and theoretical integration. *Psychosis*, *21*(8), 1143–

1192. https://doi.org/10.1016/S0272-7358(01)00106-4

Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., Øhlenschlaeger, J., le Quach, P., . . .

Nordentoft, M. (2008). Five-year follow-up of a randomized multicenter trial of intensive early

intervention vs standard treatment for patients with a first episode of psychotic illness:

the OPUS trial. *Archive of General Psychiatry, 65,* 762–71.

Bertrand, M. C., Sutton H., Achim, A. M., Malla, A. K., & Lepage, M (2007). Social cognitive

impairments in first episode psychosis. *Schizophrenia Research. 95*(1–3), 124–133.

Bier, A., Schreiber, J. L., Dyer, J., & Pickar, D. (1991) National Institute of Mental Health

longitudinal study of chronic schizophrenia: prognosis and predictors of outcome.

Archives of General Psychiatry 48, 239-246.

Birchwood, M. (2003). Pathways to emotional dysfunction in first-episode psychosis. *The

British Journal of Psychiatry. 182*(5), 373-375.

Birchwood, M., Fowler, D., & Jackson, C. (2001). *Early intervention in psychosis.*

Chichester: John Wiley and Son

Birchwood, M., Iqbal, Z., Chadwick, P., & Trower, P. (2000). Cognitive approach to depression

and suicidal thinking in psychosis, I. Ontogony of post psychotic depression. *British

Journal of Psychiatry*, *177*, 516–521.

Birchwood, M., & Jackson, C. (2001). *Schizophrenia. Clinical Psychology: A modular course.* Psychology Press.

Birchwood, M., McGorry, P., & Jackson, H. (1997). Early intervention in schizophrenia. *British Journal of Psychiatry, 170,* 2 – 5.

Birchwood, M., Todd, P., & Jackson, C. (1998). Early intervention in psychosis: the critical-period hypothesis. *British Journal of Psychiatry Supplement. 172*(33), 53-9.

Blakemore, S. (2008). Development of the social brain during adolescence. *The Quarterly Journal of Experimental Psychopathology. 61*(1), 40-49.

Bond, G. R., Drake, R. E., & Luciano, A. (2014). Employment and educational outcomes in early intervention programmes for early psychosis: a systematic review. *Epidemiology and psychiatric sciences*, 24(05), 1-12

Bora, E., Yücel, M., & Pantelis, C. (2009). Theory of mind impairment: a distinct trait-marker for schizophrenia spectrum disorders and bipolar disorder? *Acta Psychiatrica Scandinavica*, *120*(4), 253–264. https://doi.org/10.1111/j.1600-0447.2009.01414.x

Borod, J. C., C. Martin, C., Alpert, M., Brozgold, A., & Welkowitz, J. (1993). Perception of facial emotion in schizophrenic and right brain-damaged patients. *The Journal of Nervous and Mental Disease, 181*(8), 494-502. https://doi.org/10.1097/00005053-199308000-00004

Bosia, M., Riccaboni, R., & Poletti, S. (2012). Neurofunctional correlates of theory of mind deficits in schizophrenia. *Current Topics in Medicinal Chemistry*, *12*(21), 2284-2302.

Brekke, J., & Long, J. D. (2000). Community-based psychosocial rehabilitation and prospective change in functional, clinical, and subjective experience variables in schizophrenia. *Schizophrenia Bulletin, 26*, 667–680.

Brekke, J., Kay, D. D., Lee, K. S., & Green, M. F. (2005). Biosocial pathways to functional outcome in schizophrenia. *Schizophrenia Research*, *80*(2), 213–225.

https://doi.org/10.1016/j.schres.2005.07.008

Brett, M. C., Anton, J.-L., Valabregue, R., & Poline, J.-B. (2002). Region of interest analysis using the MarsBar toolbox for SPM 99. *Neuroimage*, *16* 497.

Brill, N., Reichenberg, A., Weiser, M., & Rabinowitz, J. (2007). Validity of the Premorbid Adjustment Scale. *Schizophrenia Bulletin, 34(5),* 981-983. https://doi.org/10.1093/schbul/sbm128

Brissos, S., Molodynski, A., Dias, V. V., & Figueira, M. L. (2011). The importance of measuring psychosocial functioning in schiophrenia. *Annals of General Psychiatry, 10,* 18.

Brothers, L. (1990). The neural basis of primate social communication. *Motivation and Emotion*, *14*(2), 81–91. https://doi.org/10.1007/BF00991637

Brothers, L. (2002). The social brain: A project for integrating primate behavior and neurophysiology in a new domain. *Concepts in Neuroscience*, *1*, 27–51.

Brune, M. (2005) "Theory of mind" in schizophrenia: a review of the literature. *Schizophrenia Bulletin. 31*(1), 21–42.

Brunet, E., Sarfati, Y., Hardy-Bayle, M. C., & Decety, J. (2003). Abnormalities of brain function during a nonverbal theory of mind task in schizophrenia. *Neuropsychologia, 41,* 1574–1582.

Buck, K. D., McLeod, H. J., Gumley, A., Dimaggio, G., Buck, B. E., Minor, K. S., … Lysaker, P. H. (2014). Anhedonia in prolonged schizophrenia spectrum patients with relatively lower vs. higher levels of depression disorders: Associations with deficits in social cognition and metacognition. *Consciousness and Cognition*, *29* (Supplement C), 68–75. https://doi.org/10.1016/j.concog.2014.07.005

Burnett, S., & Blakemore, S.J. (2009). The development of adolescent social cognition. *Values, Empathy, and Fairness Across Social Barriers, 1167,* 51-56.

Burns, R., & Burns, R. (2008). *Business Research Methods and Statistics Using SPSS*. Sage Publications.

Burns, T., & Patrick, D. (2007). Social functioning as an outcome measure schizophrenia studies. *Acta Psychiatrica Scandanavica, 116*(6), 403-418.

Cacciotti-Saija, C., Langdon, R., Ward, P. B., Hickie, I. B., & Guastella, A. J. (2016). Clinical symptoms predict concurrent social and global functioning in an early psychosis sample. *Early Intervention in Psychiatry*. 1-8. https://doi.org/10.1111/eip.12295

Campos, C., Santos, S., Gagen, E., Machado, S., Rocha, S., Kurtz, M. M., & Rocha, N. B. (2016). Neuroplastic changes following social cognition training in schizophrenia: A systematic review. *Neuropsychology Review*, *26*(3), 310–328. https://doi.org/10.1007/s11065-016-9326-0

Cannon, M., Jones, P., Gilvarry, C., Rifkin, L., McKenzie, K., Foerster, A., & Murray, R. (1997). Premorbid social functioning in schizophrenia and bipolar disorder: Similarities and differences. *American Journal of Psychiatry, 154*(11), 1544-1550. https://doi.org/10.1176/ajp.154.11.1544

Cheng, F., Kirkbride, J. B., Lennoz, B. R., Perez, J., Masson, K., Lawrence, K., . . . Jones, P. (2011). Administrative incidence of psychosis assessed in early intervention services in England: first epidemiological evidence from a diverse, rural and urban setting. *Psychological Medicine. 41*(5), 949-958.

Choudhury, S., Blakemore, S.-J., & Charman, T. (2006). Social cognitive development during adolescence. *Social Cognitive and Affective Neuroscience*, *1*(3), 165–174. https://doi.org/10.1093/scan/nsl024

Chudleigh, C., Naismith, S., Blaszczynski, A., Hermens, D., Redoblado Hodge, M., & Hickie, I. (2011). How does social functioning in the early stages of psychosis relate to depression and social anxiety? *Early Intervention in Psychiatry,* 5(3), 224-232.

https://doi.org/10.1111/j.1751-7893.2011.00280.x

Chung, Y. S., Kang D., Shin, N. Y., Yoo, S. Y., & Kwon, J. S. (2008). Deficits of

Theory of Mind in individuals at ultra-high risk for Schizophrenia. *Schizophrenia Research. 99,* 111-118.

Ciaramidaro, A., Adenzato, M., Enrici, I., Erk, S., Pia, L., G Bara, B., & Walter, H. (2007). The intentional network: How the brain reads varieties of intentions. *Neuropsychologia, 45*(13), 3105-3113. https://doi.org/10.1016/j.neuropsychologia.2007.05.011

Cohen, J. (1988), *Statistical power analysis for the behavioral sciences* (2nd ed.), New Jer sey: Lawrence Erlbaum Associates.

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*(1-3), 112-116.

Combs, D. R., Wicher, M., & Waldheter, E. (2007). The Ambiguous Intentions Hostility Questionnaire (AIHQ): A new measure for evaluating hostile social cognitive biases in paranoia. *Cognitive Neuropsychiatry, 12*(2), 128-143.

Corcoran, R., Mercder, G., & Frith, C. (1995). Schizophrenia symptomatology and social inference – Investigating Theory of Mind in people with schizophrenia. *Schizophrenia Research, 17*(1), 5–13. https://doi.org/10.1016/0920-9964(95)00024-G

Cornblatt, B. A., Auther, A. M., Niendam, T., Smith, C. W., Zinberg, J., Bearden, C. E., & Cannon, T. D. (2007). Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. *Schizophrenia Bulletin, 33*, 688-702.

Cornblatt, B.A., Carrio ´n, R.E., Addington, J., Seidmen, L., Walker, E. F., Cannon, T. D. . . . Lencz, T. (2012). Risk factors for psychosis: impaired social and role functioning. *Schizophrenia Bulletin, 38,* 1247–1257.

Couture, S. M., Penn, D. L., & Roberts, D. L. (2006). The functional significance of

    social cognition in schizophrenia: A Review. *Schizophrenia Bulletin, 32*(1), 44-63.

Craig, T. K. J., Garety, P., Power, P., Rahaman, N., Susannah, C., Fornells-Ambrojo, M., &

    Dunn, G. (2004). The Lambeth Early Onset (LEO) team: randomised controlled trial of

    the effectiveness of specialised care for early psychosis. *British Medical Journal, 329*,

    1067.

Cutting, J., & Murphy, D. (1988). Schizophrenic thought disorder. A psychological and organic

    interpretation. *The British Journal of Psychiatry*, *152*(3), 310–319.

    https://doi.org/10.1192/bjp.152.3.310

Cutting, J., & Murphy, D. (1990). Impaired ability of schizophrenics, relative to manics or

    depressives, to appreciate social knowledge about their culture. *British Journal of

    Psychiatry, 157*, 355-258. https://doi.org/10.1192/bjp.157.3.355

Cuzzocreo, J., Yassa, M., Verduzco, G., Honeycutt, N., Scott, D., & Bassett, S. (2009). Effect

    of handedness on fMRI activation in the medial temporal lobe during an auditory

    verbal memory task. *Human Brain Mapping, 30*(4), 1271-1278.

    https://doi.org/10.1002/hbm.20596

Davidson, C. A., Lesser, R., Parente, L. T., & Fiszdon, J. M. (2017). Psychometrics of social

    cognitive measures for psychosis treatment research. *Schizophrenia Research*, 1-7.

    https://doi.org/10.1016/j.schres.2017.06.018

Davis, J. P., & G. Gibson, M. (2000). Recognition of posed and genuine facial expression of

    emotion in paranoid and nonparanoid schizophrenia. *Journal of Abnormal Psychology,

    109*(3), 445-450. https://doi.org/10.1037/0021-843X.109.3.445

Dickerson, F. B. (1997). Assessing clinical outcome: The community functioning of per

    sons with serious mental illness. *Psychiatric Services, 48*(7), 897-901.

Dodell-Feder, D., Tully, L., & Hooker, C. (2015). Social impairment in schizophrenia: New

approaches to treating a persistent problem. *Current Opinion in Psychiatry*, *28*(00), 1–7.

Eack, S. M., Greenwald, D. P., Hogarty, S. S., Cooley, S. J., DiBarry, A. L., Montrose, D. M., & Keshavan, M. S. (2009). Cognitive enhancement therapy for early-course schizophrenia: Effects of a two-year randomized controlled trial. *Psychiatric Services*, *60*(11), 1468–1476. https://doi.org/10.1176/ps.2009.60.11.1468

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior Research Methods, Instruments, & Computers*, *28*(1), 1–11. https://doi.org/10.3758/BF03203630

Evensen, J., Rossberg, J., Barder, H., Haahr, U., Hegelstad, W., Joa, I., … Mcglashan, T. (2012). Apathy in first episode psychosis patients: A ten year longitudinal follow-up study. *Schizophrenia Research, 136*(1-3), 19-24. https://doi.org/10.1016/j.schres.2011.12.019

Fetemi, S. H., & Folsom, T. D. (2009). The neurodevelopment approach to schizophrenia re visited. *Schizophrenia Bulletin, 35*(3). 528-548.

Fett, A-K., Viechtbauer, W., Dominguez, M., Penn, D.L, van Os, J., & Krabbendam, L. (2011). The relationship between neurocognition and social cognition with functional outcomes in psychosis. *Neuroscience and Behavioural Reviews, 35,* 573-588.

Fenton, S. W., & Mcglashan, T. (1994). Antecedents, symptom progression, and long-term outcome of the deficit syndrome in schizophrenia. *The American Journal of Psychiatry, 151*(3), 351-356. https://doi.org/10.1176/ajp.151.3.351.

Field, A. (2005). *Discovering Statistics Using SPSS (Introducing Statistical Methods series).* Sage Publications, London. ISBN 0761944524

Figueira, M. L., & Brissos, S. (2011). Measuring psychosocial outcomes in schizophrenia patients. *Current Opinion in Psychiatry, 24,* 91-99.

Fornito, A., Yoon, J., Zalesky, A., Bullmore, E. T., & Carter, C. S. (2011). General and spe

cific functional connectivity disturbances in first-episode schizophrenia during

cognitive control performance. *Biological Psychiatry*, *70*(1), 64-72. DOI:

10.1016/j.biopsych.2011.02.019.

Fowler, D., French, P., Hodgekins, J., Lower, R., Turner, R., Burton, S., & Wilson, J. (2013)

CBT to address and prevent social disability in early and emerging psychosis, in CBT

for schizophrenia: evidence-based interventions and future directions (ed C. Steel),

John Wiley & Sons, Ltd, Oxford. doi: 10.1002/9781118330029.

Fowler, D., Hodgekins, J., French, P., Marshall, M., Freemantle, N., McCrone, P., …

Birchwood, M. (2017). Social recovery therapy in combination with early intervention

services for enhancement of social recovery in patients with first-episode psychosis

(SUPEREDEN3): a single-blind, randomised controlled trial. *The Lancet Psychiatry*,

5(1), 41-50. https://doi.org/10.1016/S2215-0366(17)30476-5.

Fowler, D., Hodgekins, J., Painter, M., Reilly, T., Crane, C., Macmillan, I., . . . Jones, P. B.

(2009). Cognitive behaviour therapy for improving social recovery in psychosis: a

report from the ISREP MRC Trial Platform study (Improving Social Recovery in Early

Psychosis). *Psychological Medicine*, *39*(10), 1627-1636.

Friston, K., P. Holmes, A., & J. Worsley, K. (1999). How many subjects constitute a study?

Neuroimage, 10(1), 1-5. https://doi.org/10.1006/nimg.1999.0439

Frith, C. D. (1992). *The cognitive neuropsychology of schizophrenia (Psychology).* Psychol

ogy Press, London.

Frith, C. D. (2004). Schizophrenia and theory of mind. *Psychology Medicine,*

34, 385–389.

Fu, S., Czajkowski, N., Rund, B. R., & Torgalsbøen, A.-K. (n.d.). The relationship between

level of cognitive impairments and functional outcome trajectories in first-episode

schizophrenia. *Schizophrenia Research*, *190*, 144–149.

https://doi.org/10.1016/j.schres.2017.03.002

Fusar-Poli, P., Byrne, M., Valmaggia, L., Day, F., Tabraham, P., Johns, L., & McGuire, P.

(2010). Social dysfunction predicts two years clinical outcome in people at ultra-high

risk for psychosis. *Journal of Psychiatric Research, 44,* 294-301.

Gallagher, H. L., & Frith, C. D. (2003). Functional Imaging of "Theory of

Mind". *Trends in Cognitive Sciences, 7,* 77-83.

Gard, D. E., Fisher, M., Garett, C., Genevsky, A., & Vinogradov, S. (2009). Motivation and its

relationship to neurocognition, social cognition and functional outcome in

schizophrenia. *Schizophrenia Research, 115,* 74-81.

Garety, P.A., Craig, T. K., Dunn, G., Fornells-Ambrojo, M., Colbert, S., Rahaman, N., Reed,

& J., Power, P. (2006) Specialised care for early psychosis: symptoms, social

functioning and patient satisfaction: randomised controlled trial. *British Journal of

Psychiatry, 188*, 37-45.

Garety, P. A., Fowler, D., Kuipers, E., Freeman, D., Dunn, G., Bebbington, P. E., . . . Jones,

S. (1997). The London east Anglia randomised controlled trial of cognitive behaviour

therapy for psychosis II: predictors of outcome. *British Journal of Psychiatry, 171*, 319–

327.

Gee, B., Hodgekins, J., Birchwood, M., Marshall, M., Everard, L., Lester, H., . . . Fowler, D.

(2016). The course of negative symptom in first episode psychosis and the relationship

with social recovery. *Schizophrenia Research, 174*(1-3), 165-171.

Gilbert, T. D., Pelham, B., & Krull, D. (1988). *On cognitive busyness: When person perceivers

meet persons perceived*, *54*(5), 733-740. https://doi.org/10.1037/0022-3514.54.5.733

Goldberg, T. E., Goldman, R.S., Burdick, K.E., Malthotra, A. K., Lencz, T., Patel, R. C..,

Woerner, M. G., . . . Robinson, D.G., (2007). Cognitive improvement after treatment

with second-generation antipsychotic medications in first-episode schizophrenia: Is it a practice effect? *Archives of General Psychiatry*, *64* (10), 1115–1122. https://doi.org/10.1001/archpsyc.64.10.1115

González-Blanch, C., Gleeson, J. F., Cotton, S. M., McGorry, P. D., Alvarez-Jimenez, M. (2016). Social Functioning Trajectories of Young First-Episode Psychosis Patients with and without Cannabis Misuse: A 30-Month Follow-Up Study. *Plos One,* 1-14.

Grant, N., Lawrence, M., Preti, A., Wykes, T., & Cella, M. (2017). Social cognition interventions for people with schizophrenia: a systematic review focussing on methodological quality and intervention modality. *Clinical Psychology Review*, *56* (Supplement C), 55–64. https://doi.org/10.1016/j.cpr.2017.06.001

Gravetter, F. J., & Wallnau, L. B. (2000). *Statistics for the behavioral sciences* (5th edition., Instructor's edition). Australia Wadsworth/Thomson Learning.

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* (1), 119–136. https://doi.org/10.1093/oxfordjournals.schbul.a033430

Green, M. F., Kern, R. S., & Heaton, R. K. (2004). Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophrenia Research*, *72* (1), 41–51. https://doi.org/10.1016/j.schres.2004.09.009

Green, M. F., Penn, D. L., Bentall, R., Carpenter, W. T., Gaebel, W., Gur, R. C., … Heinssen, R. (2008). Social cognition in schizophrenia: An NIMH workshop on definitions, assessment, and research opportunities. *Schizophrenia Bulletin*, *34* (6), 1211–1220. https://doi.org/10.1093/schbul/sbm145

Hafner, H., & an der Heiden, W. (1999). The course of schizophrenia in the light of modern

follow-up studies: the ABC and WHO studies. *European Archives of Psychiatry and Clinical Neuroscience, 249*, 14-26.

