A metacognitive account for the relationship between neurocognition and functional outcome in first-episode psychosis.

By

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is also why I appreciate it! It has an inherent value in my head due to the personal resource that went into it.

Personals…(turn away now!).

I first became unwell 11 years ago, a toxic mixture of the indignity and stigma of having to drop out of a Russell Group university due to my mental health, an education in a selective schooling system in which there was no room for vulnerability, and an unwillingness to admit there was a problem. I was unable to leave the bed or house at times and I remember the first time I walked to the local shops with crippling panic, anxiety and intrusive thoughts. That journey seemed insurmountable then and, in some ways, was just as difficult as my PhD. This body of work began just as much 11 years ago with that trip as it did 3 (and a bit!) years ago when I started at Sussex. I know the impact upon one's self-worth of such a combination of events and this is why, when I talk about recovery and functional outcome, I do not use these terms glibly. This thesis indelibly marks my personal road to recovery as much as academic achievement and I try to draw on this when I meet young people through work. This was also coincidently the year that Early Intervention in Psychosis services were being rolled out across the UK and I feel a certain affinity with them as such. I'm so glad that young people have these available to them in modern mental health and practitioners are trained to deal with their unique needs. Since then, I have returned to university, I have held down full-time jobs, I've completed a Masters degree and I am about to submit a PhD. I haven't done this without the help of lots of people along the way and I hope that over the coming years, I will get the opportunity to repay the faith that others have shown in me.

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Big love to all of you xxx

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Statement

I hereby declare that this thesis has not been and will not be submitted in whole or in part to another University for the award of any other degree.

Geoff Davies

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Summary

Neurocognitive and functional outcome deficits have long been acknowledged in schizophrenia and are considered a core feature of the disorder. Neurocognition has been found to account for functional disability to a greater extent than psychopathology however much of the variance in functional outcome still remains unexplained. How functional outcome is measured also requires clarification. By investigating the relationship between neurocognition and functional outcome in First-Episode Psychosis (FEP), much can be learnt about the trajectory of disability and the course of illness in schizophrenia.

Metacognition, or thinking about thinking, has been proposed as a mediating variable between neurocognition and functional outcome. Despite different theoretical backgrounds, authors generally converge on there being higher-order, explicit, conscious metacognitive knowledge and lower-order, implicit metacognitive processes. How these relate to each other requires clarification. The prefrontal cortex (PFC) has been implicated in higher-order thought and metacognitive processing, and deficits have been observed in PFC Grey Matter (GM) volume in schizophrenia. These metacognitive deficits may contribute to the relationship between cognitive ability and community functioning.

A preliminary meta-analysis demonstrated that a moderate effect size is found between neurocognition and metacognition and a moderate effect size exists between metacognition and functional outcome. The present thesis investigated whether metacognition mediates the relationship between neurocognition and functional outcome in FEP (N=80). Path models were created to investigate the different relationships between neurocognition, metacognition and both capacity to perform everyday tasks and objective functioning in the community. A secondary Voxel-based Morphometry (VBM) analysis was also conducted investigating perceptual metacognitive accuracy and its relationship to GM volume in both FEP (N=41) and a matched healthy control sample (N=21).

Current findings support the model that metacognition and negative symptoms mediate the relationship between neurocognition and functional capacity in FEP. Path models also demonstrated a significant mediation effect of metacognition between neorocognition and objective function, and functional capacity and objective function. Significant group differences were found between FEP and controls in perceptual metacognitive accuracy however no significant relationship was found between metacognition and GM volume in the PFC.

The present thesis suggests that metacognitive deficits are present at first episode and may account for the relationship between cognitive ability and functioning in the community. Findings also suggest that cognitive remediation programmes may wish to focus on metacognition to maximise the transfer of cognitive skills to community functioning. The findings also suggest the presence of two metacognitive processing routes; explicit, declarable, higher-order knowledge and implicit, intuition-based, lower-order experience which can be accounted for by Nelson and Narens (1990) metacognitive model.

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Chapter 1: General introduction

1.1 Schizophrenia and psychosis

Schizophrenia is thought to affect between 0.5% and 1% of the population and is viewed as a severe and chronic mental illness (Nuechterlein et al., 2012) estimated to cost the National Health Service £11.8 billion a year (Schizophrenia Commission, 2012). The most recent DSM V diagnostic criteria for schizophrenia requires two (or more) symptoms of delusions, hallucinations, disorganised speech, grossly disorganised or catatonic behaviour, or negative symptoms (affective flattening, alogia or avolition). At least one symptom must be present from the first three symptoms (American Psychiatric Association, 2013). The diagnostic criteria also emphasises that the symptoms must persist for at least 6 months unless otherwise treated, and have a significant impact on social or occupational functioning (Tandon et al., 2013). Research into functioning and recovery is therefore of utmost importance for treatment.

The aforementioned symptoms relate to an episode of psychosis which is central to a schizophrenia spectrum disorder diagnosis. This can occur in the absence of a formal diagnosis of schizophrenia and is comprised of a profile of percept-like experiences, which are not in the control of the individual, and have the same force or impact as the corresponding actual experience (Slade & Bentall, 1988).

The exact aetiology of schizophrenia is unclear; neurodevelopmental models suggest that genetics and early environment predisposes an individual toward psychosis (Aas et al., 2014) with social factors relegated to mere triggers in the process. Critics of this model suggest that genetic models fail to demonstrate the presence of a unitary disease process (Ruggeri & Tansella, 2009). Other authors adopt a psychosocial model of psychosis and posit that factors such as childhood trauma and hypothalamus-pituitary-adrenal axis (HPA) function can give rise to psychotic experiences (Read, Bentall, & Fosse, 2009). This matter is further complicated by the seeming heterogeneity in presentation between those given a diagnosis making causal models difficult to defend (Cochrane, Petch, & Pickering, 2010). Biological accounts for psychosis also fail to consider social factors, the timing of typical symptoms development, and subclinical psychotic experiences (Broome et al., 2005). Garety, in an influential model, suggests that biological vulnerability, cognitive, social and emotional factors are pertinent to the development of psychosis and the relationship between cognition and biology is a bidirectional one (Garety, Bebbington, Fowler, Freeman, & Kuipers, 2007). Regardless

of trajectory and cause of psychosis symptoms, modern research acknowledges the cause and cost of cognitive deficits in psychosis.

1.2 Schizophrenia and neurocognitive function

Kraeplin (1919) in his early dementia praecox work, observed the presence of cognitive deficits in serious mental illness and to this day they are considered a core feature of schizophrenia (Reichenberg & Harvey, 2007). Neurocognition is a constellation of cognitive processes such as speed of processing, attention, verbal and working memory, and executive function (Schmidt, Mueller, & Roder, 2011). Early influential studies estimated that 90% of patients demonstrate a clinically meaningful deficit in one cognitive domain and 75% in two or more (Palmer, Heaton, Paulsen, Kuck, Braff et al., 1997). More recent studies consider these estimates to be conservative (Green, Kern, & Heaton, 2004).

Early work on cognitive disturbances focused upon the attentional disturbances characterised in schizophrenia measured in reaction time experiments. Keeping with the zeitgeist of 1970s experimental psychology, those with a diagnosis of schizophrenia were found to be unable to integrate a series of tasks over time (Zahn, Rosenthal & Shakow, 1963) demonstrating two marked deficits; problems with control of attention and goal maintenance (Carter, Barch, Buchanan, Bullmore, Krystal et al., 2008). Bellissimo and Steffy (1972) also provide corollary evidence with their redundancy-association deficit work demonstrating deterioration in attention when cognitive demand increased. Finally, another discovery of the era which would shape later schizophrenia illness trajectory considerations, was that these pervasive impairments to attentional focus were stable across chronic and acute phases (Nuechterlein & Dawson, 1984).

Research has demonstrated that those with a diagnosis of schizophrenia show impairment on selective attention tasks; Kerns (2007) showed a schizophrenia sample to perform poorly on a Stroop Attention Interference Test with deteriorated performance compared to healthy controls in both accuracy and reaction times. In a meta-analysis, Kerns and Berenbaum (2002) also reveal a strong correlation between impaired executive functioning and thought disorder linking cognition to psychopathology. This executive function impairment has been interpreted as those with a schizophrenia diagnosis having cognitive disruptions that prevent the inhibition of competing responses and difficulties integrating contextual information into cognitive processes (Elvevaag, Duncan & McKenna, 2000). However, inferences on executive functioning must be made with caution as not all replications have found specific deficits in schizophrenia samples beyond a general ‘slowing’ effect (Gold, Rondolph & Coppola, 1992). In a Continuous

Performance Task, a cognitive test of vigilance, Servan-Schreiber, Cohen and Steingard (1998) found that, when the delay between cue and stimulus was increased, the schizophrenia sample responses were disproportionately inaccurate. The authors suggest this is indicative of disruption to alternative cognitive pathways to the aforementioned Stroop response neural structures. Poor performance on a CPT task has also been identified as a vulnerability marker for schizophrenia (Nuechterlein, Bauchsbaum & Dawson, 1994). However Elvevaag et al., (2000) were unable to replicate these findings instead reporting that response discrepancies occurred at shorter delay intervals. Goldberg and Green (2002) interpret these findings to be symptomatic of erroneous rapid encoding and acting upon stimuli processing or bias perceptual conceptualisation of target stimuli in the executive system. The aforementioned studies demonstrate a deficit in attention and information processing in those with a diagnosis of schizophrenia.

Executive function deficits in schizophrenia have also been investigated and notable impairments have been well described in literature. Experimental paradigms involving a Wisconsin Card Sorting Test which indexes demands on set shifting, cognitive abstraction and integrating feedback, find those with a diagnosis of schizophrenia to perform more poorly than controls (Heinrichs & Zakzanis, 1998; Lee & Park, 2005) and display performance levels comparable to frontal lobe lesion patients (Pantelis, Barber, Barnes, Nelson, Owen et al., 1999). Furthermore, Weickert, Goldberg, Gold, Bigelow, Egan et al., (2000) found these impairments to be present in chronic schizophrenia regardless of compromised premorbid intellectual function, preserved intellectual function and normal premorbid function that declined after onset. This indicates that executive function deficits comprise a core deficit in schizophrenia and are not accounted for by general IQ. Leeson, Sharma, Harrison, Ron, Barnes et al., (2009) also found executive function deficits in verbal learning and spatial working memory regardless of IQ however measures of IQ prove problematic in schizophrenia. Language deficits are a primary symptom of schizophrenia (Kuperberg, 2011) thus poor performance on IQ tests could reflect linguistic rather than cognitive abilities.

However some research indicates that these cognitive deficits are not necessarily certain or symptomatic of global cognitive impairment; Other researchers have found that a patient population ‘neuropsychologically within normal range’ exists (Palmer et al., 1997; Kremen et al., 2000). Whether this deficit is present prior or as a result of illness is also problematic to assert; Leeson et al., (2011) suggest that general IQ function post first-episode is most predictive of longer-term cognitive function rather than premorbid

assessment, indicating that the profile of neurocognition is not straightforward. Other authors have investigated neuropsychological profiles of people with schizophrenia to look for distinct subtypes; Hill, Ragland, Gur and Gur, (2002) report there to be 4 distinct clusters of cognitive profile; one of severe global cognitive impairment, a second of more milder general impairment with a deficit in verbal memory. Profiles three and four, although demonstrating moderate-to-severe impairments, showed an interaction between memory and executive skills with cluster 3 demonstrating greater impairment in executive skills but retained memory and cluster 4 demonstrating the opposite. The authors suggest this could have a large impact on cognitive interventions with tailored, profile specific remediation plans catering for specific rather than global deficits having a greater impact on recovery to the individual. Despite cognitive impairment being relatively stable post first episode, larger deficits have been observed in verbal learning and memory (Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009) and verbal learning also demonstrated a significant decline at 2 year follow-up (Torgalsbøen, Mohn, Czajkowski, & Rund, 2015) compared to other cognitive domains which remained stable. Unravelling the key cognitive determinants of both function and further cognitive deterioration is of upmost importance and authors remain equivocal on whether there is a global or domain specific cognitive deficit in schizophrenia.

1.3 Neurocognition in FEP

Neurocognitive impairment has also been investigated in FEP specifically. Mesholam-Gately, Giuliano, Goff, Faraone and Seidman, (2009) in a meta-analysis, demonstrate that similar deficits to chronic schizophrenia are found in FEP and support Leeson et al's (2011) subsequent suggestion that longer-term cognitive prognosis is stable to post-illness levels rather than premorbid function. Medium to large effect sizes are present across 10 neurocognitive domains with particularly noticeable deficits in verbal memory and processing speed however once again, there was considerable heterogeneity in effect sizes across studies. Fioravanti, Bianchi, & Cinti, (2012) interpret the heterogeneity in findings and attribute the unstable effect sizes across studies to be symptomatic of inconsistency in measurement and patient sample selection. Ayesa-Arriola et al., (2012) in a three-year longitudinal study found that 59% of FEP patients demonstrated cognitive impairment and sociodemographic and clinical characteristics at baseline were not predictive of impairment at 3 years. The authors also unexpectedly did not find that baseline cognition predicted 3 year functional disability however this could be due to the method chosen to measure function; the authors employed self-report measures with the suggestion that future recreations may wish to include functional capacity outcome measures instead as a more reliable indicator (Ayesa-Arriola et al., 2013) (see section

1.7 for review of outcome measurement). In a review, Bozikas and Andreou, (2011) also report both cognitive deficits in FEP, and that these deficits remain stable over time with the exception of verbal memory which may deteriorate further. The studies included in the review however were inconsistent and the authors suggest that those demonstrating a further decline could be due to different follow-up schedules. The authors suggest a subgroup of neurocognitively unimpaired people with a diagnosis of schizophrenia may exist and the relationship between this feature and psychosocial outcome is important to understand. This study however only included non-affective psychosis undermining external validity so generalisability to other types of psychosis is restricted. Haatveit et al., (2015) found similar stability in FEP for executive function across multiple measures between baseline and 1 year follow up with no significant change across time points. Furthermore, Greenwood, Morris, Sigmundsson, Landau, and Wykes, (2008) found little difference between FEP and chronic cohorts on executive function and memory tasks and differences between groups were determined from disorganisation symptoms rather than chronicity.

However previous research has to be evaluated against intrinsic limitations of cognitive assessments and the use of psychometric battery tests; Kuperberg (2010) saliently argues that, whilst these standardised batteries have the advantage of being well validated, they often probe multiple cognitive processes thus which specific domain each tasks assesses may vary between authors. There has been a concerted effort within experimental psychology and neuroscience to identify the component constructs that comprise neurocognitive processing and, whilst new measures have been devised that assess the 'cognitively pure' processes (Barch, Braver, Carter, Poldrack & Robins, 2009), research employing them is still to percolate through academic publishing. In short, if studies measured cognition with comparable or standardised tests which have strong validation and reliability information, comparing and contrasting across multiple populations would prove more defensible.

Summary

In summary, global deficits are observed in those with a diagnosis of schizophrenia however the exact cognitive profiles differ between individuals across domains. Working verbal memory, executive function and processing speed appear to have the most evidence of deficit pre and post first-episode however this could be due to selective measures being used in research. How cognition relates to function will be addressed in the next section.

1.4 Recovery and function in schizophrenia

Early Kraeplinian definitions of psychosis adopted the disease model and assumed the trajectory of illness as a progressive and degenerative process (Kraeplin, 1919). Traditionally the dominant theme of recovery in psychiatry was symptom reduction, hospital discharge and relapse prevention (Harvey & Bellack, 2009). Any improvements in presentation were largely interpreted as temporary symptom remission (Kraepelin, 1953) however the advent of antipsychotic medication in the 1950s and the discharge of patients to the community has led to a change in attitude. The dichotomy between medical and consumer defined definitions of recovery has merged with contemporary considerations of recovery largely regarded as a process rather than a definitive outcome (Harvey & Bellack, 2009). The recovery definition is changing in psychiatric care to a service-user defined one involving developing a positive sense of self-identity (Abdresen et al., 2003) and choosing and pursuing meaningful goals and aspirations (Davidson, 2005). In a recent review, Lin, Wood and Yung, (2013) argue that understanding psychosocial function in FEP is imperative to comprehending the cause of schizophrenia and highlight the importance of considering the patient's subjective experience of recovery in research design. With this shift in recovery attitude, new measures are required to capture the concept of recovery and return to function.

1.5 Models of recovery

A consensus held by the Centre for the Mental Health Services of the Substance Abuse and Mental Health Services Administration (SAMHSA 2008) outlined the following fundamental components of recovery; it must have self-direction, be individualised and person centred, develop empowerment, be holistic, nonlinear, strengths based, contain peer support, respect, responsibility and hope. Pitt et al., (2007) devised a service-user led study examining the subjective experience of recovery from psychosis. The authors conclude that recovery is a complex process to evaluate and suggest that the concept should incorporate rebuilding one's life, rebuilding the self and fostering hope for a better future. Leamy, Bird, Le Boutiller, Williams and Slade (2011) in a systematic review also acknowledge the importance of culturally specific definitions of recovery; recovery for individuals of black and minority ethnic origins also demonstrated a greater emphasis on spirituality and reducing stigma in subjective sense of recovery.

The involvement of service-users in defining recovery is pragmatic and encouraging however a working definition employable in research is still to be developed. Definitions that are too stringent make them impossible to realise and of little value however if the working definition is non-defined and too broad, it makes the achievement unimportant (Bellack, 2006). Shrivastava et al., (2010) conclude that outcome measures must be

multidimensional incorporating both social and clinical features but future attempts to measure these still find discrepancies between symptoms remission and functional outcome despite more sophisticated measurement techniques (Oorschot et al., 2012). Oorschot et al., (2012) attribute disparities between sufficient symptom remission and poor real-life functioning to i) cognitive dysfunction ii) low mood or, due to non-completion of social milestones, iii) return to poor premorbid function.

1.6 Functional outcome

The medical perspective on recovery is derived from the definition of schizophrenia as a disease and reflects an elimination or significant reduction of symptoms and a return to premorbid levels of function (Torgalsbøen, 2005). This measure is problematic for a number of reasons however; there is no account for situations wherein there is symptom remission but the illness persists, it fails to consider the potential for profound alterations to premorbid status but a return of function and thirdly, the measurement is empirically vague. How long must symptoms dissipate for, what extent of remission is required and how is premorbid functioning or potential measured retrospectively? (Bellack, 2006).

Even if symptom remission is achieved, these alterations do not necessarily translate to improvements in social factors or functional outcome (Shrivastave et al., 2010). Furthermore, the relevant aspects of recovery and the choice of person to complete the rating (service-user, family member or clinician) has been shown to affect measure outcome (McCabe et al., 2007).

1.7 Self-report measures

Self-report instruments are simple and inexpensive however they are problematic as they are influenced by poor insight and cognitive function (Atkinson et al., 1997). Further Bowie et al., (2007) found that accurate self-raters had the highest social skill function and over-estimators had the most deteriorated cognitive functioning which questions the conclusion that positive self-report ratings are direct reflections of better function or capacity. This suggests that an individual with poor cognitive function may inaccurately rate themselves as performing better than they are. Subjective illness belief, or the subjective belief in disability or recovery, is also confounded by insight and depressive symptoms; improved clinical insight has been associated with depressive symptoms which lead to less accurate, more negative subjective ratings of recovery (Cavelti, Beck, Kvrgic, Kossowsky, & Vauth, 2012). Thus those that are doing objectively better may report worse functioning or less enjoyment of life.

1.8 Global measures

Another common measurement of function is the clinician-rated Global Assessment of Functioning (GAF) measure wherein clinicians assign a score across 10 domains to signify a single value for overall level of functioning (0-100 total). This is the recommended tool by the DSM-IV to capture social, occupational and psychological functioning and relies upon the clinician's opinion of patient functioning. The GAF has been assessed for reliability and validity (Jones et al., 1995) and is one of the most widely used measures of current functioning in research (Robertson et al., 2013). Reviews question the consistency in interrater reliability (Mausbach, Moore, Bowie, Cardenas, & Patterson, 2009) and other studies fail to demonstrate an ability to associate with real-world social function (Roy-Byrne et al., 1996), This raises questions pertaining to the scales internal and external reliability. In a study of FEP, Vesterager et al., (2012) found that the GAF was 'impressionistic' and lacking in nuance neglecting the grey areas present in independency. Robertson et al., (2013) also report that, whilst the GAF is sensitive to changes in clinical presentation, it misses some aspects of social function and the authors advise the inclusion of supplementary outcome measures when capturing psychosocial outcomes.

1.9 Objective measures

Early objective measures of function were generally based on dichotomous variables such as whether employed or living independently. However, these are victim to a host of social factors (such as background socio-demographic circumstances and socio-political climate) rather than just recovery processes (Patterson & Mausbach, 2010).

Other research has adopted a more sophisticated objective measure of social functioning. The Time Use Survey (TUS), developed by the Office for National Statistics (ONS) looks to directly measure the amount of time an individual spends in structured activities over the preceding month. Existing measures of objective function have been criticised for lack of sensitivity and meaning (Shepherd et al., 2008) and for overemphasis on employment alone (Killackey et al., 2008). The TUS taps a multitude of occupational, educational, social, exercise and household domains and calculates the average number of hours spent per week in each type of activity in the real-world (Fowler et al., 2009). In addition, due to the National Survey 2000 employing the same measure, meaningful comparisons can be made between people with a diagnosis of schizophrenia or FEP and similar cohorts in the general population (Hodgekins et al., 2015).

Many functional recovery approaches also compare functioning to those in the general population or rate recovery on indices appropriate for normative samples. Wunderink, Sytema, Nienhuis, & Wiersma, (2009) consider this a difficult concept and question how

expected levels of functioning are to be determined for an individual that's been through psychosis. Around two-thirds of a FEP sample remained functionally impaired despite being classified as in symptom remission and the authors also question the time frame in which follow-up functional measures are to be performed in order to be meaningful. Follow-up measure timeframes may vary from 1 month to 10 years and selecting a meaningful window in which to measure functional outcome isn't standardised. Symptom and functional trajectories demonstrate different pathways in FEP too; Ventura et al., (2008) found that at 12 month follow-up 22% of a FEP cohort demonstrated symptom remission however only 7% were in functional remission. Also, premorbid social functioning significantly predicted 2 year follow-up functional status, with other studies suggesting that social dysfunction is present in prodromal (Niendam et al., 2009) and premorbid phases (Bratlien et al., 2013). Thus whether social disabilities are caused by or a contributing factor to psychosis is difficult to tease apart. By conducting research into functional outcome in FEP, some of these questions can begin to be addressed by understanding factors present at onset.

McKibbin et al., (2004) assessed direct observations of people with a diagnosis of schizophrenia in their natural setting completing daily tasks and found these assessments to be reliable and comprehensive. These assessments however are costly to administer in addition to being time consuming and lacking in standardisation which has led to the development of performance-based task measurements. Real-life activities and scenarios are set up wherein the participant has to negotiate daily tasks under observation, thus measuring individual capacity in a controlled environment.

1.10 Functional capacity

Measures of functional capacity assess the extent to which an individual can complete necessary tasks or activities in their daily life (Patterson & Mausbach, 2010). These assessments such as the UCSD Performance-Based Assessment (UPSA: Patterson et al., 2001) are victim to criticisms regarding ecological validity (McKibben et al., 2004), but the UPSA has demonstrated good interrater reliability (Harvey et al., 2004) and test-retest reliability (Green et al., 2008). Furthermore, the UPSA has demonstrated sound criterion validity (Twamley et al., 2002) and Mausbach et al., (2009) in a review suggests that, whilst there is no 'gold standard' in functional measurement, the UPSA demonstrates a closer relationship to real-world outcome. The authors suggest that performance-based measures of functional capacity may provide the most sensitive and valid measure of functional recovery in psychosis. Finally, Faber et al., (2011) raise the issue of a need for a standardised criteria for assessing functional outcome as the

multitude of measures employed currently make cross-study comparisons difficult to interpret.

Performance-based measures are employed as a proxy measure of real-world behaviour and the discrepancy between what an individual is capable of and what they actually do has become an area of intrigue in recovery research. The relationship between neurocognition and functional capacity has been found consistently (e.g. Keefe, Poe, Walker, & Harvey, 2006) however which factors bridge the relationship between capacity and actual outcome is less clear cut. A host of variables have been suggested to mediate the relationship between functional capacity and functional outcome such as negative symptoms, motivation (Bowie et al., 2008) and social cognition (Pinkham et al., 2006). Accounts vary however depending on which measure of functional outcome is employed and the effects are sometimes lost once demographic and symptoms are included in analysis (Mausbach et al., 2010). Social competency (Mancuso, Horan, Kern, & Green, 2011), self-efficacy (Cardenas et al., 2012a) but not recent experience (Gupta, Bassett, Iftene, & Bowie, 2012) have all been suggested as potential variables to bridge the gap between capacity and actual performance but no clear picture has been identified. It appears that real-world function does depend on capacity as studies demonstrate the two to converge however, when there are disparities between performance in the two domains, what is inhibiting the former when the latter skills are present is less simplistic to assert.

Summary

In summary, there are a variety of measures available for capturing function with differing qualities. As models of recovery have shifted, so too has the way recovery is viewed and, as a primary treatment target, understanding more about the concept is critical. The performance-based measures of capacity appear to be the most validated however their ecological validity is questionable. This suggests that research designs may want to include additional real-life objective measures of function as well. An approach adopting multiple measures of function is important to further understand the relationship between illness and outcome. By combining a validated calculation of personal capacity to complete typical daily tasks and a meaningful objective measure of the actual time spent in structured activities in the community, both aspects of functional outcome can be measured and investigated. Whilst the experience of the individual and personal extent to which they feel part of the community and recovered is of tantamount importance for treatment, it proves problematic for research into functional outcome due to a multitude of confounding variables such as insight and mood. Likewise, clinician or family-member rated measures of global function are subjective, do not consider the individual's

experience and underestimate the subtlety of different types of recovery. Individuals can recover in some domains and not others making an overall global function measure difficult to interpret.

1.11 Neurocognition and functional outcome

Whilst neurocognitive impairments in schizophrenia have been well documented throughout the 20th century, it was the assertion that specific neurocognitive processes may be linked to functional outcome and therefore the target for therapeutic interventions that caused a consolidation of academic focus in the 1990s (Green 1996; Green et al., 2004). Despite nascent studies being atheoretical and underpowered due to small sample groups (Goldberg & Gold, 2002), they identified the critical role of neurocognition in functional outcome and provided research with the impetus to scrutinise cognitive impairments in schizophrenia with a new focus. Neurocognitive deficits are present in chronic, acute and symptom remission stages of illness (Hoff, Svetina, Maurizio, Crow & Spokes, 2005) and they are a more robust predictor of functional outcome than clinical symptoms alone (Palmer, Dawes & Heaton, 2009). In a seminal study, Green (1996) highlighted the role of neurocognition in accounting for outcome in 3 domains; independence in community function, skill acquisition and social problem solving. Both cross sectional and longitudinal studies have determined that neurocognition predicts work performance, social skills and community functioning (Green et al., 2000) and is thus a valid target for psychosocial interventions (Lincoln, Hehl, Kesting & Rief, 2011). Further, a more profound interaction has been found between cognition with negative symptoms than positive symptoms (Greenwood et al. 2005; Schmidt, Mueller and Roder, 2011) in predicting function.

Improved working memory has been associated with increased occupational functioning (Hofer et al., 2005), clinical and functional outcomes (Gagan Fervaha, Agid, Foussias, & Remington, 2014) and processing speed with improved social and functional skills (Bowie et al., 2008. Fett et al., (2011) in a meta-analysis found the strongest relationship between neurocognition and function to lay between verbal fluency and community function, and reasoning and problem solving with social problem solving. The authors note that, whilst various domains of neurocognition demonstrate small to large correlations with functional domains, the overall variance explained was relatively low (23.3%). This means that over 75% of the variance in functional outcome remains unaccounted for by neurocognition and the authors also remark on the different definitions of functioning within the research community. This finding is comparable but even smaller than Green's early paper suggesting that 40-60% of the relationship is

understood (Green et al., 2004) however, with the greater number of studies available to Fett et al., there is no reason to doubt this more up-to-date estimation.

Couture, Penn and Roberts (2006) provide support for Fett et al., and report that studies exceeding 40% of variance were the exception rather than the norm leaving 60-80% of the relationship unexplained. Some studies, whilst demonstrating a significant relationship find even lower variance in their model with neurocognition, social cognition and negative symptoms only accounting for 7.3% of the variance in self-reported functioning (Couture, Granholm, & Fish, 2011). The method of measurement however (self-report rather than interview or capacity measurement) may explain this particularly low figure. To complicate an already complex picture, neurocognition has been found to account for objective but not subjective experience of outcome (Tas et al., 2013) highlighting that definitions and measurement of outcome is critical to results. This spearheaded the search for possible mediating or moderating variables to more parsimoniously explain the resulting functional outcomes deficits in schizophrenia.

1.12 Neurocognition and functional outcome in FEP

Functional outcome has also been investigated in FEP with working and visual memory found to be significant predictors of functional capacity (Vesterager et al., 2012). Stouten, Veling, Laan, van der Helm and van der Gaag (2014) report that, whilst psychopathology was most predictive of psychosocial function at baseline, neurocognitive domains significantly predicted 12 month follow-up general function. However, the relationship is not as linear as expected; general cognition (Addington & Gleeson, 2005) and verbal learning (Milev, Ho, Arndt, & Andreasen, 2005) have been found to strongly predict function but these predictors were not replicated in the Stouten et al., (2014) study which found an emphatic effect of visual learning on outcome. Where a relationship has been found in FEP between improved cognitive function and better functional outcome, the variance accounted for is often lower than in chronic samples (e.g. Ayesa-Arriola et al., 2012). Tandberg, Ueland, Andreassen, Sundet, and Melle, (2012) found no significant difference between occupational outcome based on neurocognitive ability and Bratlien et al., (2013) found a significant relationship between improved psychomotor speed, but not verbal memory, working memory or executive function, on social function. Finally, O'Connor et al., (2013) found that only negative symptoms significantly predicted functional outcome at 12 months with, contrary to their hypothesis, cognitive ability not contributing to their overall predictive model.

Summary

The aforementioned studies reflect the trend of cognitive dysfunction and reduced functional outcome in FEP however the results differ in effect size magnitude and across

cognitive domains. Some of the difference in findings are due to the different methods of capturing functional outcome; some authors suggest their findings do not align with existing work due to overall global functioning scales failing to capture heterogeneity in outcome. There is a clear relationship between functional capacity and functional outcome but they appear to be related but separate concepts; having the ability to complete a task and integrating this into complicated daily life requires different levels of recovery and function. The latter being influenced by a range of other external factors as well. It is clear that measuring functional outcome requires multiple measurements in experimental design. In addition, self-report and global measures of overall function are difficult to assert specific causal relationships between domains of function and the mechanisms driving them. Finally, whilst a relationship exists between improved neurocognitive ability and better community outcomes, many of the review papers demonstrate that neurocognition only accounts for a small-to-medium amount of the variance in functional outcome. This suggests that other factors may account for functional outcome and provide a more parsimonious account for the relationship with cognition. The relationship at first onset is less clear cut; with studies such as O'Connor et al., (2013) finding no clear relationship whereas Milev et al., (2005) reporting a strong relationship between cognition and functional outcome. Whether negative symptoms or neurocognition drives functional outcome most at this stage needs clarification. By conducting research at this crucial stage, the factors which impact on return to function are less impacted by medication, access to treatment and chronic social disability. If more is understood about this early phase of illness, meaningful initiatives can be introduced to get those experiencing psychosis 'back on track' before continued social atrophy.

1.13 Neurocognition and functional outcome: The search for further explanation

Early authors identified the need to find additional variables to fully account for the relationship between neurocognition and functional recovery (e.g. Green, Kern, Braff, & Mintz, 2000) and later reviews have suggested that mediating variables offer a greater account for the mechanism between cognition and function (Bell, Corbera, Johannesen, Fiszdon, & Wexler, 2011). Social cognition has been proposed as both a mediator of neurocognition and function, and as a predictor of functional outcome (Brekke & Nakagami, 2010) as it has been demonstrated to show consistent relationships with both constructs. Social cognition refers to the cognitive operations which underpin social interactions such as the perception, interpretation, and response generation to the disposition and intentions of others (Couture, Penn, & Roberts, 2006). The role of social cognition in functional outcome has been galvanised from a variety of sources with

Adolphs (2009) demonstrating in a neuroimaging study that social and non-social information processing rely on semi-independent neural pathways. Social cognition encompasses a multitude of cognitive tasks however research has tended to focus upon emotional and social perception, social schema and knowledge, social attributions and Theory of Mind (ToM) (Schmidt et al., 2011). Studies have shown social cognition to account for an additional amount of variance in outcome after controlling for neurocognition (Addington, Saeedi & Addington, 2006). Fanning, Bell, and Fiszdon, (2012) sought to extend this research rationale and test whether both concepts were mutually exclusive and found that normal range neurocognition is a prerequisite but not a guarantee of good social cognition. Social cognition appears to certainly relate to social competence and relationships however the extent to which it predicts general functional recovery is less certain. Fett et al., (2011) in a meta-analysis of this relationship, report that social cognition accounts for a greater amount of the variance in functional outcome than neurocognition alone (16% versus 6%), however a large portion of functional outcome remains unaccounted for.

Other candidate variables have also been suggested as mediators of the relationship between neurocognition and functional outcome. Defeatist beliefs have been proposed to precede functional outcome after social cognition on a pathway model (Green et al., 2012) and Grant and Beck, (2008) report defeatist beliefs to mediate the relationship between neurocognitive function and outcome. The authors do however stipulate that the pathway between neurocognition and defeatist beliefs could be bidirectional (defeatist beliefs could dictate worse neurocognitive performance) so causal pathways are difficult to determine. Defeatist beliefs have also been associated with motivation; Nakagami, Xie, Hoe and Brekke, (2008) found that intrinsic motivation mediated the relationship between neurocognition and psychosocial function. Nakagami, Hoe and Brekke, (2010) investigated this relationship further with a longitudinal study and found that intrinsic motivation correlated with neurocognition at baseline however it did not predict functional outcome at later time points. Rather, baseline motivation did predict future neurocognitive ability with the authors concluding that motivation may underpin cognitive recovery. In a more recent study, Fervaha, Foussias, Agid and Remington, (2014) investigated this relationship further and report that, whilst both neurocognition and motivation significantly predicted function, the contribution was independent from each other.

The relationship between symptoms and functioning has demonstrated mixed findings. Positive symptoms have shown a lack of relationship with functional capacity (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006) and functional outcome (Vesterager

et al., 2012) and a similar lack of relationship is found between disorganised symptoms and social outcomes (Tandberg et al., 2012). Although a number of other studies do show relationships between disorganisation and occupational function (e.g. Liddle and Morris 1991). Negative symptoms have been found to have a significant relationship with neurocognition (Couture et al., 2011), social functioning (Bratlien et al., 2013) and quality of life (Fervaha, Foussias, Agid, & Remington, 2014) and the impact of cognition and negative symptoms on outcome may be synergistic (Greenwood, Landau, & Wykes, 2005). However other authors suggest the explanatory power of cognition and negative symptoms may overlap with each other rather than functioning as unique determinants of outcome. In a follow-up study interestingly Stouten et al., (2014) found that negative symptoms have more of an impact on functioning at baseline but cognitive abilities are better predictors of functional recovery in FEP.

Studies have directly tested the ability of negative symptoms to mediate the relationship between neurocognition and psychosocial function with significant mediation effects (Lin et al., 2013) and partial mediation effects found (Ventura, Hellemann, Thames, Koellner, & Nuechterlein, 2009).

Summary

The relationship between neurcognition and functional outcome is an established one however the scope of neurocognition to account for total variance in function is limited. Candidate mediating variables have been suggested however none so far offer a parsimonious account for this relationship and only offer slightly more explanation than neurocognition alone. Estimates vary but 40-60% of the relationship is yet to be accounted for with traditional models and how functional outcome is measured needs to be better defined in study design.

Another suggested candidate variable to account for the relationship between neurocognition and functional outcome is metacognition. The gap between possessing the raw cognitive abilities and implementing them into the social world may be due to a deficit in monitoring and regulating the cognitive component and reflecting back on mental states to improve social outcomes. Metacognition will be defined and discussed in the following section.

1.14 Models of Metacognition

Despite a ‘fuzzy’ and inconsistent definition in 30 years of research, (Akturk & Sahin, 2011) contemporary epistemological accounts of metacognition incorporate a finer grained definition than the generic ‘thinking about thinking’ description and acknowledge the multifaceted nature of a complex neural system. Many modern conceptualisations

report a duality in form or a dual processing model of metacognitive function however theorists differ in distinctions to be made across a variety of indices.

Schraw and Moshman, (1995) propose there to be 3 types of metacognitive theory; *Formal* theories are highly developed and systemised accounts of cognitive phenomenon demonstrating an expertise that allows the individual explicit access to the constructive nature of internal theories and so that they can be the architect of self-regulation (Kuhn et al., 1992). *Informal* theories are fractured and not fully integrated into an ubiquitous metacognitive system; the individual will have domain specific beliefs or assumptions about a cognitive matter thus they are partially explicit and therefore adaptable and testable for development and refinement (Schraw & Moshman, 1995). *Tacit* theories in comparison are developed without an explicit awareness that they are possessed, and are thus not cognitively scrutinised or tested against relevant data (Kuhn, 1989).

Flavell (1981) marks a distinction between metacognitive *knowledge* and *experience*; knowledge refers to the known, explicit understanding of internal mechanisms relating to goals and actions in both the self and others whereas experiences are conscious, affective states relating to a particular cognitive process (Flavell, 1981). In later work, Flavell (2000) also advocates that experiences relate to the planning, monitoring and regulation of thoughts in an executive coordination manner with the addition of integrating emotional states that accompany intellectual activity. Koriat (2000) further dissembles metacognitive experience into two levels of operation relating to consciousness; a higher level, *theory*-driven, explicit mode of operation incorporating a high level of both consciousness and control, and a lower-order *experience*-based form of metacognitive judgement that is often subconscious and intuitive (Koriat & Levy-Sadot, 1999; Koriat, 2000). More pertinently, research indicates that these intuition based, implicit judgments are commonly relied upon without scrutiny (Koriat, 2007) and resistant to change (Nussinson & Koriat, 2008).

Saxe and Offen (2012) also differentiate between different hierarchal levels of metacognitive function in neuropsychiatric literature. *Attributive* metacognition can be considered akin to metacognitive knowledge and concerns the capacity to relate beliefs and desires to one's self to inform self-knowledge. This can be compared to *strategic* metacognition describing the control and monitoring of online mental processes. Thus, attributive metacognition concerns beliefs and desires in relation to the self whereas strategic metacognition relates to mental activities and processes. The resulting actions inform self-explanation in the attributive stage, and monitoring in the service of control in

strategic metacognition (Saxe & Offen, 2012). Furthermore, Nichols and Stich (2001) offer similar hypotheses with a distinction between thinking about and monitoring inner states; they propose that different mechanisms are involved in *thinking about* internal processes and *monitoring* them which can be considered in light of Tulving's (2005) distinction between conscious autoneotic and unconscious noetic processes.

Metacognition: a fractionated system?

Muñoz (2010) attempts to consolidate these different processing avenues by categorising theories into two camps; metarepresentational and control theories. Metarepresentational theories adopt the abstract, explicit 'thinking about thinking' approach and relate to the self-ascription of mental states based on an earlier mental state attribution in order to rationalise and interpret behaviour (Proust, 2007). Thus metacognition is conceptually likened to 'turning our mindreading capacity upon ourselves' (Carruthers, 2009). This approach adopts similar conceptual architecture to ToM processing in that behavioural cues are interpreted (either self or other's) and mental inferences or second order representations are based on this framework (Muñoz, 2010). Control theories view metacognition purely as a monitoring and evaluation process in the form of an offline simulation of currently engaged cognitive processes to assist with prediction and adjustment to the task at hand (Proust, 2007). Muñoz (2010) attempts to consolidate these two approaches into a homunculus-like integrated system of cognitive appraisal and control. The lower order control theories based on feeling-induced control heuristics to adjust and monitor tasks without requiring the resources that a higher metarepresentional level of processing require.

Both components interact with each other in this dual-process model either through bottom-up instigation of higher order processes (a feeling of uncertainty in monitoring may trigger the instigation of higher order processing) or top down processes wherein metarepresentations align with lower order affective states to become more salient. A further interaction may be the inhibition of lower-order processing from the second-order belief that a mistake is going to be made; this feeling of uncertainty may lead to the initiation of more cognitive scrutiny of lower-order processing to avoid potential errors. Schwarz and Vaughan (2002) demonstrated this effect by exposing participants to a theory relating to the unreliability of feelings in relation to task performance. The information questioning the reliability of feelings of familiarity facilitated participants reporting more apprehension to rely on a feeling of familiarity and engage additional, higher order strategies when processing information.

Previous explanations for metacognitive processing appear to be approaching a consensus on there being a stratified or layered system at play. Despite contrasting definitions and terminology, some clarity is found between lower-order processes relating to unconscious, monitoring functions of subservient cognitive mechanisms and a higher-order metarepresentation system incorporating stored references to these representations across a variety of tasks.

Lysaker et al., (2005) propose a hierarchal model of metacognition with incremental stages of increasing metacognitive sophistication. This commences with acknowledging that an individual has mental functions all the way through to a ninth stage wherein cognitive and emotional states are integrated into a coherent, social narrative. This rubric has then been employed to assess metacognitive capacity through clinical, semi-structured interviews and to inform psychotherapy (Lysaker et al., 2011). Lysaker et al., (2011) relate metacognition to a series of interrelated processes such as the ability to form a representation of one's mental state and the mental states of others, and relate these to emotion and behaviour in evolving social contexts. Whilst social cognition requires the identification of mental state information of 'the other' through discrete judgements, this is based on cues such as emotional perception and facial expressions or language. The more synthetic self-mental state representation requires declarative knowledge of higher-order thoughts based on self-reflection and behavioural integration. Thus, social cognition and metacognition are suggested to require different processing pathways (Lysaker et al., 2013) although it must be noted that not all authors agree on this point (see Carruthers (2009). This inability to produce representations, scrutinise them for fallibility and problem solve in daily life (Dimaggio, Lysaker, Carcione, Nicolò, & Semerari, 2008) leads to synthetic deficits in thought and results in impoverished functioning (Lysaker et al., 2005). This synthetic metacognitive ability has been found to be related to but conceptually unique from deficits in neurocognition (Lysaker et al., 2013) and accounts for deficits in social function (Lysaker et al., 2011).

