The impact of Metacognitive Training for Psychosis on neurocognition

Clayton Jeffrey
Department of Psychiatry
McGill University, Montreal, Canada
August 2024

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Master's in Science, Mental Health Thesis.

Table of Contents

ABSTRACT

Through performing a methodologically rigorous systematic review and meta-analysis, this thesis aims to clarify the impact of metacognitive training for psychosis (MCT) on neurocognition. Previous research has elucidated that MCT offers benefits for addressing a range of hallmark deficits and symptoms in psychosis, including reductions in cognitive biases and positive symptoms such as delusions, as well as improvements in social cognition, and an overall increase in functioning. Mixed results have been yielded pertaining to the relationship between MCT and neurocognition, where some randomized controlled trials (RCTs) have suggested it may enhance neurocognitive performance, and others have found no relationship whatsoever. A comprehensive understanding of the nature of this relationship would significantly contribute to the existing literature and provide valuable insights to clinicians regarding the potential added value of MCT as a cognitive intervention for psychosis. Therefore, this thesis aims to determine the efficacy of MCT in improving neurocognitive performance in psychosis by conducting a systematic review and meta-analysis. Across eleven electronic databases, 1312 sources were identified, and 14 studies that evaluated effects of MCT on neurocognitive outcomes for individuals with a psychotic disorder were included in this review. Measures of estimated effect sizes were calculated with Hedge's *g*, moderator analyses used Cochrane's *Q* statistic and significance tests to measure group differences according to control conditions including passive and active control interventions. Twelve studies, 11 RCTs and 1 non-RCT, were included in the main meta-analyses, consisting of 673 participants (n_{MCT}=345, $n_{control}$=328). When comparing MCT against control interventions, non-significant differences in estimated effect sizes were observed across all six neurocognitive domains considered (speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning

and memory, reasoning and problem-solving) when evaluating pre–post changes in neurocognition ($g \leq 0.1$, $p > 0.05$). Likewise, moderator analyses revealed that no significant differences were observed between passive or active control conditions for any of the timepoint comparisons (all *ps* > 0.05). Two additional studies were included in a narrative review, corroborating these results. By systematically comparing against control conditions, these findings suggest that MCT does not significantly improve cognitive performance over and beyond the comparator interventions examined across the six neurocognitive domains assessed. These results indicate that general practice/learning effects are likely the main contributor of improvement in neurocognitive performance, and not a difference of intervention allocation when considering MCT against the included control comparators. These findings help establish our understanding of the specificity of the effects of MCT.

RÉSUMÉ

Cette thèse vise à clarifier l'impact de l'entraînement métacognitif pour la psychose (MCT) sur la neurocognition en réalisant une revue systématique et une méta-analyse rigoureuses sur le plan méthodologique. Des recherches antérieures ont révélé que la MCT offre des avantages pour traiter toute une série de déficits caractéristiques et de symptômes dans la psychose, notamment des réductions des biais cognitifs et des symptômes positifs tels que les délires, ainsi que des améliorations de la cognition sociale et une augmentation globale du fonctionnement. Des résultats mitigés ont été obtenus concernant la relation entre la MCT et la neurocognition, où certains essais contrôlés randomisés (ECR) ont suggéré qu'elle pourrait améliorer les performances neurocognitives, tandis que d'autres n'ont trouvé aucune relation du tout. Une compréhension approfondie de la nature de cette relation contribuerait significativement à la littérature existante et fournirait des informations précieuses aux cliniciens concernant la valeur ajoutée potentielle de la MCT en tant qu'intervention cognitive pour la psychose. Par conséquent, cette thèse vise à déterminer l'efficacité de la MCT dans l'amélioration des performances neurocognitives dans la psychose en réalisant une revue systématique et une méta-analyse. À l'aide de onze bases de données électroniques, 1312 sources ont été identifiées, et 14 études qui ont évalué les effets de la MCT sur les résultats neurocognitifs des personnes souffrant de troubles psychotiques ont été incluses dans cette revue. Les mesures des tailles d'effet estimées ont été calculées avec le *g* de Hedge, des analyses de modération ont utilisé le test *Q* de Cochrane et des tests de signification pour mesurer les différences de groupe selon les conditions de contrôle, y compris les interventions de contrôle passives et actives. Douze études, 11 ECRs et 1 non-ECR, ont été incluses dans les méta-analyses principales, comprenant 673 participants (n_{MCT}=345, $n_{contrôle}$=328). Lors de la comparaison de la MCT avec les interventions de contrôle,

aucune différence significative dans les tailles d'effet estimées n'a été observée dans les six domaines neurocognitifs considérés (vitesse de traitement, attention/vigilance, mémoire de travail, apprentissage et mémoire verbale, apprentissage et mémoire visuels, raisonnement et résolution de problèmes) lors de l'évaluation des changements pré-post en neurocognition ($g \leq 0.1$, $p > 0.05$). De même, les analyses de modération ont démontré qu'aucune différence significative n'a été observée entre les conditions de contrôle passives ou actives pour aucune des comparaisons de moment dans le temps ($p > 0.05$). Deux études supplémentaires ont été incluses dans une revue narrative, corroborant ces résultats. Ces résultats suggèrent que la MCT ne présente pas de différence statistiquement significative par rapport aux interventions de contrôle dans les six domaines neurocognitifs évalués. Ces résultats indiquent que les effets généraux de la pratique/apprentissage sont probablement le principal facteur contribuant à l'amélioration des performances neurocognitives, et non une différence d'allocation d'intervention lorsqu'on considère la MCT par rapport aux comparateurs de contrôle inclus. Ces résultats contribuent à établir la spécificité des effets de la MCT.

ACKNOWLEDGEMENTS

This thesis would not have been possible without the web of support that I have been overwhelmingly fortunate to fall into, including that of my family, supervisor, laboratory colleagues and funders. An especially deserved acknowledgment goes out to my wife Kiersten for her never-ceasing support of my goals and for helping me shoulder the snowballing weight of graduate school.

Dr. Martin Lepage's Comprehensive Research Into Schizophrenia and other Psychopathologies (CRISP) laboratory has been instrumental in my development as a researcher; the support I received from students and staff have been paramount to my ability to conduct these contributions to the field of cognitive interventional research in psychosis.

I would like to take this opportunity to acknowledge and thank the Canadian Institute for Health Research whose funding of my graduate work has enabled this research to come to fruition.

An additional note of thanks is extended to my thesis advisory committee, which has played a crucial role in guiding the methodology and analytical framework of my research. Thank you to Drs. Manuela Ferrari, Geneviève Sauvé and Martin Lepage, for your support and feedback throughout this process.

CONTRIBUTION OF THE AUTHORS

Clayton Jeffrey is the primary author of this thesis and the included manuscript. He led the conceptualization and goals of the project, performed the search update, completed the data extraction and synthesis, ran the analyses, interpreted the results and formulated the discussion of the findings. The writing of this thesis is his own.

Dr Lepage had full access to the data in the systematic review and meta-analysis and takes responsibility for its integrity and the accuracy of the analysis. All authors contributed to the concept and design of this study. The acquisition, analysis, and interpretation of data was led by Jeffrey, followed by Penney, Sauvé, Mendelson, Thibaudeau and Lepage. Drafting of the manuscript was completed by Jeffrey. The critical revision of the included manuscript for important intellectual content included authors Penney, Sauvé, Mendelson, Thibaudeau, Moritz, Hotte-Meunier and Lepage. The statistical analyses were conducted by Jeffrey and supervised by Sauvé. Funding for this work was obtained by Lepage and Jeffrey. Administrative, technical, and material support was provided by Jeffrey, Penney, Moritz and Hotte-Meunier. Supervision for this work was provided by Lepage, Penney and Sauvé.

LIST OF ABBREVIATIONS

CBT: Cognitive Behavioural Therapy

CIHR: Canadian Institutes of Health Research

CR: Cognitive Remediation

CRISP: Comprehensive Research Into Schizophrenia and other Psychopathologies

CTL: Control

FRQS: Fonds de recherche Québec

HBHL: Healthy Brains, Healthy Lives

ITT: Intent to treat

MATRICS: Measurement and Treatment Research to Improve Cognition in Schizophrenia

MCT: Metacognitive Training for Psychosis

MMAT: Mixed Methods Appraisal Tool

OT: Occupational therapy

PP: Per-protocol

RCT: Randomized controlled trial

TAU: Treatment as usual

LIST OF FIGURES AND TABLES

CHAPTER 1: Introduction & Literature Review

Background

Schizophrenia and other psychotic disorders directly affect approximately 4% of the Canadian population (Lecomte et al., 2022). The psychosis spectrum is characterized by a slew of psychosocial difficulties including impairments of mental functions, activity limitations and participation restrictions (Świtaj et al., 2012). This illness typically manifests in adolescence and/or early adulthood, which is a critical developmental window for young people that can dictate functional trajectories across the lifespan of those directly or indirectly impacted. As such, psychosis is considered to be one of the leading causes of disease-related disability globally (Tandon et al., 2008) and is consistently demonstrated to have a detrimental impact on quality of life (Attepe Özden et al., 2023). Across psychotic disorders, typical dimensional presentations of the illness include a range of positive symptoms (e.g., hallucinations and delusions), negative symptoms (e.g., flattened affect, avolition) as well as cognitive symptoms (Kahn et al., 2015).

Individuals with schizophrenia and related psychotic disorders characteristically experience deficits in neurocognitive performance, which are typically two standard deviations below the mean performance of healthy controls (Keefe et al., 2011a). Gaining consensus as a core feature of the disorder, neurocognitive deficits have been designated as vulnerability indicators, as enduring abnormalities in clinical remission, and as critical rate-limiting factors of functional recovery (Nuechterlein et al., 2012). They have been tied to key clinical outcomes such as ability to maintain independent living arrangements and employment (Kharawala et al., 2023; Green, 1996). In contrast, higher performance on neurocognitive assessments has been linked with increased self-reported quality of life (Addington & Addington, 2000) as well as

improvement in social and occupational functioning outcomes (Jaeger et al., 2003; Stirling et al., 2003). In sum, these neurocognitive deficits considerably account for impaired functioning associated with psychosis (McCutcheon et al., 2023). Although the association between neurocognition and functional outcome is evident in psychosis, the relationship is not direct; this has introduced a consideration of mediating variables such as metacognition to clarify the full picture of the link between neurocognitive performance and functioning (Schmidt et al., 2011).

Cognitive health is frequently diminished in psychosis and has become an increasingly prominent area of concern in the treatment of individuals with a psychotic disorder (Saperstein et al. 2021). Broadly, two main categories capture a breadth of deficits in cognitive health in psychosis: cognitive distortions and cognitive impairments. Cognitive interventions for psychosis tend to focus their efforts on either reframing cognitive distortions, remediating cognitive impairments, or both of these areas when addressing cognitive health. MCT is well-established in its ability to benefit various aspects of symptomatology under the former category of cognitive distortions, including cognitive biases and delusions (Penney et al., 2022). However, MCT's efficacy on addressing cognitive impairments are less well understood.

Structure of MCT

Developed in 2007 by Moritz and Woodward, MCT is a free and open-source cognitive intervention that focuses on bringing cognitive biases and thought distortions to the awareness of patients. By targeting cognitive errors and maladaptive thinking styles that are typical of psychosis, it aims to challenge the cognitive infrastructure of delusional ideation. This modularized intervention emphasizes metacognitive exercises, encouraging patients to think about their own thinking and consider alternative problem-solving strategies to arrive at more adaptive inferences. Thus, the intervention employs a 'back-door approach,' focusing on

improving thought distortions and reducing cognitive biases to treat psychotic symptoms such as delusions. MCT is offered in a variety of adaptations, including group or individualized therapy, as well as remote or in-person delivery. Unlike other psychological therapies that require extensive training and resources to facilitate treatment, MCT is a low-threshold program that is highly accessible to both patients and trainees with accommodating delivery platforms and feasible training certifications (Moritz et al., 2014).

Typical variations of MCT range from a minimum of 8 to a maximum of 16 modules; across all adaptations the intervention covers 8 core modules. These highlight key concepts of cognitive errors/biases such as attribution: blaming and taking credit (to reframe one-sided and distorted attributions), jumping to conclusions (to reassess the validity of immediate inferences), changing beliefs (to address a lack of cognitive flexibility), empathy (to focus on impairments in social cognition), memory (to confront overconfidence in one's judgements), and mood (to bring self-awareness of one's tendency to depressive patterns of thought). Additional modules include an extended focus on affective problems in areas such as self-esteem and dealing with prejudices/stigma.

MCT bears similarities to popular cognitive interventions to psychosis such as cognitive behavioural therapy (CBT) and cognitive remediation (CR), but uniquely raises an awareness of cognitive distortions that are typical of psychotic experiences in a modularized format. MCT does not directly and actively target neurocognition, as an intervention like CR would, but by reducing cognitive biases that can potentially obstruct neurocognitive performance, it is hypothesized that MCT may indirectly lead to benefits in neurocognition.

Cognitive distortions: cognitive bias

Cognitive distortions encompass problematic reasoning patterns or thinking errors and can be described as cognitive biases. These are prevalent in non-clinical, and clinical populations, however in disorders like psychosis, such thinking patterns are often maladaptive and may undergird symptomatology. In the psychosis literature, common cognitive biases include but are not limited to jumping to conclusions bias (Dudley et al., 2015), bias against disconfirmatory evidence (Moritz et al., 2010), overconfidence in errors bias (Ryan P. Balzan, 2016), and attributional biases (Savulich, Shergill, & Yiend, 2012; Woodward & Menon, 2013). Such cognitive biases are strongly associated with delusional content and have been theorized to be the building blocks for delusion formation and maintenance in psychosis (Broyd et al., 2017).

Historically, antipsychotic medications have been, and in many cases continue to be, the primary treatment focus for reducing delusional beliefs. However, discontinuation rates of such pharmacological therapies tend to be high in psychosis, with a number of negative subjective responses to medication (Byerly, Nakonezny, & Lescouflair, 2007). From a cognitive perspective, antipsychotic agents are suggested to promote reasoning biases (Andreou et al., 2013) increase doubt, emotional/cognitive numbing and social withdrawal (Moritz et al., 2013) as well as lead to emotional detachment (Mizrahi et al., 2006). In addition to these well-documented aversive experiences, there is growing evidence that suggests potential neurodegenerative effects of some antipsychotic medication (Ho et al., 2011; Moncrieff, 2011). Furthermore, health complications such as increased risk of sudden cardiac death and excessive weight gain have been associated with antipsychotic medication (Alvarez -Jiménez et al., 2008; Ray et al., 2009). Recent meta-analytic research on the claimed improvements of antipsychotic medication has called its benefits into question, given the limited clinical relevance observed of

such pharmacological approaches (Lepping et al., 2011). Reduced confidence in the partial efficacy of antipsychotic medication weighed against its potentially aversive effects in combination with the advances of our understanding of underlying psychological processes of psychosis has led to the consideration of a new landscape of complementary psychotherapeutic interventions to address symptoms such as delusions.

Psychological interventions that effectively address cognitive biases often adopt a metacognitive approach. Metacognition refers to the act of thinking about thinking to better understand an individual's cognitive processes (Flavell, 1979). Metacognitive activities range from lower level processes like the ability to interpret facial expressions and recognize information that has been presented, to higher level processes such as the ability to make integrated representations of oneself and others as well as an understanding of their interactions in the social world (McGuire et al., 2024). Overall, metacognition enables individuals to create/revise their experiences and beliefs in a variety of contexts (Lysaker et al., 2010). In psychosis, there is a consistently reported degree of impairment of metacognitive abilities, including difficulties determining the source of internal experiences, having a sense of agency in the world, and theory of mind deficits when considering the intentions and emotions of others (Brüne, 2005; Lafargue & Franck, 2009). Psychological interventions like MCT that focus on restoring/improving metacognitive processes have demonstrated a strong history of efficacy in alleviating cognitive biases, increasing insight and benefiting positive symptoms in psychosis (Sauvé et al., 2022; Moritz et al., 2014; Penney et al., 2022).

Cognitive impairments: neurocognition

Cognitive impairments consist of a characteristic pattern of cognitive deficits that are relatively stable over time and independent of an individual's symptomatic presentation (Gold,

2004). Broad cognitive deficits have consistently been observed in schizophrenia and have long been characteristic of the illness (Heinrichs & Zakzanis, 1998). These deficits directly and indirectly have an impact on interpersonal behaviour, occupational and household functioning (Wykes et al., 2007; Fiszdon et al. 2008). Recognizing the robust relationship between cognitive impairment and disability, as well as poor functional outcomes associated with the illness, there has been a turning point in psychosis treatment in the last twenty years, drawing attention to cognitive impairment as a clinical outcome (Green et al., 2004). This changing landscape of psychosis treatment led to the formation and establishment of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus, which identifies the neurocognitive domains most prevalent and amenable in psychosis (Nuechterlein et al., 2008). These domains, serving as a guide to the neurocognitive focus of the current study, include speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving, and social cognition.

A great deal of interventional efforts, including pharmacological and non-pharmacological, have been made to restore and improve cognitive capacities associated with psychosis. Non-pharmacological interventions such as CR directly target neurocognitive performance through training, including task practice and the acquisition of cognitive strategies that are generalizable to impact functioning (Keefe et al., 2011b). There is strong evidence that such interventions are efficacious in restoring neurocognitive performance to varying degrees; a recent review of CR's efficacy demonstrated significant small to moderate changes in effect size across all MATRICS neurocognitive domains (Vita et al., 2021). Moreover, CR has demonstrated durable positive on global cognition and global functioning in psychosis (Vita et al., 2024). As a cognitive intervention for psychosis, MCT has been compared to CR, but it does not take the

same direct approach of considering neurocognitive performance or consider neurocognition as a proximally targeted outcome. For instance, a cognitive task in MCT may primarily focus on attenuating maladaptive thinking processes like overconfidence in errors, and not necessarily on increasing accuracy in a cognitive task. However, the possibility of an indirect effect, where increases in neurocognitive performance occur as a consequence of training such metacognitive processes, has yet to be ruled out and is of primary interest in this work.

Ambiguity in the literature pertaining to the impact of MCT on neurocognition across several studies has precluded a unitary understanding of the intervention's true impact on neurocognitive performance. Positive effects of MCT on neurocognition have been documented; however, the observed benefits to neurocognition vary by neurocognitive domain. For instance, individual studies have reported benefits to verbal learning and memory (e.g., Fekete et al., 2022), working memory (e.g., Fekete et al., 2022; Moritz et al., 2011; Ruiz-Delgado et al., 2022; Shan et al., 2021; Wang et al., 2022), attention and vigilance (e.g., Wang et al., 2022), reasoning and problem solving (e.g., Ruiz-Delgado et al., 2022; Ussorio et al., 2015), and even visual learning and memory (e.g., Wang et al., 2022). In contrast, other randomized controlled trials (RCTs) have also reported no positive effects whatsoever of MCT on neurocognitive performance (e.g., Balzan et al. 2019; Gaweda et al., 2015; Haga et al., 2022). Therefore, this work seeks to clarify the resultant relationship of MCT and neurocognitive performance in psychosis by collecting and synthesizing the applicable extant literature to conduct a systematic review and meta-analysis.

One key element to consider when disentangling the true impact of an intervention like MCT on neurocognitive performance is in accounting for practice/learning effects that are not specific to the treatment. Non-specific effects of psychological interventions present challenges

in interpreting outcome changes, but practice effects in particular are a prominent concern in evaluating changes in neurocognitive performance. Rather than as a consequence of genuine improvement/recovery, score increases in performance as a result of memory for specific test items, learned strategies, and the degree of sophistication of a neurocognitive test (affecting the likelihood of practice to improve performance) cloud judgement of observed changes in neurocognition (McCaffrey et al., 2000). For instance, it is commonly observed that scores are augmented when retested regardless of the content of an intervention; failure to account for practice effects can lead to the incorrect interpretation of changes in neurocognitive functioning (Calamia et al., 2012).