Happé, F. G. E. (1994). An advanced test of theory of mind: Understanding of story characters' thoughts and feelings by able autistic, mentally handicapped, and normal children and adults. *Journal of Autism Developmental Disorders, 24,* 129. https://doi.org/10.1007/BF02172093

Harrington, L., Siegert, R., & McClure, J. (2005). Theory of mind in schizophrenia: A critical review. *Cognitive Neuropsychiatry*, *10* (4), 249–286. https://doi.org/10.1080/13546800444000056

Harvey, P.D., & Bellack, A. S. (2009). Toward a terminology for functional recovery in schiz ophrenia: is functional remission a viable concept? *Schizophrenia Bulletin, 35*, 300-306.

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* (Supplement C), 108–137. https://doi.org/10.1016/j.cpr.2016.10.001

Heinrichs, W., & K. Zakzanis, K. (1998). *Neurocognitive Deficit in Schizophrenia: A Quantitative Review of the Evidence*, *12*(3), 426-445. https://doi.org/10.1037/0894-4105.12.3.426

Ho, S. S., Kuzniesky, R. I., Gilliam, F., Faught, E., Bebin, M., & Morawetz, R. (1998). Congenital porencephaly: MR features and relationship to hippocampal sclerosis. *American Journal of Neuroradiology, 19*(1), 135-141.

Hoekert, M., Kahn, R. S., Pijnenborg, M., & Aleman, A. (2007). Impaired recognition and expression of emotional prosody in schizophrenia: Review and meta-analysis. *Schizophrenia research, 96*, 135-145.

Hodgekins, J., French, P., Birchwood, M., Mugford, M., Christopher, R., Marshall, M., . . . Fowler, D. (2015). Comparing time use in individuals at different stages of psychosis and a non-clinical comparison group. *Schizophrenia Research, 161,* 188-193.

Hodgekins, J., Birchwood, M., Christopher, R., Marshall, M., Coker, S., Everard, L., . . . Fowler, D. (2015). Investigating trajectories of social recovery in individuals with first episode psychosis: a latent class growth analysis. *The British Journal of Psychiatry, 207*, 536-543.

Holthausen E. A. E., Wiersma D., Cahn W., Kahn R. S., Dingemans P.M., Schene A. H., & van den Bosch R. J. (2007). Predictive value of cognition for different domains of outcome in recent-onset schizophrenia. *Psychiatry Research*, *149***,** 71–80.

Horan, W. P., & Green, M. F. (2017). Treatment of social cognition in schizophrenia: Current status and future directions. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2017.07.013

Horan, W. P., Green, M. F., DeGroot, M., Fiske, A., Hellemann, G., Kee, K., … Nuechterlein, K. H. (2012). Social cognition in schizophrenia, Part 2: 12-month stability and prediction of functional outcome in first-episode patients. *Schizophrenia Bulletin*, *38* (4), 865–872. https://doi.org/10.1093/schbul/sbr001

Jackson, C., Knott, C., Skeate, A., & Birchwood, M. (2004). The trauma of first episode psychosis: The role of cognitive mediation. *Australian and New Zealand Journal of Psychiatry, 38*, 327–333.

Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollbergh, W., de Graaf, R., & van Os, J. (2003). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandanavica, 109* (1), 38-45.

Jeppesen, P., Petersen, L., Thorup, A., Abel A-B., Øhlenschlæger, J., Christensen, T. O., . . .

Nornedtoft, M. (2008). The association between pre-morbid adjustment, duration of untreated psychosis and outcome in first-episode psychosis. *Psychological Medicine, 38* (8), 1157-1166.

Jones, P., Rodgers, B., Murray, R., & Marmot, M. (1994). Child developmental risk factors for adults with schizophrenia in the British 1946 birth cohort. *Lancet, 344*, 1398–1402.

Kaney, S., & Bentall, R. P. (1989). Persecutory delusions and attributional style. British *Journal of Medical Psychology, 62*, 191-198

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin, 13*, 261-276.

Kay, S. R., & Lindernmayer, J. (1987). Outcome predictors in acute schizophrenia: Positive significance of background and clinical dimensions. *Journal of Nervous and Mental Disease, 175*, 152-160.

Kirch, D.G., Lieberman, J.A., & Matthews, S.M. (1992). First-episode psychosis: Part I. Editors' introduction. *Schizophrenia Bulletin, 18* (2), 177-178.

Kirkbride, J. B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., . . . Jones, P. B. (2012). Incidence of schizophrenia and other psychoses in England, 1950-2009: a systematic review and meta-analyses. *Plos one, 7*(3). Retrieved from: https://doi.org/10.1371/journal.pone.0031660.

Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., . . . Jones, P. B. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Archive of General Psychiatry, 63* (3), 250-258.

Kirkpatrick, B., Buchanan, R. W., Ross, D. E., & Carpenter, W. T. Jr. (2001). A separate disease within the syndrome of schizophrenia. *Archive of General Psychiatry, 58,* 165-171.

Kirkpatrick, B., Fenton, W.S., Carpenter, W.T. Jr., & Marder, S.R. (2006). The NIMH-MA

TRICS consensus statement on negative symptoms. *Schizophrenia Bulletin, 32* (2), 14–

219.

Knecht, S., Dräger, B., Deppe, M., Bobe, L., Lohmann, H., Flöel, A., … Henningsen, H. (2000).

Handedness and hemispheric language dominance in healthy humans. *Brain*, *123* (12),

2512–2518. https://doi.org/10.1093/brain/123.12.2512

Kohler, C. G., Walker, J. B., Martin, E. A., Healey, K. M., & Moberg, P. J. (2010). Facial

emotion perception in schizophrenia: a meta-analytic review. *Schizophrenia Bulletin*,

36 (5), 1009—1019. https://doi.org/10.1093/schbul/sbn192

Koster-Hale, J., & Saxe, R. (2017). Theory of Mind: A neural prediction problem. *Neuron*, *79*

(5), 836–848. https://doi.org/10.1016/j.neuron.2013.08.020

Krstev, H., Jackson, H., & Maude, D. (2010). *An investigation of attributional style in first-

episode psychosis*, 38(2), 181-194. https://doi.org/10.1348/014466599162737

Kuipers, E., Garety, P., Fowler, D., Dunn, G., Bebbington, P., Freeman, D. & Hadley, C.

(1997). London—East Anglia randomised controlled trial of cognitive—behavioural

therapy for psychosis. I. Effects of the treatment phase. *British Journal of Psychiatry,

171*, 319 -327.

Kurtz, M. M., Gagen, E., Rocha, N. B. F., Machado, S., & Penn, D. L. (2016). Comprehensive

treatments for social cognitive deficits in schizophrenia: A critical review and effect-

size analysis of controlled studies. *Clinical Psychology Review*, *43* (Supplement C), 80–

89. https://doi.org/10.1016/j.cpr.2015.09.003

Langdon, R., & Coltheart, M. (1999). Mentalising, schizotypy, and schizophrenia. *Cognition*,

71(1), 43–71. https://doi.org/10.1016/S0010-0277(99)00018-9

Langdon, R., Connors, M. H., Still, M., Ward, P. B., & Catts, S. (2014). Theory of mind and

neurocognition in early psychosis: a quasi-experimental study. *BMC Psychiatry*, *14* (1),

316. https://doi.org/10.1186/s12888-014-0316-6

Langdon, R., Ward, P. B., & Coltheart, M. (2010). Reasoning anomalies associated with delusions in schizophrenia. *Schizophrenia Bulletin*, *36*(2), 321–330. https://doi.org/10.1093/schbul/sbn069

Larrabee, G., L. Kane, R., & R. Schuck, J. (1983). *Factor analysis of the WAIS and Wechsler Memory Scale: An analysis of the construct validity of the Wechsler Memory Scale*, *5*(2), 159-168. https://doi.org/10.1080/01688638308401162

Larsen, T. K., Melle, I., Auestad, B., Friis, S., Haahr, U., Johannessen, J. O., … McGlashan, T. H. (2006). Substance abuse in first-episode non-affective psychosis. *Schizophrenia Research*, *88*(1), 55–62. https://doi.org/10.1016/j.schres.2006.07.018

Larsen, T. K., McGlashan, T. H., & Moe, L. C. (1996). First-episode Schizophrenia: I. Early Course Parameters. *Schizophrenia Bulletin*, *22*(2), 241–256. https://doi.org/10.1093/schbul/22.2.241

Lauronen, E., Miettunen, J., Karhu, M., Jones. P.B., & Isohanni, M. (2007). Outcome and its predictors in schizophrenia within the Northern Finland 1966 birth cohort. *European Psychiatry, 22,* 129-136.

Lee, K.H., Brown, W.H., Egleston, P.N., Green, R. D. J., Farrow, T. F. D., Hunter, M.D., . . . Woodruff, P. D. R. (2006). A functional magnetic resonance imaging study of social cognition in schizophrenia during an acute episode and after recovery. *American Journal of Psychiatry, 163,*1926–1933.

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* (1), 28–34. https://doi.org/10.1016/j.schres.2015.02.008

Liberman, R.P., Glynn, S., Blair, K.E., Ross, D., & Marder, S.R. (2002). In vivo amplified skills

training: promoting generalization of independent living skills for clients with schizophrenia. *Psychiatry, 65* (2), 137–155.

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* (1), 231-237.

Lin, A., Wood, S. J., Nelson, B., Brewer, W. J., Spiliotacopoulos, D., Bruxner, A., . . . Yung, A. R. (2011). Neurocognitive predictors of functional outcome two to 13 years after identification as ultra-high risk for psychosis. *Schizophrenia research*, *132* (1), 1-7.

Lin, A., Reniers, R. L. E. P., & Wood, S. J. (2013). Clinical staging in severe mental disorder: evidence from neurocognition and neuroimaging. *The British Journal of Psychiatry*, *202* (54), s11–s17. https://doi.org/10.1192/bjp.bp.112.119156

Lin, A., Wood, S. J., & Yung, A. R. (2013). Measuring psychosocial outcome is good. *Current Opinion in Psychiatry, 26* (2), 138-143.

Logothetis, N. K., & Wandell, B. A. (2004). Interpreting the BOLD Signal. *Annual Review of Physiology*, *66* (1), 735–769. https://doi.org/10.1146/annurev.physiol.66.082602.092845

Lucas, S., Redobaldo-Hodge, M., Shores, A, Brennan, J., & Harris, A. (2008). Predictors of outcome three years after diagnosis of first episode psychosis. *Psychiatry Research*, *161,* 11-18.

Ludwig, K. A., Pinkham, A. E., Harvey, P. D., Kelsven, S., & Penn, D. L. (2017). Social Cognition Psychometric Evaluation (SCOPE) in people with early psychosis: A preliminary study. *Schizophrenia Research*, *190* (Supplement C), 136–143. https://doi.org/10.1016/j.schres.2017.03.001

Lysaker, P. H., & Davis, L. W. (2004). Social function in schizophrenia and schizoaffective disorder: Associations with personality, symptoms and neurocognition. *Health and Quality of Life Outcomes*, *2* (1), 15. https://doi.org/10.1186/1477-7525-2-15

Lysaker, P. H., & Dimaggio, G. (2014). Metacognitive Capacities for Reflection in Schizophrenia: Implications for Developing Treatments. *Schizophrenia Bulletin*, *40*(3), 487–491. https://doi.org/10.1093/schbul/sbu038

Lysaker, P. H., Gumley, A., Luedtke, B., Buck, K. D., Ringer, J. M., Olesek, K., … Dimaggio, G. (2013). Social cognition and metacognition in schizophrenia: evidence of their independence and linkage with outcomes. *Acta Psychiatrica Scandinavica*, *127*(3), 239–247. https://doi.org/10.1111/acps.12012

Lysaker, P. H., Kukla, M., Dubreucq, J., Gumley, A., McLeod, H., Vohs, J. L., … Dimaggio, G. (2015). Metacognitive deficits predict future levels of negative symptoms in schizophrenia controlling for neurocognition, affect recognition, and self-expectation of goal attainment. *Schizophrenia Research*, *168*(1), 267–272. https://doi.org/10.1016/j.schres.2015.06.015

Lysaker, P., S Lancaster, R., Nees, M., & Davis, L. (2004). *Attributional bias and symptoms as predictors of social function in schizophrenia*, 60(1), 21. https://doi.org/10.1016/S0920-9964(03)80061-0

MacBeth, A., Gumley, A., Schwannauer, M., Carcione, A., Fisher, R., McLeod, H. J., & Dimaggio, G. (2014). Metacognition, symptoms and premorbid functioning in a First Episode Psychosis sample. *Comprehensive Psychiatry*, *55*(2), 268–273. https://doi.org/10.1016/j.comppsych.2013.08.027

MacBeth, A., Gumley, A., Schwannauer, M., & Fisher, R. (2011). Attachment states of mind, mentalization, and their correlates in a first-episode psychosis sample. *Psychology and Psychotherapy: Theory, Research and Practice*, *84*(1), 42–57.

https://doi.org/10.1348/147608310X530246

Madeira, N., Caldeira, S., Bajouco, M., Pereira, A., Martins, M., & Macedo, A. (2016). Social cognition, negative symptoms and psychosocial functioning in schizophrenia. *International Journal of Clinical Neurosciences and Mental Health, 3*(1), 1-10. https://doi.org/10.21035/ijcnmh.2016.3.1

Malla, A., & Payne, J. (2005). First-episode psychosis: psychopathology, quality of life, and functional outcome. *Schizophrenia Bulletin, 31*, 650–671

Mangalore, R. & Knapp, M. (2007). Cost of schizophrenia in England. *The Journal of Mental Health Policy and Economics, 10*, 23-41.

Mars, R. B., Sallet, J., Schüffelgen, U., Jbabdi, S., Toni, I., & Rushworth, M. F. S. (2012). Connectivity-Based Subdivisions of the Human Right "Temporoparietal Junction Area": Evidence for different areas participating in different cortical networks. *Cerebral Cortex, 22*(8), 1894–1903. https://doi.org/10.1093/cercor/bhr268

Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005). Association between duration of untreated psychosis and outcome in cohorts of first episode patients: a systematic review. *Archives of General Psychiatry, 62*(9), 975 983.

Matza, L. S., Buchanan, R., Purdon, S., Brewster-Jordan, J., Zhao, Y., & Revicki, D. A. (2006). Measuring changes in functional status among patients with schizophrenia: The link with cognitive impairment. *Schizophrenia Bulletin, 32*(4), 666–678. https://doi.org/10.1093/schbul/sbl004

Mayer, J. D., Salovey, P., & Caruso, D. R. (2002). *Mayer– Salovey–Caruso Emotional Intel ligence Test (MSCEIT) item booklet.* Toronto, Ontario, Canada: MHS Publishers.

Mayer, J. D., Salovey, P., Caruso, D. R., & Sitarenios, G. (2003). Measuring emotional

intelligence with the MSCEIT V2. 0. *Emotion, 3*, 97-105. doi: 10.1037/1528-3542.3.1.97.

McCabe, K. L., Maloney, E. A., Stain, H. J., Loughland, C. M., & Carr, V. J. (2012). Relationship between childhood adversity and clinical and cognitive features in schizophrenia. *Journal of Psychiatric Research*, *46*(5), 600–607. https://doi.org/10.1016/j.jpsychires.2012.01.023

McCrone, P., Craig, T. K. J., Power, P., & Garety, P.A. (2010). Cost-effectiveness of an early intervention service for people with psychosis. *British Journal of Psychiatry, 196,* 377–82.

McEvoy, J. P., Lieberman, J. A., Perkins, D. O., Hamer, R. M., Hongbin, G.U., Lazurus, A., . . . Strakowski, S. D. (2007). Efficacy and tolerability of olanzapine, quetiapine, and risperidone in the treatment of early psychosis: a randomized, double-blind 52-week comparison. *American Journal of Psychiatry, 164*(7), 1050-60.

McGlashan, T., & Hoffman, R. (2000). Schizophrenia as a disorder of developmentally reduced synaptic connectivity. *Archives of General Psychiatry*, *57*(7), 637–648. https://doi.org/10.1001/archpsyc.57.7.637

McGorry, P. D. (n.d.). Evidence and Perspectives in Early Recognition and Intervention for Psychosis and Beyond. Retrieved from: http://www.iris-initiative.org.uk/silo/files/early-intervention-in-pychosis--clinical-effectiveness.pdf.

McGorry, P. D. (2007). Issues for DSM-V: Clinical staging: A heuristic pathway to valid nosology and safer, more effective treatment in psychiatry. *American Journal of Psychiatry*, *164* (6), 859–860. https://doi.org/10.1176/ajp.2007.164.6.859

McGorry, P. D., Killackey, E., & Yung, A. (2008). Early Intervention in psychosis: concepts, evidence and future directions. *World Psychiatry. 7,* 148-156

Mcguffin, P., Farmer, A., & Harvey, I. (1991). A polydiagnostic application of operational

criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Archive of General Psychiatry, 48*(8), 764-770.

Mehta, U. M., Bhagyavathi, H. D., & Thirthalli, J. (2014). Understanding the interplay between motivation and social cognition performance in schizophrenia. *Australian & New Zealand Journal of Psychiatry*, *49*(3), 296–297. https://doi.org/10.1177/0004867414559549

Meyer, E. C., Carrión, R. E., Cornblatt, B. A., Addington, J., Cadenhead, K. S., Cannon, T. D., … Seidman, L. J. (2014). The relationship of neurocognition and negative symptoms to social and role functioning over time in individuals at clinical high risk in the first phase of the North American Prodrome Longitudinal Study. *Schizophrenia Bulletin*, *40*(6), 1452–1461. https://doi.org/10.1093/schbul/sbt235

Meyers, L.S., Gamst, G., & Guarino, A. J. (2017) *Applied Multivariate Research: Design and Interpretation.* 3nd Edition. Thousand Oaks, CA: Sage Publications.

Michail, M., & Birchwood, M. (2014). Social anxiety disorder and shame cognitions in psycho sis. *Psychological Medicine, 43,* 133-142.

Mishara, A. L., & Goldberg, T. E. (2004). A meta-analysis and critical review of the effects of conventional neuroleptic treatment on cognition in schizophrenia: opening a closed book. *Biological Psychiatry, 55,* 1013–22

Nagelkerke, N. J. D. (1991). A note on a general definition of the coefficient of determination. *Biometrika*, *78*(3), 691–692. https://doi.org/10.1093/biomet/78.3.691

National Institute for Health and Clinical Excellence. (2014). *Schizophrenia: Core Interventions in the treatment and management of schizophrenia*. London: National Institute for Health and Clinical Excellence.

Niendam, T. A., Bearden, C. E., Johnson, J. K., & Cannon, T. D. (2006). Global Functioning: Role Scale (GF: Role). Los Angeles, CA: University of California.

Niendam, T. A., Jalbrzikowski, M. & Bearde, C.E. (2009). Exploring predictors of outcome in the psychosis prodrome: Implications for early identification and intervention. *Neuropsychology Review, 19,* 280-293.

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., & Heaton, R. K. (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research*, *72*(1), 29–39. https://doi.org/10.1016/j.schres.2004.09.007

Orygen Youth Health (2002). *The Early Diagnosis and Management of Psychosis*. Retrieved from: http://oyh.org.au/sites/oyh.org.au/files/gp_manual.pdf.

Pallant, J. (2001) *SPSS survival manual*. 1st Edition, Open University Press, Buckingham.