The relationship between cognitive processes and how we regulate them has been considered in Nelson and Naren's (1990) influential model of metacognitive control (figure 1 below).

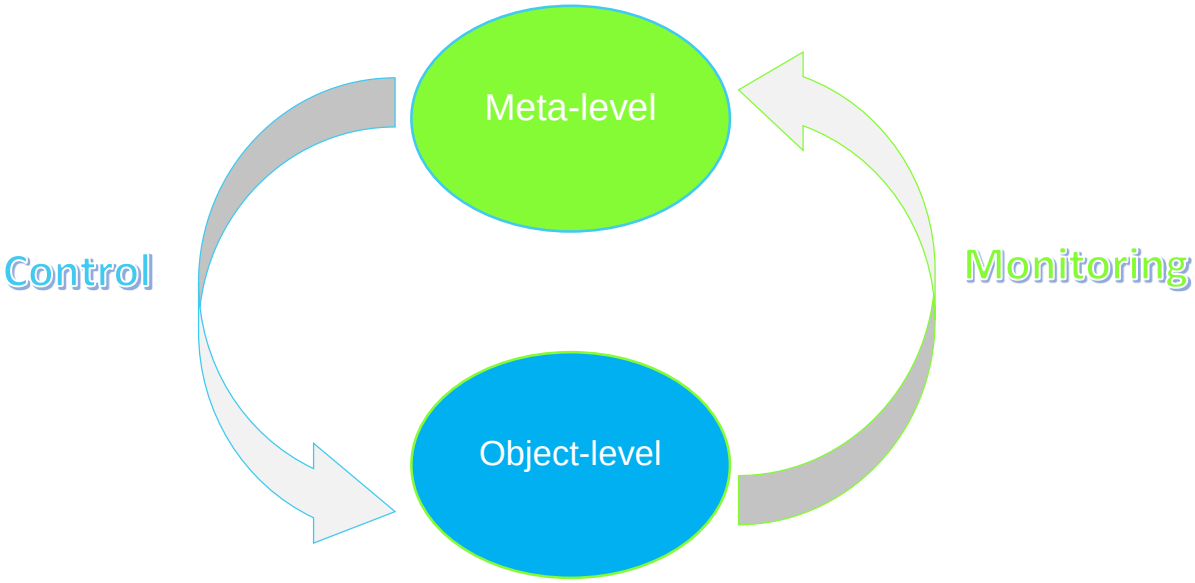

Figure 1: Adapted from Nelson and Narens, (1990)

Nelson and Narens originally proposed their model to account for memory processing. They posit that cognitive processes function on two interrelated levels; object and meta-level. Object-level processing pertains to basic cognitive processes (perception, memory, etc.) that send feedback up to the meta-level structure through monitoring processes. The meta-level structure has an abstract plan of object-level function, appraises the effectiveness of cognitive or behavioural strategies and exerts control through initiating, terminating or allowing object-level processes to continue. This dyadic model has been applied to emotional disorder (Wells & Matthews, 1995) and mapped onto hierarchal brain structure through posterior and prefrontal cortices (Shimamura, 2008).

One distinction made in the literature is between metacognitive knowledge and regulation or experience. Metacognitive knowledge broadly corresponds to the information individual's possess about their cognition and the factors that impact on it. Regulation in comparison refers to the executive control and resource allocation given to cognitive tasks and the planning, checking, and error detection in performance (Brown, Bransford, Campione & Ferrara, 1983). Metacognitive knowledge can be explicit (conscious, accessible and declarable) or implicit (not conscious, often intuitive and feeling based) and aligns with Frith's (2012) model of metacognitive control. Metacognitive experiences in comparison are appraisals that the individual makes of mental events and their meaning and judgements about the status of cognitions. Metacognitive experience is the 'online' use of metacognitive knowledge wherein cognitive process are appraised and processed at either task or complex judgement level (Efklides, 2008) and has been observed in 'tip of the tongue' phenomena (Shimamura, 2008). Metacognitive skill or control is the response the individual makes in regulating

slave cognitive systems and directs the individual toward a desired goal based on feedback from the cognitive system (Jankowski & Holas, 2014). This latter concept can be seen in the control aspect of the Nelson and Narens model (figure 1) whereas the variety of metacognitive knowledge resides in the meta-level structure.

1.15 Neural underpinnings of metacognition

Metacognitive processing has been implicated in frontal regions through a series of studies. Investigations in Korsakoff's syndrome demonstrate deficits in metamemory processing (Shimamura, 2000) and this finding has also been found in patients with frontal lobe lesions (Pannu & Kaszniak, 2005). Increased activation has been observed in the inferior frontal gyrus for correct FoK judgments (Kikyo, Ohki, & Miyashita, 2002) and increased activity in the ventromedial PFC has been seen to correlate with more accurate prospective Judgements of Learning (JOL) (Kao, Davis, & Gabrieli, 2005). Fleming et al., (2010) in a retrospective confidence-based metacognitive judgement task, found a relationship between increased GM volume and metacognitive accuracy in BA10 and greater white-matter microstructure connecting the PFC to the corpus callosum. This indicates that both the local processing and the integration of multiple processing routes may be important aspects of accurate metacognitive ability. Buchy, Stowkowy, Macmaster, Nyman and Addington (2015) report reduced cortical thickness in the insula, frontal and temporal regions in relation to lower metacognitive ability as measured by the MAS in a clinically high risk (CHR) cohort. Furthermore, (Vohs et al., 2015) found greater GM density in the medial prefrontal cortex and ventral striatum correlated with improved metacognition. These regions have been seen to be implicated in cortical atrophy in schizophrenia (Watson et al., 2012) and may account for the metacognitive deficits also observed in the same sample.

1.16 Measuring metacognition

Metacognition has been measured in a variety of ways illustrated in table 1 below. Depending on the adopted working definition, measurement is difficult due to metacognition not being a directly observable behaviour and individual's not always being aware of the process (Akturk & Sahin, 2011). Fleming and Dolan (2012) distinguish between prospective and retrospective judgements; metamemory research has asked participants to make prospective judgements of learning assessments of future task performance (Do Lam et al., 2012). Feeling of Knowing and tip-of-the-tongue states are employed with recognition tasks where an item cannot be recalled; a participant is asked to indicate whether they 'feel' they know the item although deficits have not been reported in schizophrenia literature for this domain (Elisabeth Bacon & Izaute, 2009). Learning theorists have also investigated working metacognition through 'think aloud

protocols ‘asking participants to verbally report on current cognition. Such measurement strategies however are time consuming, interfere with the cognitive task at hand and only access declarable meta-level processes (Akturk & Sahin, 2011). Questionnaires have also been employed such as the metacognitions questionnaire (MCQ), the Metacognitive Awareness Inventory (Schraw & Dennison, 1994) and the Metamemory Inventory in Adulthood (MIA) (Dixon et al., 1988) tapping general beliefs about cognition and perception of memory. These questionnaire-based methods are cost-effective and allow for the widespread investigation of metacognition however they are not task specific and do not offer insight into the basis for the belief or judgement. A factor analysis of the Metacognitive Awareness Inventory also revealed that, despite the original authors suggestion of an overall metacognitive system, that the concept is distinctly multivariate (Rahman & Masrur, 2011). This suggests that deficits may occur in multiple domains although this may be more of an indictment on the validity of the questionnaire than reflective of metacognition per se. Self-reflection has also been assessed and considered a metacognitive domain through the Beck Cognitive Insight Scale (BCIS) (Beck, Baruch, Balter, Steer, & Warman, 2004) and the Self-reflection and Insight Scale (SRIS) (Grant et al., 2002) which are questionnaire-based measures requiring the individual to reflect back on general mental processes.

Table 1 Summary table of metacognition measurement in studies

Authors	*Task*	*Method*	*Measurement*
Do Lam et al., (2012)	Face recognition	Behavioural	JoL (prospective estimate remember versus forget x correct or incorrect recall)
Bacon & Izaute, (2009)	Word recognition	Behavioural	FoK (estimate of number of letters recalled versus actual letters recalled)
Schraw & Dennison, (1994)	Memory	Questionnaire	Belief about memory abilities (108 items, 1-5 likert scale)
Beck et al., (2004)	Cognitive Insight (BCIS)	Questionnaire	Belief about cognition (15 items, 0-4 likert scale)
Moritz et al., (2015)	'Who wants to be a millionaire' quiz	Behavioural	Correct versus incorrect, confidence (1-4)
Koren et al., (2006)	Executive function (WCST)	Behavioural	Correct versus incorrect, confidence (1-100), include in overall score
Fleming et al., (2010)	Visual perception	Behavioural	Correct versus incorrect, confidence rating (1-6) (meta-*d'*)
Köther et al., (2012)	Mental state attribution	Behavioural	Correct versus incorrect, confidence (1-4)
Semerari et al., (2003)	Synthetic metacognitive awareness (MAS)	Clinical interview	3 (self-reflection, mind of other, mastery) domains, score of 1-9
Cartwright-Hatton & Wells, (1997)	Metacognitive beliefs (MCQ)	Questionnaire	65 items relating to beliefs about worry (1-4 likert scale)
Dixon, Hultsch & Herzog, (1998)	Metamemory in Adulthood (MIA)	Questionnaire	7 scales, 108 items (1-5 likert scale)
Persaud, McLeod & Cowey (2007)	Visual awareness (Iowa gambling task)	Behavioural	Correct versus incorrect, wager 0, 50p £1)

The more popular measure of metacognitive judgement in experimental psychology is the retrospective self-assessment of performance on a cognitive task. Participants are typically asked to complete a task and then rate their confidence regarding their performance. An objective task performance score is obtained and related to subjective confidence in accuracy reports to compute a value of metacognitive judgement. Some authors have questioned the motivation for participants to honestly report their confidence (Dienes & Scott, 2005) and whether this method reflects on real-world decisions based on metacognitive judgements (Koren, Seidman, Goldsmith, & Harvey, 2006). The post-metacognitive judgement decision wager strategy (i.e. participants are asked to place a financial bet on their accuracy) addresses motivation concerns (Persaud, McLeod, & Cowey, 2007) however has been criticised for not directly measuring conscious awareness as the process itself is not necessarily what the wager is based upon (Seth, 2008). Koren et al., (2006) suggest that, in order to measure

metacognitive reflections researchers should take a measure of the objective performance on a task, the subjective assessment of performance but also an option for the participant to decide whether they want to include each trial in their overall score. This combination of forced and free-choice decision making is more predictive of real life functioning and the use of metacognitive appraisals of cognitive performance (Koren et al., 2005). Thus participants are forced to attribute a confidence level to a judgement but also have the option of including or excluding the decision in a running total of their score which is more reflective of real-life.

The relationship of objective performance and subjective ratings of performance have also been developed using Signal Detection Theory (SDT) modelling paradigms. A measure of metacognition is distilled from participants' ability to discriminate 'signal' from 'noise' in that for good metacognitive accuracy, incorrect decisions should be associated with low confidence and correct judgements should be associated with high confidence (Maniscalco & Lau, 2012). This measure of metacognitive sensitivity or meta-*d'* addresses individual propensity to rate higher or lower in confidence and have a bias for particular stimuli. Concerns have been raised however about task difficulty; as metacognitive judgements have been found to differ in the same individual between easy and hard tasks. Fleming and Lau, (2014) in their own study artificially maintain task performance at a set level across trials to address this concern. This is corroborated as important to control for by Moritz et al., (2015) who found that patients demonstrated a significantly greater 'confidence gap' (overconfidence in errors and underconfidence in correct responses) than controls in an easy but not a hard task.

In clinical literature, Semerari et al., (2003) suggest metacognition should be assessed through the participant's free narrative account of their own mental processes called the Metacognitive Assessment Scale (MAS). A semi-structured clinical interview is administered and guided by the researcher. The participant's responses are rated based on the participant's capacity to identify and describe mental states, reflect back on cognitions and their relationship to emotions and behaviour, consider thoughts as subjective and view their own mental states as different from other's. The measure assesses metacognition as the ability to reflect back on one's own mental states and products (self-reflection or the understanding of one's own mind), the ability to assess the mental state of others (understanding the mind of other or decentration), and the ability to use mental state information to solve psychological problems (mastery). Lysaker et al., (2005) suggests that traditional explicit task based metacognitive judgements do not capture the nuance of real life reflections on cognitive states. The MAS therefore provides a more ecologically valid assessment method appropriate for

understanding functional deficits in schizophrenia. This measurement of metacognition requires the highest order meta-level processing of the measures mentioned thus far.

The MAS, a measure of synthetic metacognition, is one of the most well used measures in clinical research and offers an insight into a host of processes. It captures the complexity of integrating constituent skills such as mental state attribution and, linking thoughts to emotions and behaviours. This offers rich data for accounting for outcome. The BCIS also offers a faster, overall reflection of willingness to consider cognition as fallible and subjective and has also been validated in a variety of populations. In terms of measuring specific perceptual judgements, the SDT theory of meta-*d'* offers a real numerical representation of participants ability to differentiate correct from incorrect responses avoiding bias seen in other measures such as stimuli bias and individual difference in tendency to use extreme scores. It is yet to be employed in studies involving those with a schizophrenia diagnosis however and would benefit from such validation.

The relationships between these different measures of metacognition are not clear. The MAS domain of understanding one's own mind and total score and the BCIS self-reflectivity subscale have been investigated together and found to positively associate (Lysaker et al., 2008). In addition, in a factor analysis investigation, BCIS total and MAS total scores were found to inhabit a shared factor separable from social cognition, measures of affect recognition and theory of mind (Lysaker et al., 2013). The BCIS has also been investigated in relation to confidence-based metacognitive judgements on a perceptual decision making task however no significant correlation was found with either self-reflectiveness or self-certainty (Fleming, Huijgen, & Dolan, 2012).The self-certainty subscale has been found to correlate with over-confidence in erroneous decision in a social cognition task however (Köther et al., 2012). This may be indicative of the scales measuring different aspects of a multilevel metacognitive system but the relationship between measures needs to be elucidated further.

1.17 Metacognition and neurocognition

The relationship between cognitive and metacognitive abilities has been assessed in a variety of studies and will be considered further in chapter two. Palmer, David and Fleming (2014) investigated two measures of metacognition; perceptual and memory metacognitive efficiency and found a significant association between the latter but not the former on the Wechsler Memory Scale and no significant relationship with either measure and IQ or executive function. Other measures of metacognition have been found to have significant relationships with executive function. Lysaker, Dimaggio, Buck, Carcione and Nicolò, (2007) found significant relationships between the MAS subscales of decentration, self-reflectivity, understanding one's own mind, overall total MAS score

and executive function at both baseline and 6 months (Hamm et al., 2012). The BCIS self-certainty has also been found to be associated with executive function (Orfei, Spoletini, Banfi, Caltagirone, & Spalletta, 2010), and the self-certainty subscale was negatively associated with working memory. Visual memory was significantly associated with understanding one's own mind and understanding the mind of others (Lysaker et al., 2005). Verbal IQ has been associated with the metacognitive domain of mastery (Nicolò et al., 2012), understanding one's own mind (Abu-Akel & Bo, 2013) however a combined measure of MAS total and BCIS failed to obtain significance with verbal IQ indicating that relationships may be domain specific rather than global. Finally processing speed has been associated with mastery (Lysaker, McCormick, et al., 2011), understanding one's own mind and the mind of others (Nicolò et al., 2012). The relationship between metacognition and neurocognition has yet to be investigated in FEP which the present thesis will also seek to address.

1.18 Metacognition and functional outcome

In terms of relationship to function, the BCIS total and self-reflectivity scales have been associated with global assessments of functioning (Giusti, Mazza, Pollice, Casacchia, & Roncone, 2013) but the self-certainty scale demonstrated a non-significant negative association. In relation to the MAS, metacognitive mastery has been associated with improved functional capacity in the domain of comprehension and planning but not other areas (Lysaker et al., 2011), to correlate with increased social relationships (Lysaker, Dimaggio, et al., 2010) and mastery has also been found to mediate the relationship between neurcognition and social functioning (Lysaker et al., 2010) (see chapter two for further details).

In FEP, understanding of one's own mind and the mind of others have been associated with premorbid social functioning (Macbeth et al., 2014). O'Connor et al., (2013) found that cognitive insight did predict psychopathology but not global measures of function. The authors speculate that the role of cognitive insight in functional outcome may be a delayed process and become important after immediate symptoms have subsided Massé and Lecomte (2015) divided FEP service-users into three metacognitive profiles; (i) overall better metacognition across all domains, ii) overall worse metacognition with retained mastery, iii) worse metacognition and impoverished mastery. They investigated a variety of social functioning domains however the authors found conflicting results. No differences were found with understanding one's own mind and interpersonal functioning however some indices of metacognitive function were associated with less social contact. Whilst the profiles did not differ overall on all measures of social function, interestingly, the retained mastery ability did differentiate between the second and third groups on

frequency of social contacts and ability to perform social functioning tasks. No significant differences however were found on social functioning measures between high and low scorers on understanding one's own mind and understanding the mind of others. Whilst surprising, the authors suggest future studies should define the measurement of social relationships as this could be due to question interpretation rather than an accurate reflection of performance in FEP. Participants may have rated friendships and social contacts inaccurately due to a lack of awareness of the other persons' perspective. Alternatively, those with improved self-knowledge, may also be more aware of social stigma and therefore withdraw from social contacts. Further, the measures of function were all self-report and may be victim to factors discussed earlier with self-report measures of function.

The aforementioned studies demonstrate that the different measures of metacognition are indicative of a multi-layered metacognitive system. Self-reflectivity and understanding of one's own mind appear to be more closely related to each other however the different measurement options available may assess different structures or metacognitive abilities described in the Nelson and Narens' model. The nature of these relationships, particularly in relation to functioning, need clarification and assessment in non-chronic samples to separate from the effects of medication exposure and psychological treatments (Lysaker et al., 2008).

1.19 Cognition, negative symptoms and functional outcome

Frith, in an early paper, identified the relationship between cognition and symptomatology suggesting that the behavioural signs and symptoms of schizophrenia were the result of cognitive deficits (Frith, 1993). Kerns and Berenbaum (2002) offer a meta-analysis of executive function impairment and found mixed findings for the cognitive underpinnings of symptom development; formal thought disorder was found to be significantly associated with both impaired executive function and impaired semantic processing. Formal thought disorder was especially evident in executive function tasks that involved high context memory and inhibition demands to a similar degree and Stirling, Hellewell, Blakey and Deakin (2006) propose that the relationship requires further elaboration in research.

Velligan et al., (1997) found that cognition related to both symptom score and function with the relationship between function and symptoms attributed to shared variance with cognitive ability. Cognitive ability was negatively correlated with negative symptoms and both factors significantly predicted social adaptive functioning in a follow-up paper (Harvey et al., 1998). Milev, Ho, Arndt and Andreasen (2005) found that both cognitive ability and negative symptoms significantly predicted follow-up psychosocial function

however the total variance accounted for was relatively low (3.4% and 11% respectively) in their model. Couture, Granholm and Fish (2011) investigated the relationship between neurocognition, negative symptoms and self-reported function and found that negative symptoms were directly predictive of function and mediated the relationship between neurocognition and function. In contrast to Green's (2004) suggestion that between 20-60% of the relationship is accounted for; both factors only accounted for 7.3% of the variance in self-reported function. This could however be attributable to the use of self-reported data which is victim to a number of problems with validity (see section 1.7). Ventura, Hellemann, Thames, Koellner and Nuechterlein (2009) performed a meta-analytic technique to assess this relationship and also found negative symptoms to partially mediate the relationship between cognition and functional outcome and report a much larger effect size (r=.42) however caution must be applied when interpreting such a finding. The meta-analysis required the inclusion of multiple domains of outcome and multiple measures of negative symptoms. The SANS and measures of function may overlap as they ask similar questions and the nuanced relationship between different domains of function and cognition was not investigated.

1.20 Metacognition and negative symptoms

From the literature reviewed thus far, metacognition and negative symptoms appear to be the most validated and novel potential mediators to explain the relationship between neurocognition and functional outcome. Some work has looked at the relationship between the two concepts; earlier work found that understanding one's own mind correlated with emotional withdrawal (Lysaker et al., 2005) and metacognition mediates between cognitive ability and social functioning whilst controlling for symptoms in the model. This indicates that metacognition accounts for the relationship uniquely to negative symptoms (Lysaker et al., 2010). Newer research has looked at the relationship between the concepts specifically; Self-reflectivity, understanding the mind of others and mastery have all been found to correlate with negative symptom domains (Nicolò et al., 2012).

In FEP, McLeod, Gumley, Macbeth, Schwannauer, and Lysaker, (2014) found that 62% of the variance in negative symptoms at 12 month follow-up from FEP was accounted for by a model comprised of metacognition (MAS) and demographic details. This implicates metacognition in symptom trajectory and function. Baseline Negative symptoms have also been found to predict functional outcome at 12 months in FEP and, when entered into a hierarchal regression model to predict functional outcome, cognitive insight was no longer a significant predictor of social functioning (O'Connor et al., 2013). Furthermore, baseline cognitive insight was found to predict 12 month psychopathology

function as measured by the GAF. This suggests that, whilst cognitive insight does predict functional outcome, negative symptoms offered a greater contribution to the model. This relationship however has not been fully investigated as, in most studies, symptoms have only been controlled for in a mediation model rather than investigated alongside metacognition.

Summary

There have been multiple theories and definitions for metacognition in academic literature and this largely determines how it is measured. As a higher-order metacognitive knowledge process, the MAS captures one's ability to synthesise a wealth of information regarding mental states and draws upon declarative knowledge. The BCIS appears to be a general sense of reflection on cognition whereas retrospective confidence judgements are moment-to-moment reflection on processing accuracy for specific tasks. Retrospective confidence judgements would sit in a lower-order section of the Nelson & Narens model specified above. Evidence suggests a layered system with differing levels of access and awareness to meta-level processing and appraisal of cognitive systems. How these different measurements relate to each other is less well known, the most investigated in clinical literature appears to be cognitive insight and declarative, synthetic metacognitive awareness as captured in the MAS. Relationships have also been found between these variables and both neurocognition and functional outcome. The extent that differing levels of metacognitive processing mediate this relationship however is not known or fully understood. By understanding this relationship better, the preceding factors to functional recovery can be better understood and clinical interventions catered to what really helps individuals recover autonomy and independence. The relationship between metacognition and negative symptoms in relation to functional recovery also requires clarification although preliminary evidence suggests both may be important for functioning in differing ways.

1.21 Therapeutic intervention

As discussed previously, research suggests that an individual's cognitive skills predict their ability to function in the community. This notion as early as the 1960s (Rund & Borg, 1999) underpinned the idea that, if clinicians can help patients improve their cognitive processing abilities, then this should also improve functional outcomes and assist with recovery. This intervention approach has been called *cognitive remediation* therapy and the programme is comprised of behavioural interventions focused on the cognitive deficits associated with poor psychosocial outcomes (Ostergaard et al., 2014). The method adopted vaies with some favouring more 'drill and practice' approaches based on neuroplasticity and specific, behavioural strategies (Eack et al., 2010) and others

targeting compensatory strategies to circumvent neurocognitive impairment (Twamley, 2010). Some programs are cognitive domain specific, others target multiple domains, and some function as part of a stand-alone programme (Medalis & Saperstein, 2013) whereas others are integrated into a package also containing behavioural skills or vocational rehabilitation (Bell et al., 2008).

The efficacy of such initiatives has been demonstrated with moderate to large effect sizes observed (Krabbendam & Aleman, 2003). Assessment of cognitive remediation feasibility studies is problematic however; there is a large variability in method of administration, target population and outcome measurement has been identified in other reviews (Twamley, 2003). Furthermore, the generalisation of therapeutic improvements to the 'real-world' is also mixed (Krabbendam & Aleman, 2003). Wykes et al., (2014) do report that, when method and nature of programme is controlled for in a meta-analytic review, small to moderate effects are still observed and other variables can improve programme efficacy such as addressing negative symptoms in addition to cognitive process (Greenwood, Landau & Wykes, 2005), employing a strategic approach rather than drill and practice, and aligning the intervention to other occupational rehabilitation programs (Wykes et al., 2011).

Another avenue more recently identified to enhance cognitive remediation programmes involves the metacognitive monitoring of cognitive processes and information integration when learning new skills. Metacognition's formative development was largely based in metamemory and learning styles (Flavell, 1979) and this has been applied to cognitive remediation. Metacognitive knowledge pertains to the knowledge individuals' possess in relation to the accuracy of their own cognitive products and metacognitive regulation involves the planning ahead of cognitive processes, monitoring of current strategies and ability to update and revise the cognitive techniques employed based on self-reflection (Flavell, 1979). An early feasibility study (Cella, Reeder & Wykes, 2015) demonstrates the utility of such techniques in improving neurocognitive performance, negative symptoms and cognitive complaints. Metacognitive learning strategies in the guise of raising awareness of procedural rules and plans when delivering cognitive remediation has begun to be assessed. By giving learners insight to monitor their own learning style and increasing self-assessment of competence, may aid integration of skills into the real-world. Whether these gains can optimise the integration of such remediation strategies into functional improvements has yet to be investigated however and validation is required in larger samples (Cella, Reeder & Wykes, 2015).

Metacognitive training (MCT) has also been suggested by other authors to facilitate self-awareness of cognitive deficits; if an individual is aware of dysfunctional processing or that they are less able in a particular domain, they can adopt more conservative strategies (Frith, 2012) or ask for assistance (Koren, 2006) which may help with community functioning. MCT may also address deficits such as jumping to conclusion (JTC) bias, self-serving bias, bias against disconfirmatory evidence (Bartholomeusz & Allot, 2012) and overconfidence in errors (Bruno, 2012). Whilst early studies demonstrated a small association with less JTC and reduced positive symptoms (Aghotor et al., 2010) and less conviction in delusions (Ross, Freeman, Dunn & Garety, 2011), these changes failed to achieve statistical significance. A recent review into the efficacy of MCT also reports little support for the reviewed studies with a non-significant mean effect size of treatment (Oosterhout et al., 2015). The authors do concede that, due to the poor study design and low power of the studies included, definitive conclusions are difficult to draw. Also, for the purpose of the current review, MCT has not been assessed for impact on function; previous studies have only looked at cognitive bias and symptoms as outcome measures. The impact on functional recovery is to this day unknown.

1.22 Summary of introduction

The aforementioned work describes how neurocognitive deficits are predictive of longer-term functional recovery in schizophrenia. These cognitive deficits are observed in pre-morbid, prodromal, FEP and chronic stage schizophrenia and relate to psychosocial functioning across a number of domains. In order to maintain social and occupational relationships and conduct everyday tasks, certain cognitive skills are drawn upon. These already compromised skills may erode further due to illness, and therapy designed to enhance these abilities has been shown to improve community outcome. One's cognitive abilities are more important than psychopathology alone in recovery although how they interact and impact on negative symptoms is less clear. The definition and measurement of recovery and community functioning is also fluid and hinders comparisons between existing studies. The service-user focused models of recovery reflect changes in mental health care provision however self-report measures, despite being an important factor in understanding the individual, are victim to a variety of biases. Instead, objective and capacity based measures offer a more scientific assessment of an individual's ability and actual community functioning. A greater understanding of this relationship is critical to informing treatment initiatives. Giving the individual the tools to integrate raw skills into the complicated real-world setting is paramount to assisting with recovery.

The integration of our cognitive abilities into functional contexts appears to be potentially explained by our knowledge into our own metacognition. The reflection back on life experiences and learning from them may be a key distinction between partial and full recovery from psychosis. Conversely, being unaware of inaccurate cognitions may lead to less scrutiny of erroneous decisions and propagate continued incorrect strategy selections in social and occupational settings. If we are unaware of deficits in cognitive skills, we are less likely to seek help or support externally. Deficits in our representations of the world may also underpin and exacerbate social withdrawal and inhibit motivation to attempt daily tasks or the pleasure derived from completing them. This loss of pleasure may germinate the development of negative symptoms discussed previously. A lack of comprehension as to why a social situation went wrong may render the world a confusing and frustrating place inhibiting the individual from attempting future social interactions. The relationship between negative symptoms and metacognition may offer answers to these suggestions. How the currently disparately defined mental state measures are related also needs further refinement.

1.23 Conceptual models

The preceding literature review suggests that metacognition and negative symptoms may offer important insights into the relationship between neurocognition and functional outcome in FEP. In order to assess the extent to which they offer greater insight in this relationship the present thesis proposes to test the theoretical models described below. Higher order metacognitive knowledge will be represented through the MAI and cognitive insight measures. Implicit lower-order metacognitive processing will be investigated in the final empirical chapter through retrospective confidence based metacognitive accuracy (meta-*d'*).

Both metacognition (conceptual model 1, figure 2) and negative symptoms' (conceptual model 2, figure 3) relationship with neurocognition and functional outcome will be investigated for mediation effects through pathway models analysis.

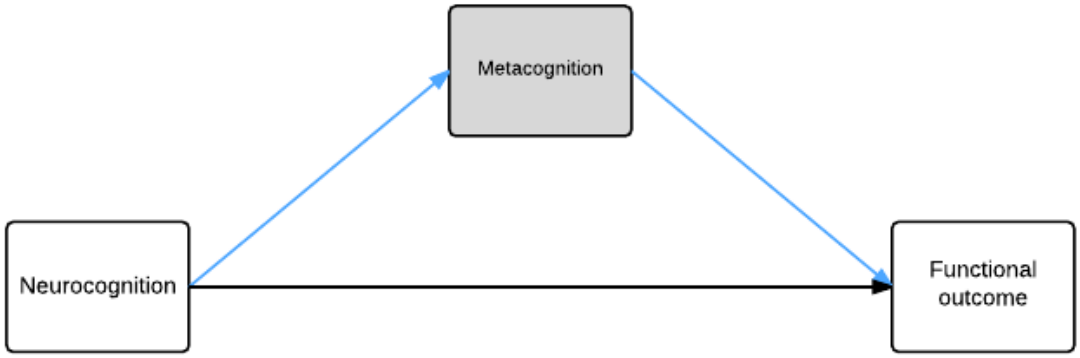

Figure 2 Conceptual model of neurocognition, metacognition and functional outcome. Note: blue line signifies a proposed mediation pathway

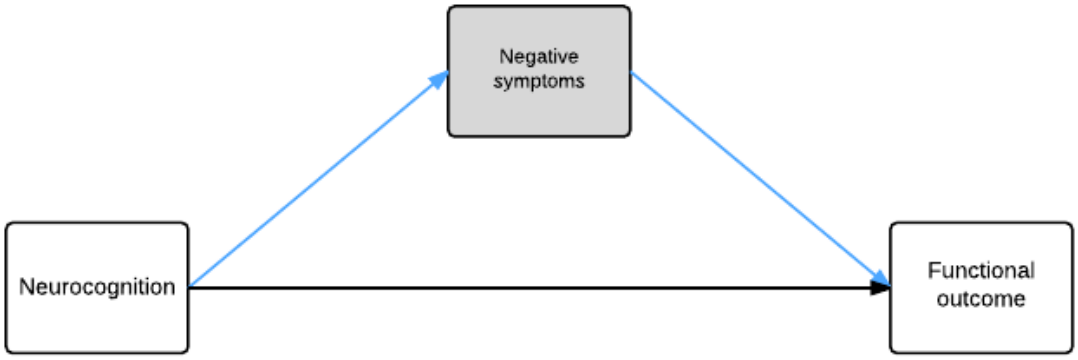

Figure 3 Conceptual model of neurocognition, negative symptoms and functional outcome. *Note:* blue line signifies a proposed mediation pathway

Having investigated individual model characteristics, both constructs will be assessed in a larger model to investigate the relationship between neurocognition, metacognition, negative symptoms and functional outcome in psychosis (figure 4).

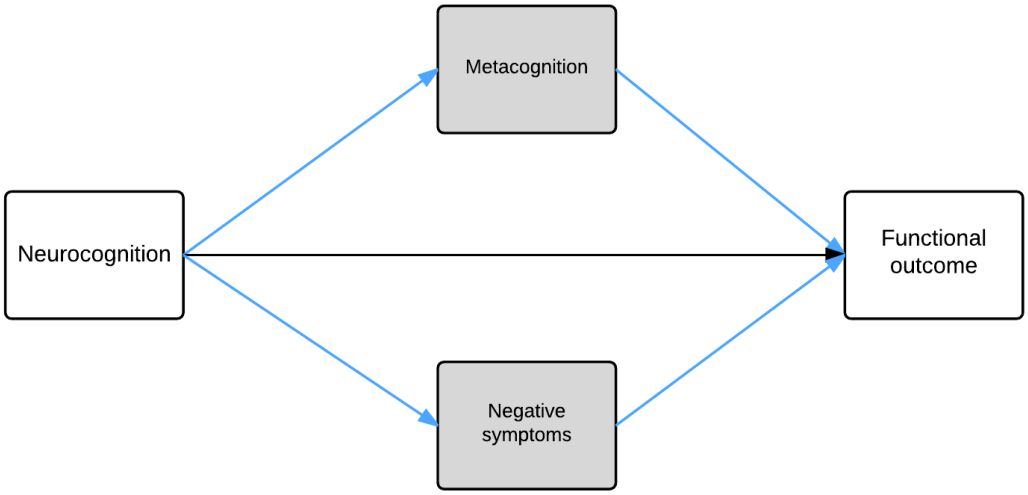

Figure 4 Conceptual model of neurocognition, metacognition, negative symptoms and functional outcome. Note: blue line signifies proposed mediation

Finally, the individual cognitive domains' identified in the meta-analyses in chapter two (memory, IQ and executive function) relationship with metacognition and functional outcome will also be investigated in a series of pathway models. This will evaluate whether specific cognitive skills are more important in accounting for functional outcome in a more nuanced method.

1.24 Overview of empirical chapters

The empirical work in the present thesis is designed to elucidate a greater understanding of the components of neurocognition (memory, executive function and IQ), metacognition (cognitive insight, synthetic metacognition and perceptual metacognitive accuracy) and functional outcome (both real-world performance and personal capacity to complete everyday tasks). An overarching goal is to evaluate hypotheses about how the subcomponents of these constructs relate to each other. A primary research question concerns how the overall construct of metacognition, accounts or mediates the relationship between neurocognition and different components of functional outcome. Secondly, having established the role of metacognition in accounting for the relationship between neurocognition and functional outcome, the role of negative symptoms will be investigated through i) being controlled for in mediation models to assess the unique contribution of metacognition and ii) as a mediation pathway in itself. Finally a neurobiological account for metacognition will be explored through a grey matter structural analysis through voxel-based morphometry. The extent that metacognitive dysfunction is accounted for by potential neurological deficits post psychosis will add to the behavioural data reported in chapter 3.

Measures of neurocognition have been investigated comprehensively in previous research. However, different measurement strategies regarding metacognition have a more equivocal evidence base, and the analysis of this construct must therefore be considered more exploratory in nature. The variables of synthetic metacognition and cognitive insight were selected for chapter 3 as they have a more established evidence base in relation to functional outcome in schizophrenia. Conceptually, our ability to reflect back on cognition, accept it as potentially subjective and open to interpretation, and identify how cognition is synthesised into relationships, behaviour and the social world is a more natural bedfellow for functioning in the community. Perceptual metacognitive accuracy was selected for chapter 4 due to known relationships to structural deficits in the prefrontal cortex. This has the added advantage of allowing a correlational analysis of all three measures of metacognition also provided in chapter 4.

A first-episode psychosis sample will be selected as this allows for the investigation of the association described above whilst minimising the impact of differing exposure between participants to neuroleptic medication and access to psychological services present in chronic cohorts. However the extent to which a classification of FEP confirms a homogenous group of service-users is less well known. Whilst every effort was made to recruit participants at first point of contact into care teams, estimating duration of untreated psychosis (DUP) is problematic and there may be variation between participants in terms of when symptoms first arose and the gap between being accepted onto full caseload and recruitment into the research studies. It must be noted that to assist addressing this, psychopathology was included in analysis in chapter 3. This only

The present thesis will attempt to address these issues with the known research in psychosis. The current evidence for the relationship between neurocognition and metacognition will first be addressed in chapter two through a meta-analytic technique to synergise known evidence. Secondly, the relationship between metacognition and functional outcome will also be investigated in chapter two as groundwork for a mediation analysis through pathway modelling in chapter three. How neurocognition, metacognition and functional outcome are defined in this analysis will first be validated through factor analysis in chapter three. This will allow a better understanding of the composite constructs and offer insights into how the proposed indicators in the literature of neurocognition, metacognition and functional outcome relate to each other. Chapter 3 will assess the validity of the aforementioned mediation models through pathway model analysis and mediation effects.

Finally, chapter four will investigate how organic brain structural measures of GM volume relate to perceptual metacognitive accuracy through a MRI study comparing healthy controls to FEP participants. The fundamental neurological determinants of metacognitive accuracy may offer more insight into behavioural measures in the community and demonstrate that dysfunction may occur at a neuroanatomical level in FEP. The relationship between higher-order metacognitive knowledge (MAI and BCIS) and lower order metacognitive experience (metacognitive accuracy) will also be investigated.

Chapter 2: A systematic review of the relationship between neurocognition, metacognition and functional outcome in schizophrenia.

2.1 Introduction

Cognitive impairment in schizophrenia is a core deficit of the disorder (Heinrichs & Zakzanis, 1998) and observed across prodromal (Jahshan, Heaton, Golshan, & Cadenhead, 2010), first-episode (Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009) and into remission stages (Hoff, Svetina, Shields, Stewart, & DeLisi, 2005). Whilst cognitive deterioration has generally not been found to be progressive in FEP (Leeson et al., 2011), improvements after illness remain diminutive in certain domains such as IQ, working memory and processing speed (Gonzalez-Ortega et al., 2013). Cognitive performance has also been implicated in predicting functional status in patients with schizophrenia (Tolman & Kurtz, 2010) and found to be a better determinant of outcome than psychopathology (Green, 1996). Green et al. (2004) in a review, report cognitive impairment to explain between 20-60% of variance in outcome with Couture, Penn, and Roberts, (2006) in further review positing that studies exceeding 40% of variance were very much the exception.

The relationship identified between cognitive ability and community function led to the development of cognitive remediation programs with the ethos of improving the cognitive skills possessed by those with a diagnosis of schizophrenia to improve their community functioning. Despite some gains in function from remediation initiatives (Wykes et al., 2007), not all of the skills necessarily translated into real-world improvements (Wykes et al., 2012) and led researchers to look for mediating variables to account for this relationship. Studies have suggested social cognition (Addington, Saeedi & Addington, 2006), social discomfort (Bell, Tsang, Greig, & Bryson, 2009), defeatist beliefs (Grant & Beck, 2009), intrinsic motivation (Nakagami, Xie, Hoe, & Brekke, 2008) and negative symptoms (Couture et al., 2011) as potential mediating variables between cognition and functional outcome. Proposed variables however haven't yet provided conclusive results and much of the relationship between neurocognition and functional outcome still remains unaccounted for (Fett et al., 2011). One approach has been to implicate

metacognition in this model (Lysaker, Shea, et al., 2010; Addington, Saeedi & addington, 2006) and research has begun to explore the relationship between cognition and metacognition. By improving an individual's metacognitive abilities, the cognitive skill improvements can potentially be integrated into social and occupational situations (Lysaker, Shea, et al., 2010).

Metacognition refers to the cognitive processes involved in thinking about thinking (Flavell, 1979) and incorporates how we monitor and control slave cognitive mechanisms (Frith, 2012) (see chapter 1.14 for further details). Most models of metacognition propose a multi-level hierarchical system, with a higher order theory and knowledge based (Koriat & Levy-Sadot 1999) meta-level processing (Nelson & Narens 1994) comprising of explicit, effortful processes (Frith 2012) and the synthesis of complex information to compile a representation of one's cognitive world (Lysaker et al., 2008). This higher-order metacognitive knowledge interacts with lower-order subjective experience-based (Koriat & Levy-Sadot 1999) automatic, implicit (Frith 2012) metacognitive judgements to regulate object-level processing units. Metacognition requires the ability to have an awareness of and monitor one's own mental states, consider the fallibility of cognitive products and be able to form, revise and so control one's mental states in rapidly evolving contexts (Lysaker et al., 2010a). Thus metacognition potentially draws upon memory, working memory and executive monitoring and control processes.

An inability to integrate ideas about oneself and others may lead to misinterpretation of social situations and avoidance of participating in them (Lysaker et al., 2012). The inability to consider the bigger picture and one's role in it may lead to the poor identification and solving of social and psychological problems (Lysaker et al., 2011). Thus a deficit in the ability to access metacognitive knowledge may leave individuals with basic evolutionary responses such as fight-or-flight to respond to challenges and frequent employment of anxious arousal and hyper-vigilance (Gilbert, 2001). The improved ability to reflect on cognitive products as fallible may also assist with challenging positive symptoms and delusional thoughts (Brüne et al., 2011). The ability to produce an accurate representation of one's cognition and to reflect back on it will lead to improved control over cognition and better application of cognition to the real world (Lysaker et al., 2011). Thus improved metacognitive knowledge will lead to improved functional outcome in the community.

Whilst neurocognitive deficits have proven links to impoverished psychosocial function (Green, 1999), metacognition may offer an explanation independent to neurocognition. Despite being considered relatively trait-like in schizophrenia (Lysaker & Dimaggio,

2014), metacognitive capacity is impacted by situational, cognitive and emotional demands (Dimaggio et al., 2007) and may therefore impact differently on capacity to complete daily tasks and actual real-world functioning. The ability to reflect back on cognitive products may be essential to the regulation of internal states and behaviours, which are crucial to global function (Beck et al., 2004).