Since practice effects in neurocognitive assessment tend to be uninfluenced by other demographic and clinical characteristics (Duff et al., 2012), we do not envision additional measures to be taken into account other than comparing changes in neurocognitive performance from patients in MCT against those in a control intervention group. We expect that gains to neurocognitive performance observed as an artefact of practice effects will be independent of the actual neurocognitive benefits of the intervention, which would become apparent when compared against the included control groups.

Interrelations of neurocognition and cognitive bias

A rapid increase in the development and incorporation of cognitive interventions into treatment for psychosis has sought to restore/improve neurocognitive capacities with the hope of increasing functional recovery (Farreny et al., 2012; Wykes et al., 2011). Although neurocognition and functioning are related, this relationship is not direct, which has led to the evaluation of other cognitive processes, such as metacognition, that may play a role along the pathway to impacting functional outcomes (Ruiz-Delgado et al., 2022). Small to moderate effect

sizes have been observed between neurocognition and metacognition, with dysfunctional metacognitive processing being associated with poor cognitive processing (Davies & Greenwood, 2020). Relationships between neurocognition and metacognition have been suggested in mediation models of functioning such as the notion that by improving metacognitive abilities, cognitive skill improvements can be better integrated into social/occupational environments (Lysaker et al., 2010). It has also been suggested that metacognition may be instrumental in early psychosis in the process of translating neurocognitive and functional outcomes into real-world scenarios (Davies et al., 2017). Due to the high degree of interrelations among these cognitive constructs, one may be tempted to ask whether these are even separate components in the picture of cognitive health. However, principal component analyses demonstrate that neurocognitive deficits and cognitive biases are indeed separable areas of cognitive health in psychosis (Eifler et al., 2015; Moritz et al., 2010). In light of these findings, and the premise that improving neurocognition alone is not proportional to improvements in functional outcome, new CR interventions have even begun to incorporate a focus on developing metacognitive exercises into their programs (Reeder et al., 2017).

If metacognitive capacities are diminished or dysfunctional, the prevalence and severity of cognitive biases are likely increased and are hypothesized to have detrimental effects on neurocognitive performance. For instance, it has been observed that difficulties with the metacognitive process of evidence integration captures a range of cognitive biases, including jumping to conclusions bias, bias against disconfirmatory evidence, theory of mind, and metamemory abilities (Eifler et al., 2014; Moritz et al., 2008). A breadth of literature has evaluated and found interrelations between neuropsychological profiles and evidence integration

in psychosis (e.g. Eifler et al. 2015; Eisenacher et al., 2015; Garety et al., 2013; Woodward et al., 2009). Furthermore, a meta-analysis on the relationship between neurocognition and insight, the cognitive process of understanding the extent of one's illness in psychosis, suggests that neuropsychological dysfunction contributes to poor insight in the disorder (Aleman et al., 2006). In sum, these findings have led to the reasoning that neurocognitive abilities are one of the mechanisms at play in higher order metacognitive processes in psychosis (Eisenacher & Zink, 2017).

Of particular interest to this work is the nature of the directionality of the relationship between neurocognition and metacognition. Do lower level neurocognitive functions have an upstream influence on metacognition, or would higher level metacognitive processes have a downstream impact on neurocognition– or could this relationship even be bidirectional? Results from studies such as Lysaker and colleagues (2010) have indicated that better neurocognitive performance is associated with increased metacognitive performance. This suggests that a degree of neurocognitive capacity is needed in order to navigate metacognitive processes, which would be consistent with the possibility that this relationship operates from a bottom-up perspective. In contrast, the current study predicts that a top-down effect of alleviating cognitive biases through training metacognitive processes would lead to increases in observed neurocognitive performance. For example, by bringing awareness to cognitive biases in MCT, an individual's ability to monitor themselves and inhibit irrelevant information may demonstrate benefits to performance on a task that evaluates a neurocognitive domain such as attention/vigilance. Similar arguments can be made for other MATRICS neurocognitive domains, and potentially to varying degrees depending on the nature of the domain. For instance, MCT may disproportionately benefit a higher-level neurocognitive domain such as reasoning and problem

solving compared to a lower-level domain like speed of processing. Because of the theoretical domain-specific inquiries of this research question, and in light of the observed mixed effects in the literature where MCT's benefits vary across MATRICS domains, this work will evaluate each neurocognitive domain individually in their relationship to undergoing MCT against control comparators.

Research aims and objectives

To the best of our knowledge, this is the first systematic review and meta-analysis to examine the role of metacognitive training for psychosis (MCT) on neurocognition. The main objective of this work is to identify the neurocognitive efficacy and specificity of MCT, a relatively novel cognitive intervention for psychosis that has had its direct and distal outcomes extensively studied in previous meta-analytic projects, including two recent meta-analytic studies completed by our research group within the Comprehensive Research Into Schizophrenia and Other Psychopathologies laboratory (Hotte-Meunier et al., 2023; Penney et al., 2022). In the most recent meta-analysis by Hotte-Meunier and colleagues (2023), MCT demonstrated significant changes of small effect size in social cognition outcomes for individuals with schizophrenia and related psychotic disorders. As we continue to evaluate the impact of MCT on a landscape of symptomatology and impairment in psychosis, these social cognition findings provide a foundation for and complement our justification of an in-depth analysis of the peripherally related area of neurocognition in psychosis. Furthermore, recent evidence will be discussed from individual RCTs suggesting the possible presence of a distal relationship between MCT and neurocognitive functioning; this project seeks to clarify the unique benefits to neurocognitive performance posed by MCT. Practically, this work can inform clinicians and service-providers of the potential added benefits, or specificity of MCT to address

neurocognitive impairment in the treatment of patients with psychosis. Therefore, this thesis demonstrates the extent to which MCT, as a cognitive intervention for psychosis, is suited to improve neurocognitive performance compared to the control interventions examined in this review.

CHAPTER 2: Does Metacognitive Training for Psychosis (MCT) Improve Neurocognitive Performance? A Systematic Review and Meta-Analysis.

Clayton Jeffrey[1,4], Danielle Penney[1,3], Geneviève Sauvé[1,6], Daniel Mendelson[1,2], Élisabeth Thibaudeau[1,4], Steffen Moritz[5], Adèle Hotte-Meunier [1,6], and Martin Lepage[1,4].

1. Douglas Research Centre, Montreal, Canada

2. Department of Psychology, McGill University, Montreal, Canada

3. Department of Psychology, Université du Québec à Montréal, Canada

4. Department of Psychiatry, McGill University, Montreal, Canada

5. Department of Psychiatry and Psychotherapy, University Medical Centre Hamburg, Germany

6. Department of Education and Pedagogy, Université du Québec à Montréal, Canada

Author Note

Dr. Steffen Moritz is the co-developer of metacognitive training and therefore was not involved in any aspect of data analysis or synthesis. Dr. Martin Lepage's Comprehensive Research Into Schizophrenia and other Psychopathologies (CRISP) group is currently offering metacognitive training at the Douglas Mental Health University Institute.

Correspondence concerning this article should be addressed to Martin Lepage, Douglas Research Centre, 6875 Boul Lasalle, Verdun, Qc, H4H 1R3, Canada. Email: martin.lepage@mcgill.ca

ABSTRACT

Background: Metacognitive training for psychosis (MCT) offers benefits for addressing hallmark deficits/symptoms in schizophrenia spectrum disorders including reductions in cognitive biases and positive/negative symptoms as well as improvements in social cognition and functioning. However, differing results exist regarding the relationship between MCT and neurocognition. A comprehensive understanding of the nature of this relationship would significantly contribute to the existing literature and our understanding of the potential added value of MCT as a cognitive intervention for psychosis.

Methods: Across eleven electronic databases, 1312 sources were identified, and 14 studies examining MCT and neurocognition in psychosis were included in this review. Measures of estimated effect sizes were calculated with Hedge's *g*, moderator analyses used Cochrane's *Q* statistic and significance tests to measure group differences according to control conditions.

Results: Twelve studies, 11 RCTs and 1 non-RCT, were included in the main meta-analyses, consisting of 673 participants (n_{MCT} =345, $n_{control}$ = 328). When comparing MCT against control interventions, non-significant differences in estimated effect sizes were observed across all neurocognitive domains when evaluating pre–post changes ($g \leq 0.1$, $p > 0.05$). Two additional studies corroborated these results in a narrative review.

Conclusion: These findings suggest that when compared against control conditions, MCT does not pose a statistically meaningful benefit to neurocognitive performance. General practice/learning effects are likely the main contributor that explains improvement in neurocognitive performance, and not a difference of intervention allocation when considering MCT against the included control comparators. These findings help establish the specificity of the effects of MCT.

Key Words: Metacognition, neurocognition, cognitive intervention, schizophrenia, psychosis.

Protocol Registration:

https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=374276

1. Introduction

Individuals with schizophrenia and related psychotic disorders characteristically experience deficits in neurocognitive performance, which considerably accounts for impaired functioning associated with psychosis (McCutcheon et al., 2023). Such deficits are especially determinant of functional outcomes in areas such as community and occupational functioning (Cowman et al., 2021; McCleery & Nuechterlein, 2019). Among these core deficits, the most prevalent and malleable domains of neurocognition in psychosis as defined by the *Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS*) consensus include speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, as well as reasoning and problem solving (Nuechterlein et al., 2008). Several non-pharmacological interventions exist that effectively increase neurocognitive performance in psychosis such as cognitive remediation (CR), which have well-established benefits in improving both neurocognition as well as functioning (Lejeune et al., 2021; Vita et al., 2021). Metacognitive training for psychosis (MCT) is a widely used intervention developed to promote an awareness for cognitive biases (Moritz & Woodward, 2007). It has been described as a blend of CR and cognitive behavioural therapy (CBT) with a grounding in psychoeducation (Sauvé et al., 2020). Given the similarities that MCT shares with interventions such as CR and CBT, which are known to benefit neurocognition in this population (Kukla et al., 2018), it is possible that MCT may also have an effect on neurocognitive performance.

MCT is an open-source intervention that focuses on bringing distorted cognitive biases to the awareness of patients; it encourages thinking about underlying cognitive/social processes and attenuates overconfidence in beliefs through a series of structured sessions in either group or individualized formats (Moritz et al., 2019). In a recent meta-analysis of 43

studies and 1816 participants (30 RCTs, 11 non-RCTs, 2 quantitative descriptive studies), MCT led to significant differences of small to medium effect size magnitude on reducing positive symptoms, delusions, cognitive biases, and negative symptoms as well as on increasing self-esteem and functioning (Penney et al., 2022). Although MCT principally aims to improve cognitive biases, the intervention has demonstrated effects on distal outcomes too, which begs the question of whether it may influence neurocognitive mechanisms as well.

Parenthetical to neurocognition, our group recently observed a significant effect of MCT on social cognition (Hotte-Meunier et al. 2023). Several RCTs have recently reported that MCT is beneficial in improving some aspect of observed neurocognitive functioning in psychosis such as verbal learning and memory, visual learning and memory, working memory, attention/vigilance, as well as reasoning and problem solving (Fekete et al., 2022; Moritz et al., 2011; Ruiz-Delgado et al., 2022; Shan et al., 2021; Wang et al., 2022). However, these RCTs differ in the specific neurocognitive domains affected, and other individual studies reported no positive effects whatsoever (Balzan et al. 2019; Gaweda et al., 2015; Haga et al., 2022). Therefore, by using a quantitative approach this systematic review and meta-analysis was conducted to synthesize the literature on this topic and clarify the resultant impact of MCT across neurocognitive domains.

To the best of our knowledge, no systematic review and meta-analysis has examined the distal effect of metacognitive training (MCT) on neurocognitive performance in psychosis. MCT targets core features of delusions that are not confined to delusional/pathological beliefs but represent problematic thinking styles that have been attributed as foundational pillars of observable delusional behaviour in the disorder (Moritz et al., 2014). It is hypothesized that through the attenuation of problematic thinking styles that are common to psychosis such as

overconfidence, incorrigibility, and hasty decision-making, a distal effect on neurocognitive performance will be observed. For example, “cold cognition” capacities like working memory are not likely increased by the intervention directly, rather the process of explaining how memory is constructive and should be challenged may lead to benefits in performance on working memory tasks. In stark comparison to cognitive interventions that principally aim to improve neurocognition such as CR, none of the available MCT modules deliberately focus on augmenting neurocognitive performance outside of addressing cognitive biases related to broad areas such as memory. Hence, any distal impact that MCT has on neurocognitive performance is proposed to be through an indirect mechanism of ameliorating cognitive biases that otherwise inhibit neurocognitive performance. One caveat to evaluating changes in neurocognitive performance in psychosis is controlling for practice/learning effects, which may lead to increases in performance across assessment timepoints regardless of the impact of the intervention (Goldberg et al., 2010). To control for this commonly observed phenomenon, this systematic review and meta-analysis of MCT’s effect on neurocognitive performance is evaluated against control comparators, and hypothesizes that MCT will demonstrate efficacy in improving neurocognition over and beyond potential gains attributed to practice/learning effects.

2. Methods

The protocol for this systematic review and meta-analysis can be found registered on PROSPERO (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=374276). The search scoured 11 electronic databases including a search of the grey literature to find all the relevant literature contributing to our knowledge on the potential effects of MCT on neurocognition in psychosis. Following 2020 PRISMA guidelines, the appropriate flowchart can be found in Fig. 1, and PRISMA checklists can be viewed in eAppendix 1 of the Supplement.

2.1. Search strategy and selection criteria

This systematic review and meta-analysis expands upon two former reviews that are considered a series of studies to the current project by Penney et al. (2022) and Hotte-Meunier et al. (2023). The search strategy for this systematic review and meta-analysis both relied on and was extrapolated from Penney et al. (2022) (see eTable 1 of Penney et al. 2022 supplemental). The search was updated to include additional studies from the end of the former search to present; studies that did not include neurocognitive outcomes (the focus of this work) were excluded. This includes a comprehensive review of the relevant literature from the outset of the first study published on MCT on June 3, 2007 (Moritz & Woodward, 2007) until November 22, 2022. Using this search criteria, a Web of Science alert was created to include any pertinent studies in the systematic review until the analysis phase commenced (November 1st, 2023). Stand-alone versions of the updated PRISMA flowchart and search strategy for the present study can be viewed in the Supplement (see eTable 1, eFig. 1). No limitations were imposed on the study language selection; any foreign language materials were processed through the online translator DeepL, and when necessary, our multi-lingual team members provided interpretations in English, French, German, and Spanish. Following the search all abstracts were screened, whereafter a full text review was conducted for eligible reports, followed by data extraction and synthesis for records included. Studies needed to meet specific eligibility criteria, which required them to report sample sizes, means, and standard deviations for outcome measures pre-treatment and post-treatment. If available, data after one year of the intervention in both the treatment and control conditions were also included.

2.2. Intervention and comparator(s)

MCT is the experimental condition of this meta-analysis, which is an open-source intervention that focuses on "sowing seeds of doubt" in the problematic thinking styles of patients through conscious reflections on cognitive processes (Moritz et al., 2019). Included studies either consisted of the original version or accepted individual/group adaptations of MCT. Acceptable adaptations included variability in the number of sessions provided and session duration. Across the course of the administered MCT adaptations, each of the hourly sessions are highly structured and aim to raise patients' awareness of cognitive traps and biases that are common to experiences along the psychosis continuum. Prepared modules for both individualized and group-facilitated variations for MCT as well as additional resources are made publicly available (www.uke.de/mct).

2.3. Main outcome(s)

Changes from pre–post intervention and post–follow-up were assessed using means and standard deviations of reported neurocognitive outcomes. As defined by the MATRICS consensus (Nuechterlein et al., 2008), the main neurocognitive outcomes of concern were speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, as well as reasoning and problem solving. Although also a MATRICS domain, social cognition has already been evaluated in a systematic review and meta-analysis in a former study from our group, and therefore was not accounted for in the current paper (Hotte-Meunier et al., 2023).

2.4. Measures of effect

Means and standard deviations of experimental and control groups were extracted for pre-intervention, post-intervention and at follow-up timepoints. Where applicable, measures of

effect size for mean difference were collected/calculated in Cohen's *d* and converted to Hedge's *g* and 95% confidence intervals to consider changes in neurocognitive performance using a random effects model. Where appropriate, effect size averages were calculated to control for nested effects when a single study had included multiple distinct outcomes that were used to measure the same neurocognitive domain (Cheung, 2019).

2.5. Data synthesis procedure

The extraction and coding of data were carried out by authors CJ, DP, DM and ET, utilizing a piloted template that was created by co-author GS. The first author (CJ) completed quality control for extracted data. In instances where means and standard deviations were not reported, the corresponding author(s) were successfully contacted by email. Additional study characteristics including available demographic information (e.g., study design, country of origin, sex, age, illness duration) and intervention/comparator details were extracted. Included data for the meta-analyses were synthesized using Metafor (version 4.0.0), Shiny (version 1.7.4), and ggplot2 version (3.4.2) packages in R. Forest plots are used to illustrate the results of the meta-analyses.

2.6. Methodological quality assessment

The Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018) was used by authors CJ, DP, DM to assess the methodological quality of the individual studies included in the meta-analysis. Any discrepancies between the authors were resolved through a collaborative process involving examination and discussion of MMAT criteria (see eTable 2). Risk of publication bias was assessed using Egger's asymmetry test for funnel plot asymmetry, by examining the portrayal of the funnel plots and with Rosenthal's fail-safe n (Egger et al., 1997; Kendall, 1938; Rosenthal, 1979). Heterogeneity across studies was estimated with Cochran's Q and the I^2

statistic (Cochran, 1954; Higgins et al., 2003). A sensitivity analysis was conducted to assess the impact of study design on the robustness of our results by restricting inclusion to RCTs.

3. Results

3.1. Search results

Of the 1312 studies screened in this review, 14 met the desired inclusion/exclusion criteria, and 12 were eligible to be assessed in the meta-analysis– of which main study characteristics are summarized in Table 1. Additionally, two studies have been included in a narrative review, corroborating the overall findings from the main analyses. Meta-analyses were calculated for each of the MATRICS neurocognitive domains.

Changes in neurocognitive performance were evaluated between MCT and the control comparator from baseline assessment before the start of the intervention (pre) to the assessment immediately following the completion of the intervention (post) to determine the immediate efficacy of the interventions on neurocognition. To evaluate maintenance effects, secondary analyses from post to one-year following the initial assessment (follow-up) were also conducted.

3.2. Preliminary analyses

Initial meta-analyses were conducted to portray general trends of change in neurocognitive performance that are observed from pre–post assessment, where MCT is not evaluated against its control comparator and vice-versa. For the MCT groups, these results indicate significant small–moderate magnitudes of change in performance across all neurocognitive domains (g = 0.33–0.71; $p < .05$). The control groups parallel these results across neurocognitive domains, indicating significant (trending towards significance for visual learning and memory; $p = .08$) small–moderate magnitudes of change for all neurocognitive domains (g = 0.29–0.63; $p < .05$). These preliminary results are portrayed in the Supplement (see eTable 9).