Pallant, J. (2011) *SPSS sul 32e432rvival manual: A step by step guide to data analysis using the SPSS*

program. 4th Edition, Allen & Unwin, Berkshire.

Pantelis, C., & Bartholomeusz, C. F. (2014). Social neuroscience in psychiatry: pathways to discovering neurobiological risk and resilience. *World Psychiatry*, *13*(2), 146–147. https://doi.org/10.1002/wps.20123

Pena, J., Segarna, R., Ojeda, N., Garcia, J., Eguiluz, J. I., & Gutierrez, M. (2012). Do the same factors predict outcome in schizophrenia and nonschizophrenia syndromes after first-episode psychosis? A two-year follow-up. *Journal of Psychiatric Research, 46*, 774-781.

Penn, D., Combs, D., & Mohamed, S. (2001) *Social cognition and social functioning in schizophrenia*. Corrigan, P. W., Penn, D., (Eds.), Social cognition and schizophrenia, American Psychological Association, Washington, DC, pp. 27-121

Penn, D. L., Roberts, D. L., Combs, D., & Sterne A. (2007). Best practices: The development of the Social Cognition and Interaction Training program for schizophrenia spectrum disorders. *Psychiatric Services, 58,* 449.

Petersen, L., Jeppensen, P., Thorup, A., Abel, M-B., Ohlenshlaeger, J., Christenses, T. O., . . .
Krarup, G. (2005). A randomised multicentre trial of integrated versus standard
treatment for patients with first episode psychotic illness. *British Medical Journal, 331,*
602.

Peyroux, É., & Franck, N. (2014). *RC2S: A Cognitive Remediation Program to Improve
Social Cognition in Schizophrenia and Related Disorders, 8,* 1-11.
https://doi.org/10.3389/fnhum.2014.00400

Pinkham, A. E., Penn, D. L., Green, M. F., Buck, B., Healey, K., & Harvey, P. D. (2014). The
social cognition psychometric evaluation study: Results of the expert survey and RAND
Panel. *Schizophrenia Bulletin*, *40*(4), 813–823. https://doi.org/10.1093/schbul/sbt081

Pinkham, A. E., Penn, D. L., Perkins, D. O., Graham, K. A., & Siegel, M. (2007). Emotion
perception and social skill over the course of psychosis: A comparison of individuals
"at-risk" for psychosis and individuals with early and chronic schizophrenia spectrum
illness. *Cognitive Neuropsychiatry*, *12*(3), 198–212.
https://doi.org/10.1080/13546800600985557

Pinkham, A. E., Penn, D. L., Perkins, D. O., & Lieberman, J. (2003). Implications for the neural
basis of social cognition for the study of schizophrenia. *American Journal of Psychiatry*,
160(5), 815–824. https://doi.org/10.1176/appi.ajp.160.5.815

Piskulic, D., Addington, J., Auther, A., & A Cornblatt, B. (2011). *Using the global
functioning social and role scales in a first-episode sample*, 5(3), 219-223.
https://doi.org/10.1111/j.1751-7893.2011.00263.x

Piskulic, D., Addington, J., Cadenhead, K., Cannon, T., A Cornblatt, B., Heinssen, R., …
Mcglashan, T. (2012). *Negative symptoms in individuals at clinical high risk of
psychosis*, *196*(2-3), 22-224. https://doi.org/10.1016/j.psychres.2012.02.018

Poldrack, A. R., Mumford, J., & Nichols, T. (2011). *Handbook of Functional MRI Data*

Analysis. Cambridge, Cambridge University Press.

https://doi.org/10.1017/CBO9780511895029

Potkin, S. G., Weiden, P. J., Loebel, A. D., Warrington, L. E., Watsky, E. J., & Siu, C. O.

(2009). Remission in schizophrenia: 196-week, double-blind treatment with ziprasidone

vs. haloperidol. *International Journal of Neuropsychopharmacology, 12,* 1233-1248.

Ram, R., Bromet, E. J., Eaton, W. W., Pato, C., & Schwartz, J. E. (1992). The Natural course

of schizophrenia: A review of first-admission studies. *Schizophrenia Bulletin*, *18*(2),

185–207. https://doi.org/10.1093/schbul/18.2.185

Rammou, A., Fisher, H. L., Johnson, S., Major, B., Rahaman, N., Chamberlain-Kent, N., &

Stone, J. M. (2017). Negative symptoms in first-episode psychosis: Clinical correlates

and 1-year follow-up outcomes in London Early Intervention Services. *Early

Intervention in Psychiatry*. https://doi.org/10.1111/eip.12502

Roberts, D. L., Combs, D. R., Willoughby, M., Mintz, J., Gibson, C., Rupp, B., & Penn, D. L.

(2014). A randomized, controlled trial of Social Cognition and Interaction Training

(SCIT) for outpatients with schizophrenia spectrum disorders. *British Journal of

Clinical Psychology*, *53*(3), 281–298. https://doi.org/10.1111/bjc.12044

Roder, V., Mueller, D. R., Mueser, K. T., & Brenner, H. D. (2006). Integrated Psychological

Therapy (IPT) for schizophrenia: Is it effective? *Schizophrenia Bulletin*, *32*

(Supplement 1), S81–S93. https://doi.org/10.1093/schbul/sbl021

Roder, V., Mueller, D. R., & Schmidt, S. J. (2011). Effectiveness of Integrated Psychological

Therapy (IPT) for schizophrenia patients: A research update. *Schizophrenia Bulletin*, *37*

(supplement 2), S71–S79. https://doi.org/10.1093/schbul/sbr072

Rodwell, L., Romaniuk, H., Nilsen, W., B Carlin, J., J Lee, K., & C Patton, G. (2018).

Adolescent mental health and behavioural predictors of being NEET: A prospective

study of young adults not in employment, education, or training. *Psychological*

Medicine, 48, 861-871. https://doi.org/10.1017/S0033291717002434

Rorden, C., & Brett, M. (2000). *Stereotaxic Display of Brain Lesion*, 12(4), 191-200.

   https://doi.org/10.1155/2000/421719

Rowland, J., Hamilton, M., Vella, N., Lino, B., Mitchell, P., & Green, M. (2013). Adaptive

   associations between social cognition and emotion regulation are absent in

   schizophrenia and bipolar disorder. *Frontiers in Psychology*, *3*, 607.

   https://doi.org/10.3389/fpsyg.2012.00607

Santesteban-Echarri, O., Paino, M., Rice1, S., González-Blanch, C., McGorry, P. D.,

   Gleeson, J. & Alvarez-Jimenez, M. (2017). Predictors of functional recovery in first-

   episode psychosis: A systematic review and meta-analysis of longitudinal studies.

   Clinical Psychology Review, 58, 59-75.

Savla, G. N., Vella, L., Armstrong, C. C., Penn, D. L., & Twamley, E. W. (2013). Deficits in

   domains of social cognition in schizophrenia: A meta-analysis of the empirical

   evidence. *Schizophrenia Bulletin*, *39*(5), 979–992.

   https://doi.org/10.1093/schbul/sbs080

Saxe, R. (2006). Uniquely human social cognition. *Cognitive Neuroscience*, *16*(2), 235–239.

   https://doi.org/10.1016/j.conb.2006.03.001

Saxe, R., Carey, S., & Kanwisher, N. (2004). Understanding other minds: Linking

   developmental psychology and functional neuroimaging. *Annual Review of Psychology*,

   55(1), 87–124. https://doi.org/10.1146/annurev.psych.55.090902.142044.

Seddon, J. L.**,** Birchwood, M., Copello, A., Everard, L., Jones, P., Fowler, D., Amos, T…
   Sharma, V. (2016). 'Cannabis use is associated with increased psychotic symptoms

   and poorer psycho-social functioning in first-episode psychosis: A report from the UK

   National EDEN study. *Schizophrenia Bulletin, 42*(3), 619-625.

Sergi, M. J., Rassovsky, Y., Widmark, C., Reist, C., Erhart, S., Braff, D. L., … Green, M. F.

   (2007). Social cognition in schizophrenia: Relationships with neurocognition and

negative symptoms. *Schizophrenia Research*, *90*(1), 316–324.

https://doi.org/10.1016/j.schres.2006.09.028.

Sheehan, D., Lecrubier, Y., Harnett-Sheehan, K., A. Amorim, P., Janavs, J., Weiller, E., … C. L. Dunbar, G. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry, 59*(20), 34-57.

Shiers, D., & Lester, H. E, (2004). Early intervention in first episode psychosis. *The British Medical Journal, 328,* 1451-1452.

Short, S. (2006). *Review of the UK 2000 Time Use Survey*. London: Office for National Statistics.

Siegel, S. J., Irani, F., Brensinger, C. M., Kohler, C. G., Bilker, W. B., Ragland, J. D., ... Gur, R. E. (2006). Prognostic variables at intake and long-term level of function in schizophrenia. *American Journal of Psychiatry*, *163*(3), 433-441. DOI: 10.1176/appi.ajp.163.3.433.

Sprong, M., Schothorst, P., Vos, E., Hox, J., & Van Engeland, H. (2007). Theory of mind in schizophrenia. *The British Journal of Psychiatry*, *191*(1), 5. https://doi.org/10.1192/bjp.bp.107.035899

Stain, H. J., Brønnick, K., Hegelstad, W. T. V., Joa, I., Johannessen, Johannes, J. O., . . . Larsen, T. K. (2013). Impact of interpersonal trauma on the social functioning of adults with first-episode psychosis. *Schizophrenia Bulletin, 40*(6), 1491-1498.

Stoffers, J. M., Vollm, B. A., Rucker, G., Timmer, A., Huband, N., & Lieb, K. (2012). Psychological therapies for people with borderline personality disorder. *Cochrane Database Systematic Review*. 8: CD005652.

Stouten, L. H., Veling, W., Laan, W., van der Helm, M., & van der Gaag, M. (2014). Psychotic symptoms, cognition and affect as predictors of psychosocial problems and functional

change in first-episode psychosis. *Schizophrenia Research*, *158*(1), 113–119. https://doi.org/10.1016/j.schres.2014.06.023

Strauss, J. S., & Carpenter, W. T. Jr. (1977). Prediction of outcome in schizophrenia: III. Five-yearn outcome and its predictors. *Archives of General Psychiatry*, *34*(2), 159–163. https://doi.org/10.1001/archpsyc.1977.01770140049005

Sullivan, S., Lewis, G., Mohr, C., Herzig, D., Corcoran, R., Drake, R., & Evans, J. (2014). The longitudinal association between social functioning and theory of mind in first-episode psychosis. *Cognitive Neuropsychiatry*, *19*(1), 58–80. https://doi.org/10.1080/13546805.2013.799463

Tabachnick, B. G., & Fidell, L. S. (1996). *Using multivariate statistics.* (3rd Edition), New York: Harper Collins.

Tandberg, M., Ueland, T., Andreassen, O.A., Sundet, K., & Melle, I. (2012). Factors associated with occupational and academic status in patients with first-episode psychosis with a particular focus on neurocognition. *Social Psychiatry and Psychiatric Epidemiology, 47*, 1763–1773.

Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008). Schizophrenia, "Just the Facts" What we know in 2008. 2. Epidemiology and etiology. *Schizophrenia Research, 102*(1–3), 1-18.

Tarrier, N., Beckett, R., Harwood, S., Baker, A., Yusupoff, L., & Ugarteburu, I. (1993). A trial of two cognitive—behavioural methods of treating drug-resistant residual psychotic symptoms in schizophrenic patients. 1. Outcome. *British Journal of Psychiatry, 162*, 524 -532.

Thompson, A., Papas, A., Bartholomeusz, C., Allott, K., Amminger, G. P., Nelson, B., … Yung, A. (2012). Social cognition in clinical "at risk" for psychosis and first episode psychosis populations. *Schizophrenia Research*, *141*(2), 204–209.

https://doi.org/10.1016/j.schres.2012.08.007

Tugwell, J. R., Goulden, N., & Mullins, P. (2017). Alleviating anxiety in patients prior to MRI:
A pilot single-centre single-blinded randomised controlled trial to compare video
demonstration or telephone conversation with a radiographer versus routine
intervention. *Radiography*. https://doi.org/10.1016/j.radi.2017.10.001

van Os, J., & Kapur, S. (2009). Schizophrenia. *The Lancet, 374* (9690), 635-645.

van Os, J., Kenis, G., & Rutten, B. P. F. (2010). The environment and schizophrenia. *Nature.*
468, 203-212.

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., . . . Bentall, R.
(2012). Childhood adversities increase the risk of psychosis: a meta-analysis of patient,
control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin, 38,*
661–671.

Vauth, R., Rusch, N., Wirtz, M., & Corrigan, P. W. (2004). Does social cognition influence
the relation between neurocognitive deficits and vocational functioning in
schizophrenia? *Psychiatry Research, 128*, 155-16.

Velthorst, E., Nieman, D. H., Linszen, D., Becker, H., de Haan, L., Dingemans, P. M., . . .
Ruhrmann, S. (2010). Disability in people clinically at high risk of psychosis. *British*
Journal of Psychiatry, 197, 278-284.

Ventura, J., Hellemann, G. S., Thames, A. D., Koellner, V., & Neuchterlein, K. H. (2009).
Symptoms and mediators of the relationship between neurocognition and functional
outcome in schizophrenia: meta-analysis. *Schizophrenia Research, 113*, 189-199.

Ventura, J., Wood, R. C., & Hellemann, G. S. (2011). Symptom domains and neurocognitive
functioning can help differentiate social cognitive processes in schizophrenia: A meta-
analysis. *Schizophrenia Bulletin*, *39*(1), 102-111. doi: 10.1093/schbul/sbr067.

Voges, M., & Addington, J. (2005). The association between social anxiety and social

functioning in first episode psychosis. *Schizophrenia Research*, *76*(2), 287–292. https://doi.org/10.1016/j.schres.2005.01.001.

Waldheter, E. J., Jones, N. T., Johnson, E. R., & Penn, D. L. (2005). Utility of social cognition and insight in the prediction of inpatient violence among individuals with a severe mental illness. *The Journal of Nervous and Mental Disease*, *193*(9). Retrieved from http://journals.lww.com/jonmd/Fulltext/2005/09000/Utility_of_Social_Cognition_and_Insight_in_the.6.aspx

Walter, H., Adenzato, M., Ciaramidaro, A., Enrici, I., Pia, L., & Bara, B.G. (2004). Understanding intentions in social interaction: The role of the anterior paracingulate cortex. *Journal of Cognitive Neuroscience, 16,* 1854–1863.

Walter, H., Ciaramidaro, A., Adenzato, M., Vasic, N., Ardito, R. D., Erk, S., & Bara, B. G. (2009). Dysfunction of the social brain in schizophrenia is modulated by intention type. *Social Cognitive and Affective Neuroscience, 4*(2), 166-176.

Walter, H., Schnell, K., Erk, S., Arnold, P., Kirsch, C., Esslinger, C., . . . Meyer-Lindenberg, A. (2011). Effects of genome-wide supported psychosis risk variant on neural activation during a Theory-of-Mind task. *Molecular Psychiatry, 16(4),* 462-70.

Wechsler, D. (1981). *WAIS-R manual: Wechsler Adult Intelligence Scale-Revised.* New York: Psychological Corporation.

Wechsler, D. (1987) *Manual for the Wechsler Memory Scale-Revised*. San Antonia: The Psychological Corporation.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale–Fourth Edition.* Pearson; San Antonio, TX.

Weiskopf, N., Scharnowski, F., Veit, R., Goebel, R., Birbaumer, N., & Mathiak, K. (2004). Self-regulation of local brain activity using real-time functional magnetic resonance imaging (fMRI). *Decoding and interfacing the brain: From neuronal assemblies to*

cyborgs, *98*(4), 357–373. https://doi.org/10.1016/j.jphysparis.2005.09.019

Wiersma, D., Wanderling, J., Dragomirecka, E., Ganev, K., Harrison, G., an der Heiden, W., . . . Walsh, D., (2000). Social disability in schizophrenia: its development and prediction over 15 years in incidence cohorts in six European centres. *Psychological Medicine, 30*, 1155-1167.

Williams, J., Farmer, A. E., Ackenheil, M., Kaufmann, C.A., & McGuffin, P. (1996). A multicentre inter-rater reliability study using the OPCRIT computerized diagnostic system. *Psychologial Medicine, 26*, 775–783.

Williams, L. M., Whitford, T. J., Flynn, G., Wong, W., Liddell, B. J., Silverstein, S., … Gordon, E. (2008). General and social cognition in first episode schizophrenia: Identification of separable factors and prediction of functional outcome using the IntegNeuro test battery. *Schizophrenia Research*, *99*(1), 182–191. https://doi.org/10.1016/j.schres.2007.10.019

Wimmer, H., & Perner, J (1983). Beliefs about beliefs: Representation and constraining function of wrong beliefs in young children's understanding of deception, *Cognition, 13*, 103-128.

Wood, S. J., Yung, A. R., McGorry, P. D., & Pantelis, C. (2011). Neuroimaging and treatment evidence for clinical staging in psychotic disorders: From the At-Risk Mental State to chronic schizophrenia. *Biological Psychiatry*, *70*(7), 619–625. https://doi.org/10.1016/j.biopsych.2011.05.034

World Health Organisation (1991). *WHO Quality of Life-BREF (WHOQOL-BREF).* Retrieved from http://www.who.int/substance_abuse/research_tools/whoqolbref/en/

World Health Organisation (1992). *The ICD-10 Classification of mental and behavioural disorders: Clinical descriptors and diagnosis guidelines.* Geneva: WHO.

Wunderink, L., Sytema, S., Nienhuis,F. J., & Wiersma, D. (2009). Clinical recovery in first episode psychosis. *Schizophrenia Bulletin. 35*, 362–9.

Yager, J. A., *& Ehmann, T. S. (2006). Untangling social functioning and social cognition: A review of the concepts and measurement. *Psychiatry, 69*(1), 47-68.

Yung, A. R., & McGorry, P. D. (1996). The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophrenia Bulletin, 22*(2), 353-37

Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010). Should a "Risk Syndrome for Psychosis" be included in the DSMV? *Schizophrenia Research*, *120*(1-3), 7-15. DOI: 10.1016/j.schres.2010.03.017.

Yung, A. R., Phillips, L. J., Yuen, H. P., Francey, S. M., McFarlane, C. A., ... McGorry, P. D. (2003). Psychosis prediction: 12-Month follow up of a high-risk ("prodromal") group. *Schizophrenia Research*, *60*(1), 21-32.

APPENDIX A:

RECRUITMENT AND CONSENT MATERIAL

A – 1 ETHICAL APPROVAL

A – 1 ETHICAL APPROVAL

A-2 Participant Information Sheet for Study 1

THE UNIVERSITY
OF BIRMINGHAM

PARTICIPANT INFORMATION

22nd December 2011, Version 2

Study Title: **Predictors of Functional Outcome in First Episode Pyschosis**

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear, or if you would like more information.

The purpose of the study:
The aim of the study is to help us understand how young people with psychosis function in their day-to-day lives, and to look at why some people continue to function well, while others do not.
This study is being undertaken for educational purposes, as part of a PhD degree in Psychology.

Why have I been chosen?
We are inviting everyone who has been referred to the Early Intervention Service in Birmingham and Solihull to take part in this study.

Do I have to take part?
No – involvement in this study is voluntary. However, if you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of health care you receive now or in the future.

What will happen to me if I take part?
The researcher will meet with you at your home or at a health centre to carry out some assessments with you. These assessments will look at how you think and reason, but also how you understand and function in your social world.