Metacognition can impact on function independently from cognition (Koriat & Goldsmith, 1999). Koren, Seidman, Goldsmith, and Harvey, (2006) argue that functioning can persist in spite of poor cognitive processes through imparting the correct confidence on cognitive products (metacognitive monitoring) (i.e. being aware they may be erroneous) and metacognitive control (requesting for help). Improved awareness can precipitate the identification of inappropriate strategies (Lysaker et al., 2011b), allow better psychological problem solving, insight into symptoms, prevent overconfidence in erroneous cognitive products and therefore improve function (Nicolò et al., 2012). Thus, intact metacognition may bestow benefits on function independently from cognition.

Previous studies have included varying measures of both metacognition and functional outcome each with differing design problems. Functional capacity is the ability to successfully complete everyday tasks under observation from a researcher (see section 1.10 for further details). Capacity measures only assess the ability to conduct a task but not whether these are employed in real-life (Mckibben et al., 2004) and self-report measures of outcome are victim to bias and level of insight (Atkinson et al., 1997). Likewise, studies have often employed individual measures of metacognition (see table 1) and investigating whether these relationships to functional outcome are observed across indices would therefore be valuable to understand.

Previous research indicates that there is a relationship between measures of general cognition, aspects of metacognition, and functional outcome however the specific processing streams need further investigation (Nicolo et al., 2012; Lysaker et al., 2010b). In relation to bridging the relationship between neurocognition and function, deficits in monitoring one's own mind and the mind of others may underpin functional deficits in those with schizophrenia (Frith 2012) and provide a unique barrier to functional recovery. A better understanding of the mechanisms driving functional recovery is essential to guiding clinical care and providing those with pertinent skills to return to community functioning after a period of illness. The present study will function as a ground clearing exercise to synthesis the nascent available evidence in a comprehensive fashion to provide support to further, refined investigation. To this end, the primary study aim will be to compare across studies the impact of neurocognition on metacognition, and

metacognition on function in schizophrenia and FEP. The magnitude and consistency of current evidence will be assessed towards this end.

2.1.1 Study aims

The primary goals of this review will therefore be to a) identify the patterns across studies for the relationship between cognition and metacognition, and b) to assess the overall relationship between metacognition and functional outcome across studies through a meta-analytic technique.

2.2 Method

Studies investigating the relationship between cognition and metacognition were identified through a computerised search of the electronic databases Medline (PubMed), PsychINFO and Embase incorporating publications from the years 1983-2013. The syntax (schiz$ OR psychosis) AND (cogn$ or neurocogn$) AND (metacogn$) was included in the search strategy. Studies investigating the relationship between metacognition and functional outcome were also identified through a second computerised search with the syntax (schiz$ OR psychosis) AND (metacogn$) AND (function$). A secondary search of the grey literature to find unpublished data and PhD dissertations was completed with no additional papers found. Duplicate articles were removed, articles not written in English, editorials, study protocols, non-human populations, articles published solely in abstract form and conference proceedings and dissertation articles were also removed. Review articles and meta-analyses were excluded however the reference lists were systematically explored to ensure that any further articles missed in the original search strategy were included in the review. The retrieved studies' abstract and reference sections were hand-screened for additional citations.

For the purpose of this review social cognition was included as a cognitive variable as advised by factor analysis studies (Lysaker et al., 2013; Mehta et al., 2013) and correlational evidence strongly linking it to cognition (e.g. Bell et al., 2009). Articles looking at metacognition, confidence-based measures of performance and Beck's cognitive insight (BCIS) (Beck et al., 2004), were grouped together as measures of metacognition. Self-reported measures of function have been shown to be victim to confounding factors such as insight, depression (Mckibben et al., 2004) and psychopathology (Atkinson et al., 1997) therefore only clinician-rated and objective measures of function were included in the overall analysis

2.2.1 Statistical analysis

The observed correlations from each study were subjected to Fisher's r-to-z transformations as advised by Hedges and Olkin (1985). The z-transformed correlations were then weighted by their inverse standard error. The sum of weights and sum of weighted effect sizes were calculated to produce the weighted mean effect size and heterogeneity was investigated using the Q and I^2 statistic. Q statistics were then compared to critical values to ensure no violations of homogeneity (Hedges & Olkin, 1985). Confidence intervals were calculated for all studies in addition to mean effect

sizes. A random effects model was employed (Hedge and Olkin, 1985) and results (Z_r) were transformed back to the r-metric prior to reporting.

2.3 Results

2.3.1 Neurocognition's relationship with metacognition

Table 2 *Systematic review results table: Neurocognition and functional outcome*

Year	Author	Sample	N	Cognition								Metacognition			
				Memory	Attention	Executive Function	Social Cognition	Processing Speed	Visual-Spatial	IQ	General Cognition	MAS	BCIS	Confidence-rating	Questionnaire
2013	Abu-Akel & Bo	ICD-10 diagnosis schizophrenia	42							✓		✓			
2013	Lysaker et al., (2013)	SCID diagnosis for schizophrenia or schizoaffective disorder	95			✓	✓					✓	✓		
2013	Giusti et al.,	Schizophrenia	20	✓		✓	✓		✓		✓		✓		
2013	Mehta & Thirthalli	Remitted schizophrenia	60				✓						✓		
2012	Kother et al.,	MINI criteria for schizophrenia or schizoaffective disorder	76	✓										✓	
2012	Bruno et al.,	DSM-IV criteria for schizophrenia	28			✓							✓	✓	
2012	Hamm et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	49			✓	✓					✓			
2012	Nicolo et al.,	DSM-IV criteria for schizophrenia	45	✓		✓		✓				✓			
2012	Luedtke et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	41				✓							✓	

Table 2 *Systematic review results table: Neurocognition and functional outcome*

Year	Author	Sample	N	Cognition								Metacognition			
				Memory	Attention	Executive Function	Social Cognition	Processing Speed	Visual-Spatial	IQ	General Cognition	MAS	BCIS	Confidence-rating	Questionnaire
2011a	Lysaker, et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	98	✓		✓		✓				✓			
2011b	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	101	✓	✓	✓		✓				✓			
2011	Stratta et al.,	DSM-IV criteria for schizophrenia	42				✓							✓	
2011	Bacon et al.,	DSM-IV criteria for schizophrenia	34	✓											✓
2011b	Lysaker et al,	SCID diagnosis for schizophrenia or schizoaffective disorder	35				✓						✓		
2010b	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	102								✓	✓			
2010a	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	37	✓		✓						✓			
2010	Orfei et al.,	DSM-IV criteria for schizophrenia	84	✓		✓			✓				✓		

Table 2 *Systematic review results table: Neurocognition and functional outcome*

Year	Author	Sample	N	Cognition								Metacognition			
				Memory	Attention	Executive Function	Social Cognition	Processing Speed	Visual-Spatial	IQ	General Cognition	MAS	BCIS	Confidence-rating	Questionnaire
2009	Bacon & Izaute,	DSM-IV criteria for schizophrenia	21											✓	
2008	Lepage et al., (200	FEP	51	✓	✓		✓	✓					✓		
2008	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	49			✓						✓	✓		
2007	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	69	✓		✓	✓	✓	✓			✓			
2006	Souchay et al.,	DSM-IV criteria for schizophrenia	16											✓	
2005	Lysaker et al.,	SCID diagnosis for schizophrenia or schizoaffective disorder	61	✓		✓		✓				✓			
2001	Bacon et al.	DSM-IIIR diagnosis of schizophrenia	19	✓										✓	

The literature search identified 24 final papers that reported a relationship between cognition and metacognition. Based on findings from Lysaker et al., (2013) who found that the MAS and BCIS measures loaded on the same component in a Principle Component Analysis (PCA), these variables were combined when considering the relationship between metacognition and both cognition and functional outcome. Executive function comprised measures of WCST perseverations (1) and categories (6) and the Delis Kaplan Executive Function System categories subscale (1). Verbal IQ included the WAIS vocabulary subset (5 studies) and the National Adult Reading Test (1). For the memory analysis, the Hopkins Verbal Learning Test (1), Weschler Memory Scale visual reproduction or logical memory test (4), the N-back verbal memory task (1) and the Rey-15 word test (1) were combined. Social Cognition measures of the Bell-Lysaker Emotional Recognition Task (4), the Four Factor Test of Social Intelligence (1), The False-Belief Task (1) and the Reading the mind in the Eyes Task (1) were combined to account for social cognition.

The papers all included adult schizophrenia or FEP samples with the majority using a DSM-IV diagnostic criteria. The mean age of participants included in the review was 39.54 (range 23.2-50.4).

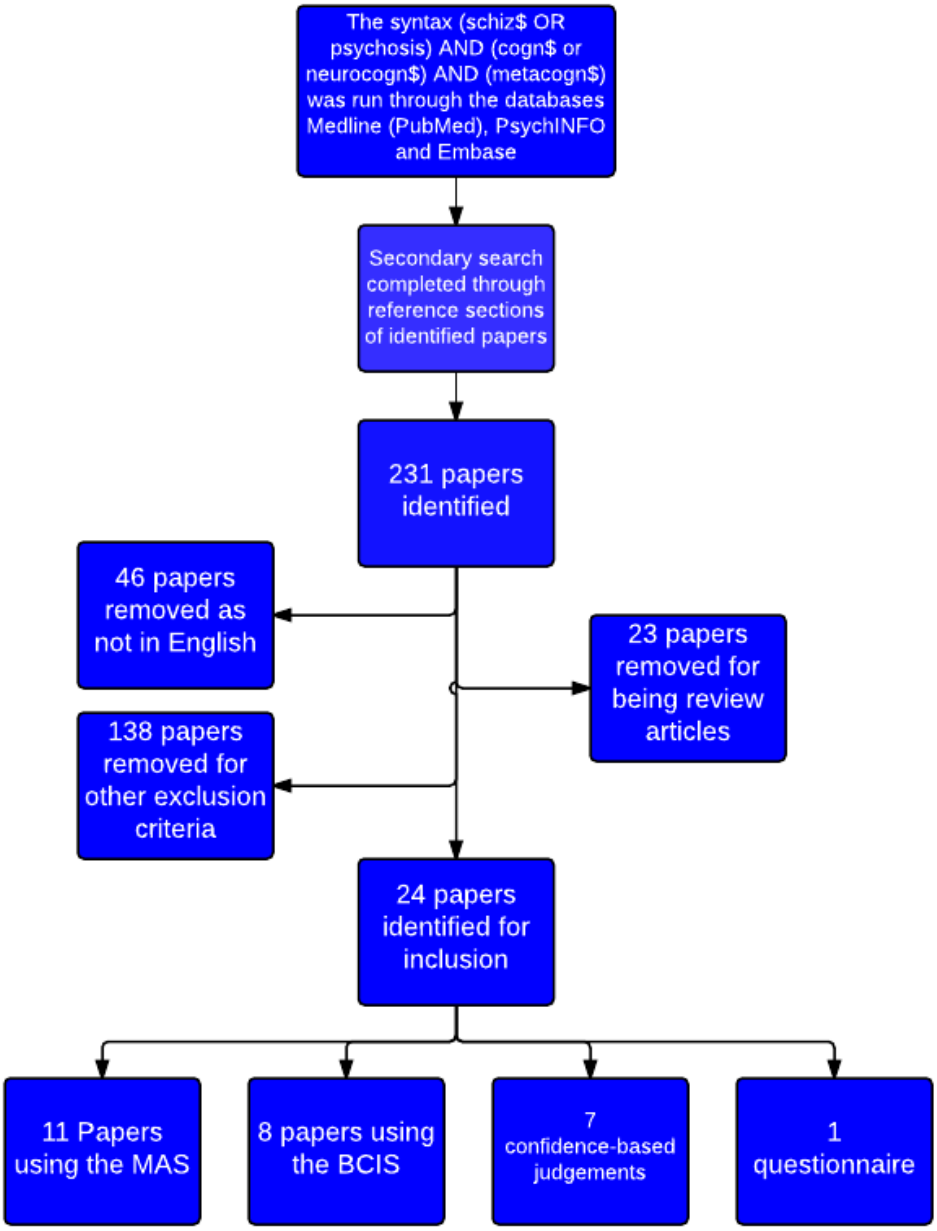

Figure 5 Neurocognition and metacognition search result consort diagram

2.3.2 Metacognition measurement

Metacognition was measured through a variety of methods in the papers included. The MAS uses the Indiana Psychiatric Illness Interview (IPII), a semi-structured interview designed to explore narratives of both the self and illness in those with schizophrenia. The interview is designed to be conversational and participants are required to generate a personal narrative and self-reflect which can be analysed in terms of metacognitive capacity. The scale is comprised of 4 subscales; *understanding one's own mind* or *self-reflectivity*, *understanding others' mind*, *mastery* and *decentration*. A higher score translates to improved metacognitive ability (see Lysaker et al., 2007 for validity and

reliability information). The MAS appears to assess synthetic forms of metacognitive processing which are effortful, deliberate and naturally occurring within personal narrative.

The Beck Cognitive Insight Scale (BCIS) is a 15-item questionnaire assessing how participants assess their own judgements. The measure contains two subscales; *self-reflectivity* and *self-certainty* relating to the ability to reflect back on cognition and confidence in cognitive products. An overall score of cognitive insight or *composite index* score is obtained by subtracting the self-certainty score from the self-reflectivity score (see Beck et al., 2004 for scale validation). The BCIS is a general reflection upon one's thinking and is not context specific.

The other main measure of metacognition was a confidence versus accuracy performance on a cognitive task measured through a correlation between the two measures. Bruno et al., (2012) adopt Koren's meta-WCST paradigm which also includes the choice to include a response in the final total arguing that this is a more ecologically valid form of processing which addresses both the control and monitoring components of Nelson and Narens' (2003) model.

2.3.3 Overall cognition and metacognition

An initial analysis was run to investigate the relationship between cognition and metacognition. Only one effect size from each paper was included to prevent the sample population being included twice. In the situation where two cognitive tasks were available from the same cognitive domain for a paper, the most commonly reported measure's effect size was selected to match other papers in the analysis.

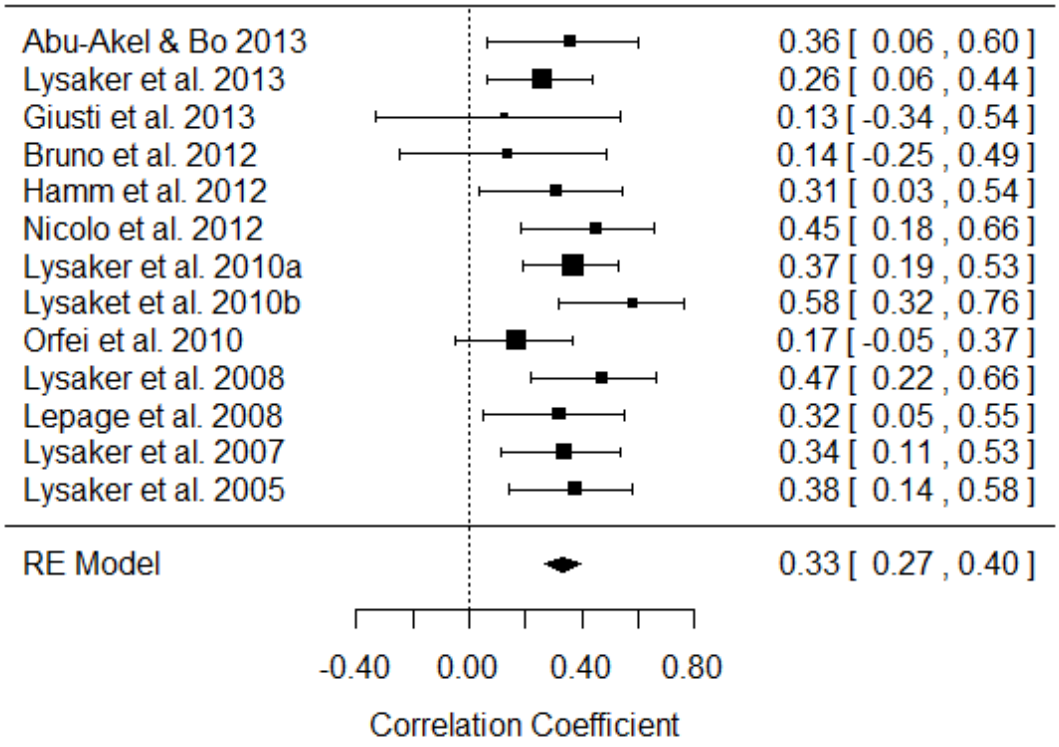

Figure 6 Cognition and metacognition forest plot

Effect sizes were extracted from 13 papers to assess the relationship ranging from .13-.58 and a total of 732 participants were pooled. The Q statistic was non-significant (Q=10.86, df=12, *p*>.05) and I^2= 0 suggesting homogeneity of variance. The Z statistic suggests a significant relationship between cognition and metacognition (Z= 9.14, *p*<.001) and a mean effect size ($\overline{ES}$) of .33 (95%+/- CI: .27, .40) suggests a moderate positive relationship exists between the variables. The study effect sizes and confidence intervals are available in figure 6 above.

In regards to publication bias, the fail-safe N suggests that 374 studies with 0 effect sizes would need to exist to dissolve this significant effect and Kendall's Tau also suggests little evidence for publication bias (τ(N=13)=.04 p=.855). The funnel plot is available in figure 7 below.

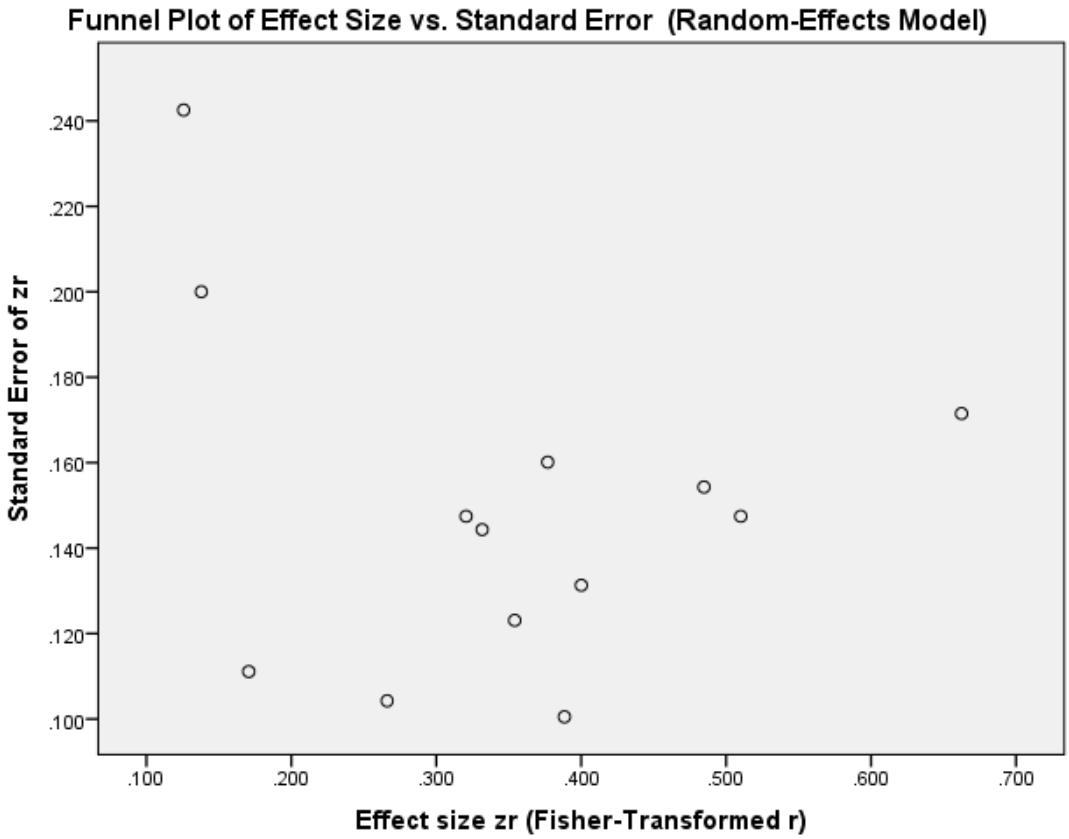

Figure 7 Funnel plot for cognition's relationship to metacognition

Next, the relationship between individual cognitive domains and metacognition was investigated in separate analyses.

2.3.4 Executive Function

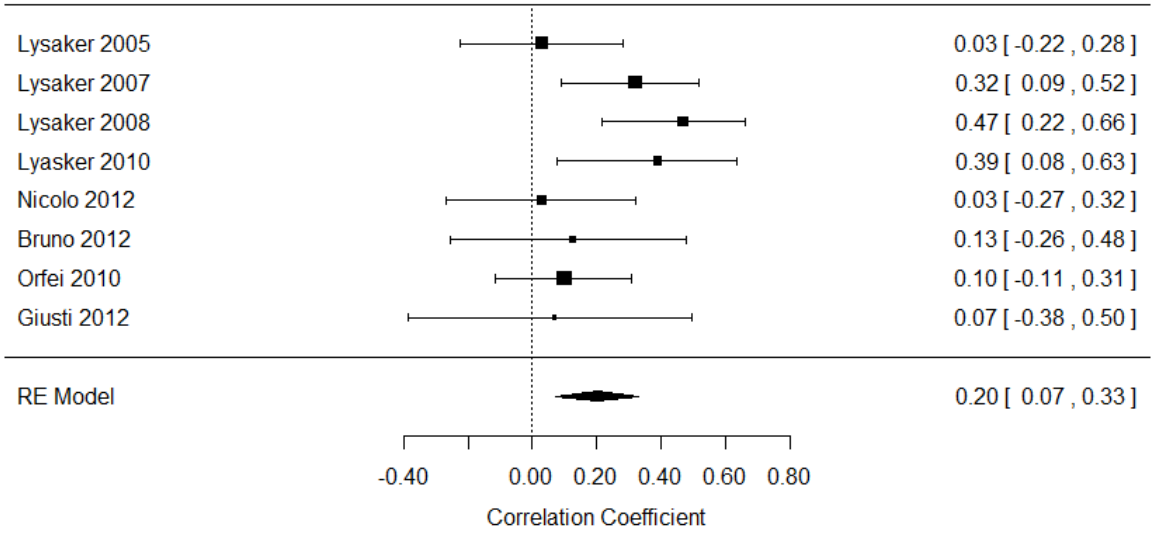

Figure 8 Executive function and metacognition forest plot (effect size and confidence intervals)

Of the studies included for meta-analysis for the relationship between executive function and metacognition, the effect size range was from 0.03-0.47 and the total sample size

was 393 participants. The Q statistic was not significant across studies (Q= 11.25, df=7, p>.05) and the I^2 statistic reports low heterogeneity across studies (I^2= 12.5) suggesting homogeneity of cognitive measurement. The mean effect sizes across studies was 0.20 (95%+/- CI: 0.10-0.31) and a significant Z score was also observed (z= 3.05, p=.002). The individual study effect sizes and confidence intervals are available in figure 8. This infers a small-moderate positive effect size (Cohen, 1992) between executive function and metacognitive processing therefore better executive function is associated with better metacognitive ability.

An inspection of the fail-safe N value indicates that there would need to be 35 unpublished studies with 0 effect sizes to ameliorate the significant effect found and an inspection of Kendall's Tau suggests little publication bias (τ(N=8)=.07, p=.805). Despite a small number of studies present, the funnel plot provides corollary evidence for no significant publication bias being present (see figure 9 below).

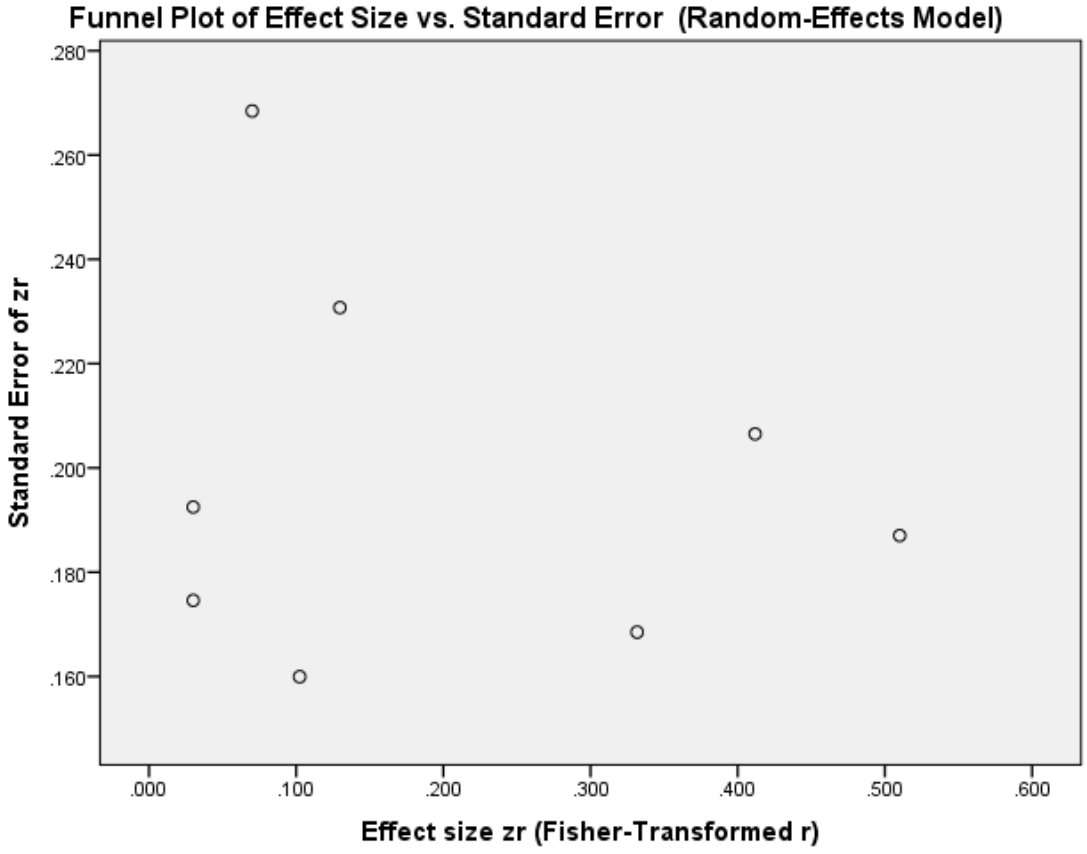

Figure 9 Executive function and metacognition funnel plot

Higher executive function (as measured with the WCST) was found to be positively correlated with decentration and self-reflectivity, understanding one's own mind (Lysaker et al., 2007), total MAS at baseline and 6 months (Hamm et al., 2012), and negatively

correlated with self-certainty (Orfei et al., 2010). This relationship to self-certainty persisted across measure of executive function (Guisti et al., 2013) however it must be noted that Lysaker et al., (2007) did not find this relationship for decentration alone and Bruno et al., (2012) found no significant association between executive function and any of the BCIS scores. This indicates that having trouble maintaining abstract concepts online and fluidly shifting from one abstract concept to another associates with being unable to identify one's thoughts and feelings. Thus retained executive function is required for superior metacognitive ability.

In summary, executive function appears conceptually to be critical to metacognitive processing as the ability to self-reflect requires shifting between different mental states and the integration of feedback to correct erroneous judgements. Poor executive function can lead to over-certainty in false beliefs. In addition, inhibition is also required to inhibit one's own perspective in order to correctly interpret the mental states of others. Effect sizes however in the meta-analysis were small to moderate indicating that executive function on its own does not account for metacognition and other cognitive processes may be just as important.

2.3.5 Memory

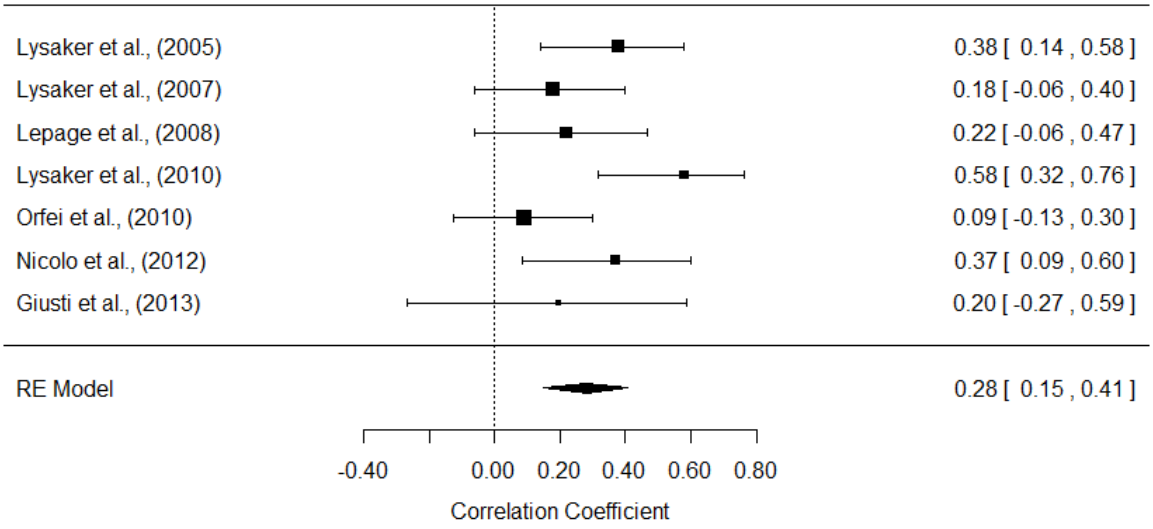

Figure 10 Memory and metacognition forest plot (effect size and confidence intervals)

Memory, alongside executive function, was one of the most consistently investigated cognitive variables throughout the papers. In regards to heterogeneity, the Q statistic was not found to be significant across studies for memory (Q=4.79, df=5, p>.05) and the I^2 statistics confirms this (I^2= 0). The range of effect sizes included in the meta-analysis was 0.09-0.58 and the individual study effect sizes and confidence intervals are available in figure 10. The 7 papers included 367 participants in total. The mean effect size for

memory's relationship to metacognition was 0.28 (95%+/- CI 0.15:0.41) indicating a medium effect size. The Z statistic indicates a significant effect of memory on metacognition (Z= 4.07, *p*<.001). This infers that better memory performance is associated with better metacognitive processing.

An inspection of the fail-safe N value indicates that there would need to be 66 unpublished studies with 0 effect sizes to ameliorate the significant effect found and an inspection of Kendall's Tau suggests little publication bias (τ(N=7)=.52, *p*=.099). Despite a small number of studies present, the funnel plot provides supprting evidence for no significant publication bias being present (see figure 11 below).

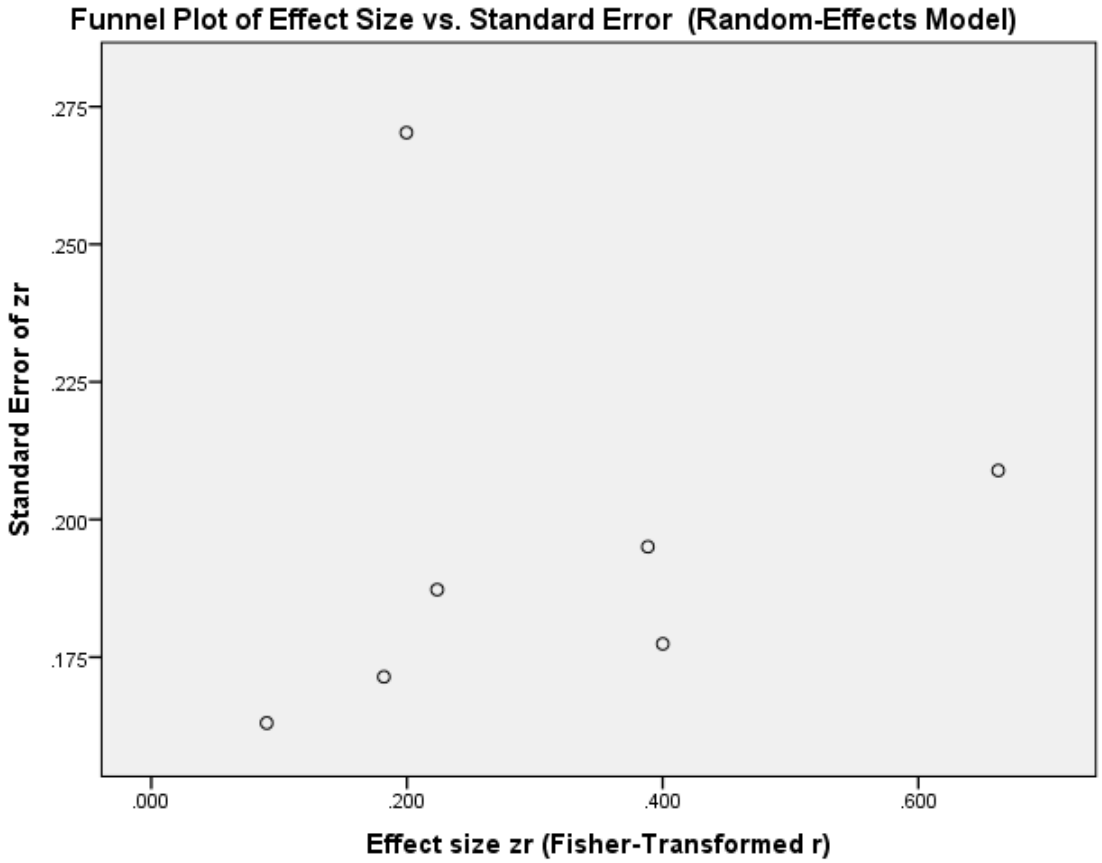

Figure 11 Memory and metacognition funnel plot

Positive correlations have been found between visual memory and understanding one's own mind (Lysaker et al., 2005; 2007) and understanding the mind of others (Lysaker et al., 2005) and a negative relationship was found with self-certainty (Orfei et al., 2010). A similar relationship was found with verbal working memory and understanding the mind of others (Lysaker et al., 2005), understanding one's own mind (Lysaker et al., 2005; 2011), total MAS (Lysaker et al., 2011) and an inverse relationship with self-certainty (Orfei et al., 2010). Mastery was positively associated with verbal memory in Lysaker's 2005 study but this was not replicated in the 2010 or 2011b papers. Giusti et al., (2013)

found no relationship between immediate and delayed memory and indices of cognitive insight and Bruno et al., (2011) found no significant relationship with general memory and metamemory ability. Bruno et al., (2011) however did find more correct answers on a memory test to correlate with a low feeling of knowing compared to healthy controls. Lepage (2008) in an early paper, found a significant correlation with overall cognitive insight but this relationship was not found with self-reflectivity (the measure included for this review) and this effect was similarly found by Orfei et al., (2010). This could suggest that the relationship with self-certainty rather than reflectivity underpinned memory performance. Being less certain may lead to correcting erroneous performances and more conservative strategy adoption when completing tasks leading to improved performance. Finally, Kother et al, (2012) report that poor immediate recall was correlated with number of high confidence incorrect responses.

In summary, metacognition measured over multiple indices has been found to relate to different aspects of memory. The most pronounced effect appears to be in the relationship between immediate memory and the metacognitive domain of understanding one's own mind. In order to reflect back on one's cognition, it must be held online for appraisal and often multiple pieces of information (e.g. the cognition, behaviour and outcome) must be simultaneously recalled which requires functional working memory. Furthermore, longer term memory may also be implicated as one needs to remember past events and mental states to begin with to inform future behaviours and behavioural strategy choices. The results of the meta-analysis suggest that working memory appears critical to metacognitive processing however Lysaker warns that for the true relationship to be revealed, a broader set of assessment methods must be incorporated into future study designs. There also seems to be a less linear relationship between cognitive insight and memory; this however could be an artefact of metacognitive measurement. The MAS requires in the moment assessment of previous mental states and therefore the information to be recalled and assessed. The BCIS with whom less consistent findings were available, only requires the individual to reflect generally with no specific information held online at the time of reflection.

2.3.6 IQ

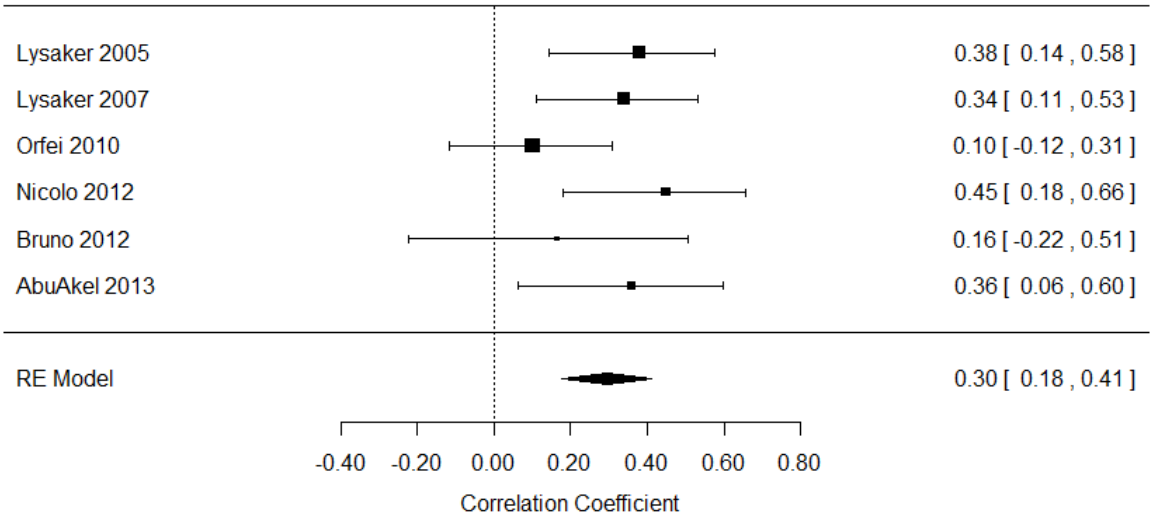

Figure 12 IQ and metacognition forest plot (effect sizes and confidence intervals)

Individual study and mean effect sizes are available in figure 12. In regards to heterogeneity, the Q statistic was not found to be significant across studies for verbal IQ (Q= 6.02, df=5, p>.05) and the I^2 statistic was also low (I^2= 16) meaning a consistent relationship across studies and a total of 329 participants were included in the overall sample. The Z statistic reports a significant effect across studies (Z= 4.83, p <.001). The range of effect sizes for studies included in the meta-analysis was 0.10-0.48 and the mean effect size calculated across studies was 0.30 (95%+/-CI: 0.18:0.41). This infers a moderate effect size for verbal IQ's relationship with metacognitive processing and demonstrates that as verbal IQ increases, metacognitive processing also improves.

The fail-safe N statistic suggest that 58 unpublished studies would need to be available to negate the significant result obtained and Kendall's Tau suggests little publication bias (τ(N=6)=.20, p=.573). Despite a small number of studies present, the funnel plot provides corollary evidence for no significant publication bias being present (see figure 13 below) although this must be interpreted with the fact that only 6 papers were included in analysis.

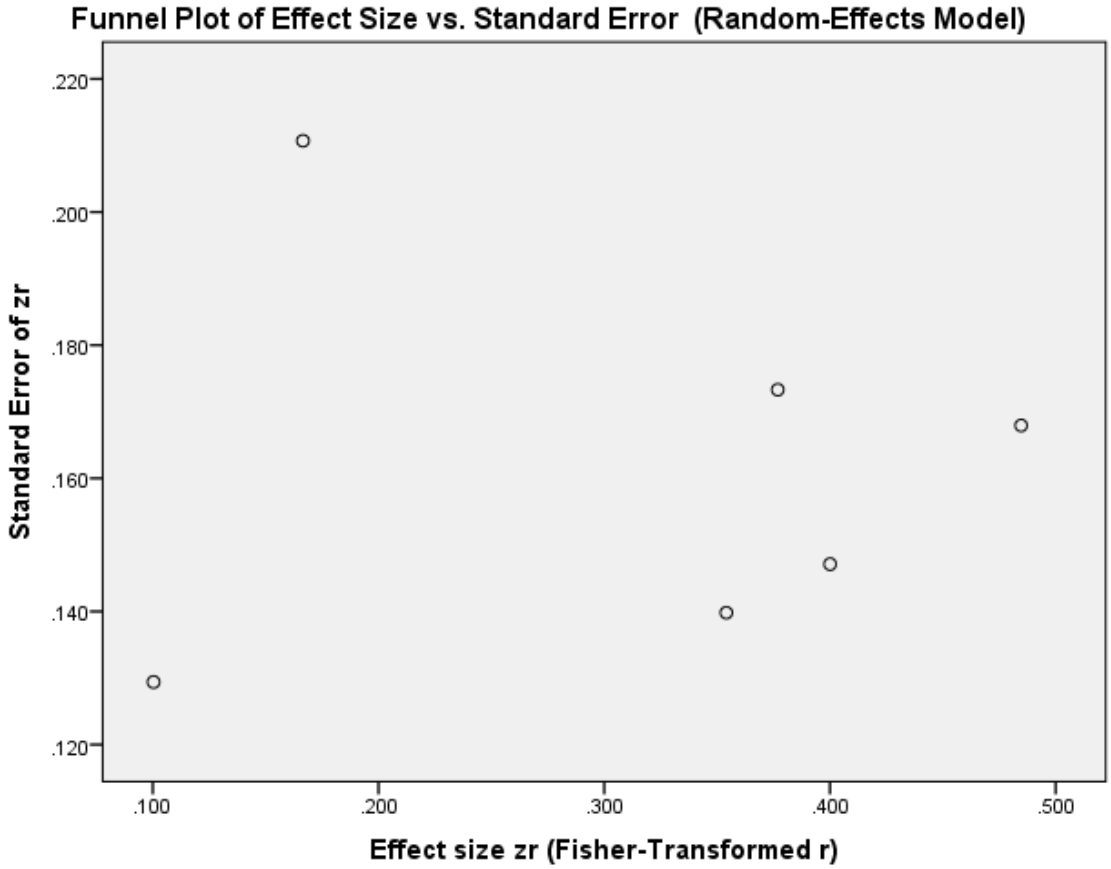

Figure 13 IQ and metacognition funnel plot

Correlations are reported between verbal IQ and mastery (Nicolo et al., 2012; Lysaker et al., 2011a), understanding one's own mind (Lysaker et al., 2007; Abu-Akel & Bo, 2013; Nicolo et al., 2012), total MAS score and understanding the mind of others (Abu-Akel & Bo, 2013; Nicolo et al., 2012). This pattern of relationship to understanding one's own mind but not to decentration further persists across other IQ domains including arithmetic and block design (Lysaker et al., 2007). This suggests that a) metacognition associates with IQ across measures and b) that a stronger relationship exists with understanding one's own mind than understanding that others have a different perspective to our own.