3.3. Neurocognitive outcomes

The main meta-analysis results indicate negligible non-significant differences in effect sizes when comparing changes in neurocognitive performance of MCT interventions against control comparator interventions across all MATRICS domains assessed: speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem-solving (all $p > .05$; see eTable 3 of the Supplement). Non-significant findings ($p > .05$) for immediate effects evaluated by pre–post comparisons were observed across all pre–post considerations (see forest plots in Fig. 2). Secondary analyses of maintenance effects via post–follow-up comparisons yielded similar non-significant findings across all neurocognitive domains assessed ($p > .05$) and can be viewed in the Supplement (eTable 3).

3.4. Publication bias

Non-significant ($p > .05$) results for heterogeneity from Cochran's Q statistic were obtained for all timepoint comparisons for each neurocognitive outcome; likewise, the I^2 test results suggest very low heterogeneity for each neurocognitive domain across timepoint comparisons (eTable 4 of the Supplement). Rosenthal's fail-safe N demonstrated non-significant results, further demonstrating low risk of publication bias in this meta-analysis ($p > .05$). A visual assessment of the funnel plots aligned with the non-significant findings of Egger's regression tests for funnel plot asymmetry ($p > .05$) (see eTable 5 of the Supplement).

3.5. Moderator analyses

Included studies ranged in their comparator to MCT from passive interventions such as treatment as usual (TAU) and occupational therapy (OT) to active evidence-based interventions such as Psychosocial Skills Training, Psychoeducation, Cognitive Remediation, Action-Based

Cognitive Remediation and CogPack. By grouping comparators into intervention types, moderator analyses were performed to evaluate subgroup differences.

Due to the nature of the control conditions differing substantially from each other practically and demonstrating high within-group heterogeneity, subgroup analyses were conducted by including the two main categories of control group as moderators: passive and active control groups. Non-significant ($p > .05$) between group heterogeneity tests using the Q statistic were found when comparing differences between passive and active group comparisons for each of the six neurocognitive domains assessed for comparisons of pre–post and post–follow-up (full subgroup analyses can be viewed in eTable 6 of the Supplement).

3.6. Sensitivity analysis

A sensitivity analysis repeated these subgroup analyses while excluding studies with control groups that consisted of cognitive interventions such as CR (Balzan et al., 2019), CogPack (Moritz et al., 2013) and Action-Based Cognitive Remediation (Mendelson et al., 2022). The rationale being that such comparators may not be the most accurate control conditions for assessing changes in neurocognitive performance, since they are interventions that target cognitive outcomes. However, this sensitivity analysis yielded no substantial differences from the main analyses (see eTable 7 of the Supplement).

Two additional studies, one single-group study with no control group, and one longitudinal study reporting three-year data, could not be included in the meta-analytic synthesis but were instead incorporated into this work as a narrative review. see Table 2 for rationale and results summary). These studies further corroborate the observed findings, where general neurocognitive benefits of the MCT intervention are observed in absence of a control comparator (e.g., Ussorio et al., 2016), however where a control group exists for comparison, MCT groups

are not meaningfully different in improvement of neurocognitive performance from their comparator intervention group (e.g., Moritz et al., 2014).

4. Discussion

This methodologically rigorous and analytically comprehensive systematic review and meta-analysis provides clarity in our current understanding of the efficacy of MCT on neurocognition. Preliminary analyses portray that when considered without a comparison group both MCT and control groups seem to demonstrate clear, significant benefits to neurocognitive performance that vary in effect size magnitude from small–moderate across neurocognitive domain. However, the main contribution of this work is in examining the efficacy of MCT on neurocognitive performance when comparing changes against control conditions. Across pre–post timepoints, non-significant differences were found for each neurocognitive domain, which indicates that benefits to neurocognitive performance are not significantly different between MCT and their control comparators. These robust findings were unchanged when considering subgroup and sensitivity analyses. Therefore, increases in raw neurocognitive performance that are commonly observed are more likely attributable to factors such as practice/learning effects, or otherwise qualities that are common across the interventions included in this review such as non-specific effects. The findings of studies included in a narrative review corroborate the preliminary and main meta-analytic results, where without a control group to compare against, MCT intervention groups demonstrate increases in neurocognitive performance, whereas when a control group exists, this effect is diminished. Altogether, these findings valuably capture the specificity of MCT as an intervention not uniquely suited to addressing neurocognitive deficits in psychosis.

Due to the domain-specific differences observed in the literature pertaining to MCT's impact on neurocognitive performance, which this project sought to clarify, no global measure of

neurocognition was created. Given the findings of this work, we would not expect a global measure to reflect any new or valuable insight from the consistent null findings of MCT's impact on individual neurocognitive domains compared to control comparators. In this study, the post–follow-up group analyses consisted of a much smaller sample size, ranging from 2-4 studies by neurocognitive domain, which would suggest these are underpowered compared to the pre–post analyses. Although we would not expect the results to substantially differ from the pre–post findings, in order to be confident in the results of the present systematic review and meta-analysis of the post–follow-up data further RCTs of MCT that track long-term changes in neurocognitive performance would solidify our understanding of the maintenance effects of MCT on neurocognition. Given the precedent of other observed sleeper effects that have been documented in MCT (see Moritz et al., 2014), it may be worthwhile for a future meta-analysis to determine the degree to which MCT may benefit neurocognition in the long-term with a greater sample size to draw from. Generalizability of these findings across sex is limited due to a lack of sex-differentiated analyses of the effect of MCT on neurocognition based on the available data in this review.

Although the alternative hypothesis theorized distal effects where MCT may be uniquely beneficial in improving neurocognition compared to control comparators, no such relationship was demonstrated to exist in this review. Though not captured in this study, it could still be the case that neurocognitive abilities are potentially enhanced in MCT by an alleviation of cognitive biases that would otherwise inhibit neurocognitive capacities. Caution has been advised when interpreting neurocognitive changes through serial testing of the same cognitive tests/batteries, which may not enable patients to demonstrate intervention-specific changes to underlying neurocognitive processes. Practice effects are also generally observed in greater magnitude

between initial and second assessment, which elaborates on the potential value for future work to include additional long-term assessment timepoints that are less prone to demonstrate incremental benefits from practice effects (Goldberg et al., 2010). In their own right, practice effects may speak to cognitive capacities connected to memory consolidation, but methodological steps from future studies that are designed to mitigate practice/learning effects would contribute valuable information to making confident claims on MCT's unique efficacy or lack thereof compared to control conditions on neurocognition in psychosis.

5. Conclusion

Given these findings, this review helps clarify the existing ambiguity in the literature regarding the mixed effects of MCT on neurocognition, in that it does not significantly differ from the other control comparators that were assessed. Although MCT has demonstrated its efficacy in symptom amelioration across other core domains of issues characteristic of psychosis, it is not currently recommended as an intervention to specifically target neurocognition if that is a priority outcome of concern.

Acknowledgements

We would like to recognize Dr. Manuela Ferrari's contributions to the general support of this project as an advisory committee member to CJ's M.Sc. Thesis. The authors have no writing assistance disclosures to report.

Declaration of Interests

Steffen Moritz is the co-developer of metacognitive training. His role in this study is to consult with the co-authors to ensure the inclusion of all relevant studies. Dr. Moritz was not involved in any aspect of data analysis or synthesis. We also wish to disclose that the Comprehensive Research Into Schizophrenia and other Psychopathologies (CRISP) group (Dr. Lepage) is currently offering metacognitive training at the Douglas Mental Health University Institute. There are no other known conflicts of interest.

Role of the Funding Source

Research funding for this project is supported by the Canada First Research Excellence Fund, awarded through McGill University's Healthy Brains, Healthy Lives (HBHL) initiative (HBHL 3c-KM-56). CJ is funded by the Canada Graduate Scholarships Master's– Canadian Institutes of Health Research (CIHR). DP is supported by a doctoral training award from the Fonds de recherche Québec - Santé (FRQS, #315157). GS is supported by a research scholar salary award (FRQS, #339871). ET is supported by a postdoctoral fellowship grant from the Canadian Institutes of Health Research (CIHR, #171198). ML is supported by a James McGill Professorship from McGill University. No funding agency or sponsor had any role in the study design, data collection, analysis, or in the means of publication of this research. Steffen Moritz is the co-developer of metacognitive training. His role in this study is to consult with the co-authors to ensure the inclusion of all relevant studies. Dr. Moritz was not involved in any aspect

of data analysis or synthesis. We also wish to disclose that the Comprehensive Research Into Schizophrenia and other Psychopathologies (CRISP) group (Dr. Lepage) is currently offering metacognitive training at the Douglas Mental Health University Institute. There are no other known conflicts of interest.

Table 1. Summary of study characteristics.

Source	Country	Design	Group type	Age, mean (SD), y	Illness Duration, mean (SD), y	Sample Size, No.	Sex Ratio (M:F)
Balzan et al. (2019)	Australia	Randomized controlled trial	MCT	35.37 (9.84)	9.85 (8.47)	27	15:12
			Cognitive Remediation	39.04 (7.48)	12.37 (7.95)	27	17:10
Fekete et al. (2021)	Hungary	Randomized controlled trial	MCT	44.22 (10.45)	16.16 (7.76)	23	11:12
			TAU	38.39 (10.41)	11.32 (8.74)	23	11:12
Fujii et al. (2021)	Japan	Randomized controlled trial	MCT	54.00 (7.60)	31.78 (6.16)	9	6:3
			OT	54.50 (8.63)	33.38 (10.43)	8	4:4
Gaweda et al. (2015)	Poland	Randomized controlled trial	MCT	50.41 (10.79)	22.96 (10.05)	23	11:12
			TAU	51.65 (10.25)	20.61 (11.30)	21	11:10
Haga et al. (2022)	Japan	Randomized controlled trial	MCT	44.25 (8.54)	21.75 (12.49)	8	5:3
			OT	43.25 (7.98)	17.88 (11.11)	8	3:5
Mendelson et al. (2022)	Canada	Non-randomized controlled trial	MCT	31.9 (12.3)	7.9 (9.9)	17	9:8
			Action-Based Cognitive Remediation	32.6 (9.2)	7.8 (8.0)	11	6:5
Moritz et al. (2013)	Germany	Randomized controlled trial	MCT	36.82 (11.12)	N/R	76	45:31
			CogPack	32.68 (9.54)	N/R	74	49:25
Moritz et al. (2011)	Germany	Randomized controlled trial	MCT	33.6 (8.8)	N/R	18	15:3
			TAU	31.9 (7.0)	N/R	18	13:5
Ruiz-Delgado et al. (2022)	Spain	Randomized controlled trial	MCT	27.05 (7.94)	2.15 (2.01)	65	44:21
			Psychoeducation	28.21 (6.73)	2.46 (2.07)	57	41:16
Shan et al. (2021)	China	Randomized controlled trial	MCT	26.05 (5.81)	N/R	19	12:7
			Non-Specific Therapeutic Program	22.75 (4.38)	N/R	20	15:5
Wang et al. (2022)	China	Randomized controlled trial	MCT	44.66 (9.61)	N/R	50	23:27
			TAU	44.34 (8.53)	N/R	50	21:29
Yildiz et al. (2019)	Turkey	Randomized controlled trial	MCT	33.1 (10.7)	13.6 (6.1)	10	6:4
			Psychosocial Skills Training	37.4 (4.6)	13.2 (8.4)	11	7:4

Table 2. Narrative Review Results.

Source	Outcomes of interest	Narrative Review Reasoning	Neurocognition Results
Moritz et al., 2014	Neurocognition (processing speed, reasoning and executive functions, verbal learning and memory, attention).	This is the only included study that reported long-term data at the three-year mark, based on a previous RCT (Moritz 2013). With no other studies to compare three-year follow-up data to, this cannot be used in the meta-analysis.	Non-significant differences between MCT and CTL conditions for both intent-to-treat (ITT) analyses and per-protocol (PP) analyses for processing speed, reasoning and executive functions, verbal learning, and memory. Non-significant differences for PP, but significant differences for ITT in attention were demonstrated in favour of the neuropsychological CTL condition.
Ussorio et al., 2016	Neurocognition (verbal learning and memory, processing speed, reasoning and executive functions, attention).	Non-randomized controlled trial with no comparator intervention.	Both short and long-duration of untreated psychosis groups experienced significant neurocognitive benefits in verbal learning and memory, processing speed, reasoning and executive functions, and attention.

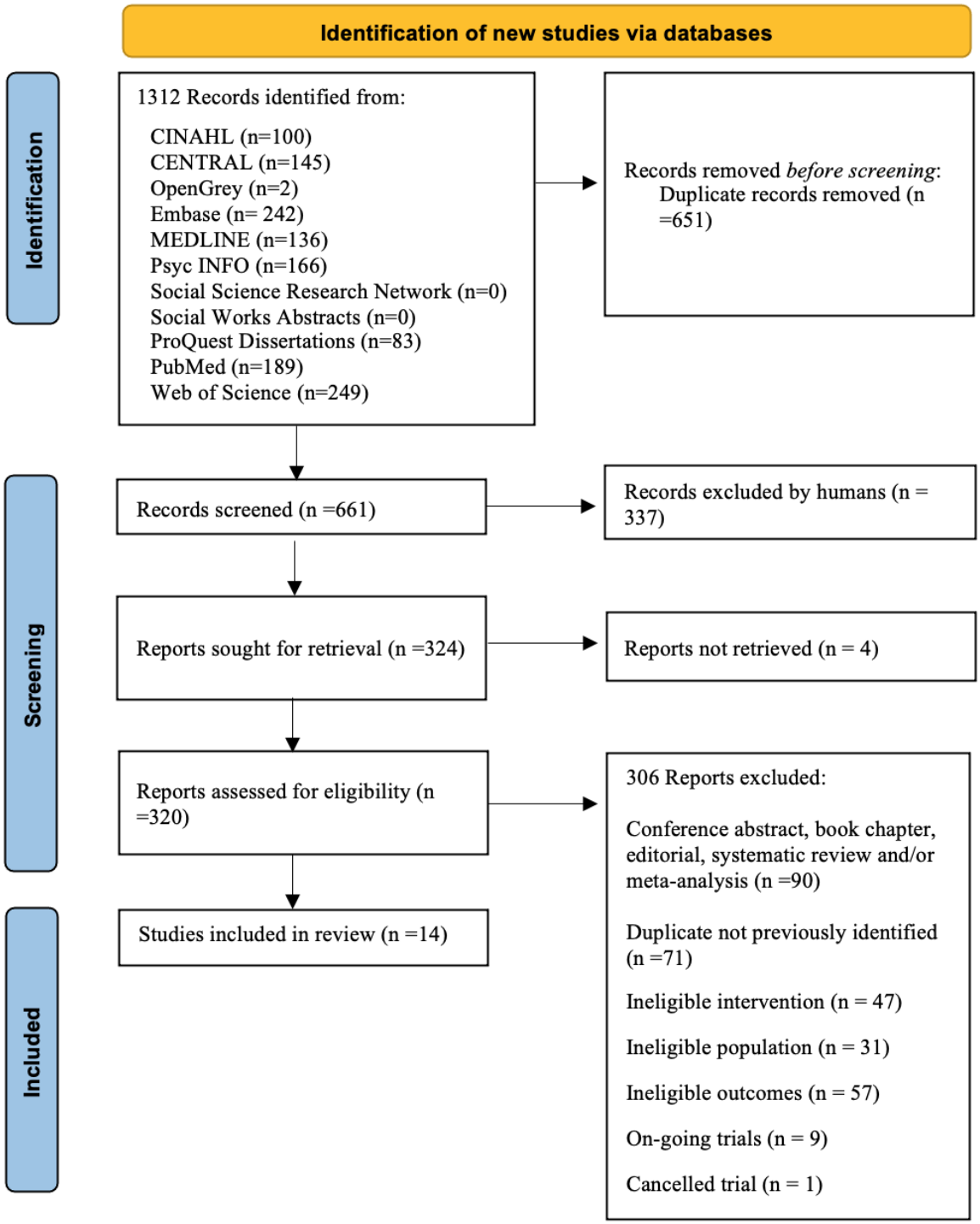


Fig. 1. PRISMA flowchart for systematic reviews and meta-analyses (2020).

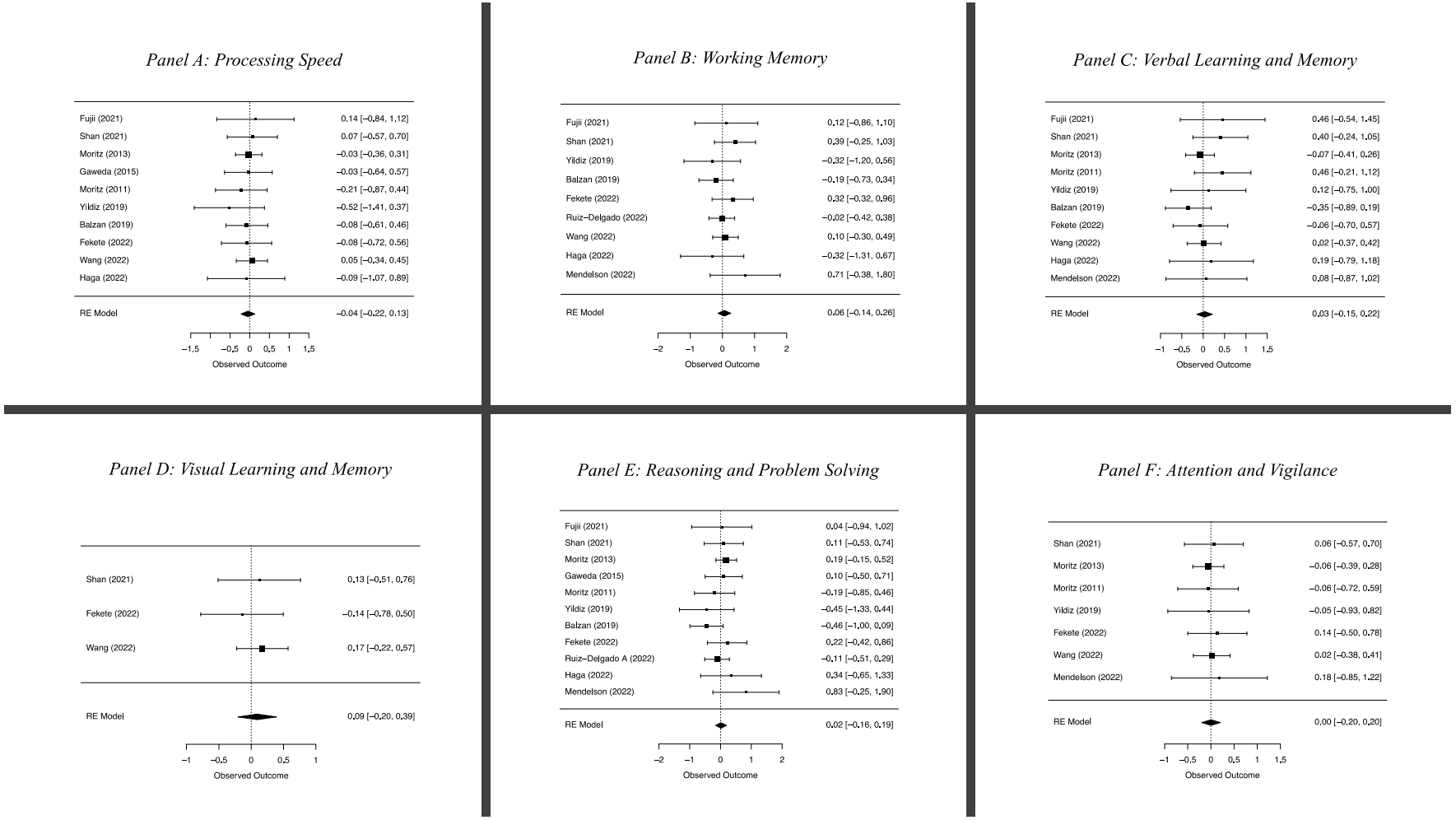


Fig. 2. Forest plot panels of all neurocognitive outcomes (pre–post); right favours improvement, left favours deterioration using Hedges *g* and 95% confidence intervals.