These assessments will take approximately one hour to complete, and you will receive **£20** in recognition of your time and expenses, upon completion of assessments. We will also make contact with you in twelve months time, to complete the same assessments.

You may also be asked permission for the research team to contact a friend to ask if they would also be interested in taking part in this research. This contact will only be made with your permission. The purpose of this contact is to invite your friends to complete similar assessments to which you have been

asked to complete; this will help us build a wider picture of how young people understand their social world.

What are the possible side effects of taking part?
We do not expect that any part of this study will cause harm to anyone taking part in it. However, you do not have to answer anything that you do not feel comfortable with, and you can stop at any time.

What are the possible benefits of taking part?
On a personal level, participants from previous studies have found meeting up and talking with a study researcher to be helpful. Although we cannot promise the study will help you, the information we get from this study may help improve social outcomes for young people experiencing a first episode of psychosis.

What will happen when the research study stops?
The data will be put into a database and analysed together with data from other participants under the care of the Early Intervention Service (EIS). All data will be anonymised. The results will be published in journal articles. We can send you a summary of the results of the study when they are ready. We will ask you at the appointment if you would like to see these results.

Will my taking part in this study be kept confidential?
All information collected as part of this research (including questionnaires), will be kept in a locked filing cabinet and/or on secure IT systems at the University of Birmingham. Any information from or about you will have your name, address and any other identifying features removed so that you cannot be recognised from it. This means that your anonymity will be preserved at all times during and after the study period. The data will be destroyed 5 years after the study has been completed, in line with University of Birmingham research policy.

What will happen to the results of the research study?
The results of the study will be written up for publication in health professional journals and will be presented at conferences in the UK and abroad, however, your anonymity will be preserved at all times.

Who is organising and funding the research?
The research is sponsored by The University of Birmingham and is undertaken as part of a PhD.

What if there is a problem?
If you are worried or concerned about any aspect of the study, you should talk to the researcher. If they are unable to address your concerns, you can contact your local Patient Advice and Liaison Service [0800 917 2855], should you wish to make a complaint about the study.
Who has reviewed the study?
All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed by the Black Country Research Ethics Committee.

Contact for further information
Please contact Lowri Griffiths (Doctoral Researcher) on ▓▓▓▓▓▓▓ School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT.

If you agree to participate, you will be given a copy of this Information Sheet and a copy of the signed consent form to keep.

Thank you for reading this.

A-3 Participant Consent Form for Study 1

THE UNIVERSITY
OF BIRMINGHAM

Patient Identification No for this study:

PATIENT CONSENT FORM (Over 16 years)

22nd December 2011 (Version 2)

Study Title: A Prospective 12 - month Follow - Up Study examining the predictors of Functional Outcome Trajectories in a First Episode Cohort.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated December 2011 (version 2) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.

3. I understand that sections of any of my medical notes may be looked at by responsible individuals from the Early Intervention Service, and/or research staff from the University of Birmingham or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

4. I understand that I have given permission for the researcher to use the data from the information gathered during the routine intake assessments at the Early Intervention Service.

5. I agree to take part in the above study.

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

A-4 Healthy Control Participant Information Sheet

THE UNIVERSITY
OF BIRMINGHAM

PARTICIPANT INFORMATION

September 2011, Version 1

Study Title: Predictors of Functional Outcome in First Episode Psychosis.

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

The purpose of the study
The aim of the study is to help us understand how young people with psychosis function in their day-to-day lives and to look at why some people continue to function well while others do not. As part of this, we would like to study how young people with a first episode of psychosis compare with their peers on tasks which assess their ability to understand their social world.

Why have I been chosen?
We are inviting young people between the ages of 16-35 years who have no history of mental illness to take part in this study.

Do I have to take part?
No – involvement in this study is voluntary. However, if you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect your legal rights.

What will happen to me if I take part?
If you are happy to go ahead with the research, the researcher will arrange a time to meet with you at the University of Birmingham to carry out some assessments with you.

The purpose of these assessments is to get an idea of how you understand your social world. These assessments will take approximately one hour to complete and you will receive **£20** in recognition of your time and expenses, upon completion of assessments.

What are the possible side effects of taking part?
We do not expect that any part of this study will cause harm to anyone taking part in it. However, you do not have to answer anything that you do not feel comfortable with and you can stop at any time.

What are the possible benefits of taking part?
On a personal level, participants in previous studies have enjoyed taking part in research. Although we cannot promise the study will help you, the information we get from this study may help improve social outcomes for young people experiencing a first episode of psychosis.

What will happen when the research study stops?

The data will be put onto a database and analysed together with data from other participants. All data will be anonymised. The results will be published in journal articles. We can send you a summary of the results of the study when they are ready. We will ask you at the appointment if you would like to see these results.

Will my taking part in this study be kept confidential?

All information collected as part of this research, including questionnaires, will be kept in a locked filing cabinet and on secure IT systems at the University of Birmingham. Any information from you, or about you, will have your name, address, and any other identifying features removed so that you cannot be recognised from it. This means that your anonymity will be preserved at all times during and after the study time period. The data will be destroyed 5 years after the study has been completed, in line with University of Birmingham research policy.

What will happen to the results of the research study?

The results of the study will be written up for publication in health professional journals and will be presented at conferences in the UK and abroad, however, your anonymity will be preserved at all times.

Who is organising and funding the research?

The research is sponsored by The University of Birmingham and is undertaken as part of a PhD.

What if there is a problem?

If you are worried or concerned about any aspect of the study, you should talk to the researcher. The researcher can be contacted on the number below between the hours of 9am-5pm, Monday to Friday.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed by the Black Country Research Ethics Committee.

Contact for Further Information

Please contact Lowri Griffiths (Doctoral Researcher) on [redacted] School of Psychology. University of Birmingham, Edgbaston, Birmingham, B15 2TT.

If you agree to participate, you will be given a copy of this Information Sheet and a copy the signed consent form to keep.

Thank you for reading this.

A-5 Healthy Control Participant Consent Form

**THE UNIVERSITY
OF BIRMINGHAM**

Patient Identification No for this study:

PARTICIPANT CONSENT FORM (Over 16 years)

September 2011 (Version 1)

Study Title: A Prospective 12 month Follow up Study examining the predictors of Functional Outcome Trajectories in a First Episode Cohort.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated September 2011 (version 1) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.

3. I agree to take part in the above study.

_____   _____   _____
Name of participant   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

A-6 Participant Information Sheet for the SUPEREDEN Study (Study 2)

UNIVERSITY OF BIRMINGHAM

Birmingham and Solihull NHS
Mental Health NHS Foundation Trust

Super EDEN Study 3

Funded by the NIHR

Improving social recovery in young people with emerging severe social disability: A proof of principle randomised controlled trial.

Participant Information Sheet

Invitation Paragraph
You are being invited to take part in a research study. Before you decide, whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.   Thank you for reading this

What is the purpose of the study?
People who have episodes of worrying, distressing or unusual experiences or beliefs often recover from the worst of these experiences, but may continue to have difficulties in maintaining social contacts and social activities or in returning to or taking up employment or educational opportunities. We think people can be helped to make a better social recovery by working with a therapist using a therapy called **Social Recovery oriented Cognitive Behaviour Therapy (SRCBT).** The study aims to see if working with a therapist helps to improve social recovery and to reduce symptoms of hopelessness and anxiety if present.

Why have I been chosen?
We are approaching people who have been receiving care from the Early Intervention Service for between 1 and 2 years, who display severe levels of social disability. The whole study will involve 150 patients across Birmingham, Lancashire and Norfolk Early Intervention Teams.

Do I have to take part?
No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

If you do agree to take part, you will meet with a researcher who will ask about your current problems and social situation, after this you will be randomly offered either SRCBT and your usual treatment or your usual treatment with your team alone. After nine months you will then meet with the researcher again to repeat the assessments and again after a further 6 months. The research assessments will take approximately an hour and a half to complete, and will include a maximum of 23 measures, many of these being self-report questionnaires. You will not have to do this in one sitting, if you prefer, the researcher can spread the assessments over 2 visits, whichever is more convenient and comfortable for you.

This is a randomised trial, which means we do not know which treatment works best, therefore, people will be divided into two groups, one group will receive the SRCBT and the other group will not, this will allow comparisons to be made. The groups will be selected by a computer which has no information about the individual i.e. by chance. Patients in each group then have a different treatment and these are compared. You will have a 50/50 chance of receiving SRCBT or treatment as usual.

What do I have to do?
If you are randomly allocated to the SRCBT treatment group, it will involve weekly or fortnightly meetings with a therapist for up to nine months which will be arranged at a time and location convenient for you.

What is the therapy being tested?
The aims of SRCBT are: to carefully identify activities and occupations which are meaningful for the person; to understand any barriers people may have to undertaking the activity the person wants to do; and to help people prepare for work or leisure activities by practicing in safe and low stress environments. This kind of help is called Social Recovery oriented Cognitive Behaviour Therapy (SRCBT). Social recovery is the aim. CBT tries to help you to understand what you are experiencing and feeling, cope with it differently, and feel less worried when you are trying to do new things.

SRCBT is a relatively new treatment. We still do not know how exactly it helps people to improve. The main aim of the study is therefore to see if SRCBT works, but we also want to improve our understanding of this type of treatment so that we can develop it further to be more helpful.

What are the possible disadvantages and risks of taking part?
If people feel pressurised into undertaking new activities they can sometimes have a recurrence of symptoms. However, the aim of SRCBT is to help people explore new activities they want to do while taking care to minimise the risk of symptom recurrence.

What are the possible benefits of taking part?
We hope that all the treatments will help you. However, this cannot be guaranteed. The information we get from this study may help us treat future patients better.

What happens when the research study stops?
When the research study finishes, all participants will receive normal care from Early Intervention Services

What happens if something goes wrong?
If you are harmed by taking part in a research project there are no special compensation arrangements. If you are harmed by someone's negligence you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the study, the normal National Health Service complaints mechanisms should be available to you.

Will my taking part in this study be kept confidential?

All information collected as part of this research including questionnaires, typed up notes of interviews and recording of interviews will be kept in a locked filing cabinet and secure IT systems in the University/NHS trust sites. Any information from or about you will have your name, address and any other identifying features removed so that you cannot be recognised from it. This means that your anonymity will be preserved at all times during and after the study time period. The tapes will be destroyed 7 years after the study has been completed in line with NHS research policy.

If you consent, we will inform your consultant psychiatrist and the team responsible for your care about your involvement in the study.

Since we are trying to provide the very best treatment possible, we would like to audio tape some sessions that you have with your therapist. The reason for this is to check that the therapy is carried out in the way that we expect it to be.

Where and how long will records be stored?
Data will be stored in locked cabinets in local health care or university premises. It will be kept for 7 years after the completion of the study and then destroyed.

What will happen to the results of the research study?
The results of the study will be written up for publication in health professional journals and will be presented at conferences in the UK and abroad, however your anonymity will be preserved at all times.

Who is organising and funding the research?
The research is funded by the National Institute of Health Research (NIHR) and sponsored by Birmingham and Solihull Mental Health NHS Foundation Trust. It is being carried out by researchers from Birmingham and Solihull Mental Health NHS Foundation Trust, Birmingham University, Lancashire Care Trust and Norfolk and Waveney Mental Health Foundation Trust.

Who has reviewed the study?
The research has been considered and approved by the West Midlands – Black Country Research Ethics Committee.

Thank you for reading this. If you need further information, please contact a member of the research team. The names of people to contact are given below.

We will give you this information sheet to keep as well as a signed consent form if you agree to take part in the study.

Contact for further information:
Chief Investigator: Prof Max Birchwood. School of Psychology, FranklandBuilding. University of Birmingham. Edgbaston. Birmingham B15 2TT. Tel:

Programme Manager: Linda McCarthy. The Early Intervention Service. 1 Miller Street. Aston. Birmingham. B6 4NF. Tel:

A-7 – Participant Consent Form for the SUPEREDEN Study (Study 2)

UNIVERSITY OF BIRMINGHAM

Birmingham and Solihull NHS
Mental Health NHS Foundation Trust

Funded by the NIHR

Super EDEN Study 3

Super EDEN Project Team
{insert address and contact details of local study teams}

CONSENT FORM

Title of Project: Improving social recovery in young people with emerging severe social disability: A proof of principle randomised controlled trial.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated 19/03/2012 (version 1) for the above study and have had the opportunity to ask questions.

   ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

   ☐

3. I understand that sections of any of my medical notes may be looked at by responsible individuals working on the project or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

   ☐

4. I am willing for my care team/consultant psychiatrist to be informed of my participation in this project, and for assessment information regarding my current problems and social circumstances to be shared with my care team/consultant psychiatrist.

   ☐

5. I give my consent for tape recordings of assessment and treatment sessions to be made. I understand that this is for the purposes of training and supervision, and that any person hearing the tape will sign a declaration of confidentiality and that recordings will be stored under locked conditions.

☐

4.   I agree to take part in the above study.

☐

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

A-8 Participant Information Sheet for the fMRI Study (Study 3)

THE UNIVERSITY OF BIRMINGHAM

PARTICIPANT INFORMATION

2nd May 2012, Version 2

Study Title: Investigating the Neural Correlates of Theory of Mind Ability as a Predictor of Functional Outcome in a Sample of Socially Disabled Young People with First Episode Psychosis.

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear, or if you would like more information.

The purpose of the study:
This study will examine how your brain functions when you undertake a task which measures a type of social ability using Magnetic Resonance Imaging (see next section). The study will also explore any changes in brain function before and after you have received therapy on the SuperEDEN study.

What is magnetic resonance imaging?
Magnetic resonance imaging (MRI) involves changes in the gradient of magnetic field to produce shifts in the alignment of atoms in the body of the person being scanned. The changes in alignment can be used to measure the structure and function of the tissues. When the brain is scanned, we can derive information about both brain structure and function. The procedure is non-invasive and carries no known harm outside of safety issues for operating in high magnetic field (e.g. if you have a cardiac pacemaker). For this reason you will be asked to go through a safety questionnaire with a scan operator prior to being allowed to proceed into the scanning environment.

Why have I been chosen?
We are inviting service users of the Early Intervention Service who are receiving the Social Recovery-oriented Cognitive Behavioural Therapy to take part in this study.

Do I have to take part?
No – involvement in this study is voluntary. However, if you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a

decision not to take part, will not affect the standard of health care you receive now or in the future.

What will happen to me if I take part?
You will undergo an MRI scan and you will also be asked to carry out a task while in the MRI scanner. As you carry out the task, we will measure changes in brain activity; this will inform us about which brain areas operate while the task is being undertaken. The scanning session will last approx. 45 min. during which time you will be asked to lie still.

You will be invited to undergo scanning on two occasions; at the start of the therapy, and after 9 months (at the end of therapy). You will receive £20 for your time and expenses.

What kind of stimuli will be presented?
While in the scanner we will be asking you to perform a task which will involve looking at cartoon drawings. The cartoon drawings will depict a story; your task is to decide on the most logical ending to the story

What are the possible benefits of taking part?
It is hoped that this study will provide future treatment targets for improving social recovery in young people with a first episode psychosis, and also allow us to identify individuals who will benefit form therapy.

What are the possible side effects of taking part?
The MRI procedure is considered to be completely safe and non-invasive. However, the scanner is noisy so all participants will wear earplugs and headphones. The enclosed space of the scanner can produce claustrophobia, so any participant with a history of claustrophobia will be excluded. Other participants will be introduced carefully to the scanner and allowed to leave at any stage. Furthermore, whilst lying motionless on the scanner bed, participants can experience back and neck pain. This will be minimized by the use of comfortable padding and positioning.

There is no known extra risk in conducting MRI scans on women who are pregnant. However, based on the precautionary principle that an unknown risk may not be a zero risk, it is conventional to exclude women who are pregnant from research using MRI scans. A pregnancy test kit will be available should women wish to use it before undergoing a scan.

Whilst in the scanner, participants can talk to the operator at any time and will be holding a panic button which they can squeeze during a scan in the event of distress. The effect of this will be to activate an alarm and cause the operator to immediately stop the scan.

What will happen when the research study stops?
The results will be written up for scientific publication. All data will be reported anonymously.

Will my taking part in this study be kept confidential?
Our procedures for handling, processing, storing, and destroying your data will be compliant with the Data Protection Act 1998. All information that is collected about you during the course of the research will be kept strictly confidential.

What will happen to the results of the research study?

The results of the study will be written up for publication in health professional journals and will be presented at conferences in the UK and abroad, however, your anonymity will be preserved at all times.

Who is organising and funding the research?
The research is being undertaken as part of a PhD at the University of Birmingham.

What if there is a problem?
If you are worried or concerned about any aspect of the study, you should talk to the researcher. If they are unable to address your concerns, you can contact your local Patient Advice and Liaison Service [0800 917 2855], should you wish to make a complaint about the study.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed by The Black Country NRES committee.

Contact for further information
Please contact Lowri Griffiths (Doctoral Researcher) on ⬚⬚⬚⬚⬚⬚⬚. School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT.

If you agree to participate, you will be given a copy of this Information Sheet and a copy of the signed consent form to keep.

Thank you for reading this.

A-9 Participant Consent Form for the fMRI Study (Study 3)

THE UNIVERSITY OF BIRMINGHAM

PARTICIPANT CONSENT FORM (Over 16 years)

May 5th 2012 (Version 2)

Study Title: Neurobiological Predictors of Functional Outcome in First Episode Psychosis.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated May 2nd 2012 (version 2) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.

3. I understand that sections of any of my medical notes may be looked at by responsible individuals from the Early Intervention Service, and/or research staff from the University of Birmingham or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

4. I understand that I have given permission for the researcher to use the data from the information gathered as part of SuperEDEN study assessments.

5. I agree to take part in the above study.

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person taking consent   Date   Signature
(if different from researcher)

_____   _____   _____
Researcher   Date   Signature

A-10 Table Showing Comparisons Between the Groups Who Completed Cognitive Assessments at Baseline in the SRCBT trial Compared to Those Who Did Not (Study 2).

	Group Completing Cognitive Assessments at Baseline on the SRCBT trial (N= 123)	Group Not Completing Cognitive Assessments at Baseline on the SRCBT Trail (N = 30)	Statistical Significance
Mean Age (years)	25.4	25.7	NS [a]
Males (n; %)	97; 78.9	18; 60	NS [bc]
Years in Education (mean)	12.2	11.7	NS [a]
Hour per week in Structured activity (Time Use Survey)	11	13.6	NS [a]
Ethnicity (%)			
Caucasian	74.8	86.7	
Asian	13.8	3.3	NS [b]
Black	5.7	3.3	
Other	5.7	6.7	
Symptoms (PANSS)			
Positive	13.7	15	NS [a]
Negative	16.2	15.4	NS [a]
General	32.4	36.9	.013 [a]
Delay of Untreated Psychosis (DUP; days)	326	209.4	NS [a]

[a] One-way Analysis of Variance (ANOVA). [b] Chi-Square test. [c] Yates' Correction for Continuity statistic was reported as it compensates for the overestimation of the chi-square value in 2x2 design.
NS = Non – significant. SRCBT – Social Recovery Cognitive Behavioural Therapy

APPENDIX B:

QUESTIONNAIRES AND MEASURES

B-1 The Global Functionig Scales (Role Functioning and Social Functioning)

GLOBAL FUNCTIONING: SOCIAL
SCALE

Specific questions to aid in rating the GF: Social scales are provided below. Be sure to assess for changes in social functioning over the previous year (to rate highest and lowest) as well as current functioning in the past month.