Bruno et al., (2012) found borderline significant negative correlations between verbal performance and total IQ performance and the self-certainty subscale of the BCIS however little to no association was demonstrated on the other measures of cognitive insight (Orfei et al., 2010). In addition Bacon et al., (2009; 2001) and Souchay et al., (2006) all found no significant relationship between IQ and metamemory performance as measured by confidence ratings and Feeling of Knowing (FoK) judgements. In Lysaker et al's., (2013) paper, verbal IQ failed to reach significance to an overall metacognitive factor which combined the MAS and BCIS total scores. This could infer

differing relationships between IQ and cognitive insight and metacognitive reflection which studies only including one measurement component suggest.

Taken together, these findings suggest that deficits observed in metacognition cannot be straightforwardly attributed to overall intellectual impairment because certain cognitive domains may influence aspects of synthetic metacognition and self-reflection uniquely.

2.3.7 Social Cognition

Social cognition has one of the most clearly defined relationships with metacognition and the literature search found 9 papers investigating the relationship with metacognition. This relationship was so developed that some authors have progressed to assessing it's distinctness from indices of metacognition (Efklides, 2008; Lincoln et al., 2011). A meta-analytic technique was run with effect sizes extracted from 7 of the papers with effect sizes ranging from .07-.73 and a total of 358 participants.

The Q (Q=6.89, df= 6, p>.05) and I^2 (I^2=.13) statistics suggest homogeneity in study findings and a significant Z statistic (Z= 3.64, p<.001) suggest a significant relationship between social cognition and metacognition. A means effect size of .35 (+/-95% CI:.17, .51) once again suggest a moderate positive relationship between social cognition and metacognition (individual study effect sizes and confidence intervals are available in figure 14 below).

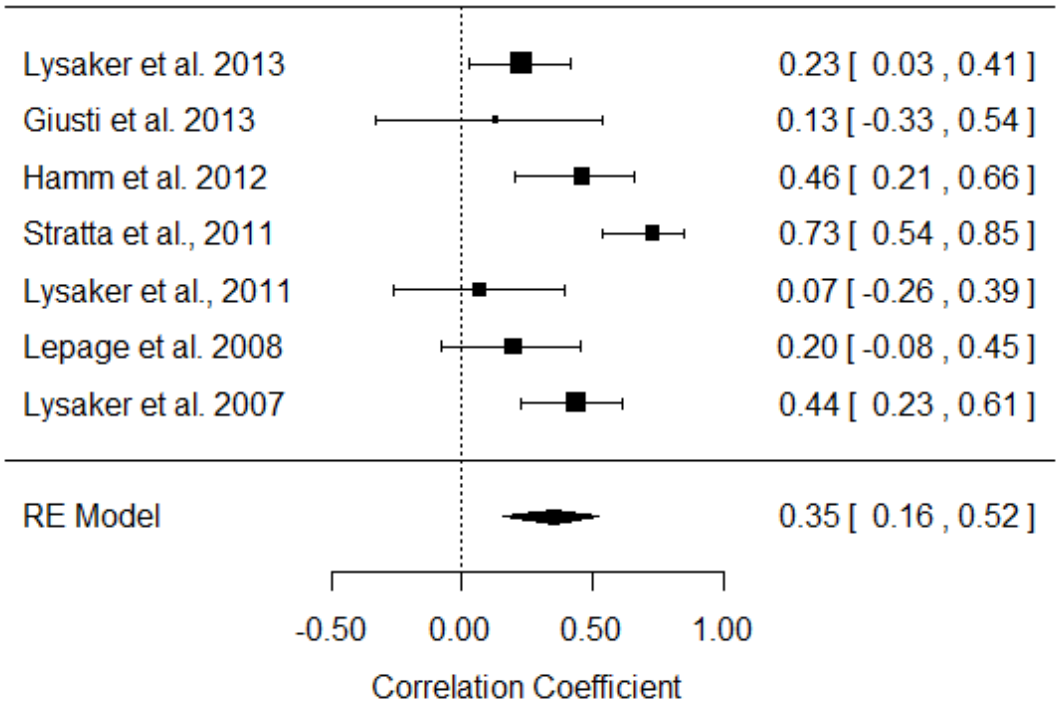

Figure 14 Social cognition and metacognition forest plot

The fail-safe N value suggests that 104 unpublished studies would need to be available to negate the significant finding and Kendall's Tau was also non-significant (τ(N=7)=.05, *p*=.881) providing little evidence of publication bias. The funnel plot is available in figure 15 below.

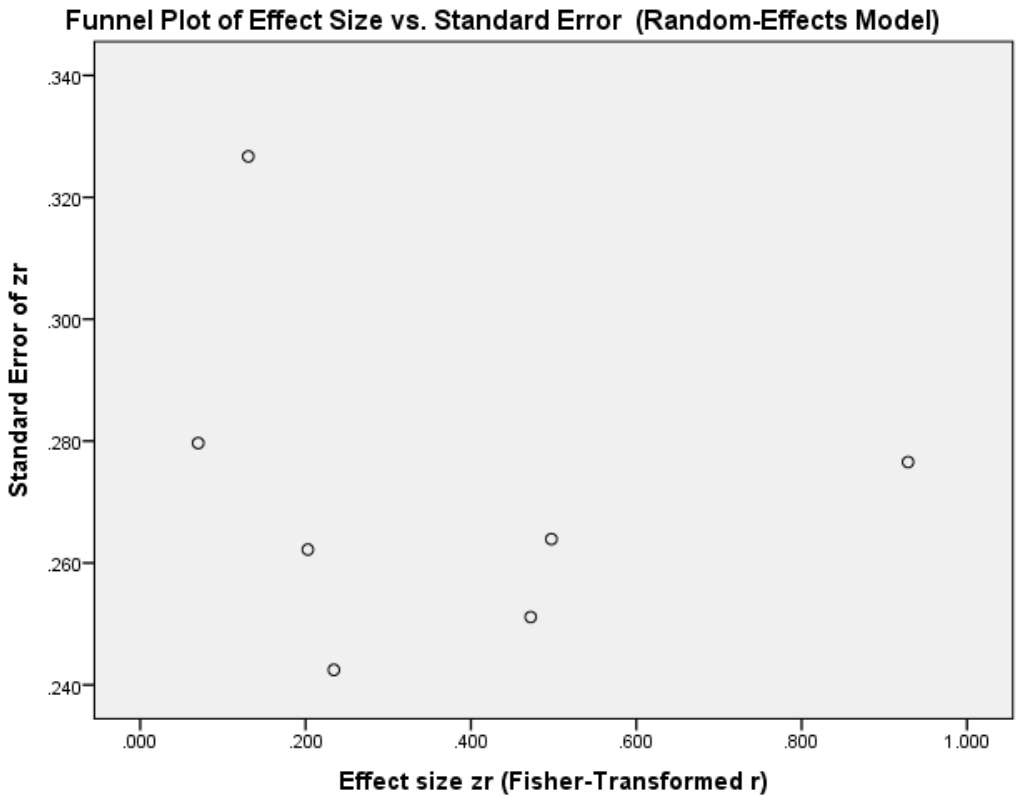

Figure 15 Funnel plot of effect sizes for social cognition and metacognition

Lysaker et al., back in 2007 determined that identification of negative emotions was significantly correlated with understanding one's own mind, and with decentration at both baseline and 6 month follow-up (Hamm et al., 2012). However these results surprisingly were not replicated when identifying positive emotions. Identification of negative emotions in the other was also found in higher scoring individuals on the self-reflectivity subscale of the MAS. The lack of difference between the decentered and non-decentered groups on the emotional recognition measure (BLERT) indicates that making sense of other' intentions is a more sophisticated skill than identifying emotions alone. The relationship of metacognition with poor negative emotion identification in others therefore may exacerbate or precipitate social avoidance and symptoms such as paranoia. By inaccurately concluding that others are experiencing negative emotions towards you, may allow paranoia to develop. Identifying the perspective of another is contingent upon being able to correctly interpret emotional states so a relationship between these variables makes sense to interpret.

Lysaker et al., (2011b) look to further tease this relationship apart investigating the relationship between different facets of social cognition and cognitive insight. They found that social cognitive tasks correlated with each other but the aggregated social cognitive

variables did not correlate with BCIS self-reflection and self-certainty measures. This is evidence for a semi-independent function in social cognition and cognitive insight; thus the ability to clearly judge one's own thoughts (self-reflection) requires a metarepresentation of internal processes and is distinct conceptually from the ability to deduce emotions and thoughts in another. The theory of an overarching, unitary 'mentalizing system' is hard to justify with this evidence; indeed Lysaker et al., (2013) undertook a factor analysis of emotional recognition, ToM, MAS and BCIS scores and found two distinct components relating to social cognition (BLERT, Eyes Test and hinting task) and metacognitive awareness (MAS and BCIS). This distinction has also been found by Mehta and Thirthalli (2013).

Lysaker et al., (2013) advocate that the study demonstrates separate processing for an ability to interpret discrete ideas about the thoughts and feelings of others (social cognition) and the ability to formulate synthetic, complex representations of both oneself and oneself in relation to another (metacognition). However these separate processing routes are indelibly linked.

2.3.8 Attention

Attention has received considerably less investigation than the aforementioned cognitive domains with only two papers in the present review investigating this relationship specifically. Lysaker et al., (2011) employed the Conner Continuous Performance Test (CPT) and compared groups based upon MAS self-reflectivity and social cognition profiles. Despite other cognitive domains demonstrating significant differences across groups, selective attention failed to obtain this with the self-aware/other aware actually demonstrating a slight decrease in attention. Lepage et al., (2008) also failed to find a significant association between attention and self-reflectivity although the self-certainty and composite index scores found trend level significant relationships.

2.3.9 Processing Speed

Five papers included processing speed and it has been demonstrated to associate with understanding one's own mind (Lysaker et al., 2005; 2011) and mastery (Lysaker et al., 2011) however not with understanding the mind of others (Lysaker et al., 2005). Furthermore, processing speed was found to predict 10% of the variance in understanding one's own mind. The authors conclude that the metacognitive ability to understand one's own mind is influenced by markers of general cognitive function. This finding is replicated in later papers in the domains of self-reflectivity and mastery (Lysaker et al., 2011) with participants high in both metacognitive domains

demonstrating significantly faster processing speed scores. Nicolo et al., (2012) in comparison found significant correlations between processing speed and understanding one's own mind, understanding the mind of others and mastery, extending previous findings in a more emphatic manner. Overall, studies indicate that processing speed is important to metacognitive function however the current evidence available needs refinement and the exact mechanisms need to be determined in relation to other cognitive variables. Presumably higher order metacognitive tasks require mental flexibility and the ability to switch between mental states in order to assess them successfully which relies on processing speed.

2.3.10 Visual-Spatial Intelligence

Three studies included assessments of visual-spatial abilities, often considered a measurement of non-verbal intelligence; Lysaker et al., (2007), Orfei et al., (2010) and Giusti et al., (2013). Lysaker et al., report a significant association between the block design task and understanding one's own mind and found a significant difference between those high in self-reflectivity and decentration and those low and without decentration. Giusti et al., (2013) report a significant positive correlation between the self-reflectivity subscale of the BCIS and visual-spatial intelligence. The composite index and self-certainty subscales failed to achieve significance. Orfei et al., (2010) failed to find any significant correlations between visual-spatial function, and the BCIS. These equivocal findings indicate that visual-spatial intelligence may relate to metacognitive function as a reflection of general cognitive impairment rather than having a specific relationship itself.

2.3.11 General Cognition

Finally, 2 papers completed PCA analysis on a variety of cognitive tasks to produce a composite cognition factor. Guisti et al., (2013) found no significant relationship between overall cognition and any of the BCIS scales however Lysaker et al., (2010) found a significant relationship between cognition and the MAS subscale of Mastery. Lysaker et al., (2010) assess this finding and report that in order to respond to psychological and interpersonal difficulties, a degree of neurocognition is required to process and react appropriately. It should be noted however that whilst both papers employed a version of the WCST task of executive function, the other composite tasks were different and may explain the difference in findings. Which variable(s) are driving the relationship remains hidden and future research in the area must focus on unearthing the mechanics of the relationship between general cognition and metacognitive processing.

2.4.1 Metacognition's relationship with functional outcome

Table three contains the individual study information for those included in the meta-analysis of the relationship between metacognition and functional outcome. Metacognition was measured through a variety of methods in the papers included. Three of the studies included the Metacognition Assessment Scale (MAS) as their measurement of metacognitive processing, one the WCST-meta paradigm and one the Beck Cognitive Insight Scale. The WCST-meta measure of metcognition involves a confidence versus accuracy performance on a cognitive task measured as a correlation. Stratta et al., (2009) adopt Koren's WCST-meta paradigm which also includes the choice to include a response in the final total arguing that this is a more ecologically valid form of processing which addresses both the control and monitoring components of Nelson and Narens' (2003) metacognitive model.

The outcome measures were more disparate in their scope. Luedtke et al., (2012) estimate outcome by comparing the partcipant self-rating of work performance to the rating attributed by a researcher. Tas et al., (2012) likewise employ the difference between predicted performance and actual performance on a task and Lysaker et al., (2011) measure functional capacity through the performance-based skills assessment battery (UPSA). The aforementioned outcome measures are considered to measure functional capacity and are the first 3 studies included in the forest plot above. The latter 2 studies employed the GAF which is a measure of objective functional outcome.

Table 3 Systematic review results table: Metacognition and functional outcome

Study	*Diagnosis*	*Population*	*Metacognition measure*	*Outcome measure*	*Effect size*
Luedtke et al., (2012)	SCID DSM-IV criteria schizophrenia/schizoaffective disorder	41	Metacognition Assessment Scale	Accuracy of Work Performance Appraisal	.55
Tas et al., (2012)	SCID DSM-IV criteria schizophrenia/schizoaffective disorder	52	Metacognition Assessment Scale	Learning Potential	.32
Lysaker et al., (2011)	DSM-IV criteria for schizophrenia	45	Metacognition Assessment Scale	Functional Capacity	.2
Stratta et al., 2009)	DSM-IV criteria for schizophrenia	20	Wisconsin Card Sorting Task-meta	Global Assessment of Functioning	.57
O'Connor et al., (2013)	DSM-IV criteria schizophrenia or related disorder, or affective disorder with psychotic features	127	Beck Cognitive Insight Scale	Global Assessment of Functioning	.14

The five studies included for the meta-analysis had an effect size range of 0.14 to 0.57 and the total sample size was 285. The Q (Q= 3.96, df=4, p>.05) and I^2 (I^2= 0) statistic suggest homogeneity was present across study domains indicating that there was not a significant difference in effect sizes found across studies. The mean effect size across studies was .33, the confidence intervals ($CI_{.95}$) were .15 (lower) to .49 (upper) and a highly significant associated Z score between studies was also observed (*z*= 3.42, p=.001). The forest plot with individual study and mean effect size and confidence intervals is available in figure 16 below. This infers a moderate positive (Cohen, 1992) relationship between metacognitive ability and function therefore as metacognitive ability improves so does function.

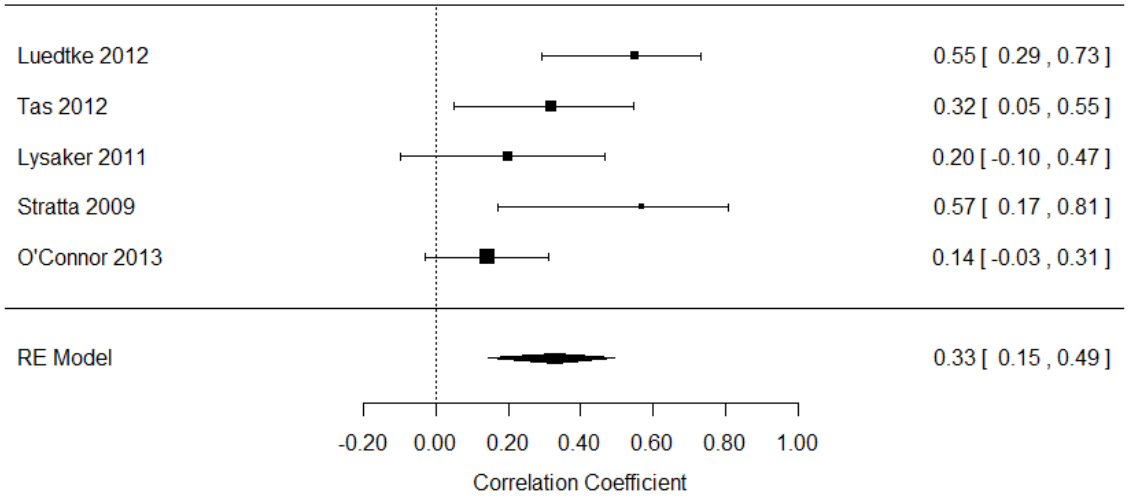

Figure 16 Metacognition and functional outcome forest plot (effect sizes and confidence intervals)

An inspection of the fail-safe N value indicates that there would need to be 46 unpublished studies with 0 effect sizes to ameliorate the significant effect found and an inspection of Kendall's Tau suggests little publication bias (τ(N=5)=.6, p=.142). Despite a small number of studies present, the funnel plot provides corollary evidence for no significant publication bias being present (see figure 17 below).

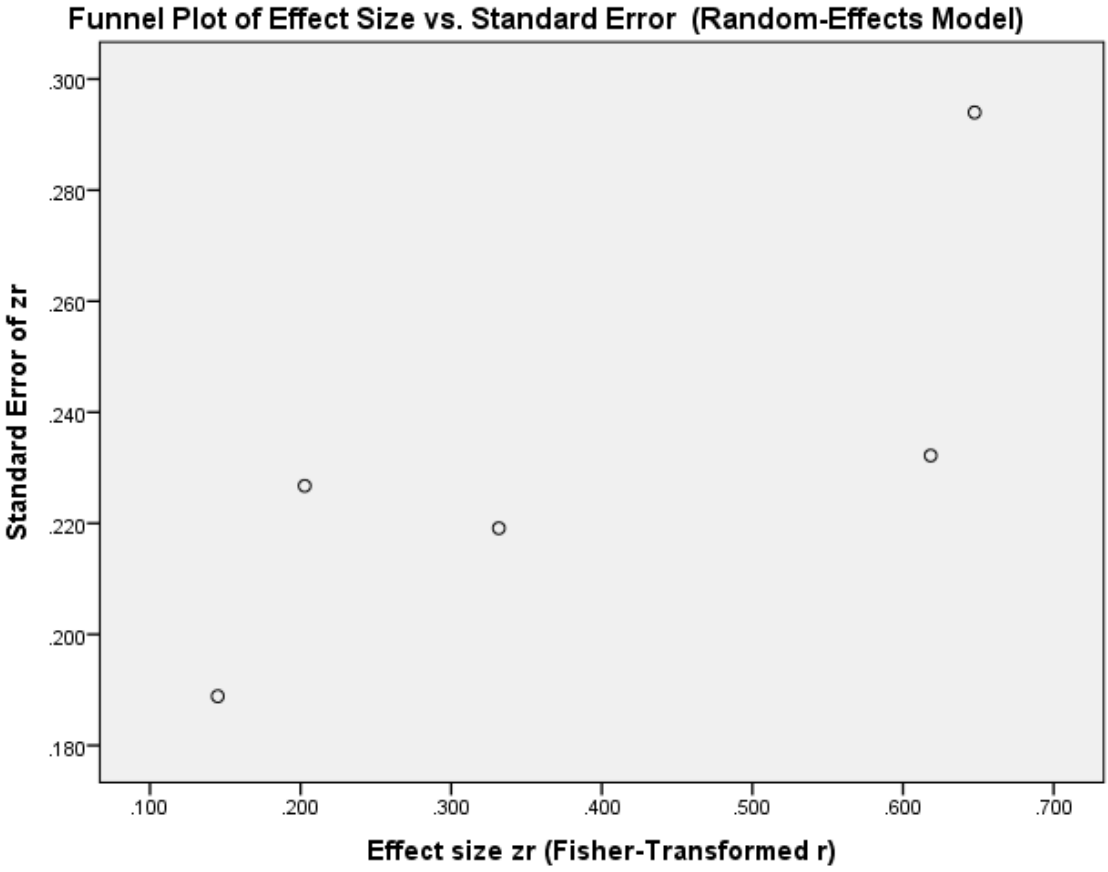

Figure 17 Metacognition and functional outcome funnel plot

2.5 Discussion

The results indicate that dysfunctional metacognitive processing is associated with impoverished cognitive processing as demonstrated in cross-sectional studies gathered from the last 15 years. The individual meta-analyses results indicate a small to moderate effect size for different aspects of cognition on metacognitive processing. The most striking effect size was observed in the cognitive domain of social cognition in the present study. The second analysis confirms that there is a moderate relationship between metacognition and functional outcome across studies.

2.5.1 The relationship between cognition and metacognition

Firstly, an overall significant relationship was found between combined measures of cognition and metacognition and a moderate mean effect size was reported. In relation to individual cognitive domains and metacognition, executive function was the most frequently investigated cognitive domain however the present meta-analysis only indicated a small-moderate effect size. The relationship between executive function and confidence-based measures of metacognition rather than the MAS and BCIS is made slightly more complicated by the fact that a measure of executive function was often incorporated into the metacognitive judgement in design (such as in the case of the meta-WCST). This makes the relationship slightly harder to tease apart. In terms of metacognitive knowledge, conceptually the relationship makes sense. In order to produce and form mental states, a series of cognitive abilities (recall, emotional recognition) are required, however in order to do this successfully, one must be able to switch between tasks effectively and inhibit irrelevant information to judge and reflect. Likewise, in relation to the BCIS, executive function in addition to memory may be required in order to hold contextual information online to assess judgements and notice distortions or erroneous outputs/conclusions.

Working Memory has certainly been associated with the MAS as, in order to consider mental states, these mental states need to be recalled in the first instance. Episodic memory is required to remember previous events, contextual and self-relevant aspects to the event, and why one chose particular strategies during the situation. Similarly, memory deficits were reported in the majority of studies incorporating the BCIS as a measure of metacognition; in order to assess the validity of one's previous judgements and success, memory is required to reflect back accurately. The confidence-based measures in comparison, are immediate inferences and are seemingly less dependent upon memory (although still draw upon this to an extent) as decisions are made straight after attending to a task. One concern in terms of assessing memory in the above reviews appears to be a lack of consensus on measurement tasks and types of memory

assessed; a variety of memory aspects have been investigated through different designs. Working memory and delayed verbal memory may related differently to metacognition.

Social cognition demonstrated the strongest relationship to metacognition with a moderate effect size. This relationship validates the speculations among authors to ensure that they are indeed distinct from one another however Lysaker et al., (2013) did find this. The task with the strongest effect sizes appears to be the BLERT which requires participants to assess emotional states within others; this may overlap with understanding the mind of others contained in the MAS although once again, authors do suggest that these are processing units from discrete versus synthetic higher-order processing. They are related but distinct processing avenues drawing on related but separate processing pathways (Lysaker et al., 2013).

Processing speed deficits have been well documented in schizophrenia research and the papers reviewed here offer some evidence for a relationship with metacognition too. However it is noteworthy that none of the papers incorporating confidence-based measures or the BCIS included processing speed so comments offered on this aspect of metacognition are limited to conjecture. Dickinson, Ramsey and Gold (2007) argue that processing speed underpins higher cognitive faculties such as executive function therefore impaired processing speed may underlie the relation between executive function and metacognitive performance. Whether a poverty in processing speed inhibits moment-by-moment assessment of cognitive performance would be worth further investigation. Intuitively, this appeals more to confidence-based measures or implicit metacognitive processing rather than the reflective nature of the BCIS however further evidence is warranted before assertions can be made. Confidence-based judgements are typically made immediately after a task therefore may be contingent on processing both the task and making a decision on how accurate the performance was whereas reflexive metacognitive knowledge may be more dependent on memory and executive function.

Attention appeared to have the weakest relationship with either measure of metacognition. This could infer that completing metacognitive tasks requires little more attention than required for the task itself. One interpretation is that reflection and mental state assessment do not require much attention and any trend level effects could just be echoes from a general cognitive blunting however this is speculative as the present review could not investigate this relationship.

2.5.2 Limitations

As with all meta-analysis, there were some systemic problems in the data included in analysis. Firstly, due to different study designs, the analysis had to find a balance between conceptual integrity when combining variables, and running analysis on a meaningful amount of data. The verbal IQ analysis was conducted on six studies and the executive function and memory on eight. Whilst there is preliminary evidence to suggest that the MAS and BCIS are homogenous in measurement (Lysaker et al., 2013), more work needs to be completed in the area to improve confidence in this conceptual alignment. Previous meta-analyses have reported that cognitive function deficits in schizophrenia that measure IQ by the WAIS produce larger effect sizes than those investigated by non-WAIS assessment (Heinrichs & Zakanis, 1998; Mesholam-gately et al., 2009). They attribute this to differential degrees of sensitivity within intellectual ability testing. The effect sizes included in the meta-analysis for verbal IQ were larger in the studies that included the WAIS (0.34-0.38) than those that used non-WAIS measures (0.1-0.165) thus the mean effect size observed may be attributable to the WAIS sensitivity. This potentially could underpin the effects found in other cognitive domains and systematic reviews comparing different methods of cognitive function measurement may wish to investigate this.

Similarly, the meta-analysis employed multiple measures of memory when calculating mean effect sizes. In order to complete a meta-analysis, studies had to be grouped together across measures for numbers however there is some evidence alluding to memory deficits being more pronounced in some modalities rather than others (Aas et al., 2014). The most severe deficits appear to be observed in verbal working memory. Future studies may want to assess the differing functional domains and compare the impact of different types of memory on metacognition although it must be noted that a heterogeneity analysis did not raise any significant concerns.

The lack of consistently employed, standardised measures makes cross-study comparisons difficult (Green et al., 2008). There has been a consensus in schizophrenia research to address this problem and great steps have been made in introducing the MATRICS neurocognitive battery (Nuechterlein et al., 2012) however the studies reported in this review have yet to benefit from this initiative. Likewise, even studies employing the MAS tended to report different subscales, and infrequently total scores, which prevents assessing the influence of differing cognitive domains on different aspects of metacognitive function.

Metacognition is defined differently by authors and the search term may also have been problematic; some papers looking at related areas may have been missed due to using

a different description such as mentalizing (Abu-Akel & Bo, 2013) or high-order thought (Rosenthal, 2000) which are metacognitive in nature.

Due to the nascent research area, fewer studies were available and, publication bias can be a factor in meta-analyses as significant results tend to be reported in papers and non-significant results omitted. Whilst in the present review authors took every step to avoid this, not all authors were able to be contacted to obtain any related data therefore some data may be missing. A final problem was found in the sample descriptions; whilst some studies reported that the sample recruited was from a higher-functioning cohort, some of the studies employed different diagnostic entry criteria and some gave little description other than 'persons with schizophrenia'. Thus certainty that similar clinical profiles are being compared is difficult to claim. Likewise, only one of the studies was completed in FEP; whilst work on both neurocognition (Meshalom-Gately et al., 2013) and metacognition (Macbeth et al., 2014) have been investigated in FEP, the relationship between neurocognition, metacognition and functional outcome specifically has not. Lepage et al., (2008) found no significant relationship between the BCIS and memory however whether this is symptomatic of the relationship having not manifest in early-onset samples or whether this was due to measures selection is hard to elucidate due to the dearth of studies.

2.5.3.Future directions

One of the main suggestions made in the studies included in the present review relates to future studies needing to replicate findings in different cohorts. Many of the confidence–based designs employed small sample sizes and higher-functioning samples which place restrictions on inferences that can be made on results. A plethora of studies list sample selection as a potential problem, with schizophrenia samples largely comprised of middle-aged, chronic presentation males. The relationships found may be due to treatment exposures, neuroleptic medication administration or rehabilitation efforts therefore replication must be made in more diverse samples such as FEP, those refusing treatment and female participants. For example, neuroleptic medication has been demonstrated to impair processing speed in schizophrenia (Veselinovic et al., 2013) and processing speed has been linked to both working memory and executive function. Whether the deficits observed in these domains is due to cognitive impairment or impairment due to medication exposure would be valuable to investigate. The metacognitive profiles may be different in earlier phases of illness and neurocognitive function can be assessed prior to extended treatment effects. Towards this end, future studies need to be completed in FEP to i) address the aforementioned potential confounding variables ii) to assess at which stage of illness the deficits may

occur and iii) to understanding the causes of schizophrenia. Similarly, the majority of investigations were cross-sectional and only employed restricted measures of both neurocognition and metacognition. Future researchers need to employ multiple measures of both neurocognition and metacognition across longitudinal designs to really excavate the relationship between these concepts.

Social cognition also requires further clarification as to how different aspects relate to each other. Studies have employed multiple measures of emotional recognition, theory of mind and social inference and headway has been made in looking at the relationship between neurocognition and function (e.g. Horan et al., 2011). Studies in the present review appear to have mainly included the Reading the Mind in the Eyes test and the BLERT which provide conflicting results. As to how much they measure the same skill and are therefore combinable for a review needs clarification. The relationship between discrete social processing and synthetic metacognitive processing also needs more refinement as conceptually they appear to overlap to a degree. Hamm et al., (2012) did look into the two concepts and found a distinct but significant relationship. Preliminary research infers that social cognition is multifaceted (Bell et al., 2009) and may have two tiers of function; emotional perception and emotional regulation (Lin et al., 2012) and higher order inferential tasks such as egocentricity (Bell et al., 2009). These higher-order social cognitive tasks have been omitted from studies to date. To what extent these inferential tasks overlap with metacognition, symptoms and ultimately function needs further investigation as higher-order social cognition such as the ability to detach oneself from the other may be closer to metacognitive processing than social cognition.

2.5.4 The relationship between metacognition and functional outcome

The results of the second meta-analysis indicate that metacognitive processing has a moderate sized effect on functional outcome in schizophrenia. Furthermore, These individual effects observed in the preliminary studies are consistently found across designs. Put simply, better metacognitive abilities relate to better functional outcome in those with a diagnosis of schizophrenia as demonstrated across a larger participant pool in the present study. Despite the few studies included in this exploratory meta-analysis, there is little indication of publication bias and a large amount of unpublished studies would need to be present in order to ameliorate the observed relationship found in analysis.

Functional outcome

Cognitive insight as a measure of metacognition correlated with functional outcome in the O'Connor study and metacognitive accuracy was significantly related to the same

outcome measure (Stratta et al., 2009). The authors suggest that the monitoring and control of cognitive strategies assessed using the WCST-meta paradigm are also required for the initiation and maintenance of interpersonal relationship. These metacognitive abilities may be more pertinent skills to successful community integration than cognitive ability alone. Interestingly, O'Connor et al., (2009) found that once negative symptoms, ethnicity and gender were controlled for in analysis, this relationship between cognitive insight and outcome was not significant. This may be reflective of cognitive insight having a more pronounced impact on function longer term as measurements were only taken 12 months from baseline. A stronger correlation was found between cognitive insight and the symptom severity construct of the GAF (.32) and a significant relationship was also found between cognitive insight and psychopathology as measured by the PANSS. This may also indicate that cognitive insight is more closely related to general psychopathology then psychosocial function. The authors speculate that the translation of these impairments to functional impairment rather than psychopathology may occur later into the illness course therefore studies looking at this dynamic overtime may prove valuable. Another potential explanation is that this relationship may be reciprocal rather than unidimensional; a lack of cognitive insight may foster symptom development unchecked and the persistence of symptoms may hinder self-reflection through cognitive disruption and bias assessment of cognition. This symbiotic cycle may lead to functional disability and holding down social and occupational relationships may be impacted. The relationship between cognitive insight and psychopathology has been inconsistently found across studies (Favrod et al., 2008) therefore the direction of this relationship may be important to further investigate.

Functional capacity

The metacognitive domain of mastery (Lysaker et al., 2011; Tas et al., 2011) and self-reflectivity (Luedtke et al., 2011) were significantly related to overall functional capacity across studies and specific outcome measures. Mastery, being a measure of the ability to use metacognitive knowledge to respond to challenges and solve psychological problems, and self-reflectivity, may underpin the ability to learn new tasks and solve problems. These are critical skills for successful occupational function. The ability to identify solutions to interpersonal social problems and reflect back and identify social strategy choices as either successful or erroneous is critical to regaining community function. Conversely, an inability to use metacognitive strategies to respond to difficult situations may lead to a reliance upon basic evolutionary defences (Gilbert, 2001), an avoidance of difficult or confusing social situations and the atrophy of functional skills (Lysaker et al., 2011). Further analysis of Lysaker's study reveals that the association

between mastery and functional capacity is largely underpinned by the comprehension/planning subscale of the UPSA. This is indicative of metacognition being required to anticipate future events, situations and interpersonal interactions as a pre-emptive measure rather than solely relying upon online metacognitive processes to react to current circumstances in the moment. Tas et al., (2012) also incorporate intrinsic motivation into analysis and suggest that improved metacognitive processing allows the personal relevance of a task to become more integrated thus improving learning potential.

2.5.5 Limitations and recommendations

The present analysis must be considered exploratory rather than definitive and inferences must be made with certain limitations in mind. Firstly, only 5 studies were included in the sample which restricts the power of the analysis and the scope of the investigation. An inclusion criteria had to be decided upon which lead to the exclusion of many papers. This is reflective of the disparate measurement of both variables in research. Despite preceding studies offering support to metacognitive variables relating to one another, a refined understanding of how they interact and whether they measure explicitly the same metacognitive domain is yet to be produced. Most modern models of metacognition report there to be different 'levels' of processing at play, the WCST-meta task reflects more intuitive, subconscious, implicit knowledge of cognitive processes whereas the MAS is an explicit, conscious, narrative of mental states integration in social contexts. Whilst they are in most conceptualisations part of a meta-level system, a lack of standardisation in measurement of metacognition makes cross-study comparisons problematic. Different metacognitive abilities may relate independently to function and if more studies were available, a separate analysis would shed light on specific pathways between levels of metacognitive process and constituent parts of function. Likewise, the studies included were of a correlational nature restricting the inference of causal links between variables. Study designs incorporating multiple measures of both metacognition and different indices of outcome would be a valuable addition to the research landscape. Likewise, longitudinal studies tracking the relationship between metacognition and function over time would also provide a valuable insight as all the studies included were cross-sectional in nature.

One of the main problems identified in the literature is capturing the nature of functioning in schizophrenia. In two of the studies, the index of actual performance by which the self-reported performance data was compared was a clinician-based assessment. Performance-based measures are being suggested as a better measurement of function (Depp et al., 2012) however only one study in the present review assessed functional outcome this way. The Tas et al., (2012) paper employed learning potential as an

outcome measure however, with Wykes and Reeder's (2005) suggestions that learned skills do not necessarily convert to utilisation in the community, this is arguably a prerequisite rather than a guarantee of psychosocial function. Finally, Tas et al., (2012) included a measure of functional outcome that assessed actual performance against expected performance based on WCST performance. How researchers measure an expected trajectory of learning potential on basic demographic and cognitive abilities is difficult to defend with the multi-faceted determinants of expected outcome.

Whilst the inspection of publication bias did not highlight any significant 'file-draw' problems, studies did not always report all of the gathered data across constructs. The full reporting of different aspects of outcome and refraining from the use of composite aspects of function would make comparisons more impactful. Likewise in the case of the MAS, the scale has 4 subscales, and studies varied in which domain was included as a measure of metacognition and often only reported one of them. If all 4 domains were included in reporting a more comprehensive comparison could be made.

2.5.6 Conclusions

In conclusion, the present meta-analysis found small to moderate effects across the domains of executive function, memory and verbal IQ on metacognitive processing and a moderate effect of metacognition on function. A better understanding of the mechanics driving individual recovery in function with schizophrenia is essential and may be used to further the known relationship between neurocognition and function. Aspects of metacognition have the scope to contribute to the ability for an individual to return to work, maintain social relationships, live independently and manage symptoms in the community. Questions remain about the manner in which negative symptoms (also implicated in functional outcome) interact with metacognition and functional outcome. Also, how these relationships change over time may of importance to understanding recovery. Potentially symptoms may be more predictive of cross-sectional functioning however longer-term, metacognition may be of importance once symptoms have been addressed. By understanding the relationship further, cognitive remediation and metacognitive behavioural therapy can be focused and refined to give those with a schizophrenia diagnosis the raw skills to regain both functional abilities and symptom management.

2.6 Chapter summary

The aforementioned reviews demonstrate that existing research i) empirically confirms a relationship between cognitive and metacognitive function ii) improved metacognition is associated with better functional capacity and outcome. If this is considered with the findings in chapter one that neurocognition is related to function but does not account for

the entire relationship, metacognition may bridge the gap in the relationship. This could offer insight into the determinants of recovery from schizophrenia.

2.7 Chapter limitations

The aforementioned conclusions must be made with limitations in mind however. Due to multiple measures being used in different studies, the exact nature of relationships and comparisons between studies is problematic. Different measurements of metacognition may draw on different cognitive domains so synthesising studies is conceptually difficult to consolidate despite known correlations between the MAS and BCIS. Less is known about the relationship between confidence-based judgements, BCIS and the MAS and these were combined in the first analysis. Likewise, functional capacity and outcome are known to be related but distinct concepts and were combined in the second analysis. Therefore this review must function as a ground-clearing rather than definitive assessment of the literature. The main drawback of the evidence included in this review is the research being grounded in chronic schizophrenia samples. This makes it difficult to unpick whether relationships observed are due to longer-term exposure to medication or differing access to therapies. Work conducted in early stage psychosis will avoid some of these concerns. These limitations will be addressed in the next two empirical chapters through a mediation analysis looking directly at neurocognition, metacognition and both objective and functional capacity and an MRI structural investigation.

Chapter 3: Metacognition as a mediator between neurocognition and functional outcome in FEP.

3.1 Introduction

3.1.1Neurocognition

Neurocognitive deficits in schizophrenia have long been observed (Kraeplin, 1919), considered a core feature of the disorder (Reichenberg & Harvey, 2007) and even been considered a vulnerability marker for later schizophrenia development (Nuechterlein et al., 2012). Deficits are observed in working memory (Lee & Park, 2005) executive function (Sullivan, Shear, Zipursky, Sagar, & Pfefferbaum, 1994), language (Kuperberg, 2010), attention and general IQ (Heinrichs & Zakzanis, 1998b) amongst a host of other indices. Researchers differ over whether the cognitive deficits can be considered a consequence of generalised impairment (Dickinson, Iannone, Wilk, & Gold, 2004) or whether there are distinct cognitive deficit profiles (Reichenberg et al., 2009). In addition, different neurocognitive processing domains have been found to relate to differing symptom profiles (Nieuwenstein, Aleman, & de Haan, 2001; Greenwood et al. 2008) (see section 1.2).

3.1.2 Relationship with functional outcome

Whilst cognitive deficits have been known to exist for a long time, it was Michael Green's work in the 1990s that highlighted the importance of cognitive ability in predicting functional recovery in the community and placed neurocognition as a focal point in the eye of then contemporary research (Green, 1996; Green et al., 2000). Cognitive performance has been associated with improved self-reported quality of life (Addington & Addington, 2000), social (Stirling et al., 2003) and occupational outcomes (Jaeger et al., 2003) and these relationships persist in longitudinal designs (see Green, Kern, & Heaton, 2004 for a review). However later reviews found inconsistent measurement of cognition across studies (Green, Nuechterlein, et al., 2004) and the magnitude of the relationship appears limited (Schmidt et al., 2011). Cognitive remediation programmes were introduced to exploit this relationship; by improving an individual's cognitive skills, community outcomes would also improve (Wykes et al., 2011). However these interventions did not necessarily lead to real-world improvements in functional status (Wykes & Reeder, 2008) (see section 1.11). This led to the search for mediating variables between the two constructs to account for the relationship.

One such candidate variable to explain the unaccounted for variance in the relationship between neurocognition and functional outcome is metacognition (see chapter 1, section 1.13 for further details) which has been observed to have a relationship between both neurocognition (Nicolò et al., 2012) and functional status (e.g. Lysaker et al., 2011) (see chapter 2 for a full review of these relationships).

3.1.3 Metacognition

Metacognition is broadly defined as 'thinking about thinking' (Frith, 2012) and relates to our ability to inspect cognitive products and mental states (Lysaker et al., 2005) and objectively scrutinise them (Brüne et al., 2011). This higher-order ability draws upon cognitive skills to process self-referential information and may be essential to the integration of raw cognitive processing into a complex and constantly evolving social world (Lysaker et al., 2010). Thus it is what we know that we know that is important (Koriat, 2008), Being unaware of erroneous decisions may lead to inaccurate social interpretations and poor behavioural response choices fostering social disability.

Metacognition can be both conceptualised and measured in a number of ways (see section 1.14 for further details). One particular approach has been through assessing an individual's ability to describe and reflect back on their own cognition, differentiate between mental state transitions, their relationship to emotion and behaviour and to differentiate between one's own and the mental states of others (Lysaker et al., 2008; Semerari et al., 2003). The *Metacognitive Assessment Interview* (MAI) encourages the interviewee to describe their own mental products in a free narrative account guided by the interviewer. This ability has been associated with the insight we have into our own cognition called *cognitive insight* (Beck et al., 2004) which places demands upon the individual to demonstrate an awareness of the fallibility of cognition and consider alternative interpretations of events. Both assessments of metacognition have been found to relate to functioning (Giusti, Mazza, Pollice, Casacchia, & Roncone, 2013; Lysaker, Shea, et al., 2010) and neurocognition (Lysaker, Dimaggio, Buck, Carcione, & Nicolò, 2007) although the findings for cognitive insight appear more mixed (Lepage et al., 2008). In addition, few studies have investigated the extent to which the two measures overlap although Lysaker et al., (2013) did find them to load onto a metacognitive awareness factor separable from neurocognition in a factor analysis. This would provide insight into the extent that different measures of metacognitive processing inhabit a shared ubiquitous metacognitive system and relate to functioning.