References

Balzan, R. P., Mattiske, J. K., Delfabbro, P., Liu, D., & Galletly, C. (2019). Individualized Metacognitive Training (MCT+) Reduces Delusional Symptoms in Psychosis: A Randomized Clinical Trial. *Schizophr Bull, 45*(1), 27-36. doi:10.1093/schbul/sby152

Cheung, M. W.–L. (2019). A guide to conducting a meta-analysis with non-independent effect sizes. Neuropsychology Review, 29(4), 387–396. 10.1007/s11065-019-09415-6

Cochran W.G. (1954). The combination of estimates from different experiments. *Biometrics*, *10*(1):101-129. doi:10.2307/3001666

Cowman, M., Holleran, L., Lonergan, E., O'Connor, K., Birchwood, M., & Donohoe, G. (2021). Cognitive Predictors of Social and Occupational Functioning in Early Psychosis: A Systematic Review and Meta-analysis of Cross-Sectional and Longitudinal Data. *Schizophr Bull, 47*(5), 1243-1253. doi:10.1093/schbul/sbab033

Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-634. doi:10.1136/bmj.315.7109.629

Fekete, Z., Vass, E., Balajthy, R., Tana, Ü., Nagy, A. C., Oláh, B., Domján, N., & Kuritárné, I. S. (2022). Efficacy of metacognitive training on symptom severity, neurocognition and social cognition in patients with schizophrenia: A single-blind randomized controlled trial. *Scandinavian journal of psychology*, *63*(4), 321–333. https://doi.org/10.1111/sjop.12811

Fujii, K., Kobayashi, M., Funasaka, K., Kurokawa, S., & Hamagami, K. (2021). Effectiveness of Metacognitive Training for Long-Term Hospitalized Patients with Schizophrenia: A Pilot Study with a Crossover Design. *Asian Journal of Occupational Therapy, 17*(1), 45-52. doi:10.11596/asiajot.17.45

Gaweda, L., Krezolek, M., Olbrys, J., Turska, A., & Kokoszka, A. (2015). Decreasing self-reported cognitive biases and increasing clinical insight through meta-cognitive training in patients with chronic schizophrenia. *J Behav Ther Exp Psychiatry, 48*, 98-104. doi:10.1016/j.jbtep.2015.02.002

Goldberg, T. E., Keefe, R. S., Goldman, R. S., Robinson, D. G., & Harvey, P. D. (2010). Circumstances under which practice does not make perfect: a review of the practice effect literature in schizophrenia and its relevance to clinical treatment studies. *Neuropsychopharmacology, 35*(5), 1053-1062. doi:10.1038/npp.2009.211

Haga, S., Kobayashi, M., Takehara, A., Kawano, K., & Endo, K. (2022). Efficacy of Metacognitive Training for Patients With Schizophrenia in Psychiatric Emergency Wards: A Pilot Randomized Controlled Trial. *Front Psychol, 13*, 861102. doi:10.3389/fpsyg.2022.861102

Higgins J.P., Thompson S.G., Deeks J.J., Altman D.G. (2003). Measuring inconsistency in meta-analyses. *BMJ, 327*(7414):557-560. doi:10.1136/bmj.327.7414.557

Hong, Q. N., Pluye, P., Fàbregues, S., Bartlett, G., Boardman, F., Cargo, M., Dagenais, P., Gagnon, M., Griffiths, F., Nicolau, B., O'Cathain, A., Rousseau, M., & Vedel, I. (2018, August 1). Mixed methods appraisal tool (MMAT) version 2018 [pdf]. http://mixed methodsappraisaltoolpublic. pbworks.com/w/file/fetch/127916259/MMAT_2018_ criteria-manual_2018-08-01_ENG.pdf.

Hotte-Meunier, A., Penney, D., Mendelson, D., Thibaudeau, E., Moritz, S., Lepage, M., & Sauve, G. (2023). Effects of metacognitive training (MCT) on social cognition for

schizophrenia spectrum and related psychotic disorders: a systematic review and meta-analysis. *Psychological* Medicine, 1-7. doi:10.1017/S0033291723002611

Kukla, M., Bell, M. D., & Lysaker, P. H. (2018). A randomized controlled trial examining a cognitive behavioral therapy intervention enhanced with cognitive remediation to improve work and neurocognition outcomes among persons with schizophrenia spectrum disorders. *Schizophrenia research*, *197*, 400–406. https://doi.org/10.1016/j.schres.2018.01.012

Lejeune, J. A., Northrop, A., & Kurtz, M. M. (2021). A Meta-analysis of Cognitive Remediation for Schizophrenia: Efficacy and the Role of Participant and Treatment Factors. *Schizophr Bull*, *47*(4), 997-1006. doi:10.1093/schbul/sbab022

McCleery, A., & Nuechterlein, K. H. (2019). Cognitive impairment in psychotic illness: prevalence, profile of impairment, developmental course, and treatment considerations. *Dialogues Clin Neurosci*, *21*(3), 239-248. doi:10.31887/DCNS.2019.21.3/amccleery

McCutcheon, R. A., Keefe, R. S. E., & McGuire, P. K. (2023). Cognitive impairment in schizophrenia: aetiology, pathophysiology, and treatment. *Mol Psychiatry*. doi:10.1038/s41380-023-01949-9

McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., and Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *Am. J. Psychiatry 164*, 1791–1802. doi: 10.1176/appi.ajp.2007.07060906

Mendelson, D., Thibaudeau, E., Sauve, G., Lavigne, K. M., Bowie, C. R., Menon, M., Raucher-Chene, D. (2022). Remote group therapies for cognitive health in schizophrenia-spectrum disorders: Feasible, acceptable, engaging. *Schizophr Res Cogn*, *28*, 100230. doi:10.1016/j.scog.2021.100230

Moritz, S., Andreou, C., Schneider, B. C., Wittekind, C. E., Menon, M., Balzan, R. P., & Woodward, T. S. (2014). Sowing the seeds of doubt: a narrative review on metacognitive training in schizophrenia. *Clin Psychol Rev*, *34*(4), 358-366. doi:10.1016/j.cpr.2014.04.004

Moritz, S., Veckenstedt, R., Andreou, C., Bohn, F., Hottenrott, B., Leighton, L., Köther, U., Woodward, T. S., Treszl, A., Menon, M., Schneider, B. C., Pfueller, U., & Roesch-Ely, D. (2014). Sustained and "sleeper" effects of group metacognitive training for schizophrenia: a randomized clinical trial. *JAMA psychiatry*, *71*(10), 1103–1111. https://doi.org/10.1001/jamapsychiatry.2014.1038

Moritz, S., Veckenstedt, R., Bohn, F., Hottenrott, B., Scheu, F., Randjbar, S., Aghotor, J., Köther, U., Woodward, T. S., Treszl, A., Andreou, C., Pfueller, U., & Roesch-Ely, D. (2013). Complementary group Metacognitive Training (MCT) reduces delusional ideation in schizophrenia. *Schizophrenia research*, *151*(1-3), 61–69. https://doi.org/10.1016/j.schres.2013.10.007

Moritz, S., Kerstan, A., Veckenstedt, R., Randjbar, S., Vitzthum, F., Schmidt, C., Heise, M., & Woodward, T. S. (2011). Further evidence for the efficacy of a metacognitive group training in schizophrenia. *Behaviour research and therapy*, *49*(3), 151–157. https://doi.org/10.1016/j.brat.2010.11.010

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., & Marder, S. R. (2008). The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *American Journal of Psychiatry*, *165*(2), 203-213.

Penney, D., Sauvé, G., Mendelson, D., Thibaudeau, É., Moritz, S., & Lepage, M. (2022).

Immediate and sustained outcomes and moderators associated with metacognitive training for psychosis: a systematic review and meta-analysis. *JAMA psychiatry*.

Rosenthal R. The file drawer problem and tolerance for null results. Psychol Bull. 1979;86(3): 638. doi:10.1037/0033-2909.86.3.638

Ruiz-Delgado, I., Moreno-Küstner, B., García-Medina, M., Barrigón, M. L., Gonzalez-Higueras, F., López-Carrilero, R., Barrios-Mellado, I., Barajas, A., Pousa, E., Lorente-Rovira, E., Grasa, E., Cid, J., Barrau-Sastre, P., Moritz, S., Ochoa, S., & Spanish Metacognition Group (2022). Is Metacognitive Training effective for improving neurocognitive function in patients with a recent onset of psychosis?. *Psychiatry research*, *318*, 114941. https://doi.org/10.1016/j.psychres.2022.114941

Sauve, G., Lavigne, K. M., Pochiet, G., Brodeur, M. B., & Lepage, M. (2020). Efficacy of psychological interventions targeting cognitive biases in schizophrenia: A systematic review and meta-analysis. *Clin Psychol Rev, 78*, 101854. doi:10.1016/j.cpr.2020.101854

Shan, X., Liao, R., Ou, Y., Pan, P., Ding, Y., Liu, F., Chen, J., Zhao, J., Guo, W., & He, Y. (2021). Increased regional homogeneity modulated by metacognitive training predicts therapeutic efficacy in patients with schizophrenia. *European archives of psychiatry and clinical neuroscience*, *271*(4), 783–798. https://doi.org/10.1007/s00406-020-01119-w

Ussorio, D., Giusti, L., Wittekind, C. E., Bianchini, V., Malavolta, M., Pollice, R., Casacchia, M., & Roncone, R. (2016). Metacognitive training for young subjects (MCT young version) in the early stages of psychosis: Is the duration of untreated psychosis a limiting factor?. *Psychology and psychotherapy*, *89*(1), 50–65. https://doi.org/10.1111/papt.12059

Vita, A., Barlati, S., Ceraso, A., Nibbio, G., Ariu, C., Deste, G., & Wykes, T. (2021). Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Psychiatry, 78*(8), 848-858. doi:10.1001/jamapsychiatry.2021.0620

Wang, C., Chong, Y., Zhang, J., Cao, Y., & Wang, Y. (2022). The Efficacy of Extended Metacognitive Training on Neurocognitive Function in Schizophrenia: A Randomized Controlled Trial. *Brain sciences*, *12*(3), 413. https://doi.org/10.3390/brainsci12030413

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., and Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am. J. Psychiatry 168*, 472–485. doi: 10.1176/appi.ajp.2010.10060855

Yildiz, M., Ozaslan, Z., Incedere, A., Kircali, A., Kiras, F., & Ipci, K. (2019). The Effect of Psychosocial Skills Training and Metacognitive Training on Social and Cognitive Functioning in Schizophrenia. *Noro Psikiyatr Ars, 56*(2), 139-143. doi:10.29399/npa.23095

Supplementary Materials

Jeffrey, C.M., Penney, D., Sauvé, G., Mendelson, D., Thibaudeau, É., Moritz, S., Hotte-Meunier, A., Lepage, M. (2024). Does Metacognitive Training for Psychosis (MCT) Improve Neurocognitive Performance? A Systematic Review and Meta-Analysis.

These supplementary materials have been provided by the authors to provide readers with additional information about this work.

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

eAppendix 1. PRISMA checklists.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p. 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p. 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	pp. 4-6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	pp. 4-5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	pp. 6-7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	pp. 6-7
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	pp. 6-7
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p. 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p. 9
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p. 8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	pp. 8-9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p. 9
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pp. 8-9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	pp. 7-8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	p. 9

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	p. 9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	pp. 8-9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	pp. 9-10
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	p. 10
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	p. 9
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	pp. 8-9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	p. 10
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	p. 10
Study characteristics	17	Cite each included study and present its characteristics.	Table 1.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	eTable 2, p.7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	eTable 3, p. 11
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pp. 10-11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	eTable 3-4, p. 11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	eTable 4-5, p. 11
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	eTable 7, p. 11-12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	p. 11
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	pp. 11-12
DISCUSSION			

Section and Topic	Item #	Checklist item	Location where item is reported
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	pp. 12-13
	23b	Discuss any limitations of the evidence included in the review.	pp. 13-14
	23c	Discuss any limitations of the review processes used.	pp. 13-14
	23d	Discuss implications of the results for practice, policy, and future research.	p. 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	p. 3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	p. 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	pp. 15-16
Competing interests	26	Declare any competing interests of review authors.	p. 15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

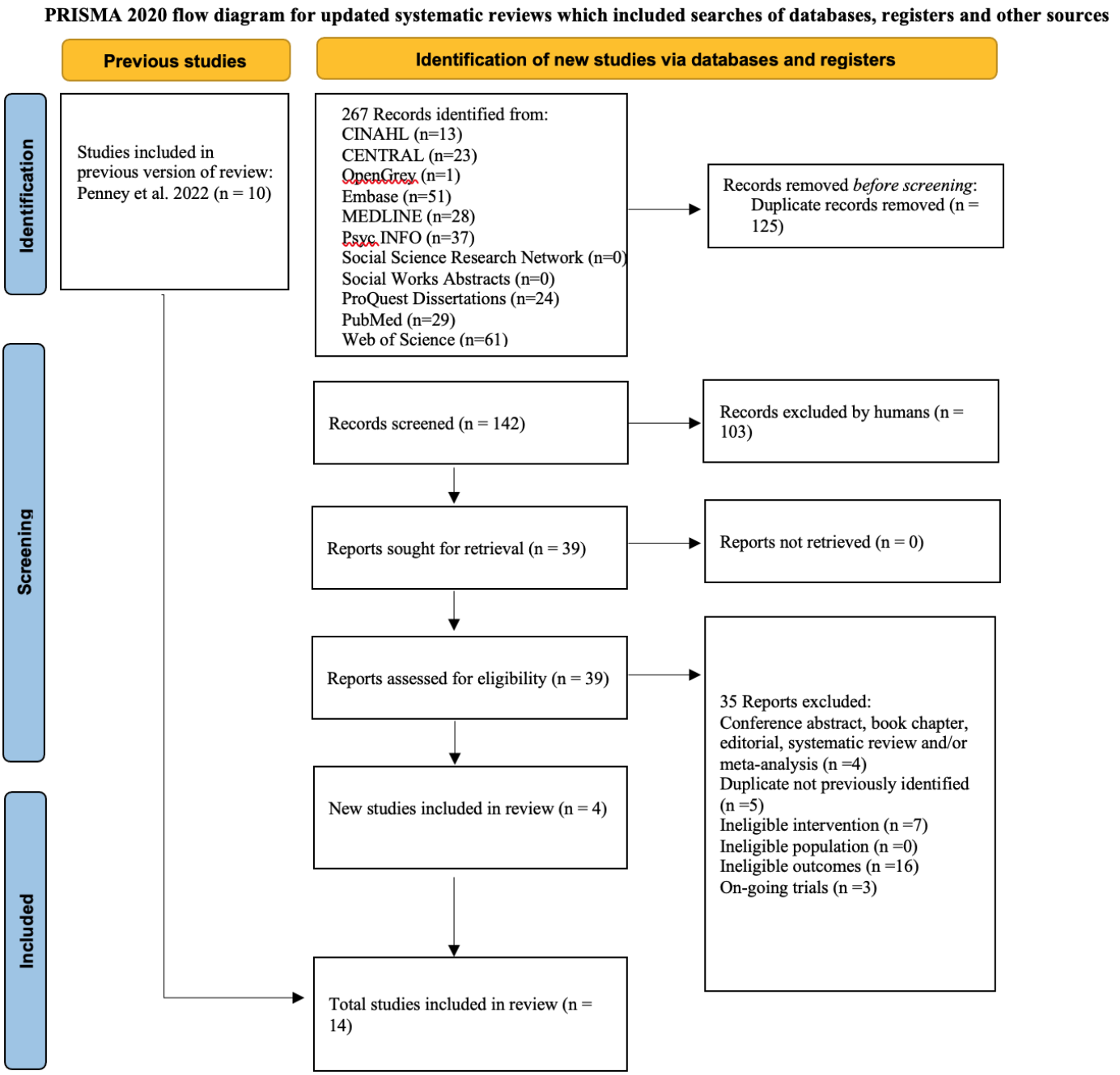
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

eTable 1. Search strategy.

Database	Search
CINAHL	TX ((schizo* or delusion* or psychosis or psychoses or psychotic* or first episode* or first-episode* or fep*)) AND TI ((metacognitive train* or meta-cognitive train*)) OR AB ((metacognitive train* or meta-cognitive train*)) OR TX ((metacognitive train* or meta-cognitive train*)) Results: 13
Cochrane (Central)	"#1 MeSH descriptor (Schizophrenia Spectrum and Other Psychotic Disorders) 20 #2 (schizo* or delusion* or psychosis or psychoses or psychotic* or first episode* or first-episode* or fep*) 39740 #3 (""metacognitive"" NEXT train*) 169 #4 (""meta-cognitive"" NEXT train*) 21 #5 MCT 1368 #6 #1 or #2 39740 #7 #3 or #4 or #5 1428 #8 #6 and #7 with Cochrane Library publication date Between Sep 2021 and Dec 2022 23". Results: 23
OpenGrey	"(schizo* OR delusion* OR psychosis OR psychoses OR psychotic* OR first episode* OR first-episode* OR fep*) AND (((""meta-cognitive"" NEAR train*)OR(""metacognitive"" NEAR train*) OR(MCT))" Results: 1
Embase (Ovid)	"1 exp psychosis/ or exp acute psychosis/ or exp affective psychosis/ or exp brief psychotic disorder/ or exp childhood psychosis/ or exp delusion/ or exp depressive psychosis/ or exp endogenous psychosis/ or exp hallucination/ or exp intensive care psychosis/ or exp manic psychosis/ or exp paranoid psychosis/ or exp puerperal psychosis/ or exp schizophrenia/ 2 (schizo* or delusion* or psychos* or psychotic* or first episode* or first-episode* or fep*).mp. 3 (metacognitive train* or meta-cognitive train*).mp. 4 MCT.mp. 5 1 or 2 6 4 and 5 7 3 or 6. limit 7 to yr=""2021 -Current""" Results: 51
MEDLINE (Ovid)	"exp ""schizophrenia spectrum and other psychotic disorders""/ (schizo* or delusion* or psychos* or psychotic* or first episode* or first-episode* or fep*).tw,kf. (((""metacognitive"" adj train*) or (""meta-cognitive"" adj train*)).mp. MCT.tw,kf. 1 or 2 3 or 4 5 and 6 limit 7 to yr=""2021 -Current""" Results: 28
Psyc INFO Ovid	"1 psychosis/ or exp acute psychosis/ or exp affective psychosis/ or exp childhood psychosis/ or exp chronic psychosis/ or exp ""paranoia (psychosis)""/ or exp schizophrenia/ or exp paranoid schizophrenia/ 2 (schizo* or delusion* or psychos* or psychotic* or first episode* or first-episode* or fep*).mp. 3 (metacognitive train* or meta-cognitive train*).mp. 4 MCT.mp. 5 1 or 2 6 4 and 5 7 3 or 6 Limit 7 to YR= 2021- Current " Results: 37
Social Works Abstracts (Ovid)	"1 (schizo* or delusion* or psychos* or psychotic* or first episode* or first-episode* or fep*).mp. 2 (metacognitive train* or meta-cognitive train*).mp. 3 MCT.mp. 4 1 and 3 5 2 or 4 6 limit 5 to yr=""2021 -Current""" Results: 0
ProQuest Dissertations	(schizo* OR delusion* OR psychosis OR psychoses OR psychotic* OR first episode* OR first-episode* OR fep*) AND (("meta-cognitive training") OR ("metacognitive training ")) Results: 24
PubMed	((("Schizophrenia Spectrum and Other Psychotic Disorders"[Mesh]) OR (schizo* or delusion* or psychosis or psychoses or psychotic* or first episode* or first-episode* or fep)) AND ((("metacognitive" train*) OR ("meta-cognitive" train*) OR (MCT))) AND (("2021/09/01"[Date - Publication] : "3000"[Date - Publication])) Results: 29

Web of Science	"ALL=(schizo* or delusion* OR psychosis OR psychoses OR psychotic* OR first episode* OR first-episode* OR fep*) AND TS=((""metacognitive"" NEAR train*) OR (""meta-cognitive"" NEAR train*) OR (MCT)) AND PY=(2007-2021) TOPIC: (schizophrenia spectrum disorders) OR ALL FIELDS: ((schizo* or delusion* OR psychosis OR psychoses OR psychotic* OR first episode* OR first-episode* OR fep*)) AND ALL FIELDS: ((metacognitive train* OR meta-cognitive train* OR MCT)) AND YEAR PUBLISHED: (2021-2023) Results: 60" Results: 61



eFig. 1. Stand-alone version of search update, PRISMA flowchart for systematic reviews and meta-analyses (2020).

eTable 2. Quality assessment ratings of included studies using the Mixed Methods Appraisal Tool (MMAT).

FIRST AUTHOR	YEAR	STUDY DESIGN	1. SCREENING QUESTIONS		2. RANDOMIZED CONTROLLED TRIALS					3. NON-RANDOMIZED STUDIES					MMAT SCORE
			1.1 Are there clear research questions?	1.2. Do the collected data allow to address the research questions?	2.1. Is randomization appropriately performed?	2.2. Are the groups comparable at baseline?	2.3. Are there complete outcome data?	2.4. Are outcome assessors blinded to the intervention provided?	2.5 Did the participants adhere to the assigned intervention?	3.1. Are the participants representative of the target population?	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	3.3. Are there complete outcome data?	3.4. Are the confounders accounted for in the design and analysis?	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?	
Balzan	2019	RCT	yes	yes	yes	no	yes	no	yes						3
Fujii	2021	RCT	yes	yes	yes	yes	no	no	no						2
Gaweda	2015	RCT	yes	yes	yes	yes	yes	no	yes						4
Moritz	2013	RCT	yes	yes	no	yes	yes	yes	yes						4
Moritz	2011	RCT	yes	yes	yes	yes	yes	yes	yes						5
Shan	2021	RCT	yes	yes	yes	yes	yes	yes	yes						5
Yildiz	2019	RCT	yes	yes	no	yes	yes	yes	yes						4
Fekete	2021	RCT	yes	yes	yes	yes	no	yes	yes						4
Ruiz-Delgado	2022	RCT	yes	yes	yes	yes	no	yes	yes						4
Wang	2022	RCT	yes	yes	yes	yes	yes	yes	yes						5
Haga	2022	RCT	yes	yes	yes	yes	no	no	yes						3
Mendelson	2022	Non-RCT	yes	yes						yes	yes	no	no	yes	3

eTable 3. Neurocognition results.

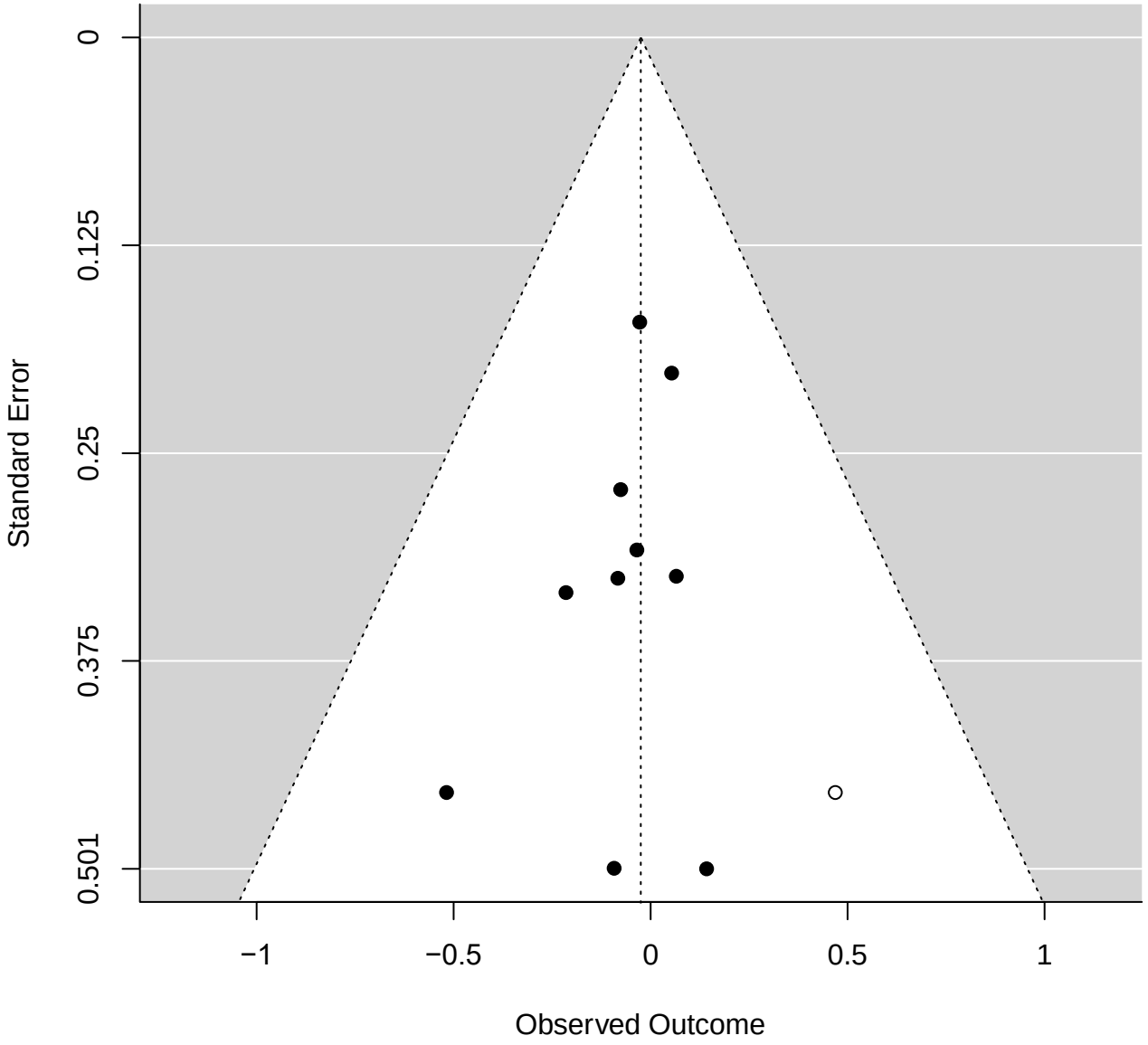
Comparison	Neurocognitive Domain	Number of Studies	Effect Size (*g*)	Lower 95% CI	Upper 95% CI	*p*-value
Pre–Post	Processing Speed	10	-0.04	-0.22	0.13	0.63
Pre–Post	Working Memory	9	0.06	−0.14	0.26	0.55
Pre–Post	Attention and Vigilance	7	0	−0.20	0.2	0.98
Pre–Post	Verbal Learning and Memory	10	0.03	−0.15	0.22	0.71
Pre–Post	Visual Learning and Memory	3	0.09	−0.20	0.39	0.54
Pre–Post	Reasoning and Problem Solving	11	0.02	−0.16	0.19	0.85
Post–Follow-Up	Processing Speed	4	−0.03	−0.25	0.2	0.82
Post–Follow-Up	Working Memory	4	−0.06	−0.30	0.19	0.64
Post–Follow-Up	Attention and Vigilance	3	−0.00	−0.25	0.25	0.99
Post–Follow-Up	Verbal Learning and Memory	4	0.09	−0.14	0.32	0.43
Post–Follow-Up	Visual Learning and Memory	2	0.01	−0.34	0.37	0.95
Post–Follow-Up	Reasoning and Problem Solving	4	0.09	−0.15	0.32	0.47

eTable 4. Heterogeneity assessment by neurocognitive domain and timepoint comparison.

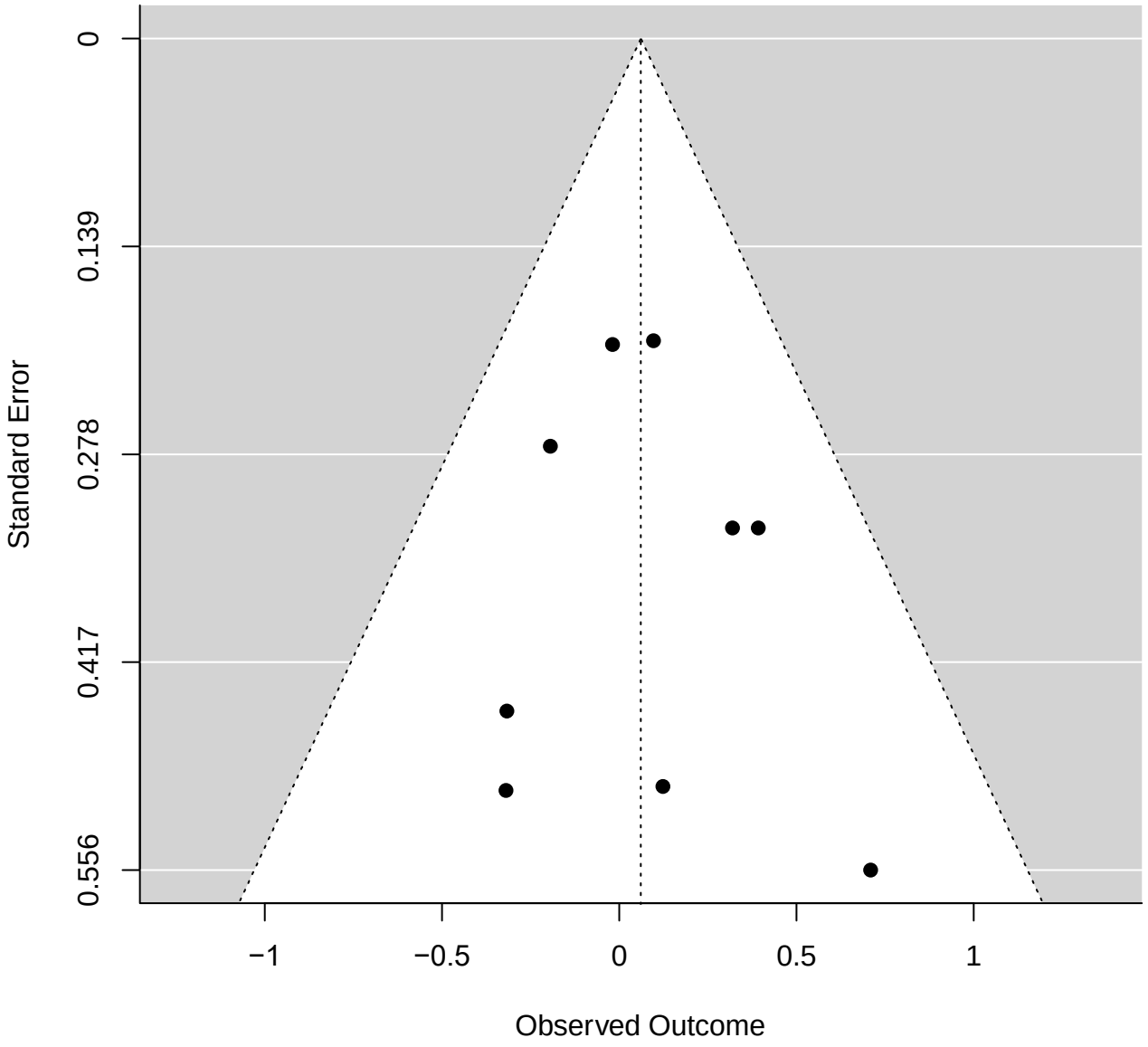
Comparison	Outcome	Number of Studies	*Q*-value	df	*p*-value	I^2
Pre–Post	Processing Speed	10	1.88	9	0.99	0.00
Pre–Post	Working Memory	9	5.35	8	0.72	0.00
Pre–Post	Attention and Vigilance	7	0.50	6	1.00	0.00
Pre–Post	Verbal Learning and Memory	10	6.11	9	0.73	0.00
Pre–Post	Visual Learning and Memory	3	0.68	2	0.71	0.00
Pre–Post	Reasoning and Problem Solving	11	8.88	10	0.54	0.00
Post–Follow-Up	Processing Speed	4	0.60	3	0.90	0.00
Post–Follow-Up	Working Memory	4	1.50	3	0.68	0.00
Post–Follow-Up	Attention and Vigilance	3	0.07	2	0.97	0.00
Post–Follow-Up	Verbal Learning and Memory	4	0.32	3	0.96	0.00
Post–Follow-Up	Visual Learning and Memory	2	0.82	1	0.37	0.00
Post–Follow-Up	Reasoning and Problem Solving	4	1.38	3	0.71	0.00

eTable 5. Rosenthal's fail-safe N and funnel plot asymmetry (Egger) tests for pre–post outcomes.

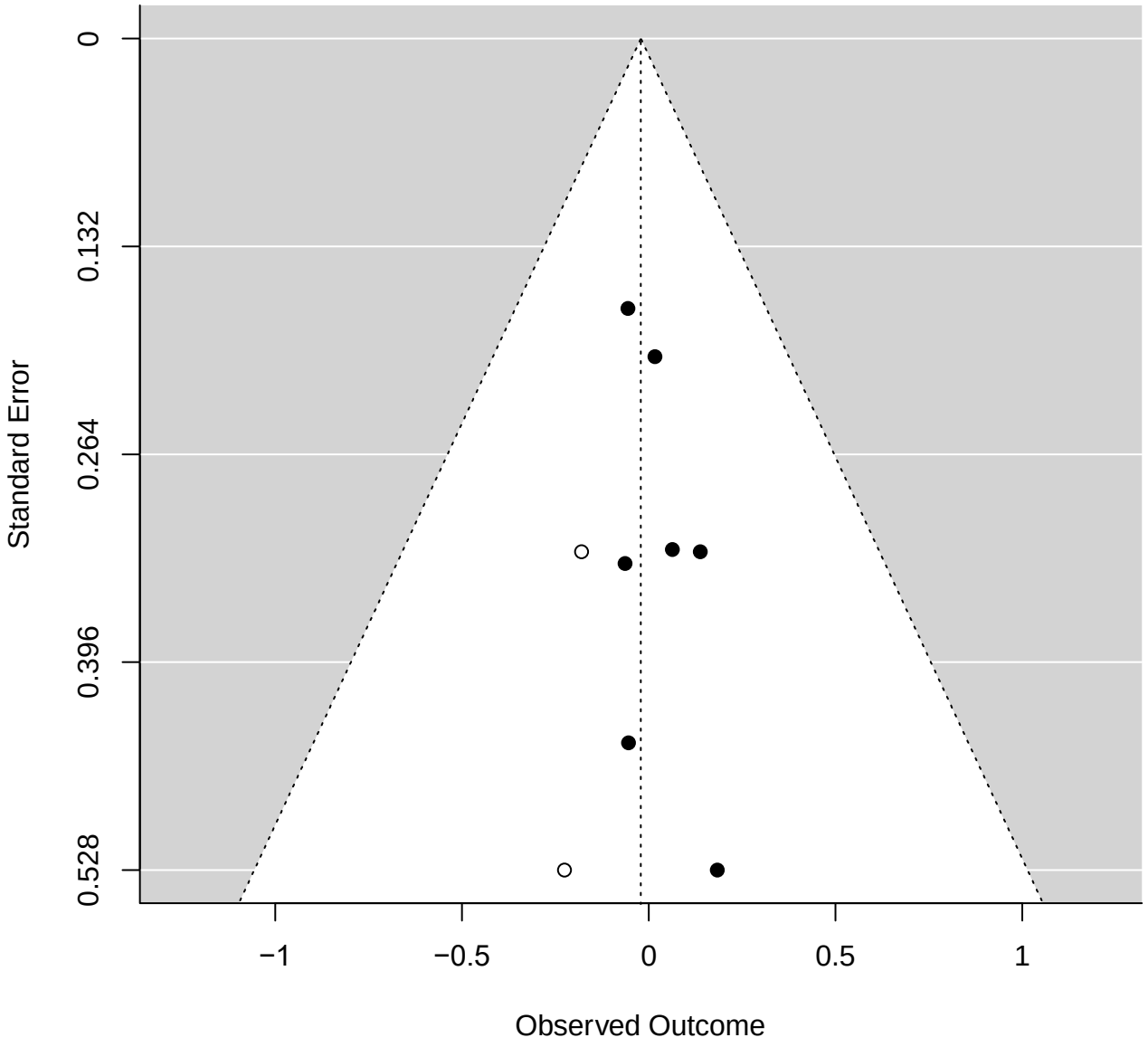
Outcome	Fail-Safe N	Intercept (*b*)	*t*-statistic	df	Lower 95% CI	Upper 95% CI	*p*-value
Processing Speed	0.00	0.09	-1.20	8	-0.18	0.36	0.26
Working Memory	0.00	-0.03	0.38	7	-0.62	0.57	0.72
Attention and Vigilance	0.00	-0.10	1.38	5	-0.29	0.10	0.23
Verbal Learning and Memory	0.00	-0.26	1.62	8	-0.70	0.19	0.14
Visual Learning and Memory	0.00	0.47	-1.02	1	-4.34	5.29	0.49
Reasoning and Problem Solving	0.00	-0.05	0.28	9	-0.61	0.52	0.79



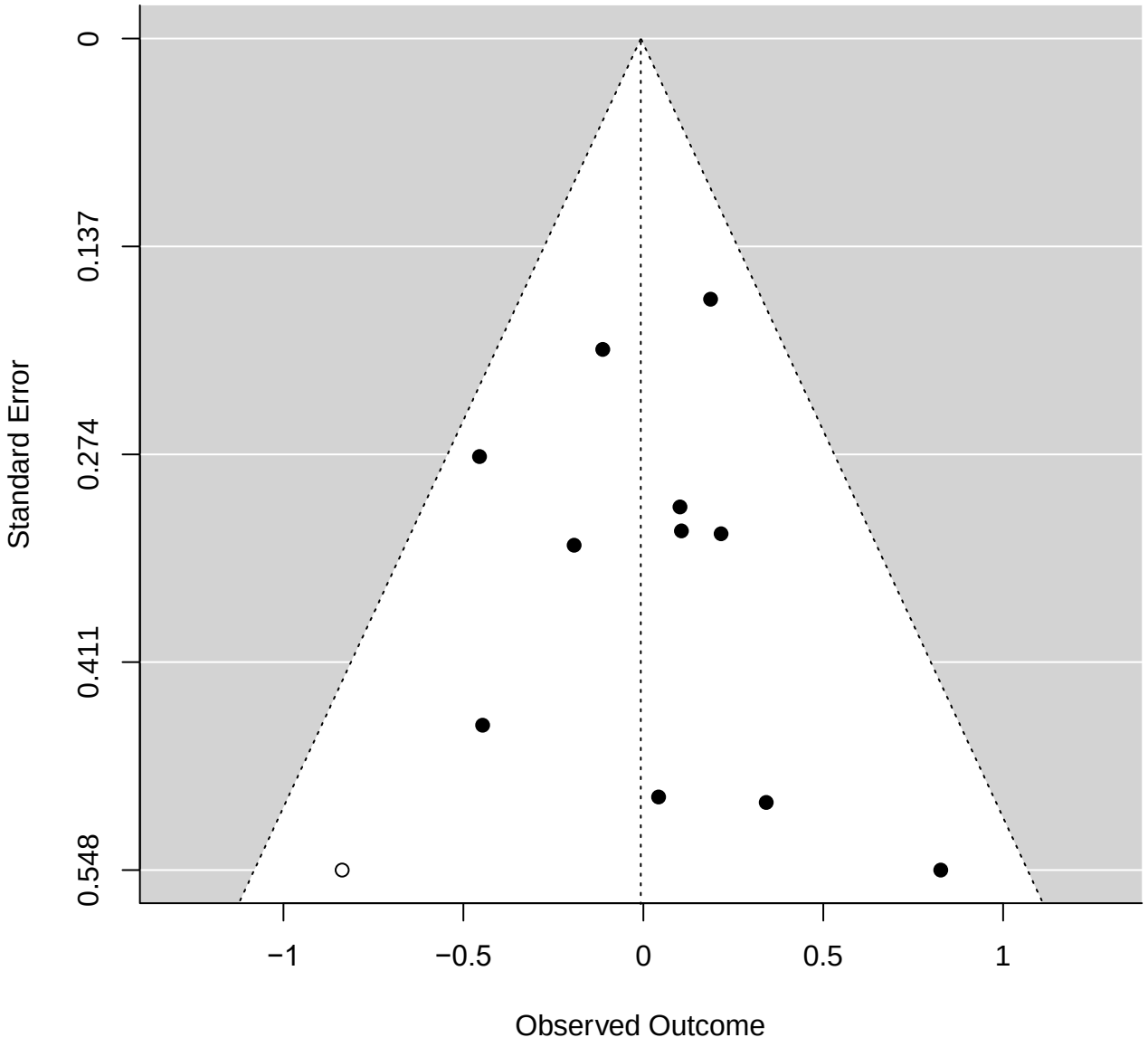
eFig. 2.1. Funnel plot of processing speed for pre–post comparison.



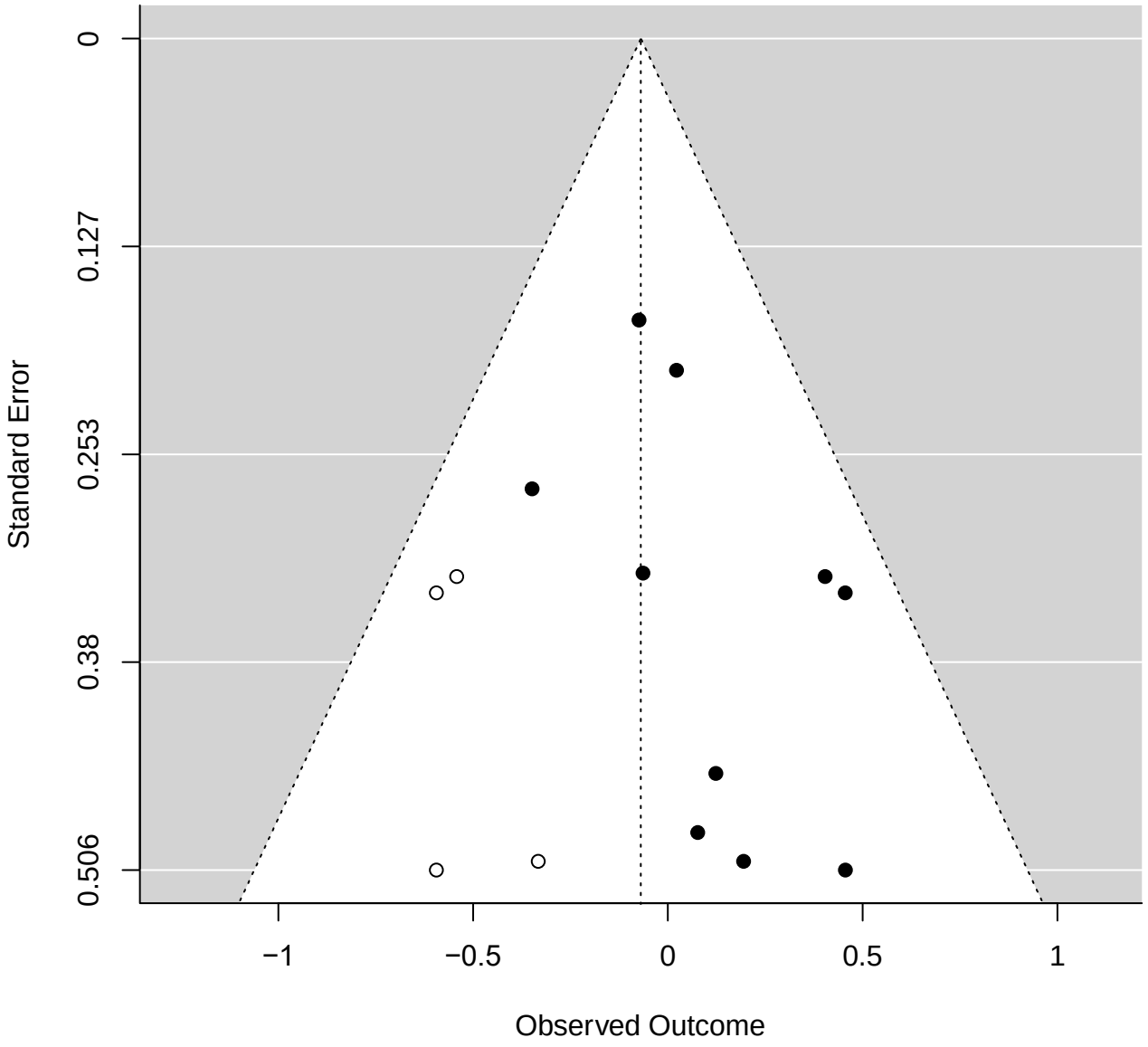
eFig. 2.2. Funnel plot of working memory for pre–post comparison.



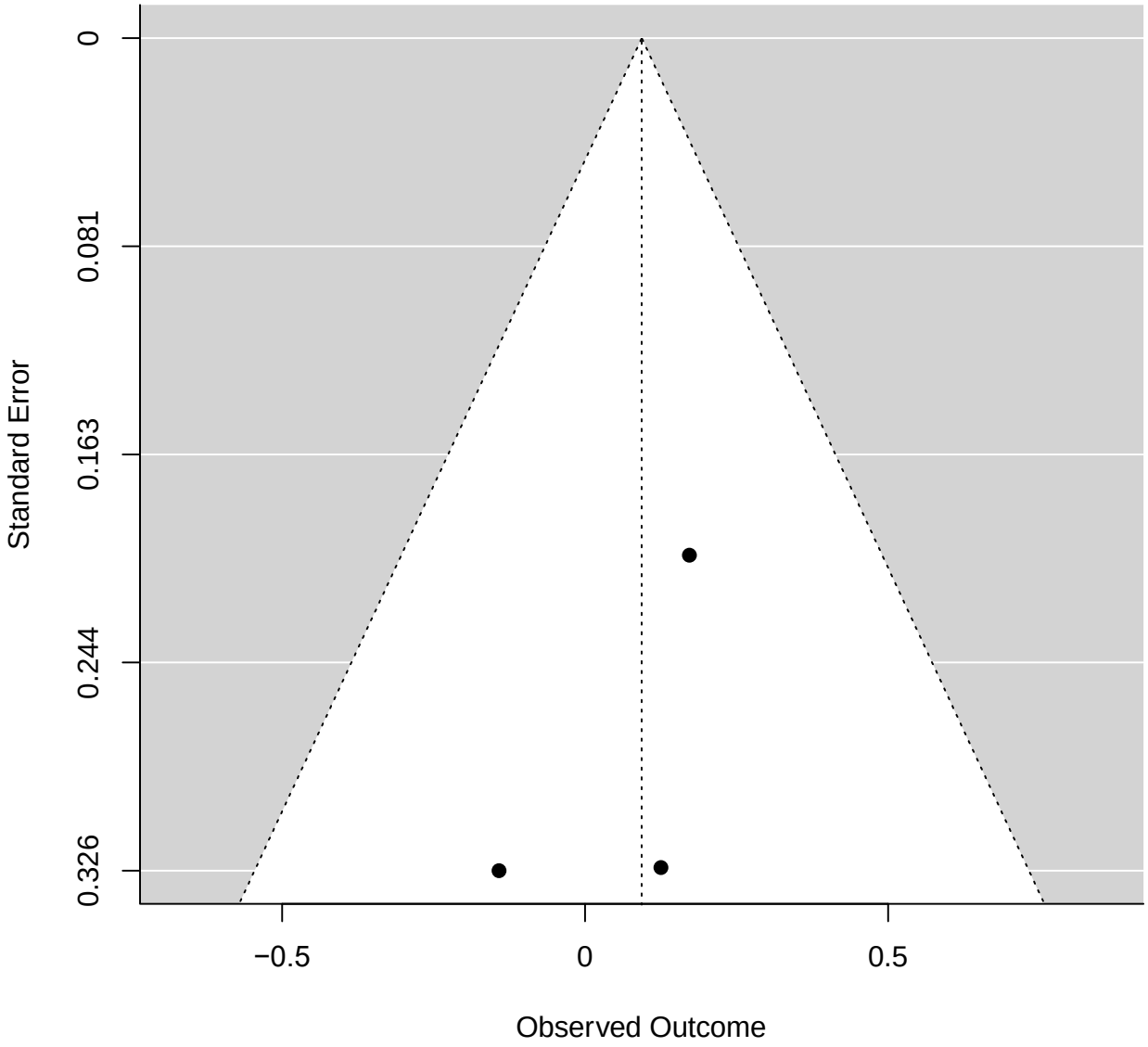
eFig. 2.3. Funnel plot of attention and vigilance for pre–post comparison.



eFig. 2.4. Funnel plot of reasoning and problem solving for pre–post comparison.



eFig. 2.5. Funnel plot of verbal learning and memory for pre–post comparison.



eFig. 2.6. Funnel plot of visual learning and memory for pre–post comparison.

eTable 6. Moderator analysis of subgroup differences in comparison group (passive and active).

Comparison	Outcome	Number of Studies (Passive: Active)	$Q_{between}$-statistic	*p*-value
Pre–Post	Processing Speed	10 (6:4)	0.04	0.84
Pre–Post	Working Memory	9 (4:5)	0.17	0.68
Pre–Post	Attention and Vigilance	7 (3:4)	0.05	0.83
Pre–Post	Verbal Learning and Memory	10 (5:5)	0.78	0.38
Pre–Post	Visual Learning and Memory	3 (2:1)	0.01	0.91
Pre–Post	Reasoning and Problem Solving	11 (5:6)	0.20	0.66
Post–Follow-Up	Processing Speed	4 (2:2)	0.01	0.91
Post–Follow-Up	Working Memory	4 (2:2)	0.00	0.98
Post–Follow-Up	Attention and Vigilance	3 (2:1)	0.00	0.98
Post–Follow-Up	Verbal Learning and Memory	4 (2:2)	0.25	0.62
Post–Follow-Up	Visual Learning and Memory	1 (1:0)	0.00	1.00
Post–Follow-Up	Reasoning and Problem Solving	4 (1:3)	0.40	0.53

eTable 7. Sensitivity analysis of neurocognition results.

Comparison	Neurocognitive Domain	Number of Studies	Estimated Effect Size (*g*)	Lower 95% CI	Upper 95% CI	*p*-value
Pre–Post	Processing Speed	8	−0.05	−0.27	0.18	0.69
Pre–Post	Working Memory	7	0.08	−0.14	0.3	0.49
Pre–Post	Attention and Vigilance	5	0.03	−0.23	0.28	0.85
Pre–Post	Verbal Learning and Memory	7	0.17	−0.08	0.41	0.18
Pre–Post	Visual Learning and Memory	3	0.09	−0.20	0.39	0.54
Pre–Post	Reasoning and Problem Solving	8	−0.01	−0.24	0.21	0.91
Post–Follow-Up	Processing Speed	2	−0.04	−0.40	0.31	0.82
Post–Follow-Up	Working Memory	3	−0.11	−0.38	0.17	0.45
Post–Follow-Up	Attention and Vigilance	2	−0.01	−0.36	0.35	0.97
Post–Follow-Up	Verbal Learning and Memory	2	0.02	−0.33	0.38	0.91
Post–Follow-Up	Visual Learning and Memory	2	0.01	−0.34	0.37	0.95
Post–Follow-Up	Reasoning and Problem Solving	2	0.13	−0.24	0.51	0.49

eTable 8. List of excluded studies and ongoing trials.

First Author	Year/Trial #	Title	Exclusion Reasoning/Link to Protocol
So	2021/NCT03449394	A randomised controlled trial of metacognitive training for psychosis, depression, and belief flexibility	Only collected neurocognitive data at baseline; https://clinicaltrials.gov/study/NCT03449394
Ochoa	2022/NCT05455593	Effectiveness of the Combination of Water Aerobics and Metacognitive Training	Mixed intervention, ongoing clinical trial; https://clinicaltrials.gov/show/NCT05455593
Ochoa	2022/NCT05358457	Pilot Study to Evaluate the Effectiveness of Online Familiar Metacognitive Training (MCTf)	Mixed intervention, ongoing clinical trial; https://clinicaltrials.gov/show/NCT05358457
Fekete	2022	Basic demographic outcomes: additional findings of a single-blind, randomised, controlled trial on metacognitive training for psychosis	Only collected neurocognitive data at baseline.
González-Blanch	2021	Moderators of cognitive insight outcome in metacognitive training for first-episode psychosis	Only collected neurocognitive data at baseline.
Lopez-Morinigo	2022/NCT04104347	Investigating the Contribution of Decision-Making, Cognitive Insight, and Theory of Mind in Insight in Schizophrenia: A Cross-Sectional Study	Only collected neurocognitive data at baseline; https://clinicaltrials.gov/ct2/show/NCT04104347
Kim	2022	Effectiveness of group metacognitive training and cognitive-behavioural therapy in a transdiagnostic manner for young patients with psychotic and non-psychotic disorders	Mixed intervention, no control group.

eTable 9. Preliminary analyses: neurocognition results (no comparator group).

Comparison	Neurocognitive Domain	Number of Studies	Effect Size (*g*)	Lower 95% CI	Upper 95% CI	*p*-value
		MCT				
Pre–Post	Processing Speed	10	0.33	0.08	0.58	0.01
Pre–Post	Working Memory	9	0.50	0.10	0.90	0.01
Pre–Post	Attention and Vigilance	7	0.37	0.11	0.63	0.00
Pre–Post	Verbal Learning and Memory	10	0.48	0.16	0.79	0.00
Pre–Post	Visual Learning and Memory	3	0.71	0.00	1.41	0.05
Pre–Post	Reasoning and Problem Solving	11	0.33	0.12	0.53	0.00
		Control				
Pre–Post	Processing Speed	10	0.33	0.14	0.51	0.00
Pre–Post	Working Memory	9	0.29	0.03	0.55	0.03
Pre–Post	Attention and Vigilance	7	0.45	0.07	0.84	0.02
Pre–Post	Verbal Learning and Memory	10	0.43	0.18	0.68	0.00
Pre–Post	Visual Learning and Memory	3	0.63	0.08	1.34	0.08
Pre–Post	Reasoning and Problem Solving	11	0.30	0.01	0.58	0.04

eTable 10. Preliminary analyses: heterogeneity assessment by neurocognitive domain (no comparator group).

Comparison	Outcome	Number of Studies	*Q*-value	df	*p*-value	I^2
		MCT				
Pre–Post	Processing Speed	10	15.78	9	0.07	41.90
Pre–Post	Working Memory	9	25.04	8	0.00	72.88
Pre–Post	Attention and Vigilance	7	10.95	6	0.09	33.95
Pre–Post	Verbal Learning and Memory	10	21.15	9	0.01	61.62
Pre–Post	Visual Learning and Memory	3	8.43	2	0.01	79.29
Pre–Post	Reasoning and Problem Solving	11	14.17	10	0.17	27.09
		Control				
Pre–Post	Processing Speed	10	8.32	9	0.50	3.79
Pre–Post	Working Memory	9	12.20	8	0.14	33.32
Pre–Post	Attention and Vigilance	7	15.46	6	0.02	66.69
Pre–Post	Verbal Learning and Memory	10	14.00	9	0.12	37.31
Pre–Post	Visual Learning and Memory	3	9.33	2	0.01	78.60
Pre–Post	Reasoning and Problem Solving	11	21.32	10	0.02	55.33

eTable 11. Preliminary analyses: Rosenthal's fail-safe N and funnel plot asymmetry (Egger) tests for pre–post outcomes (no comparator group).

Outcome	Fail-Safe N	Intercept (*b*)	*t*-statistic	df	Lower 95% CI	Upper 95% CI	*p*-value
			MCT				
Processing Speed	36	0.0955	0.6369	8	-0.7145	0.9054	0.542
Working Memory	53	-0.3299	1.5995	7	-1.4143	0.7544	0.1537
Attention and Vigilance	32	-0.2669	2.0634	5	-1.0561	0.5223	0.094
Verbal Learning and Memory	75	0.1217	0.8216	8	-0.7854	1.0287	0.4351
Visual Learning and Memory	16	-0.9419	1.6869	1	-12.5249	10.6412	0.3407
Reasoning and Problem Solving	50	-0.0717	1.4436	9	-0.6923	0.5489	0.1827
			Control				
Processing Speed	43	0.0325	1.2664	8	-0.5368	0.6018	0.241
Working Memory	17	-0.0458	0.8565	7	-0.9399	0.8483	0.42
Attention and Vigilance	33	-0.1481	1.2063	5	-1.3031	1.0068	0.2817
Verbal Learning and Memory	56	0.5579	-0.37	8	-0.2395	1.3553	0.721
Visual Learning and Memory	11	-1.0991	1.7326	1	-12.8972	10.699	0.3333
Reasoning and Problem Solving	28	0.1622	0.3139	9	-0.7232	1.0477	0.7607

eAppendix 2. References of Studies Included in the Systematic Review and Meta-Analysis, and Narrative Review.

Balzan, R. P., Mattiske, J. K., Delfabbro, P., Liu, D., & Galletly, C. (2019). Individualized Metacognitive Training (MCT+) Reduces Delusional Symptoms in Psychosis: A Randomized Clinical Trial. *Schizophr Bull, 45*(1), 27-36. doi:10.1093/schbul/sby152

Fekete, Z.-.-V., Edit-//-Balajthy, Ramóna-//-Tana, Ünige-//-Nagy, Attila Csaba-//-Oláh, Barnabás-//-Domján, Nóra-//-Kuritárné, Ildikó Szabó. (2022). Efficacy of metacognitive training on symptom severity, neurocognition and social cognition in patients with schizophrenia: A single-blind randomized controlled trial. *Scandinavian Journal of Psychology, 63*(4), 321-333. doi:10.1111/sjop.12811

Fujii, K., Kobayashi, M., Funasaka, K., Kurokawa, S., & Hamagami, K. (2021). Effectiveness of Metacognitive Training for Long-Term Hospitalized Patients with Schizophrenia: A Pilot Study with a Crossover Design. *Asian Journal of Occupational Therapy, 17*(1), 45-52. doi:10.11596/asiajot.17.45

Gaweda, L., Krezolek, M., Olbrys, J., Turska, A., & Kokoszka, A. (2015). Decreasing self-reported cognitive biases and increasing clinical insight through meta-cognitive training in patients with chronic schizophrenia. *J Behav Ther Exp Psychiatry, 48*, 98-104. doi:10.1016/j.jbtep.2015.02.002

Haga, S.-.-K., Masayoshi-//-Takehara, Ayako-//-Kawano, Kojiro-//-Endo, Kenji. (2022). Efficacy of Metacognitive Training for Patients With Schizophrenia in Psychiatric Emergency Wards: A Pilot Randomized Controlled Trial. *Frontiers in psychology, 13*, 861102. doi:https://dx.doi.org/10.3389/fpsyg.2022.861102

Mendelson, D.-.-T., E.-//-Sauve, G.-//-Lavigne, K. M.-//-Bowie, C. R.-//-Menon, M.-//-Woodward, T. S.-//-Lepage, M.-//-Raucher-Chene, D. (2022). Remote group therapies for cognitive health in schizophrenia-spectrum disorders: Feasible, acceptable, engaging. *Schizophrenia Research: Cognition, 28*, 100230. doi:https://dx.doi.org/10.1016/j.scog.2021.100230

Moritz, S., Kerstan, A., Veckenstedt, R., Randjbar, S., Vitzthum, F., Schmidt, C., . . . Woodward, T. S. (2011). Further evidence for the efficacy of a metacognitive group training in schizophrenia. *Behav Res Ther, 49*(3), 151-157. doi:10.1016/j.brat.2010.11.010

Moritz, S., Veckenstedt, R., Bohn, F., Hottenrott, B., Scheu, F., Randjbar, S., . . . Roesch-Ely, D. (2013). Complementary group Metacognitive Training (MCT) reduces delusional ideation in schizophrenia. *Schizophr Res, 151*(1-3), 61-69. doi:10.1016/j.schres.2013.10.007

Moritz, S., Veckenstedt, R., Andreou, C., Bohn, F., Hottenrott, B., Leighton, L., . . . Roesch-Ely, D. (2014). Sustained and "sleeper" effects of group metacognitive training for schizophrenia: a randomized clinical trial. *JAMA Psychiatry, 71*(10), 1103-1111. doi:10.1001/jamapsychiatry.2014.1038

Ruiz-Delgado, I.-.-M.-K., Berta-//-Garcia-Medina, Monica-//-Barrigon, Maria Luisa-//-Gonzalez-Higueras, Fermin-//-Lopez-Carrilero, Raquel-//-Barrios-Mellado, Irene-//-Barajas, Ana-//-Pousa, Esther-//-Lorente-Rovira, Esther-//-Grasa, Eva-//-Cid, Jordi-//-Barrau-Sastre, Paula-//-Moritz, Steffen-//-Ochoa, Susana-//-Spanish Metacognition, Group. (2022). Is Metacognitive Training effective for improving neurocognitive function in patients with a recent onset of psychosis? *Psychiatry Research, 318*, 114941. doi:https://dx.doi.org/10.1016/j.psychres.2022.114941

Shan, X. X.-.-L., R. Y.-//-Ou, Y. P.-//-Pan, P.-//-Ding, Y. D.-//-Liu, F.-//-Chen, J. D.-//-Zhao, J. P.-//-Guo, W. B.-//-He, Y. Q. (2021). Increased regional homogeneity modulated by metacognitive training predicts therapeutic efficacy in patients with schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience, 271*(4), 783-798. doi:10.1007/s00406-020-01119-w

Ussorio, D., Giusti, L., Wittekind, C. E., Bianchini, V., Malavolta, M., Pollice, R., . . . Roncone, R. (2016). Metacognitive training for young subjects (MCT young version) in the early stages of psychosis: Is the duration of untreated psychosis a limiting factor? *Psychol Psychother, 89*(1), 50-65. doi:10.1111/papt.12059

Wang, C.-.-C., Y.-//-Zhang, J. C.-//-Cao, Y. L.-//-Wang, Y. B. (2022). The Efficacy of Extended Metacognitive Training on Neurocognitive Function in Schizophrenia: A Randomized Controlled Trial. *Brain sciences, 12*(3). doi:10.3390/brainsci12030413

Yildiz, M., Ozaslan, Z., Incedere, A., Kircali, A., Kiras, F., & Ipci, K. (2019). The Effect of Psychosocial Skills Training and Metacognitive Training on Social and Cognitive Functioning in Schizophrenia. *Noro Psikiyatr Ars, 56*(2), 139-143. doi:10.29399/npa.23095

CHAPTER 3: Comprehensive Discussion

Strengths

This project set out to determine the extent to which neurocognition is uniquely impacted by MCT in psychosis. This thesis has comprehensively synthesized the literature from existing datasets that met our inclusion criteria and could adequately compare MCT against a breadth of control comparator interventions to evaluate its impact on neurocognitive performance. Through a methodologically rigorous approach, this project effectively addressed the research question. It relied on an established pipeline based on the framework of two previous meta-analyses within our research group (Hotte-Meunier et al., 2023; Penney et al., 2022) that considered this dataset. This approach helped shed light on the potential added value (or lack thereof) of MCT as a cognitive intervention to improve neurocognitive functioning in psychosis. The alternative hypothesis posited that MCT would present a unique benefit to neurocognitive performance, and that this true effect would be independent of practice effects when compared against control interventions. However, the findings of this systematic review and meta-analysis demonstrate no such relationship between MCT and neurocognition. Rather, the negative findings observed of MCT across all six MATRICS neurocognitive domains when compared to control interventions were robust against sensitivity and moderator analyses. This provides substantial confidence to conclude that this intervention while having multiple well-documented benefits, is not uniquely suited to restore/improve neurocognitive performance in psychosis compared to the passive and active control interventions that were evaluated. This valuably contributes to the growing field of research on MCT, and of particular importance has clinical relevance as this informs clinicians of MCT's specificity as a cognitive intervention for psychosis. If remediating neurocognitive deficits is a priority area for treatment, then other psychosocial interventions such as CR, which

directly target neurocognition and have been rigorously studied to demonstrate clear benefits to neurocognitive performance, should be considered (Vita et al., 2021).

Limitations

This systematic review and meta-analysis primarily include data from shorter durations between initial and post-assessment, focusing on the immediate effects of MCT on neurocognition. Similar to the limitations identified in a recent meta-analysis on neurocognitive performance in first-episode psychosis (Catalan et al., 2024), the likelihood of practice effects existing in a dataset is greatest in short-term retesting comparisons. This complicates determining whether a true effect exists, as it may be obscured by the magnitude of practice effects. It is reassuring that the same negative findings, suggesting a general practice effect on changes in neurocognitive performance from pre- to post-assessments, were also observed in our limited comparisons of maintenance effects from post- to follow-up assessments. However, in ideal circumstances we would have liked for our dataset to consist of more long-term data, from at least one-year follow-up or even longer, so the scarcity of available long-term data is noted as a limitation of the current work. Unlike Catalan et al. (2024), we did not observe different levels of consistency in neurocognitive areas affected by practice effects. Instead, we found consistent negative relationships across all neurocognitive domains from pre–post comparisons, enhancing confidence in the validity of our negative findings.

Criticism may be drawn to the variance in the number of studies included in the examination of individual neurocognitive domains between pre–post assessment, and of course in the post–follow-up comparisons that had even fewer studies to draw data from. Of the 12 studies included in the meta-analyses of the pre–post data, there were as many as 11 studies incorporated into the domain of reasoning and problem solving, 10 each for both processing

speed and verbal learning and memory, 9 for working memory, 7 for attention and vigilance, and as few as 3 to inform our understanding of MCT's impact on visual learning and memory. When considering the certainty of the evidence from a power perspective for the pre–post comparisons that demonstrate the immediate effects of MCT on neurocognitive performance, different levels of confidence should be attributed to various meta-analyses. Less confidence should be placed on meta-analyses for neurocognitive domains like visual learning and memory, which pool fewer studies. In contrast, greater confidence should be placed on meta-analyses for domains like reasoning and problem solving, which draw from a larger pool of individual studies. This issue is exacerbated when considering the comparatively underpowered pre–follow-up data assessed to understand maintenance effects of MCT on neurocognitive performance. At most, 4 individual studies included data at one-year post-assessment for reasoning and problem solving, verbal learning and memory, working memory and processing speed. 3 studies were included for attention and vigilance, and 1 study was examined for visual learning and memory. Therefore, low confidence can be attributed to these long-term negative findings, particularly for the neurocognitive domain of visual learning and memory. For these reasons, the post–follow-up meta-analyses of the maintenance effects are not the primary focus of this thesis and are considered complementary analyses that bolster the validity of the pre–post comparisons for immediate effects.

Recognizing the overall concerns about the relatively small number of studies that constitute this work, these negative findings, and their implications are limited. Future analyses that draw a greater pool of individual studies would provide greater certainty as to the true effects (or lack thereof) of MCT on neurocognitive performance. Although the lack of a power analyses might be considered a limitation to the current work, we have rationalized that post-hoc

power analyses would not be informative or useful in the context of this study. Such analyses have been considered to be conceptually flawed and misleading from an analytical perspective (Heckman et al., 2022; Zhang et al., 2019). Furthermore, since we have demonstrated negative findings, any post-hoc power calculations would be considered insufficient by definition (Hoenig et al., 2001).

Implications

MCT is an intervention that is chiefly focused on addressing cognitive biases through metacognitive processes rather than drawing explicit attention to improving accuracy in neurocognitive exercises/tests. We originally hypothesized that improving metacognitive functioning by alleviating cognitive biases would have a top-down effect on neurocognitive functioning. However, the conclusions drawn from the negative findings observed do not support this model. It could be extrapolated that these findings do support the notion that cognitive deficits and cognitive biases are independent components in the picture of cognitive health in psychosis. This underscores the value of considering both these aspects of cognitive health: cognitive distortions (i.e. cognitive biases) and cognitive deficits (i.e. neurocognition). When addressing the latter category of cognitive deficits, cognitive interventions that have been developed to target neurocognitive domains and increase accuracy in performance such as CR should be prioritized compared to MCT. Complementary approaches that address both sides of this cognitive coin may offer broader benefits that encapsulate a breadth of perspectives on cognitive health. For example, the non-randomized concurrent control designed iCog CA project, (Au-Yeung et al., 2024) provides opportunities to engage in both MCT and action-based cognitive remediation– a form of CR that is particularly focused on extrapolating neurocognitive gains into real-world scenarios (Bowie et al., 2017). Considering the mediating role that

metacognition has been theorized to play between neurocognition and functional outcome (Wright et al., 2020), such complementary approaches may also provide benefits to the real-world applicability of the skills learned and recovery made in these interventions.

Is there a spectrum of higher versus lower-level neurocognitive domains that may be more or less likely impacted by MCT? If this were the case, we would expect to have seen domain-specific differences in the current review, which were not demonstrated. However, considering a recent meta-analysis that demonstrated small positive effects for social cognition, this question may warrant more attention. Social cognition is itself considered a MATRICS domain, although it was not examined in the current study because a recent meta-analysis had already synthesized this literature and found small benefits as a consequence of engaging in MCT (Hotte-Meunier et al., 2023). The negative findings of the current review for the other six MATRICS domains indicate that social cognition is unique from the other neurocognitive domains in its response to MCT. This may be because social cognition incorporates higher-level processes that are more consciously influenced by a focus on cognitive biases and metacognitive processes. Following this reasoning, a range of neurocognitive domains may be expected to be more or less influenced by metacognitive processes. For example, one may expect reasoning and problem solving– a relatively higher-level neurocognitive domain– to be differentially impacted by addressing metacognition compared to a lower-level neurocognitive domain such as processing speed. However, in the current study, no such relationships were demonstrated. Another argument is that core and additional MCT modules focus directly on social cognition, presumably amplifying benefits in this domain compared to the hypothesized indirect effects on other neurocognitive domains that were studied in this work.

Future directions

In this study, the included population consisted of a range of presentations across the psychosis spectrum, including those experiencing a first episode of psychosis, those diagnosed with chronic schizophrenia, individuals with schizoaffective disorder, and other psychotic disorders. Future work may wish to investigate presentation-specific differences on the relationship between MCT and neurocognitive performance. For example, delineating MCT's neurocognitive efficacy between affective and non-affective psychosis may answer interesting research questions about the nature of one's ability to incorporate metacognitive gains to neurocognitive performance in psychosis. An argument may be made that cognitive capacity could differ between such presentations, which was not examined in the current work.

Another area of interest to the current work could be examining neurocognitive batteries that are sensitive to practice/learning effects when evaluating the impact of MCT on neurocognition in psychosis. Three strategies have been suggested by Goldberg and colleagues (2015) to attenuate practice effects in serial testing circumstances. One strategy is to incorporate mass practice at a pre-baseline timepoint to reduce effects of familiarity with task question/instruction comprehension, simple strategies, and stimulus response mapping. Another strategy is to incorporate neurocognitive batteries that consist of multiple similar items to reduce recall of individual items. A third strategy recommended is to utilize well-matched alternate forms of assessment to minimize item exposure. Future studies that consider any of these strategies would provide a clearer understanding of the magnitude of practice effects that have been demonstrated to exist in the current review.

Final conclusion

In summary, this thesis has explored the specificity of MCT as a cognitive intervention for psychosis. It has demonstrated that this intervention is not uniquely suited to improve neurocognitive performance in psychosis relative to various passive and active control interventions assessed in this review. These findings were robust across the six MATRICS neurocognitive domains observed in both pre–post comparisons of immediate effects, as well as in post–follow-up comparisons of maintenance effects. It is our hope that these findings will provide insights to both clinicians treating and patients experiencing psychosis to better understand the utility and potential benefits of MCT in treatment. This work complements recent systematic reviews and meta-analyses conducted by the CRISP research group (Hotte-Meunier et al., 2023; Penney et al., 2022) that consider MCT's efficacy, as well as a growing body of literature concerning the treatment implications of this relatively novel and promising cognitive intervention for psychosis.

REFERENCES

Addington, J., & Addington, D. (2000). Neurocognitive and social functioning in schizophrenia: a 2.5 year follow-up study. *Schizophrenia Research, 44*(1), 47-56. doi:https://doi.org/10.1016/S0920-9964(99)00160-7

Aleman, A., Agrawal, N., Morgan, K. D., & David, A. S. (2006). Insight in psychosis and neuropsychological function: meta-analysis. *Br J Psychiatry, 189*, 204-212. doi:10.1192/bjp.189.3.204

Alvarez-Jiménez, M., Hetrick, S. E., González-Blanch, C., Gleeson, J. F., & McGorry, P. D. (2008). Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials. *Br J Psychiatry, 193*(2), 101-107. doi:10.1192/bjp.bp.107.042853

Andreou, C., Moritz, S., Veith, K., Veckenstedt, R., & Naber, D. (2013). Dopaminergic Modulation of Probabilistic Reasoning and Overconfidence in Errors: A Double-Blind Study. *Schizophrenia Bulletin, 40*(3), 558-565. doi:10.1093/schbul/sbt064

Antonio Vita, M.D., Ph.D. ,, Stefano Barlati, M.D. ,, Anna Ceraso, M.D. ,, Gabriele Nibbio, M.D. ,, Francesca Durante, M.D. ,, Michele Facchi, M.D. ,, . . . Til Wykes, D.Phil. (2024). Durability of Effects of Cognitive Remediation on Cognition and Psychosocial Functioning in Schizophrenia: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *American Journal of Psychiatry, 181*(6), 520-531. doi:10.1176/appi.ajp.20230396

Attepe Özden, S., Tekindal, M., & Tekindal, M. A. (2023). Quality of Life of people with Schizophrenia: A meta-analysis. *Int J Soc Psychiatry, 69*(6), 1444-1452. doi:10.1177/00207640231164019

Au-Yeung C, Thai H, Best M, Bowie CR, Guimond S, Lavigne KM, Menon M, Moritz S, Piat M, Sauvé G, Sousa AE, Thibaudeau E, Woodward TS, Lepage M, Raucher-Chéné D iCogCA: An innovative protocol promoting cognitive health through online group interventions for individuals living with a schizophrenia-spectrum disorder JMIR Preprints. 14/06/2024:63269

Balzan, R. P. (2016). Overconfidence in psychosis: The foundation of delusional conviction? *Cogent Psychology, 3*(1), 1135855. doi:10.1080/23311908.2015.1135855

Balzan, R. P., Mattiske, J. K., Delfabbro, P., Liu, D., & Galletly, C. (2019). Individualized Metacognitive Training (MCT+) Reduces Delusional Symptoms in Psychosis: A Randomized Clinical Trial. *Schizophr Bull, 45*(1), 27-36. doi:10.1093/schbul/sby152

Bowie, C. R., Grossman, M., Gupta, M., Holshausen, K., & Best, M. W. (2017). Action-based cognitive remediation for individuals with serious mental illnesses: Effects of real-world simulations and goal setting on functional and vocational outcomes. *Psychiatr Rehabil J, 40*(1), 53-60. doi:10.1037/prj0000189

Broyd, A., Balzan, R. P., Woodward, T. S., & Allen, P. (2017). Dopamine, cognitive biases and assessment of certainty: A neurocognitive model of delusions. *Clinical Psychology Review, 54*, 96-106. doi:https://doi.org/10.1016/j.cpr.2017.04.006

Brüne, M. (2005). "Theory of mind" in schizophrenia: a review of the literature. *Schizophr Bull, 31*(1), 21-42. doi:10.1093/schbul/sbi002

Byerly, M. J., Nakonezny, P. A., & Lescouflair, E. (2007). Antipsychotic Medication Adherence in Schizophrenia. *Psychiatric Clinics of North America, 30*(3), 437-452. doi:https://doi.org/10.1016/j.psc.2007.04.002

Calamia, M., Markon, K., & Tranel, D. (2012). Scoring Higher the Second Time Around: Meta-Analyses of Practice Effects in Neuropsychological Assessment. *The Clinical Neuropsychologist, 26*(4), 543-570. doi:10.1080/13854046.2012.680913

Catalan, A., McCutcheon, R. A., Aymerich, C., Pedruzo, B., Radua, J., Rodríguez, V., . . . Fusar-Poli, P. (2024). The magnitude and variability of neurocognitive performance in first-episode psychosis: a systematic review and meta-analysis of longitudinal studies. *Translational Psychiatry, 14*(1), 15. doi:10.1038/s41398-023-02718-6

Davies, G., Fowler, D., & Greenwood, K. (2016). Metacognition as a Mediating Variable Between Neurocognition and Functional Outcome in First Episode Psychosis. *Schizophrenia Bulletin, 43*(4), 824-832. doi:10.1093/schbul/sbw128

Davies, G., & Greenwood, K. (2020). A meta-analytic review of the relationship between neurocognition, metacognition and functional outcome in schizophrenia. *Journal of Mental Health, 29*(5), 496-505. doi:10.1080/09638237.2018.1521930

Dudley, R., Taylor, P., Wickham, S., & Hutton, P. (2015). Psychosis, Delusions and the "Jumping to Conclusions" Reasoning Bias: A Systematic Review and Meta-analysis. *Schizophrenia Bulletin, 42*(3), 652-665. doi:10.1093/schbul/sbv150

Duff, K., Callister, C., Dennett, K., & Tometich, D. (2012). Practice effects: a unique cognitive variable. *Clin Neuropsychol, 26*(7), 1117-1127. doi:10.1080/13854046.2012.722685

Eifler, S., Rausch, F., Schirmbeck, F., Veckenstedt, R., Englisch, S., Meyer-Lindenberg, A., . . . Zink, M. (2014). Neurocognitive capabilities modulate the integration of evidence in schizophrenia. *Psychiatry Research, 219*(1), 72-78. doi:https://doi.org/10.1016/j.psychres.2014.04.056

Eifler, S., Rausch, F., Schirmbeck, F., Veckenstedt, R., Mier, D., Esslinger, C., . . . Zink, M. (2015). Metamemory in schizophrenia: Retrospective confidence ratings interact with neurocognitive deficits. *Psychiatry Research, 225*(3), 596-603. doi:https://doi.org/10.1016/j.psychres.2014.11.040

Eisenacher, S., Rausch, F., Ainser, F., Mier, D., Veckenstedt, R., Schirmbeck, F., . . . Zink, M. (2015). Investigation of metamemory functioning in the at-risk mental state for psychosis. *PSYCHOLOGICAL MEDICINE, 45*(15), 3329-3340. doi:10.1017/S0033291715001373

Eisenacher, S., & Zink, M. (2017). Holding on to false beliefs: The bias against disconfirmatory evidence over the course of psychosis. *Journal of Behavior Therapy and Experimental Psychiatry, 56*, 79-89. doi:https://doi.org/10.1016/j.jbtep.2016.08.015

Farreny, A., Aguado, J., Ochoa, S., Huerta-Ramos, E., Marsà, F., López-Carrilero, R., . . . Usall, J. (2012). REPYFLEC cognitive remediation group training in schizophrenia: Looking for an integrative approach. *Schizophrenia Research, 142*(1), 137-144. doi:https://doi.org/10.1016/j.schres.2012.08.035

Fekete, Z., Vass, E., Balajthy, R., Tana, Ü., Nagy, A. C., Oláh, B., Domján, N., & Kuritárné, I. S. (2022). Efficacy of metacognitive training on symptom severity, neurocognition and social cognition in patients with schizophrenia: A single-blind randomized controlled trial. *Scandinavian journal of psychology, 63*(4), 321–333. https://doi.org/10.1111/sjop.12811

Fiszdon, J. M., Choi, J., Goulet, J., & Bell, M. D. (2008). Temporal relationship between change in cognition and change in functioning in schizophrenia. *Schizophr Res, 105*(1-3), 105-113. doi:10.1016/j.schres.2008.06.010

Flavell, J. H. (1979). Metacognition and cognitive monitoring: A new area of cognitive–developmental inquiry. *American Psychologist, 34*(10), 906-911. https://doi.org/10.1037/0003-066X.34.10.906

Garety, P., Joyce, E., Jolley, S., Emsley, R., Waller, H., Kuipers, E., Bebbington, P., Fowler, D., Dunn, G., & Freeman, D. (2013). Neuropsychological functioning and jumping to conclusions in delusions. *Schizophrenia research*, *150*(2-3), 570–574. https://doi.org/10.1016/j.schres.2013.08.035

Gaweda, L., Krezolek, M., Olbrys, J., Turska, A., & Kokoszka, A. (2015). Decreasing self-reported cognitive biases and increasing clinical insight through meta-cognitive training in patients with chronic schizophrenia. *J Behav Ther Exp Psychiatry, 48*, 98-104. doi:10.1016/j.jbtep.2015.02.002

Gold, J. M. (2004). Cognitive deficits as treatment targets in schizophrenia. *Schizophrenia Research, 72*(1), 21-28. doi:https://doi.org/10.1016/j.schres.2004.09.008

Goldberg, T. E., Harvey, P. D., Wesnes, K. A., Snyder, P. J., & Schneider, L. S. (2015). Practice effects due to serial cognitive assessment: Implications for preclinical Alzheimer's disease randomized controlled trials. *Alzheimers Dement (Amst), 1*(1), 103-111. doi:10.1016/j.dadm.2014.11.003

Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *Am J Psychiatry, 153*(3), 321-330. doi:10.1176/ajp.153.3.321

Haga, S., Kobayashi, M., Takehara, A., Kawano, K., & Endo, K. (2022). Efficacy of Metacognitive Training for Patients With Schizophrenia in Psychiatric Emergency Wards: A Pilot Randomized Controlled Trial. *Frontiers in psychology*, *13*, 861102. https://doi.org/10.3389/fpsyg.2022.861102

Heckman, M. G., Davis, J. M., & Crowson, C. S. (2022). Post Hoc Power Calculations: An Inappropriate Method for Interpreting the Findings of a Research Study. *The Journal of Rheumatology*, *49*(8), 867-870. doi:10.3899/jrheum.211115

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*(3), 426-445. doi:10.1037/0894-4105.12.3.426

Ho, B.-C., Andreasen, N. C., Ziebell, S., Pierson, R., & Magnotta, V. (2011). Long-term Antipsychotic Treatment and Brain Volumes: A Longitudinal Study of First-Episode Schizophrenia. *Archives of General Psychiatry, 68*(2), 128-137. doi:10.1001/archgenpsychiatry.2010.199

Hoenig, J. M., & Heisey, D. M. (2001). The Abuse of Power. *The American Statistician, 55*(1), 19-24. doi:10.1198/000313001300339897

Hotte-Meunier, A., Penney, D., Mendelson, D., Thibaudeau, E., Moritz, S., Lepage, M., & Sauve, G. (2023). Effects of metacognitive training (MCT) on social cognition for schizophrenia spectrum and related psychotic disorders: a systematic review and meta-analysis. *Psychol Med*, 1-7. doi:10.1017/S0033291723002611

Jaeger, J., Czobor, P., & Berns, S. M. (2003). Basic neuropsychological dimensions in schizophrenia. *Schizophrenia Research, 65*(2), 105-116. doi:https://doi.org/10.1016/S0920-9964(03)00052-5

Kahn, R. S., Sommer, I. E., Murray, R. M., Meyer-Lindenberg, A., Weinberger, D. R., Cannon, T. D., O'Donovan, M., Correll, C. U., Kane, J. M., van Os, J., & Insel, T. R. (2015). Schizophrenia. *Nature reviews. Disease primers*, *1*, 15067. https://doi.org/10.1038/nrdp.2015.67

Keefe, R. S., Fox, K. H., Harvey, P. D., Cucchiaro, J., Siu, C., & Loebel, A. (2011). Characteristics of the MATRICS Consensus Cognitive Battery in a 29-site antipsychotic schizophrenia clinical trial. *Schizophr Res, 125*(2-3), 161-168. doi:10.1016/j.schres.2010.09.015

Keefe, R. S., Vinogradov, S., Medalia, A., Silverstein, S. M., Bell, M. D., Dickinson, D., . . . Stroup, T. S. (2011). Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophr Bull, 37*(5), 1057-1065. doi:10.1093/schbul/sbq010

Kharawala, S., Hastedt, C., Podhorna, J., Shukla, H., Kappelhoff, B., & Harvey, P. D. (2022). The relationship between cognition and functioning in schizophrenia: A semi-systematic review. *Schizophr Res Cogn, 27*, 100217. doi:10.1016/j.scog.2021.100217

Lafargue, G., & Franck, N. (2009). Effort awareness and sense of volition in schizophrenia. *Conscious Cogn, 18*(1), 277-289. doi:10.1016/j.concog.2008.05.004

Lecomte, T., Addington, J., Bowie, C., Lepage, M., Potvin, S., Shah, J., . . . Tibbo, P. (2022). The Canadian Network for Research in Schizophrenia and Psychoses: A Nationally Focused Approach to Psychosis and Schizophrenia Research. *Can J Psychiatry, 67*(3), 172-175. doi:10.1177/07067437211009122

Lejeune, J. A., Northrop, A., & Kurtz, M. M. (2021). A Meta-analysis of Cognitive Remediation for Schizophrenia: Efficacy and the Role of Participant and Treatment Factors. *Schizophr Bull, 47*(4), 997-1006. doi:10.1093/schbul/sbab022

Lepping, P., Sambhi, R. S., Whittington, R., Lane, S., & Poole, R. (2011). Clinical relevance of findings in trials of antipsychotics: systematic review. *British Journal of Psychiatry, 198*(5), 341-345. doi:10.1192/bjp.bp.109.075366

Lysaker, P. H., Molly Erickson, M. A., Buck, K. D., Procacci, M., Nicolò, G., & Dimaggio, G. (2010). Metacognition in schizophrenia spectrum disorders: Methods of assessment and associations with neurocognition and function. *The European Journal of Psychiatry, 24*, 220-226. Retrieved from http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-61632010000400004&nrm=iso

Lysaker, P. H., Shea, A. M., Buck, K. D., Dimaggio, G., Nicolò, G., Procacci, M., . . . Rand, K. L. (2010). Metacognition as a mediator of the effects of impairments in neurocognition on social function in schizophrenia spectrum disorders. *ACTA PSYCHIATRICA SCANDINAVICA, 122*(5), 405-413. doi:https://doi.org/10.1111/j.1600-0447.2010.01554.x

McCaffrey, R. J., Duff, K., & Westervelt, H. J. (2013). *Practitioner's guide to evaluating change with neuropsychological assessment instruments*: Springer Science & Business Media.

McCutcheon, R. A., Keefe, R. S. E., & McGuire, P. K. (2023). Cognitive impairment in schizophrenia: aetiology, pathophysiology, and treatment. *Mol Psychiatry*. doi:10.1038/s41380-023-01949-9

McGuire, N., Gumley, A., Hasson-Ohayon, I., Allan, S., Aunjitsakul, W., Aydin, O., Bo, S., Bonfils, K. A., Bröcker, A. L., de Jong, S., Dimaggio, G., Inchausti, F., Jansen, J. E., Lecomte, T., Luther, L., MacBeth, A., Montag, C., Pedersen, M. B., Pijnenborg, G. H. M., Popolo, R., … McLeod, H. (2024). Investigating the relationship between specific negative symptoms and metacognitive functioning in psychosis: A systematic review. *Psychology and psychotherapy*, *97*(2), 191–214. https://doi.org/10.1111/papt.12505

Mizrahi, R., Kiang, M., Mamo, D. C., Arenovich, T., Bagby, R. M., Zipursky, R. B., & Kapur, S. (2006). The selective effect of antipsychotics on the different dimensions of the experience of psychosis in schizophrenia spectrum disorders. *Schizophrenia Research, 88*(1), 111-118. doi:https://doi.org/10.1016/j.schres.2006.07.013

Moncrieff, J. (2011). Questioning the 'neuroprotective' hypothesis: does drug treatment prevent brain damage in early psychosis or schizophrenia? *British Journal of Psychiatry, 198*(2), 85-87. doi:10.1192/bjp.bp.110.085795

Moritz, S., Andreou, C., Klingberg, S., Thoering, T., & Peters, M. J. V. (2013). Assessment of subjective cognitive and emotional effects of antipsychotic drugs. Effect by defect? *Neuropharmacology, 72*, 179-186. doi:https://doi.org/10.1016/j.neuropharm.2013.04.039

Moritz, S., Andreou, C., Schneider, B. C., Wittekind, C. E., Menon, M., Balzan, R. P., & Woodward, T. S. (2014). Sowing the seeds of doubt: a narrative review on metacognitive training in schizophrenia. *Clin Psychol Rev, 34*(4), 358-366. doi:10.1016/j.cpr.2014.04.004

Moritz, S., Kerstan, A., Veckenstedt, R., Randjbar, S., Vitzthum, F., Schmidt, C., Heise, M., & Woodward, T. S. (2011). Further evidence for the efficacy of a metacognitive group training in schizophrenia. *Behaviour research and therapy, 49*(3), 151–157. https://doi.org/10.1016/j.brat.2010.11.010

Moritz, S., Vitzthum, F., Randjbar, S., Veckenstedt, R., & Woodward, T. S. (2010). Detecting and defusing cognitive traps: metacognitive intervention in schizophrenia. *Current Opinion in Psychiatry, 23*(6), 561-569. doi:10.1097/YCO.0b013e32833d16a8

Moritz, S., & Woodward, T. S. (2007). Metacognitive training for schizophrenia patients (MCT): A pilot study on feasibility, treatment adherence, and subjective efficacy. *German Journal of Psychiatry, 10*(3), 69-78.

Moritz, S., Woodward, T. S., Jelinek, L., & Klinge, R. (2008). Memory and metamemory in schizophrenia: a liberal acceptance account of psychosis. *PSYCHOLOGICAL MEDICINE, 38*(6), 825-832. doi:10.1017/S0033291707002553

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., Essock, S., Fenton, W. S., Frese, F. J., 3rd, Gold, J. M., Goldberg, T., Heaton, R. K., Keefe, R. S., Kraemer, H., Mesholam-Gately, R., Seidman, L. J., Stover, E., Weinberger, D. R., Young, A. S., Zalcman, S., … Marder, S. R. (2008). The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. *The American journal of psychiatry, 165*(2), 203–213. https://doi.org/10.1176/appi.ajp.2007.07010042

Nuechterlein, K. H., Subotnik, K. L., Ventura, J., Green, M. F., Gretchen-Doorly, D., & Asarnow, R. F. (2012). The puzzle of schizophrenia: Tracking the core role of cognitive deficits. *Development and Psychopathology, 24*(2), 529-536. doi:10.1017/S0954579412000132

Penney, D., Sauvé, G., Mendelson, D., Thibaudeau, É., Moritz, S., & Lepage, M. (2022). Immediate and Sustained Outcomes and Moderators Associated With Metacognitive Training for Psychosis: A Systematic Review and Meta-analysis. *JAMA Psychiatry, 79*(5), 417-429. doi:10.1001/jamapsychiatry.2022.0277

Ray, W. A., Chung, C. P., Murray, K. T., Hall, K., & Stein, C. M. (2009). Atypical antipsychotic drugs and the risk of sudden cardiac death. *N Engl J Med, 360*(3), 225-235. doi:10.1056/NEJMoa0806994

Reeder, C., Huddy, V., Cella, M., Taylor, R., Greenwood, K., Landau, S., & Wykes, T. (2017). A new generation computerised metacognitive cognitive remediation programme for

schizophrenia (CIRCuiTS): a randomised controlled trial. *PSYCHOLOGICAL MEDICINE, 47*(15), 2720-2730. doi:10.1017/S0033291717001234

Ruiz-Delgado, I., Moreno-Küstner, B., García-Medina, M., Barrigón, M. L., Gonzalez-Higueras, F., López-Carrilero, R., Barrios-Mellado, I., Barajas, A., Pousa, E., Lorente-Rovira, E., Grasa, E., Cid, J., Barrau-Sastre, P., Moritz, S., Ochoa, S., & Spanish Metacognition Group (2022). Is Metacognitive Training effective for improving neurocognitive function in patients with a recent onset of psychosis?. *Psychiatry research*, *318*, 114941. https://doi.org/10.1016/j.psychres.2022.114941

Saperstein, A. M., Medalia, A., Bello, I., & Dixon, L. B. (2021). Addressing cognitive health in coordinated specialty care for early psychosis: Real-world perspectives. *Early Intervention in Psychiatry, 15*(2), 374-379. doi:https://doi.org/10.1111/eip.12966

Saperstein, A. M., Medalia, A., Malinovsky, I., Bello, I., & Dixon, L. B. (2021). Toolkit for assessing and addressing cognitive health in early psychosis: Evaluation of feasibility and utility in a coordinated specialty care setting. *Early Intervention in Psychiatry, 15*(5), 1376-1381. doi:https://doi.org/10.1111/eip.13070

Sauve, G., Lavigne, K. M., Pochiet, G., Brodeur, M. B., & Lepage, M. (2020). Efficacy of psychological interventions targeting cognitive biases in schizophrenia: A systematic review and meta-analysis. *Clin Psychol Rev, 78*, 101854. doi:10.1016/j.cpr.2020.101854

Savulich, G., Shergill, S., & Yiend, J. (2012). Biased Cognition in Psychosis. *Journal of Experimental Psychopathology, 3*(4), 514-536. doi:10.5127/jep.016711

Schmidt, S. J., Mueller, D. R., & Roder, V. (2011). Social Cognition as a Mediator Variable Between Neurocognition and Functional Outcome in Schizophrenia: Empirical Review and New Results by Structural Equation Modeling. *Schizophrenia Bulletin, 37*(suppl_2), S41-S54. doi:10.1093/schbul/sbr079

Shan, X., Liao, R., Ou, Y., Pan, P., Ding, Y., Liu, F., Chen, J., Zhao, J., Guo, W., & He, Y. (2021). Increased regional homogeneity modulated by metacognitive training predicts therapeutic efficacy in patients with schizophrenia. *European archives of psychiatry and clinical neuroscience*, *271*(4), 783–798. https://doi.org/10.1007/s00406-020-01119-w

Stirling, J., White, C., Lewis, S., Hopkins, R., Tantam, D., Huddy, A., & Montague, L. (2003). Neurocognitive function and outcome in first-episode schizophrenia: a 10-year follow-up of an epidemiological cohort. *Schizophrenia Research, 65*(2), 75-86. doi:https://doi.org/10.1016/S0920-9964(03)00014-8

Świtaj, P., Anczewska, M., Chrostek, A., Sabariego, C., Cieza, A., Bickenbach, J., & Chatterji, S. (2012). Disability and schizophrenia: a systematic review of experienced psychosocial difficulties. *BMC psychiatry, 12*, 193. doi:10.1186/1471-244x-12-193

Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008). Schizophrenia, "Just the Facts": what we know in 2008 part 1: overview. *Schizophr Res, 100*(1-3), 4-19. doi:10.1016/j.schres.2008.01.022

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *The American journal of psychiatry*, *168*(5), 472–485. https://doi.org/10.1176/appi.ajp.2010.10060855

Ussorio, D., Giusti, L., Wittekind, C. E., Bianchini, V., Malavolta, M., Pollice, R., Casacchia, M., & Roncone, R. (2016). Metacognitive training for young subjects (MCT young version) in the early stages of psychosis: Is the duration of untreated psychosis a limiting factor?. *Psychology and psychotherapy*, *89*(1), 50–65. https://doi.org/10.1111/papt.12059

Vita, A., Barlati, S., Ceraso, A., Nibbio, G., Ariu, C., Deste, G., & Wykes, T. (2021). Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Psychiatry, 78*(8), 848-858. doi:10.1001/jamapsychiatry.2021.0620

Wang, C., Chong, Y., Zhang, J., Cao, Y., & Wang, Y. (2022). The Efficacy of Extended Metacognitive Training on Neurocognitive Function in Schizophrenia: A Randomized Controlled Trial. *Brain Sci, 12*(3). doi:10.3390/brainsci12030413

Woodward, T. S., & Menon, M. (2013). Misattribution Models (II): Source Monitoring in Hallucinating Schizophrenia Subjects. In R. Jardri, A. Cachia, P. Thomas, & D. Pins (Eds.), *The Neuroscience of Hallucinations* (pp. 169-184). New York, NY: Springer New York.

Woodward, T. S., Mizrahi, R., Menon, M., & Christensen, B. K. (2009). Correspondences between theory of mind, jumping to conclusions, neuropsychological measures and the symptoms of schizophrenia. *Psychiatry Research, 170*(2), 119-123. doi:https://doi.org/10.1016/j.psychres.2008.10.018

Wright, A., Fowler, D., & Greenwood, K. (2020). Influences on functional outcome and subjective recovery in individuals with and without First Episode Psychosis: A metacognitive model. *Psychiatry Research, 284*, 112643. doi:https://doi.org/10.1016/j.psychres.2019.112643

Wykes, T., Newton, E., Landau, S., Rice, C., Thompson, N., & Frangou, S. (2007). Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. *Schizophr Res, 94*(1-3), 221-230. doi:10.1016/j.schres.2007.03.030

Zhang, Y., Hedo, R., Rivera, A., Rull, R., Richardson, S., & Tu, X. M. (2019). Post hoc power analysis: is it an informative and meaningful analysis? *Gen Psychiatr, 32*(4), e100069. doi:10.1136/gpsych-2019-100069