1) Tell me about your social life. Do you have friends?

2) Are they casual or close friends? If only casual – are they school or work friends only? If close – how long have you been close friends?

3) How often do you see friends? Do you see them outside of work/school? When was the last time you saw one of your friends outside of work/school? (Attempt to determine actual amount of social contact versus perceived amount of social contact.)

4) Do you usually initiate contact or activities with friends or do they typically call or invite you? Do you ever avoid contact with friends?

5) Do you ever have problems/falling outs with friends? Arguments or fights? How are they typically resolved?

6) Are you dating or interested in dating? (Alter as needed to assess age appropriate intimate relationships)

7) Do you spend time with family members (at home)? How often do you communicate with them? Do you ever avoid contact with family members?

GLOBAL FUNCTIONING: SOCIAL SCALE (GF: Social)

CURRENT _____	LOWEST PAST YEAR _____	HIGHEST PAST YEAR _____

☐   Check here if this is a retrospective rating

Please rate the patient's most impaired level of social functioning for the specified time period by selecting the lowest level which describes his/her functioning within that time frame. For current, rate most impaired level of functioning in the **past month**. Rate actual functioning regardless of etiology of social problems.

Note: The emphasis is on social contact/interactions with people other than family members, unless these are the only interpersonal contacts a person has (e.g., the lower end of the scale). Also note that ratings of intimate relationships are secondary to the rating of primary friendships and should take into account the age of the individual. For example, older individuals may be expected to have intimate relationships involving steady dating, cohabitation, or marriage whereas younger individuals may be expected to have only romantic interests (i.e., flirtations or crushes) or close friendships.

SUPERIOR SOCIAL/INTERPERSONAL FUNCTIONING		
Criteria: **10**		**Superior functioning in a wide range of social and interpersonal activities.** Frequently seeks out others and has multiple satisfying interpersonal relationships, including multiple close and casual friends. Is sought out by others because of his or her many positive qualities. Age appropriate involvement in intimate relationships.
ABOVE AVERAGE SOCIAL/INTERPERSONAL FUNCTIONING		
Criteria: **9**		**Good functioning in all social areas, and interpersonally effective.** Interested and involved in a wide range of social and interpersonal activities, including both close and casual friends. Age appropriate involvement in intimate relationships. No more than everyday interpersonal problems or concerns (e.g., an occasional argument with spouse, girlfriend/boyfriend, friends, co-workers, or classmates). Able to resolve such conflicts appropriately.
GOOD SOCIAL/INTERPERSONAL FUNCTIONING		
Criteria: **8**		**Some transient mild impairment in social functioning.** Mild social impairment is present, but transient and expectable reactions to psychosocial stressors (e.g., after minor arguments with spouse, girlfriend/boyfriend, friends, co-workers, or classmates). Has some meaningful interpersonal relationships with peers (casual and close friends), and/or age appropriate intimate relationships. Infrequent interpersonal conflict with peers.
MILD PROBLEMS IN SOCIAL/INTERPERSONAL FUNCTIONING		

Criteria: 7	**Some persistent mild difficulty in social functioning.** Mild impairment present that is NOT just expectable reaction to psychosocial stressors (e.g., mild conflicts with peers, co-workers or classmates; difficulty resolving conflicts appropriately). Has some meaningful interpersonal relationships with peers (casual and/or close friends). Some difficulty developing or maintaining age appropriate intimate relationships (e.g., multiple short-term relationships).

MODERATE IMPAIRMENT IN SOCIAL/INTERPERSONAL FUNCTIONING

Criteria: 6	**Moderate impairment in social functioning.** Moderate impairment present (e.g., few close friends; significant but intermittent conflicts with peers, co-workers or classmates). Moderate difficulty developing age appropriate intimate relationships (e.g., infrequent dating). Occasionally seeks out others, but will respond if invited by others to participate in an activity.

SERIOUS IMPAIRMENT IN SOCIAL/INTERPERSONAL FUNCTIONING

Criteria: 5	**Serious impairment in social functioning.** No close friends or intimate partner, but has some casual social contacts (e.g., acquaintances, school/work friends only). Rarely seeks out others. Occasional combative or verbally argumentative behavior with peers. Beginning to withdraw from family members (e.g., doesn't initiate conversation with family, but will respond if addressed).

MAJOR IMPAIRMENT IN SOCIAL AND INTERPERSONAL FUNCTIONING

Criteria: 4	**Major impairment in social functioning.** Serious impairment in relationships with friends or peers (e.g., very few or no friends, frequent conflicts with friends, or frequently avoids friends). Frequent combative or verbally argumentative behavior with peers. Infrequent contact with family members (e.g., sometimes does not respond to family or avoids family members).

MARGINAL ABILITY TO FUNCTION SOCIALLY

Criteria: 3	**Marginal ability to function socially or maintain interpersonal relationships.** Frequently alone and socially isolated. Serious impairment in relationships with all peers, including acquaintances. Few interactions with family members (e.g., often alone in room). Serious impairment in communication with others (e.g., avoids participating in most social activities).

INABILITY TO FUNCTION SOCIALLY

Criteria: 2	**Unable to function socially or to maintain any interpersonal relationships.** Typically alone and socially isolated. Rarely leaves home. Rarely answers the phone or the door. Rarely participates in interactions with others at home or in other settings (e.g., work, school).

EXTREME SOCIAL ISOLATION

Criteria: 1	**Extreme social isolation.** No social or family member contact at all. Doesn't leave home. Refuses to answer the phone or door.

GLOBAL FUNCTIONING: ROLE SCALE

Specific questions to aid in rating the GF: Role scales are provided below. Be sure to assess for changes in role functioning over the previous year (to rate highest and lowest) as well as **current functioning within the past month**. Determine and rate functioning for <u>primary role setting</u> (work, school, or home) based upon questions below. However, if the subject is engaged in multiple roles, consider TOTAL amount of time spent in role-related activities (i.e., part-time school plus part-time work equals full-time role status).

1) How do you spend your time during the day?

2) **IF CURRENTLY WORKING:**

   a. Where do you work? What are your job responsibilities?

   b. How many hours a week do you work?

   c. How long have you been at your current job? Have you had any recent changes in your job status (e.g., lost job, stopped working, changed position or workload)?

   d. Do you usually need assistance or regular supervision at work? How often do you need extra help? Are there any tasks that you are not able to do alone?

   e. Do you ever have trouble keeping up? Are you able to catch up if you fall behind?

   f. Have you received any comments (positive or negative) or formal reviews regarding your performance? Have others pointed out things that you've done well or poorly?

3) **IF CURRENTLY ATTENDING SCHOOL:**

   a. What type of school do you attend? (general education, non-public school, residential/hospital)

b. Have you ever been in special education classes or other non-general education classes?

c. How long have you been at this school? Have you had any recent changes in your school placement?

d. Do you receive any extra help or accommodations in your classes? Do you receive tutoring or extra help in school or after school? Do you receive extra time to take tests or are you able to leave the classroom to take tests in a quiet place?

e. Do you have trouble keeping up with your coursework? Are you able to catch up if you fall behind?

f. How are your grades? Are you failing any classes?

4) IF A HOMEMAKER:

a. What are your responsibilities around the house or for the family?

b. How long have you been in charge of the home?

c. How many hours per week do you spend working on household tasks?

d. Are you able to keep up with the demands of your household? Do you ever fall behind? If so, are you able to catch up or do you need others' help? Are you avoiding any tasks? Do you need regular assistance or supervision for any tasks within the home?

e. Have you received any comments (positive or negative) regarding your performance? Have others pointed out things that you've done well or poorly?

GLOBAL FUNCTIONING: ROLE SCALE (GF: Role)

CURRENT _____	LOWEST PAST YEAR _____	HIGHEST PAST YEAR _____

☐ Check here if this is a retrospective rating

Please rate the patient's <u>lowest</u> level of functioning in occupational, educational, and/or homemaker roles, as appropriate, within specified time frame. For **current**, rate most impaired level of functioning for the **past month**. Rate actual functioning regardless of etiology of occupational/educational problems.

<u>NOTE</u>: This scale emphasizes the level of support provided within the individual's environment <u>and</u> the individual's performance given such support. The term "independently" as used throughout this instrument implies that an individual is functioning at an <u>age-appropriate level</u> without the assistance of external supports or accommodations. Examples of independent functioning include (1) age-appropriate functioning in a mainstream school without out requiring extra help, special classes, or special consideration for testing, (2) competitive full-time employment without additional guidance, support, job coaching, or other forms of special assistance, and (3) full-time homemaker responsible for generating, organizing and pacing of household tasks and activities for a family without additional guidance, support or supervision.

SUPERIOR ROLE FUNCTIONING	
Criteria: **10**	Independently maintains superior functioning in demanding roles. Obtains only superior performance evaluations at competitive work placement. Obtains all A's in mainstream school. Generates, organizes & completes all homemaking tasks with ease.
ABOVE AVERAGE ROLE FUNCTIONING	
Criteria: **9**	Independently maintains very good functioning in demanding roles. Rarely absent or unable to perform. Obtains good to superior performance evaluations at competitive work placement. Obtains grades in A and B range in all courses in mainstream school. Generates, organizes and completes all homemaking tasks.
GOOD ROLE FUNCTIONING	
Criteria: **8**	Independently maintains good role functioning in demanding roles. Occasionally falls behind on tasks BUT always catches up. Obtains satisfactory performance evaluations at competitive work placement. Obtains grades of C and above in mainstream school. Occasional difficulty generating or organizing homemaking tasks. **OR** Maintains above average performance with minimal support (e.g., tutoring; reduced academic course load at 4-year university; attends community college; may receive additional guidance at work less than 1-2x week). Receives As & Bs, good work/school evaluations, completes all tasks with this level of support.
MILD IMPAIRMENT IN ROLE FUNCTIONING	
Criteria: **7**	Mildly impaired functioning in demanding roles independently. Frequently behind on tasks or unable to perform. Frequently obtains poor performance evaluations at competitive work placement or grades of Ds or better in mainstream school. Frequent difficulty generating or organizing homemaking

	tasks. **OR** Maintains good performance with minimal support (e.g., minimal accommodations/special considerations in general education classroom; receives additional guidance/support at work 1-2x week). Receives Cs or higher, satisfactory work/school evaluations, and completes most homemaking tasks with this level of support.
MODERATE IMPAIRMENT IN ROLE FUNCTIONING	
Criteria: **6**	Moderate impairment independently. May receive occasional F in mainstream courses, persistently poor performance evaluations at competitive work placement, may change jobs because of poor performance, persistent difficulty generating or organizing homemaking tasks. **Or** Requires partial support (some resource or special education courses; receives guidance/support at work 2+ times/week). May requires less demanding or part-time jobs and/or some supervision in home environment BUT functions well or adequately given these supports (may fall behind but eventually completes assigned tasks, obtains satisfactory evaluations at work or passing grades in school).
SERIOUS IMPAIRMENT IN ROLE FUNCTIONING	
Criteria: **5**	Serious impairment independently. Failing multiple courses in mainstream school, may lose job, or unable to complete most homemaking tasks independently. **OR** In entirely special education classes, requires less demanding job/daily support or guidance, may require vocational rehabilitation, and/or some supervision in home environment BUT maintains <u>above average</u> performance - receives As & Bs, good evaluations at work/school, completes all tasks.
MAJOR IMPAIRMENT IN ROLE FUNCTIONING	
Criteria: **4**	Very serious impairment independently. All Fs in mainstream school or failing out of school. Can't obtain or hold independent job, or unable to complete virtually any homemaking tasks independently. **OR** Adequate to good functioning with major support. Requires assisted work environment, entirely special education classes, non-public or psychiatric school, and/or supported home environment BUT functions adequately given these supports (may fall behind but completes assigned tasks, obtains satisfactory performance evaluations at work or passing grades).
MARGINAL ABILITY TO FUNCTION	
Criteria: **3**	Impaired functioning with major support. Requires supported work environment, entirely special education classes, non-public or psychiatric school, and/or supported home environment BUT functions poorly despite these supports (persistently behind on tasks, frequently unable to perform, obtains poor performance evaluations at work or fails courses at school).
INABILITY TO FUNCTION	
Criteria: **2**	Disabled but participates in structured activities. On disability or equivalent non-independent status. Not working for pay, attending classes for grades, or living independently. Spends 5 or more hours a week in structured role-related activities (e.g., residential treatment, volunteering, tutoring, sheltered work programs).
EXTREME ROLE DYSFUNCTION	
Criteria: **1**	Severely disabled. On disability or equivalent non-independent status. Not working for pay, attending classes for grades, or living independently. Spends fewer than 5 hours a week in structured role-related activities.

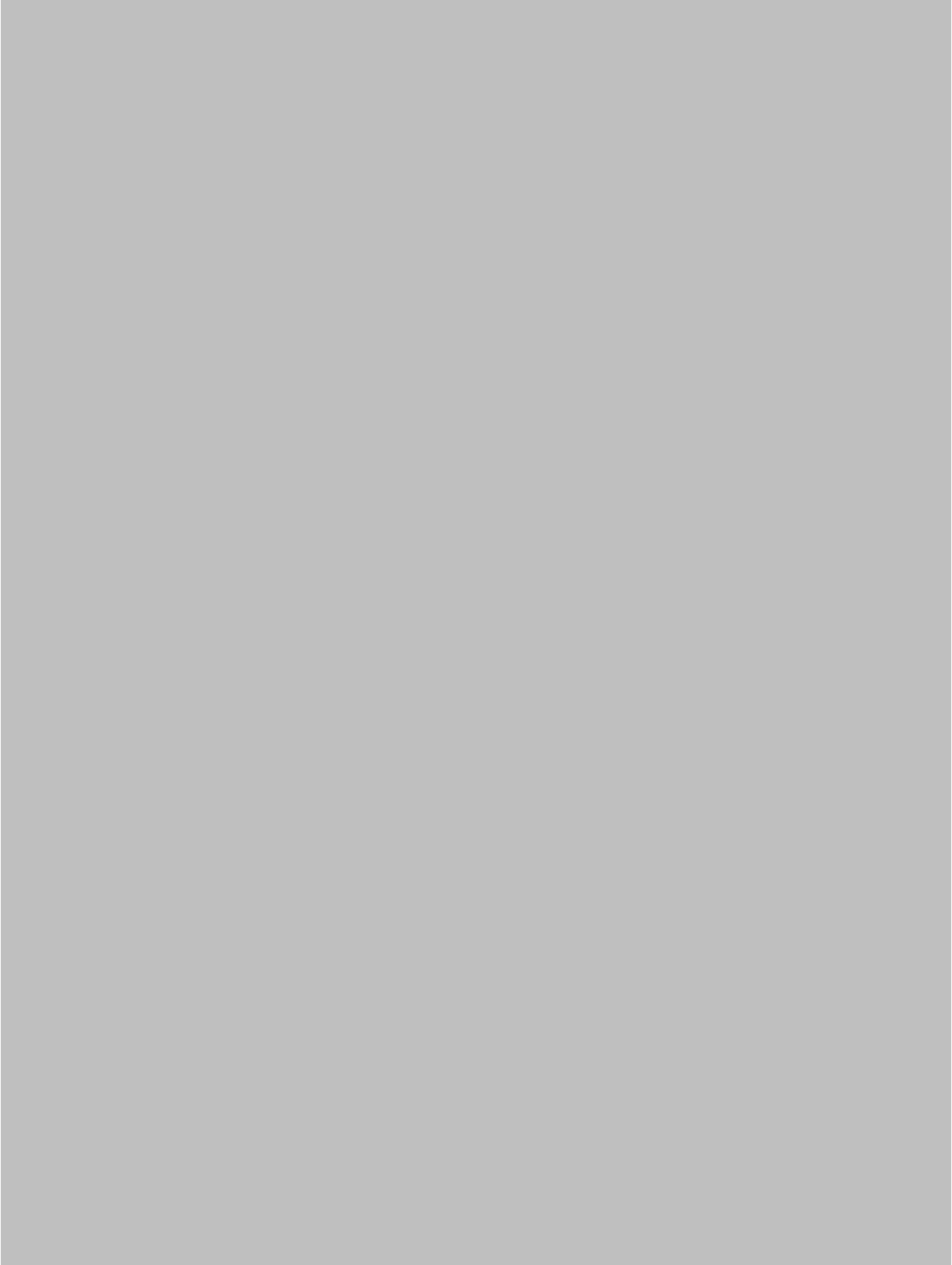## B-2 Positive and Negative Syndrome Scale (PANSS)