3.1.4 Metacognition as a mediator

A domain of metacognition (*mastery* or the ability to use mental state information to solve psychological challenges) has been found to mediate the relationship between neurocognition and social functioning in a chronic schizophrenia sample (Lysaker, Shea, et al., 2010). However whether this mediation is pervasive or specific to this aspect of metacognition, and whether it is present in early stage samples, needs to be addressed (Lysaker et al., 2010). This will assess whether deficits are present before chronic stages of illness or as a result of them. Also, the preceding authors employed only one measure of outcome (the frequency of social contacts); functional recovery is considered a multi-faceted concept including a host of occupational (Bell et al., 2009), social involvement (Robertson et al., 2013), ability to complete daily tasks (Leifker, Patterson, Heaton, & Harvey, 2011) and subjective sense of recovery (Andresen, Oades, & Caputi, 2003) aspects to its measurement. Research needs to account for different measures of outcome after illness and explore the relationship between cognitive abilities and metacognition. Having the ability to reflect back and learn may be critical to integrating cognitive skills into real-world situations. Furthermore, incorporating metacognitive processing into cognitive remediation programmes has already begun in small trials with positive results thus far (Cella, Reeder, & Wykes, 2015). These metacognitive skills may aid the learning of new information, improve social and occupational recovery and promote self-management in the community.

Preceding research has also been predominantly completed on chronic cohorts and the effects observed are difficult to disentangle from the longer-term impact of neuroleptic medication and differing access to psychological therapies (lysaker et al., 2008). New research needs to be completed in early stage, non-chronic schizophrenia to evade some of these potential pitfalls. Furthermore, reviews suggest that neurcognition only accounts for around 40% of the relationship between cognitive ability and functional outcome and metacognition may offer further insight into this relationship (see section 1.13).

3.1.5 Summary

In summary, metacognition has been found to relate to both neurocognition and function however the extent to which it may relate to different measurements of functional outcome has not been addressed. How metacognition impacts on functional capacity *and* objective function requires clarification as few designs have differentiated between these variables. Negative but not positive symptoms have also been implicated in the relationship between neurocognition and function (Greenwood et al., 2005; Strassnig et al., 2015) and as such, will be also be investigated in the present study. Furthermore, by

conducting research in FEP, the aforementioned confounds of medication and therapy exposure can be reduced. Whether metacognitive deficits are an aspect of longer-term illness chronicity or whether present at an early stage of psychosis can also be addressed.

3.1.6 Study aims

This first study aim will be to determine the construct structure of different measurements of neurocognition, metacognition and functional outcome through a series of factor analysis procedures. The following hypotheses will then be addressed:

Study hypotheses

i) That the relationship between neurocognition and functional capacity will be mediated by metacognition.

ii) That the relationship between neurocognition and objective function will be mediated by metacognition.

iii) The relationship between neurocognition and time spent in structured activities will be mediated by functional capacity.

iv) The relationship between functional capacity and time spent in structured activities will be mediated by metacognition.

v) The relationship between neurocognition and functional capacity is mediated by metacognition and negative symptoms.

vi) The relationship between memory, IQ and executive function, and functional outcome (functional capacity and objective function) will be mediated by metacognition and negative symptoms.

These hypotheses will be evaluated through a series of path models looking at the relationships independently.

3.2 Method

3.2.1 Design

A cross-sectional design was employed with neurocognitive, metacognitive and functional measures being administered as well as symptom and demographic information recorded (see list of measures in section 3.2.5).

3.2.2 Participants

A convenience sample of participants were recruited from Early Intervention in Psychosis (EIP) services in Sussex Partnership NHS Foundation Trust.

Inclusion criteria

The study inclusion criteria was that all participants:

i) Held a diagnosis of first-episode of psychosis
ii) Were currently on full caseload of an EIP service
iii) Over the age of 18
iv) Had capacity to give informed consent
v) Had sufficient English language skills.

Exclusion criteria

The exclusion criteria were that participants:

i) Had a primary diagnosis of substance misuse
ii) Had a diagnosis of organic neurological impairment

3.2.3 Procedure

Ethical approval was obtained from the London-Camden and Islington NHS Research and Ethics Committee (Ref: 11/LO/1877, project ID 72141; see appendix A). The study recruitment target was calculated by consulting Fritz (2007) for sensitivity to detect mediation effects and the effect sizes calculated in chapter 2 were employed in analysis. As the meta-analytic technique suggests that moderate effect sizes may exist between neurocognition and metacognition, and metacognition and functional outcome, a recruitment target of 80 was set as suggested by Fritz (2007). Participants were recruited through either current registration on a research database operated by Sussex Partnership NHS Foundation Trust giving consent to be contacted by a researcher or through their care team. In the latter case, care teams were approached by a member of the research team and permission was sought from the service-user via their care co-ordinator. This permission allowed a researcher to contact them to explain the study and provide a participant information sheet. Demographic and

medication information was recorded at the beginning of study participation and medication information was converted to Olanzapine atypical equivalent doses with conversion tables from Leucht et al., (2014). The neurocognition measures were completed first, participants were offered a short break, then the metacognition and functional outcome measures were completed. After another short break, an assessment of psychopathology was completed. Participants were also encouraged to take any additional breaks should they feel the need. Upon completion of the study, participants were given £20 as compensation for their time. Participants were recruited from November 2013 until February 2015.

3.2.5 Measurement of variables

Neurocognition

Several specific domains of neurocognitive function were selected as previous research identifies the need for more comprehensive (Lysaker et al., 2007) and more standardised (Green et al., 2004) measurement of neurocognitive impairment. Preceding research identifies memory, executive function (Aas et al., 2014), and general cognitive performance (IQ) (Tandberg et al., 2012) to be impaired in psychosis and implicated in community function (Leeson et al., 2011). The results of the previously run meta-analysis (chapter two) were also used to select neurocognitive measurement. The results of the meta-analysis suggest that existing research demonstrates a relationship between executive function, memory and IQ, and metacognition, and therefore offers grounds for these processes to be investigated in the present study. By selecting measures more commonly used, greater comparisons can be made with existing research.

Memory

Memory was assessed using the Logical Memory (LM) and Letter-Number Sequencing (LNS) subscales from the Wechsler Memory Scale (WMS-III) (Wechsler, 1987). The LM test is a way of capturing verbal memory ability in which participants are instructed to listen to and repeat back two stories as a measure of immediate verbal memory (LM1). Participant responses are scored for accuracy on a scale of 0-25 per story, and 0-75 in total, as the second story is repeated and recalled twice. Participants are then asked to repeat the stories 25-35 minutes later as a measure of delayed verbal memory (LM2) on a scale of 0-50. The WMS is reliable and validate across a number of populations (Selnes, 1991) and employed in FEP (Torgalsbøen et al., 2015). For comparison with other studies, the raw scores were also converted to age-scaled standardised z scores using the population means from normative data provided by Wechsler (1987).

The LNS is a measure of working memory. The administrator reads a mixed sequence of letters and numbers aloud and participants are asked to repeat the list back with the numbers in ascending order and the letters in alphabetical order. The length of the sequence commences with 2 items, and becomes progressively longer with correct responses. The task requires participants to store a list of information online and manipulate the sequence to adhere to the task rules. The total score ranges from 0-21. The raw scores were also transformed into standardised age-scaled z scores using the normative data in Wechsler (1987).

Executive Function

Executive function was assessed through the Verbal Fluency (VF) task for letters (phonological) (e.g. Benton et al., 1994) and semantic categories (Heaton et al., 2004). The administrator asks the participant to list as many words beginning with a letter (F, A and S) or exemplars of a category (four-legged animals) within 60 seconds. Participants are informed that proper nouns are not accepted (excludes names, numbers and places) and repetitions of the same root word with different suffixes are only counted once. The VF task requires initiation, inhibition and cognitive flexibility (Mitrushina et al., 2005). The total number of correct responses for phonological and semantic categories were used as a score. Raw scores were also converted into age-scaled standardised scores using the normative data in Tombaugh, Kozak, and Rees (1999).

Executive function was also measured using the Trailmaking Task (TMT) as a measure of attention, visuomotor skills and cognitive flexibility. The task has two sections: Part A contains a page with the numbers 1-25 scattered in circles across the sheet. Participants are asked to draw a single line connecting the numbers up in ascending numerical order as quickly as possible. Part B contains both numbers (1-13) and letters (A-L) and participants are instructed to draw a line connecting the numbers and letters in ascending numerical and alphabetical order alternating between number and letter (e.g. 1-A-2-B-3-C etc.). The participant's score (time taken to complete the task) on task A was subtracted from their time on task B to give a measure of cognitive flexibility and set-shifting (as described in Tombaugh, 2004). Raw scores were converted into age-scaled z scores using the normative data from Tombaugh, (2004).

General IQ

The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 2008) was developed as a screening tool for IQ assessment and cognitive impairment The

vocabulary subscale is a measure of verbal intelligence wherein participants are asked to provide a definition for a list of 40 words. The scores range from 0-80 with an individual word scoring scale of 0-2. The Matrix Reasoning subscale is a measure of nonverbal fluid reasoning within Performance IQ. Participants are shown a coloured geometric pattern with 3 shapes and one missing shape. They must select from 5 options which is the correct missing section to complete the pattern. Scores range from 0-35 and raw scores were converted to age scaled scores using validation data. Age-scaled scores were converted into z scores using the normative data from The Psychological Corporation, (1999).

Metacognition

Metacognition in this study was assessed through two measures; the Metacognitive Assessment Interview (MAI) (Semerari et al., 2012) and the Beck Cognitive Insight Scale (BCIS) (Beck et al., 2004). These measures were selected for their frequency of use as metacognitive measures in psychosis, as confirmed also in the meta-analysis (chapter two).

The MAI is a semi-structured clinical interview designed to assess 4 domains of metacognition; *monitoring*, *integration, differentiation* and *decentralisation*. A manualised set of interview questions are conducted with the participant response guiding the interview sequence to assess the aforementioned domains. In the event that a participant fails to describe or identify the relevant metacognitive domain after the initial question, extra prompt questions are also asked to capture the ability level. A self-generated description with no prompting from the interviewer for the domain would be attributed a score of 5, with additional prompt questions the score falls in value. If the participant, despite prompt questions, demonstrates no awareness of the metacognitive domain, a score of 0 is given. The *monitoring* subsection is comprised of questions that capture the interviewee's ability to identify and monitor the thoughts and emotions that make up their own mental state. The *integration* subscale assesses the individual's ability to reflect back on the transitions between their own mental states and identify causal reasons behind the transitions. The *differentiation* subscale assesses the individual's ability to consider their point of view as subjective and fallible and distinguish between fantasies, beliefs and assumptions about reality in relation to factual events. The final *decentralisation* subscale requires the participant to describe and interpret the mental state of another person and how that person's beliefs, values and perspective is separate from their own. The benefit of the MAI is it offers an assessment of in vivo metacognitive knowledge in response to a personally relevant,

social situation. This offers an insight into a real-life cognitive event and how the individual is able to describe and assess their cognitive processing.

Each subscale consists of 4 exemplar domains (see table 9 below) (16 items in total), which are scored on a scale of 0 (no evidence of metacognitive skill) to 5 (clear evidence of ability without prompting). The MAI is an adaptation of the Metacognitive Assessment Scale (Semerari et al., 2003) but has the advantage that it directly assesses domains of metacognition rather than discretely through psychotherapy sessions and is thus less time consuming. The measure has been validated in a non-clinical population (Semerari et al., 2012). The MAS, from which it derives, has been validated across numerous clinical populations (see Lysaker et al., 2005) including psychosis (Macbeth et al., 2014). The MAI was selected as this encapsulates higher-order, declarative metacognitive knowledge as described by Wells (2000), considered in the Nelson and Narens model (1990) and discussed in chapter 1. The MAS has been previously validated in schizophrenia (Lysaker et al., 2013b; Semerari et al., 2003) and checked for reliability (Buck, Warman, Huddy, & Lysaker, 2012) and employed in FEP (McLeod, Gumley, MacBeth, Schwannauer, & Lysaker, 2014) although not fully validated in this population.

The BCIS captures the participant's self-reported ability to assess their own cognitive products, distance themselves from and re-evaluate thoughts and beliefs, and subjective interpretations (Beck et al., 2004). It comprises 2 subscales; the self-reflectiveness scale assesses the individual's willingness to reflect upon and be objective about thoughts and openness to feedback. The self-certainty subscale relates to the individual's certainty about being right and resistance to correction. This information is measured through 15 self-report questionnaire items rated from 0 (do not agree at all) to 3 (agree completely). The BCIS was included as a higher-order aspect of metacognitive knowledge; the measure requires general reflection on cognition however is not elaborative or mental state specific but rather a general ability to question the fallibility of cognition, and reflect back on one's thoughts. The BCIS has been assessed for validity and reliability (Beck et al., 2004; Riggs, Grant, Perivoliotis, & Beck, 2012) and employed in FEP (Tranulis, Lepage, & Malla, 2008).

The MAI and BCIS scales are available in appendix C and D.

Symptoms

Symptoms were measured by the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). The PANSS is a 30 item observer-rated, semi-structured clinical

interview designed to assess the severity of symptoms in schizophrenia. The interview produces scores for positive symptoms (7 items), negative symptoms (7 items) and general psychopathology (16 items), has been well validated in research (Peralta & Zorita, 1994) and employed in FEP (McLeod, Gumley, MacBeth, et al., 2014).

Functional outcome

Functional outcome was measured through two methods; functional capacity and objective functioning. Functional capacity was measured by the UCSD Performance-Based Skills Assessment (UPSA) (Patterson et al., 2001) and objective functioning was captured by the Time Use Survey (Fowler et al., 2006). The UPSA is an instrument to assess capacity to complete everyday tasks across five domains; finance, communication, comprehension and planning, transportation and household chores. Participants are provided with equipment and asked to complete a list of tasks designed to replicate skills required in daily life. Participant performance is then scored by the researcher from the manualised guidelines and converted to a score out of 20 for each domain (0-100 in total). The UPSA has been assessed for reliability and validated in schizophrenia (Velligan et al., 2013) however has not been used in FEP before (although the shorter UPSA-B has in Vesterager et al., 2012).

The Time Use Survey is a semi-structured interview in which the participant is asked about the amount of time spent undertaking a variety of activities in the preceding month. The activities capture a host of functional domains including employment, education, voluntary work, leisure and sport, childcare and household maintenance. Two summary scores are produced; Constructive Economic Activity (CEA) is comprised of time spent undertaking employment, education, voluntary work, childcare and household chores whereas Structured Activity (SA) also includes time spent in leisure and sport activities. As previous research has focused on the structured activity score (Fowler et al., 2009; Hodgekins et al., 2015), the total number of hours per week spent engaged in all structured activity was used as an outcome measure. The Time Use survey has been used in FEP and CHR groups (Hodgekins et al., 2015) in previous research.

3.2.6 Analysis Plan

The primary research questions will be assessed through a series of analysis steps.

i) The raw data will be inspected for normality and outliers.

ii) The measurement variables' construct validity will be assessed through factor analysis to justify inclusion in latent variable pathway analysis.

iii) Reliability statistics will also be run to ensure internal reliability

iv) A series of pathway models (outlined in chapter 1) will be built using SEM and potential mediation effects will be tested in each model.

3.2.7 Factor analysis data analysis

Data processing

Normal distribution and outliers

Prior to analysis, the raw data was inspected for the presence of non-normal distribution and potential outliers. Univariate distribution was investigated with visual inspection of Q-Q and box plots and histogram distributions. Distribution was also empirically investigated with Kolmogorov-Smirnov (K-S) tests. In the case of non-normal distribution, the standard errors can be corrected by use of a more robust statistical estimator (Finney & DiStefano, 2006). Skewness and kurtosis were also investigated through SPSS (version 22) descriptive statistics.

Multivariate distribution

Multivariate outliers were assessed through the Mahalanobis' distance statistic which looks at the combinations of scores between variables to assess for unexpected relationships outside of the estimated multivariate normal distribution (Penny, 1996). Mahalanobis' distance was calculated in SPSS and a critical values table was consulted to look for values a significant distance from the expected distribution ($p<.001$).

Suitability for Factor Analysis

The suitability of the data for factor analysis was screened through the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity. Finally the determinant of the matrix was consulted to detect multicollinearity; a figure below .00001 is considered indicative of multicollinearity and reflects all variables loading on one structure (Field, 2013).

Where there are concerns about normality, a Maximum Likelihood Robust (MLR) model will be run instead of Maximum Likelihood (ML) as suggested by Kline, (2012) as this takes into account non-normality in estimation.

Factor Analysis assessment

Factor Analysis (FA) (Spearman, 1904) is a widely used research technique to investigate interdependencies within observed variables. The relationships between observed variables can be used to inform about underlying theoretical *factors* or *latent*

variables both in terms of function and structure (Jung & Lee, 2011). Exploratory Factor Analysis (EFA) is employed to determine the number of constructs represented by items and to provide a framework to evaluate a multitude of individual measures. Where, the underlying factor structure of the observed variables is estimated with no a priori framework placed over the item shared variance (Floyd & Widaman, 1995). Confirmatory Factor Analysis (CFA) in comparison is a technique used to determine whether a known prescribed factor model fits the observed data (Floyd & Widman, 1995) with cross-factor loadings constrained to 0.

Exploratory Structural Equation Modeling (ESEM) is a relatively new technique allowing for exploration of factor structure. Many CFA models fail to provide support for established EFA models (Marsh et al., 2009) due to EFA allowing for freely estimated loadings in model structure whereas CFA imposes a predefined structure on item level observations using independent cluster modelling. This constrains cross loadings of items on multiple factors to zero which, in behavioural science data, is arguably too restrictive for real life data which can have multiple relationships (Marsh et al., 2014).

The use of ESEM allows the researcher more a priori control over factor structure for the testing of theoretically driven structures (or confirmation of model). ESEM also offers model fit statistics similar to CFA allowing the researcher to assess factor and model contribution of constituent items. CFA however can lead to the use of non-theory driven model modifications which render it more exploratory than confirmatory and the misspecification of zero loadings can lead to distorted factors (Asparouhov & Muthen, 2009). Thus item loadings can be assessed on both hypothesised factors and other related factors due to the allowed cross-loading framework althought the rotation does ‘push’ the items towards the pre-specified factor structure (Asparouhov & Muthen, 2009). By running ESEM in Mplus, standard error values are calculated so which items significantly predict the factor can also be assessed. Marsh et al., (2014) advocate that both CFA and ESEM should be applied to model assessment. CFA, and ESEM were used where appropriate to validate variable structure. In the case of a measure having previous validation data through EFA or CFA, the structure was checked on the current sample through CFA. Where no previous measure validation data in FEP is available, ESEM was run.

Model fit assessment

The extent to which the model (or covariance matrix) imposed by the researcher is an accurate reflection of the raw data (or sample covariance matrix) is assessed by model fit statistics. If the discrepancy is too great (i.e. the data covariance speaks against the model applied) the difference is not attributable to chance or sampling error and the researcher must justify the model-to-data discrepancy or revise the model (Kline, 2012). This is typically assessed by a multitude of model fit indices; the chi-square test (χ^2) assesses the magnitude of difference between the sample and model fitted covariance matrices and expressed as a conventional significance test (Gierl & Mulvenon, 1995). The Bentler Comparative Fit Index (CFI) and the Tucker Lewis Index (TLI) are incremental fit indices which measure the improvement of the proposed model to the baseline (or independence model) and the author's suggest a value of 0.9 indicates an acceptable and 0.95 a good fit. The TLI is however less impacted by sample size. The Root-Mean-Square Error of Approximation (RMSEA) conversely is a measure of model misfit or poor fit per degree of freedom and a value of .08 implies acceptable model fit and .05 good model fit (Browne & Cudek, 1990). Such 'rules-of-thumb' cut-off criteria however must be employed with caution as these are victim to sample size and distribution bias, especially the chi-square test, thus no one fit should be considered absolute (Hu & Bentler, 1999) and models should not be viewed as 'correct' or 'incorrect' (see Yuan, 2005 for a review of model fit statistics). Instead, the extent to which observed data fits applied factor(s) structure will be assessed with multiple fit statistics reported based on the aforementioned criterion.

Internal reliability

The construct robustness will also be considered through Cronbach's alpha (Cronbach, 1951) statistics.

Inter-rater reliability:

To ensure standardised assessment and the reliability of the measure of metacognition, inter-rater reliability was assessed using Intraclass Correlation Coefficient (ICC) analysis.

3.2.8 Pathway model analysis

The relationship between latent and observed variables can be investigated through path analysis and conducted in a SEM framework. A path analysis is a multivariate regression model which can incorporate multiple dependent and independent variables whereas traditional regression techniques restrict analysis to a single dependent variable (Geiser, 2012). The increasing popularity of the technique can also

be attributed to allowing researchers to investigate both *direct* and *indirect* relationships between variables (MacKinnon, 2008) in theoretical models. An indirect effect is one wherein a third variable explains the mechanism through which one variable affects another (Baron & Kenny, 1986; Hayes, 2009).

Traditional approaches to mediation analysis frequently employ the *causal steps strategy* (Baron & Kenny, 1986) whereby a series of conditions have to be met in order to claim mediation involving:

1) A significant relationship between the independent and mediating variable;
2) A significant relationship between independent variable and dependent;
3) The mediating variable significantly predicts the dependent variable when the independent is controlled for;
4) The relationship between independent and dependent decreases substantially when the mediating variable is entered simultaneously with the independent as a predictor of the dependent variable.

This approach has been criticized however as a significant relationship between predictor and outcome variable is not required for mediation to be claimed (Mackinnon, Krull & Lockwood, 2000), the estimation of standard error for the mediation pathway is theoretically flawed (McKinnon et al., 2002) and the requirement of normally distributed data for deriving the significance value of the indirect effect being unlikely in all but the largest samples (Preacher & Hayes, 2008). Instead, one proposed method advocates for bootstrapping wherein the data is repeatedly sampled from, and the indirect effect is estimated in each subset over thousands of iterations to develop an empirical estimation of sampling distribution (Preach & Hayes, 2008). Thus confidence intervals can be calculated for the assessment of indirect effects. Current thinking also suggests that mediation can be present in the absence of a correlation between independent and dependent variable on the condition that a relationship is present between both independent and mediating variable, and mediating and dependent variable (Rucker et al., 2011). All models will be estimated through Maximum Likelihood algorithms (ML) as the bootstrapping method addresses any concerns about normality of data and 5000 iterations will be run.

Assessment of mediation effects

Mediation will be investigated on the proviso that the aforementioned conditions are met and assessed through a) significant regression pathways in the model and b) CIs

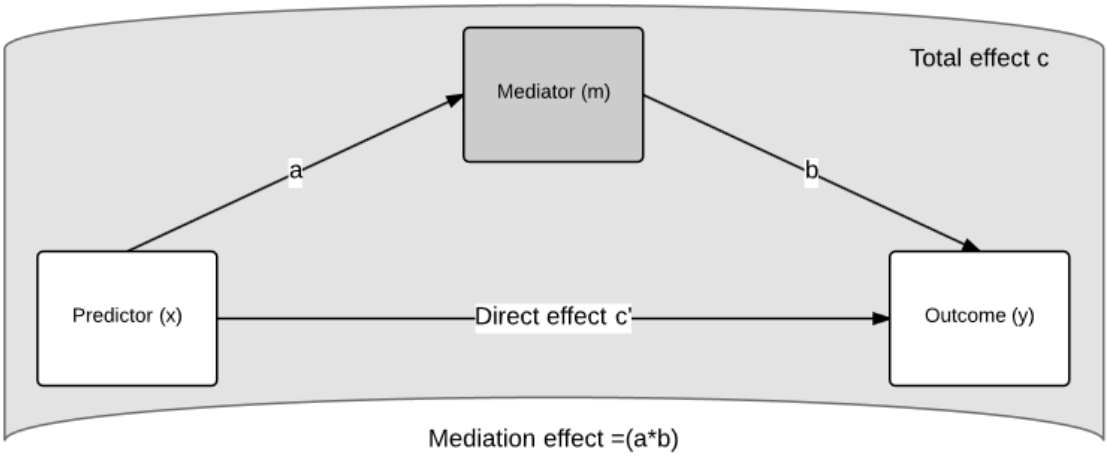

Figure 18 Mediation pathway model

not containing 0 (Preacher & Hayes, 2008). The pathway model will be run in one estimation model. The mediation model will be investigated through direct regression pathways between i) predictor variable and mediating variable (a), ii) mediating variable and outcome variable (b) iii) predictor variable and outcome variable (c') and the overall total effect of the model (c) which is calculated as the beta weight of c'+ (a*b). The indirect or mediation effect will also be calculated to assess for mediation (a*b) (see figure 18 above for the theoretical mediation model). The size of associations will also be investigated through R^2 statistics and coefficient values. To assess the magnitude of effect, Cohen (1988) suggests that an R^2 value of .01=a small effect, .09= a medium effect and >.25= a large effect with the respective standardised coefficient values of .1= small, .3= medium and <.5= large. Finally, as the data is cross-sectional, the direction of the proposed effect will be assessed through reverse causality model testing. By reversing the model structure and assessing whether mediation is still present, the possible direction of the relationship can be indicated. If the model structure is reversed and the mediation effect is lost, more confidence can be placed on the direction of observed effect. The reverse models will be run by swapping X and Y variables and by swapping Y and M variables to assess direction of causality.

Overall model fit statistics will also be investigated through the criteria identified in section 3.2.7.

3.3 Results

3.3.1 Sample statistics

Eighty FEP patients were recruited in total, mean age 26.08 (SD. 5.53, range 18-40) and the sample was comprised of 49 male and 31 female patients (see table 4 for demographic information). One hundred and eighty-six FEP service-users were provisionally identified, 27 declined to participate via their care co-ordinator, 37 were deemed too unwell by their care co-ordinators and 28 service-users the researcher was unable to contact. The remaining 14 participants failed to attend appointments or could not participate for other reasons.

Table 4 Sample characteristic summary table

Sample characteristics	Mean (SD)
Age	26.08 (5.53
Gender (M/F)	49/31
Symptoms (positive)	12.01
Symptoms (negative)	13.6
Symptoms (general)	28.35
Prescribed anti-psychotic medication (Y/N)	48/32
Olanzapine equivalent dose (of those prescribed medication) (mg/day)	12.77 (7.79)

3.3.2 Factor analysis

3.3.3 Neurocognition

The patient sample were overall -.86 standard deviations below the population mean with the highest deficit observed in the trailmaking task (-1.53) closely followed by logical memory (-1.3/-1.26). The best performance was found for non-verbal IQ with the mean performance being just above what would be expected from the general population (.17).

Table 5 Sample neurocognitive performance descriptive statistics

Cognitive Task	Raw score mean (SD)	Range	Z score mean (SD)
Logical Memory I $^{(0-75)}$	27.7 (10.9)	(10-55)	-1.3 (1.12)
Logical Memory II $^{(0-50)}$	16.28 (8.26)	(0-35)	-1.26 (1.12)
Letter-number Sequencing $^{(0-21)}$	8.64 (2.46)	(4-15)	-1.08 (.94)
Verbal Fluency (phonemic)	32.28 (10.27)	(5-56)	-1.01 (.91)
Verbal Fluency (semantic)	18.49 (4.77)	(9-29)	-.55 (.94)
Matrix Reasoning $^{(0-35)}$	25.82 (4.13)	(13-34)	.17 (.85)
Vocabulary $^{(0-80)}$	52.8 (11.67)	(11-73)	-.35 (1.17)
Trailmaking Task (B-A)	37.99 (33.88)		-1.52 (2.54)
Overall neurocognition mean	27.5		-.86

Key: Scale total range indicated in brackets after name $^{(x-x)}$

Data Assumptions

All neurocognitive variables were explored for normal distribution through histogram, Q-Q and box plots, and SPSS Kolmogorov-Smirnov tests of normality, skewness and kurtosis statistics. The Kolmogorov-Smirnov test indicated that LM1 (p=.005), LNS (.011) and TMT (.004) may violate the normality assumption. TMT was the only significant violation of the skewness statistic (statistic/standard error= -3.97) and an inspection of the histogram plots indicated a negative skew on the data distribution (Field, 2012). All other skew and kurtosis were within expected range. The determinant reported <.0001 therefore multicollinearity was not present in the data.

Neurocognitive variables were therefore also inspected for outliers prior to analysis. Box plots revealed some data outside of the standard error bar for TMT and LNS however the departure was not major and individual cases were not unique within the sample therefore the data was not transformed.

Multivariate distribution

Multivariate outliers were also investigated using Mahalanobis' distance. Mahalanobis' distance was calculated using SPSS and no scores were significant at p<.001.

Correlation analysis

The neurocognitive measures were initially inspected for correlations. All items were significantly correlated with each other (table 6) indicating intercorrelation however LM1 and LM2 were highly correlated (R= .897, p<.001). As they are both measures taken from the same scale, this may account for the high correlation therefore were left in subsequent analysis steps. The Bartlett's test was significant (p<.001) indicating appropriate relationships between variables for factor analysis. The Kaiser-Meyer-

Olkin measure of sampling adequacy also exceeded .5 (.75) suggesting that the data are suitable for factor analysis.

Table 6 Bivariate correlations among cognitive variables

	LM1	*LM2*	*LNS*	*FAS*	*Animals*	*Vocab*	*MR*	*TMT*
LM1	1	.89***	.36**	.26*	.28*	.47***	.41***	.37**
LM2		1	.36**	24*	.25*	.44***	.44***	.38***
LNS			1	.46***	.26*	.53***	.38**	.46***
FAS				1	.57***	.48***	.33**	.49***
Animals					1	.33**	38**	.35**
Vocab						1	.56***	.40**
MR							1	.48***
TMT								1

A host of previous studies have assessed and validated neurocognition through a composite score (e.g. Bowie et al., 2010; Harvey et al., 1998; Vesterager et al., 2012) so to check the suitability of the present cognitive variables representing a neurocognitive factor in the present study, CFA was deemed appropriate. A GEOMIN rotation was used as an oblique rotation is recommended in social sciences to achieve simple structure due to theoretical grounds to assume that the factors will be correlated (Costello & Osborne, 2005). A MLR parameter estimation was used as a conservative response to potential non-normality of data as advised by Yuan & Bentler, (2000) and analysis run in Mplus (version 6.0; Muthén & Muthén, 1998-2010).

Model Fit

The CFA suggests a one factor solution demonstrating good model fit indices (χ^2 (29) = 29.55, *p*=.06, CFI= 0.96, TLI=0.95 RMSEA= 0.08).

Internal reliability

Cronbach's alpha was .81 for the general cognition factor indicating good factor reliability. Factor loadings are available in table 7 below.

Table 7 Neurocognition CFA rotated factor loadings

Measure	Factor
	Neurocognition
Logical Memory 1	.56
Logical Memory 2	.55
Letter-number Sequencing	.65
Verbal Fluency phonemic	.66
Verbal Fluency semantic	.54
WASI vocabulary	.75
Trailmaking Task	.65
WASI matrix reasoning	.66

The results of the CFA confirm the suitability of neurocognition being structured as one factor.

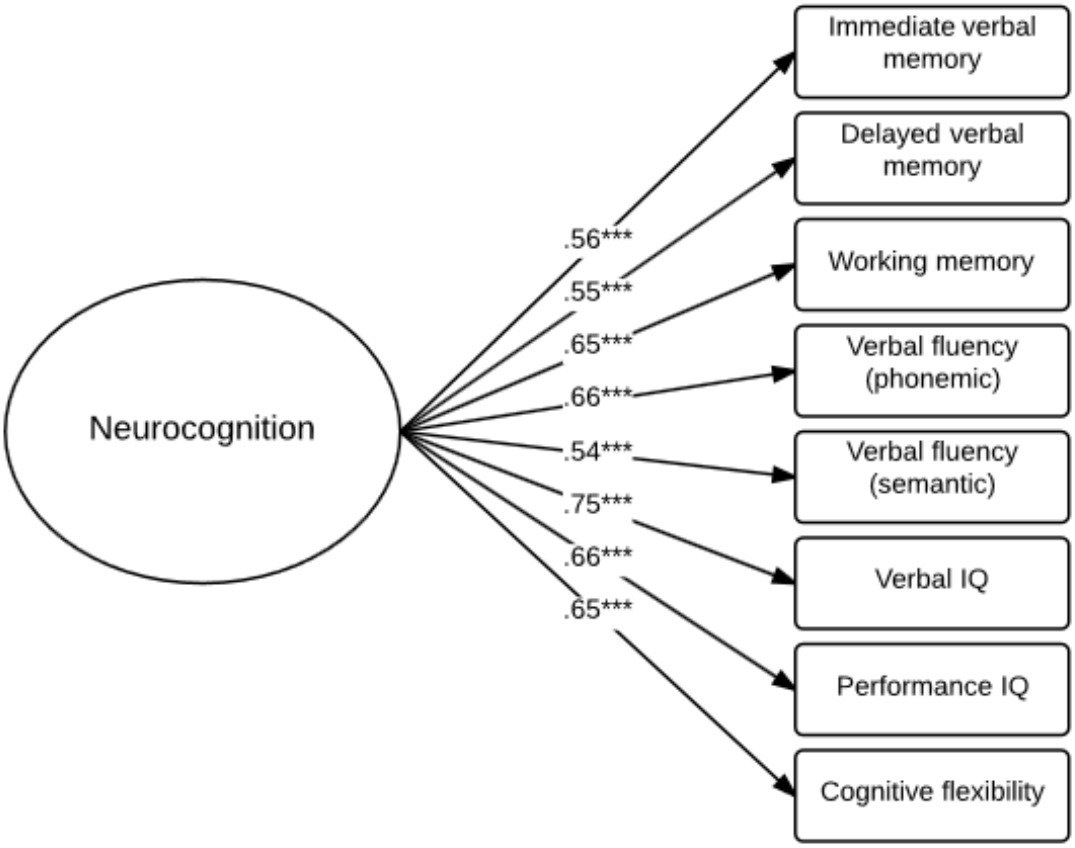

Figure 19 Neurocognition factor loadings

3.3.4 Metacognition

Metacognitive Assessment Interview

Inter-rater reliability:

All interviews were undertaken and rated by the same researcher (GD). Three MAI interviews were recorded and marked independently by a second trained researcher to check for inter-rater reliability. An Intraclass Correlation Coefficient (ICC) method

was used to assess inter-rater reliability through a two-way mixed absolute agreement model for all 16 items in the MAI. The ICC demonstrated excellent agreement (0.9, p<.001) (Fleiss, 1981) between interview ratings across the 16 items.

Data assumptions

The K-S statistics reported significant violations of normal distribution for all items. An inspection of the histogram graphs indicate some negative skew for MAI items however the Q-Q plots indicated some adherence to the expected distribution. The Box plots indicated no outliers present. As the violation to normal distribution was not of a severe magnitude this was addressed by running a MLR model.

Descriptive statistics

Table 8 Metacognitive Assessment Interview subscale mean scores

Measure	Subscale	Mean (SD)
Metacognitive Assessment Interview	Monitoring	2.93 (1.25)
	Differentiation	2.77 (1.17)
	Integration	2.83 (1.22)
	Decentralism	2.57 (1.43)

The mean and standard deviation values for the MAI are available in table 8 above. Participants demonstrated the highest mean performance for monitoring and the lowest for decentralism however the large standard deviation relative to the mean demonstrates a large variance in individual performance.

Correlation analysis

The factor structure of the MAI was first inspected for suitability for factor analysis. The correlation matrix indicated high correlation between items. Bartlett's test revealed a significant value (p<.001) and the Kaiser-Meyer-Olkin measure of sampling adequacy was also sufficient (.97) indicating that continued investigation was merited. The determinant indicated the presence of multicollinearity (<.00001) suggesting the presence of one structure.

Model fit

Due to a previous EFA validation study (Semerari et al., 2012), the structure of the MAI was confirmed in the present study through CFA. A CFA was run with the original author's suggested two factor structure (self-reflectivity of one's own mind, and the understanding of the mind of the other) however extremely high factor correlation (.98)

was observed and a violation in the determinant statistic (>.00001) therefore the 2 factor solution was rejected. An ESEM was then run to investigate factor structure.

The ESEM was run with a GEOMIN rotation as the default in Mplus and a MLR parameter estimate model was selected due to concerns about normality of items. The ESEM suggested a 1 factor solution (χ^2 (101) = 122.41, *p*=.07, CFI= 0.99, TFI=.99, RMSEA= 0.05) with good model fit suggested on all model fit indices. The scree plot also suggests a one factor solution and there was only one eigenvalue above 1. All items loaded highly on one factor (see table 9) and cronbach's alpha suggests good internal reliability of the scale loading on one factor (α =.987). The results of the second ESEM analysis suggest the MAI is determined by one latent structure; synthetic metacognitive ability. The results of the scree plot are presented in figure 20 below.

Table 9 MAI single factor item loadings

Subscale	Item	Factor
		Metacognition
Monitoring	*Identifies and specifies emotions*	**.87**
Monitoring	*Describes and relates to thoughts*	**.89**
Monitoring	*Relates behaviour to aspects of mental state*	**.91**
Monitoring	*Connects thoughts to emotional states*	**.93**
Differentiation	*Aware that world representation is subjective*	**.87**
Differentiation	*Offers plausible interpretation of events*	**.93**
Differentiation	*Can reflect and evaluate events*	**.94**
Differentiation	*Can differentiate between different representations*	**.76**
Integration	*Can demonstrate a coherent connection between thoughts, emotions, events and behaviours*	**.95**
Integration	*Can identify transitions between mental states*	**.89**
Integration	*Awareness of continuity in thoughts and emotions*	**.95**
Integration	*Can describe and rebuild narration of mental function with order and clarity*	**.91**
Decentralism	*Can describe the psychology of other*	**.92**
Decentralism	*Describes intentions of others based on their beliefs*	**.95**
Decentralism	*Able to understand same event can have differing relevance to people*	**.95**
Decentralism	*Able to understand the psychological process of others independent from self*	**.94**

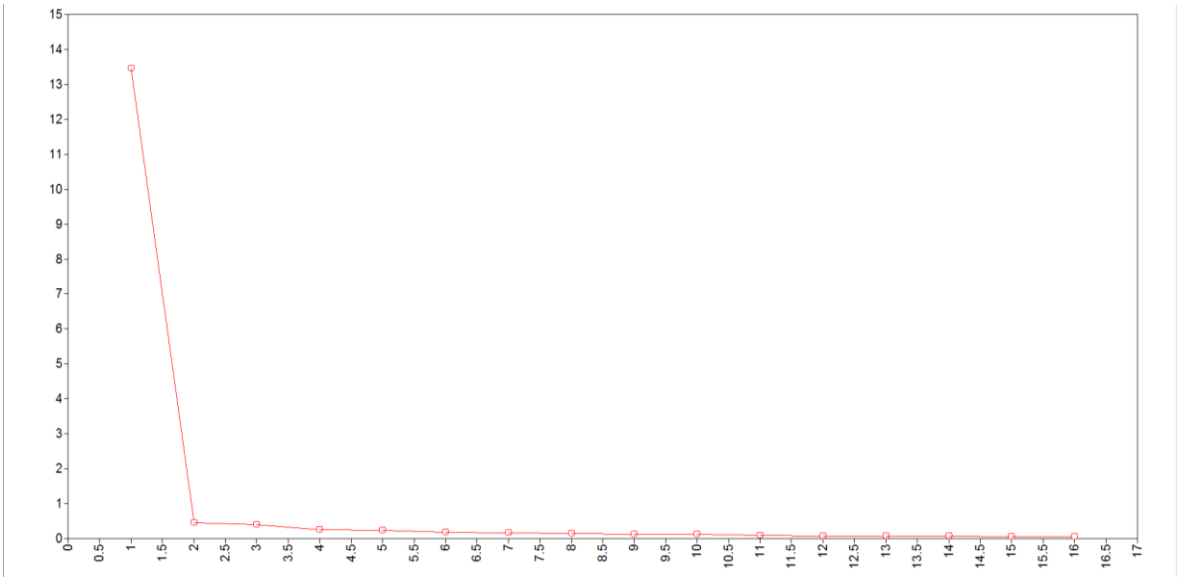

Figure 20 MAI item scree plot

The Beck Cognitive Insight Scale:

Data assumptions

The mean and standard deviation information for the BCIS is available in table 10 below. On average participants scored 14.3 for self-reflectivity and 5.88 for self-certainty which is comparable to the FEP findings reported by Buchy et al., (2010) of 13.3 for self-reflectivity however slightly lower than the 8.3 mean score on for self-certainty. The questionnaire items were inspected for normality and the Kolmogorov-Smirnov indicated non-normality within the individual items. An inspection of the correlation matrix table indicated no correlations between items >.8 and Bartlett's test revealed a significant finding (p<.001). The determinant was <.0001 indicating no multicollinearity.

Mahalanobis' distance was also calculated and no variables were significant at p<.001 indicating no violation of multivariate distribution.

Correlation Analysis

The correlation matrix demonstrated that the correlation between all items was below .8 (see table 13).

Confirmatory Factor Analysis

Due to a multitude of prior studies having investigated the factor structure of the BCIS and reporting a two factor solution, a CFA was conducted to assess factor structure in a FEP sample. The CFA was run with MLR due to non-normality in the data distribution and revealed poor model fit for a 2 factor solution (χ^2 (89)=140.52 , p<.001, CFI= .77,

RMSEA= .087). Model fit statistics were inspected and covariance paths were added incrementally however the overall model fit could not be improved. As outlined previously, ESEM allows for factor models with approximately zero cross-loadings which are potentially more suitable for such psychological variables, It was therefore decided to re-test the 2-factor structure through ESEM.