STRUCTURED CLINICAL INTERVIEW
FOR THE POSITIVE AND NEGATIVE SYNDROME SCALE
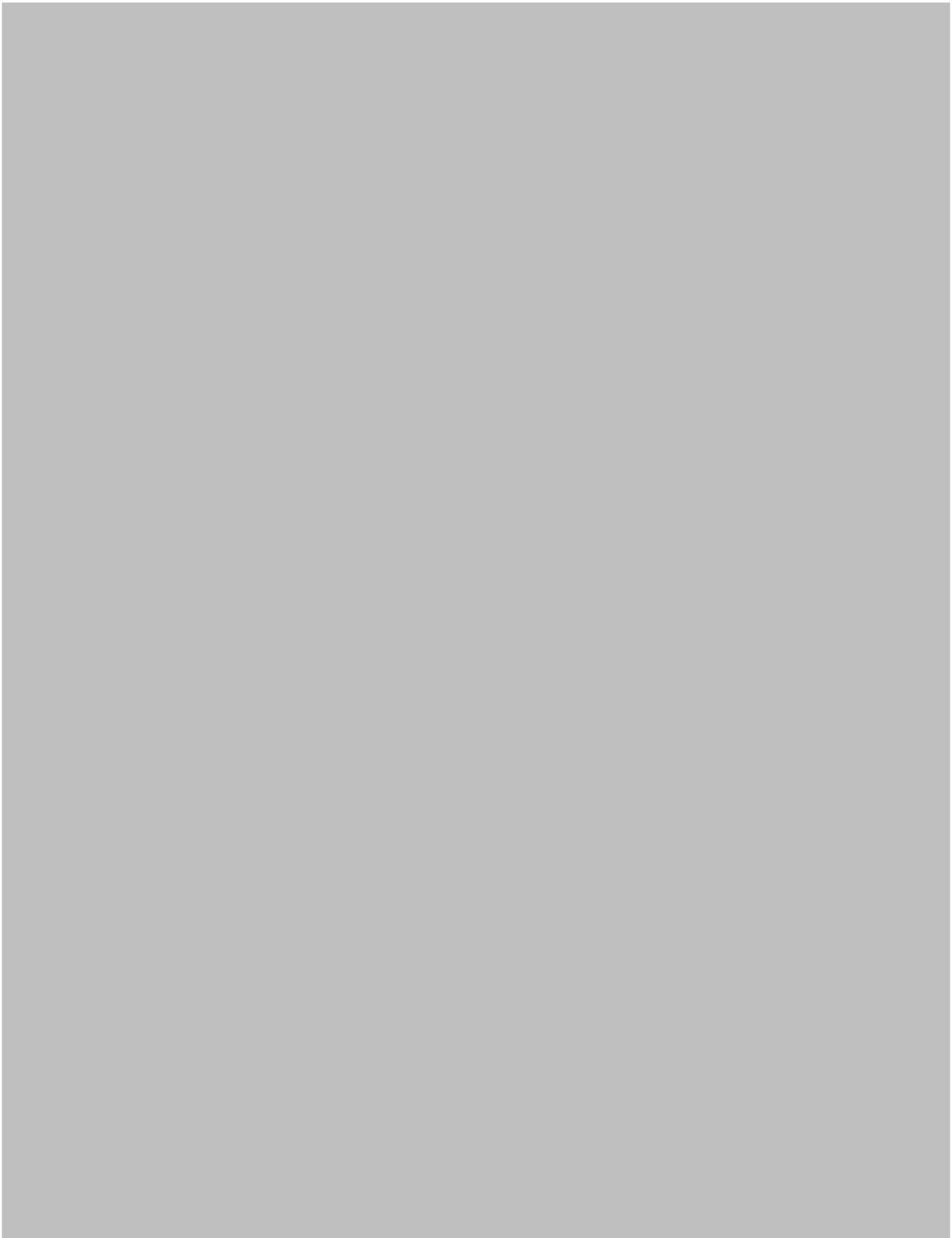# (SCI-PANSS)
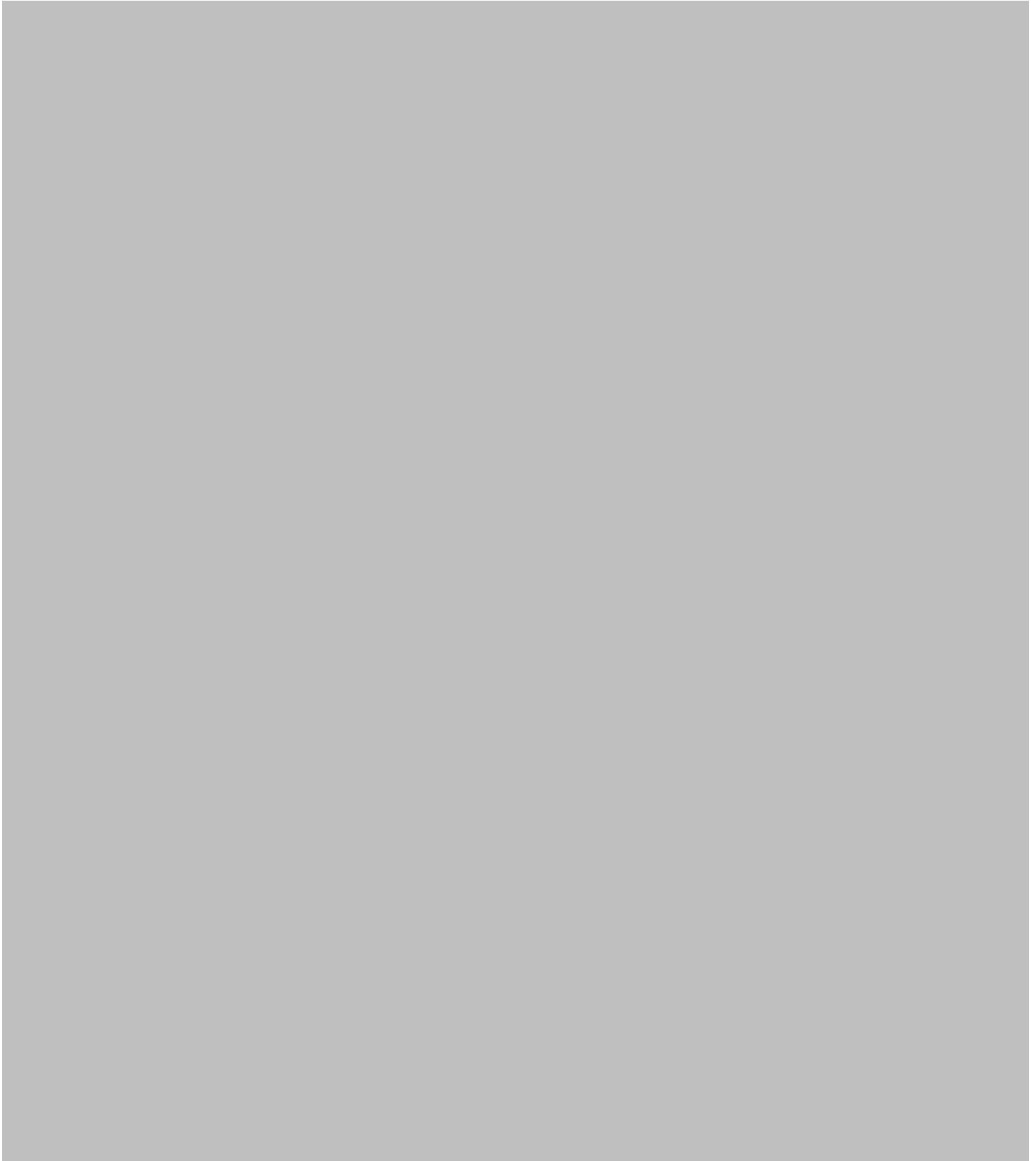
Data on **HALLUCINATORY BEHAVIOUR** and **ASSOCIATED DELUSIONS.**
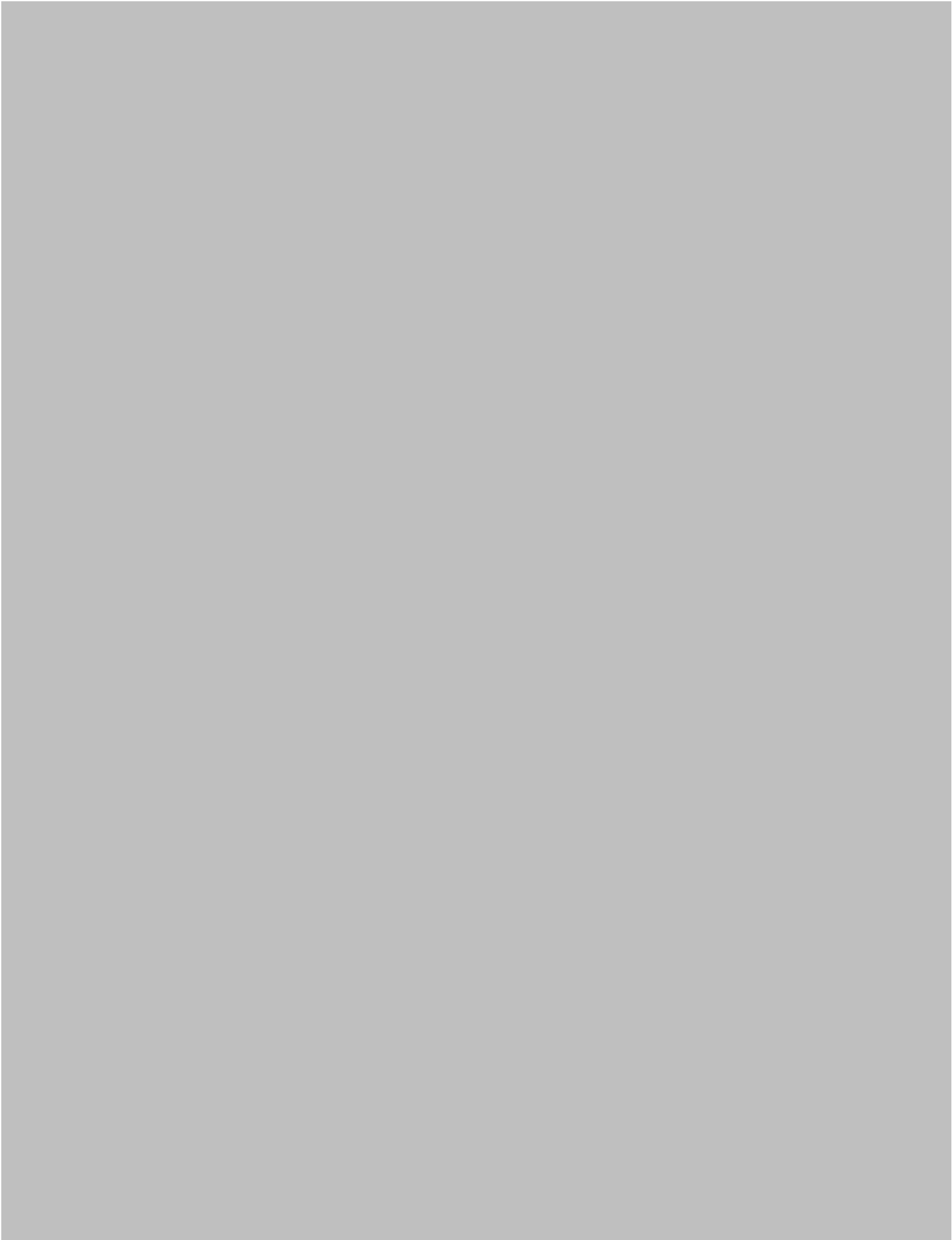
*Appendix A: Items for assessing SIMILARITIES in the evaluation of **DIFFICULTY IN ABSTRACT THINKING.***

2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	1. How are a ball and orange alike? 2. Apple and banana? 3. Pencil and pen? 4. Nickel and dime?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	5. Table and chair? 6. Tiger and elephant? 7. Hat and shirt? 8. Bus and train?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	9. Arm and leg? 10. Rose and tulip? 11. Uncle and cousin? 12. The sun and the moon?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	13. Painting and poem? 14. Hilltop and valley? 15. Air and water? 16. Peace and prosperity?

Appendix B: Items for assessing PROVERB INTERPRETATION in the evaluation of
DIFFICULTY IN ABSTRACT THINKING.

What does the saying mean:

2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	1. "Plain as the nose on you face"? 2. "Carrying a chip on your shoulder"? 3. "Two heads are better than one"? 4. "Two many cooks spoil the broth"?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	5. "Don't judge a book by its cover"? 6. "One man's food is another man's poison"? 7. "All that glitters is not gold"? 8. "Don't cross the bridge until you come to it"?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	9. "What's good for the goose is good for the gander"? 10. "The grass always looks greener on the other side"? 11. "Don't keep all your eggs in one basket"? 12. "One swallow does not make a Summer"?
2-year assessment **Baseline/6mth assessment** **1-year/Discharge/18mth assessment** **Acute ward assessment**	13. "A stitch in time saves nine"? 14. "A rolling stone gathers no moss"? 15. "The acorn never falls far from the tree"? 16. "People who live in glass houses should not throw stones at others"?

		absent	minimal	mild	moderate	moderate severe	severe	extreme
P1	Delusions	1	2	3	4	5	6	7
P2	Conceptual disorganisation	1	2	3	4	5	6	7
P3	Hallucinatory behaviour	1	2	3	4	5	6	7
P4	Excitement	1	2	3	4	5	6	7
P5	Grandiosity	1	2	3	4	5	6	7
P6	Suspiciousness/persecution	1	2	3	4	5	6	7
P7	Hostility	1	2	3	4	5	6	7
N1	Blunted affect	1	2	3	4	5	6	7
N2	Emotional withdrawal	1	2	3	4	5	6	7
N3	Poor rapport	1	2	3	4	5	6	7
N4	Passive/apathetic social withdrawal	1	2	3	4	5	6	7
N5	Difficulty in abstract thinking	1	2	3	4	5	6	7
N6	Lack of spontaneity & flow of conversation	1	2	3	4	5	6	7
N7	Stereotyped thinking	1	2	3	4	5	6	7
G1	Somatic concern	1	2	3	4	5	6	7
G2	Anxiety	1	2	3	4	5	6	7
G3	Guilt feelings	1	2	3	4	5	6	7
G4	Tension	1	2	3	4	5	6	7
G5	Mannerisms & posturing	1	2	3	4	5	6	7
G6	Depression	1	2	3	4	5	6	7
G7	Motor retardation	1	2	3	4	5	6	7
G8	Uncooperativeness	1	2	3	4	5	6	7
G9	Unusual thought content	1	2	3	4	5	6	7
G10	Disorientation	1	2	3	4	5	6	7
G11	Poor attention	1	2	3	4	5	6	7

G12	Lack of judgement & insight	1	2	3	4	5	6	7
G13	Disturbance of volition	1	2	3	4	5	6	7
G14	Poor impulse control	1	2	3	4	5	6	7
G15	Preoccupation	1	2	3	4	5	6	7
G16	Active social avoidance	1	2	3	4	5	6	7

$P_{tot} =$ _____ $N_{tot} =$ _____ $P_{tot} - N_{tot} =$ _____ $G_{tot} =$ _____

B-3 The Premorbid Social Adjustment Scale (PAS)

PREMORBID ADJUSTMENT SCALE
Sample Questions for Individuals Interview

Corresponding to "childhood (up through age 11)"

1. Establish time period and any major life events at this stage; i.e. which junior/infants school(s) did you go to at this time? Describe what you were like at this stage.

2. In general, how do you get on at school; did you find it enjoyable and interesting?

3. How did you find the work? Were you at the top, bottom or middle of your class? If 'streamed' (according to ability) which groups were you in?

4. How did you get on with other students and teachers?

5. Were you a member of any teams, clubs or groups at this school?

6. Did you ever get into trouble at school? Did you play truant or refuse to go to school?

7. Did you have many friends? Were these close/best friends or casual friends? Were your friends about the same age as you?

8. How regularly did you see these friends?

9. Did you spend much time on your own at this age?

10. Were you a shy person at this age? Would you approach other children to talk to or play with or did you usually wait until others asked you to join in?

11. At this age did you spend much time day dreaming or 'in your own world'?

Corresponding to "Adolescence (Early ages 12-15)"

12. Establish time period and any major life events at this stage. (I.e. which secondary school(s) did you go to at this time?) In what ways did you change as you got older?

13. In general, how did you get on at school; did you find it interesting and enjoyable?

14. How did you find the work? Were you at the top, bottom or middle of your class? If 'streamed' (according to ability) which groups were you in?

15. How did you get on with other students and teachers?

16. Were you a member of any teams, clubs or groups at this school?

17. Did you ever get into trouble at school? Did you play truant or refuse to go to school?

18. Did you have many friends? Were these close/best friends or casual friends? Were your friends about the same age as you?

19. How regularly did you see these friends?

20. Did you spend much time on your own at this age?

21. Were you a shy person at this age? Would you approach other people or did you wait until others asked you to join them?

22. At this age did you spend much time day dreaming or 'in your own world'?

23. Did you have male/female (use opposite gender to the client) friends at this age?

24. Did you go out on dates? Did you have a boyfriend(s)/girlfriend(s)?

25. Did you show physical signs of affection such as hugging or kissing? Did you have a sexual relationship with any of your girlfriends/boyfriends?

26. (if person did not date at this age) Were there boys/girls who you liked/were interested in/fancied?

Corresponding to "Adolescence (Late ages 16-18)"

27. Establish time period and any major life events at this stage. I.e. did you stay on at school after your GCSE's or did you decide to work/go to college or a training course? Did you experience the onset of illness or other problems?

28. In general, how did you get on at school/college/work; did you find it interesting and enjoyable?

29. How did you get on with other students/colleagues and teachers/lecturers/managers?

30. How did you find the work/your studies? Did you get good marks for your work or did you get praise/promotion/acknowledgments from bosses/managers?

31. Were you a member of any teams, clubs or groups at this age?

32. Did you ever get into trouble at school/college/work? Did you have a good attendance record?

33. Did you have many friends? Were these close/best friends or casual friends? Were your friends about the same age as you?

34. How regularly did you see these friends, what sort of things did you do together?

35. Did you spend much time on your own at this age?

36. Did you ever organise social events (going to the cinema, pub ect.) with others, or would you wait to be asked? are you a shy person at this age?

37. At this age did you spend much time day dreaming or 'in your own world'?

38. Did you have male/female (use opposite gender to the client) friends at this age?

39. Did you have a boyfriend(s)/girlfriend(s)? Would you describe any of these relationships as serious/long term?

40. Did you show physical signs of affection such as hugging or kissing? Did you have a sexual relationship with any of your girlfriends/boyfriends?

41. (if person did not date at this age) Were there men/women who you liked/were interested in/fancied?

<u>Corresponding to "Adulthood (Ages 19 and above)"</u>
Miss this section if the client became ill before they were 19 years of age.

42. Establish time period on a 'timeline' – include work history, major life events and onset of illness/hospitalisation. Include details of how your illness affected you particularly at work/in relationships. What examinations did you pass (+ grades)? Describe what you were like before your illness.

43. Did you have many friends? Were these close/best friends or casual friends? Were your friends about the same age as you?

44. How regularly did you see these friends, what sort of things did you do together?

45. Did you prefer to be on your own at this age?

46. Did you ever organise social events (going to the cinema, pub ect.) with others, or would you wait to be asked? Would you describe yourself as a shy person at this age?

47. At this age did you spend much time day dreaming or 'in your own world'?

48. Are you/have you been married or in a long-term relationship? (if in a long term relationship do you/have you lived together?) (if 'NO' go to question 52).

49. How long have you been/were you together? Are/were you happy in your relationship with your partner (husband/wife)?

50. Do you/did you have a close relationship? Do you/did you show physical signs of affection such as hugging and kissing?

51. Are you having/did you have a sexual relationship? Were there any problems?

(If questions 48-51 have been answered, go to question 55)

52. Did you ever go out on dates? Did you have a boyfriend(s)/girlfriend(s)? Were any of these relationships serious? How long did it/they last on average? Did you ever talk about marriage or serious commitment?

53. Did you show physical signs of affection such as hugging or kissing? Did you have a sexual relationship with any of your girlfriends/boyfriends? Were there any problems?

54. (If person did not date at this age) Were there men/women who you liked/were interested in/fancied?

Corresponding to "general section"

55. (If living with parents) Have you ever tried living on your own? How did you get on? Do you have your own income or do your parents manage your money?

56. Describe how you spent your time before your illness, (e.g. involvement with home, family, friends, work, sport, art, pets, gardening, social activities, music, and drama). How would you describe your involvement/interest in any of the items that you have selected?

57. Does it appear that the client was able to function successfully in and take pleasure from a) school or job b) friends c) intimate sexual relationships d) church, hobbies (ask more questions if there is not sufficient information to answer the above question).

58. Since childhood have you been involved in any societies, clubs or groups? Describe the level of your involvement. Did you ever have a leadership or organisation role in any of the groups?

59. Before your illness did you feel motivated? Did you take things on or did you spend a lot of time watching TV or sleeping? Did you find things to that challenged you in some way (i.e. challenging sport, hobby or career)?

60. If you were faced with a problem or difficulty what was your typical reaction? How might you tackle it; did you see it as a challenge or would you avoid it?
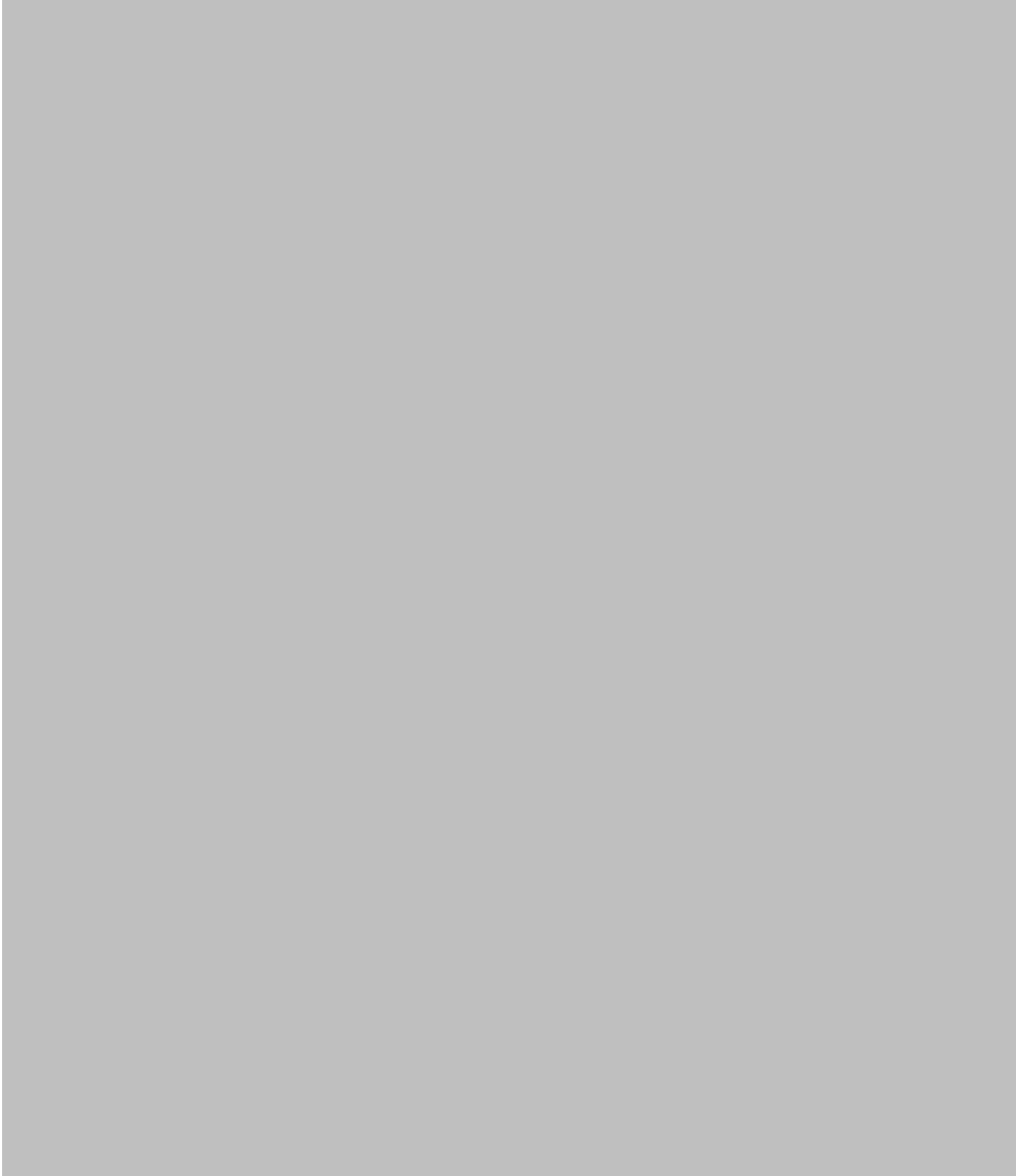
ANY ADDITIONAL INFORMATION?

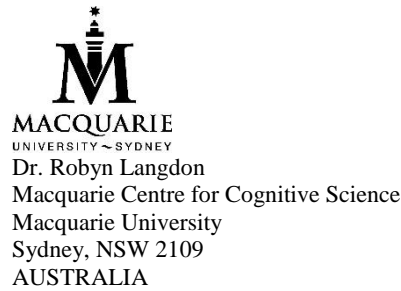## B-4 Logical Memory subtest - Wechsler Memory Scale Revised – IV

B-5 Vocabulary subtest Wechsler Adult Intelligence Scale – IV: Example of Word List

B-6 Block Design subtest Wechsler Adult Intelligence Scale – IV:

Score Sheet

B-6 Block Design subtest Wechsler Adult Intelligence Scale – IV:

Score Sheet

B-7 Picture sequencing task: Administration and scoring sheet

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To Whom It May Concern:

After downloading the files from the website, you should have a copy of the 4-card picture sequences used in the *Cognition* study (Langdon & Coltheart, 1999), a response sheet, and a sheet of the current administration and scoring instructions. We ask that you reference the task appropriately in any publications. There are 2 practice sequences and 16 experimental sequences. There are four types of experimental sequences: mechanical, social script, false belief and capture (4 sequences of each type; 4 cards in each sequence). Each file is labeled with the sequence type, sequence number and card number. There's also an alternate set of cards, labeled "fbeliefold" that can be used instead of False-Belief story 1. I think that False-Belief story 1 may be slightly more difficult. I leave it up to you to decide which to use.

The pictures were presented on cards, thick enough so that the line drawing could not be seen from the back of the card. The drawings were all black on white with no other distinguishing marks on the face of the cards. There was a small number on the back of each card to identify which sequence it came from. The four cards of each sequence were then kept together in a similarly labeled envelope. You will probably need to mark the backs of individual cards with random meaningless symbols (eg. #, *, $, &; or coloured dots) so that it's easy for you to record the order in which subjects arrange cards and to then calculate a position score.

In the original version of the task each subject saw a random order of the 16 sequences and the cards in each sequence were randomly ordered and positioned in a 2 x 2 square layout. More recently I have used a predetermined random order of cards for each sequence and have placed the cards upside down side by side in a line. I have also been using a pre-arranged fixed random order of sequences. I find that this simplifies administration; the change hasn't had any effect on the pattern of results that I usually find when testing clinical patients with schizophrenia. I will include a response sheet that I have recently used. In this case we used coloured dots on the backs of the cards (B=blue; O=orange; Y=yellow; G=green); the coloured dots were placed on each card sequence as per the listing in the 'Correct Order' column. The 'Layout Order' column indicates the order in which cards were placed face down in front of subjects.

Best wishes,

Robyn Langdon

Australian Research Council Australian Research Fellow
Picture Sequencing Task

Hold up one of the practice sequences and say, **"In each of these envelopes I have four cards. On the back of each card is a number. The number does not mean anything. I simply use the numbers to pre-arrange a mixed-up order of stories for each person to see. There are also coloured dots. I simply use these to record the order of cards when you've arranged them. I am going to put these four cards face-down in front of you."** Place the cards in the pre-arranged order on the table face-down.

Say, **"When we are ready to start, I will ask you to turn the cards over. You can do that in any order that you like, that's entirely up to you. Once you have turned the cards over, your task is to line the cards up in a straight line, like a comic-strip, first card here, second card here, etc."** (Point to where you want the cards lined up on the table.) **"You need to arrange the cards in the correct order so that they show a logical sequence of events."**

Say**, "When you are happy that you have the cards in the correct order, or that you have done your best to work out an order that makes the most sense, I want you to say 'finished'. I will be using this stopwatch to record how long you take from the time that I say turn the cards over 'now' to the time that you say 'finished'. Having said that, I don't want you to worry about being timed. It is more important to get the cards in the correct order than it is to be fast. Let's try the first story. This is a practice so that you can get used to doing the task. When I say 'now', I want you to turn the cards over. Ready, turn the cards over now".**

Start the stopwatch on 'now', and proceed to give the participant feedback as to whether they were correct or not. Also use this teddy-bear picture sequence to point out to subjects that these are not the sort of picture sequences where every detail of the story is shown on every card. For example.. **"Notice that in this sequence you can't tell that the boy wants the teddy-bear until the last card. In all of the sequences that you will do the cards are like that. You will need to make some inferences to work out how best to put the cards together"**.

Say, **"Now we'll do a second practice"** and proceed as above.

Say, **"Now we'll move on to the other stories. There are 16 stories in total. You may find that some of these stories are less straightforward than others. If you find a set of cards confusing, just do your best to put the cards in an order which you think is the most sensible. You will see the 16 stories in a mixed-up order. That means that the stories will not start out easy and get progressively harder. You might do one story that seems a bit confusing and then the very next story could be very easy. Just work through each story at your own pace. Do you have any questions? OK, let's start with this story".**

Lay the first story out in the predetermined order (L-R for participant. R-L from examiner's view) and Say "**You can turn the cards over now**". Begin timing.

Stop timing when the participant indicates they are finished and record the order of the cards on the score sheet and the time taken. Pickup from R-L from examiner's view and fan downwards. Record any errors before allowing the participant to fix them.

Scoring

Each sequence has a scoring ranging from 0 to 6, calculated as follows:

If the correct card is in the first position	2 points
If the correct card is in the last position	2 points
If the correct card is in the second position	1 point
If the correct card is in the third position	1 point

(This scoring equates the beginning middle and end of stories – eg. If the first and fourth card are correct, the two interim cards are either both correct or both incorrect)

Options

You may want to ask the participant to "tell the story that the cards tell". Stories are then tape recorded and scored for use of mental state language as per Langdon et.al. (1997, *Cognitive Neuropsychiatry*).

Hints

Label the backs of the cards with meaningless symbols (!, *, etc) or coloured dots in order to record order of cards and then check with correct order when scoring. Mark top of reverse side of cards in some way to ensure that when they are initially placed facedown, none of them are upside down.

Key for Story Number Listed on Response Sheet

Story Number	Story Type
1	Practice 1
2	Practice 2
3	Social Script 1
4	Social Script 2
5	Social Script 3
6	Social Script 4
7	Mechanical 1
8	Mechanical 2
9	Mechanical 3
10	Mechanical 4
11	Capture 1
12	Capture 2
13	Capture 3
14	Capture 4
15	False-Belief 1
16	False-Belief 2
17	False-Belief 3
18	False-Belief 4

Picture Sequencing Task

Sub ID: _____

Story	Layout order	Time taken	Subject order (colour id → no. id)	Correct order	Score	Story
Prac 1						Prac 1
Prac 2						Prac 2
3	OGYB			BYGO		3
9	YGBO			BYGO		9
17	OBYG			GYOB		17
12	GYOB			GYBO		12
18	YBOG			BGOY		18
10	YOBG			GYBO		10
5	YGBO			YOBG		5
14	OYBG			YBOG		14
8	YBOG			GBYO		8
15	BGYO			YOGB		15
7	GOYB			OBYG		7
11	BGYO			YBGO		11
4	BGOY			OBYG		4
13	GBOY			OBYG or OBGY		13
16	GYOB			BOYG		16
6	GYBO			OYGB		6

B-8 Picture sequencing task: Example of a False Belief Story

B-9 Mayer-Salovey-Caruso Emotional Intelligence Test – Perceiving Emotions: Faces Task Example

B-10 Mayer-Salovey-Caruso Emotional Intelligence Test – Perceiving Emotions: Picture Task Example

B-11 Ambiguous Intentions Hostility Questionnaire (AIHQ)

AIHQ

SUBJECT NAME/ID#_____   DATE_____

PLEASE READ EACH OF THE SITUATIONS LISTED BELOW AND IMAGINE THE SITUATION
HAPPENING TO YOU. FOR EACH SITUATION, WRITE DOWN A BRIEF REASON FOR IT. THEN,
RATE WHETHER YOU THINK THE PERSON ACTED THAT WAY TOWARD YOU ON PURPOSE. YOU
WILL THEN BE ASKED TO RATE HOW ANGRY THAT SITUATION MAKES YOU FEEL AND HOW MUCH
YOU BLAME THE OTHER PERSON. FINALLY, PLEASE WRITE DOWN WHAT YOU WOULD DO ABOUT
THAT SITUATION. A RESPONSE OF "I DON'T KNOW" IS NOT ACCEPTABLE. YOU NEED TO
DESCRIBE SOME TYPE OF BEHAVIORAL RESPONSE.

1.   1.   Someone jumps in front of you on the grocery line and says, "I'm in a rush."

    A.   What do you think was the real reason why someone jumped in line in front of you?

        _____

    B.   Did that person jump in front of you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

    C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

    D.   How much would you blame that person for jumping in front of you on line?

1	2	3	4	5
Not at All				Very Much

    E.   What would you do about it?

        _____

2.   A friend of yours slips on the ice, knocking you onto the ground.

    A.   What do you think was the real reason why your friend knocked you to the ground?

        _____

    B.   Do you think your friend knocked you onto the ground on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

    C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

    D.   How much would you blame your friend for knocking you onto the ground?

1	2	3	4	5
Not at All				Very Much

E.   What would you do about it?

_____

3.   You've been at a new job for three weeks. One day, you see one of your new co-workers on the street. You start to walk up to this person and start to say hello, but she/he passes by you without saying hello.

A.   What do you think was the real reason why your coworker passed by you without saying hello?

_____

B.   Do you think your co-worker did this to you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D.   How much would you blame the co-worker for passing by you?

1	2	3	4	5
Not at All				Very Much

E.   What would you do about it?

_____

4.   While walking outside during the rain, a car swerves to avoid hitting a cat, and drives into a puddle, splashing water onto you.

A.   What do you think was the real reason why the car splashed water onto you?

_____

B.   Do you think the driver of the car splashed water onto you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D.   How much would you blame the person in the car for splashing water onto you?

1	2	3	4	5
Not at All				Very Much

E.   What would you do about it?

_____

5.   You have an appointment with an important person. When you arrive at your appointment, the secretary informs you that the person is not in; they took the day off.

A.   What do you think was the real reason why the person didn't keep your appointment?

B.   Do you think the person did this to you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D.   How much would you blame the person for not keeping your appointment?

1	2	3	4	5
Not at All				Very Much

E.   What would you do about it?

_____

You are on a bus sitting in an aisle seat. A person gets on the bus at the next stop, begins walking as the bus moves, and steps on your foot.

A.   What do you think was the real reason why the person stepped on your foot?

_____

B.   Do you think the person did this to you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D.   How much would you blame the person for stepping on your foot?

1	2	3	4	5
Not at All				Very Much

E.   What would you do about it?

_____

Your neighbors are playing loud music. You knock on the door and ask them to turn it down. Fifteen minutes later, the music is loud again.

A.   What do you think was the real reason why your neighbors made the music loud again?

_____

B.   Do you think your neighbors raised the music on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D. How much would you blame them for raising the music again?

1	2	3	4	5
Not at All				Very Much

E. What would you do about it?

_____

8. You walk past a bunch of teenagers at a mall and your hear them start to laugh.

A. What do think was the real reason why the teenagers started to laugh after you walked past them?

_____

B. Do you think the teenagers did this to you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C. How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D. How much would you blame the teenagers for laughing as you walked past them?

1	2	3	4	5
Not at All				Very Much

E. What would you do about it?

_____

9. While driving, the person in the car behind you honks their horn and then cuts you off.

A. What do you think was the real reason why the person cut you off while driving?

_____

B. Do you think the person cut you off on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C. How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D. How much would you blame the driver of the car for cutting you off on the road?

1	2	3	4	5
Not at All				Very Much

E. What would you do about it?

A. What do you think was the real reason why your new friend didn't show up at the restaurant?

_____

B. Do you think your new friend did this to you on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C. How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D. How much would you blame your new friend for not showing up at the restaurant?

1	2	3	4	5
Not at All				Very Much

E. What would you do about it?

_____

11. You've been looking for a parking spot for awhile, when you see one up ahead. You put your signal on, proceed toward the spot, but someone passes your car and takes the parking space.

A. What do you think was the real reason why the person in the other car took your parking space?

_____

B. Do you think the person in the other car took your parking space on purpose?

1	2	3	4	5	6
Definitely No	Probably No	Maybe No	Maybe Yes	Probably Yes	Definitely Yes

C. How angry would this make you feel?

1	2	3	4	5
Not at all Angry				Very Angry

D. How much would you blame the person in the other car for taking your parking space?

1	2	3	4	5
Not at All				Very Much

E. What would you do about it?

_____

12. You're dancing at a club and someone bumps into you from behind.

A. What do you think was the real reason why the person in the club bumped into you from behind?

_____

B. Do you think the person bumped into you on purpose?

1	2	3	4	5	6
Definitely	Probably	Maybe	Maybe	Probably	Definitely

No	No	No	Yes	Yes	Yes

C.   How angry would this make you feel?

     1   2   3   4   5

Not at   Very
all Angry   Angry

D.   How much would you blame the person for bumping into you at the club?

     1   2   3   4   5

Not at   Very
All   Much

E.   What would you do about it?

_____

13.   You call a friend and leave a message on their answering machine, asking them to call you back. One week passes and they have not called you back.

A.   What do you think was the real reason why your friend didn't call you back?

_____

B.   Do you think your friend didn't call you back on purpose?

     1   2   3   4   5   6

Definitely   Probably   Maybe   Maybe   Probably   Definitely
No   No   No   Yes   Yes   Yes

C.   How angry would this make you feel?

     1   2   3   4   5

Not at   Very
all Angry   Angry

D.   How much would you blame your friend for not calling you back?

     1   2   3   4   5

Not at   Very
All   Much

E.   What would you do about it?

_____

14.   You're at a bar watching a football game and having a drink. Suddenly, the home team scores, people begin to cheer, and someone hits your arm, spilling the drink onto your clothes.

A.   What do you think was the real reason why the other person hit your arm?

_____

B.   Did the other person hit your arm on purpose?

     1   2   3   4   5   6

Definitely   Probably   Maybe   Maybe   Probably   Definitely
No   No   No   Yes   Yes   Yes

C.   How angry would this make you feel?

     1   2   3   4   5

Not at   Very
all Angry   Angry

D.   How much would you blame the other person for hitting your arm?

     1   2   3   4   5

Not at   Very

All   Much

E.   What would you do about it?

_____

15.   A day before meeting someone for a date, she/he calls to cancel. This is the third straight time
they've done that.

A.   What do you think was the real reason why the other person cancelled the date with you?

_____

B.   Did the other person cancel the date on purpose?

1	2	3	4	5	6
Definitely	Probably	Maybe	Maybe	Probably	Definitely
No	No	No	Yes	Yes	Yes

C.   How angry would this make you feel?

1	2	3	4	5
Not at				Very
all Angry				Angry

D.   How much would you blame the other person for canceling the date?

1	2	3	4	5
Not at				Very
All				Much

E.   What would you do about it?

_____

B-12 Ambiguous Intentions Hostility Questionnaire (AIHQ):

Scoring Examples

AIHQ Scoring Examples

Hostility Bias

For this item you must rate the participant's perceptions that the other person is deliberately intending to harm them (hostile intention). Base your ratings on the presence of two parts: 1) purpose/intention and 2) harm.

Score of 1: Not at all hostile (an accident)
"It was an accident"
"They did not see me or know I was there."
Any mention of situational factors (e.g., "They are busy" or "Their car broke down")
Any mention of something about the person doing the rating ("I deserved it." or "It was probably my fault.")

Score of 2

"The person was being careless or in a rush."
"They may have had something better to do."
"The person is only looking out for him or her self"
Hint: The person may suggest some intention or harm, but it is vague.   The person may have been careless, not aware of situation, or had other plans. In these cases you are not sure if there was intention to harm or not.

Score of 3: Moderately hostile (The person feels that the other person does not like them or they offer a negative description of why the person acted they way they did)
"The person is rude or a jerk"
"They do not like me."
"The person ran into me, but did not want knock me down."

Score of 4

"The person did that on purpose"
"The person is trying to get back at me"
Profanity based descriptions of the other person or their motives are rated as a 4.
Hint: The person clearly mentions intention and the wording suggests negative or harmful consequences may occur.

Score of 5: Very hostile (Other person clearly intended to inflict harm)
"The person is trying to make me mad" (purpose and intention are evident)
"The person is trying to hurt me"
"Person wanted to ruin my clothes."

"The person is trying to get me fired from my job"
Hint: Scores of 5 have both intention and harm mentioned
Aggression Bias

When rating this item you must examine what the participant does in response to the situation. Rate the behaviors in response to the situation.