ESEM

ESEM was run allowing all items to load on both factors with a 2 factor solution however a TARGET rotation was employed to push cross loadings *towards* zero. The initial model demonstrated poor model fit statistics (χ^2 (76)=133.15, p<.001, CFI= .74, TLI= .64, RMSEA= .1) however model fit statistics suggested the addition of correlated error terms between 2 of the self-reflectivity items. With the inclusion of these correlated error terms, the model demonstrated good model fit (χ^2 (74)=87.75, p=.13, CFI= .94, TLI= .91, RMSEA= .05).

Internal reliability was also investigated. The self-reflectivity scale demonstrated acceptable internal reliability (α =.793). The self-certainty scale was bordering on acceptability (α =.642) with no improvement made through item deletion.

As a result of the factor analysis, and in light of the previous research in this area supporting a theoretical distinction between these 2 processes, it was decided to keep the BCIS as a two factor structure containing self-reflectivity and self-certainty factors.

Table 10 Beck Cognitive Insight subscale mean scores

Measure	Subscale	Mean (SD)
Beck Cognitive Insight Scale	Self-reflectivity$^{(0\text{-}27)}$	14.3 (5.06)
	Self-certainty$^{(0\text{-}18)}$	5.88 (2.88)

Key: Scale total range indicated in brackets after name $^{(x\text{-}x)}$

Overall Metacognitive structure

To investigate how the metacognitive domains related to each other, ESEM was run with the factors determined in the previous steps. An ESEM was run as there is preceding evidence (and therefore a priori structure to apply) to suggest a relationship between the MAI and BCIS (Lysaker et al., 2013b) although the specific construct has not been refined enough to require a CFA. This was run as a second step in determining metacognitive factor structure, rather than as a second order analysis, due to the small sample size. As discussed previously, ESEM provides standard error

statistics thus allowing significance testing of whether indicators significantly predict the latent variable. The factor analyses already presented were used to generate factor scores to include in analysis for the 3 factors (self-reflectivity, self-certainty (BCIS) and synthetic metacognition (MAI)).

Data assumptions

The results of the K-S test suggested some concern over the distribution of the self-certainty BCIS factor and the MAI factor however the Q-Q and histogram plots suggest that this possible violation was not severe. The box plot also suggested 2 potential outliers however as they were not major violations, they were included in analysis.

Mahalanobis' distance was also calculated and no variables were significant at $p<.001$ indicating no violation of multivariate distribution.

Correlation analysis

The correlation matrix found significant relationships between the self-reflectivity and the MAI factor and the self-certainty factor showed a negative relationship to other variables. The KMO (.58) and Bartlett's test ($p<.001$) suggest that a factor analysis is appropriate for the data and the determinant confirmed that multicollinearity was not present.

Exploratory Factor Analysis

A GEOMIN rotation was run with a MLR estimation model due to potentially non-normally distributed data.

The factor loading information was inspected for individual model contribution with the MAI (.77), self-reflectivity (.52) positively loading on the factor. The rotated loadings however suggested that the self-certainty structure had a small and negative loading on metacognition construct (-.20) and was not a significant predictor ($p=.127$) so was deleted from the model in further analysis. The final factor loadings are reported in table 11 below

Table 11 Metacognition rotated factor loadings

Variable	Factor loading
Self-reflectivity (BCIS)	.66
Synthetic metacognition	.60

The results of the ESEM suggest that the domains of metacognition investigated thus far are suitable to be combined into an overall metacognition latent variable. The metacognitive factor will be comprised of the self-reflection and synthetic metacognition (see diagram in figure 21 below).

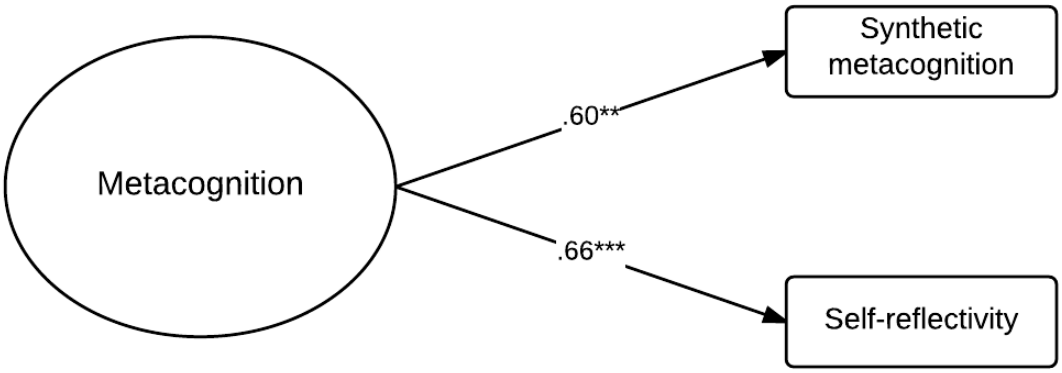

Figure 21 Metacognition measurement model

The internal reliability analysis suggested only limited construct reliability (α =.603) but it was not possible to improve this value by deleting items due to the construct only consisting of two items which may account for the low figure.

3.3.4 Functional Outcome

Functional capacity

The distribution histogram was consulted and confirmed some non-normal distribution for the UPSA. The violation was not of significant magnitude however to warrant data transformation and, to address this concern, a MLR estimation model was run in the pathway model. Participants on average scored 66.48 out of a possible 100 which is comparable the other study employing the UPSA-B in FEP who found a mean score of 70 (Roche et al., 2014).

Table 11 Functional outcome descriptive statistics

Measure	Subscale	Mean (SD)	Range
UPSA	*Finance* $^{(0\text{-}20)}$	15.68 (3.06)	(7.27-20)
	Communication $^{(0\text{-}20)}$	12.99 (3.69)	(5-18.33)
	Comprehension & planning $^{(0\text{-}20)}$	12.48 (4.65)	(0-20)
	Transport $^{(0\text{-}20)}$	15.12 (3.03)	(8.89-20)
	Household $^{(0\text{-}20)}$	15.75 (4.42)	(0-20)
	Total $^{(0\text{-}100)}$	66.48 (23.89)	(36.62-95.24)
Time Use	*Structured activity (total hours per week)*	24.97 (23.09)	(2.3-96.74)

Scale total range indicated in brackets after name $^{(x\text{-}x)}$

Data assumptions

The functional capacity variables were inspected for normal distribution and the K-S tests revealed significant results for all variables (p<.01) indicating non-normally distributed data. The UPSA household, communication and planning histograms indicate negative skew which is confirmed in the skewness statistics. The box plots indicate the presence of outliers on the household subscale of the UPSA.

The KMO test indicated suitable sampling adequacy (.765) and Bartlett's test was significant (p<.001). The correlation matrix indicates that all variables were significantly associated with each other (p<.05) however no correlations exceeded .8. The determinant value was above .0001 confirming that multicollinearity was not present in the data.

Mahalanobis' distance was also calculated and no variables were significant at p<.001 indicating no violation of multivariate distribution.

Correlation analysis

All UPSA domains were significantly correlated with each other (p=/<.001) however no correlations exceeded .8 between items.

Confirmatory Factor Analysis

The original authors devised the UPSA to measure 5 domains of functional capacity based on everyday tasks encountered by patients in the community (finances, comprehension and planning, communication, household maintenance and transportation) however many designs include functional capacity as a total score to capture overall capacity (e.g. Patterson et al., 2001). Previous studies have validated the measure so to confirm the factor structure in the present sample, a confirmatory factor analysis was run.

Due to the non-normal data distribution and skewness a MLR model estimate was run in analysis, with GEOMIN rotation

Model fit

The CFA indicated borderline-acceptable model fit for a one factor solution of the UPSA performance-based skills assessment test (χ^2 (5)=10.59, p=.06, CFI= .94, TLI= .89, RMSEA= .13). The scree plot also endorses the presence of only one factor with a drop in magnitude after the first factor (figure 22 below).

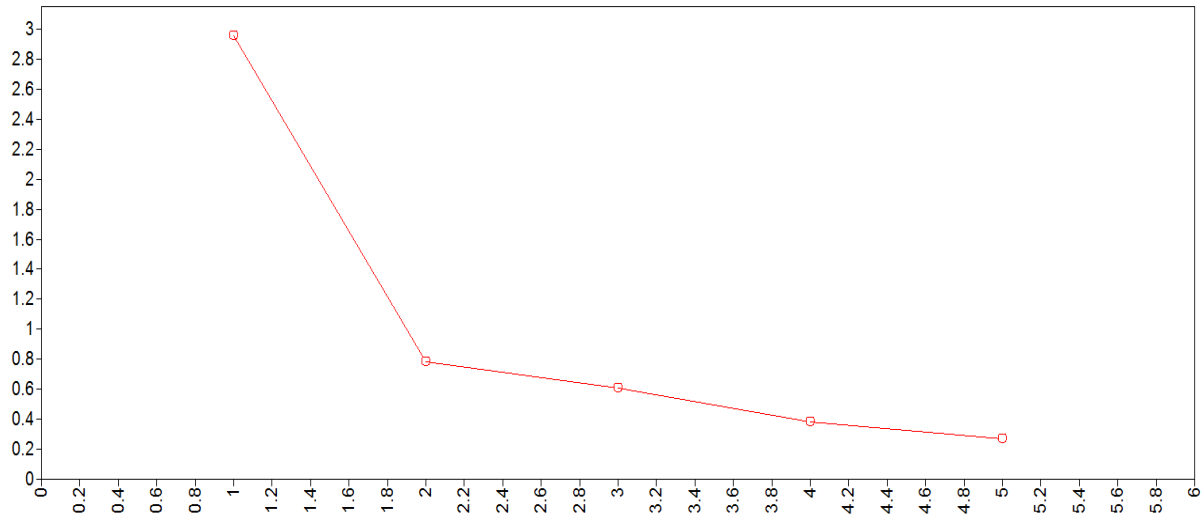

Figure 22 UPSA scree plot

Objective Function

Data assumptions

The Time Use Survey was initially assessed for normal distribution. The K-S test reported a significant result (p<.001) and an inspection of the histogram suggests a positive skew which the Q-Q plot and skewness statistic confirmed. The box plot indicates no outliers were present. On average, participants spent 24.97 hours per week in structured activities and this ranged from 2.3-96.74 hours.

As there was only one measure, no factor analysis was run.

Functional outcome is therefore determined by a one factor solution for functional capacity and objective function is measured by the Structured Activity domain of the Time Use Survey.

3.3.5 Pathway analysis

The primary analysis concerned the extent that metacognition mediates the relationship between neurocognition and function. The results of the factor analysis to determine variable structure were carried over to formulate the latent variables of neurocognition, metacognition and function (both capacity and objective).

3.3.6 Measures:

Neurocognition

Neurocognition was measured by a factor score derived from participant performance on the logical memory, letter-number sequencing, verbal fluency, trailmaking tasks and the WASI verbal and performance IQ scales. A higher score denotes better cognitive function.

Metacognition

The results of the factor analysis suggested that metacognitive ability is best captured by the MAI and the BCIS self-reflectivity scale. Both factor scores were entered as a measurement model into the pathway model to produce the latent variable metacognitive ability. A higher score represents better metacognitive ability.

Psychopathology

Participant scores on positive, negative and total symptoms were included in analysis as covariates. Negative symptoms were also investigated as a mediating variable between neurocognition and functional outcome (both capacity and objective function) as previous studies demonstrate a relationship between negative but not positive symptoms and functional outcome (Fulford et al., 2013). A higher score represents greater symptom severity.

Functional outcome

Two domains of function were investigated; functional capacity measured through a factor score of the subdomains of the UPSA performance-based measure and objective function through total Structured Activity score on the Time Use Survey. A higher score on functional capacity represents increased ability to complete everyday tasks and a higher score on the Time Use Survey denotes more time spent in structured activities each week over the preceding month.

3.3.7 Correlation analysis

Bivariate correlations

The relationship between pathway variables was first investigated through correlational analysis. Cognitive ability was significantly correlated with both functional capacity (r=.70, p<.001) and objective function (r=.48, p<.001) and the MAI factor score (r=.61, p<.001) but not the BCIS self-reflectivity scale (r=.19, p=.096). The MAI was significantly associated with self-reflectivity (r=.43, p<.001), functional capacity (r=.81, p<.001) and objective function (r=.84, p<.001). BCIS self-reflectivity was also significantly associated with functional capacity (r=.31, p<.011) and objective function (r=.33, p<.004). The BCIS self-certainty was not significantly associated with any variable (intercorrelation values available in table 13).

Table 13 Bivariate correlations between neurocognition, metacognitive, function outcome and symptoms measures

	Neurocognition	BCIS self-reflectivity	BCIS self-certainty	MAI	UPSA	Time Use
Neurocognition	1					
Beck Cognitive Insight Scale: self-reflectivity	.19	1				
Beck Cognitive Insight Scale: Self-certainty	.02	-.2	1			
Reportable metacognition (MAI)	.61***	.43***	-.13	1		
Functional capacity (UPSA)	.70***	.31**	-.01	.81***	1	
Objective function (Time Use)	.48***	.33**	-.07	.84***	.64***	1
Positive symptoms	-.21	-.01	-.14	-.14	-.23	-.10
Negative symptoms	-.43***	-.33**	-.03	-.64***	-.68***	-.49***
General symptoms	-.22	-.14	-.1	-.39**	-.37**	-.27*

***p<.001, **p<.01, *p<.05

Table 13 reveals that, as suggested by previous research, that neurocognitive ability is significantly associated with one's ability to conduct everyday tasks and the amount of time spent in structured activities. Higher neurocognitive ability is associated with better individual functioning. The analysis also demonstrates that metacognitive ability, both measured by the MAI and the BCIS self-reflectivity scale, is positively associated with both functional capacity and objective functioning. This suggests that better metacognitive function is associated with greater capacity to complete daily living tasks and spending more time in structured activities. Positive symptoms were not significantly associated with any other variables whereas negative symptoms were negatively associated with cognition, metacognitive variables and functional capacity

and objective functioning. General psychopathology was significantly negatively associated with both functional capacity and objective function but not metacognitive or cognitive ability. No significant association was found between medication dose and metacognition (*p*=.687) or functional capacity (*p*=.407) or objective function (*p*=.369).

In relation to time spent in structured activities, the present sample are comparable to other studies in FEP (table 14 below). The EDEN project found that on average young people experiencing their first episode of psychosis spent 25.17 hours per week in structured activities and the present study reports on average 24.97 hours per week.

Table 14 Time Use Survey comparison table

Study	N	Min-Max	Mean (SD)
Non-clinical (UK 2000 Time Use Survey)	5686	0-140.00	63.49 (25.89)
At-risk mental state (EDIE-II)	199	1.31-139.19	35.61 (29.68)
FEP (National EDEN)	878	0-140.00	25.17 (26.22)
FEP (present study)	80	2.3-96.74	24.97 (23.09)

3.3.8 Model 1: That the relationship between neurocognition and functional capacity will be mediated by metacognition

The relationship between neurocognition, metacognition and functional capacity will be assessed in the first model through direct and indirect effects. The overall model demonstrated good model fit statistics ($\chi^2(1) = .03$, *p*=.86, CFI= 1.00, TLI=1.00 RMSEA= 0.00) which indicated that the theoretical framework placed on the observed data was a good fit.

The results of the mediation analysis confirm that cognition does significantly predict metacognitive ability ($\beta = .56$, *p*=.02), metacognition significantly predicts functional capacity ($\beta = .51$, *p*=.005) and there is a significant direct relationship between neurocognition and functional capacity ($\beta = .42$, *p*<.001). The mediation analysis confirms that metacognition significantly mediates the relationship between neurocognition and functional capacity as demonstrated by the indirect pathway ($\beta = .29$, *p*=.009) and this is corroborated by the CIs ($\beta = .28$, +/-95%[.50, .07]).

The mediation model accounted for 67% of the variance in functional capacity ($R^2 = .673$) and 31% ($R^2 = .313$) of the variation in metacognitive function which are large effect sizes. Negative symptoms were also included as a covariate and metacognition and functional capacity were regressed onto negative symptoms. The mediation model

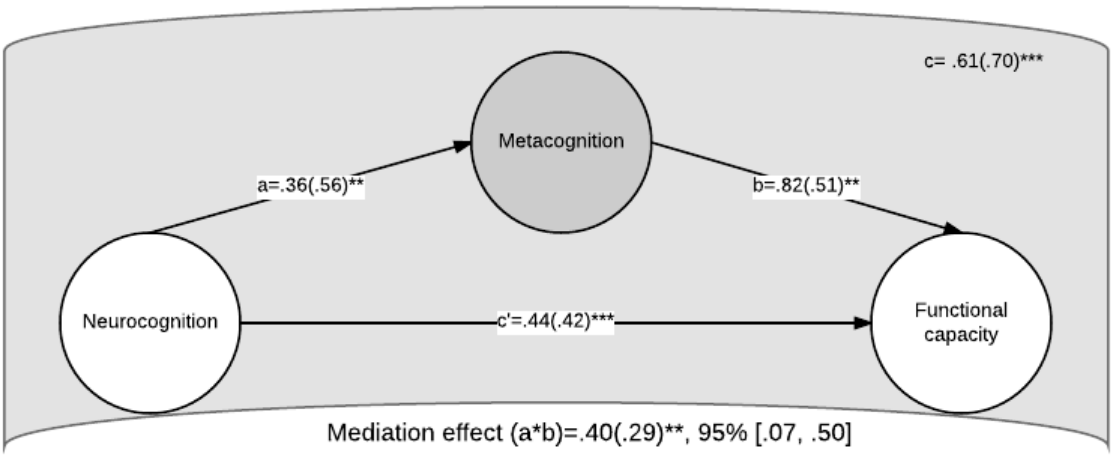

*Figure 23 Mediation of the effect of neurocognition on functional capacity through metacognition. ***p<.001, ** p<.01, *p<.05*

however failed to retain significance suggesting that negative symptoms also account for this relationship (a*b= .16, *p*=.074, 95%CI [-.01, .31]). When negative symptoms were solely controlled for on functional capacity (and not metacognition), the model was once again significant (a*b= .22, *p*=.012, 95%CI [.05, .39]). The reverse model was also assessed (Y-M-X) and the significant mediation effect was lost suggesting that metacognition mediates the relationship of neurocognition on functional capacity rather than functional capacity's impact on neurocognition.

In summary, one's cognitive ability significantly impacts on the ability to complete everyday tasks however this relationship is also mediated by metacognitive function.

3.3.9 Model 2: That the relationship between neurocognition and objective function will be mediated by metacognition.

Next, the relationship between neurocognition, metacognition and objective function was investigated through pathway analysis. The overall model fit was once again a good fit ($\chi^2(1) = .11$, $p=.74$, CFI= 1.00, TLI=1.00 RMSEA= 0.00).

The pathway model confirmed that neurocognition significantly predicts metacognitive function ($\beta=.56$, $p=.004$), metacognition significantly predicts objective function ($\beta=.74$, $p=.01$) however neurocognitive ability did not significantly predict objective function ($\beta=.06$, $p=.61$). The mediation analysis confirms that metacognition mediates the relationship between neurocognition and objective function as demonstrated by the indirect pathway ($\beta=.41$, $p<.001$ and CIs ($\beta=.41$, +/-95%[.62, .31]).

The mediation model accounted for 59% ($R^2=.594$) of the variation in time spent in structured activity and 32% of the variation in metacognitive ability ($R^2=.317$) which

are large effect sizes. The standardized and unstandardized pathway coefficients are available in figure 24 below and overall model summaries are available in table 16. In summary, improved neurocognitive ability predicts increased metacognitive function which predicts more time spend in structured activities. Neurocognitive ability alone however did not significantly predict time spent in structured activities. This mediation effect persisted with the inclusion of negative symptoms as a covariate in the model (a*b= .34, *p*=.01, 95% CI[.08, .59]). Finally, the reverse model was assessed and the significant mediation effect was lost suggesting that metacognition mediates the relationship between neurocognition and objective function rather than objective function's impact on neurocognition.

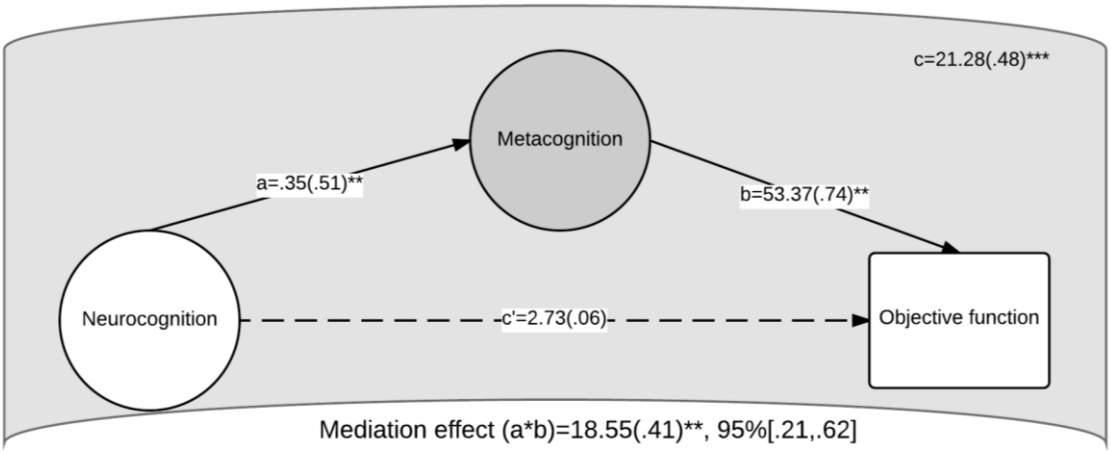

*Figure 24 Mediation of the effect of neurocognition on community function through metacognition***p<.001, ** p<.01, *p<.05*

3.3.10 Model 3: The relationship between neurocognition and time spent in structured activities will be mediated by functional capacity.

The relationship between neurocognitive ability and objective function was investigated with functional capacity included as a mediating variable.

The model confirmed that cognitive ability significantly predicted function capacity (β = .70, *p*<.001) and that functional capacity significantly predicts objective functioning (β = .58, *p*<.001) however neurocognition did not significantly predict objective function (β =.09, *p*=.44).

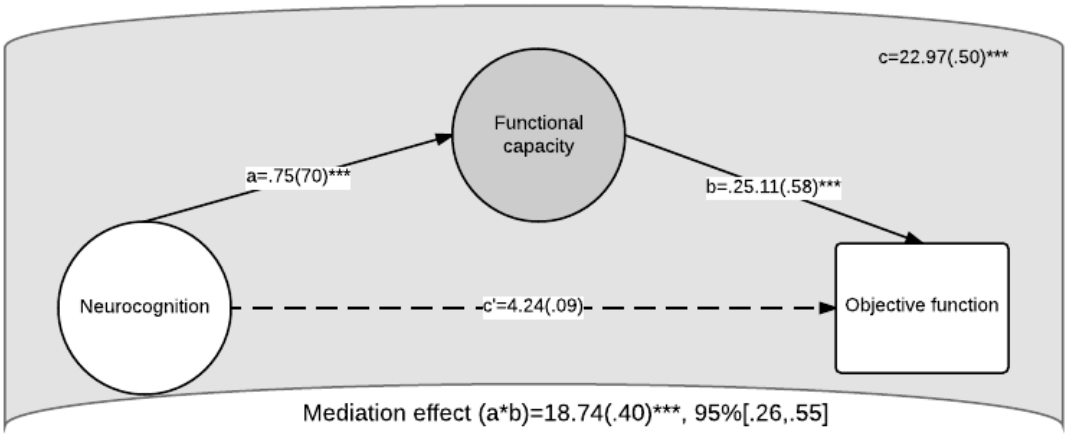

*Figure 25 Mediation effect of functional capacity on the relationship between cognitive ability and objective community functioning. Key: ***p<.001, ** p<.01, *p<.05*

The mediation analysis reports that functional capacity significantly mediates the relationship between neurocognition and objective function (β =.40, +/-95% [.26, .55]). The model explained 50% of the variance in functional capacity and 41% of the variance in objective functioning. The model retained significant mediation even with the inclusion of negative symptoms in analysis (a*b=.27, *p*=.001, 95%CI [.11, .43]). The reverse model was run to assess the direction of the relationship and functional capacity was found to significantly mediate the relationship between objective function and neurocognition (a*b=.32, *p*<.001, 95%CI [.16, .47]). This suggests that the reverse relationship is also true and as someone functions more in the community, better cognitive abilities are found to through their increased capacity to complete daily living tasks

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3.3.11 Model 4: The relationship between functional capacity and time spent in structured activities will be mediated by metacognition.

A model was run to investigate whether functional capacity predicts functional outcome with metacognition mediating this relationship (figure 26 below). Firstly, the overall model fit was investigated and the pathway model achieved good fit statistics ($\chi^2(1)$ = .17, *p*=.68, CFI= 1.00, TLI=1.00 RMSEA= 0.00).

Functional capacity significantly predicted metacognition (β = .77, *p*=.001) and metacognition significantly predicted objective function (β =.77, *p*=.006). The relationship between functional capacity and objective function however failed to obtain significance (*p*=.81). The indirect effect of metacognition on objective function reported a significant mediation effect however (β =.60, *p*=.001) and the confidence intervals corroborate this finding (+/-95%[.24, .95]. The model reports a large effect

size with 66% (R^2= .66) of the variation in objective function being accounted for. The model was run with negative symptoms as a covariate and retained significant mediation effects (a*b=.59, *p*=.006, 95%CI [.17, 1.01]. The reverse model of metacognition mediating the relationship between objective function and functional capacity was assessed and no significant relationship was found. The reverse model of functional capacity mediating the relationship between metacognition and objective function was also run and the mediation analysis was non-significant. Finally, the model of both metacognition and negative symptoms mediating the relationship of functional capacity and objective function was run and negative symptoms were not a significant mediator of this relationship.

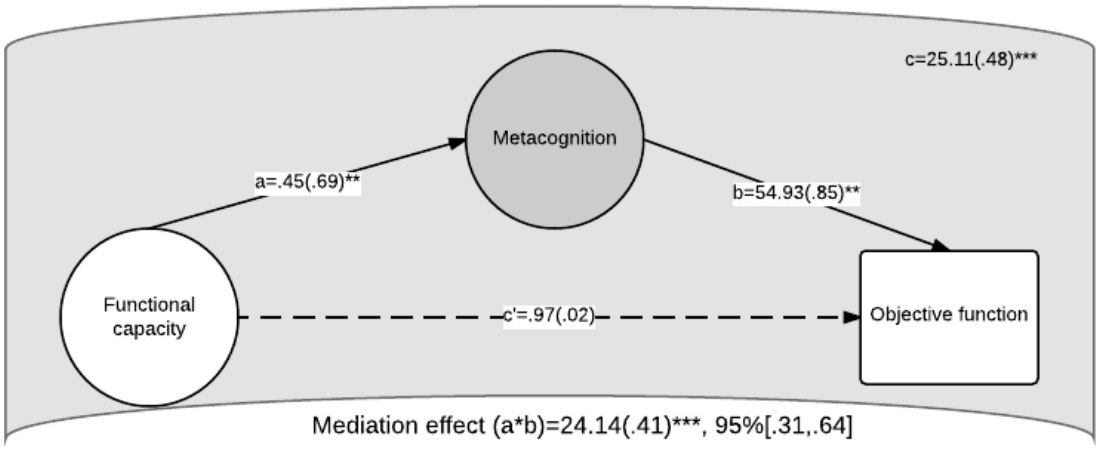

*Figure 26 Suggested mediation model of functional capacity to relationship objective community function mediated by metacognition. Key: ***p<.001, ** p<.01, *p<.05*

3.3.12 Model 5: The relationship between neurocognition and functional capacity is mediated by metacognition and negative symptoms.

First, the model of neurcognition on functional capacity was re-run with both negative symptoms and metacognition as mediating pathways between neurocognition and functional capacity. Both metacognition (β = .40, p=.015) and negative symptoms (β =-.27, *p*=.004) signficantly predicted functional capacity and neurocognition signficantly predicted metacognition (β =.56, *p*=.021) and negative symptoms (β =-.43, *p*<.001). Next the mediation pathways were inspected and metacognition (a*b= .22, *p*=.012, 95% CI[.05, .39]) and negative symptoms (a*b=.12, *p*=.015, 95% CI[.02, .21]) mediate the relationship between cognitive ability and functional capacity. The R^2 statistic suggests that 71% of the variance in functional capacity is accounted for by the overall model.

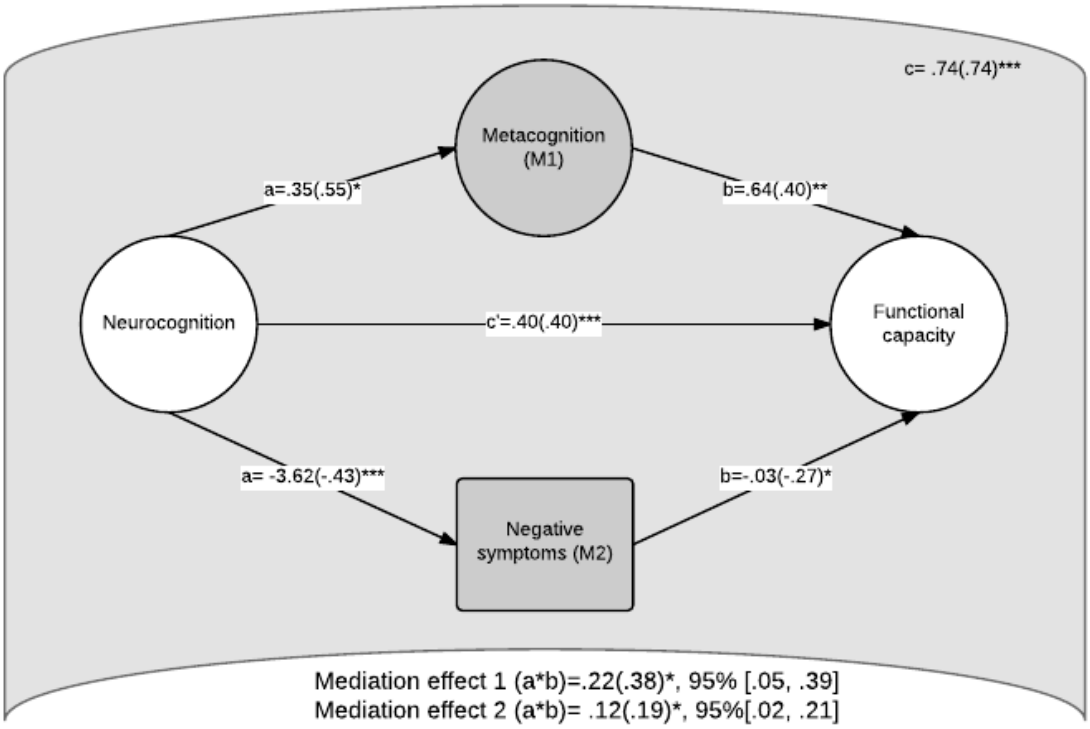

*Figure 27 Mediation model: metacognition and negative symptoms as mediators for the relationship between neurocognition and functional capacity. Key: ***p<.001, ** p<.01, *p<.05*

The model was also run to investigate the relationship of metacognition and negative symptoms on objective function however no signifcant pathway was present between negative symptoms and objective function (β = .07, p=.376) therefore one of the conditions for mediation was not met.

3.3.13 Model 6: Memory, IQ and executive function, metacognition and functional outcome (functional capacity and objective function)

Finally, the individual cognitive domains included in the meta-analysis discussed in chapter two were also investigated. Memory, IQ and executive function were entered into the model as predictors of functional capacity and functional outcome with metacognition and negative symptoms included as covariates. The analysis results are displayed in table 15 below.

Table 15 Summary table of individual cognitive predictors, metacognition and functional outcome

Predictor	*Mediator*	*Outcome*	*Covariate*	*a*	*b*	*Direct (C')*	*Indirect (a*b,[95%CI])*
Memory	MC	Fx		.12(.)*	.77(.48)**	.26(.49)***	.14(.26)*[.05, .29]
Memory	MC	Fx	Neg	.16(.53)**	53.37(.68)**	.21(.39)***	.08(.15) [-.02, .31]
Memory	MC	FO		.23(.31)*	54.8(.79)*	.55 (.02)	6.54(.26)*[.04, .45]
Memory	MC	FO	Neg	.08 (.20)*	55.92(.83)*	.21 (.05)	4.36(.16) [-.03, .36]
IQ	MC	Fx		.01 (.55)*	.84 (.52)**	.01 (.41)***	.01(.29)* [.06, .52]
IQ	MC	Fx	Neg	.01(.38)*	.62(.36)*	.01(.34)**	.01(.14) [-.06, .35]
IQ	MC	FO		.01(.59)**	57.94(.86)*	-07(-.50)	.74(.51)*** [.26, .76]
IQ	MC	FO	Neg	.09(.40)*	61.02(.94)**	-.12(-.8)	.52(.38)* [.08, .68]
EF	MC	Fx		.18(.40)*	1.07(.65)**	.14(.19)*	.19(.3)* [.07, .45]
EF	MC	Fx	Neg	.10(.22)	.84(.51)**	.08(.11)	.08(.11) [-.03, .25]
EF	MC	FO		.17(.40)*	.53.63(.72)**	2.2(.07)	8.85(.29)**[.13, .44]
EF	MC	FO	Neg	.10(.22)	54.79(.80)**	.47(.02)	5.27(.18)* [.01, .35]

*Key: ***=p<.001, **=p<.01, *= p<.05. Notes: NC=neurocognition, MC=metacognition, Fx=functional capacity, FO=objective function, Neg=negative symptoms, ( )= standardised values*

Metacognition was found to significantly mediate the relationship between all 3 cognitive domains and functional capacity however all three mediation pathways failed to obtain significance once negative symptoms were also included as a covariate. This suggests that negative symptoms also contribute to the mediation effect observed. In relation to objective function, metacognition was found to significantly mediate the relationship between all three individual cognitive domains and time spent in structured activity. When negative symptoms were included as a covariate, the significant mediation effect was lost in the memory and executive function domains. IQ however retained significance even controlling for negative symptoms.

This suggests that metacognition uniquely accounts for the relationship between IQ and objective function distinct from negative symptoms. This suggests that executive function and memory may be more related to negative symptoms than IQ and account for the loss of significant pathways once negative symptoms were included in the model.

Table 16 Mediation model summary table including model fit and pathway estimates

Predictor	*Mediator*	*Outcome*	*Model fit (χ^2 (df), p)*	*CFI/TFI/RMSEA*	*a*	*b*	*Total (c)*	*Direct (C')*	*Indirect (a*b,[95%CI])*	*R^2_{med}*	*R^2_{out}*
NC	MC	FX	.03(1), .86	1.00, 1.04, .00	.36(.56)*	.82(.51)**	.61(.70) ***	.44(.42) ***	.40(.29)**[.07, .50]	.313	.673
NC	MC	FO	.11(1), .74	1.00, 1.04, .00	.35(.51) **	53.37(.74) **	21.28(.48) ***	2.73(.06)	18.55(.41) ***[.31, .64]	.317	.594
NC	FX	FO	.00(0), .00[a]	1.00, 1.00, .00	.75(.70) ***	25.11(.58) ***	22.97(.50) ***	4.24(.09)	18.74(.40) ***[.26, .55]	.495	.413
FX	MC	FO	.17(1), 68	1.00, 1.00, 0.00	.45(.69)	54.93(.85)	25.11(.48)	.97(.02)	24.14(.41) ***[.31, .64]	.314	.66
NC	MC, Neg	FX	.22(3), .00	.89, .63, .00	.50(.77) ***	51.80(.77) **	27.69(.64) ***	2.01(.05)	25.68(.60) **[.24, .95]	.595	.71

***=*p*<.001, **=*p*<.01, *= *p*<.05. Notes: NC=neurocognition, MC=metacognition, FX=functional capacity, FO=objective function, Neg=negative symptoms, [a]= just identified model, ( )= standardised values

3.4. Discussion

In relation to the first study aim, the results of the factor analysis suggested that metacognition is best represented by the self-reflectivity subscale of the BCIS and a total score of the MAI. This model demonstrated good overall fit statistics. The self-certainty subscale was found to have a non-significant relationship with both other metacognitive variables and outcome measures. The factor analysis suggests that neurocognition is also suitably represented by a one factor solution, as is functional capacity. The present study offers similar levels of functioning as Hodgekins et al's., (2015) FEP study (see table 14 above) and confirms that those with psychosis are spending under half the time in structured activities as a non-clinical comparison study. Social disability is present across FEP cohorts and highlights social disability as a key feature of psychosis.

In relation to the second and third hypotheses, neurocognition and metacognition were positively associated with both functional capacity and objective function. Negative symptoms were found to have a significant negative association with metacognition and functional capacity and objective function. The relationship between neurocognition and objective function was mediated by functional capacity and the relationship between functional capacity and objective function was also mediated by metacognition. Finally, functional capacity and objective function were found to have a significant, positive association with each other.

Functional capacity

The mediation analysis found that metacognition partially mediates the relationship between neurocognition and functional capacity explaining 67% of the overall variance in functional capacity. This suggests that cognitive skills are associated with successfully completing everyday tasks however the ability to regulate these skills through metacognition is also important to integrating these domains.

Objective function

Metacognition was found to fully mediate the relationship between neurocognition and objective function with 59% of the variance in objective community function accounted for in the model. This suggests that once again, the cognitive skills required to perform occupational, social, educational and social activities are also associated with the metacognitive abilities required to integrate them into the real world.

Furthermore, the individual cognitive domain pathways analyses suggest that the relationship between memory, executive function and IQ and functional capacity and objective function is mediated by metacognition. When negative symptoms were controlled for in mediation analysis, only the relationship with IQ persisted. This suggests that a particular relationship exists entirely separate from the influence of negative symptoms between IQ, metacognition and time spent in structured activities. This is an interesting finding in light of Hill et al., (2002) work documenting that those with a diagnosis of schizophrenia may fall into distinct cognitive profiles. However, the direct pathway between IQ and objective function was not significant suggesting that there is something unique to the relationship between metacognition and IQ accounting for the relationship to objective function as IQ individually did not significantly predict objective function.

Verbal IQ was employed for this particular analysis as most other studies also report this relationship (see chapter two). Verbal IQ is suggested as a measure of both premorbid IQ and verbal intelligence; whilst having adequate verbal skills is essential to conducting social and occupational activities, language in itself may not be enough. Likewise, if it is considered a measure of premorbid IQ this suggests that intelligence prior to psychosis is a key determinant of functional recovery after illness. However this relationship only appears when considered through metacognition; metacognition may be the essential ingredient associated with translating these abilities into actual real-life activities.

Functional capacity and objective function

In terms of the relationship between functional capacity and objective function, metacognition was found to fully mediate this relationship. This is an important finding as this suggests that, whilst individuals may possess the capacity to complete tasks essential to community function, without sufficient metacognitive abilities, these skills may not be integrated and adapted successfully to support real-world recovery. This confirms that functional capacity is required to take part in structured activities.

Negative symptoms

The relationship between neurocognition, metacognition and functional capacity and objective function was not attributable to negative symptoms as these relationships persisted even when negative symptoms were included in analysis. In addition, a second mediation pathway was observed between neurocognition and functional capacity going through negative symptoms. This confirms that negative symptoms also play a role in translating cognitive skills into functional capacity. The overall model with both

metacognition and negative symptoms accounts for 71% of total variance in functional capacity. Interestingly, no relationship was found between negative symptoms and functional outcome in model 4 which was unexpected. Conceptually, as both measures assess amount of involvement in activity (although in different ways) this is surprising and may be a power issue. However this does suggest that negative symptoms are more predictive of capacity to complete a task rather than whether you are actually engaging in community activities.

In relation to the hypotheses, the present study can confirm that metacognition partially mediates the relationship between neurocognition and functional capacity and fully mediates the relationship with objective function. Metacognition also fully mediates the relationship between functional capacity and objective function. Additionally, metacognition was found to mediate the relationship between individual cognitive domains and both functional capacity and objective function. In relation to objective function, no significant direct pathway was observed between the cognitive domains of memory, IQ and executive functioning and time spent in structured activities. Direct pathways however were found in the functional capacity models. This suggests that cognitive ability is directly related to functional capacity as it is likely that these tasks directly require raw cognitive skills. Objective function in comparison requires these cognitive pathways to be integrated into complex social environments hence metacognitive ability is more important to the relationship. This could suggest that remediation interventions may have a greater impact on equipping individuals with the capacity to complete everyday tasks by also working on a metacognitive level. If improvements in metacognition are also promoted, cognitive improvements may be passed on to improved community functioning. For example having improved working memory skills may be important to completing individual tasks in an occupational setting however managing cognitive resources and monitoring when the individual task may go wrong may be more critical to holding down employment longer-term.

Interestingly, in relation to model 3, the reverse model was also found to be significant. The relationship between time spent in structured activities and neurocognition was mediated by functional capacity. This may suggest a form or reinforcement is important to community function with spending more time in structured activities relating to better capacity and better cognitive function. Taking part in more activities may allow individuals to practice their cognitive skills and therefore improve them which facilitates increased community engagement in a cyclical relationship.

The present study corroborates Lysaker et al.'s (2010) study which also found that mastery, a form of metacognition, mediated the relationship between cognition and social function. However this builds on the study by demonstrating this effect across different measures of function and a richer overall construct of metacognition. Furthermore, as the present study employed FEP, the argument that deficits may be due to chronicity of illness and associated medication and treatment therapy exposure rather than metacognition itself are addressed.

The medication analysis also suggested no significant relationship between medication and metacognitive domains or outcome domains. Likewise, Lysaker employed a largely older, male cohort restricting the claims that can be made in terms of generalizability. Although the sample was still predominantly male, the ratio was much more even (61% male versus 39% female). This is the first study to incorporate cognitive insight into this analysis and suggests that self-reflectivity may contribute to community function in addition to cognitive ability.

In terms of the relationship with neurocognition, the present study corroborates the work of Hamm et al., (2012), Nicolò et al., (2012) and Abu-Akel & Bo, (2013) and a host of papers by Paul Lysaker (2005; 2007; 2011) in which improved neurocognition is associated with better metacognition. The present study also confirms that metacognition is an important predictor of community function as suggested by Giusti et al., (2013) and Brüne et al., (2007).

The factor analysis offers some insight into the construct of metacognition; the self-reflectivity subscale of the BCIS loaded onto a single factor with the MAI total score suggesting that they are indicators of a shared latent factor. The self-certainty subscale did not fit with this model and no significant relationships were found between self-certainty and other variables. Two findings can be concluded from this; firstly, the self-reflectivity aspect of cognitive insight may fit in a multi-layered metacognition system related to synthetic metacognition as a form of metacognitive knowledge. The self-certainty subscale measures an unrelated aspect of cognitive insight and this is supported by other studies showing mixed findings when including overall scores for cognitive insight rather than separate indices. The present study suggests that authors should use caution when using a composite index score of cognitive insight as these two factors may relate to different processing systems.

The study findings are important as they suggests that cognitive abilities are an important predictor of our capacity to complete everyday tasks however metacognition is also required to navigate the complexities of daily life. When it comes to translating these skills into a real-world setting, metacognition is potentially equally important as raw cognitive ability. Metacognition was observed to significantly mediate the relationship between cognition and objective function whilst controlling for negative symptoms however no significant direct pathway was observed between cognition and objective function. This indicates that metacognition is more important to real-world functioning than either neurocognition or negative symptoms. In summary, one's ability to reflect back on cognition and monitor the transitions between mental states may improve learning and correct strategy selection in response to both the capacity to complete daily tasks and real-world situations.

3.4.1 Limitations

Whilst the present study attempted to address many of the identified issues with known research, a number of limitations must be held in mind when considering the findings. Firstly, the present study is cross-sectional so the impact of changes in neurocognition and metacognition and how these may impact on functional levels in the individual are not known. Future studies tracking the changes in all three domains across time would offer greater insight into the mechanisms of the relationship between variables. The analysis of reverse models offers some confidence in relation to the direction of causality however how these variables interact in psychosis needs clarification.

The MAI, as a measure of synthetic and declarable metacognitive ability, relies on self-report of internal mechanisms. Language disturbances have been identified as a primary feature of schizophrenia (Kuperberg & Caplan, 2003) or as a result of current symptoms (Stirling, Hellewell, Blakey, & Deakin, 2006). As a self-report interview measure reliant upon verbalisation of internal experiences, deficits may be due to linguistic deficits or descriptive impairment rather than metacognition per se. However as one of the measures of neurocognition is verbal IQ and logical memory and verbal fluency also draws on theses abilities, both neurocognition and metacognition measurement would have been impacted on equally by language deficits in the study. This should minimise the effect language would have on the results however this should still be considered when interpreting the findings.

Secondly, the present study was potentially underpowered despite recruitment targets being calculated in advance as suggested by Fritz, (2007). Whilst exact numbers

required for factor analysis vary from author-to-author (Jung & Lee, 2011), some commentators suggest a minimum of 150 (Hutcheson & Sofroniou 1999) even when there is high correlation amongst variables as in the present study. Likewise, the models assessed were restricted due to concerns over power; ideally the pathway models would have been measurement models with all indicators included however the present study had to approach this in a piecemeal manner and run through multiple models to maintain a respectable case to parameter ratio (Bentler & Chou, 1987). Finally, due to self-certainty's poor factor loading, the latent variable of metacognition was only measures by two indicators. Whilst Kenny suggest this as a minimum number, three is a safer option (Kenny, 2012) and under estimation may lead to bias parameter estimates (Iacobucci, 2010). The significant correlation however between the two indicators acts a protective factor and helps justify the use of only two indicators (Kenny, 2012).

3.4.2 Implications

Despite these restrictions, the present study implicates metacognition in both functional capacity and real-world functioning. This builds on the work discussed in chapter 1 and 2 and confirms the relationship between neurocognition and function being mediated by metacognition. This also demonstrates that this relationship is present at early stage of illness. There are important implications of these findings; metacognition may be a critical ingredient in integrating a host of skills into occupational and social situations and this may suggest that treatment programs may wish to target this ability in care pathways. Cognitive remediation programmes have already started to incorporate metacognitive content to traditional cognitive remediation exercises and the present study suggests that this is a valuable addition. By improving both cognition and metacognition rather than solely the former, recovery from psychosis after symptoms have subsided may be maximised. The effect sizes were also larger than previous studies investigating the relationship between neurocognition and function ranging from 40%-70% of the overall variance in outcome. This offers far more explanation of functioning and highlights the importance of both metacognition and negative symptoms in outcome.

Chapter 4: A Voxel-Based Morphometry (VBM) investigation of perceptual metacognitive accuracy in FEP.

4.1 Introduction

The neurodegenerative process in schizophrenia was suggested as early as Kraeplin's (1919) description of dementia praecox and was similarly asserted by Bleuler (1911). Authors such as Bender (1947) and Watt (1978) added further evidence that early abnormal neurodevelopment may underpin the deficits observed in schizophrenia. With the advent of MRI technology, nascent studies began to suggest the presence of neurological abnormalities in schizophrenia (Crow, 1982; Smith et al., 1984), such as differences in overall brain volume, enlarged ventricles, and localised volume changes. Evidence for differences in total brain volume compared to controls has been mixed, with some studies reporting larger (e.g. Andreason et al., 1990) and others smaller (e.g. Barta et al., 1990) overall total intracranial volume. However Shenton, Dickey, Frumin and McCarley, (2001) in a review reported that 78% of studies found no difference. A more consistent finding appears to be enlarged lateral ventricles, and localised volume changes including reduced basal ganglia, prefrontal, medial temporal (Shenton et al., 2001) and hippocampal (Radulescu et al., 2014) volume. Furthermore, enlarged ventricles have been associated with a reduction of the thalamus, striatum and temporal cortex (Gaser, Nenadic, Buchsbaum, Hazlett, & Buchsbaum, 2004). Whilst longitudinal studies have not shown a continued degeneration in more advanced stages of chronic illness (Pantelis et al., 2005), progressive brain volume changes have been found post earliest phase of illness, and further degeneration has been associated with poorer clinical recovery (Lieberman, 1999). Zipursky, Reilly and Murray, (2013) warn that longitudinal studies demonstrating a longer term degenerative process must be considered with the fact that the further degeneration may be due to effects of continued exposure to antipsychotic mediation and substance abuse rather than psychosis per se.

Structural abnormalities have been found to be present at first stage of illness (Zipursky et al., 1998) and more recently, a strategy to avoid the aforementioned confounding variables has been adopted by investigating non-chronic samples. Furthermore, different GM deterioration profiles have been observed in affective versus non-affective psychosis

and are associated with worse outcomes (Rosa et al., 2015). Equally, differing GM volume and cortical thickness are associated with positive and negative symptom profiles separately (Padmanabhan et al., 2015). In FEP, reduced GM volume has been observed in limbic structures (Watson et al., 2012), frontal, temporal, occipital and cerebellum regions compared to controls and more severe GM reduction has been associated with earlier onset of psychosis (Tordesillas-gutierrez et al., 2015). Clinically high risk (CHR) groups have been investigated and researchers have found that those that converted into psychosis demonstrated a higher decline in overall GM volume than those that did not (Borgwardt et al., 2008), although other studies have only found this effect in specific brain regions such as the prefrontal cortex (Sun et al., 2009) and temporal regions (Pantelis et al., 2003). Scanlon et al., (2014) in comparison found cortical thinning of GM in temporal and caudate regions in relation to controls. However no differences were found in the local gyrification index and no relationship was found between structural abnormalities and symptom or global functioning 3 years later. Tognin et al., (2014) report reduced cortical thickness in the parahippocampal gyrus compared to controls however they found no GM volume differences between CHR individuals that transitioned to psychosis compared to those that did not. This suggests that cortical changes may not necessarily predicate transition to psychosis. Comparison among studies looking at prodromal and CHR samples are problematic as studies differ in terms of group definition, scan interval between baseline and follow-up, contain relatively small sample sizes, and employ differing MRI analysis techniques (Chung & Cannon, 2015; Tognin et al., 2014). This suggests that, whilst there are structural deficits evidenced in schizophrenia and FEP, the exact profile is not established as yet.

A further complication in considering previous research is the comparison control groups employed. Studies often fail to control for education (Smith et al., 2015), find significant difference in IQ and compare anyway (Benetti et al., 2013; Watson et al., 2012) or recruit a sample of patients with intact IQ who may not be representative of a typical schizophrenia population (Radulescu et al., 2014). Some evidence suggests the presence of a sub-profile of patients who retain cognitive abilities and may very well have a different structural profile and different clinical outcome statistics (Leeson et al., 2011). Typical meta-analysis reports suggest that IQ in FEP is -.91 standard deviations below the population mean (Mesholam-Gately et al., 2009) therefore selecting patients with above mean IQs may not be representative of the group on the whole.

In summary, structural deficits have been observed in schizophrenia and some work has begun to investigate this at early stage of illness such as FEP. How these GM deficits interact with metacognition in FEP has not been researched and will be the focus of the

next section. Understanding the relationship between neural structure and metacognitive processing in FEP may offer insight into determinants of disability in later schizophrenia.

Metacognition

Metacognition refers to 'thinking about thinking' (Flavell, 1979) and is a fundamental component of higher order cognition (Rosenthal, 2000) (see section 1.14). The ability to critically evaluate one's cognitive products requires a number of higher order skills and the preoccupation with accurate self-knowledge is not a new notion dating back Plato and Socrates. Nelson and Narens (1990) provide a model of metacognition, detailing a dual system of object and meta-level processing, wherein cognitive processes send information through a feedback loop relating to task performance, and meta-level processes regulate the cognitive resources allocated to a task. Meta-level processes are responsible for assessments of cognitive accuracy, selection of strategy and the updating of goals which allow successful learning and completion of daily tasks (see section 1.15 for further details). The monitoring and control of these processes are dependent on subjective appraisals and may be explicit (conscious) or implicit (feeling driven or 'gut instinct') and are pertinent to successful social interactions (Frith, 2012).

Dysfunction in metacognition has been found in a number of neuropsychiatric disorders (David, Bedford, Wiffen, & Gilleen, 2012) and specifically in schizophrenia (Vargas, Sendra, & Benavides, 2012) and may underpin functional deficits. Those with schizophrenia have been found to have deficits in reflecting back on their own mental states (Lysaker et al., 2013) overconfidence in erroneous conclusions (Köther et al., 2012) and these deficits have been associated with a jumping to conclusions bias (Buck et al., 2012) due to inaccurate assessments of self-knowledge. Koren, Seidman, Goldsmith and Harvey (2006) suggest that successful metacognitive ability depends on the ability to perform a task, an appropriate level of confidence in performance (i.e. which tracks objective performance) and, thirdly, the decision to act on these confidence judgements in real-life. They argue that these processes may be essential to social recovery. The preceding research suggests presence of deficits in metacognitive processing in schizophrenia and FEP. Being aware that one may be wrong will lead to more caution in decision making whereas overconfidence may lead to inappropriate social strategies being employed leading to poor social and occupational function.

Research has investigated these metacognitive judgements in schizophrenia and psychosis through prospective learning assessments (JOLs) (Do Lam et al., 2012) and feelings of knowing (Bacon & Izaute, 2009). More recently retrospective reports of confidence in accuracy have been employed to estimate metacognitive control (Fleming,

Weil, Nagy, Dolan, & Rees, 2010) using signal detection theory (SDT) to model the ability to discriminate signal from noise (Maniscalco & Lau, 2012) (see section 1.16 for further details on measurement). To have good metacognitive efficiency, an individual should be confident in correct responses and unconfident in incorrect decisions. Perceptual metacognition has been used in previous research (Fleming et al., 2010; Palmer et al., 2014) and using SDT gives a 'bias free' estimate of metacognitive accuracy without the confounds of task performance or stimuli bias (Fleming & Lau, 2014). In relation to the Nelson and Narens (1990) metacognitive model, metacognitive accuracy is considered a lower-order metacognitive experience.

The study of the neural basis of these judgements has become of increasing interest in research (for a review, see Fleming & Dolan, 2012). The frontal cortex has been associated with mentalizing about one's self since the beginning of the 21st century (Frith & Frith, 2003). More recently, the processing of self-referential information and engaging in introspective behaviours has been associated with increased activity in the dorsomedial PFC and Schmitz et al., (2004) found a relationship between the dorsolateral PFC and self-evaluative metacognition. Higher activity was demonstrated when responding to self versus other evaluations. Retrospective confidence judgements have been found to be associated with the lateral PFC (Fleming & Dolan, 2012) and lesion studies implicate the rostrolateral PFC in subjective reporting of conscious perception (Del Cul, Dehaene, Reyes, Bravo, & Slachevsky, 2009). Beyond studies of brain activation, metacognitive judgements have been investigated in relation to structural volume. Fleming, Weil, Nagy, Dolan and Rees (2010) found a correlation between metacognitive accuracy and GM volume in the anterior PFC, and white-matter microstructure connecting the anterior PFC. However the authors failed to control for age which has since been implicated in GM volume (Terribilli et al., 2011) and metacognitive accuracy (Palmer et al., 2014).

In schizophrenia, Spalletta, Piras, Piras, Caltagirone and Orfei, (2014) assessed metacognitive insight through a questionnaire design and found poor self-reflection associated with reduced volume in the ventrolateral and right dorsolateral PFC. Vohs et al., (2015) investigated metacognition using the Metacognitive Assessment Scale (MAS), a semi-structured interview free narrative account of mental state reflection in the self and others. It was found that greater GM density in the medial PFC and ventral striatum was associated with increased metacognitive ability across a number of indices. Buchy, Stowkowy, Macmaster, Nyman and Addington, (2015) investigated metacognitive ability within a CHR group and found associations between cortical thickness and inferior and middle frontal gyri, superior temporal and insula regions, and higher scores on the MAS.

Finally, metacognition has been associated with functional outcome in psychosis and schizophrenia (Lysaker et al., 2010; McLeod, Gumley, Macbeth, Schwannauer, & Lysaker, 2014). It is thus essential to understand how metacognitive processing and neurological structure interact in FEP. The ability to correctly appraise cognitive products for accuracy can assist with social (Frith, 2012) and occupational (Giusti et al., 2013) performance and lead to requesting help at an earlier point before community deterioration (Koren et al., 2006). This metacognitive ability may also predicate self-management of symptoms and is also implicated in delayed recovery (Nicolò et al., 2012). The ability to form complex representations of one's self may allow for the revision of negative self-beliefs and assist with motivational deficits (Hamm et al., 2012). In relation to Nelson and Narens (1990) metacognitive model, (section 1.13), metacognitive accuracy is considered an implicit form of lower-order metacognitive processing. How this relates to high-order, synthetic metacognitive knowledge discussed in chapter three will also be investigated.

The previous evidence provides a number of suggestions; i) that GM differences can be present at early stage of illness, ii) these deficits are more subtle than at chronic stages iii) that worse symptom outcomes are associated with greater GM deterioration. However the nature of this relationship is as yet unclear and the profile of continued GM degeneration is not certain after first episode. There appears to be sub profiles of those experiencing their first-episode of psychosis; a proportion make a full recovery however others deteriorate into chronic schizophrenia and longer term social disability. Understanding variables that predict recovery at first point of illness is critical to understanding the causal factors of schizophrenia.

Metacognition is a higher-order mentalisation process and has been linked to frontal regions which have also been proposed to be deteriorated in FEP. How the two may interact is yet to be investigated and retrospective judgments of cognitive processes has also not been explored in FEP. The forced-choice metacognitive efficiency appraisal may be part of a different processing level to the MAI. How this appraisal process relates to brain structure in FEP may be of relevance for community outcome; incorrect confidence judgements of cognitive processes may lead to the individual assigning incorrect credence to self-judgements. If incorrect confidence is attributed to cognitive products, this could lead to poor real-world decision making. Deficits in metacognition at early stage of illness may underpin the functional deficits observed in the real-world that are a core feature of later schizophrenia. Structural deficits in the PFC and impoverished metacognitive ability may indeed be a marker for FEP.

4.1.1 Hypotheses

Metacognitive accuracy has already been associated with GM volume (Fleming et al., 2010) however whether this relationship is evident in FEP is unknown. GM volume deficits may account for metacognitive impairment seen in schizophrenia and FEP. To address these questions, the present study will (i) investigate whether patients with FEP have a deficit in metacognitive accuracy compared to matched healthy controls; (ii) investigate structural GM differences between FEP and healthy controls. The present study will focus on temporal and frontal gyri and the PFC, as there are clear a priori implications for these regions in both metacognitive processing and GM volume deficits; (iii) to investigate the relationship between structural GM volume and metacognitive processing in FEP and healthy controls; (iv) assess the extent to which this lower-order metacognitive accuracy relates to high-order, synthetic metacognition (discussed in chapter 3) in patients with FEP.

4.2 Method

4.2.1 Design

A cross-sectional design was employed with a convenience sample of FEP service-users who were recruited from Early Intervention in Psychosis (EIP) services from the Sussex Partnership Trust.

4.2.2 Participants

Potential participants were identified through either being registered on an existing research database or referred by EIP service care co-ordinators.

Inclusion criteria

All FEP participants were diagnosed as having their first-episode of psychosis and accepted onto full caseload of an EIP service. Inclusion criteria included a primary diagnosis of first-episode psychosis, being over the age of 18 and an exclusion criteria of organic neurological impairment and primary diagnosis of substance misuse were applied.

Twenty-one age, sex and education matched control participants were recruited from the community through local media outlets and were screened for relevant psychiatric, substance misuse or medical history. MRI safety protocol contradictions such as existing heart condition, non-removable metallic piercings and pregnancy were also reasons for exclusion.

4.2.3 Procedure

Ethical approval was obtained from the London-Camden and Islington NHS Research and Ethics Committee (Ref: 11/LO/1877, project ID 72141; see appendix A) and a local NHS research governance committee (appendix B). Participants were recruited through either current registration on a research database operated by Sussex Partnership Trust giving consent to be contacted by a researcher or through their care team. In the latter case, care teams were approached by a member of the research team and permission was sought from the service-user via their care co-ordinator for a researcher to contact them to explain the study and provide a participant information sheet. The FEP sample were advised to discuss taking part in the study with a family member or member of their care team and both groups were compensated for their time by £20.Informed consent was obtained by a) checking capacity with a member of the care team and b) by discussion with the service-user on the day of the study. A short version of the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987) and the Time Use survey (Constructive Economic Activity subscale) (Short et al., 2000) were also collected in addition to the behavioural task and the MRI scan acquisition on the day of

the study. Neuroleptic medication information was taken and converted to Olanzapine equivalent doses (Leucht et al., 2014) for correlational analysis with other variables of interest. Measures of metacognition (MAI and BCIS) collected as part of the study reported in chapter 3 were included for the investigation for how different metacognitive variables relate to each other (N=30). See table 18 for clinical characteristics information.

4.2.4 Behavioural Task; perceptual metacognitive accuracy

All participants received a standardised instruction sheet describing the task and a researcher was available to answer any questions prior to commencement. Participants were seated in a darkened room and positioned approximately 60 cms from a PC computer screen. The task was programmed and administered on MATLAB 8 (Mathworks Inc., Natick, MA, USA) using the COGENT 2000 toolbox.

Perceptual metacognitive accuracy was investigated through a computerised visual perception task adapted from a previous study (Fleming et al., 2010). Participants undertook a forced choice visual perception task wherein they were presented with 2 screens one after the other. Each screen contained 6 Gabor patch stimuli (circular patches containing alternate black and white vertical bars presented at 1.5 visual angle, 2.2 cycles per degree) arranged around a central fixation point (see figure 28). One of the Gabors in each screen was manipulated to 'pop-out' by increasing the contrast in the patch itself compared to neighbour patches. The contrast of the background Gabors was set to 20% luminance, the target Gabor was set to vary from 40% (little difference) to 100% (large difference) contrasts. All stimuli and instructions were presented on a grey background.

Stimuli array screens were presented for 200ms with an interval of 300ms between stimuli displays. The target Gabor's location was randomly alternated both in terms of screen location and which presentation screen (first or second) it would appear. Participants were requested to state which screen they believed the target Gabor had appeared in (1 or 2) by pressing an assigned key on a standard qwerty keyboard. They were given 2500ms to respond or a message stating 'too slow' would appear. Participants were then asked to report their confidence regarding with their decision on a scale of 1 (low confidence) to 6 (high confidence) by pressing a labelled key on the computer keyboard. They had 4000ms to make this decision before the next trial would automatically commence. Participants were encouraged to use the full range of the scale and a red box would surround their selected responses. The response window was increased from the original study (Fleming et al., 2010) (stimuli response was 2000ms and confidence response was 3500ms) to account for the potentially slower FEP sample response speed and ensure a suitable level of accuracy was achieved.

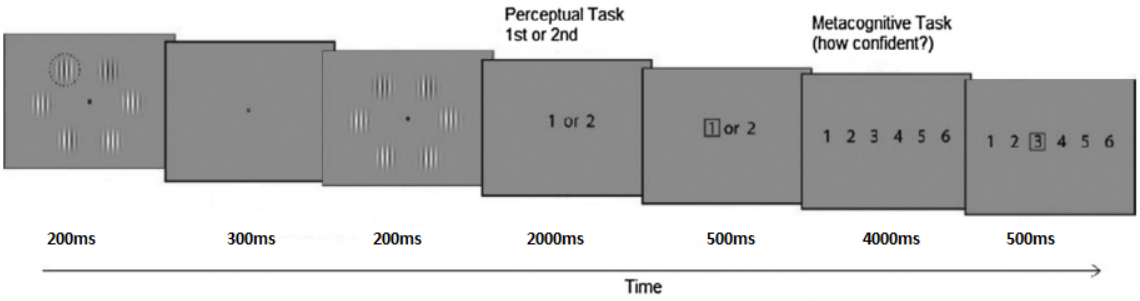

Figure 28 Perceptual metacognition 'pop out' task. Adapted from (Fleming et al., 2010)

To avoid metacognitive accuracy being confounded by general performance, the Gabor patch contrast was set using a 1-up-2 down staircase procedure to maintain participant accuracy at ~70%. One incorrect response would lead to a 3 % increase in contrast and two consecutive correct judgements would lead to a 3% decrease in contrast. All participants received a practice block containing 10 trials to familiarise themselves with the procedure and ensure task comprehension. The main task consisted of 4 blocks of 50 trials with a short break between each block. Due to the clinical sample, the number of trials was reduced to 200 from the 600 included in the original study to reduce task demands.

Perceptual metacognitive accuracy was calculated using the Maniscalco and Lau (2012) type 2 SDT method for meta-*d*' and quantified as meta-*d'*/*d'*. Meta-*d'*/*d'* is measure of how aware the individual is of their accuracy given their processing capacity (*d'*). A value of 1 equates to 'perfect' or optimal metacognitive awareness where confidence tracks accuracy in response to the task and values less than 1 demonstrates lack of metacognitive awareness or suboptimal metacognition. Meta-*d'* was calculated using a Matlab code available at http://www.columbia.edu/~bsm2105/type2sdt/ (Maniscalco & Lau, 2012).

4.2.5 Image Acquisition

All participants underwent the same imaging protocol. Structural MRI scans were obtained using a Siemens Avanto 1.5 T scanner. A T1-weighted MPRAGE sequence was performed with the following parameters: TR/TE = 2730ms/3.57ms, GRAPPA acceleration 2, an in-plane matrix of 256x 256 pixels over a FOV of 256mm x 240mm, flip angle 7°, slice thickness 1mm yielding 192 sagittal plane slices, coronal and axial resolution 1mm, acquisition time 5 min 58 seconds. All images were inspected for image and motion artefacts prior to analysis.

4.2.6 Voxel-Based Morphometry

Structural data was preprocessed and analysed using FSL-VBM (Douaud et al., 2007, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLVBM) with an optimised Voxel-Based Morphometry

(VBM) protocol (Good et al., 2001) in FMRIB software library (FSL) version 5.0.7 (Smith et al., 2004). For the purpose of creating the study template, a sample (21) of the FEP were randomly selected to match the number of controls, using an in-house MATLAB script. This is necessary because mismatching group numbers may lead to a biased template being used in analysis. In the first stage of FSL-VBM, the T1 images were skull-stripped using the FSL Brain Extraction Tool (BET), using a fractional intensity threshold of 0.15 with the options –R for a more robust brain centre estimation and–N to counteract the presence of greater neck volume in the images. The resulting images were inspected for suitability to be included in the study template. Two participant images did not show satisfactory skull stripping and were then separately re-processed with BET using a fractional intensity threshold of 0.1 with options –R, -S and –B to address residual eye, optic nerve and neck voxels. In the next step of FSL-VBM, the skull-stripped images were segmented to extract grey matter only and registered to the MNI 152 standard space using non-linear registration (Andersson et al., 2007). The resulting images were then averaged and flipped along the x-axis to create a left-right symmetric study-specific grey matter template. A modulation process was then run to compensate for the enlargement/contraction required for non-linear spatial registration wherein each voxel of each grey matter image was divided by the Jacobian of the warp field (Good et al., 2001). All normalised grey matter images were then smoothed with an isotropic Gaussian kernel with a sigma value of 3 (equal to a full width half maximum of 7 mm). Finally voxelwise GLM was applied using permutation-based non-parametric inference testing correcting for multiple comparisons across voxels. Whole-brain analyses were conducted across all GM voxels within the template. In addition, given the clear role for prefrontal cortex in metacognition, region of interest analyses were conducted across GM voxels within a frontal lobe mask, as defined by the frontal lobe region in the FSL Harvard-Oxford Cortical Atlas.

4.2.7 Design matrix

A design matrix was compiled with the FSL general linear model tool. The following contrasts were run to investigate the main effect of group on GM volume, the main effect of metacognitive accuracy on GM volume, and the interaction between group and metacognitive accuracy in GM volume. Contrasts were also run to explore age and gender. In the main effect and interaction contrasts, age and gender were controlled. All covariates were demeaned before entering to the design (see http://mumford.fmripower.org/mean_centering/ for details on demeaning variables) matrix. Contrast and design matrices are available in table 17.

Table 17 VBM analysis contrasts

	Variable					
Contrast	$\beta_{control}$	β_{FEP}	$\beta_{control*meta\text{-}d'}$	$\beta_{FEP*meta\text{-}d'}$	β_{gender}	β_{age}
Group (con>FEP)	1	-1	0	0	0	0
Group (FEP>con)	-1	1	0	0	0	0
Metacognition (positive)	0	0	1	1	0	0
Metacognition (negative)	0	0	-1	-1	0	0
Group*Metacognition (con>FEP)	0	0	1	-1	0	0
Group*Metacognition (FEP>con)	0	0	-1	1	0	0
Gender (female>male)	0	0	0	0	1	0
Gender (male>female)	0	0	0	0	-1	0
Age (positive)	0	0	0	0	0	1
Age (negative	0	0	0	0	0	-1

Statistical analysis was conducted using the FSL tool randomise, which allows for inference testing on statistical maps through a permutation method. Permutation methods allow inferential testing against the null hypothesis when little is known about the normality of the data and when there are multiple comparison concerns to control against false-positives (Bullmore et al., 1999), by drawing a null distribution on the basis of the data. Using randomise, the data were analysed using 5000 permutations with Threshold-Free Cluster Enhancement (TFCE) (Smith & Nichols, 2009). More information on the permutation method in neuroimaging is available elsewhere (Winkler et al., 2014; Nichols & Holmes, 2001).

4.3 Results

4.3.1 Sample

Forty-one psychosis participants were recruited in total, 32 male, 9 female with an age range of 19-39 (mean age 25.95) (see table 18 for demographic information). Thirteen patients were medication free for one month or more and 28 were receiving antipsychotic medication (see Table 18 for mean Olanzapine equivalent daily dose calculated for those prescribed medication). Seven patients did not complete the metacognition task due to fatigue and one was removed as a statistical outlier. One patient was excluded from further analysis due to poor quality T1 MPRAGE and one due to atypical neurology.

Table 18 FEP and control participant demographic information

	FEP (N=41)	HC (N=21)	
Age (SD)	25.95 (5.66)	24.43 (5.62)	P>.05
Gender (female/male	9/32	6/15	P>.05
Education (years) (SD)	13.27 (1.64)	13.71 (1.76)	P>.05
Time Use Survey (CEA) (hours/week)	19.97	N/A	
Medication (olanzapine equivalent mg/day) (SD)	12.91 (7.19)	N/A	
PANSS (3 item) positive symptoms (mean) (SD)	5.35 (2.38)	N/A	
PANSS (2 item) cognitive disorganisation (mean) (SD)	3.33 (1.43)	N/A	
PANSS (3 item) negative symptoms (mean) (SD)	5.67 (2.8)	N/A	

4.3.2 Perceptual metacognitive accuracy

Group comparisons

Variables were inspected for normal distribution prior to analysis, despite a slight positive skew, no significant violations were observed. An analysis of covariance was run to investigate metacognitive accuracy between the control (N= 19) and FEP (N=32) samples with age controlled for as previous evidence suggests this is implicated in metacognitive accuracy (Palmer et al., 2014). A significant difference was found between groups ($F(1, 48)= 4.54$, $p=.038$) with the control sample demonstrating increased metacognitive accuracy (M=.42, SD=.34) compared to the FEP sample (M=.22, SD=.36), despite equivalent performance accuracy as ensured by the staircase procedure built into the task. The magnitude of the effect size indicates a medium sized effect of group on metacognitive accuracy (Cohen's $d = .57$).

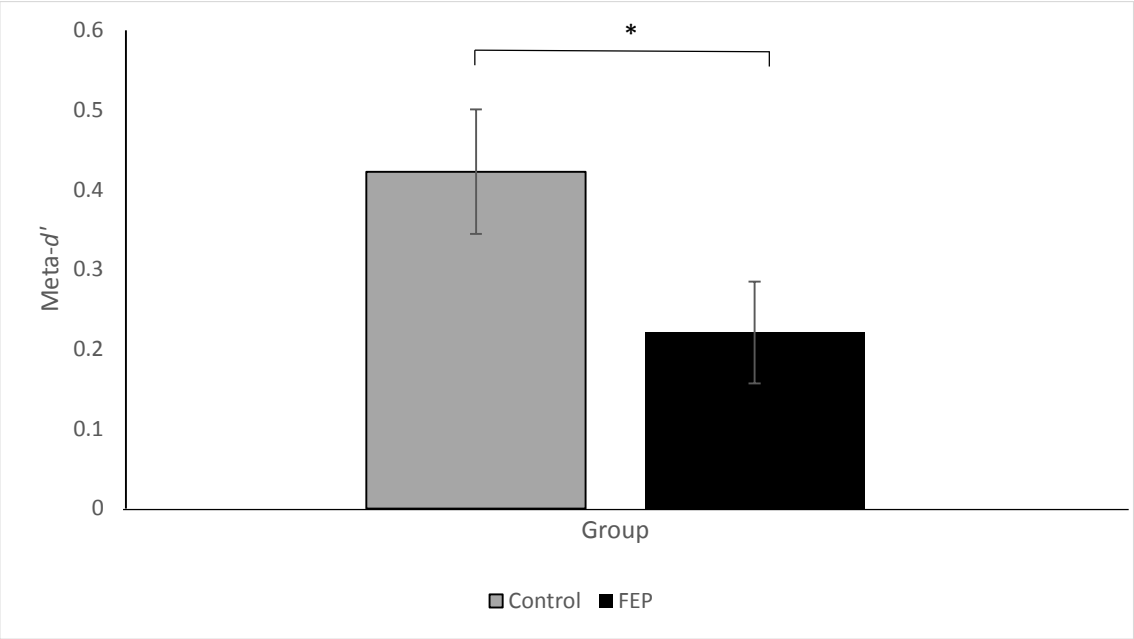

Figure 29 Perceptual metacognitive accuracy between FEP and control participants. Error bars represent standard error of the mean.

4.3.3 Relationship of different metacognitive measures.

FEP performance on the perceptual metacognition task was also investigated in relation to the other measures of metacognition outlined in chapter three with a subset of FEP participants who had completed all three measures (N=30). No significant correlations were observed between meta-*d'*, and the MAI or the BCIS subscales (p>.05). No significant associations were observed between meta-*d'* and symptoms, medication dose (r=.18, *p*=.33) or time spent in structured activities (r=.15, *p*=.41). Time spent in structured activities did however demonstrate a significant association with negative symptoms (r= -.49, *p*=.002) and cognitive disorganisation (r= -.44, *p*=.005) but not positive symptoms (r= -.05, *p*=.763).

4.3.4 VBM analysis: whole-brain

A threshold—free cluster enhancement (TFCE) correction was applied to correct for multiple comparisons across all GM voxels within the template, with Family-Wise Error rate (FWE) p<0.05.

Whole-brain group difference

In a whole-brain analysis testing for a group difference with control GM volume greater than FEP, no voxel clusters were significant at *p*=.05 when controlling for multiple comparisons. Two clusters were found at a trend significance level of *p*=.07, in the right middle occipital gyrus (figure 30 below), with FEP having reduced GM volume compared to control participants (clusters localised using the MNI structural atlas within FSL). A significant association (p<.05) was found between i) age and decreased GM volume,

with lateral caudate nucleus, putamen and frontal gyri regions showing decreased GM volume with increased age and ii) gender, with the cerebella regions showing greater GM volume in male participants (see table 19 below).

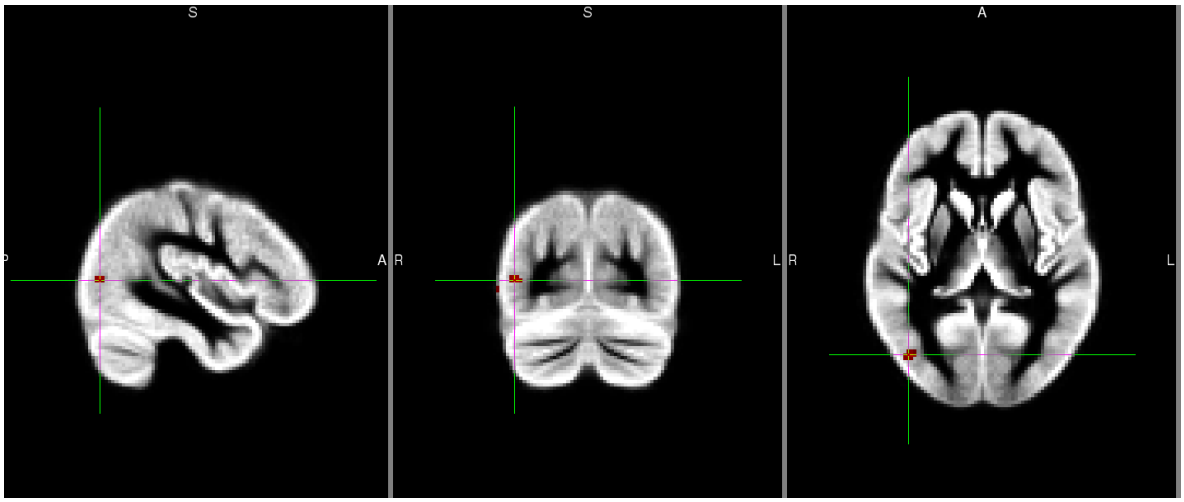

Figure 30 Full brain analysis: significant 18 cluster, peak coordinate 44, -74, 6 shown at p<0.07 FWE

Table 19 Whole brain analysis for GM volume and relationship to variables. Regions localised according to the Harvard-Oxford atlas in FSL

Contrast	Peak coordinate (x y z)		voxel	Cluster size (voxels)	Region	*P* value
HC>FEP	44	-74	6	18	Right middle occipital gyrus	.07
HC>FEP	54	-74	0	3	Right middle occipital gyrus	.07
Age (negative)	-12	12	6	196	L caudate nucleus	.05
Age (negative)	-34	32	-18	112	L inferior frontal gyrus	.05
Age (negative)	-30	-14	4	105	L Putamen	.05
Age (negative)	-42	48	-16	102	L inferior frontal gyrus	.05
Gender (M>F)	-12	-54	-64	6608	Cerebellum	.05

4.3.5 VBM analysis: Frontal lobe mask

An investigation was run with regions of interest specified encompassing the frontal lobe. A GM mask was created using the Harvard-Oxford Cortical Atlas. This includes the frontal pole region highlighted in previous research as specifically relevant for metacognition (Fleming et al., 2010; Buchy et al., 2015). This a priori region of interest approach allows researchers to investigate specific motivated brain regions while reducing the number of corrections required to exceed FWE p<0.05 threshold (Haller et al., 2011).

Frontal mask group difference

A significant group difference was found within the frontal lobe, with the FEP sample having significantly lower GM volume in the right superior medial gyrus (p<.05) controlling for multiple comparisons (figure 31).

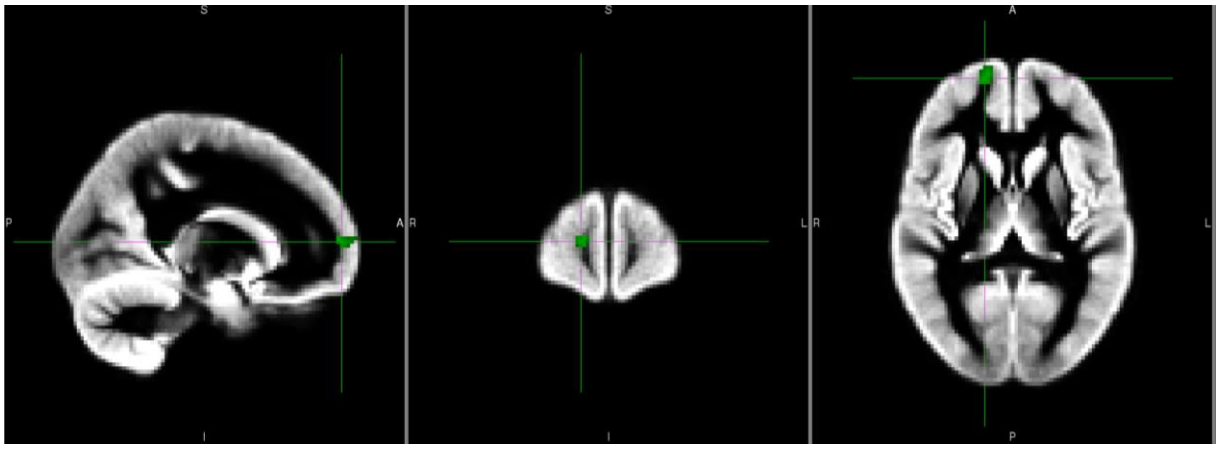

Figure 31: significant 47 voxel cluster from frontal mask region of interest analysis, peak coordinate 16 58 8, shown at p<0.05 FWE.

Main effect of perceptual metacognitive accuracy

Metacognitive accuracy was also investigated however contrary to the hypothesis, there was a trend level negative relationship with GM volume (p=.07) in the frontal gyri region. Better metacognitive accuracy was associated with lower GM volume in both FEP and controls.

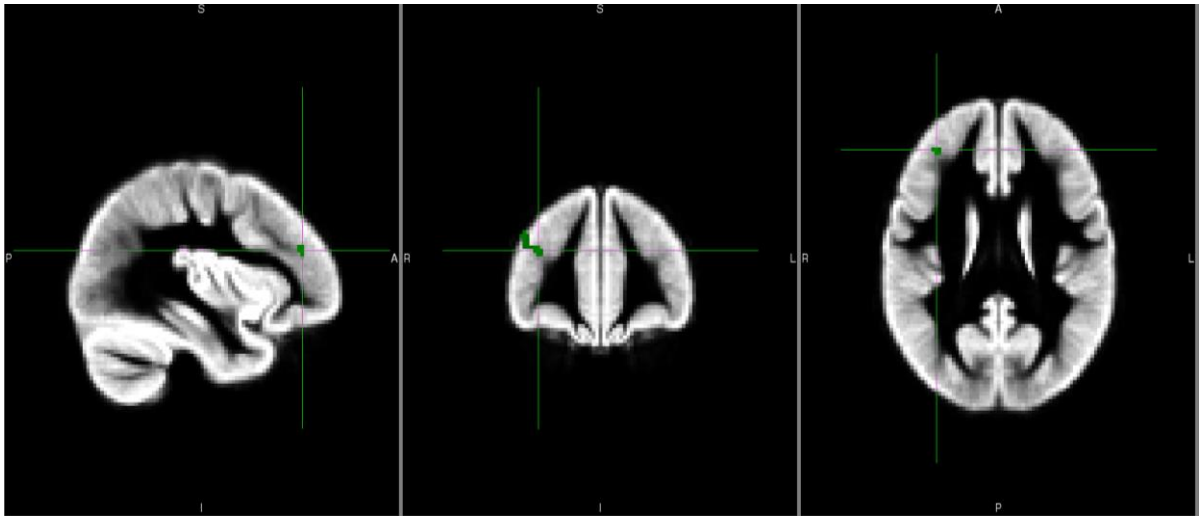

Figure 32: Metacognitive accuracy 34 voxel cluster from frontal mask region of interest analysis, peak coordinate 27, 83, 47, shown at p<0.07 FWE.

Metacognitive accuracy and relationship to group

No significant (p<0.05 FWE) interaction effects were found between metacognitive accuracy and group on GM volume, suggesting that the relationship between

metacognitive accuracy and GM volume did not significantly differ between FEP and controls

Age

There was a significant negative association (p<.05) between age and GM volume in the left and right inferior frontal gyrus and the right superior medial gyrus. As age increases, GM volume was lower across participants in both FEP and controls.

Table 20 Contrast results got GM volume and relationship to variables. All clusters reported were tested with a frontal lobe region of interest mask and FWE corrections. Regions localised according to the Harvard-Oxford atlas in FSL

Contrast	*Peak voxel coordinate (x y z)*			*Cluster size (voxels)*	*Region*	*P value*
HC>FEP	16	58	8	47	superior medial-frontal gyrus	.05
Metacognitive accuracy (negative)	44	40	30	34	R middle frontal gyrus	.07
Metacognitive accuracy (negative)	52	34	26	1	R inferior frontal gyrus	.07
Age	-34	32	-18	634	L inferior frontal gyrus	.05
Age	10	50	44	257	R superior medial gyrus	.05
Age	48	40	0	239	R inferior frontal gyrus	.05
Age	-54	36	-12	7	None	.05
Age	22	44	-20	3	R middle orbital gyrus	.05
Age	20	54	-22	1	None	.05

4.4. Discussion

The results of the study confirm that the FEP participants demonstrated significantly worse metacognitive accuracy compared to healthy controls matched on age, gender and education level. This is indicative of a specific processing deficit in the metacognitive domain and not attributable to objective task ability. The second hypothesis relating to structural deficits within the population is less clear. In a whole-brain analysis, trend level volume differences were observed in the occipital gyri and when applying a frontal lobe region of interest mask, significant medial-frontal gyrus differences were found in GM volume compared to controls. No interaction was found however between group and metacognitive accuracy and no significant relationship was found between metacognitive accuracy and GM volume. In relation to the structure of the metacognitive system, no relationship was found between perceptual metacognitive accuracy and synthetic metacognitive knowledge (MAI and BCIS). No relationship was found between medication and measures of metacognition.

The first finding is novel and confirms the deficits observed in metacognition in other studies. Köther et al., (2012) found a similar effect in overconfidence in relation to incorrect decisions on a social cognition task compared to controls and Warman, Lysaker, & Martin, (2007) found less self-reflectivity and increased certainty in patients versus control participants. Cartwright-Hatton and Wells (1997) found differences in patients compared to controls for a metacognition questionnaire relating to worry and, in another questionnaire design, Bacon, Huet, and Danion, (2011) found patients to have less awareness of their mental state than controls. Importantly, whilst the above measures relate to social cognitive insight, this study experimentally demonstrates metacognitive deficits in FEP in perceptual decision-making.

In relation to the neural underpinnings of metacognition, Fleming et al., (2010) found an association between metacognitive accuracy and the BA10 and precuneus regions. The present study failed to replicate Fleming et al.,'s (2010) findings. The present study included both control and FEP patients whereas the original authors only investigated members of the general population which may account for the failure to replicate the original authors' findings. Furthermore the present study also controlled for age in analysis due to subsequent research implicating this as a factor in metacognitive accuracy which the original did not. This may account for the disparity in results. Other papers have failed to find a relationship between cortical thickness and task performance instead suggesting that task performance and cognitive function is more related to white-matter function (Ziegler et al., 2010). The relationship between function and structure

may be more complicated than merely differences in straightforward GM volume and may be more related to white-matter integrity which Fleming et al., (2010) also found.

The GM volume group differences appear in line with other VBM studies (Watson et al., 2012; Buchy et al., 2015) however in an attenuated form. The present findings generally relate to the right hemisphere rather than bilaterally which may indicate a specific deficit in cortical symmetry as found in Kawasaki et al., (2008). The lower GM volume in the superior medial gyrus in the present study is an interesting finding; Lesion studies have found a deficit in this region compared to controls and a relationship with inhibitory control (Aron, Robbins, & Poldrack, 2004). This may account for the suggestion that people with FEP struggle to inhibit competing cognitive responses and the process of excessive or *hypermentalization* observed in schizophrenia (Schimansky, David, Rössler, & Haker, 2010) which impacts on sense of agency. Other studies have implicated middle occipital regions in attention shifting (Kim et al., 1999) which may be involved in attentional deficits observed in schizophrenia (Shakeel & Docherty, 2012). However further investigation revealed that the deficits were more severe on the left, not right hemisphere.

There could, however, be a number of reasons behind the less pronounced cortical differences found compared to other existing studies: the healthy controls to whom the FEP sample was compared were a better match in terms of education level and demographic information and half the FEP sample were not exposed to antipsychotic medication. Previous studies, such as Smith et al., (2015), have failed to match on education level or studied long-term populations (Douaud et al., 2007). The more severe deficits reported elsewhere could be attributed to these factors rather than FEP status alone. Other studies appear to have recruited those with mean level IQs which are not typical for the cohort and may also be a factor. The causal factor in GM atrophy post illness may have a multifaceted aetiology which includes illness trajectory, symptoms, changes in IQ and access to treatments. Mental health care provision varies country-to-country and, even within Early Intervention in Psychosis services in the UK, there is some heterogeneity in acceptance criteria for caseload. The surrounding location of the present study was a city with two large university campuses so the patient sample may contain a higher than typical concentration of those with higher IQs and different sociodemographic details. The mean level of education in the present sample was higher than other studies (Rosa et al., 2015) which may also explain the attenuated structural deterioration despite every precaution being made to find matched controls. Future studies may wish to control for both years of education and take a measure of IQ.

4.4.1 Limitations

Finally, whilst the present study recruited those from FEP and medication information was taken, inclusion in analysis would have been difficult to do due to the group comparison. Medication dose was investigated in relation to metacognitive accuracy and no significant relationship was noted suggesting that metacognitive dysfunction in FEP is not attributable to medication alone. None of the controls were on medication so an analysis would have been reflective of group membership rather than impact of medication. The present study employed a 1.5T scanner, if the scan had occurred in a more powerful 3T MRI scanner, it may have picked up more subtle group differences and more accurate GM volume readings. Finally power may have been lower than ideal. Fusar-Poli et al., (2014) suggest that detecting group differences increases with sample size in VBM investigations; recruitment of more participants may have revealed more pronounced group differences.

Participants in the study completed the behavioural task after they had been through a long MRI scan. As the study also recruited FEP participants, in order to minimise the potential distress caused the number of trials completed in the perceptual task was reduced from Fleming's original study to 200. This is considered the lower end of the number required to obtain an accurate reading however the present study's mean performance is lower than in other studies employing a similar design. Whilst this could be due to a clinical population, the matched controls were also lower which could be an artefact of the reduced number of trials. This may have impacted on the GM investigation. However as both comparison groups completed the same task, this should not have affected the group comparison analysis in which a significant difference was observed.

The nature of research may also be inhibitory in capturing the true manifestation of psychosis. Recruitment into studies is dependent on social circumstance, living conditions and current level of recovery. Most patients recruited into studies may be at the higher end of the functioning and social spectrum which may impact on getting a true reflection of psychosis. The present study additionally was a cross-sectional design; ideally the pattern of deterioration assessed longitudinally, rather than a one-off cross-sectional scan may be of greater value. Comparing how metacognitive accuracy changes with deterioration in structural volume may offer better insights into the relationship between the two. Whilst the task would need to be validated for practice effects, tracking metacognitive accuracy with structural changes may offer a richer insight into the neural basis of metacognition so future studies may wish to consider a longitudinal design. Incorporating functional outcome measures would also allow for inspection of the relationship between metacognition, GM volume and functioning in the

community. The impact that neural deterioration has on actual real-world outcome, as well as on a cognitive task, would offer valuable information as to the impact of metacognitive and structural profiles in schizophrenia. Metacognition may function for example as a protective factor in maintaining independence in the community and compensating for cognitive deficits and cortical atrophy.

4.4.2 Implications

The metacognitive system may be a cluster of related but distinct individual processing routes; the finding that metacognitive accuracy does not significantly associate with other forms of metacognition can be explained through the Nelson and Narens (1990) model. Metacognition may function on both higher-order and lower-order levels and perceptual metacognitive accuracy is performed at a lower-order section of an overall metacognitive system. Metacognitive dysfunction in FEP may be impacted by deficits in different processing routes and these routes may offer unique contributions accounting for functional disability in both FEP and chronic schizophrenia. The fact that these lower-order metacognitive deficits are present at first episode suggests they may play a causal role in the development of schizophrenia.

4.4.3 Conclusions

In conclusion, the present study offers new insights into the structural differences at early stages of illness and into metacognitive deficits in schizophrenia. The profile of GM volume deficits in FEP appears less linear and more subtle than in other studies and the nature of GM atrophy in psychosis is likely not a definitive trajectory. The metacognitive deficits, which the present study demonstrates are present, were not explained through structural difference as previous work suggests. How these differences interact with community function would be a useful next step as the real-life social cost of psychosis should be of the upmost importance to researchers adopting an anatomical approach.

Chapter 5: General discussion

5.1 Summary of chapters

Reduced social function is a core feature of psychotic disorder and part of the diagnostic criteria for schizophrenia. Social impairment has been observed in prodromal (Cornblatt et al., 2007) and FEP samples (Hodgekins et al., 2015) compared to control participants. The development and trajectory of dysfunction post-treatment can be impacted by a range of factors; investigation in FEP is critical to understanding the underlying factors which lead to longer-term disability (Bratlien et al., 2013) and the causes of schizophrenia (Lin et al., 2013). Previous evidence implicates neurocognitive impairment (Green et al., 2000), negative symptoms (Ventura et al., 2009) and metacognition (Lysaker, Mccormick, et al., 2011) in accounting for this disability. The extent to which metacognition mediates the relationship between neurocognition and functioning, and whether this relationship is present at early stages of illness remains unexplained. In addition, the extent that different measurements of metacognition relate to each other also has not been explored in research. How different aspects of functional capacity and the extent to which the individual actually engages in community activities interact with each other, and with neurocognitive and metacognitive dysfunction has also not been addressed sufficiently. Understanding the predictors of capacity and real-world function is important to recovery in psychosis and ensuring that treatment pathways are targeting 'the right stuff'.

5.1 Integrated overview of chapter findings

Chapter one identified that a relationship between neurocognition and functional outcome has been well documented in experimental research however the extent to which variance in outcome has been accounted for is limited. Metacognition has been suggested as a mediating variable and some work has begun to assess this possibility (e.g. Lysaker et al., 2010). Metacognition as a concept has developed from a host of disciplines with different measurement strategies suggested as capturing the ability and Nelson and Narens (1990) provides a model for how meta and object-related processing avenues interact with each other. The chapter ends with a conceptual model being suggested as to how metacognition may mediate the relationship between neurocognition and different aspects of functional outcome. The different measurements of metacognition may be accounted for in the Nelson and Narens (1990) model and relate to higher and lower-order abilities that may be impacted in those with a diagnosis of schizophrenia.

Chapter two demonstrated through a meta-analytic technique that a relationship exists across studies between neurocognition and metacognition, and also between metacognition and functional outcome. Small to moderate effect sizes were found across different cognitive domains and a moderate effect size was found between cognition and metacognition, and metacognition and functional outcome. The papers reviewed suggested that more work is needed at an earlier point of illness and across multiple measures of both neurocognition and functional outcome. Papers also suggested that how different measurements of metacognition relate to each other also required clarification.

Chapter three addresses these aforementioned points. A factor analysis suggests that from the measures selected, the construct of metacognition is most stably captured by synthetic metacognition and the self-reflectivity component of cognitive insight. Objective function was also significantly associated with functional capacity suggesting some shared skill in both domains. It is possible that the capacity to complete daily tasks is a pre-requisite to actually performing these skills in real-life but not a guarantee that this will happen successfully. The mediation analysis confirmed that metacognition does mediate the relationship between neurocognition and both functional capacity and objective function. This relationship is not attributable to negative symptoms as both of these models withstood the inclusion of negative symptoms as a covariate and the direction of the relationship is maintained by the non-significant reverse models tested. Negative symptoms, in addition to metacognition, were found to also mediate the relationship between neurocognition and functional capacity but not objective function which is an unexpected but interesting finding. This suggests that metacognition offers a unique account separate from negative symptoms for the relationship between neurocognition and objective function. Services should therefore focus on assisting with metacognitive skills rather than symptoms in order to assist return to function in the real-world.

Chapter 3 also found that, when metacognition was included as a mediating variable between functional capacity and objective function, there was no longer a significant direct pathway between capacity and objective function. This is an important finding as this suggests that the relationship between functional capacity and objective function is accounted for through metacognition. In order to assist those with FEP translating functional capacity skills into the real-world, metacognition should be targeted by services. However these suggestions have to be made with the low power of the study in mind; a larger sample may have revealed a relationship with negative symptoms too. The final model is available in figure 33 below.

5.2 Final study model

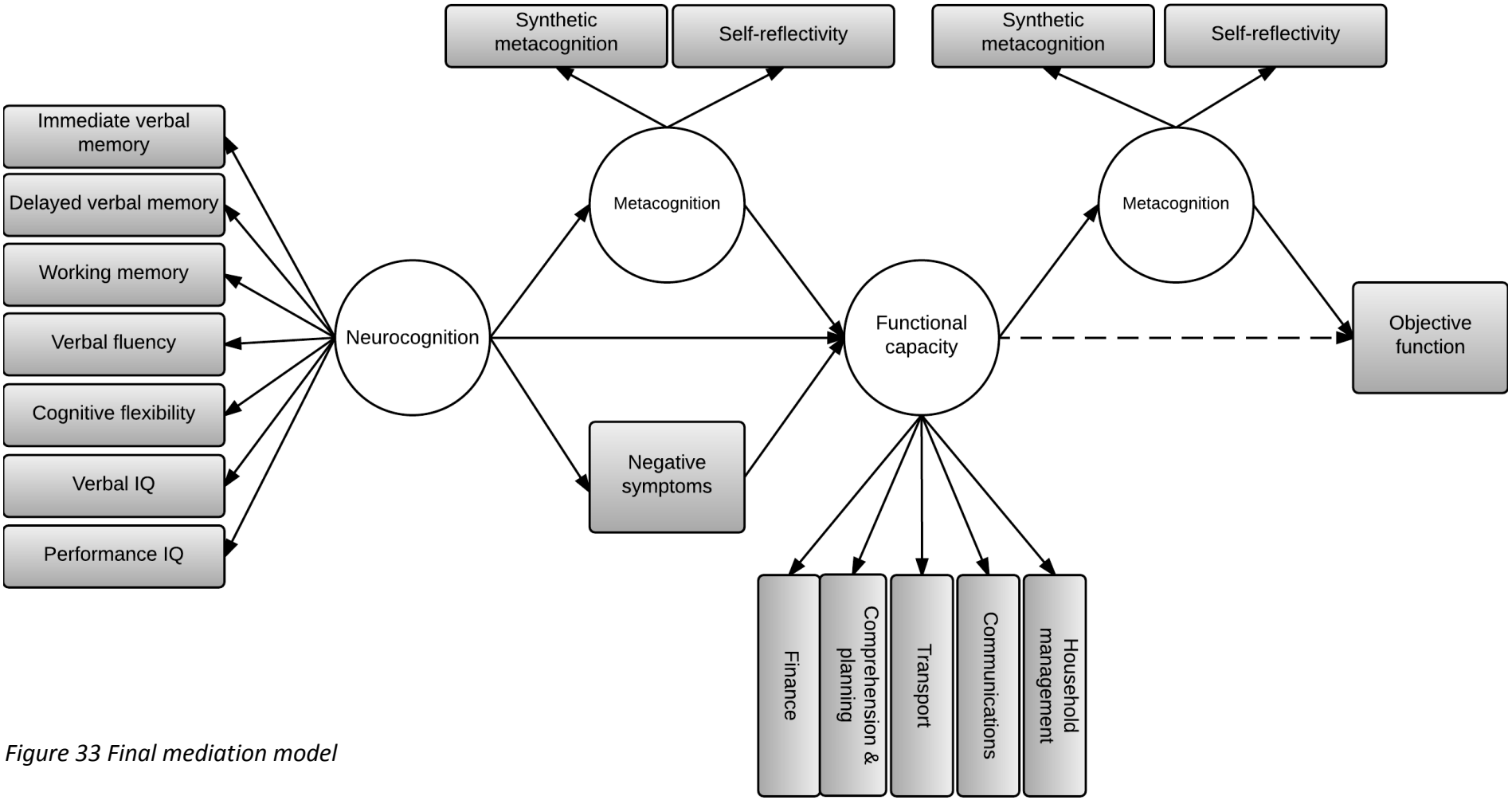

Figure 33 Final mediation model

Chapter three also contains another interesting finding; the mean neurocognitive impairment in the present study was -.86. Meta-analytic investigations of cognitive impairment (e.g. Mesholam-Gately et al., 2009) found mean neurocognitive deficits of -.91 across studies suggesting a similar level of function between the present study and other known assessments. Likewise, the present study found similar amounts of time spent in structured activity to those found in the large EDEN project (24.97 compared to 25.17) (Hodgekins et al., 2015). This suggests that deficits in both domains are pervasive across studies and are defining features of early stage illness.

Chapter four addressed the lower-order aspect of metacognitive experience documented in the Nelson and Narens (1990) model and how metacognitive accuracy relates to GM volume through an MRI investigation. The study demonstrates that FEP performed significantly worse than matched healthy controls on the perceptual metacognitive accuracy task and that the FEP had GM volume deficits in frontal regions associated with higher-order thought. An interaction between metacognitive accuracy and GM volume was not found however suggesting that the relationship between cognitive performance and neural decline is more complicated than GM architecture alone or that similar effects are found in both FEP and controls. Surprisingly, a negative trend level relationship was found between better metacognitive accuracy and lower GM volume. This is difficult to interpret however and may suggest that the relationship between cognitive performance and GM volume is not a straightforward one thus other factors may account for this relationship. Finally, participant scores on a metacognitive accuracy task did not associate with either cognitive insight or synthetic metacognition suggesting that a separate, lower-order processing pathway may exist as part of the same system described in chapter one. These claims have to be made with power in mind again; only 30 of the FEP sample managed to complete all measures, a larger sample may offer a different conclusion. How generalizable metacognitive accuracy is across tasks would also benefit from further investigation; Palmer et al. (2014) found no significant relationship between metacognitive efficiency on a memory and perceptual task. This suggests that how models of lower-order metacognitive accuracy, and upon what information these decisions are made, needs further clarification in research.

5.3 Clinical implications

Functional outcome is a multifaceted concept not easily captured in research. The present study suggests that the ability that an individual has to complete tasks required to function successfully in the community does not have a direct relationship with actually having an active, structured life across domains of occupation and social indices. There exists a related but conceptually distinct pathway to objective function that involves

recovering the cognitive skills that underpin function but also the higher-order knowledge of one's own cognition that allows these skills to be integrated into real-life. Neurocognition was directly predictive of functional capacity but not objective functioning in the pathway models suggesting that having the raw cognitive skills is not enough in itself to maintain real-world function. Rather, metacognitive skills are associated with integrating these cognitive abilities into both the ability to complete daily tasks (model 1) and importantly to transfer these capacity skills into the real-world (model 3).

The present study investigated metacognition in relation to functional outcome in FEP. Whilst the direction of the relationship was considered through reverse model testing, it is possible that functioning may also have a reciprocal impact on metacognition. Frith (2012) discusses the role of metacognition in human social interactions and suggests that the knowledge we possess into our own actions and perceptions is improved through social interactions and discussion with others. Social interactions and functional activity can impart knowledge into our own cognitive processes and therefore build more accurate accounts of the world and ourselves (Frith, 2012). Thus, whilst metacognitive dysfunction may inhibit social and occupational interaction, the lack of interaction may also then feedback into poorer insight into our own cognitive worlds. Greenwood et al., (2005) also report this relationship and suggest that our cognitive and functional skills may be improved by increased functional activity. Thus the more we use these cognitive and functional skills through use in daily life, the better they become. The number of hours spent in structured activity was very low on average for the FEP participants (<25 hours per week) compared to a non-clinical matched sample (63 hours). The lack of exposure to social and occupational interactions may function to exacerbate existing metacognitive deficits in a cyclical fashion.

The role of metacognition in remediation is also highlighted by the present study. Metacognitive awareness and learning encoding skills may assist both recovery and the success of cognitive remediation initiatives. Whilst the efficacy of MCT has received mixed reviews, this may be due to the treatment outcome measures used. The presented work assessed MCT success on symptoms remission scores however the same analysis with measures of function may provide different results. Integrating metacognitive ability into traditional CBT and remediation programs may assist adoption of these skills in the real-world. Other authors have begun to suggest the value of such approaches (e.g. Cella, Reeder, & Wykes, 2015) and the present study offers support to these notions. The current research extends the literature by extending this relationship to FEP. By targeting these skills in FEP skills that promote better functioning can be developed prior

to longer-term disability. The idea of a critical period in which to ameliorate the course of illness in psychosis is not new (Birchwood, Todd & Jackson, 1998). By offering interventions targeting the skills associated with improved psychosocial function, this would address the costs to both the individual and society relating to chronic illness. Improving the skills required to complete everyday tasks (or capacity) may not be enough to ensure actual real-world (objective function) improvements however without addressing metacognition.

Clinically speaking, the present study confirms the lack of a clear relationship between total and positive symptoms, and outcome. Negative symptoms were seen to be important in the relationship between neurocognition and functional capacity but not objective function. More importantly, the overall models were still significant when controlling for symptoms in analysis as predictors of both metacognition and function. This confirms that metacognition offers a unique contribution to functional recovery that cannot be attributed to psychopathology.

5.4 Implications on metacognition

Metacognitive Assessment Interview

The current research offers new information on how different measurements of metacognition relate to each other. Firstly, the original authors of the MAI suggest two separate domains of metacognition (knowledge of one's own mind and the other) and the MAS suggests there to be three (knowledge of own mind, mind of the other and mastery). The present factor analysis however suggests a high correlation between knowledge of one's own mind and the mind of other's. This could be due to a relatively small sample for factor analysis (see section 3.5 for further comment on sample size) or the fragmentation of processes may have not manifest at early stages of illness such as FEP. The early deterioration rather could be a global one in metacognitive capacity however further investigation would be required before this claim could be substantiated. The domain specific deficits reported elsewhere may develop with chronicity.

Relationship between the MAI, cognitive insight and perceptual metacognitive accuracy

The aspects of metacognition captured in the MAI and BCIS have a clear relationship that can be considered through Nelson and Narens (1990) model as high-order, declarable metacognitive knowledge. The moment-to-moment retrospective metacognitive accuracy judgements (meta-*d'*) may relate to metacognitive feelings or intuition and fall under implicit or lower-order judgements of a specific object-level task. Exactly what these trial-by-trial judgements are based on is hard to stipulate. Both forms of metacognition are accounted for in the model however and may rely on separable

processing routes which would explain the lack of relationship found. Whilst both may be important in functioning, they may relate differently to individual domains; metacognitive accuracy may account for error monitoring of object-level processes whereas higher-order knowledge-based awareness may govern overall strategy choice and the complex synthesis of contextual and personal information. The present research suggests that synthetic metacognition and cognitive insight are considered metacognitive knowledge based processes whereas perceptual metacognitive judgements may fit better as metacognitive experiences. Deficits in implicit metacognition may account for other reported deficits in clinical research such as JTC bias. An overconfidence in cognitive products based on inaccurate intuition may have a knock-on effect leading to erroneous conclusions, and causal relationships being assumed with little evidence. This may underpin symptoms such as delusions and paranoia.

Metacognitive knowledge based decisions require deliberate consideration of higher-order thought; presumably, in order to conduct inspection of synthetic metacognition (MAI), one must first possess and be willing to use general self-reflection skills (BCIS). Perceptual metacognitive judgements only require a degree of accurate self-certainty to be aware when one may have been inaccurate rather than the reflective skills to consider specific cognitive products. The self-certainty subscale was not found to adequately load on the metacognitive factor produced in chapter three. This suggests that self-certainty may reflect an entirely different processing route and future studies may wish to investigate this in relation to function in itself.

Whilst perceptual metacognitive judgements were assessed in chapter four, how metacognitive judgements across different cognitive (or object level) tasks relate to each other was not addressed in the present thesis. Palmer, David, and Fleming (2014) found significantly different performance levels between perceptual and memory metacognitive judgements in a general population sample suggesting that metacognitive substrates may exist. A profile similar to cognitive abilities within psychosis may exist where individual's may demonstrate better and worse ability across different domains and this would relate to functioning in different ways.

Finally, the original authors suggest that the MAI detects ability in two domains of metacognitive knowledge; awareness of our own mind and the mind of others (Semerari et a., 2003; Semerari et al., 2012). The present study however failed to find evidence of a separate underlying structure but rather that both substructures were reflective of an overall metacognitive system. If there is a separable mind of other processing system how this relates to social cognition and ToM would also be valuable to establish. Social

cognition and metacognition have been found to load onto separate factors in previous research (Lysaker et al., 2013) however their relationship to each other in FEP needs clarification. The extent to which impairment can be present in one but not the other system would reveal insight into how knowledge of our own minds and others interact. Also, the relationship between how we conceptualise the perspective of other people and awareness of our own mental states may be determinant of our social and occupational functioning. If research could delineate the relationship between each metacognitive ability and remediation programmes focus on specific deficits, this may optimise returning to functioning after illness.

5.5 Research implications

Understanding the different components of metacognition and how they relate is important for real-world functioning. MCT teaches metacognitive awareness of cognitive biases (Aghotor, Pfueller, Moritz, Weisbrod, & Roesch-Ely, 2010) and assists the identification of errant cognition through higher-order awareness. Whilst a recent review found mixed findings for the success of MCT (van Oosterhout et al., 2015), the main index of efficacy was positive and general symptoms reduction rather than functional recovery. The present study suggests that metacognition is a larger determinant of community function than symptoms and may assist with this domain rather than symptom reduction alone. By improving metacognitive knowledge, a knock on effect may occur with lower-order metacognitive accuracy and assist outcome in multiple ways. More caution may be applied to intuitive judgements and more conservative strategies employed to confidence-based judgements leading to error reduction in decision making. Whilst previous reviews find mixed evidence for MCT efficacy, a re-evaluation looking at impact on functional skills rather than psychopathology may offer different and important conclusions.

Chapter four failed to find a relationship between GM volume and metacognitive accuracy or an interaction effect between GM volume and metacognitive accuracy between groups. This is particularly surprising in light of Fleming et al., (2010) suggesting that reduced volume in the BA10 was associated with worse metacognitive accuracy. Subsequent studies have demonstrated an effect of age on metacognitive accuracy (Palmer, Dawes, & Heaton, 2009) which was controlled for in the present study but not Fleming's. This may account for the disparity in results. GM deterioration has been associated with chronicity of illness and worse psychopathology (Rosa et al., 2015) however the present study suggests that the relationship is less clear cut than previously thought. The interaction between IQ, GM volume and function may be of more importance than just GM volume alone. The results have to be considered with the

imbalance of FEP (N=32) versus control (N=19) participants and a more balanced design would have had greater power and sensitivity to detect effects. Also, as subjects were matched on years of education rather than raw IQ, this may have addressed sociodemographic disparities between patient and control participants. Those at university are found to have come from higher sociodemographic backgrounds (James, 2007) so by matching control and FEP participants on years of education this may have addressed sociodemographic status as well. This may underpin the more widespread differences found in previous structural investigations due to the groups being more discrepant on IQ and education.

Future studies may also wish to investigate the relationship between neural structure and functional outcome. Guo et al., (2015) report that less progressive brain volume loss in chronic schizophrenia is associated with preserved social and occupational functioning however a causal relationship is difficult to establish due to medication exposure and time spent in hospital. Likewise, Allen et al., (2015) investigated the neurobiological underpinning of functional outcome in a UHR population and found that 'good' or 'poor' functioning at 18 month follow-up was predicted by cortical and subcortical function and lower prefrontal-striatal activation. By investigating the neurobiological underpinnings of functioning at first point of illness a greater understanding could be gained into the onset of cortical deterioration in schizophrenia and its relationship to social disability. Whether functional disability is a result of cortical decline or whether a symbiotic relationship exists is not known and would be of value to know.

5.6 Limitations of empirical chapters

Sample size

One drawback of the analysis in chapter three was the number of participants entered into the factor analysis and pathway models. The factor analysis had to be broken into separate analyses between metacognition and neurocognition; demonstrating the distinction of individual scales to cognitive and metacognitive components by entering them simultaneously into a factor analytic technique would reveal more about how they relate to each other. An analysis with a higher number of participants may offer more information on the clarity with which component items comprise metacognition and neurocognition. The pathway models also had to be broken down into smaller components to allow the detection of meaningful effects whilst maintaining a sufficient case-to parameter ratio (Bentler & Chou, 1987). Increased power would have allowed the model to have run as a measurement model allowing more sophisticated effect detection (Fritz & MacKinnon, 2007). A larger sample would also have allowed items

rather than subscales to have been entered into both cognitive and functional capacity factor analyses offering more subtlety of investigation.

Omitted variables

Due to the relatively small sample size, sociodemographic information could not also be entered into the models in addition to metacognition and psychopathology. Some authors suggest that sociodemographic factors are predictive of social opportunity, recovery post-illness (O'Connor et al., 2013) and defeatist beliefs (Grant & Beck, 2009) however decisions had to be made to focus on negative symptoms and metacognition as the most important predictors of functioning based on available evidence.

Measuring functional outcome

The current research, based on known evidence identified in chapter one, decided to measure both functional capacity and objective functioning due to their validity and reliability statistics (Cardenas et al., 2012; Hodgekins et al., 2015) and ability to be compared with other both clinical and non-clinical samples. However the subjective sense of recovery and functioning was not assessed due to reliability studies (McKibbin, Brekke, Sires, Jeste, & Patterson, 2004) suggesting concerns over the comparability of self-report and subjective sense of recovery indices. The recovery models of psychosis suggest this as a primary target of mental health services and the relationship between metacognition and a subjective sense of inclusion in society and recovery would have been interesting to ascertain. Whether better metacognition allows for more accurate self-assessments of recovery may be important to know. Future studies may want to investigate this measure of functioning in relation to other measures of functional outcome as well in FEP.

The Time Use Survey relies on self-report data which, as discussed in chapter one (section 1.7), can be problematic (Bowie et al., 2007). Whilst the questions asked remain concrete (i.e. how many hours spent in employment/education/social situations) they assume a level of accuracy in recall. Sabbag et al., (2012) suggest that accurate self-reporting of function is associated with improved neurocognitive ability thus there is a possibility that the increased objective function is due to more accurate reporting. However the evidence suggests that poor neurocognitive function is associated with *overestimation* rather than *underestimation* of functioning so this possibility is unlikely to be responsible for the effects demonstrated. Also, functional capacity is not influenced by self-report bias (Sabbag et al., 2012) so the mediation effect of metacognition between neurocognition and functional capacity would not be victim to such confounding variables.

Design

The present research was cross-sectional in nature which restricts the conclusions which can be drawn in terms of causal direction. Whilst reverse model testing allows a greater degree of inference about the direction of effects, how neurocognitive impairment predicts function through metacognition over time would be more valuable to know. By looking at changes across time points latent growth curve modelling could be applied to look at the interaction of variables across recovery. Capturing outcomes of psychosis would be best served by up to 10 year follow-ups which has been investigated through cognitive trajectories (Hoff et al., 2005). The true impact of metacognition after initial symptoms have subsided would allow interventions to target the most important deficits that relate to disability. However, higher-order metacognitive knowledge seems likely to constitute one such target.

Some evidence suggests that DUP has an impact on social disability (Bratlien et al., 2013). Whilst the current study attempted to recruit participants at first point of contact with clinical services, DUP information was not included in analysis. Studies suggest a present but weak effect of DUP on neurocognitive and functional outcome (Faber et al., 2011) and some participants would have had greater access to therapy due to differing gaps between entry into care teams and recruitment to the study which may underpin findings. Ideally all participants would be recruited at first point and DUP information would be taken for inclusion in analysis however this is victim to capacity to take part in research. Many of those first into services are too unwell to participate in research studies so this particular issue is difficult to address.

5.7 Conclusions

The main implications of this thesis are that metacognitive processes may be part of an overall system but are distinct from each other. They can be accounted for through Nelson and Narens (1990) higher–order metacognitive knowledge and lower-order metacognitive experience pathways and the present study suggests they may relate to functioning independently from each other. This thesis also extends the previous understanding of the role of metacognition in bridging the gap between neurocognition and functional outcome and demonstrates this at early stages of illness. In addition, negative symptoms may impact on functional capacity uniquely.

The relationship between metacognition and functional outcome is an important one as Early Intervention in Psychosis services place community recovery as a primary objective of their care pathway. By understanding more of the mechanisms that underpin social disability, teams can offer treatment initiatives that target important determinants

of longer-term functioning. Metacognitive skills can be integrated into traditional cognitive remediation and vocational rehab programs in a ‘two-pronged’ approach to equipping those experiencing their first episode of psychosis with the skills required to function in the real-world. Social disability and neurocognitive impairment are unfortunately core features of psychosis and schizophrenia as demonstrated in chapter three however by understanding the relationship between them, clinicians on the frontline can target the right skills. More refinement of this relationship is required across longitudinal designs before this can be brought to the policy makers of contemporary mental health services.

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Appendices A: NHS Research and Ethics Committee (REC) approval letter

NHS
Health Research Authority

NRES Committee London - Camden & Islington
North East REC Office
Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
Tyne & Wear
NE32 3DT

Tel: 0191 428 3566
Fax: 0191 428 3432

25 July 2013

Dr Richard Whale
Consultant Psychiatrist / Senior Lecturer
Sussex Partnership Foundation NHS Trust / Brighton and Sussex Medical School
The White House
54 New Church Road
Hove
BN3 4FL

Dear Dr Whale

Study title: **Sussex First Episode Psychosis Outcome Study**
REC reference: **11/LO/1877**
Amendment number: **2**
Amendment date: **12 July 2013**
IRAS project ID: **72141**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Summary of changes to protocol and REC form		01 July 2013
Participant Consent Form	2	01 July 2013
Participant Information Sheet	3	01 July 2013
Protocol		
Notice of Substantial Amendment (non-CTIMPs)	2	12 July 2013

UCSD Performance-Based Skills Assessment (UPSA-2)		
Metacognitive Interview Scale (MAI)		
Weschler Scales		
Cohort Data Pack		
Covering Letter		12 July 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

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

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

11/LO/1877:	**Please quote this number on all correspondence**

Yours sincerely

J Brown

***pp* Mrs Rosie Glazebrook**
Chair

E-mail: nrescommittee.london-camdenandislington@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Tanya Telling, Sussex Partnership NHS Foundation Trust*

NRES Committee London - Camden & Islington

Attendance at Sub-Committee of the REC meeting on 25 July 2013

Name	*Profession*	*Capacity*
Dr Sati Ariyanayagam	Consultant Physician	Expert
Mrs Rosie Glazebrook (Chair)	Consumer Marketing	Lay

Appendix B: Sussex Partnership Trust (SPT) governance approval letter

Sussex Partnership NHS
NHS Foundation Trust

26th July 2013

Research and Development
Sussex Education Centre
Mill View Hospital
Nevill Avenue
Hove BN3 7HZ

Tel: 01273 265928
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www.sussexpartnership.nhs.uk

Dr Richard Whale
Sussex Partnership NHS Foundation Trust
The White House
54 New Church Road
Hove
BN3 4FLPI

Study title: Sussex First Episode Psychosis Outcome Study

R&D Ref: 5005-2012
REC reference: 11/LO/1877
Amendment number: 2
Amendment date: 12 July 2013

Further to the initial study approval letter on 01/06/2012, a substantial amendment (2) has been received for research governance review and approval.

I am pleased to inform you that the substantial amendment has been approved, and so may proceed.

The final list of substantial amendment documents reviewed and approved is as follows:

Document	Version	Date
Participant Consent Form	2	1 July 2013
Participant Information Sheet	3	1 July 2013
Protocol		
UCSD Performance Based Skills Assessment (UPSA-2)		
Metacognitive Interview Scale (MAI)		
Weschler Scales		
Cohort Data Pack		
Summary of Changes to Protocol and REC form		1 July 2013

Conditions of approval

The approval covers the period stated in the Research Ethics Committee (REC) application and will be extended in line with any amendments agreed by the REC. Research must commence within 12 months of the issue date of this letter. Any delay beyond this may require a new review of the project resources.

Please alert the Research and Development Office if significant developments occur as the study progresses, whether in relation to the safety of individuals or to scientific direction.

Please ensure that you comply fully with the Department of Health Research Governance Framework, in particular that you are aware of and fully discharge your

Sussex Partnership NHS
NHS Foundation Trust

responsibilities in respect to Data Protection, Health and Safety, financial probity, ethics and scientific quality. You should refer in particular to Sections 3.5 and 3.6 of the Research Governance Framework.

Please ensure that all information regarding patients or staff remains secure and strictly confidential at all times. Ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice, Data Protection Act and Human Rights Act. Unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

Amendments

Project amendment details dated after the issue of this approval letter should be emailed to the Research and Development Office for formal approval.

NIHR Adoption

This project has been adopted by the NIHR and as Principal Investigator for this site you are responsible for ensuring accrual numbers are submitted to the co-ordinating centre for study. If you need any support to manage this please contact me.

ICH-GCP Monitoring

The Trust has a duty to ensure that all research is conducted in accordance with the Research Governance Framework and to ICH-GCP standards. In order to ensure compliance the Trust undertakes random audits. If your project is selected you will be given 4 weeks notice to prepare all documentation for inspection. The trust undertakes annual monitoring of all research studies, please respond to any requests for information. Failure to do this will result in the suspension of research governance approval.

I wish you luck with your project and would be grateful if you could inform me when the project is complete or due to be closed on this site.

Yours sincerely,

Tanya Telling
Research and Development Manager

Appendix C: Beck Cognitive Insight Scale

	Do not agree at all	*Agree slightly*	*Agree a lot*	*Agree completely*
At times, I have misunderstood other people's attitudes towards me.				
My interpretations of my experiences are definitely right.				
Other people can understand the cause of my unusual experiences better than I can				
I have jumped to conclusions too fast				
Some of my experiences that have seemed very real may have been due to my imagination				
Some of the ideas I was certain were true turned out to be false				
If something feels right, it means that it is right				
Even though I feel strongly that I am right, I could be wrong				
I know better than anyone else what my problems are.				
When people disagree with me, they are generally wrong				
I cannot trust other people's opinion about my experiences				
If somebody points out that my beliefs are wrong, I am willing to consider it				
I can trust my own judgement at all times				
There is often more than one explanation for why people act the way they do				
My unusual experiences may be due to my being upset or stressed				

Appendix D: Metacognition Assessment Interview

INSTRUCTIONS:

"Dear Mr. / Madam, I am Geoff ...., I thank you for agreeing to do this interview created with the aim of a better understanding of the way people think.

The purpose of this interview is not to give any diagnosis, nor to perform a therapeutic intervention, but to look at your "way of being" in the relationships with others. We think that this psychological element is very important to better understand the relevant clinical questions.

You will be asked a series of questions about a recent episode in your relational life that was important to you. We apologize if, in some occasions, the questions may seem repetitive or obvious. These repetitions are useful for evaluating your way of relating to others. We consider important that you keep in mind that in this test there are no right or wrong answers, and there are not any better or worse performances from your part.

QUESTION:

"Can you tell me, what - from a psychological point of view -was the worst event or interpersonal situation, that you had to face in the last 6 months?" Possibly a relationship episode, that means an episode that involved another person and it was meaningful to you on a psychological level.

1) Regarding the episode just described, how were you feeling?
2) What emotions did you experience?
3) What was the origin of these emotions?
4) What were your thoughts?
5) What was the cause of these thoughts?
6) What did you do? What behavioural choice did you make?
7) What motivated you to behave in a certain way?
8) So, trying to sum up the episode that just told me, you felt this ... thought this... and reacted by... What was your aim at that time?
9) What did you want most? What made you feel afraid in that situation?
10) So, you told me you were feeling (refers back to described emotions). When did your state of mood change?
11) How did it change?
12) What, in your opinion, caused it to change?
13) You told me you were thinking .. (the interviewer refers to the episode recounted). How deeply did you believe, in that moment, that .. (reported thinking)?
14) On a scale of one to ten how much did you believe this to be true?
15) Do you think it was possible to have a different interpretation of the facts?

16a) If yes: which kind of interpretation?
17a) If yes: What has changed?
18a) If yes: What encouraged this change?
19) Looking back now, is there something that has changed your point of view compared to 6 months ago?
16b) If no: Do you think that, in future, that your point of view on what has happened may change?

17b) If not: What could help you to revise your point of view on what has happened?

20) During the episode described, did you feel like you were in a state of confusion as if in a dream or had a sense of not being in reality like the event was only imagined?
21) Have you ever had an experience that felt a sense of confusion, like being in a dream or fog like state?
21a) If yes: Did it happen to enable you to immerse yourself in a fantasy such as to lose all sense of time and the relationship with the real world?
21b) If yes: Have you ever experienced very vivid memories or images that felt as if they were really happening at that time? Can you give me some examples?
21c) If yes: are you feeling the same confusion now?
22) So, did you ever have such reactions (points out the described behaviour), to experience this kind of emotions…….or……? Do you often feel/think/experience/behave in these ways?
23a) If yes:How do you explain your typical reaction?
24a) Have you ever experienced a different reaction, (different emotions and thoughts) facing similar events? Can you remember and try to describe some episodes?
25a) So, sometimes you react ____ (first example interviewer here summarizes the typical state of the subject, using terminology more close as possible to that of the interviewee), while other times your reaction is____ (episode two_ the interviewer summarizes here the new story obtained through questioning). What according to you dictates which reaction occurs?
26a) Why, in your opinion, did you react in the first way?
Why, in your opinion, did you react in the second way?
23b) If not, can you remember your typical reaction facing difficult situations?
24b) If yes, How did you react in that moment? Which were your emotions in that circumstances? What about your thoughts?
23c) If not, repeat questions
27) You told me that ….(name the protagonist of the story) had a significant role in this story. I would like you to take his/her point of view. In your opinion, how did the other person emotionally perceive the situation?
28) What emotions did he/she feel?
29) Why did he/she feel this kind of emotion? What did you conclude from this?
30) What could he/she have thought?
31) Why did he/she think this way? What reasons did he/she have?
32) In your experience, is it typical of____ (character name) to think and feel this way?
32a) If yes, why is this their typical way to react?
33a) Can you make another brief example of when you tried/felt, heard and acted the same way?
32b) If not, why was it different?