Score of 1: Not at all aggressive (do nothing about it)
"I would not worry about it"
"I would let it go"
"I would not do anything since it was an accident."
"I would walk away"

Score of 2

"I would think to myself they are a jerk."
"I would think about doing something bad to them."
"Inside, I would be angry."
Hint: If the person states that they would think negative thoughts about them or mentally ruminate about reacting this would be rated as a 2. This rating is just below that of verbal aggression in which the anger is expressed.

Score of 3: Moderately aggressive (verbal aggression)
"I would yell at them"
"I would confront them and tell them off"
"I would ask them what their problem was."

Score of 4

"I would flip them off."
"I would shake my fist at them and yell 'jerk'."
"I would stare them down."
Hint: These are threatening or aggressive gestures without physical contact or injury

Score of 5: Very aggressive (physical aggression and/or damage to property)
"I would hit them or punch them in the face"
"I would follow their car and when they leave, hit it."
"I would push them down"

B-13	The Social Knowledge Questionnaire (SKQ)

Social Knowledge Questionnaire

1. Why do you think the divorce rate is so high?
   a. The birth rate is high.
   b. There are too many police around.
   c. The cost of living is high.
   d. Divorce laws now make divorce easy.

2. What do you think would be most likely to happen if suddenly there were no more police?
   a. More suicides.
   b. More people on the streets.
   c. More burglaries.
   d. Fewer cops and robbers films on TV.

3. What do you think would be the most sensible thing to say if you came across two strangers having a fight in the street?
   a. I suppose you think you're clever.
   b. The police are coming.
   c. Stop it. You'll lose your jobs.
   d. Stop it. You'll upset your mothers.

4. Why do you think that some men gamble excessively?
   a. They need continual excitement.
   b. They had overprotective mothers.
   c. They enjoy losing money.
   d. They are of low intelligence.

5. How would you tell a friend politely that they had stayed too long at your house?
   a. You'd better go. I'm fed up with you staying too long.
   b. Haven't you got anything better to do?
   c. Excuse me. I've got an appointment with a friend.
   d. There's no more coffee left.

6. What helpful thing could you say to a friend who was continually being harassed by a neighbour?
   a. Don't worry. I've heard she is unpleasant to everybody.

      b.   Why don't you throw some trash over into her yard?
      c.   You probably deserve it. You're a noisy person.
      d.   There's nothing you can do. You'll have to move.

7. Why do you think identical twins are emotionally alike?
      a.   They're brought up on the same foods.
      b.   They've inherited the same characteristics.
      c.   They probably get the same presents at Christmas.
      d.   No one will play with them because they are so strange.

8. What sort of people do you think make the best lawyers?
      a.   People who get angry with the way the country is run.
      b.   People who like talking a lot.
      c.   People who don't drink or smoke.
      d.   People with an eye for detail.

9. If you won the lottery, how would you best guarantee a large income for the rest of your life?
      a.   Buy shares in the Australian gold mine.
      b.   Bet it on the favourite in the Grand National.
      c.   Give it to your neighbour to look after.
      d.   Place it with an investment company in the city.

B-14 The Mini International Neuropsychiatric Interview (M.I.N.I.)
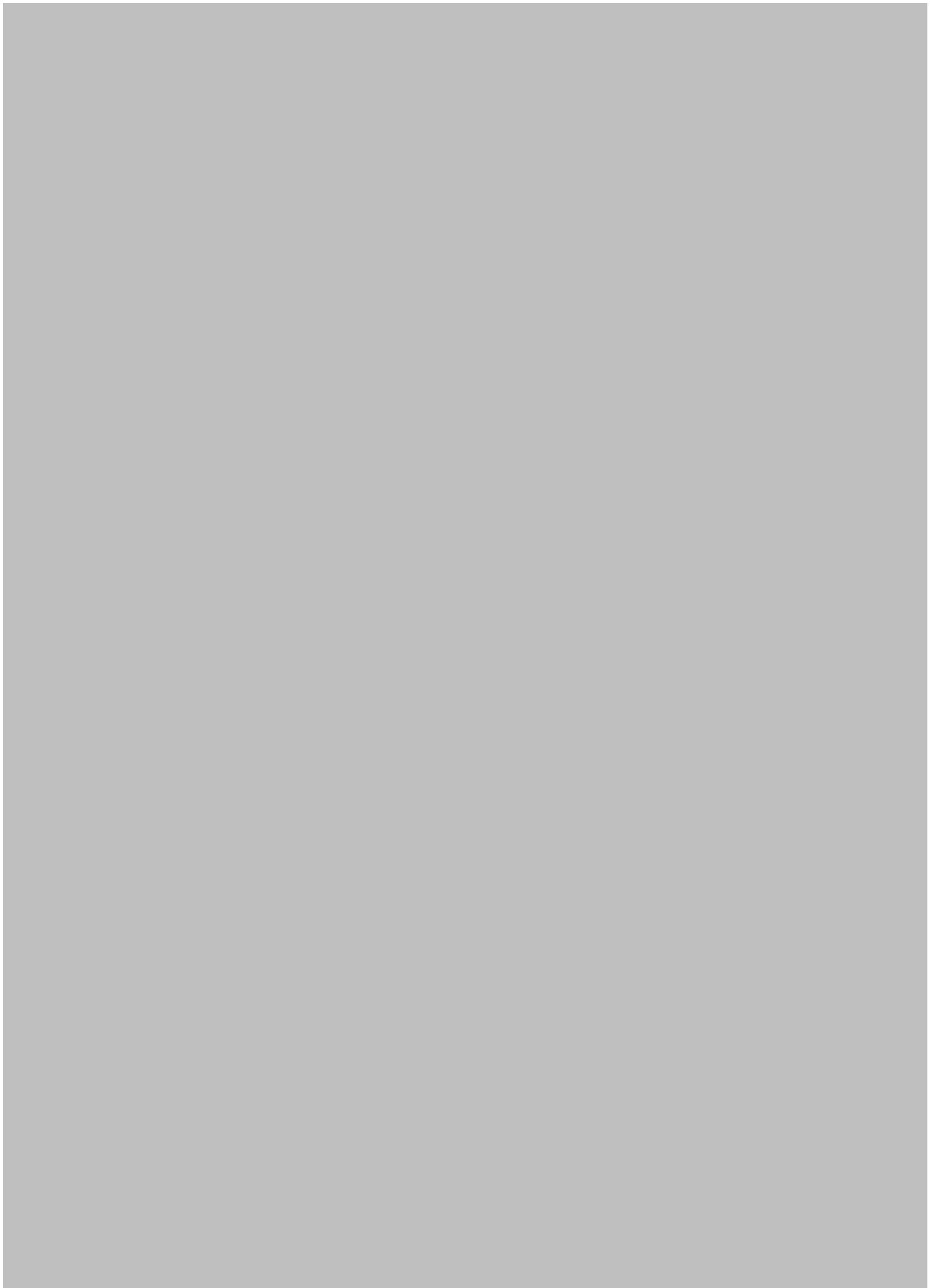
B-15 The Time Use Survey (TUS)

<u>TIME USE INTERVIEW</u>

EMPLOYMENT

1. Did you do any paid work in the last month, either as an employee or self-employed?

>   **YES** → ASK DETAILS
>   **NO**   → GO TO QU 3

Details

2. How many hours a week do you usually work in your main job? Include any overtime. How many hours have you worked in the last month?

Details

3. Over the last month have you been away from your main job?

>   **YES** → ASK DETAILS
>   **NO**   → GO TO QU 4

Details

4. Have you ever had a paid job?

>   **YES** → ASK DETAILS
>   **NO**   → GO TO 'EDUCATION AND TRAINING' SECTION

Details (What was the job? When left job, etc)

EDUCATION AND TRAINING

1. Are you studying for any formal qualifications at the moment?

> **YES**   →   ASK DETAILS
> **NO**   →   GO TO QU 2

> *Details (e.g. what, where, full/part time, hours in the last month)*

2. In the last month, have you been on any taught courses or undertaken learning of any   of the following sorts:

Taught courses meant to lead to qualifications (even if you did not obtain them)	
Taught courses designed to help you develop skills that you might use in a job	
Courses or instruction or tuition in driving, in playing a musical instrument, in an art or craft, in a sport or in any practical skill	
Evening classes (e.g. art/craft, languages, cookery)	
Learning which involved working on your own from a package of materials provided	

> **IF YES TO ANY OF THE ABOVE**   →   ASK DETAILS
> **IF NONE OF THE ABOVE**   →   GO TO 'VOLUNTARY WORK'
> SECTION

> *Details (e.g. what, where, full/part time, hours in the last month)*

3. On how many occasions in the last month did you spend time studying at home outside of teaching sessions? How many hours?

> *Details (e.g. what, where, full/part time, hours in the last month)*

VOLUNTARY WORK

Have you done any voluntary work through a group or on behalf of an organisation at any time during the last month? Have you done any unpaid work for anybody else e.g. running errands for elderly relatives?

YES	→	ASK DETAILS
NO	→	GO TO 'LEISURE ACTIVITIES'

Details of voluntary work

How many times in the past month?

How long do you normally spend doing this?

LEISURE AND SPORT ACTIVITIES

1. I am now going to ask some questions about things that some people do in their spare time. For each activity that I mention could you please tell me whether of not you have done this in the last month, AND how often?

ACTIVITY	NUMBER OF TIMES	AMOUNT OF TIME
Been to cinema		
Been to an event as a spectator (e.g. sports event, theatre, live music performance)		
Been to a museum, art gallery or heritage site		
Been to a library		
Been out to eat or drink at a café, restaurant, pub or wine bar		
Been to a shopping centre, or mall, apart from regular shopping for food and household items		
Been to some other place of entertainment (e.g. dance, club, bingo, casino)		
Been on any other outdoor trips (including going to places of natural beauty, picnics, going for a drive or going to the beach)		
Been involved in any community based activities (e.g. Scouts, going to church)		

2. I am now going to ask about sports activities. Could you please tell me whether or not you took part in any of these sports in the last month AND how often?

ACTIVITY	NUMBER OF TIMES	AMOUNT OF TIME
Swimming		
Cycling		
Gym/weight training		
Exercise classes (e.g. aerobics, martial arts)		
Team sports (e.g. rugby, football, cricket, hockey, netball)		
Racquet sports (e.g. tennis, badminton, squash)		
Jogging, cross country, road running		
Walking or hiking for 2 miles or more (recreationally)		
Climbing/mountaineering		
Fishing		
Golf		
Horse riding		
Pub games (e.g. snooker, pool, darts)		

3. How much time do you spend socialising? How many occasions in the last month have you seen friends, either visiting them or receiving visitors? How much time did you tend to spend socialising on each occasion on average?

> *Details*

CHILD CARE

1. Are you responsible for the care of any children?

YES	→	ASK 2
NO	→	GO TO 'HOUSEWORK AND CHORES'

2. How many children do you have? How old are they? Are you their primary carer?

3. How much time do you spend doing things with your children?

Physical care (e.g. feeding, dressing, washing)	
Supervision (inside and outside)	
Teaching children (e.g. helping with homework)	
Reading, playing and talking with children	
Accompanying child (e.g. to school, doctor, friend's house, etc)	

HOUSEWORK AND CHORES

How many people do you live with? Who is mainly responsible for the housework?

How much time do you spend doing housework and chores per week?

Food management and preparation	
Cleaning, dusting, vacuuming, washing dishes	
Food shopping	
Washing	
Gardening	
DIY and repairs	

B-16   MRI Safety Screening Questionnaire

MRI SAFETY SCREENING QUESTIONNAIRE

> EVERYONE must fill out this form BEFORE entering the MRI suite.
> The MRI suite has a very powerful magnetic field that may be hazardous to
> those with metallic, electronic, magnetic or mechanical implants or devices.
> All information will be kept strictly confidential.

BUIC
Birmingham University Imaging Centre

Name:		Date of Birth:	
Email:		Tel No:	

Section A – To be completed by EVERYONE entering the MRI suite

Please indicate if you have any of the following:	YES	NO	If yes please explain
Cardiac Pacemaker, pacing wires or defibrillator			
Aneurysm clip (metal clips put around blood vessels during surgery)			
Electrical Stimulator for nerves, bone or brain			
Ear or Eye implants (e.g. cochlear implants)			
Implanted insulin, drug or infusion pump			
Stent, catheter, coil or filter in any blood vessel			
Orthopaedic hardware (e.g. artificial joints, metal plates, screws)			
Any other type of prosthesis or implant			
Gun pellets, shrapnel, bullets or metal fragments			
Any surgery or an operation			

Section B – Complete ONLY if you are being scanned or intend to go inside the scanner room

Please answer the following questions carefully	YES	NO	Staff Notes
Have you had an MRI scan before?			
Are you claustrophobic?			
Have you ever been a welder, machinist, grinder or worked with metal without eye protection?			
Do you suffer from any medical condition that may be relevant (e.g. epilepsy, diabetes, asthma)?			
Do you have any tattoos or body piercings (other than earrings)?			
Do you wear dentures, a dental plate or a brace (not fillings)?			
Do you have any transdermal skin patches (e.g. nicotine patch)?			
(Females only) Are you or could you be pregnant?			
Please state your weight (kg)			
Other information (e.g. spectacle prescription)			

Please tick the boxes before being scanned or going inside the scanner room

I confirm that the above information is accurate to the best of my knowledge. ☐

I will remove all metal including mobile phones, keys, watches, coins, credit cards, body piercings, jewellery, false teeth, hearing aids etc before entering the scanner room. (Lockers available in waiting room.) ☐

I acknowledge that BUIC has taken reasonable precautions to screen for potential difficulties and is not liable for any event that might result from incorrect answers to the above. ☐

Signed:		Date:	

Form verified by (*Authorised Personnel only*):

Print Name:		Signed:		Date:	

Staff Note: This form is only valid for six months from date of initial screening   v4.0 July 2010

**B-17   fMRI Task Instructions**

08 May 2012

Theory of Mind – ATTRIBUTION OF INTENTIONS FMRI TASK
<u>Instructions to participants:</u>
While in the scanner we will be asking you to perform a task which will involve picture stories.

You will see 3 cartoons drawings presented one after the other on the screen. These will represent a story. Your task is to follow the story. After this story phase you will see two pictures displayed simultaneously on the screen. These pictures represent possible endings to the story. Your task is to choose the most logical ending by pressing the corresponding button as quickly as possible. Only one picture will represent the correct answer.

These two pictures representing the possible story ending are presented one next to the other in the middle of the screen. The left button corresponds to the picture on the left, and the right button corresponds to the picture on the right.
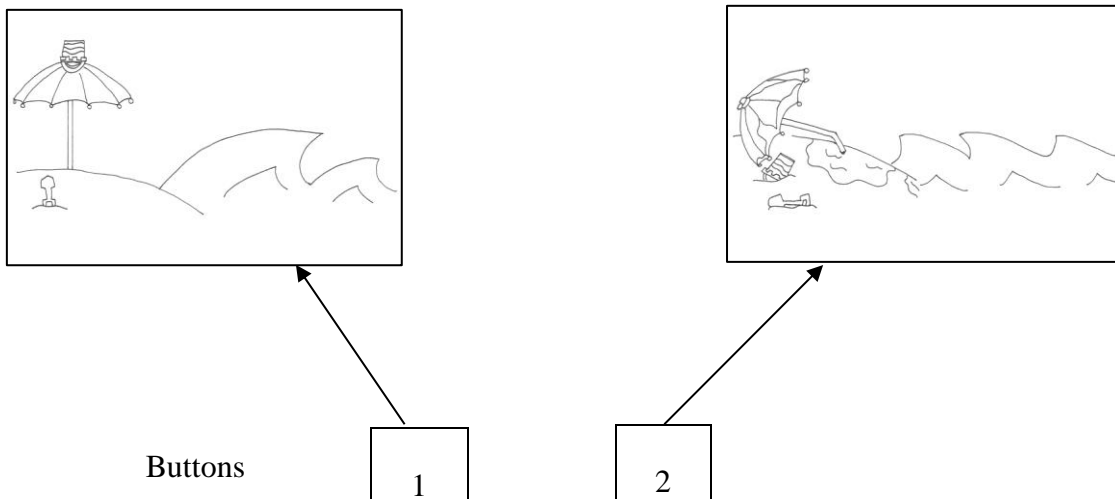
When you see a white cross or the word REST in the middle of the screen you can rest during this time but try not to look away from the middle of the screen and remember to remain as still as possible throughout the scan.

B-18	Personal Details Form

PERSONAL DETAILS FORM

NAME: _____   DOB: _____

SOCIODEMOGRAPHIC INFORMATION

Sex: 1 = Male   2 = Female

Ethnicity

White

1	British	2	Irish	3	Other White Background

Asian

4	Indian	5	Pakistani	6	Bangladeshi
7	Other Asian Background				

Black

8	Caribbean	9	African	10	Other Black Background

Mixed

11	White and Black Caribbean	12	White and Black African	13	White and Asian
14	Other Mixed Background				

Other Ethnic Groups

15	Chinese	16	Other Ethnic Group		

Country of birth (specify) _____

Fluency in English

0	No t fluent	1	Fluent - spoken	2	Fluent – spoken and written

Religious Cultural Tradition

1	Christian	2	Muslim	3	Hindu
4	Sikh	5	Other (specify)		

Marital Status

1	Married and cohabiting	2	Married but separated	3	Cohabiting > 2yrs
4	Cohabiting <2yrs	5	Single	6	Divorced
7	Widowed				

Postcode Area _____

Age at Entry to Study _____

CURRENT LIVING SITUATION

Living Status – At Baseline

1	Alone	2	With parents/guardians	3	With partner
4	Other				

Housing Type

1	Own home/parents home	2	Rented	3	Supported Accommodation
4	Temp. Accommodation	5	Long Stay Psychiatric Hospital	6	Other (specify)

EDUCATION AND EMPLOYMENT

Educational Qualifications Attained

0	No qualifications	1	GCSE/ NVQ level 1 or 2	2	A-level/ GNVQ/ BTEC/NVQ level 3
3	Degree/ HND/ NVQ level 4 or above	4	Special Needs Educational Qualifications	5	Higher Degree

Employment Status – At Baseline

1	Working (Paid)	2	Working (Voluntary)	3	Unemployed
4	Home maker	5	Student	6	Sheltered employment
7	Other (specify)				

No of hours worked per week

0	On sick leave	1	<16 hours	2	>16 hours < 36 hours
3	36 hours or more	999	N/A (Unemployed / Home maker)		

Client's Occupation: _____

Mother's Occupation: _____

Father's Occupation: _____

OTHER INFORMATION

Probable Diagnosis at Baseline

1	Unspecified Psychosis	2	Schizophrenia	3	Bi- Polar
4	Schizo-Affective Disorder	5	Drug Induced Psychosis	6	Paranoid Psychosis
7	Depression	8	Other		

No of Episodes: _____

Age at Onset   _____

No of Admissions: _____

Age at First Admission   --------Head Injury in lifetime (time spent unconscious)

0	Unknown whether injury has occurred	1	Very Mild (<5mins)	2	Mild (5 – 60 mins)
3	Moderate (1 – 24 hours)	4	Severe (1 – 7 days)	5	Very Severe (1 – 4 weeks)
6	Extremely Severe (> 4 weeks)	7	Injury – Unknown Severity	999	N/A

Epilepsy

0	None	1	Yes –No medication needed	2	Yes – Fits controlled by medication
3	Yes – Medication taken but fits not controlled	4	Other	999	Unknown

Antipsychotic Medication

Medication	Dose	Frequency

Other Information about Client

1	Possible mild learning difficulty	2	Possible moderate learning difficulty	3	Possible Autistic Spectrum Disorder
4	N/A	5		6	

Handedness: