The assessment and treatment of neurocognition and social cognition in early psychosis

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Thesis for the degree of Philosophiae Doctor

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Ágrip

Bakgrunnur: Geðrofsraskanir koma oftast fram snemma á lífsleiðinni og hafa því mikil áhrif á tækifæri ungs fólks til náms og starfa, auk þess að skerða lífsgæði. Stór hluti þeirrar skerðingar tengist truflun á vitrænni getu (s.s. athygli, minni, vinnsluhraða, stýrifærni og félagsskilningi), sem reynist hluti af einkennamynd flestra þeirra sem glíma við geðrofsraskanir. Niðurstöður úr mati á vitrænni getu hefur meira forspárgildi um batahorfur og daglega færni heldur en geðrofseinkenni og því hefur áhersla á mat og meðferð vitrænna þátta í þessum hópi aukist verulega síðustu ára. Vitræn endurhæfing hefur reynst árangursrík meðferð fyrir vitræna skerðingu, en yfirfærsla í daglegt líf hefur reynst áskorun. Sýnt hefur verið fram á að betri árangur náist ef vitræn endurhæfing er sameinuð félagsskilningsþjálfun, en rannsóknir á árangri slíkrar meðferðar fyrir ungt fólk með byrjandi geðrofsraskanir eru skammt á veg komnar. Enn fremur er lítið vitað um hvaða þættir stuðla að árangursríkri innleiðingu meðferðarinnar á deildum sem sérhæfa sig í meðhöndlun fyrsta geðrofs.

Markmið: Heildarmarkmið verkefnisins var að innleiða og framkvæma klínískt vitrænt mat og síðar, byggt á því mati, vitræna endurhæfingu með félagsskilningsþjálfun (VEF) á Laugarási, deild innan geðþjónustu Landspítala sem sérhæfir sig í meðferð ungs fólks með fyrsta geðrof. Auk þess var leitast eftir því að skoða innleiðingu á VEF með tilliti til hentugleika, áreiðanleika og viðhalds. Tilgangur fyrstu rannsóknar var að leggja mat á vitræna getu, líðan og færni í daglegu lífi hjá ungu fólki eftir geðrof og skoða tengsl félagsskilnings við aðra vitræna þætti, einkenni og færni í daglegu lífi. Einnig að kanna forspárgildi vitrænna þátta fyrir sjálfsmati og mati aðstandenda á færni í daglegu lífi. Tilgangur annarrar rannsóknar var að framkvæma árangursmat á VEF. Tilgangur þriðju rannsóknar var að kanna langtíma áhrif VEF á vitræna þætti, líðan og færni í daglegu lífi.

Aðferð: Öllum þeim sem voru innritaðir í þjónustu Laugaráss á árunum 2015–2017 var boðin þátttaka í fyrstu rannsókninni og samþykktu alls 70 einstaklingar að taka þátt, eða 82% þeirra sem voru innritaðir í þjónustu. Þátttakendur voru á aldrinum 18-30 ára og höfðu fengið sitt fyrsta geðrof innan fimm ára. Lagt var mat á vitræna getu, líðan og færni í daglegu lífi og niðurstöður bornar saman við heilbrigða samanburðarhópa. Auk þess var spágildi vitrænna þátta fyrir sjálfsmati og mati aðstandenda á færni í daglegu

lífi kannað. Þátttakendur úr fyrstu rannsókninni sem mældust meira en hálfu staðalfráviki undir meðaltali á að minnsta kosti einum vitrænum þætti var boðin þátttaka í annarri rannsókninni, sem fól í sér árangursmat á VEF. Þátttakendum (*n*=49) var raðað af handahófi í meðferðarhóp (*n*=25), sem fékk VEF auk hefðbundinnar meðferðar, eða samanburðarhóp (*n*=24), sem hélt áfram sinni hefðbundnu meðferð en var á biðlista eftir VEF. Mælingar úr fyrsta hluta verkefnisins voru nýttar sem grunnlínumælingar og voru báðir hópar metnir strax eftir að meðferð lauk með sömu matsaðferðum. Í þriðju rannsókninni voru allir þeir sem luku VEF (*n*=37) metnir með sömu matsaðferðum 12 mánuðum eftir meðferð. Gögnum um mætingu, áreiðanleika við meðferðarhandbók og endurgjöf frá þátttakendum og meðferðaraðilum var safnað til að meta innleiðingarferlið.

Niðurstöður: Frammistaða sem nam nálægt einu staðalfráviki undir heilbrigðum samanburðarhópum reyndist algeng. Mestur vandi kom fram á *Theory of Mind (ToM)* og seinkuðu yrtu minni (>1 staðalfrávik undir meðaltali). Tafarlaust yrt minni og skilningur á andlitssvipbrigðum (*emotion perception*) spáðu marktækt fyrir um mat aðstandenda á færni í daglegu lífi en eignunarstíll (*attributional style*) var eini þátturinn sem spáði fyrir um sjálfsmat á færni í daglegu lífi. Niðurstöður úr mati á árangri VEF sýndu að marktækur munur var á milli hópa á tafarlausu og seinkuðu yrtu minni, vinnsluminni, stýrifærni, ToM og eignunarstíl. Ekki kom fram marktækur munur milli hópa á mælingum á líðan eða færni í daglegu lífi við lok meðferðar. Við 12 mánaða eftirfylgd kom í ljós að árangur hélst á öllum þáttum og að munurinn á frammistöðu þátttakenda á grunnlínumælingum og við 12-mánaða endurmat var marktækur nær öllum vitrænum þáttum, neikvæðum einkennum og færni í daglegu lífi. Mæting var góð (77.6%), þátttakendur töldu meðferðina gagnlega og áreiðanleiki við meðferðarhandbækur var hár (86.6%).

Ályktanir: Meirihluti einstaklinga með byrjandi geðrofsraskanir er með skerta getu á vitrænum þáttum. Niðurstöður rannsóknarinnar auka skilning á vitrænni getu ungs fólks eftir geðrof og gefa vísbendingar um gagnsemi VEF í þessum hópi, ekki síst ef markmiðið er að efla vitræna getu og auka færni í daglegu lífi til lengri tíma.

Lykilorð: Geðrof, vitræn geta, félagsskilningur, vitræn endurhæfing, félagsskilningsþjálfun, innleiðing

Abstract

Background: Cognitive impairment is a core feature at all stages of the psychotic illness and significantly predicts functional outcomes. Targeting cognition early is theoretically attractive as a means to reverse the functional impairment before it is fully realized and thus improve the long-term outcome and quality of life of patients with psychotic disorders. Cognitive remediation is an effective treatment of cognitive deficits in schizophrenia, but generalization to everyday functioning remains a challenge. Interventions, such as strategy training combined with computerized training, and social-cognitive training have shown promise in bridging the gap between cognitive gains and functional outcomes. However, relatively little is known about the effects of integrated neuro- and social-cognitive remediation in early psychosis and what may aid in implementing these interventions into standard care for early psychosis.

Objectives: The overall aim of this thesis was to assess and treat the neuro- and social-cognitive impairment among individuals seeking treatment at an early intervention in psychosis (EIP) service in Iceland. In addition, to examine implementation outcomes of the intervention with regards to attendance, fidelity and acceptability. The specific aims of the first study were to investigate the nature of neuro- and social-cognitive impairment and explore the relationship between social cognition and neurocognition, clinical symptoms, and functional outcome. In addition, we sought to investigate the role of neuro- and social-cognitive domains in predicting variance in informant-reported and self-reported functional outcomes. the specific aims of the second study were to evaluate the effects of a novel integrative neuro- and social-cognitive remediation on cognition, clinical symptoms and functional outcome. The specific aims of the third study were to evaluate the long-term effects of the intervention on cognition, clinical symptoms, and functional outcomes.

Method: All patients between the ages of 18 and 30, who had experienced their first psychotic episode in the past five years and in seeking treatment at the EIP service between 2015-2017, were offered participation in the first study. A total of 70 patients, 82% of the total patient population receiving care agreed to participate. Cognition, clinical symptoms and functional outcome were assessed, and the results were compared to healthy comparison groups. Participants that performed one half a standard deviation below healthy norms in at least one cognitive domain were offered participation in

the second study. Participants (*n*=49) were randomly assigned to either a treatment group (*n*=25) that received integrated neuro- and social-cognitive remediation in addition to their standard treatment, or a wait-list control group (*n*=24) that continued their standard treatment. Assessments from the first study were used as baseline assessments in the second study, and both groups were reassessed with the measures at post-treatment. In the third study, all participants that received ICR during the trial (*n*=37) were reassessed on the same variables 12-months after treatment ended. Implementation outcomes were assessed with attendance data, fidelity checks, and feedback from participants and facilitators.

Results: Results suggested that, compared to healthy comparison samples, this group of early psychosis patients demonstrated broad cognitive impairments that were maximal in delayed recall and theory of mind (ToM) (<1SD below the mean). A model including both neuro- and social-cognitive domains predicted variance in informant-reported community functioning, whereas attributional style was the single predictor for self-reported functional outcomes. ICR was associated with improvements on measures of immediate verbal memory, delayed recall, working memory, cognitive flexibility, ToM, and hostile attributional style. No significant between-group differences were found on measures of functional outcomes or clinical symptoms. However, ICR participants demonstrated significant improvements on multiple measures, including cognitive, clinical symptom, and functional outcome measures at post-treatment. Performance at 12-month follow-up was significantly better than performance at baseline for most cognitive measures, and there were further significant increases in performance on processing speed, immediate verbal memory and delayed recall. The intervention had good attendance rates (77.6%), received high treatment satisfaction ratings from participants, and the fidelity to treatment manuals was high (86.6%).

Conclusions:

The findings of this thesis provide a better understanding of cognitive functioning of early psychosis patients and lend support to the relevance of implementing integrated neuro- and social-cognitive remediation at EIP services. ICR may improve both neuro- and social-cognitive domains and long-term functioning, but further conclusions on the efficacy of the intervention will require replication of the results in a larger randomized controlled trial that includes a control group at the long-term follow-up.

Keywords:
Psychosis, Neurocognition, Social Cognition, Cognitive Remediation, Social Cognitive Training, Functional Outcome, implementation

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Contents

List of abbreviations

ICD	International Classification of Diseases Classification System
WHO	World Health Organization
ToM	Theory of Mind
SD	Standard Deviation
EIP	Early Intervention in Psychosis
MATRICS	Measurement and Treatment Research to Improve Cognition in Schizophrenia
MCCB	MATRIX Consensus Cognitive Battery
BACS	Brief Assessment of Cognition in Schizophrenia
SCOPE	Social Cognition Psychometric Evaluation
CR	Cognitive Remediation
NIMH	National Institute of Mental Health
SCIT	Social Cognition and Interaction Training
IPT	Integrated Psychological Therapy
CET	Cognitive Enhancement Therapy
NICE	National Institute for Health and Care Excellence
LUH	Landspitali University Hospital
TMT	Trail Making Test
LMI	Logical Memory I
LMII	Logical Memory II
FEIT	Facial Emotion Identification Test
AIHQ-A	Ambiguous Intentions Hostility Questionnaire-Ambiguous Items
BCIS	Beck Cognitive Insight Scale
PANSS	Positive and Negative Symptom Scale

DASS-21	Depression, Anxiety and Stress Scale-21 item
DUP	Duration of Untreated Psychosis
QOLS	Quality of Life Scale
BRIEF-A	Behavior Rating Inventory of Executive Function-Adult Version
LSP	Life Skills Profile
IPS	Individual Placement and Support
ICR	Integrative Cognitive Remediation
NEAR	Neuropsychological Educational Approach to Remediation
CCT	Compensatory Cognitive Training
CBT	Cognitive Behavioral Therapy
WAIS-IV	Wechsler Adult Intelligence Scale, 4th edition
WASI-is	Wechsler Abbreviated Scale of Intelligence-Icelandic
D-KEFS	Delis-Kaplan Executive Function System
TAU	Treatment as Usual
SPSS	Statistical Package for the Social Sciences
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
NOS	Not Otherwise Specified

List of figures

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List of original papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals I-III:

I. Viðarsdóttir, Ó. G., Twamley, E. W., Roberts, D. L., Guðmundsdóttir B., Sigurðsson, E., & Magnúsdóttir, B. B. (2019). Social and non-social measures of cognition for predicting self-reported and informant-reported functional outcomes in early psychosis. *The Scandinavian Journal of Psychology, 60*, 295-303.

II. Viðarsdóttir, Ó., G., Roberts D. L., Twamley E. W., Guðmundsdóttir B., Sigurðsson, E., & Magnúsdóttir B. B. (2019). Integrative cognitive remediation for early psychosis: Results from a randomized controlled trial. *Psychiatry Research, 273*, 690-698.

III. Viðarsdóttir, O. G., Twamley, E. W., Roberts, D. L., Guðmundsdóttir, B., Sigurðsson, E., & Magnúsdóttir, B. B. (2020). Integrative cognitive remediation for early psychosis: a 12-month follow-up. *Psychiatry Research*, *288*, 112964.

Declaration of contribution

I. Ólína G. Viðarsdóttir (OGV), Brynja B. Magnúsdóttir (BBM), and Engilbert Sigurðsson (ES) were involved in the study design. OGV, BBM, Elizabeth W. Twamley (EWT), David L. Roberts (DLR), and Berglind Guðmundsdóttir (BG) were involved in the data analysis and interpretation. OGV wrote the first draft of the manuscript and was responsible for data collection. All authors critically revised the manuscript and approved the final manuscript.

II. OGV, BBM, DR, and EWT designed the study and wrote the study protocol. It was carried out by OGV, who translated the treatment manuals, served as the leading therapist and was responsible for data collection. OGV, BBM, DLR, and EWT were involved in data analysis and interpretation. OGV wrote the first draft of the manuscript and was responsible for data collection. All authors critically revised the manuscript and approved the final manuscript

III. OGV, BBM and ES designed the study. OGV, BG, DLR, and EWT were involved in data analysis and interpretation. OGV wrote the first draft of the manuscript and was responsible for data collection. All authors critically revised the manuscript and approved the final manuscript.

OGV wrote the doctoral thesis, but all members of the doctoral committee reviewed and approved the final draft of the doctoral thesis. OGV takes full responsibility for the final conclusions and any errors that remain.

1 Introduction

Psychotic disorders are chronic and severe mental disorders that affect cognition, emotions, and behavior. According to International Classification of Diseases (ICD) classification system, 10th version, developed by the World Health Organization (WHO), psychotic disorders include schizophrenia, schizoaffective disorder, acute and transient psychotic disorder, schizotypal disorder, delusional disorder, and other primary psychotic disorders. Psychosis best fits a continuum model, ranging between normality and illness, and a diagnosis of any psychotic disorder is only made when symptoms persist and functioning is markedly affected. The global prevalence of psychotic disorders varies between studies but is usually reported to be approximately 7.2 per 1000 persons per year (Jongsma et al., 2019; McGrath et al., 2008). Men are at higher risk and have an earlier onset of these disorders than women, with age ranges of 18 to 25 and 25 to 35, respectively (Jongsma et al., 2019; Ochoa et al., 2012). Prior to the first psychotic episode, there is usually a prodromal period, where a decline in functioning is seen alongside negative symptoms and sub-threshold positive symptoms, such as ideas of reference, perceptual disturbance, and paranoid ideation (Yung et al., 2003). The early onset of psychotic disorders is a major reason for high economic burden of these disorders. In addition to high costs associated with health care cost, institutional costs and unpaid care, young individuals who develop psychotic disorders have disrupted education and employment resulting in a high rate of disability pension (Andrew et al., 2012). In fact, schizophrenia ranked in the top 15 causes of disability worldwide in 2016 despite being a relatively rare disorder (Vos et al., 2017).

Clinical symptoms are a defining feature of psychotic disorders and include positive symptoms, such as delusions, hallucinations, experiences of passivity and control, disorganized behavior, and thinking. However, they also include negative symptoms, such as restrictions of affect, speech, motivation, and decreased social interaction. These symptoms vary between individuals, and most of them fluctuate over time. Despite the destabilizing effects of the defining psychotic symptoms, in particular delusions and hallucinations, these symptoms have remarkably little association with the long-term functional impairments that also characterize psychotic disorders. As a result, the goal of treatments for psychotic disorders has moved beyond

symptom management to the more important and ambitious goal of "functional recovery". One of the most consistent correlates and determinants of the functional outcome of research in this field has been cognition (Bilder, 2000; Green et al., 2012; Keefe & Harvey, 2012).

1.1 Cognition in psychotic disorders

1.1.1 Neurocognition and social cognition

Cognition encompasses neurocognitive and social-cognitive processes, two related but independent constructs (Allen et al., 2007; Fett et al., 2011). Neurocognition can be defined as processes of linking and appraising information. It includes abilities, such as processing speed: the ability to process information automatically and respond quickly without making errors; attention/vigilance: the ability to focus or concentrate; verbal and visual learning and memory: the capacity to encode and/or retrieve verbal and/or visual information over shorter or longer periods; working memory: the ability to immediately hold information in mind briefly and manipulate the information; and reasoning and problem solving (components of executive functioning): the ability to develop and apply strategies to solve problems.

Social cognition has been defined as "the domain of cognition that involves the perception, interpretation, and processing of social information" (Green et al., 2008). Social cognition is a multifaceted concept and includes four main domains: *Theory of mind* (ToM), which refers to the ability to infer the thoughts and intentions of other people from their words and behavior. It is also referred to as *perspective taking* or *mentalizing*; *Emotion perception* includes emotion expression, recognition, and experience and refers to the ability to infer another person's emotional state from facial expression or vocal tone; *Social perception* refers to the ability to identify interrelationships and social cues as well as gauge social rules and expectations. This domain also includes *social knowledge*, which refers to one's knowledge of norms and schemas surrounding social situations and interactions; *Attributional style/bias* reflects whether one typically makes inferences about the causes of positive and negative events to internal (personal), external (other person), or situational factors. These four main domains of social cognition are related yet fairly independent (Green et al., 2008; Mancuso et al., 2011), and have been categorized into two types of social-cognitive processes: *capacities* and *biases* (Roberts & Pinkham, 2013). Capacities comprise the automatic ability to generate mental and emotional state representations and the controlled ability to manipulate these representations. Social-cognitive capacities have

been described as “lower-order” social-cognitive components and include the social-cognitive domains of ToM, emotion perception, and social perception. Biases refer to the tendency for information processing functions to produce systematically distorted output and include the domain of attributional style.

1.1.2 Cognition in schizophrenia

It is well established that people diagnosed with schizophrenia consistently demonstrate performance well below healthy comparison subjects on multiple domains of neurocognition (Fioravanti et al., 2012; Forbes et al., 2009; Heinrichs & Zakzanis, 1998). The magnitude of differences in performance in schizophrenic and non-psychiatric groups approaches 1.5 standard deviations (SD) for processing speed and aspects of sensory, verbal, and working memory and averages 1.0 SD across tests of attention, executive function, language, motor and spatial abilities, as well as general intelligence. These impairments have been found to be stable over time (Heaton et al., 2001) and to manifest similarly in different regions of the world, despite linguistic and cultural differences (Schaefer et al., 2013).

Neurocognitive impairment contributes moderately to the variance in functional outcomes in schizophrenia. Such impairment is considered a core feature in psychotic disorders (Fett et al., 2011; Green et al., 2000). However, a fair amount of variance in functional outcomes remains unexplained. Over the past two decades, evidence has been growing fast which demonstrates the functional significance of social cognition in schizophrenia. Schizophrenia patients have been shown to have marked impairments, as compared with healthy controls, in all four main domains of social cognition, and these are maximal in social perception, ToM, emotion perception and emotion perception (Savla et al., 2013). Research shows that social cognition is more strongly associated with functional outcomes than neurocognition (Fett et al., 2011; Mancuso et al., 2011), and contributes incremental variance to the prediction of functional outcome above and beyond that provided by neurocognition (Pinkham & Penn, 2006). Furthermore, the relationship between neurocognition and functional outcome is partly mediated by a pathway through social-cognitive domains, with emotion perception and social knowledge emerging as the most effective mediators (Schmidt et al., 2011). Due to the variations in the selection of cognitive and outcome domains and measures, more research is needed to assess a wide range of social-cognitive domains to unravel their differential relationship with neurocognition and functional outcome.

1.1.3 Cognition in early psychosis

Those in the field of schizophrenia generally accept that earlier treatment is associated with better outcome (Correll et al., 2018; Wyatt, 1991). The aim with setting up early intervention in psychosis (EIP) services was to minimize and shorten the severity of the first episode of psychosis and facilitate as full a recovery as possible through early detection and intervention during the first 3-5 years following onset (Bilder et al., 2006). This has guided researchers to assess cognitive performance as soon as possible after the first psychotic episode as well as investigate cognitive performance at the prodromal stage of the disorder before such an episode unfolds. There are several benefits of studying cognition in early phases of psychosis as opposed to in the more chronic stages of the illness. The nature of neurocognitive dysfunction may be less confounded by the effects of age and illness- and chronicity-related variables (e.g., chronic hospitalization, effects of prolonged use of antipsychotic medication, smoking, metabolic syndrome, etc).

Consistent evidence demonstrates that neurocognitive performance is impaired long before the onset of psychotic illness and continues to deteriorate from the premorbid period to the first psychotic episode (Bilder et al., 2006; Fusar-Poli et al., 2012; Rund et al., 2007; Woodberry et al., 2008). There are indications for even further decline in performance across multiple domains, including general intellectual working memory and processing speed after the onset of the first psychotic episode.(Jahshan et al., 2010). However, the deterioration in cognitive performance varies across different domains, with some domains deteriorating while others remain relatively stable (Jahshan et al., 2010). Generally, the neurocognitive impairments found in first-episode psychosis is statistically significant and clinically meaningful across all neuropsychological domains, and maximal in verbal learning and memory and processing speed (Keefe & Harvey, 2012; Mesholam-Gately et al., 2009; Rund et al., 2007). Although most data on the functional relevance of neurocognition come from cross-sectional studies done on patients with chronic schizophrenia, the same domains are also associated with functional outcome in early psychosis individuals (Cervellione et al., 2007).

Regarding social cognition, several studies have demonstrated significant and functionally relevant impairment in all domains of social cognition at prodromal stages and early psychosis, compared to non-psychiatric groups (Healey et al., 2016; Lindgren et al., 2018; Ludwig, 2017; Thompson et al.,

2012). However, there is some debate over whether the degree of social-cognitive impairment in early psychosis matches the social-cognitive impairment at more chronic stages of psychotic illness (Horan et al., 2012; Ludwig, 2017; Savla et al., 2013). For example, some studies demonstrate that for emotion perception, the degree of impairment in early psychosis is less than that observed in chronic schizophrenia (Romero-Ferreiro et al., 2016), whereas others have not found a difference between the two groups (Addington et al., 2006b).The strongest and most consistent social-cognitive deficits in early psychosis samples appear on verbal tasks of ToM (Healey et al., 2016; Ventura et al., 2015). The literature is limited on social perception and attributional style in early psychosis, and the stability of attributional style in these samples remains unclear. Some studies demonstrating deficits (Healey et al., 2016), while others do not (Ludwig, 2017).

Consistent with results in schizophrenia, social cognition in early psychosis accounts for more variance in functional outcome than do various neurocognitive factors (Ludwig, 2017), and may be an important mediator of the relationship between neurocognition and poor functional outcome (Addington, 2010). Emotion perception, ToM, social perception and social knowledge appear to have direct or indirect effects on functional outcome in early psychosis, as well as interpersonal problem solving (Addington et al., 2006a; Addington et al., 2006b; Lindgren et al., 2018; Williams et al., 2008). Furthermore, impairments in social cognition appear to be associated with functional decline in early psychosis (Ludwig, 2017; Ventura et al., 2015), and the relationship between social cognition and functional outcomes appears to strengthen as the illness progresses (Horan et al., 2012).

1.1.4 Associations between social cognition, neurocognition, and clinical symptoms

Many systematic reviews and meta-analyses have investigated the relationships between neurocognitive and social-cognitive domains as well as how each domain associates with symptom dimensions. However, the nature and relative strength of these relationships have not been firmly established. Given the importance of neurocognition and social cognition to the course and outcome in psychotic disorders, a better understanding of these relationships is essential for the development of optimal early intervention models.

From a clinical perspective, the distinction between social-cognitive capacities and biases is helpful in understanding these relationships. The relationships between capacities and basic neurocognitive domains, such as

verbal memory, verbal fluency, processing speed, executive functioning, and visual reasoning, appear to be important moderators, with no single neurocognitive domain standing out or being dominating (Addington et al., 2006a; Mancuso et al., 2011; Meyer & Kurtz, 2009; Ventura et al., 2013). Furthermore, there is a strong link between these cognitive domains and negative and disorganized symptoms, with more severe symptoms relating to poorer cognitive performance. However, the associations with the classic positive symptoms, delusions and hallucinations, appear to be weak at best (Brown et al., 2014; Dominguez et al., 2009; Mancuso et al., 2011; Ventura et al., 2010, 2013). Some studies have reported that paranoid patients demonstrate more impairment in emotion perception and ToM than non-paranoid patients do (Pinkham et al., 2011). It is possible that difficulties in perceiving and interpreting social information may have an impact on symptom development (Bentall et al., 2001). For example, a patient who inaccurately identifies and interprets social cues may be more likely to interpret neutral facial expressions as angry or vague neutral social situations as hostile or threatening. However, this link has not been established in early psychosis.

Studies exploring the relationships between positive and negative symptoms, neurocognition, and social-cognitive capacity are comparatively common, while the relationships between bias, clinical symptoms and neurocognition are understudied. Social-cognitive bias appears to be an independent social-cognitive domain, mostly unrelated to other social-cognitive or neurocognitive domains (Mancuso et al., 2011). There are reports of weak correlations between bias and executive functioning (Mehta et al., 2014). For the most part, research has focused on understanding the relationship between this domain and positive symptoms. Researchers have found strong associations between bias and positive symptoms, in particular for paranoid delusions and beliefs (Combs et al., 2007; Healey et al., 2016; Pinkham et al., 2016a).

Results from early psychosis samples do not always replicate results from schizophrenia studies, and this field requires further research. Researchers have identified social-cognitive deficits as a relevant component in the development of various types of symptoms (Addington, 2010; Sergi et al., 2007), and they have suggested that the overlap between symptoms and social cognition affects the stability of social-cognitive deficits in early psychosis. Early psychosis samples may be more heterogeneous than chronic schizophrenia samples and have more variations in clinical stability (Bora & Pantelis, 2013; Horan et al., 2012). Results are mixed from cross-

sectional studies reporting on the relationship between social cognition and clinical symptoms in early psychosis. Several studies report significant relationships similar to those found in schizophrenia samples (An et al., 2010; Healey et al., 2016; Horan et al., 2012; Ventura et al., 2015), whereas others have not found significant relationships (Addington et al., 2006a; Bertrand et al., 2007). The same is true for longitudinal studies that reported both small reductions (Behere et al., 2009; Horan et al., 2012) and no change (Addington et al., 2006a; Addington et al., 2006b) in social-cognitive deficits following improvement in psychopathology. Understanding social cognition at the early stage of the psychotic disorder has clear implications for a greater understanding of the development of psychosis.

1.2 Measuring cognition and functional outcome

1.2.1 Measuring neurocognition and social cognition

When conducting clinical trials in schizophrenia research, it is important to consider the measurement issues. Neurocognitive domains are not consistently created using the same neuropsychological tests which makes cross-study comparisons difficult. When selecting measurements for clinical trials it is important to consider the resource availability, patient characteristics, and the purpose of the assessment. Several standardized test batteries have been developed to address this issue. The MATRICS Consensus Cognitive Battery (MCCB), a mainly pen-and-paper test, was developed to be an endpoint for clinical trials aiming to enhance cognition in schizophrenia (Kern et al., 2011; Nuechterlein et al., 2008). The MCCB assesses seven cognitive domains commonly impaired in schizophrenia, namely processing speed, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition, and has become the gold standard for cognitive assessment in behaviorally based cognitive interventions. Shorter assessments with similar reliability and validity have been developed such as the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe, 2004). The BACS is a reliable and feasible assessment alternative to MCCB and is sensitive for evaluating treatment progress and outcome (Bowie et al., 2012, 2014). Using a standardized testing battery has clear advantages but further research on the psychometric properties of different translations and normative base development is needed before a global standardized testing battery can be recommended in clinical practice and clinical trials worldwide.

Limitations in social-cognitive assessment are well known, and researchers have tried to identify tasks that are well suited for clinical trials in psychotic disorders. The overlaps between social-cognitive domains and between these domains and neurocognitive domains make it hard to determine whether the domains currently outlined are accurate. In addition, the variability in social-cognitive impairment between first-episode and chronic schizophrenia samples is even greater than for neurocognitive impairment. The Social Cognition Psychometric Evaluation (SCOPE) study (Pinkham et al., 2018) attempted to reach a consensus on the domains of social cognition and to identify suitable measures by systematically evaluating the psychometric properties of promising measures. Results from the SCOPE study showed that three social-cognitive measures had strong psychometric properties and were recommended for use in clinical trials; the Hinting Task (Corcoran et al., 1995), a measure of ToM; the Bell Lysaker Emotion Recognition Task (BLERT) (Bryson et al., 1997), a measure of emotion perception; the Penn Emotion Recognition Task (ER-40) (Kohler et al., 2003), another measure of emotion perception. Other measures, although promising, require further study. A paper published in 2017 by Ludwig et al. extended the results of SCOPE with a younger first-episode sample. They report that the Hinting task was the only social-cognitive measure that could be recommended for use in clinical research in first-episode psychosis sample. Clearly, further exploration of measures of social cognition is needed in this group of patients.

1.2.2 Measuring functional outcome

As mentioned above, valid and reliable measures of functional outcome are critical in demonstrating clinical effectiveness of an intervention. However, functional outcome is a complex phenomenon. It includes broad concepts such as interpersonal skills, community functioning, social functioning, daily-living skills, and work performance. Variability in measurement methods further complicates research on the link between functional outcome and cognition. The most commonly used methods to measure functional outcome include assessments of what the individual can do under optimal conditions (i.e., capacity-based role-plays), and what the individual actually does in real life (i.e., performance-based work outcomes), informant reports, and self-reports. Clinicians' direct observations appear to be the most reliable method, and associate closely with neurocognition and social-cognitive capacity (Bowie et al., 2008; Harvey et al., 2007; Ludwig et al., 2017). However, it is still unclear how performance on these measures translates to real-life performance.

To get a more complete picture of variance in performance across different settings, the use of informant reports and self-reports may be particularly valuable. There is evidence suggesting that informant reports from friends and relatives may reliably reflect real-world daily living skills in early psychosis (Puig et al., 2013). Self-reports may give a better idea of personally meaningful outcomes to individual patients, and it has been argued that subjects in early psychosis samples may be better able to accurately report their own functional abilities than the self-reports from chronic schizophrenia samples (Ludwig, 2017; Williams et al., 2008). Most measures are designed to capture functional impairments in schizophrenia, and researchers have adapted a few for early psychosis samples. It is unlikely that the functional impairments seen in chronic schizophrenia adequately reflect those observed in early psychosis. Younger individuals often live at home and may view social relationships (making friends, having a girlfriend/boyfriend) or schoolwork as more important than independent living or work outcomes.

To determine which, if any, informant or self-assessed measures of functioning have value for early psychosis, understanding the cognitive predictors of each method may also be important. Most research has focused on the link between social-cognitive capacity and functional outcomes, but few studies have investigated the role of bias in predicting functional outcome. There is some evidence in schizophrenia that blaming attributions predict scores of informant-reported functional outcome, rated by high-contact clinicians (Pinkham et al., 2016b). However, this link has not been demonstrated in early psychosis samples. In fact, evidence suggests that in early psychosis, attributional style is not associated with performance or capacity-based measures, but rather with self-reported functional outcome (Ludwig et al., 2017).

1.3 Treatment of cognitive deficits in psychotic disorders

1.3.1 Cognitive remediation

One of the great challenges of treatment in schizophrenia is to develop effective treatment options for the functional impairments characterizing psychotic disorders. Evidence is accumulating that antipsychotic treatment alone is insufficient to accomplish functional recovery (Lieberman et al., 2008) and has little effect on cognition in schizophrenia. As the research focus in the treatment of schizophrenia shifts from reducing psychotic symptoms to improving functional outcomes and quality of life, the research

on interventions targeting cognition has expanded rapidly in the past two decades. During this period, several psychosocial interventions designed to improve thinking or cognitive skills have emerged. They are referred to as *cognitive remediation* (CR). CR has been defined as "an intervention targeting cognitive deficit (attention, memory, executive function, social cognition or metacognition) using scientific principles of learning with the ultimate goal of improving functional outcomes" (Cognitive Remediation Expert Working Group, 2012).

In general, CR approaches fall into two major methods of treatment: *restorative* and *strategy-based/compensatory approaches.* At present, no clear evidence supports one CR treatment approach over another (Kurtz, 2016a). Restorative approaches have been most commonly used in neurocognitive remediation programs for psychosis (Wykes et al., 2011). Restoration or enhancement of cognitive function is the goal of restorative approaches targeting cognitive deficits directly through repeated practice. Strategy-based/compensatory approaches focus on acquiring internal (mental) and external (behavioral) strategies and/or on modifying the environment to circumvent cognitive difficulties. The goals of such interventions are to reduce cognitive demands in the environment, conserve cognitive energy for more complex tasks, and bypass cognitive impairment by using routines or compensatory strategies when approaching tasks (Twamley, 2016). Meta-analyses investigating treatment effects of restorative and strategy-based/compensatory approaches show that irrespective of therapy characteristics, CR has significant and durable positive effects on multiple domains of cognition in schizophrenia (McGurk et al., 2007; Wykes et al., 2011). Furthermore, compared to other widely adopted interventions in psychosis, CR produces stronger effects on targeted outcomes (Best & Bowie, 2017) and has demonstrated potential for improvements to translate to real-world outcomes (Keshavan et al., 2014).

The functional relevance of social cognition has led to a large increase in the development and study of social-cognitive interventions in the past two decades. Just like neurocognitive approaches, social-cognitive approaches include both restorative and compensatory methods. Furthermore, social-cognitive interventions may include targeted interventions that focus on one specific social-cognitive domain, comprehensive interventions that target multiple social-cognitive domains and broad-based interventions that also include neurocognitive remediation (Fiszdon, 2016b). The overarching goal of social-cognitive approaches is the same as for other CR approaches, that is, to facilitate functional recovery by targeting key domains of social cognition.

The evidence for their efficacy in improving social functioning is promising (Kurtz et al., 2016b), and in 2008, a panel of experts at an NIMH Workshop identified social cognition as a key target for psychosocial interventions in schizophrenia-spectrum illnesses (Green et al., 2008). In addition, social-cognitive interventions appear to have an advantage over other CR approaches in affecting social and interpersonal functioning in schizophrenia (Kurtz & Richardson, 2012).

1.3.2 Integrated neuro- and social-cognitive remediation

The main criticism of neurocognitive remediation has been that the effects on functional outcomes are small (at best), unless provided in the context of comprehensive psychiatric rehabilitation or other evidence-based psychosocial treatments. This has led researchers to investigate combination treatments that may enhance generalization of outcomes to everyday life. Restorative approaches most consistently benefit cognition, but generalization to real-world behavior is more likely when combining them with strategy coaching or compensatory training (Bowie et al., 2012; McGurk et al., 2007; Wykes et al., 2011). Furthermore, researchers have hypothesized that addressing social cognition may enhance the generalization of any neurocognitive gains acquired through CR to real-world functioning (Horan et al., 2016). Some evidence suggests that the effects on social functioning are greater when neuro- and social-cognitive domains are targeted, compared to targeting only neurocognitive domains (Lindenmayer et al., 2013).

There are also other reasons for combining neuro- and social-cognitive remediation. Social-cognitive dysfunction may act as an impediment to implementing cognitive remediation. Furthermore, social-cognitive dysfunction may interfere with patients' abilities to benefit from group-based approaches of cognitive remediation (Horan et al., 2016). On the flip side, neurocognitive training may improve patients' ability to apply lessons learned in social-cognitive training via improved memory to recall strategies and enhance their executive function to apply skills flexibly (Roberts & Velligan, 2012).

Existing research suggests that broad-based multi-component interventions targeting social cognition as well as neurocognition, may produce durable cognitive and functional improvements (Hogarty et al., 2006; Mueller et al., 2015; Roder et al., 2011). The best researched broad-based treatments with the most rigorous evidence base supporting their efficacy are Integrated Psychological Therapy (IPT) (Roder et al., 2011) and Cognitive Enhancement Therapy (CET) (Hogarty et al., 2004). The optimal combination

of neurocognitive and social-cognitive remediation remains a question, and some of these treatments may also require alteration to make their delivery feasible and acceptable in community treatment settings. To date, continued treatment development in this area is still needed (Horan & Green, 2019).

1.3.3 Cognitive remediation for early psychosis patients

As early intervention in psychosis is highly effective, researchers have suggested that embedding cognitive treatments early – before the cognitive and functional disabilities associated with psychotic disorders are fully realized – is important. There is evidence demonstrating that the cognitive, clinical and functional benefits of CR are greater for early psychosis patients than for those suffering from chronic schizophrenia (Bowie et al., 2014; Deste et al., 2019). On the neuro-developmental level there is evidence that cognitive remediation offers neuroprotective effects against grey matter loss that commonly occurs early in the disorder (Eack et al., 2010b), and also improves brain activation (Wykes et al., 2002). In addition, young individuals may have greater neural plasticity and be more amenable to treatment (Berger et al., 2007; Fisher et al., 2010; Pantelis et al., 2009). Furthermore, younger age and shorter duration of illness have been identified as predictors of the effectiveness of CR in schizophrenia (Barlati et al., 2012; Bowie et al., 2014).

Numerous randomized controlled trials have been conducted to evaluate the effectiveness of neurocognitive remediaiton in early psychosis. A systematic review and meta-analysis on the effectiveness of neurocognitive remediation in this population reported that it is an effective intervention that has significant positive effects on verbal learning and memory, global symptoms and functioning (Revell et al., 2015). However, some researchers have suggested that to achieve optimal functional response of neurocognitive remediation in early psychosis, it may be necessary to target both neurocognition and social cognition (Barlati et al., 2019; Bowie et al., 2014; Revell et al., 2015). As discussed earlier, this population presents with large, consistent, and functionally relevant deficits in both neuro- and social-cognitive domains. The reported success of social-cognitive interventions in improving social and interpersonal functioning makes these interventions especially relevant in early psychosis. In fact, there is evidence that social-cognitive interventions effectively improve cognition as well as social and community functioning in this population (Bartholomeusz & Allott, 2012). For younger individuals, improving their social lives (making friends, getting a girlfriend/boyfriend, improving relationships with parents) may be as

important, if not more important, than acquiring skills for independent living or employment. In addition, there is more variability in cognitive dysfunction in early psychosis samples than in chronic schizophrenia and more heterogeneity in clinical presentation, and it is unlikely that a single approach fits all.

Most of the randomized controlled trials on the efficacy of broad-based interventions include older and more chronically ill schizophrenia patients. However, the existing evidence indicates that integrated neuro- and social-cognitive interventions have substantial and durable effects on cognition and social functioning in early psychosis (Boriello et al., 2015; Eack, 2009, 2010a; Lewandowski, 2013; Ueland & Rund, 2005). The effects on cognitive flexibility and long-term memory have been found to be greater in early psychosis samples than in more chronic schizophrenia (Boriello et al., 2015). A report on the two-year effect of CET in early psychosis reported medium CET-associated effects on improvements in neurocognition and large effects on social cognition, cognitive style, social adjustment, and symptoms (Eack et al., 2010a). Eack et al. (2011) further investigated the functional improvement gained in the two-year trial and found that improvements in executive functioning and emotion management mediated functional improvement. More studies are needed to investigate the immediate and long-term effects of combined neuro- and social-cognitive remediation in young individuals early in the course of their psychotic illness.

1.3.4 Implementing integrative cognitive remediation into standard psychosis care

It is important that research informs clinical practice, and that the key findings are implemented for the benefit of current and future patients. Cognitive remediation is an evidence-based practice that should be routinely available to psychosis patients when needed (Best & Bowie, 2017). In fact, in light of the recent evidence, cognitive remediation is now recommended as part of the clinical practice guidelines in several countries, including Australia, New Zealand, Singapore, and Scotland (Galletly et al., 2016; SIGN, 2013; Verma et al., 2011). However, despite the strong and growing evidence base for cognitive remediation, clinical availability of these interventions remains sparse, creating an unsatisfactory gap between science and clinical practice (Vinogradov, 2019). Prior research indicates that CR can be successfully implemented in large scale, geographically diverse, publicly funded clinical settings (Medalia et al., 2019). Although CR has shown efficacy in short-term clinical trials, the demonstration of the effectiveness on the overall treatment

of schizophrenia (including measures of long-term illness and functional outcomes) is a critical prerequisite for its more widespread adoption. The difference between efficacy (the extent to which treatment improves a dependent variable in the short term in experimental settings) and effectiveness (the role of a treatment in the outcome of an illness in more long-term real-life clinical settings) is important to consider in this regard. A recent meta-analysis contended that the evidence supporting CR in schizophrenia was robust, and that the time had come to focus on implementation and dissemination of CR (Wykes et al., 2011). Implementation science provides a framework for facilitating implementation in diverse settings while retaining the core effective components of CR. Various implementation models have been created to aid in the successful implementation of evidence-based treatments. Dark (2016) described the implementation process for cognitive remediation where he lists five stages that are essential in the implementation of CR approaches: exploration, adoption and installation, initial implementation, implementation and maintenance. According to Dark, the estimated timeline for implementation of CR is 2-4 years (Dark, 2016). However, more studies describing successful implementation and maintenance of CR are highly needed.

2 Aims

The overall aim of this thesis was to assess and treat the neuro- and social-cognitive impairment among individuals early in the course of their psychotic illness. This thesis includes the results from the three published papers as well as the results of the implementation process.

Specifically, the main aims of the three papers described in this thesis were:

I. To examine the nature of cognitive impairment in early psychosis and the interrelationships between the social-cognitive measures and how they intercorrelated with measures of neurocognition, clinical symptoms and functional outcomes. In addition, we sought to investigate the individual contributions of neurocognitive and social-cognitive domains to self-reported and informant-reported functional outcome in this sample.

II. To evaluate the effects of integrative cognitive remediation (ICR), a novel neurocognitive and social-cognitive treatment, on cognition, clinical symptoms, and functional outcome in early psychosis.

III. To examine changes in cognition, clinical symptoms and functional outcome from baseline to a 12-month follow-up for all ICR participants and evaluate the stability of outcomes from post-treatment to 12-month follow-up.

3 Materials and methods

3.1 Study design and procedure

The study took place at an EIP service at Landspitali- the National University Hospital (LUH) in Reykjavik, Iceland. This is the only EIP service in the country. It provides support to young people (18-30 years old) experiencing their first episode of psychosis. The study was approved by LUH's Ethics Committee (20/2015, ref. 16; LSH 42-15). Written informed consent was obtained from all participants. An overview of the study design, participants, measurements and data analyses of the three papers is provided in Table 1.

Table 1. Overview of study design, participants, measurements and data analyses of the three papers.

Paper	**I**	**II**	**III**
Design	Cross-sectional	Randomized wait-list controlled trial	Longitudinal
Participants	N=70	N=49	N=37
Measurements	Neurocognition Social cognition Clinical symptoms Functional outcome	Neurocognition Social cognition Clinical symptoms Functional outcome	Neurocognition Social cognition Clinical symptoms Functional outcome
Data Analysis	Pearson correlations and linear regression	ANCOVA Intention-to-treat analysis	ANOVA

Note. ANCOVA: Analysis of covariance; ANOVA: Analysis of variance.

3.1.1 Inclusion criteria

The following inclusion criteria were applied in all three studies:

1. Meeting the ICD-10 diagnostic criteria for schizophrenia, schizoaffective disorder, acute and transient psychotic disorder, schizotypal disorder, delusional disorder or other non-unipolar or non-bipolar psychotic disorders (World Health Organization, 2008).
2. Between 18-30 years old.
3. Icelandic as first language.
4. No evidence of intellectual disability (i.e., IQ<70) or active epileptic disorder.
5. First episode of psychosis within the last five years.

For study II, in addition to the above-listed criteria, the participants with cognitive performance greater than or equal to 0.5 standard deviations below norms on any of the cognitive measures administered at baseline were eligible for and offered participation in the second study.

3.1.2 Allocation

An independent research assistant allocated participants enrolled in the second study into blocks of four and five. One went into an intervention group receiving their usual treatment, as well as integrative neuro- and social-cognitive remediation. The other group went into a wait-list control group that continued their treatment as usual.

3.2 Participants

3.2.1 Paper I

All patients seeking treatment at the EIP service between 2015 and 2017 were asked to enroll in the first study. A total of 70 agreed to participate, representing 82% of the total patients seeking treatment at the EIP service.

3.2.2 Paper II

Out of the 70 participants analyzed in the first study, 21 participants were excluded from participation in the second study either because they did not meet the inclusion criteria for participation in the trial (*n*=13) or declined participation (*n*=8). The final sample used in the between-group analyses included 49 participants, randomized into either an intervention group (*n*=25) or a wait-list control group (*n*=24). Out of the 24 participants in the waitlist group, 15 accepted treatment eventually. Participants who attended less than one third of the sessions were deemed dropouts but included in the final intent-to-treat analysis. Participants that were not available for any of the cognitive, clinical symptom, or functional outcome assessments after treatment (n=3) were not included in the final analyses. A total of 37 participants accepted treatment eventually, completed assessments and included in the final within-group analyses.

3.2.3 Paper III

At the 12-month assessments, cognitive data were collected for 32 out of these 37 participants (86.5%), assessments of psychopathology and data on informant-reported social functioning were collected for 26 (70.3%) participants, and self-reports were completed by 32 participants (86.5%). Data on occupational and educational status was collected for all 37

participants as well as for a historical control group (*n*=30) that was assessed at baseline as part of the first study but did not receive the intervention. Figure 1 describes the study cohort in papers I-III whose data were used in the various statistical analyses.

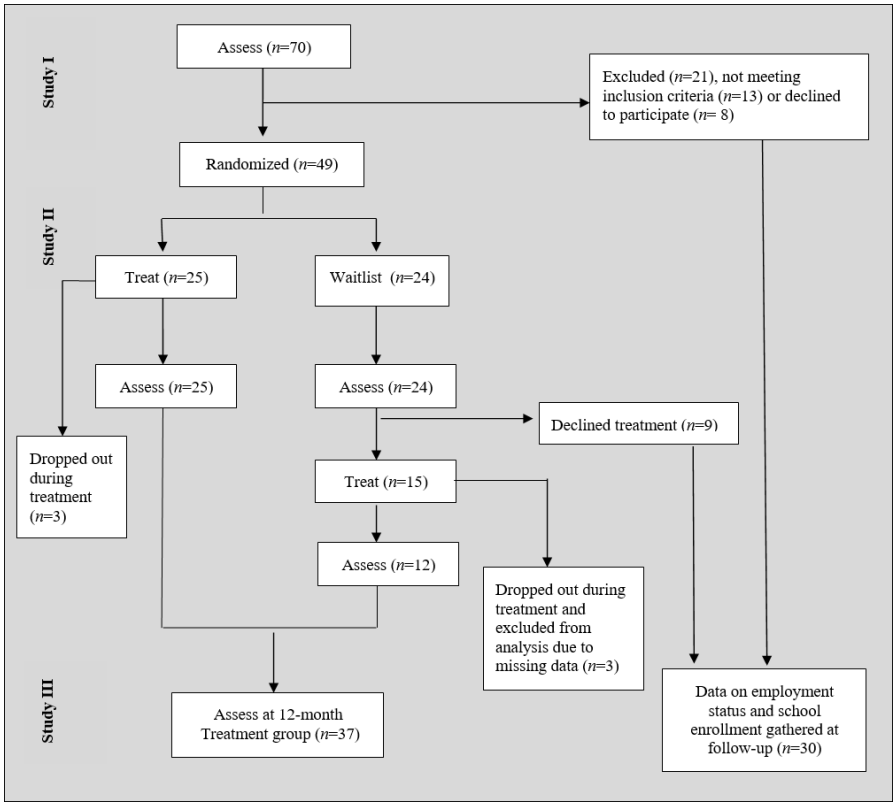

Figure 1. Consort diagram for the three studies.

3.3 Assessment (Papers I – III)

The same assessment procedure was used in all three studies. Cognitive testing took place in one session and all other assessments were performed within seven days. Cognitive assessments at baseline were completed by the doctoral candidate (OGV). Cognitive assessments post-treatment were completed by clinical psychologists blind to treatment allocation. Cognitive assessments at follow-up were completed by a clinical psychologist external to the research and treatment teams. All participants that received the intervention were followed in a naturalistic setting of care for one year. Then the same measures were re-administered to assess the long-term effects of the intervention. These participants received compensation of ISK 10,000

towards their travel expenses to attend the 12-month follow-up assessments.

A background questionnaire was used to collect socio-demographic data, and clinical characteristics were collected from medical records or their care team. All measures were administered in Icelandic. A brief description of each measure is below and, when available, psychometric properties of the Icelandic translations are provided.

3.3.1.1 Neurocognition

Neuropsychological tests that have been validated in a non-psychiatric Icelandic sample (i.e. did not have a diagnosis of a severe mental illness), and schizophrenia samples were used.

The Symbol Coding subtest from the Wechsler Adult Intelligence Scale, 4th edition (Wechsler, 2008) was used as a measure of processing speed. Total correct symbols were tallied with a higher score indicating better performance. Processing speed was also measured with the Trail Making Test A (TMT A) (Magnusdottir et al., 2019; Reitan, 1958). The total time was used for TMT A with less time reflecting better performance. The Trail Making Test B (TMT B) was used to assess cognitive flexibility (Magnusdottir et al., 2019; Reitan, 1958). The total time was used with less time reflecting better performance. A ratio score was also calculated (TMT ratio, B/A) and used as a measure of cognitive flexibility. The Digit Span subtest from the Wechsler Adult Intelligence Scale, 4th edition (Wechsler, 2008) was used to assess attention and working memory. The total score for Digit Span forward was used as a measure of attention, and working memory was assessed with Digit Span working memory span (backwards + in a row)/2). Higher scores reflected better performance. The Logical Memory subtest from the Wechsler Memory Scale, 3rd edition (Wechsler, 1997) was used to assess verbal memory. Scores were obtained for immediate recall total items (LMI), immediate recall theme score (LMI theme), delayed recall total items (LMII), and delayed recall theme score (LMII theme). A total score was obtained by adding the LMI and LMII scores. The Matrix Reasoning subtest from the Icelandic standardized version of the Wechsler Abbreviated Scale of Intelligence (Guðmundsson, 2015; Wechsler, 1999) was used to assess visual reasoning. The total score was used with higher scores reflecting better performance. The Tower subtest from the Delis-Kaplan Executive Function System (Delis, 2001) was used to assess planning. The total achievement score was used with higher scores reflecting better performance. The Stroop Color-Word test (Magnusdottir et al., 2019; Stroop, 1935) was used to assess inhibition. An interference score was calculated

(Stroop III-[(Stroop II + Stroop I)/2] (Golden, 1978) with lower scores reflecting better performance.

3.3.1.2 Social cognition

Three widely-used measures of social cognition were translated as part of this study and used to assess three out of the four main social-cognitive domains. Results from informal testing of the test-retest reliability of the social-cognitive measures are reported in Paper II for those participants with a double baseline (*n*=12) (Vidarsdottir et al., 2019a).

The Hinting Task (Corcoran et al., 1995; Fridriksson, 2016) was used to assess ToM. The Hinting Task consists of verbal description of 10 brief interactions between two characters. During this interaction, one of the characters drops a social hint that the respondent must interpret. Higher scores indicate better performance (range 0-20). Cronbach's alpha for the Icelandic version was 0.76.

The Facial Emotion Identification Task (FEIT) (Fridriksson, 2016; Kerr, 1993) was used to assess emotion perception. Participants viewed 19 facial emotion photographs and were required to indicate which of six basic emotions (happy, sad, angry, afraid, surprised, and ashamed) was conveyed in each photograph. Total scores range from 0-19, with higher scores indicating better performance. Cronbach´s alpha for the task was 0.46. Although not one of the four main social-cognitive domains, metacognitive overconfidence in social judgments has been studied as a social-cognitive domain and is targeted in the intervention used in this study. Therefore, a metacognitive measure of confidence was added to the standard administration of FEIT as an exploratory measure (Fiszdon et al., 2016a; Moritz et al., 2012). For each FEIT item, participants were asked to indicate how confident they were that their answer was correct using, a Likert-type scale ranging from *100% sure* (4) to *guessed* (1). We then calculated separate average confidence ratings for trials where participants correctly and incorrectly identified an emotion, with higher scores indicating more confidence.

The Ambiguous Intentions and Hostility Questionnaire–Ambiguous items (AIHQ-A) (Combs et al., 2007; Össurardóttir, 2018) was used to assess attributional style. The AIHQ consists of five vignettes describing ambiguous social scenarios with negative outcomes. Each vignette is followed by a series of questions assessing the amount of hostility, blame, and aggression that the participant states he or she would experience if in the situation. The

hostility and aggression bias scales range from 5-25, with higher scores indicating greater bias toward hostility or aggression. The blame scale ranges from 15-80, with higher scores indicating a tendency to blame others. Cronbach's alpha for the three subscales was 0.54 for hostility bias, 0.88 for the blame scale, and 0.33 for aggression bias.

3.3.1.3 Cognitive insight

Beck's Cognitive Insight Scale (BCIS) (Beck et al., 2004) was used to assess cognitive insight, the bias-based ability to evaluate and correct distorted beliefs and misinterpretations. The BCIS is a 15-item self-report questionnaire consisting of two subscales that measure the capacity and willingness to observe own mental productions and to consider alternative explanations (self-reflectiveness), and overconfidence in the validity of beliefs (self-certainty). Cronbach´s alpha for the self-reflectiveness scale was 0.84 and 0.61 for the self-certainty scale. A total score was obtained by subtracting the score for self-certainty scale from that of the self-reflectiveness scale. The BCIS total score ranges from -18–27 with higher scores reflecting more cognitive insight. Cronbach´s alpha for the total score was 0.56.

3.3.1.4 Clinical symptom severity

Clinical symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) (Stanley et al., 1987), a 30-item clinician-administered rating scale yielding scores for positive symptoms (range 7-49), negative symptoms (range 7-49) and general psychopathology (range 16-112). PANSS-raters were experienced clinicians who received training and guidance prior to and during the study. The Depression, Anxiety, and Stress scale 21-item (DASS-21) (Ingimarsson, 2010; Lovibond & Lovibond, 1995), a self-report that provides scores for three subscales, namely depression anxiety and stress. Higher scores reflect more symptoms (range 0-21 for each of the three scales). Cronbach´s alpha for the depression scale was 0.92, 0.82 for the anxiety scale and 0.84 for the stress scale. Duration of untreated psychosis (DUP) was assessed as the time from the first onset of psychotic symptoms to the start of the first adequate treatment of psychosis with antipsychotic medication. Given the evidence that psychotic symptoms can respond within a few days of antipsychotic medication (Agid et al., 2003), we chose initiation over more stringent criteria for the adequacy of medication treatment proposed by others.

3.3.1.5 Functional outcome

Functional outcome was assessed with three self-report measures, two informant reports, and the rate of employment and school enrolment. Informants were family members, partners, or high-contact clinicians.

The Quality of Life scale was used to assess subjective quality of life (QOLS) (Flanagan, 1978; Jónsdóttir & Sigurðardóttir, 2016), including five domains of quality of life: material and physical well-being; relationships with other people; social, community, and civic activities; personal development and fulfilment, and recreation. The QOLS ranges from 16-112, with higher scores reflecting better quality of life. Cronbach's alpha for the Icelandic version was 0.90.

The Occupational Self-Assessment (OSA) (Baron et al., 2006; Pálsdóttir & Jónsdóttir, 2005) was used to assess self-reported competence in occupational performance, with higher scores reflecting better functional capacity (range 21-84). Cronbach's alpha for the Icelandic version was 0.95.

Executive dysfunction was assessed with The Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) (Kristinsdottir, 2012; Roth et al., 2005), which includes both a self-report version and an informant-report version. The range for each scale is 75-225, with higher scores reflecting more problems related to executive functioning in everyday life. Cronbach's alpha for the self-report version was 0.96 and 0.97 for the informant report version.

The Life Skills Profile (LSP) (Jónsdóttir & Sigurðardóttir, 2016; Rosen et al., 1989) was used to assess the aspects of functioning affecting how successfully people with schizophrenia live in the community. The LSP is an informant-rated measure that includes the following five subscales: self-care, non-turbulence, social contact, communication, and responsibility. The scale has been selected as one of the best instruments for assessing real-world day-to-day living skills in schizophrenia (Leifker et al., 2011) and has adequate psychometric characteristics in adolescents with early onset psychosis (Puig et al., 2013). Scores range from 39-156, with lower scores reflecting lower levels of skill. Chronbach's alpha for the Icelandic version was 0.90.

3.4 Treatment conditions

All participants in the three studies continued their treatment as usual.

3.4.1 Treatment as usual

Treatment as usual differed across participants, based on their individual treatment plan. However, all participants had weekly or monthly contact with a member of their treatment team. The team included a psychiatrist, case-manager, and support counselor. In addition, there was one or more of the following treatment components: medication treatment, socialization at the early psychosis service (lunch, board games, all female/male groups), psychoeducation, individual or group-based exercise, individual placement and support (IPS), and family support. Some participants were enrolled in school or had part-time employment, but no participants received other organized cognitively oriented therapies.

3.4.2 Integrative cognitive remediation (ICR)

The duration of the intervention was 12 weeks, during which participants met twice a week for two hours. In addition, all group members were assigned a practice partner with whom they met once a week during the 12-week period. At the meetings, they completed intervention-related exercises designed to enhance generalization to everyday life. A practice partner is a specific person from the participants´ life, such as a family member, friend, individual therapist or acquaintance, who has agreed to help the client practice learned skills at home. Because each participant already had an assigned supportive counselor at the EIP service, these staff members were used as practice partners in ICR. The intervention integrated three evidence-based approaches to cognitive remediation. The restorative approach selected was the Neuropsychological Educational Approach to Remediation (NEAR) (Medalia et al., 2018). The strategy-based/compensatory approach selected was Compensatory Cognitive Training (CCT) (Mendella et al., 2015; Twamley et al., 2012, 2017). The social-cognitive training approach selected was the Social Cognition and Interaction Training (SCIT) (Roberts et al., 2016). These interventions have been widely researched and implemented in various settings in different countries but have not been integrated and studied in early psychosis before. The three approaches were integrated and delivered in three phases (see figure 2).

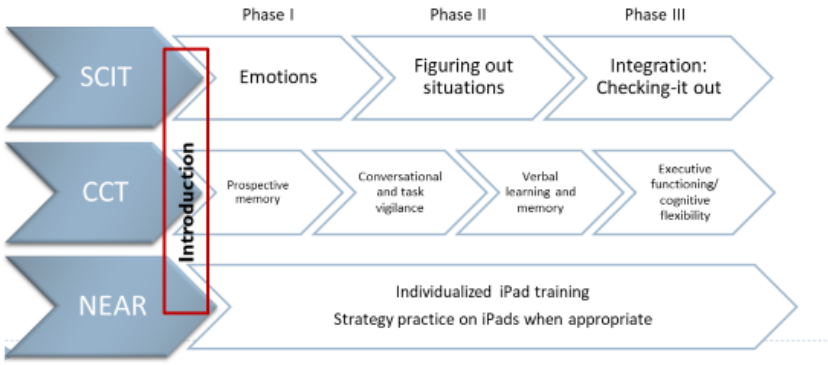

Figure 2. An overview of the three treatment phases.

3.4.2.1 Neuropsychological Educational Approach to Remediation (NEAR)

NEAR utilizes commercially available educational software to create a rich learning environment that is intrinsically motivating and rewarding. NEAR emphasizes eight major goals (1) to improve the neuropsychological (cognitive) functions identified as sufficiently impaired to hamper functional outcome, (2) to provide every client a positive learning experience, (3) to promote independent learning skills, (4) to promote a positive attitude about learning, (5) to promote awareness of learning styles, learning strengths and weaknesses, (6) to promote a sense of competence and confidence in one's ability to acquire skills, (7) to promote awareness of how the social-emotional context affects cognitive functioning, and (8) to promote optimal cognitive functioning in different everyday contexts. NEAR allows for personalized computer training, which has been found to increase motivation and cognitive gains (Medalia & Saperstein, 2017). In the ICR intervention, each participant received a summary of his own cognitive strengths and weaknesses, based on his baseline cognitive performance, and recommendations for games that target weaknesses. Figure 3 shows an example of an individual cognitive profile. Participants were always given the option of working on their weaknesses or strengths within the selected computer training programs. The computer training programs included BrainHQ (Posit Science, Inc., San Francisco, CA), Lumosity (www.lumosity.com), and Games for the Brain (www.gamesforthebrain.com).

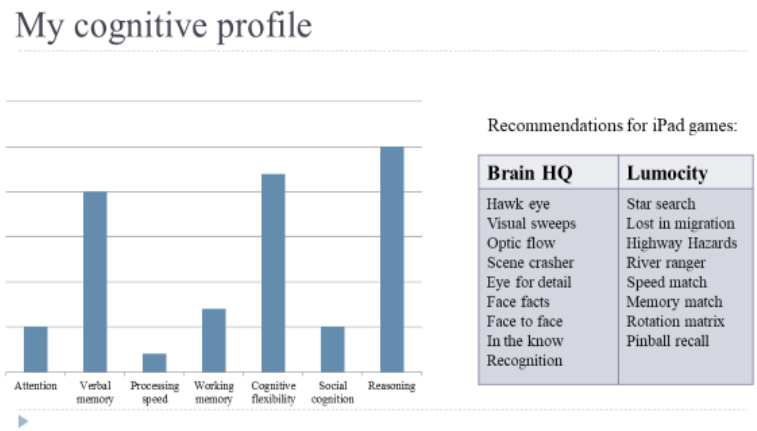

Figure 3. An individual training program based on baseline cognitive performance

3.4.2.2 Compensatory Cognitive Training (CCT)

CCT combines compensatory strategy training with client-driven environmental modifications to help clients develop cognitive strategies to form long-term habits that are meaningful in the real world. CCT training teaches clients self-management techniques as well as environmental adaptations targeting four neurocognitive domains that have been found to be modifiable and related to real-world functioning. These domains include prospective memory, attention, learning/memory, and executive functioning. The CCT manual presents a 12-session curriculum designed to be administered individually (1-hr per week for 12 weeks) or in groups of 4-8 (2-hr per week for 12 weeks).

3.4.2.3 Social Cognition and Interaction Training (SCIT)

SCIT is a manual-based group psychotherapy targeting several domains of social cognition. They include emotion perception, ToM, and attributions as well as metacognitive overconfidence and interaction skills to improve social functioning. SCIT has 24 sessions that are usually delivered once a week over a six-month period. However, although we did not edit out any material from the SCIT manual, we delivered SCIT 2x per week over a three-month period, as one part of the complete ICR intervention. SCIT draws substantially on cognitive behavioral therapy (CBT) and uses graded exposure by gradually confronting clients with increasingly self-relevant, challenging, and ambiguous social experiences. However, SCIT focuses relatively more on social-cognitive processes than cognitive content and targets dysfunctional interpretive processes that may lead to distorted or impoverished inference (Roberts et al., 2016).

3.4.3 Session structure

All sessions began with structured check-ins designed to increase emotional self-awareness. In the first two sessions, psychoeducation, goal setting, and discussion of cognitive principles followed the check-in. After the first two sessions, SCIT material was delivered, as the SCIT manual instructed, for 40-45 min. Then a 15-20 min. break was provided. After the break, one CCT strategy was introduced and practiced, and the remaining time was spent playing games on iPads. We deemed it more feasible for younger people to complete the computerized training using iPads rather than desktop computers. Evidence suggests that younger people favor iPads over desktop computers, and that there is not a significant difference in effects on cognition between the two methods (Biagianti et al., 2017). Table 2 describes the session content, treatment strategies and modifications applied to each of the three approaches.

Table 2. Session content, treatment strategies and modifications.

	SCIT	CCT	NEAR
Session content	Review of agenda, check-ins, and activities specific to the session topic	Introduction of a strategy, discussion on how to use the strategy in everyday life	Strategy practice iPad training
Strategy	*Sessions 1-6* Phase I – Emotions Introduce ICR and establish group alliance. Address emotion perception, emotion self-awareness and overconfidence by defining emotions, emotion mimicry, and understanding paranoia *Sessions 7-15* Phase II-Figuring out situations Address ToM, social perception and attributional bias by thinking up other guesses, separating social facts from guesses, and gathering more evidence *Sessions 16-24* Phase III – Checking-it-out Focus on generalizing skills to day-to-day life	*Sessions 1-6* Prospective memory Goal setting, calendar use and weekly planning Session 7-12 Conversational and task vigilance. Goals revisited, self-talk to stay focused *Sessions 13-18* Verbal learning and memory Goals revisited, reducing information and making it meaningful, writing down, and name-learning skills *Sessions 19-24* Cognitive flexibility Goals revisited, brainstorming, and 6-step problem solving method	*Sessions 1-24* Individualized iPad training using commercial programs Training programs tailored to each participant's cognitive profile. Therapists help with goal setting and use verbal encouragement and reinforcement. Therapists guided the training using questions to enhance metacognition and information processing
Modifi-cations	Discussion of homework eliminated All homework, other than meeting with a practice partner, eliminated Practice partner exercises reduced to include CCT strategies	Material adjusted to 24, 15-20 minute sessions. IPad training of strategies instead of paper-pencil Discussion of homework eliminated	CCT strategies practiced on iPads when appropriate

Note. SCIT: Social Cognition and Interaction Training; CCT: Compensatory Cognitive Training; NEAR: Neuropsychological Educational Approach to Remediation.

3.5 Implementing ICR into standard psychosis care

The research evidence supporting CR in early psychosis was examined and presented by the author (OGV) to clinical directors, leaders, and all other staff at the early psychosis clinic. The rate and nature of cognitive impairment of patients in service at the early psychosis service were evaluated in the first study.

The program facilitators were two psychologists and three occupational therapists. In addition, two master's level psychology students, two bachelor level psychology students and two supportive counsellors were a part of the treatment team. The doctoral candidate (OGV) was the treatment team leader and managed every therapy session. Prior to the study, OGV received training by the authors of the programs. OGV then provided the team with a two-day training course. Furthermore, the entire treatment team travelled to Denmark to observe a session on a neuro- and social-cognitive intervention with a similar set-up (Glenthøj et al., 2015). Finally, in addition to reading the treatment manuals, all facilitators were required to complete two online courses on cognitive dysfunction and cognitive remediation for people with psychiatric disorders provided by Columbia University (http://teachrecovery.cumc.columbia.edu/). The treatment team received consultation by DLR and/or EWT during the intervention through Skype.

3.5.1 Assessment of implementation outcomes

Implementation outcomes were assessed using data from fidelity checks, assessment of program feasibility and acceptability, and maintenance. Two fidelity scales, issued with the SCIT and the CCT treatment manuals were used. Each session was audio recorded and sessions were randomly chosen and rated for fidelity by an independent researcher who listened to 27% of randomly selected sessions and rated how well the leading therapist (OGV) delivered the intervention as designed. No material was edited out of the SCIT manual and fidelity to the manual was rated by the following eight factors: orientation and organization; review previous session activities; check-in; adherence to session goals, objective and activities; quality of the delivered intervention; conclusion and wrap-up; skill maintenance-emotion identification; skill maintenance-strategies for avoiding jumping to conclusions. Each factor was given a score ranging from 0 (poor quality), 1 (fair quality), 2 (acceptable quality) or N/A (not applicable for this session). The CCT manual was edited by the author (EWT) and OGV. The main domains targeted by the CCT program were targeted in the intervention, and most of the strategies were introduced. However, the time spent on practicing

each strategy was shorter than in the original CCT manual. The CCT fidelity scale was edited to fit the shorter version of the CCT and included different factors, based on the content of each session. All factors were rated as 0 (the criterion was not met), 1 (the criterion was met) or N/A (not applicable).

All participants receiving the intervention were asked to complete a feedback questionnaire OGV developed for this study. It had thus not been used in other studies. Participants were asked to rate the length of each session (2 hours) and the length of the intervention (12 weeks) on a 5-point Likert Scale. They were also asked to rate how useful they thought each of the three approaches was, and how useful they thought the practice partner exercises were on a 10-point Likert Scale. Finally, they were asked to state their most common reason/s for attending the sessions, and whether they would recommend the program to others. Clinicians that served as practice partners were asked to report the length of each practice partner session.

All facilitators participated in two focus group sessions. The first one was six weeks after the start of the intervention, and the second was after the intervention (12 weeks). They were asked open questions with general prompts regarding experience with computer programs, session content, the running of the intervention, and the time and practicality of the intervention. All practice partners participated in a separate focus group session at the end of the intervention.

3.6 Statistical analysis

All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 26. Variables were checked for normality and outliers. Raw scores were used for all measures. Skewed data were handled using log transformations.

3.6.1 Paper I

To examine the rate of cognitive impairment, raw scores for each of the cognitive measures were converted to z-scores, using published (WAIS-IV, WASI^{is}, D-KEFS) or local (LMI, LMII, TMT A, TMT B, and Stroop) norms that matched the general demographics of the experimental sample (Magnusdottir et al., 2019). Regarding the social-cognitive measures, z-scores were calculated, based on local age-matched healthy comparison groups (Fridriksson, 2016; Össurardóttir, 2018). A one-sample *t*-test was then used to investigate whether the proportion of impairment (>1 SD below the mean) in this population was significantly higher than what would be

expected in a healthy population based on the normal distribution (0.16). Because this study used several measures and conducted multiple simultaneous statistical tests, the significance levels for all analyses were set at 0.01 to reduce the risk of Type I error associated with multiple comparisons. Impairment or deviance from a normal cognitive function was defined as greater than 1 SD below the mean. Pearson correlations were used to explore intercorrelations between the social-cognitive measures, and how they correlated with measures of neurocognition, clinical symptoms and social functioning. To investigate the individual contributions of neuro- and social-cognitive domains to self-reported and informant-reported functional outcome a multiple linear regression was conducted. The cognitive measures correlating significantly with the social functioning measures were used as independent variables and each of the five social functioning measures were used separately as a dependent variable.

3.6.2 Paper II

Chi-square and *t*-tests were used to (a) compare individuals receiving the intervention to those who were in the wait-list control group on demographic, clinical, and cognitive variables at baseline; (b) compare individuals who dropped out during the intervention to those who completed the intervention on the same variables. Significance levels were set at 0.05. An intent-to-treat analysis was used that included all enrolled participants regardless of level of participation in the intervention. Analysis of covariance (ANCOVA) was used to examine change between the two conditions from baseline to post-treatment while controlling for pre-treatment levels.

3.6.3 Paper III

Independent *t*-tests and chi-square tests (for dichotomous variables) were used to (a) examine differences between the ICR group and the historical control group on demographic and clinical variables at baseline; (b) examine differences between the two groups on the number of participants employed and enrolled in school at baseline, post-treatment and a 12-month follow-up; (c) examine differences in cognitive, clinical symptom or functional outcome scores for individuals who had been discharged from the EIP service at follow-up and those who had not. The Mann-Whitney U test or the Friedman test was used for skewed variables. Paired sample t-tests were used to examine within-group change from baseline to 12-month follow-up on the number of participants employed and enrolled in school.

A repeated measures ANOVA with a Greenhouse-Geisser correction was conducted to examine changes in cognition, clinical symptoms, and functional outcome from baseline to the 12-month follow-up for all ICR participants. Post-hoc tests were conducted on all outcomes to evaluate the stability of outcomes from posttreatment to 12-month follow-up. To evaluate the role of clinical state on cognitive and functional outcomes we calculated change scores (follow-up minus baseline) for those variables that demonstrated significant improvement from baseline to 12-month follow-up. The correlates of these change scores with PANSS positive and negative symptom severity at baseline was then examined with Pearson correlations. Significance levels were set at 0.01 to reduce the risk for Type I error. Effect size for ANOVA was assessed by partial η^2, in which medium (>0.06) and large (>0.14) effects were considered clinically meaningful.

3.6.4 Implementation

Descriptive statistics were used to report the implementation outcomes.

4 Results

This chapter summarizes the main results from the three papers and the implementation process.

4.1 Demographics and clinical characteristics at baseline for the final samples in the three papers

Table 3 shows the demographics and clinical characteristics at baseline for the final sample in the three studies. Most of the participants in all three studies were diagnosed with schizophrenia and were taking antipsychotic medication. Although medication changes were allowed throughout the study, every effort was made to stabilize patients on an acceptable medication regimen prior to their enrolment in the intervention study.

Table 3. Demographics and clinical characteristics at baseline for the final samples in studies I – III

	Paper I	Paper II			Paper III	
	n=70	Whole sample *n*= 49	ICR *n*=25	TAU *n*=24	ICR *n*=37	Historical control group *n*=30
	M (SD)/ %	M (SD)/ %	M (SD)/ %	M (SD)/ %	M (SD)/ %	M (SD)/ %
Age (years)	24.1(3.1)	24.2 (3.2)	23.6 (3.4)	24.8 (2.9)	24.0 (3.3)	24.4 (3.9)
Education (years)	11.3 (1.7)	11.3 (1.6)	10.7 (1.2)	11.9 (1.7)	11.0 (1.4)	11.7 (1.9)
Age of onset (years)	22.2 (3.0)	22.3 (3.1)	21.6 (3.4)	23.0 (2.6)	22.0 (3.1)	22.6 (2.8)
Duration of illness (months)	25.6(17.9)	28.7 (22.0)	30.4 (26.5)	26.8 (16.4)	31.5 (24.1)	24.2 (18.4)
Number of hospitalizations	2.9 (2.1)	2.7 (1.9)	3.0 (2.2)	2.5 (1.6)	2.9 (1.9)	3.3 (2.3)
DUP (weeks)	10.6 (28.2)	9.6 (16.2)	10.6 (17.0)	8.4 (15.7)	9.9 (17.6)	NA
Gender, % male	87.1%	86.0%	92.0%	83.3%	89.2%	83.3%
Diagnosis						
Schizophrenia	84.3%	68.0%	64.0%	75.0%	70.3%	83.3%
Psychosis NOS	12.9%	28.0%	32.0%	25.0%	27.0%	13.3%
Schizoaffective disorder	2.9%	2.0%	4.0%	0%	2.7%	3.3%
Medication						
Atypical antipsychotics	81.4%	89.8%	88.0%	91.7%	89.2%	73.3%
Typical antipsychotics	2.9%	10.2%	16.0%	4.2%	13.5%	3.3.%
No antipsychotics	7.1%	6.0%	4.0%	8.3%	6.3%	23.3%

Note. ICR: Integrated Cognitive Remediation; TAU: Treatment as usual; DUP: Duration of untreated psychosis; otherwise specified; NA: Not Available.

4.2 Paper I

4.2.1 Cognitive functioning of the sample

Table 4 shows the average performance of the 70 participants assessed relative to healthy controls on clinical symptoms, functional outcome and cognitive measures. The average performance of the sample was only impaired (<1 SD below healthy comparison samples) on measures of delayed recall (LMII; z-score = -1.07), ToM (Hinting Task; z-score = -1.47), and metacognitive overconfidence (FEIT confidence in incorrect answers; z-score = -2.1). However, the proportion of impairment was significantly higher than what would be expected in a healthy population on all cognitive measures except for measures of visual reasoning (Matrix Reasoning), planning (Tower), and executive functioning (TMT ratio).

4.2.2 Associations of the social-cognitive measures

Worse performance on the Hinting Task was associated with less confidence in correct answers on the FEIT and less negative symptoms (Table 5). In addition, better performance on the Hinting Task was associated with better performance on immediate verbal memory (LMI) and delayed recall (LMII). Better performance on the FEIT was associated with more confidence in correct answers on the FEIT, better performance on both verbal memory tasks (LMI and LMII), and better performance on Matrix Reasoning. A more blaming attributional style (AIHQ blame scale) was associated with a higher tendency to interpret ambiguous situations as hostile (AIHQ hostility bias), and more positive symptoms.

Table 4. Performance of the sample (*N*=70), relative to healthy controls on clinical symptom, functional outcome, and cognitive measures.

	M (*SD*)	Range in sample	
Clinical symptoms[a]			
PANSS positive	12.5 (4.3)	7-22	
PANSS negative	14.8 (5.6)	7-22	
PANSS general	29.8 (7.4)	16-51	
DASS-21 depression	7.5 (6.3)	0-20	
DASS-21 anxiety	4.3 (4.3)	0-15	
DASS-21 stress	5.5 (4.5)	0-20	
Functional outcome			
LSP	25.5 (2.9)	19-30	
BRIEF-A informant[a]	126.0 (28.5)	73-186	
BRIEF-A self-report[a]	124.5 (25.1)	71-177	
QOLS	52.3 (13.9)	28-100	
OSA	73.5 (14.6)	30-106	
	M (*SD*)	Z-Scores (*SD*)	% impaired[b]
Social Cognition			
Hinting Task	14.2 (3.0)	-1.47 (1.87)	46.3%**
FEIT	12.8 (2.5)	-0.95 (1.40)	47.8%**
FEIT conf. correct	1.8 (0.5)	0.14 (1.68)	2.1%**
FEIT conf. incorrect[a]	2.2 (0.6)	-2.10 (0.95)	93.0%**
AIHQ hostility[a]	2.0 (0.6)	-0.55 (1.25)	31.7%**
AIHQ blame[a]	2.2 (0.8)	-0.31 (1.26)	29.5%**
AIHQ aggression[a]	1.6 (0.4)	0.12 (1.49)	25.0%**
Neurocognition			
Symbol Coding	60.7 (14.0)	-0.36 (0.82)	28.6%**
Digit Span forward	8.3 (1.8)	-0.56 (1.06)	45.7%**
Digit Span backward	7.4 (1.6)	-0.39 (0.69)	31.4%**
LMI	30.8 (10.1)	-0.91 (0.84)	46.4%**
LMII	17.8 (9.2)	-1.07 (1.04)	53.6%**
Matrix Reasoning	26.9 (4.4)	-0.12 (0.99)	17.6%
Stroop interference[a]	30.6 (10.8)	-0.46 (1.11)	26.8%**
Tower	16.4 (2.8)	-0.12 (0.77)	15.2%
TMT ratio	2.8 (0.8)	-0.02 (0.79)	6.1%

Note. FEIT: Facial Emotion Identification Task; AIHQ: Ambiguous Intentions Hostility Questionnaire; LMI and LMII: Logical Memory parts I and II; TMT ratio: Trail Making Test ratio.

[a] Higher scores reflect greater pathology.

[b] > 1 SD worse than reference mean.

*p < 0.05; **p < 0.01.

Table 5. Correlations between measures of social cognition, neurocognition, and clinical symptoms.

	Hinting Task	FEIT	FEIT conf. correct	FEIT conf. incorrect	AIHQ hostility	AIHQ blame	AIHQ aggr.
Social Cognition	‘						
Hinting Task	-						
FEIT	0.25*	-					
FEIT conf. correct	-0.32**	-0.33**	-				
FEIT conf. incorrect	-0.16	-0.15	0.75**	-			
AIHQ hostility[a]	0.15	-0.01	-0.22	-0.02	-		
AIHQ blame[a]	0.15	-0.21	-0.15	-0.12	0.65**	-	
AIHQ aggression[a]	-0.05	0.07	-0.09	-0.08	-0.26*	0.09	-
Neurocognition							
Symbol Coding	0.23	0.27*	-0.11	0.10	0.12	0.01	0.01
Digit span forward	-0.05	0.00	-0.15	-0.23	0.12	0.10	-0.16
Digit span backward	0.11	0.19	-0.02	0.01	-0.03	-0.01	0.07
LMI	0.40**	0.44**	-0.37**	-0.08	-0.01	-0.04	0.01
LMII	0.45**	0.52**	-0.26**	-0.03	-0.07	-0.10	-0.10
Matrix Reasoning	0.24	0.33**	-0.14	-0.13	-0.13	-0.04	-0.06
Stroop interference[a]	-0.17	-0.16	0.07	0.08	-0.04	0.23	0.04
Tower	0.02	0.07	0.14	0.13	-0.12	0.11	-0.10
TMT ratio	0.10	0.03	0.07	-0.09	-0.09	-0.14	0.01
Clinical symptoms							-0.23
PANSS positive[a]	-0.05	-0.17	-0.01	-0.09	0.32*	0.40**	0.12
PANSS negative[a]	-0.41**	-0.26*	0.26*	0.01	-0.27*	-0.24	

Note. FEIT: Facial Emotion Identification Task; AIHQ: Ambiguous Intentions Hostility Questionnaire; LMI and LMII: Logical Memory parts I and II; TMT: Trail Making Test; PANSS: Positive and Negative Syndrome Scale. *$p < 0.05$; **$p < 0.01$.

4.2.3 The predictive value of cognitive measures for variance in informant- and self-reported functional outcomes

Table 6 shows the correlations between cognitive measures and measures of functional outcome. In the context of multiple predictor variables, LMI and FEIT explained 16% of the variance in total scores of the LSP (Table 7). The AIHQ hostility bias and AIHQ blame scale explained 32.9% of the variance in total scores of BRIEF-A self-report. The AIHQ hostility bias and AIHQ aggression bias explained 33.9% of the variance in total scores of the OSA. BRIEF-A informant and QOLS were not significantly correlated with any of the cognitive variables and were therefore not used in regression analyses.

Table 6. Correlations between measures of functional outcome, social cognition, and neurocognition.

	Informant-report		Self-report		
	LSP	BRIEF-A[a] Informant	BRIEF-A[a] self-report	OSA	QOLS
Social Cognition					
Hinting Task	-0.07	-0.07	0.03	0.07	0.11
FEIT	0.35**	-0.29*	-0.20	0.11	0.08
FEIT conf. correct	-0.12	0.15	-0.02	0.04	-0.05
FEIT conf. incorrect	-0.02	-0.09	-0.03	0.03	-0.11
AIHQ hostility[a]	-0.19	0.17	0.41**	-0.49**	-0.27*
AIHQ blame[a]	-0.27	0.14	0.59**	-0.34*	-0.32*
AIHQ aggression[a]	0.01	-0.16	-0.25	0.44**	0.14
Neurocognition					
Symbol Coding	-0.03	0.03	-0.07	0.14	0.14
Digit span forward	-0.01	-0.04	0.14	0.01	-0.06
Digit span backward	0.07	-0.06	-0.01	0.27*	0.18
LMI	0.38**	-0.30*	-0.19	0.20	0.14
LMII	0.28*	-0.19	-0.21	0.25	0.17
Matrix Reasoning	0.05	-0.15	0.11	0.01	-0.17
Stroop interference[a]	0.15	-0.11	0.10	-0.01	-0.05
Tower	0.11	-0.20	0.30*	-0.12	-0.11
TMT ratio	0.08	0.04	-0.09	-0.08	-0.08

Note. LSP: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self-Assessment; QOLS: Quality of Life Scale; FEIT: Facial Emotion Identification Task; AIHQ: Ambiguous Intentions Hostility Questionnaire; LMI and LMII: Logical Memory Part I and II; TMT: Trail Making Test.
*$p < 0.05$; **$p < 0.01$.

Table 7. Regression analyses for cognition's incremental prediction of functional outcome.

Dependent variable	Predictor	Beta	*P*	*F* change	R^2	Adjusted R^2	Sig of the model
BRIEF-A self-report	AIHQ hostility	0.038	0.788	15.446	0.351	0.329	<0.001**
	AIHQ blame	0.574	0.001**				
OSA	AIHQ hostility	-0.422	0.001**	12.806	0.339	0.312	<0.001**
	AIHQ aggression	0.306	0.013*				
LSP	FEIT	0.232	0.098	6.061	0.190	0.160	0.004**
	LMI	0.276	0.051				

Note. BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self-Assessment; LSP: Life Skills Profile; LMI: Logical Memory part I; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task.
*$p < 0.05$; **$p < 0.01$.

4.3 Paper II

4.3.1 Baseline group differences

No significant differences in any baseline demographic, clinical, and cognitive variables were found between the ICR and TAU groups, except that the TAU group had significantly more years of education ($t(42) = -3.00$, $p = 0.006$) (Table 3). The cognitive variables that correlated with education were therefore entered as covariates with the baseline performance in the ANCOVA. These variables included Matrix Reasoning ($r = 0.381$, $p = 0.007$), Digit Span working memory ($r = 0.392$, $p = 0.006$), LMI ($r = 0.288$, $p = 0.045$), LMII ($r = 0.302$, $p = 0.035$), and the AIHQ blame scale ($r = 0.304$, $p = 0.044$). Results from these analyses demonstrated that controlling for education did not have an impact on the significance of the between-group findings.

4.3.2 Effects of ICR

Table 8 presents the ANCOVA results, comparing the two conditions at post-treatment while controlling for baseline scores. The intervention was associated with improvements on LMI theme, LMII theme, Digit Span working memory span and TMT B. Effect sizes ranged from 0.11 (LMI theme) to 0.19 (TMT B). Significant ICR-associated effects were found on the Hinting Task and AIHQ hostility bias with effect sizes 0.10 and 0.13, respectively. There were no significant ICR-associated effects on measures of functional outcome or clinical symptoms at post-treatment. A post-hoc linear regression analysis for ICR participants suggested a dose-response effect at post-treatment on LMII theme ($p = 0.038$), Digit Span working memory ($p = 0.046$) and TMT A ($p = 0.043$), with higher attendance associated with better performance.

Table 8. Analysis of covariance results comparing conditions at post-treatment and controlling for baseline scores

Measures	Baseline *M* (*SD*) TAU	Post-treatment *M* (*SD*) TAU	Baseline *M* (*SD*) ICR	Post-treatment *M* (*SD*) ICR	*F*	*P*	η^2 effect size
Neurocognition							
Symbol Coding	65.5 (14.8)	64.5 (11.5)	59.2 (14.4)	62.6 (13.6)	0.22	0.644	0.01
TMT A[a]	29.8 (8.7)	30.9 (11.3)	28.6 (10.9)	27.9 (12.0)	0.82	0.371	0.02
Digit Span forward	8.3 (1.9)	8.3 (1.5)	8.1 (1.8)	8.5 (1.7)	0.18	0.678	0.01
Digit Span WM	8.0 (1.4)	7.6 (1.3)	7.7 (1.5)	8.2 (1.4)	6.63	**0.014**	0.13
LMI	31.2 (8.7)	33.3 (10.3)	29.8 (10.5)	35.1 (12.4)	1.09	0.301	0.03
LMI theme	12.3 (2.7)	12.2 (3.3)	11.7 (3.2)	14.4 (4.6)	6.10	**0.018**	0.13
LMII	20.0 (8.2)	20.2 (8.4)	16.6 (9.4)	22.1 (9.5)	3.93	0.054	0.09
LMII theme	8.4 (2.7)	8.4 (3.0)	7.4 (3.4)	9.4 (3.1)	4.81	**0.034**	0.11
Matrix Reasoning	27.2 (4.5)	28.6 (3.8)	26.8 (4.8)	28.0 (5.2)	0.29	0.593	0.01
Stroop interference[a]	29.2 (11.7)	29.6 (9.2)	30.4 (9.3)	27.0 (7.5)	1.87	0.179	0.04
Tower	16.7 (3.5)	18.3 (4.1)	16.1 (2.6)	17.1 (4.4)	0.15	0.697	0.01
TMT B[a]	77.6 (28.7)	86.9 (32.1)	73.1 (20.4)	70.6 (14.2)	9.53	**0.004**	0.19
Social cognition							
Hinting Task	14.8 (2.9)	15.8 (3.0)	14.0 (2.7)	16.5 (2.6)	4.76	**0.035**	0.10
AIHQ hostility[a]	10.3 (3.0)	8.4 (2.7)	9.2 (2.8)	6.2 (1.9)	6.21	**0.025**	0.13
AIHQ blame[a]	34.0 (9.5)	33.1 (9.7)	34.4 (10.9)	29.8 (10.1)	0.49	0.488	0.01
AIHQ aggression[a]	8.6 (1.8)	7.9 (1.3)	7.9 (1.8)	7.7 (1.9)	0.00	0.997	0.01
FEIT	12.9 (2.2)	13.1 (2.7)	12.7 (2.7)	13.6 (2.4)	0.57	0.456	0.01
FEIT conf. correct	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	2.0 (0.5)	2.59	0.115	0.05
FEIT conf. incorrect[a]	1.2 (0.8)	1.1 (0.8)	1.2 (0.7)	1.0 (0.6)	0.14	0.714	0.01
BCIS	8.8 (6.8)	8.8 (6.5)	8.5 (6.5)	7.7 (5.9)	0.245	0.624	0.01
Functional outcome							
LSP	124.7 (13.8)	128.6 (8.6)	127.5 (15.1)	127.6 (14.5)	0.19	0.670	0.01
BRIEF-A informant[a]	127.8 (32.2)	130.3 (30.3)	130.4 (27.2)	129.9 (23.1)	0.13	0.718	0.01
BRIEF-A self-report[a]	127.0 (22.8)	128.2 (22.2)	124.9 (25.1)	119.0 (23.3)	2.73	0.110	0.06
OSA	49.2 (8.9)	47.6 (9.4)	52.06 (12.0)	49.8 (7.8)	0.41	0.526	0.01
QOLS	73.0 (13.3)	69.1 (10.2)	77.1 (14.4)	70.1 (13.6)	0.26	0.616	0.01
Clinical symptoms[a]							
PANSS positive	11.9 (4.0)	11.1 (3.8)	13.7 (5.2)	12.9 (4.9)	1.30	0.264	0.04
PANSS negative	15.6 (4.9)	13.0 (3.7)	15.6 (6.2)	14.2 (5.0)	0.89	0.354	0.03
DASS-21 depression	6.3 (5.2)	9.7 (5.9)	7.7 (6.8)	7.4 (5.4)	2.25	0.141	0.05
DASS-21 anxiety	4.2 (4.2)	6.3 (5.0)	4.8 (4.2)	4.3 (4.3)	1.37	0.249	0.03
DASS-21 stress	5.7 (4.7)	7.2 (5.5)	5.7 (4.9)	6.7 (5.1)	0.05	0.829	0.01

Note. TAU; Treatment as Usual; ICR: Integrated Cognitive Remediation; TMT: Trail Making Test; Digit Span WM: Digit Span working memory span; LMI and LMII: Logical Memory Parts I and II; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task; BCIS: Becks Cognitive Insight Scale; LSP: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function-Adult version; OSA: Occupational Self-Assessment; QOLS: Quality of Life Scale; PANSS: Positive and Negative Syndrome Scale; DASS-21: Depression, Anxiety and Stress Scale.
[a] Higher scores reflect greater pathology.
[b] Bolded significance values indicate those significant at $p < 0.01$.

4.4 Paper III

4.4.1 Baseline group differences

The ICR group and the historical control group did not differ significantly in any key demographic, clinical symptom or cognitive variables at baseline. At the 12-month follow-up, 12 (32.4%) of the ICR group had been discharged from the EIP service and 16 (53.3%) of the historical control group, but the difference between the two groups was not significant for any of the outcome variables.

4.4.2 Stability and change in cognitive functioning from baseline to 12-month follow-up

A significant increase in performance from baseline to 12-month follow-up was found for Symbol Coding, Digit Span forward, LMI, LMI theme, LMII, LMII theme, Matrix Reasoning, Stroop interference, Tower, Hinting Task and AIHQ hostility bias with large effect sizes from baseline to 12-month follow-up (Table 9). The change scores for these variables were not associated with change scores for PANSS positive or PANSS negative symptom severity at baseline. Post-hoc tests showed a significant level of continued improvement from post-treatment to 12-month follow-up on LMI ($p = 0.011$), LMII ($p = 0.009$), LMII theme ($p = 0.034$) and Symbol Coding ($p = 0.039$).Although scores on AIHQ hostility bias and TMT B were elevated, meaning that the performance on these measures was worse at 12-month follow-up than at posttreatment, the difference was not significant.

4.4.3 Changes in functional outcome and clinical symptoms from baseline to 12-month follow-up

Inspection of scores on the five functional outcome measures revealed no significant improvement in scores from baseline to 12-months follow-up (Table 9). Effect sizes for improvement on informant-reported functional outcome measures (LSP and BRIEF-A informant) was large. Effect sizes range from small to large on the three self-reports (OSA, BRIEF-A self-report and QOLS). The number of participants working increased significantly between baseline and 12-month follow-up in the ICR group ($t(36)= -3.97$, $p < 0.001$), but not in the historical control group. At baseline, 8 (21.6%) participants were employed in the ICR group and 11 (33.3%) in the historical control group. At posttreatment, 10 (37.8%) from the ICR group were employed, and 12 (56.8%). One year later, the number of participants that were employed had increased to 21 (56.8%) participant in the ICR group and 15 (46.7%) in the historical control group (Figure 2). School enrolment increased from 5 (13.5%) to 7 (18.9%) in the ICR group and from 3 (10%) to 6 (20%) in the control group, but the difference was not significant in either group. No significant between-group differences were found in occupational or educational status at the three assessment points. Although there was not a significant change in scores on measures of clinical symptoms, the effect size for improvement in negative symptoms was large (0.15).

Table 9. Results of Analyses of Variance for cognitive, functional outcome, and clinical symptom measures at baseline compared with 12-months follow-up for ICR completers

Measures	Baseline *M* (*SD*)	Post-treatment *M* (*SD*)	12-months *M* (*SD*)	*F (df), p*	η^2, effect size
Neurocognition					
Symbol Coding	61.0 (14.0)	64.8 (13.2)	68.5 (14.3)	**9.15 (1.5), 0.001**	0.23, large
TMT A[a]	29.0 (10.6)	27.7 (12.1)	26.4 (10.5)	1.84 (1.9), 0.171	0.06, small
Digit Span forward	7.9 (1.7)	8.4 (1.6)	8.6 (1.7)	**5.63 (1.7), 0.009**	0.16, large
Digit Span wm	7.6 (1.4)	8.2 (1.4)	8.4 (1.6)	3.33 (1.7), 0.049	0.10, medium
LMI	30.9 (10.3)	36.3 (12.3)	41.3 (11.3)	**19.21 (1.9), 0.000**	0.41, large
LMI theme	12.1 (3.0)	14.5 (4.6)	15.3 (3.4)	**14.96 (1.7), 0.000**	0.35, large
LMII	18.1 (9.0)	23.7 (10.1)	27.9 (8.1)	**28.71 (2), 0.000**	0.51, large
LMII theme	8.1 (3.0)	9.7 (3.0)	10.7 (2.5)	**19.51 (1.8), 0.000**	0.41, large
Matrix Reasoning	26.6 (5.1)	28.2 (5.3)	28.5 (4.4)	**5.56 (1.9), 0.007**	0.17, large
Stroop interference	31.3 (11.1)	26.5 (9.3)	26.1 (7.9)	**5.95 (1.8), 0.006**	0.17, large
Tower	16.7 (3.0)	17.8 (4.1)	19.4 (3.7)	**8.06 (2), 0.001**	0.24, large
TMT B[a]	75.1 (24.1)	68.3 (16.5)	75.8 (28.9)	1.89 (1.6), 0.180	0.06, medium
Social cognition					
Hinting Task	14.0 (2.9)	16.0 (2.8)	16.2 (2.8)	**17.25 (1.8), 0.000**	0.37, large
AIHQ hostility[a]	9.6 (3.0)	7.0 (2.4)	8.3 (2.7)	**11.96 (1.9), 0.000**	0.32, large
AIHQ blame[a]	31.2 (10.1)	31.4 (10.2)	30.1 (9.3)	0.26 (1.6), 0.728	0.01, small
AIHQ aggression[a]	8.3 (1.6)	8.2 (2.0)	8.5 (1.8)	0.40 (2), 0.675	0.02, small
FEIT	13.1 (2.5)	13.8 (2.4)	13.2 (2.5)	1.34 (1.9), 0.269	0.04, small
FEIT conf. correct	1.8 (0.4)	1.9 (0.4)	1.8 (0.4)	1.09 (2), 0.344	0.04, small
FEIT conf. incorrect[a]	1.1 (0.7)	1.0 (0.6)	1.1 (0.7)	0.69 (1), 0.414	0.02, small
BCIS	-5.9 (8,3)	-5.5 (6.7)	-6.4 (6.1)	0.21 (1.6), 0.762	0.01, small
Functional outcome					
LSP	123.3 (14.7)	127.3 (13.5)	130.0 (13.6)	3.54 (1.9), 0.040	0.15, large
BRIEF-A informant[a]	130.4 (29.7)	127.2 (27.2)	120.6 (28.1)	1.86 (2), 0.169	0.08, medium
BRIEF-A self-report[a]	125.4 (22.8)	118.8 (22.8)	116.0 (25.1)	2.89 (1.8), 0.072	0.10, small
OSA	52.6 (13.4)	54.4 (11.8)	58.0 (12.8)	3.45 (1.8), 0.047	0.14, medium
QOLS	77.6 (12.8)	74.3 (12.7)	78.6 (14.2)	2.79 (1.9), 0.073	0.10, medium
Clinical symptoms					
PANSS positive[a]	11.9 (4.4)	12.2 (4.6)	11.6 (5.4)	0.17 (1.5), 0.788	0.01, small
PANSS negative[a]	15.2 (5.6)	14.3 (4.9)	12.5 (4.4)	3.54 (1.6), 0.049	0.15, large
DASS-21 depression[a]	6.6 (6.4)	6.5 (5.1)	6.0 (5.6)	0.27 (2), 0.756	0.01, small
DASS-21 anxiety[a]	4.2 (4.2)	4.6 (4.5)	4.1 (4.0)	0.19 (1.9), 0.816	0.01, small
DASS-21 stress[a]	5.3 (4.3)	6.2 (5.0)	5.2 (4.9)	1.07 (1.9), 0.348	0.04, small

Note. TMT: Trail Making Test; Digit Span WM: Digit Span working memory span; LMI and LMII: Logical Memory part I and II; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task; BCIS: Becks Cognitive Insight Scale; LSP: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self-Assessment; QOLS: Quality of Life Scale; PANSS: Positive and Negative Syndrome Scale; DASS-21: Depression, Anxiety and Stress Scale.

[a]Higher scores reflect greater pathology.

[b]Bolded significance values indicate those significant at $p < 0.01$.

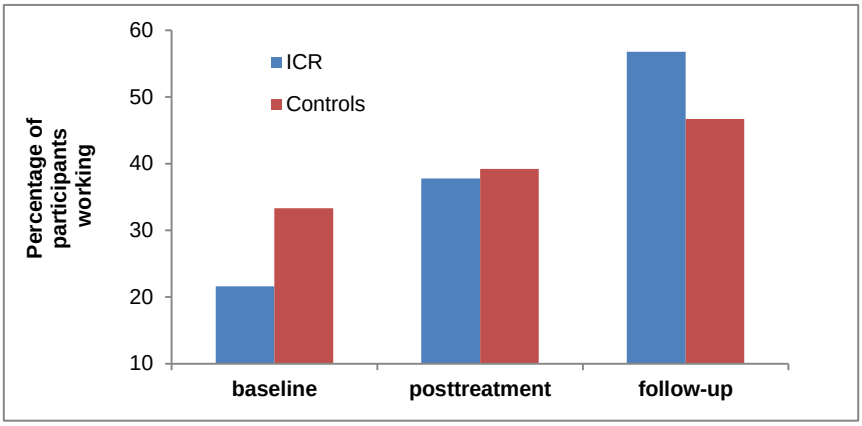

Figure 4. Longitudinal course of participants employed in the ICR and historical control groups.

4.5 Implementation outcomes

4.5.1 Fidelity

Fidelity to the SCIT manual was 86.6% (range: 71.4-100). Fidelity to the CCT treatment manual was 83.3% (range: 50-100). The combined total fidelity score for both SCIT and CCT was 86.6%.

4.5.2 Acceptability

The attendance rate was 77.6% (range 33.3-100) and the drop-out rate was 22.4%. Feedback from participants regarding the length of the intervention is depicted in figure 3.

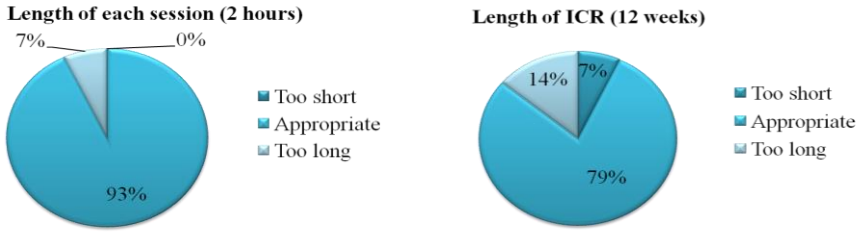

Figure 5. Participants´s feedback regarding the intensity of ICR.

The top five reasons participants listed for attending sessions were: “it was helpful (73%)”, “it was fun (53%)”, “there was good food (33%)”, “I liked the computer training (33%)”, and “I was told to attend (33%)”. The SCIT approach was rated by participants as the most useful approach (44.2%) followed by the NEAR approach (37.8%) and CCT strategies (18%). Only 33% thought that

exercises with a practice partner were helpful and the average completion rate for the practice partner exercises was 63%. On average, these exercises took 17.4 min (SD 2.2). Almost half (47%) of the participants would have preferred to have no practice partner exercises at all.

Regarding facilitators' experience with running the intervention, they thought they needed to know and understand the purpose of each computer game better. They also viewed it important to get more training on how to link material from each approach (SCIT, CCT, and the computer games) to real-world functioning as well as the goals participants were setting for themselves. We conducted a half-day workshop on this issue and included more reading material before the next group started. Facilitators mentioned that some participants were tired after about 30 minutes of playing the computer games and did not want to play any longer. We decided to discuss this issue with group members and reached a consensus that staying for 45 minutes was optimal, but participants would try to notice when they were getting tired and then take breaks more often. Furthermore, facilitators would reinforce the use of CCT strategies for attention/vigilance in these situations.

There were two issues mentioned at the practice partner focus group meeting. First of all, the practice partners often forgot to meet with participants. Second, they thought it was hard to complete exercises where participants needed to come up with their own examples and requested that more examples of situations would be included in the practice partner manual. For the following groups, all practice partners received a weekly e-mail from the facilitators with information on the content of each session. We also added more examples into the practice partner manual including examples on what would be an appropriate social situation to address and for the SCIT exercise "figuring-out-situations".

4.5.3 Maintenance

ICR was implemented at LUH as a part of this research. ICR has now been running two times per year at LUH since fall of 2016. Over the four years since the first groups started, a total of 92 patients have received the intervention (37 as part of the study). The intervention has been disseminated and is now available to all patients with a diagnosis of a psychotic disorder seeking treatment at any rehabilitation service for psychotic disorders at LUH. Furthermore, cognitive remediation based on the NEAR model is now being offered in an open-group format for a heterogeneous group seeking treatment at the psychiatric rehabilitation clinic at LUH. Eight therapists (four psychologists and five occupational therapists) have been trained in the

intervention methods. As it is important to ensure proper training for new therapists, the doctoral candidate continues to monitor and ensure that all new ICR therapists receive adequate training. To become a certified ICR therapist, an individual must complete the following:

1. A one-day course with the doctoral candidate (OGV) covering relevant topics including cognitive dysfunction in schizophrenia, cognitive remediation and social-cognitive training.
2. Three online training courses provided online by Columbia University free of charge.
3. Participate in one cycle of the intervention as a co-therapist.
4. Read intervention-related material, specifically, the manuals for each of the three interventions.

The doctoral candidate (OGV) continues to be a treatment team leader, as part of her clinical work. This entails overseeing assessments, preparation, and delivery of the intervention to ensure that it meets defined standards. Ongoing funding has been secured through funding from LUH. LUH also supports the program by providing program facilitators who are able to deliver the intervention as part of their clinical work, purchasing iPads, and paying access to computer programs.

5 Discussion

5.1 Main Findings

The aim of the studies presented in this thesis was to investigate the rate of cognitive impairment in patients seeking treatment at the only EIP service in Iceland and investigate the role of social cognition and neurocognition in predicting variance in self-reported and informant reported functional outcomes. Furthermore, we sought to implement a novel 12-week ICR and investigate the immediate and long-term effects on cognition, clinical symptoms and functional outcomes.

Overall, our findings showed significant neuro- and social-cognitive impairments compared to healthy comparison samples, which were most significant in immediate verbal memory and ToM. Results from the regression analyses indicated that in the context of multiple predictor variables, informant reported functional outcomes were predicted by immediate verbal memory and emotion perception, whereas self-reported functional outcome was best predicted by attributional style (Paper I). The intervention was associated with improvement on multiple neuro- and social-cognitive measures but there were no immediate effects on measures of functional outcome or clinical symptoms. After receiving ICR, participants showed significant improvements on most neuro- and social-cognitive domains from baseline to 12-month follow-up, and clinically meaningful long-term improvements on negative symptoms and functional outcome. The results from Paper II and Paper III provide preliminary evidence for the immediate and long-term efficacy of the intervention. The intervention was successfully implemented at the EIP service and is now among routinely available treatment options for all psychosis patients seeking service at all psychosis services at LUH.

5.2 Rate of cognitive impairment

Results suggested that the average performance of the whole sample was intact on all cognitive domains but delayed recall, ToM, and metacognitive overconfidence. However, previous evidence suggests that the variability between patients regarding cognitive performance is very high in early psychosis samples (Green et al., 2012; Horan et al., 2012; Woodberry et al., 2008), and therefore we also compared the rate of cognitive impairment in our sample to normative expectations. Results demonstrated that performance

was impaired on most neurocognitive and social-cognitive measures, which is in accordance with previous findings (Addington et al., 2003; Green et al., 2012; Healey et al., 2016; Mesholam-Gately et al., 2009). The need for cognitive remediation that targets multiple neuro- and social-cognitive domains is supported by our results.

5.3 Cognitive predictors of self-reported and informant reported functional outcomes

There were distinct differences that emerged between cognitive predictors of self-reported and informant reported functional outcome. As capturing the long-term efficacy of CR on the outcome of the psychotic illness becomes vital for the widespread implementation, these results provide valuable insights. To understand how CR interventions affect functional outcome in early psychosis it may be important to include both self-reports and informant reports in clinical trials. Furthermore, the results suggest that the distinction made by Roberts and Pinkham (2013) between social-cognitive *deficits* and *biases* is applicable in early psychosis samples. This distinction can be helpful in clinical practice in deciding which psychosocial intervention approaches to use with individual patients.

It may be that impairments in emotion perception and verbal memory affect the development of skill acquisition necessary for community functioning. The clinical symptom correlates of social-cognitive capacities suggest that negative symptoms may have specific additional contributions to the informant-reported functioning. Negative symptoms have been found to be strongly associated with functional outcome (Reichenberg et al., 2014), and even associate with community functioning when assessed with the LSP in early psychosis samples (Puig et al., 2013). Informant-reported community functioning of early psychosis samples may therefore be affected by a complex relationship between capacity-based social-cognitive domains, neurocognition and negative symptoms.

Our results replicate previous results on the importance of social-cognitive bias in predicting self-reported functioning (Ludwig et al., 2017), and imply that this domain may be an important treatment target. Adding social-cognitive training to CR may therefore be essential to achieve an overall improvement in self-reported functioning. The negative association of hostility and blame bias with self-reported occupational performance (OSA) may reflect the tendency of participants with excessively blaming or externalizing attributional style to attribute their poorer occupational performance to the hostile intentions of

others. Investigating further the subgroup of participants with high bias may shed more light on the meaning of the construct to the individual. It may also be that more bias contributes to the inaccuracy of self-reported functioning. Neurocognitive impairment, positive symptoms, insight, and depression are all factors that individually may affect the accuracy of self-reports (Bowie et al., 2007; Durand et al., 2015; Sabbag et al., 2012). The strong associations between hostile and blaming attributions and positive symptoms in our sample give indirect support for the conclusion that the relationship between bias and self-reported functioning is impacted by positive symptom severity. Furthermore, the results suggest that bias is not a trait characteristic of psychotic disorders, but specifically present in a subgroup of patients with more proneness to paranoid ideation and persecutory delusions, as has been previously suggested (Pinkham et al., 2016a). However, these assertions are speculative and should be further investigated in future studies.

The opposite significant relationship between AIHQ hostility and blame, on the one hand, and hostility and aggression on the other hand, as well as the different clinical correlates of aggression compared to hostility and blame was expected. It has been suggested that scores on the aggression scale that are higher than average but still close to midpoint may be understood as more "assertive" than "aggressive", referring to the participants´ willingness to take action or speak-up to rectify interpersonal problems (An et al., 2010). It is important to note that the psychometric properties of the aggression scale are inadequate and further developments of the scale are urgently needed.

5.4 Efficacy and effectiveness of ICR for early psychosis

The results suggest that ICR may be a promising treatment approach for both neurocognitive and social-cognitive impairment. These results add to earlier findings from broad-based cognitive remediation applied in early psychosis (Eack et al., 2009; Ueland & Rund, 2005). As discussed earlier, it is also important to determine the effectiveness of the intervention, or how the treatment impacts the overall outcome of the illness. For all participants that received the intervention, there was a clinically significant effect found on the three methods used to assess functional outcome; self-reported, informant-reported, and employment outcomes. These results suggest that ICR may add to the functional benefits associated with comprehensive treatment at EIP services.

From the results from paper I, it may be hypothesized that the main intervention-associated effects on ToM and verbal memory may in part be due

to the impaired baseline performance of the sample, with greater room for improvement. The intact baseline performance on processing speed and our inability to find ICR-associated effects on this domain also supports this claim. It is also important to note that performance on the measure of verbal memory has been reported to explain part of the variance in performance on the Hinting Task in early psychosis (Lindgren et al., 2018). The Hinting Task has heavy verbal load and our success in improving ToM may be in part due to our success in improving verbal memory. However, it may also be that targeting ToM and verbal memory simultaneously may have synergistic effects on performance on both measures. This should be investigated further.

There were no significant between-groups effects found for attention, reasoning, processing speed, or emotion perception. It may be that early psychosis samples require less training in basic cognitive domains, as the deficits found in these domains are relatively well preserved and therefore do not change much with treatment (Eack et al., 2009; Romero-Ferreiro et al., 2016). Adding more training in these domains throughout the intervention may be valuable. The significant ICR-associated improvements in working memory and cognitive flexibility support previous results (Eack et al., 2009) reporting that integrated neuro- and social-cognitive interventions successfully improve executive functioning in early psychosis. However, there was a regression in performance on measures of cognitive flexibility over time. Similarly, improvement in social cognition appears to be lost over time as we did not observe a continued improvement on any of the social-cognitive measures at 12-months follow-up. Executive functioning and social cognition is strongly linked to functioning (Fett et al., 2011; Green et al., 2000) and has been found to mediate improvement in functioning (Eack et al., 2011). In addition, improvements in executive functioning have been associated with reduced disability as well as health and social care costs (Reeder et al., 2014). Although preliminary, the results from this research are a cause of concern and warrant further investigation into the long-term effectiveness of ICR. It may be that integrated neuro- and social-cognitive interventions may be more effective in improving higher levels of cognition than lower levels of cognition in early psychosis. This may have implications as to which patients to refer to ICR. It may however be necessary to sustain intervention for longer and/or to have booster sessions. However, when interpreting these results it is important to keep in mind that the test-retest reliability of the social-cognitive measures in early psychosis is generally low (Ludwig, 2017; Vidarsdottir et al., 2019b).

Although the long-term functional improvement of the intervention group is promising, the non-significant intervention-associated effects on functioning

require further exploration. It may be that meaningful changes in real-life behavior over 12 months require more time than the 12-week intervention period used in this research. In fact, Eack et al. (2011) found that the effects of the two-year CET on functioning were robust. It may also be that the functional outcome measures used in this study do not adequately capture the functional deficits found in this population or be sensitive to change in functioning. Speculating on the results from paper I, it was demonstrated that variance in informant reported functional outcomes was predicted by both emotion perception and immediate verbal memory. It could be that the non-significant effects of the ICR intervention on informant reported functional outcome may in part be explained by our inability to improve emotion perception. The long-term improvements on measures of functional outcome may be associated with our success in improving verbal memory. Verbal memory improvements have been found to be the most reliable neurocognitive predictor of functional change in early psychosis (Eack et al., 2011). Placing these results in context with the results from paper I, i.e., that attributional style predicts variance in self-assessed functioning it is possible that the regression of performance on attributional style may have contributed to the lack of significant effects observed on the BRIEF-A self-report and the QOLS scale. This also begs the question whether attributional style has a role in the differences observed between self-assessed functional outcome and real-world functional outcomes.

5.5 The implementation of ICR

When we were deciding which CR approach to implement at the EIP service, it was important that the intervention chosen would meet the cognitive needs of this patient population, feasible and user-friendly for the EIP service and patients. ICR contains several key elements that facilitate its implementation. The intervention is group-based and relatively short (12 weeks) which was considered to be more economically feasible than an approach that consists primarily of individual-based therapy, and/or is delivered over a longer period. The positive ratings from participants regarding intensity and duration of the intervention suggest that this setup is feasible in early psychosis populations. Furthermore, comprehensive treatment manuals and other key materials for the three intervention approaches integrated in ICR are available either free of charge (CCT) or at a very low price (less than $55). Using iPads instead of computers may reduce the start-up cost for the intervention as well as the space required for cognitive training. The intervention was well received by participants. There was not a consensus amongst the participants regarding which intervention approach they thought helped them the most, which

suggest that it is important to include more than one approach to meet the often complex rehabilitation needs of each individual. This may be particularly appropriate in early psychosis samples, where there is a large variability in cognitive performance.

The intervention was successfully incorporated into the EIP service and, continues to disseminate at other psychiatric services within LUH. Ongoing organizational and financial support has been secured. The three year process of implementation is consistent with the two to four year project plan required for most such implementation projects (Fixsen et al., 2005). Although this study did not involve a formal cost-effectiveness analysis, the results on the long-term efficacy support the case for funding the program in as part of important evidence-based EIP-services in the context of continuously constrained health budgets.

6 Summary and conclusions

6.1 Implications for clinical practice

The results from the three studies included in this thesis provide some guidance for good clinical practice. First of all, the consistent impairment on multiple domains in this sample and the strong link between cognition and functional outcome suggest that assessing and addressing social-cognition as well as neurocognition is very important in routine clinical practice at EIP services. EIP services might therefore want to consider adding an integrated neuro- and social-cognitive remediation program, such as ICR, to their standard treatment. A routine screening of cognitive impairments in all patients entering EIP services would aid individually-based treatment programs for early psychosis patients. However, it is important that the measures used are psychometrically sound and capture the common impairment found in early psychosis. Furthermore, the use of multiple methods of assessing functional outcome, including self-report and informant-reports may also be of value. Although there are issues regarding error variance in self-reported functioning, it is important that this not lead to a de-emphasis on the importance of this domain. If interventions are to be recovery and consumer oriented, the subjective experience of patients of their own functioning should not be dismissed on the grounds that it is difficult to understand and interpret. Researchers should continue to work to prioritize goals, problems, obstacles and methods of therapeutic intervention as experienced through the eyes of the patients. In fact, this may help to further enhance generalization of cognitive gains to improved functioning that is meaningful to each individual.

Patient choice of the individual training packages may be an important further step once the evidence-base has been strengthened. This may lead to both immediate improvement in cognition, and long-term improvements in functioning. Although almost half of the participants would have preferred to have no practice partner exercises at all. However, we would recommend that these exercises are included as part of the intervention, as the importance of transfer techniques to enhance generalization to everyday life has been established in other research (Tas et al., 2012). However, it would be helpful to get feedback from participants about why they would have preferred to have no practice partner exercises, and what they think would be the optimal way to support them in applying learned skills in their everyday-life. Regardless, some

modifications may be required in order to increase the acceptability of the practice partner exercises.

It may also be that patients require follow-up sessions or further therapy addressing cognitive flexibility and social cognition, possibly in the form of booster sessions. Regarding further modifications to the ICR intervention, it may be of value to increase training in emotion perception within the intervention in order to enhance the positive effects on functioning. Furthermore, the tendency to interpret ambiguous situations as hostile needs further attention within the intervention and may be better improved by adding related material from other interventions such as metacognitive training, cognitive behavioral therapy, or Understanding Social Situations (USS), a new social-cognitive intervention that uses restorative methods to target higher level social-cognitive skills (Fiszdon et al., 2016a).

6.2 Strengths and limitations

6.2.1 Strengths

The study took place at the only EIP service in the country and the majority of patients experiencing a first episode of psychosis in Iceland are referred there. In Iceland, treatment at an EIP service is free of charge and the small size of Reykjavik makes it easy to reach patients. This creates and ideal setting for collecting data from a group which is generally very difficult to recruit into studies in many countries. This is most evident when considering results from Paper I where we were able to assess the majority of patients (82%) in care at the EIP service between 2015 and 2017. Second, participants were assessed and treated in a naturalistic setting at the EIP service. The study included a clinical sample of early psychosis patients with various co-morbidities, including substance, representing the entire spectrum of patients in care at EIP services. Although this may also be considered a limitation, it increases the generalizability of the results to populations seeking treatment at other EIP services. Third, this study included a comprehensive assessment of neuro- and social-cognition and used several methods to assess functional outcomes. Fourth, all treatment facilitators received extensive training, the groups were all led by the same leading therapist (OGV), and fidelity to treatment manuals was high.

6.2.2 Limitations

The studies presented in this thesis have several limitations. Limitations regarding the study design in the three papers are worth mentioning. In paper

I, the cross-sectional design makes it difficult to infer cause-and effect. In papers II and III, the wait-list design makes it impossible to evaluate the between group differences over long-term which limits our ability to associate the positive long-term effects to the intervention. The large number of analyses conducted in all three studies increases the risk for Type I error associated with multiple comparisons. In papers I and III alpha was set at 0.01 to reduce the risk of Type I error, but no corrections were made in paper II due to the small sample size and because this was a pilot study exploring potential benefits of a novel intervention targeting multiple neuro- and social-cognitive domains.

There are some limitations regarding some of the measures used in the studies. Although we used published norms for most of the neurocognitive measures, the limited number of participants in the control group for the social-cognitive measures renders the results from these measures vulnerable e.g. to bias, random and type II errors. Furthermore, the cognitive performance of the control groups was not reported. Thus, it is possible that performance could be within the average range in some instances, but statistically higher within the control group. It is possible that some results may have been due to practice effects associated with repeated measurement. This may be particularly true for memory tasks with verbal content such as the Logical Memory (LMI and LMII), which is known to produce pronounced practice effects in older adults with mild cognitive impairment (Gavett et al., 2016). However, the observed improvements were greater than observed gains of a half a standard deviations found in multiple retesting (Scharfen et al., 2018). In addition, changes seen in those treated were greater than those made by individuals who received no ICR treatment between two separate testing occasions on the measures of verbal memory. The gains due to practice effects tend to decrease with increased number of tests and longer test-retest interval (Scharfen et al., 2018) and therefore the impact of practice effects may be reduced by the number of testing occasions as well as the long test-retest interval of 12 months. It is important to point out that baseline, posttreatment and 12-month cognitive assessments were completed by different assessors. Furthermore, the PANSS-raters were not blind to treatment conditions.

The limited sample sizes in papers II and III may have resulted in too low power to detect smaller and even medium-sized treatment effects. The small sample size in paper III made it difficult to control for other factors that may impact long-term outcomes, such as clinical symptoms or other treatments participants may have received at the EIP service.

6.3 Future studies

Further demonstrations of how cognitive gains extend to different areas of functioning are needed. Adding a functional outcome measure that is scored by a high-contact clinician may be a useful addition in future trials. That method has in fact been reported to have more validity than self- or informant reported functional outcome (Bowie et al., 2007; Sabbag et al., 2011, 2012).

Furthermore, the results highlight the continued need for psychometrically sound methods for assessing cognition and functional outcomes in early psychosis. Standardization of a cognitive test battery in an Icelandic population may be of helpful for future clinical trials. However, it is important that the test battery assesses multiple domains of cognition impaired in schizophrenia but is also feasible for use in clinical practice. In some cases, the use of cognitive tests that have already been translated and standardized in an Icelandic population may be more appropriate. The cognitive measures included in the current study assess multiple domains of neuro- and social-cognition, including the five domains assessed by the BACS. Because there is an urgency to investigate the psychometric properties of the social-cognitive measures, a study is currently being conducted assessing the psychometric properties of the Hinting Task, FEIT and the cognitive insight scale (BCIS).

As the results from this pilot study were generally promising, a larger trial would be an appropriate next step. Investigating for whom and under what conditions ICR is most suitable and effective may guide which patients to refer. Although the results suggest that long-term functional improvements can be attained, further long-term studies that include a control group are obviously needed. There is also a need to investigate which factors are most strongly associated with long-term improvement. Further investigations of each CR approach is not generally recommended (Horan & Green, 2019). However, further investigations of additional factors that could bridge the gap between cognitive gains and functioning are urgently needed. A new randomized controlled trial is currently being conducted at psychosis services at LUH, investigating the immediate and long-term effects of ICR plus aerobic exercise compared with ICR alone.

Intervention studies are increasingly being conducted at EIP services as part of a comprehensive treatment program. As CR is currently included in some clinical guidelines, and may be recommended in others in the future, a cost/benefit analysis would help to investigate further whether an integrated neurocognitive and social-cognitive remediation would be worthwhile within an EIP service. Furthermore, investigation of individual factors associated with

improvement in functioning within early psychosis populations would help in guiding which patients should receive ICR, and at what time-point within the comprehensive treatment at the EIP service. Reaching a general consensus of which CR approach is most beneficial and feasible in these samples should encourage the implementation of evidence-based integrated neuro- and social-cognitive approaches into standard psychosis care worldwide.

6.4 Conclusions

This thesis demonstrates that young early psychosis patients in Iceland exhibit broad cognitive impairments compared to healthy comparison samples, supporting the rationale for an integrated neuro- and social-cognitive intervention. It further suggests that there may be a distinct difference between the predictive factors for self-reported and informant reported measures of functional outcome in this population. A 12-week group-based ICR appears to be feasible and effectively improve performance on multiple measures of neurocognition and social-cognition, including verbal and working memory, cognitive flexibility, ToM, and hostile attributions. The long-term benefits of ICR should be investigated further, although the results suggest that they can be sustainable for at least some outcomes.

The aspiration behind this thesis was to improve the serious functional impairment that affects the quality of life of young adults diagnosed with psychotic disorders. Although there is still a long way to go to enhance our knowledge in this field, adding perhaps a few relevant pieces to the puzzle and taking part in ICR becoming part of EIP services at LUH made all the hard work involved worthwhile.

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Original publications

Paper I

Cognition and Neurosciences

Social and non-social measures of cognition for predicting self-reported and informant-reported functional outcomes in early psychosis

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Vidarsdottir, O. G., Twamley, E. W., Roberts, D. L., Gudmundsdottir, B., Sigurdsson, E. & Magnusdottir, B. B. (2019). Social and non-social measures of cognition for predicting self-reported and informant-reported functional outcomes in early psychosis. *Scandinavian Journal of Psychology, 60,* 295–303.

The main aim of this study was to investigate the individual contributions of neurocognitive and social-cognitive domains to self-reported and informant-reported functional outcome in early psychosis. We also sought to further characterize the nature of cognitive impairments in this sample and explore the interrelationships between the social-cognitive measures and how they correlate with measures of neurocognition and clinical symptoms. In this study, 70 patients (mean age: 24.1; 87.1% males) with primary psychotic disorder diagnosed in the previous 5 years were assessed on multiple neurocognitive (processing speed, attention, working memory, immediate verbal memory, delayed recall, visual reasoning, inhibition, planning, cognitive flexibility), and social-cognitive domains (theory of mind (ToM), emotion recognition, attributional style, metacognitive overconfidence) as well as measures of clinical symptoms. Functional outcome was assessed with three self-reports and two informant-reports. On average, patients performed one or more *SD* below healthy controls on measures of delayed recall, ToM and metacognitive overconfidence. Emotion recognition and ToM were intercorrelated and correlated with multiple neurocognitive domains and negative symptoms. Attributional style correlated with positive symptoms. In the context of multiple variables, self-reported functional outcomes were predicted by attributional style, whereas emotion recognition and immediate verbal memory predicted variance in informant-reported community functioning. These results support the suggestion of a likely distinction between the predictive factors for self-reported and informant-reported functional outcome in early psychosis and suggest that consideration of self-assessment of functional outcome is critical when attempting to evaluate the effects attributional style has on functional disability.

Key words: Attributional style, community functioning, neuropsychological tests, schizophrenia, theory of mind.

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INTRODUCTION

Individuals with schizophrenia consistently show impairments in neurocognitive domains, which contribute moderately to the variance in functional outcomes in schizophrenia (Fett, Viechtbauer, Dominguez, Penn, van Os & Krabbendam, 2011; Keefe & Harvey, 2012; Schaefer, Giangrande, Weinberger & Dickinson, 2013; Twamley, Doshi, Nayak *et al*., 2002). However, prior research suggests that social cognition, defined as "the domain of cognition that involves the perception, interpretation, and processing of social information" (Green, Penn, Bentall *et al*., 2008), is even more strongly associated with functional outcomes than is neurocognition (Allen, Strauss, Donohue & van Kammen, 2007; Fett *et al*., 2011; Ludwig, Pinkham, Harvey, Kelsven & Penn, 2017; Pinkham & Penn, 2006) and mediates the relationship between the two constructs (Schmidt, Mueller & Roder, 2011). Social cognition includes several domains that are related but fairly independent (Mancuso, Horan, Kern & Green, 2011) and the strength of the association with functional outcome depends on the specific domain of each construct examined (Couture, Penn & Roberts, 2006). *Theory of mind* (ToM) refers to the ability to infer the thoughts and intentions of other people based on their words and behaviour. *Emotion recognition* is the ability to infer another person's emotional state based on facial expression or vocal tone. *Social perception* includes the ability to identify interrelationships and social cues as well as gauge social rules and expectations. *Attributional style* refers to an individual's tendencies in interpreting the causes of ambiguous or vague social events.

There are many published observations of important associations among neurocognition, social cognition, and functional outcomes in schizophrenia, but less is known about these relationships in early psychosis. The relationship between social cognition and functional outcomes in early psychosis appears to strengthen as the illness progresses (Horan, Green, DeGroot *et al*., 2012). Therefore, it is essential for the development of effective early interventions to gain further understanding of specific social-cognitive domains, how they relate to neurocognition and clinical symptoms, and how those relationships translate to functional outcomes.

Individuals early in the course of their psychotic illness exhibit neurocognitive impairment that is comparable to that seen in more chronic stages of illness (Mesholam-Gately, Giuliano, Faraone, Goff & Seidman, 2009). However, there is some debate as to whether early psychosis and chronic schizophrenia patients exhibit the same types and degree of social-cognitive impairment. Whereas, some studies have found similar deficits between early psychosis samples and those with chronic schizophrenia

(Addington, Saeedi & Addington, 2006a,2006b; Bertrand, 2007; Bora & Pantelis, 2013; Clayson, Kern, Nuechterlein *et al*., 2019; Green, Bearden, Cannon *et al*., 2012), others have found that social-cognitive deficits are of lesser magnitude in early psychosis samples than in chronic schizophrenia samples, in particular for emotion recognition (Healey, Bartholomeusz & Penn, 2016; Kucharska-Pietura, David, Masiak & Phillips, 2005; Ludwig, 2017; Savla, Vella, Armstrong, Penn & Twamley, 2013). Similar to results in chronic schizophrenia, evidence suggests that social cognition accounts for more variance in functional outcome than neurocognition, and is a mediator of the relationship between neurocognition and poor functional outcome (Addington, 2010; Ludwig, 2017; Ventura *et al*., 2015). However, more research is needed to make firm conclusions about whether the functional relevance of specific social-cognitive domains in chronic schizophrenia can be generalized to early psychosis samples. Early psychosis samples may be more heterogeneous and have a greater fluctuation in clinical presentation than chronic schizophrenia samples (Nuechterlein, Dawson, Gitlin *et al*., 1992), which may affect the stability and severity of social-cognitive deficits and their relationships to functional outcome (Green *et al*., 2012; Horan *et al*., 2012). Furthermore, little is known about the role of attributional style in predicting functional outcomes in early psychosis, although there is some support for its relevance to self-reported functioning (Ludwig *et al*., 2017).

Functional outcome is a multifaceted construct, and the social-cognitive and functional outcome association is further impacted by the many methods previously used to assess functional disability. These include performance-based measures of capacity, real-world observations, self-reports, and informant-reports. Each outcome domain may have its own social-cognitive predictors, but specific predictor-outcome linkages have not been established in early psychosis. Studies have indicated that informant-reports regarding the specific behaviors reflective of community functioning may be the most reliable assessment of functioning (Sabbag, Twamley, Vella, Heaton, Patterson, & Harvey, 2012). However, in outpatient samples, there are many behaviors to which the clinician has no access and the use of self-reports may be important to get a clearer picture of the subjective level of functioning of patients. Although evidence suggests that peoples with schizophrenia have substantial problems in self-reporting everyday functioning (Bowie, Twamley, Anderson *et al*., 2007), about one-third of chronic schizophrenia patients may be able to accurately report their functional abilities (Sabbag *et al*., 2012). Further, it has been suggested that this rate might even be higher in first-episode samples than in older patients (Ludwig *et al*., 2017; Williams, Whitford, Flynn *et al*., 2008).

The purpose of the present study was to investigate the role of social cognition and neurocognition in predicting self-reported and informant-reported functional outcome in early psychosis. The first aim was to investigate the domains of neurocognitive and social-cognitive impairment in all patients seeking treatment at the only early psychosis unit in Iceland between 2015 and 2017. Second, we explored the interrelationships between the social-cognitive measures and how they associate with neurocognition and clinical symptoms. Lastly, we examine the individual contributions of social and non-social measures of cognition for predicting self-reported and informant-reported functional outcomes.

METHODS

Participants

Participants were recruited from an early intervention unit for psychosis at Landspitali – The National University Hospital (Reykjavik, Iceland). This is the only early psychosis unit in the country and service users include the majority of patients developing a serious psychotic disorder among 18 and 30 years old in Iceland. The study included 70 patients, representing 82% of the total patient population in service between 2015 and 2017. To be eligible for participation they had to meet the ICD-10 diagnostic criteria for schizophrenia, schizoaffective disorder, acute and transient psychotic disorder, schizotypal disorder, delusional disorder or other non-unipolar or non-bipolar psychotic disorders (World Health Organization, 2008). Diagnoses were determined by a team of psychiatrists and specialists in clinical adult psychology. Exclusion criteria were psychotic disorders caused by a general medical condition or substance use disorder, duration of illness of more than 5 years, epilepsy, or intellectual disability (i.e. IQ < 70). A cut-off of 5 years for illness duration was used because evidence indicates that a relative stability is established two to 5 years after illness onset (Rund, Melle, Friis *et al*., 2007; Srihari, Shah & Keshavan, 2012). All participants provided written informed consent, and the study was approved by the appropriate ethics committee.

Measures

A background questionnaire was used to collect socio-demographic data and clinical characteristics were collected from medical records. All measures were administered in Icelandic. Brief descriptions of each measure are included below and, when available, psychometric properties of the Icelandic version of the measures.

Neurocognition. To capture neurocognitive domains commonly impaired in schizophrenia, a comprehensive test battery was administered by a clinical psychologist trained in standardized neuropsychological testing. Processing speed was assessed using the Digit Symbol Coding subtest from the Wechsler Adult Intelligence Scale, 4th edition (Wechsler, 2008). Attention and working memory were measured with the Digit Span forward and Digit Span backward subtests from the Wechsler Adult Intelligence Scale, 4th edition (Wechsler, 2008). Immediate verbal memory (LMI) and delayed recall (LMII) were assessed using the Logical Memory subtests from the Wechsler Memory Scale, 3rd edition (Wechsler, 1997). Visual reasoning was measured using the Matrix Reasoning subtest from the Icelandic standardized version of the Wechsler Abbreviated Scale of Intelligence (Guðmundsson, 2015; Wechsler, 1999). Planning was assessed using the Tower Test from the Delis-Kaplan Executive Function System (Delis, 2001). Inhibition was assessed using the Stroop Color-Word Interference score (Golden, 1978; Stroop, 1935). Cognitive flexibility was measured with the Trail Making Test ratio score (B/A) (Reitan, 1958).

Social cognition. Social cognition was assessed with three widely used social-cognitive measures. ToM was measured with the Hinting Task (Corcoran, Mercer & Frith, 1995; Fridriksson, 2016). The Hinting Task includes 10 brief, written vignettes including social hints that the respondent must interpret (range 0–20). Cronbach's alpha was 0.76. Emotion recognition was measured with Facial Emotion Identification Task (FEIT) (Fridriksson, 2016; Kerr, 1993). Performance on the FEIT is indexed as the total number of correctly identified emotions out of nineteen pictured faces (range 0–19). Cronbach's alpha was 0.46. Because overconfidence in social judgments has been studied as a social-cognitive domain, a measure of confidence was added to the standard administration of FEIT as an exploratory measure of metacognitive overconfidence (Fiszdon, Roberts, Penn, Choi, Tek & Choi, 2016; Moritz, Woznica, Andreou & Köther, 2012). For each FEIT item, participants were asked to indicate how confident they were that their answer was correct using a Likert-type scale ranging from *100% sure* (4) to *guessed* (1). We then calculated separate average confidence ratings for trials where participants correctly and incorrectly identified an emotion, with higher score

indicating more confidence. Attributional Style was assessed with Ambiguous Intentions and Hostility Questionnaire – Ambiguous items (AIHQ) (Combs, Penn, Wicher & Waldheter, 2007; Össurardóttir, 2018). The AIHQ yields scores for hostility, aggression, and blame. The hostility and aggression scales include rater-scored items (range 5–25 for each scale) with higher scores indicating an increased tendency to see other's actions as hostile and increased tendency to hypothetically respond in an aggressive manner. The blame scale is a self-report (range 15–80) with higher scores indicating an increased tendency to blame others for ambiguous events. Cronbach's alpha for the three subscales was 0.54 for hostility bias, 0.88 for the blame scale and 0.33 for aggression bias.

The test-retest reliability of the Icelandic versions of the social-cognitive measures was reported in a previous study by our group (Vidarsdottir *et al*., 2019).

Clinical symptoms. The Positive and Negative Syndrome Scale (PANSS), a 30-item clinician-administered rating scale, was used to assessed positive and negative symptoms of schizophrenia (range 7–49 for each of the two subscales used in this study) (Stanley, Fiszbein & Opler, 1987). PANSS raters were experienced clinicians who knew the participants well. They routinely use the measure and had received training in its use prior to the study. Symptoms of depression, anxiety, and stress were measured using the Depression Anxiety Stress Scales 21-item (DASS-21) (Ingimarsson, 2010; Lovibond & Lovibond, 1995), a self-report with each of the three subscales ranging from 0 to 21. Duration of untreated psychosis (DUP) was defined as the time from the first onset of psychotic symptoms to the start of the first adequate treatment of psychosis with antipsychotic medication.

Functional outcome. Functional outcome was assessed with three self-report measures and two informant-reports. Informants were high-contact clinicians or close family members. The self-reports included the Occupational Self Assessment (OSA) (Baron, Kielhofner, Lyenger, Goldhammer & Wolenski, 2006; Pálsdóttir & Jónsdóttir, 2005) which assesses participants' perceptions of their competence in habits and roles, performance of skills and volition for participation (range 21–84). Cronbach's alpha for OSA was 0.95. Subjective quality of life was assessed with the Quality of Life Scale (QOLS) (Flanagan, 1978; Jónsdóttir & Sigurðardóttir, 2016), which assesses five domains of quality of life: material and physical well-being; relationships with other people; social, community and civic activities; personal development and fulfillment; and recreation (range 16–112). Cronbach's alpha for the QOLS was 0.90. Self-reported executive dysfunction was assessed with the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) (Kristinsdottir, 2012; Roth, Isquith & Gioia, 2005), which includes two summary scales including a metacognitive index and a behavioral regulation index.

The BRIEF-A also includes an informant-report version and the range for each scale is 75–225. Cronbach's alpha for the self-report version was 0.96 and 0.97 for the informant-report version. Informants also rated participants' community functioning with the Life Skills Profile (LSP) (Rosen, Pavlovic-Hadzi & Parker, 1989), which includes five subscales examining self-care, non-turbulence, social contact, communication, and responsibility (range 17–32). Cronbach's alpha for the LSP was 0.90.

Statistical analyses

Statistical analyses were conducted using SPSS version 24. Variables were checked for normality and outliers. The AIHQ hostility scale, the OSA and the Stroop interference score were positively skewed and transformed with Log 10. The Hinting Task was negatively skewed and transformed with Log 10 after reflection.

To explore the rate of cognitive and social-cognitive impairment, raw scores for the neurocognitive measures were converted to z-scores using published (WAIS-IV, WASI^{is}, D-KEFS) or local (LMI, LMII, Trails, and Stroop) sex-, age- and education-matched normative data (Magnusdottir, unpublished). Z-scores for the Hinting Task and the FEIT were calculated based on an Icelandic age-matched healthy comparison group (n = 32) (Fridriksson, 2016). In the case of the AIHQ, z-scores were calculated based on an Icelandic age-matched healthy comparison group (n = 125) (Össurardóttir, 2018). A one sample t-test was used to investigate whether the proportion of impairment in this population was significantly higher than what would be expected in a healthy population (16%). Impairment was defined as greater than 1 *SD* below the mean.

Pearson correlation analyses were performed to explore intercorrelations between the social-cognitive measures and how these correlated with neurocognition and clinical symptoms. Another set of Pearson correlation analyses were performed to explore how the social-cognitive and neurocognitive measures associated with each of the five measures of functional outcome. To control for Type I error associated with multiple comparisons, alpha was set to 0.01 for significance testing. Cognitive variables that showed significant correlations with each of the five functional outcome measures were entered as single blocks in regression models to assess the explanatory power of the tasks as a group.

RESULTS

Demographic, clinical symptom, functional outcome and cognitive measures

Demographics, clinical symptom and functional outcome variables are presented in Table 1. On average, participants demonstrated low to moderate levels of psychiatric symptoms and were mostly treated with atypical antipsychotic medication. Table 1 also shows descriptive statistics and z-scores for each of the neurocognitive and social-cognitive measures. The average performance in this group fell within one *SD* below healthy comparison samples on all neurocognitive and social-cognitive measures (range 0.55−−0.95), except for LMII (z-score = −1.07), the Hinting Task (z-score = −1.47), and the FEIT confidence in incorrect answers (z-score = 2.2). The percentage of the sample performing in the impaired range exceeded normative expectation (16%) on all measures except Matrix Reasoning, Trails ratio and Tower.

Correlation analysis among social-cognitive, neurocognitive and clinical symptom measures

Among bivariate correlations between the social-cognitive measures, a lower performance on the Hinting Task was associated with higher scores on the FEIT confidence in correct answers (Table 2). FEIT confidence in correct answers was also associated with FEIT and FEIT confidence in incorrect answers. The Hinting Task and the FEIT correlated at trend level ($p < 0.05$) and were positively associated with LMI and LMII. In addition, better performance on the FEIT was also associated with better performance on Matrix Reasoning. The AIHQ hostility and blame scales were intercorrelated and a negative trend-level correlation was found between hostility and aggression bias. However, none of the AIHQ subscales correlated with any of the other cognitive variables. PANSS positive symptom severity was associated with the AIHQ blame score and PANSS negative symptom severity correlated with the Hinting Task.

Social-cognitive and neurocognitive predictors of variance in functional outcome

To explore whether any of the social-cognitive or neurocognitive variables predicted variance in functional outcome, we first

Table 1. *Demographics, clinical characteristics, functional attainment variables and cognitive measures*

	n	%
Males	61	87.1
Inpatient	12	17.1
Diagnosis		
Schizophrenia	59	84.3
Psychosis NOS	9	12.9
Schizoaffective disorder	2	2.9
Medications		
Atypical antipsychotics	57	81.4
Typical antipsychotics	2	2.9
No antipsychotics	5	7.1

	Mean (*SD*)	Range in sample
Age	24.1 (3.1)	18–30
Education (years)	11.3 (1.7)	10–17
Age of onset	22.2 (3.0)	16–28
DUP (weeks)	10.6 (28.2)	0–115
Illness duration (months)	25.6 (17.9)	1–59
Clinical symptoms[a]		
PANSS positive	12.5 (4.3)	7–22
PANSS negative	14.8 (5.6)	7–28
DASS-21 depression	7.5 (6.3)	0–20
DASS-21 anxiety	4.3 (4.3)	0–15
DASS-21 stress	5.5 (4.5)	0–20
Functional outcome		
LSP	25.5 (2.9)	19–30
Informant BRIEF-A[a]	126.0 (28.5)	73–186
Self-report BRIEF-A[a]	124.5 (25.1)	71–177
QOLS	52.3 (13.0)	28–100
OSA	73.5 (14.6)	30–106

	Mean (*SD*)	Z-Scores (*SD*)	% impaired[b]
Social Cognition			
Hinting Task	14.2 (3.0)	−1.47 (1.87)	46.3**
FEIT	12.8 (2.5)	−0.95 (1.40)	47.8**
FEIT confidence in correct answers	1.8 (0.47)	0.14 (1.68)	2.1**
FEIT confidence in incorrect answers[a]	2.2 (0.63)	−2.1 (0.95)	93.0**
AIHQ HB[a]	2.0 (0.6)	−0.55 (1.25)	31.7**
AIHQ BS[a]	2.2 (0.8)	−0.31 (1.26)	29.5**
AIHQ AB[a]	1.6 (0.4)	0.12 (1.49)	25.0**
Neurocognition			
Digit Symbol Coding	60.7 (14.0)	−0.36 (0.82)	28.6**
Digit Span forward	8.3 (1.8)	−0.56 (1.06)	45.7**
Digit Span backward	7.4 (1.6)	−0.39 (0.69)	31.4**
LMI	30.8 (10.1)	−0.91 (0.84)	46.4**
LMII	17.8 (9.2)	−1.07 (1.04)	53.6**
Matrix reasoning	26.9 (4.4)	−0.12 (0.99)	17.6
Stroop interference[a]	30.6 (10.8)	−0.46 (1.11)	26.8**
Tower	16.4 (2.8)	−0.12 (0.77)	15.2
Trails ratio	2.8 (0.8)	−0.02 (0.79)	6.1

Notes: AB = aggression bias; AIHQ = Ambiguous Intentions Hostility Questionnaire; BRIEF-A = Behavior Rating Inventory of Executive Function – Adult version; BS = blame score; DASS = Depression, Anxiety and Stress Scale; FEIT = Facial Emotion Identification Task; HB = hostility bias, LMI and LMII = Logical Memory part I and II; LSP = Life Skills Profile; OSA = Occupational Self Assessment; PANSS = Positive and Negative Syndrome Scale; QOLS = Quality of Life Scale.

[a]Higher scores reflect greater pathology.

[b]>1 *SD* worse than reference mean.

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

investigated the associations between these variables (see Table 3). The only social-cognitive measure that significantly correlated with any of the self-reported functional outcome measure was the AIHQ. The AIHQ explained 32.9% of the variance in total scores on the self-reported executive dysfunction (BRIEF-A self-report), with significant contributions from hostility bias and blame scale. Self-reported competence in occupational performance (OSA) significantly correlated with hostility and aggression bias and the regression model explained 33.9% of the total variance. Informant-reported community functioning (LSP) was significantly correlated with the FEIT and LMI, and the regression model for the LSP explained 16% of the total amount of variance (see Table 4). Subjective quality of life (QOLS) and the informant-report version of assessment of executive dysfunction (BRIEF-A informant-report) were not associated with any of the cognitive variables and were therefore not included in the regression analyses.

DISCUSSON

The primary purpose of this study was to examine the role of non-social and social-cognitive domains in predicting informant-reported and self-reported functional outcomes in early psychosis. We first aimed to investigate rate of cognitive impairment in this sample. Second, we examined the intercorrelations between the social-cognitive measures, and how they correlated with neurocognitive and clinical symptom measures. Lastly, we investigated the individual contribution of neurocognitive and social-cognitive domains in predicting variance in functional outcomes. Data from the majority of patients seeking service at the only early psychosis unit in Iceland between 2015 and 2017 were analyzed. The findings for each of the three aims are discussed in detail below.

Overall cognitive performance

On average, the patients in our sample performed in the impaired range only on measures of delayed recall (LMII), ToM (Hinting Task), and metacognitive overconfidence (FEIT confidence in incorrect answers). However, it is likely that intact performances in a subset of patients outweighed impaired performances, resulting in mean scores that were mostly within the average range. In fact, the percentage of the sample scoring in the impaired range exceeded normative expectation for all but a few measures, consistent with previous research demonstrating broad cognitive impairment in early psychosis samples (Addington, Brooks & Addington, 2003; Green *et al*., 2012; Mesholam-Gately *et al*., 2009).

Relationships between social cognition, neurocognition and symptoms

The intercorrelations between the social-cognitive measures, and how they associate with measures of neurocognition and clinical symptoms support the distinction between two types of social-cognitive functions, capacities and biases, recently highlighted by Roberts and colleagues (Roberts & Pinkham, 2013; Walss-Bass, Fernandes, Roberts, Service & Velligan,

Table 2. *Correlations between measures of social cognition, neurocognition and clinical symptoms*

	Hinting Task	FEIT	FEIT conf. correct	FEIT conf. incorrect	AIHQ HB	AIHQ BS	AIHQ AB
Social Cognition							
Hinting Task	-						
FEIT	0.25*	-					
FEIT conf. correct	**−0.32****	**−0.33****	-				
FEIT conf. incorrect	−0.16	−0.15	**0.75****	-			
AIHQ HB[a]	0.15	−0.01	−0.22	−0.02	-		
AIHQ BS[a]	0.15	−0.21	−0.15	−0.12	**0.65****	-	
AIHQ AB[a]	−0.05	0.07	−0.09	−0.08	−0.26*	0.09	-
Neurocognition							
Digit Symbol Coding	0.23	0.27*	−0.11	0.10	0.12	0.01	0.01
Digit span forward	−0.05	0.00	−0.15	−0.23	0.12	0.10	−0.16
Digit span backward	0.11	0.19	−0.02	0.01	−0.03	−0.01	0.07
LMI	**0.40****	**0.44****	**−0.37****	−0.08	−0.01	−0.04	0.01
LMII	**0.45****	**0.52****	**−0.26****	−0.03	−0.07	−0.10	−0.10
Matrix reasoning	0.24	**0.33****	−0.14	−0.13	−0.13	−0.04	−0.06
Stroop interference[a]	−0.17	−0.16	0.07	0.08	−0.04	0.23	0.04
Tower	0.02	0.07	0.14	0.13	−0.12	0.11	−0.10
Trails ratio	0.10	0.03	0.07	−0.09	−0.09	−0.14	0.01
Clinical symptoms							
PANSS positive[a]	−0.05	−0.17	−0.01	−0.09	0.32*	**0.40****	−0.23
PANSS negative[a]	**−0.41****	−0.26*	0.26*	0.01	−0.27*	−0.24	0.12

Notes: AB = aggression bias; AIHQ = Ambiguous Intentions Hostility Questionnaire; BS = blame score; FEIT = Facial Emotion Identification Task; HB = hostility bias; LMI and LMII = Logical Memory part I and II; PANSS: Positive and Negative Syndrome Scale.
[a]Higher scores reflect greater pathology.
*$p < 0.05$; **$p < 0.01$.
Bold values indicate significants of $p < 0.01$.

2013). They argue that social-cognitive capacity refers to the ability to perform an information processing function and include social-cognitive domains such as ToM and emotion recognition, whereas social-cognitive bias refers to the tendency for information processing functions to produce systematically distorted output and include domains such as attributional style and metacognitive overconfidence. This distinction has much in common with the distinction between negative and positive symptoms in schizophrenia and is most useful in selecting which social-cognitive intervention approaches to use with specific patients. In line with previous research, the capacity-based tasks (Hinting Task and FEIT) intercorrelated and correlated with several neurocognitive domains (Bora, Eryavuz, Kayahan, Sungu & Veznedaroglu, 2006; Pinkham & Penn, 2006). The bias-based task (AIHQ), however, was not associated with any of the other social-cognitive or neurocognitive domains. This suggests that capacities are a more elemental process of social cognition (Addington *et al*., 2006a,2006b; Brown, Tas, Can, Esen-Danaci & Brüne, 2014; Mancuso *et al*., 2011), and supports previous findings that attributional style is an independent social-cognitive factor (Mancuso *et al*., 2011), independent of basic neurocognitive processes (Mehta, Bhagyavathy, Thirthalli, Kumar & Gangadhar, 2014). The AIHQ correlated with positive symptoms, whereas the Hinting Task and the FEIT correlated with negative symptoms, consistent with studies in first-episode samples (An, Kang, Park, Kim, Lee & Lee 2010; Healey *et al*., 2016). As suggested by others, these results indicate that the effect of positive symptoms may be isolated to bias rather than capacity (Combs *et al*., 2007; Pinkham, Harvey & Penn, 2016).

Social and non-social cognitive predictors of informant-reported and self-reported functional outcomes

Regression analyses demonstrated that in the context of multiple predictor variables immediate verbal memory (LMI) and emotion recognition (FEIT) predicted variance in informant-reported community functioning (LSP). However, attributional style was the only cognitive measure that predicted variance in self-reported occupational competence (OSA) and self-reported executive dysfunction (BRIEF-A). These results support previous findings in early psychosis and indicate that there may be a distinct difference between the predictive factors for self-reported and informant-reported measures of functional outcome in early psychosis (Ludwig *et al*., 2017; Williams *et al*., 2008).

Our results suggest that neurocognitive domains as well as social-cognitive capacity affect everyday functional difficulties that are noticeable by others. However, although the two capacity-based measures intercorrelated and correlated with verbal memory, ToM was not related to any of the functional outcome measures. These results contradict previous results in early psychosis (Lindgren, Torniainen-Holm, Heiskanen *et al*., 2018; Ludwig *et al*., 2017; Sullivan, Herzig, Mohr *et al*., 2013; Williams *et al*., 2008), but the variability in methods used to assess ToM and functional outcomes in previous studies make comparisons between studies somewhat difficult. Unlike ToM, emotion recognition also correlated with visual reasoning (Matrix Reasoning) and processing speed (Digit Symbol Coding). From a theoretical perspective, these neurocognitive domains are considered to underlie performance on other cognitive domains and these findings extend the argument for emotion recognition being a "lower-level" social-cognitive component in schizophrenia (Mancuso *et al*., 2011). Thus, it logically follows

Table 3. *Correlations between measures of functional outcome and social cognition, neurocognition and clinical symptoms*

	LSP	Informant BRIEF-A[a]	Self-report BRIEF-A[a]	OSA	QOLS
Social cognition					
Hinting task	−0.07	−0.07	0.03	0.07	0.11
FEIT	**0.35****	−0.29*	−0.20	0.11	0.08
FEIT conf. correct	−0.12	0.15	−0.02	0.04	−0.05
FEIT conf. incorrect	−0.02	−0.09	−0.03	0.03	−0.11
AIHQ HB[a]	−0.19	0.17	**0.41****	**−0.49****	−0.27*
AIHQ BS[a]	−0.27	0.14	**0.59****	−0.34*	−0.32*
AIHQ AB[a]	0.01	−0.16	−0.25	**0.44****	0.14
Neurocognition					
Symbol coding	−0.03	0.03	−0.07	0.14	0.14
Digit span forward	−0.01	−0.04	0.14	0.01	−0.06
Digit span backward	0.07	−0.06	−0.01	0.27*	0.18
LMI	**0.38****	−0.30*	−0.19	0.20	0.14
LMII	0.28*	−0.19	−0.21	0.25	0.17
Matrix reasoning	0.05	−0.15	0.11	0.01	−0.17
Stroop interference[a]	0.15	−0.11	0.10	−0.01	−0.05
Tower	0.11	−0.20	0.30*	−0.12	−0.11
Trails ratio	0.08	0.04	−0.09	−0.08	−0.08

Notes: AB = aggression bias; AIHQ = Ambiguous Intentions Hostility Questionnaire; BRIEF-A = Behavior Rating Inventory of Executive Function – Adult version- Informant-Report and Self-Report; BS = blame score; FEIT = Facial Emotion Identification Task; HB = hostility bias; LMI and LMII = Logical Memory part I and II; LSP = Life Skills Profile; OSA = Occupational Self Assessment; QOLS = Quality of Life Scale.
[a]Higher scores reflect greater pathology.
*$p < 0.05$; **$p < 0.01$.

that difficulties in this domain may affect the development of skill acquisition necessary for community functioning. The clinical correlates of the capacity-based measures support previous findings that suggest that negative symptoms may make specific additional contributions to informant-rated community functioning (Bowie, Leung, Reichenberg *et al*., 2008; Reichenberg, Feo, Prestia, Bowie, Patterson & Harvey, 2014). Although the results from this study are correlational and cross-sectional, they indicate that community functioning is affected by a complex relationship between non-social and social-cognitive domains, and that this relationship may be further impacted by negative symptoms. The clinical implications of these results are the potential value of broad-based cognitive interventions as means to improve community functioning.

The importance of social-cognitive bias in predicting self-reported functioning in our sample replicates previous findings in early psychosis (Ludwig *et al*., 2017). It is possible that our results reflect the true disturbances bias can have on the individual's everyday-life. In this case, targeting bias may be key when the goal is to improve functional outcome. However, in light of the previous literature demonstrating that factors such as neurocognitive deficits, positive symptoms, insight and depression affect the accuracy of self-reports (Bowie *et al*., 2007; Durand, Strassnig, Sabbag *et al*., 2015; Sabbag *et al*., 2012), it may be reasonable to hypothesize that social-cognitive bias affects the individuals' ability to accurately rate their functioning. The strong associations between hostile and blaming attributions and positive symptoms give indirect support for the conclusion that this relationship is impacted by the severity of positive symptoms. However, this assertion is speculative and this should be examined more rigorously in future studies.

Unlike hostile and blaming attributions, aggression bias was not associated positive symptoms and negatively correlated with negative symptoms. In addition, individuals who were more likely to react in an aggressive way in ambiguous situations rated themselves with more occupational competence. This may appear contradictory to the argument that positive symptoms affect the relationship between bias and self-reported functional outcome. However, evaluations of the psychometric properties of the AIHQ aggression scale have reported that this subscale does not adequately distinguish patients from controls (Buck, Iwanski, Healey *et al*., 2017; Ludwig, 2017; Össurardóttir, 2018). It may be that scores on the aggression scale that are higher than average but still close to midpoint may be considered more "assertive" than "aggressive" and in this sense may actually indicate a greater awareness and self-perceived ability to take appropriate assertive social action to proactively solve interpersonal issues. Similar findings were reported in a study on ultra-high risk sample (An *et al*., 2010). In view of the heterogeneity of illness presentation in various stages of the

Table 4. *Regression analyses for cognition's incremental prediction of functional outcome*

Dependent variable	Predictor	Beta	*P sig*	*F* change	R^2	Adjusted R^2	Sig of the model
BRIEF-A self-report	AIHQ HB	0.038	0.788	15.446	0.351	0.329	<0.001**
	AIHQ BS	0.574	0.001**				
OSA	AIHQ HB	−0.422	0.001**	12.806	0.339	0.312	<0.001**
	AIHQ AB	0.306	0.013*				
LSP	FEIT	0.232	0.098	6.061	0.19	0.160	0.004**
	LMI	0.276	0.051				

Notes: AB = aggression bias; AIHQ = Ambiguous Intentions Hostility Questionnaire; BRIEF−A = Behavior Rating Inventory of Executive Function – Adult version; BS = blame score; FEIT = Facial Emotion Identification Task; HB = hostility bias; LMI = Logical Memory part I; LSP = Life Skills Profile; OSA = Occupational Self Assessment.
*$p < 0.05$; **$p < 0.01$.

psychotic illness, it would be interesting to see if the effect of bias would hold up in a longitudinal study.

It is worth highlighting that there was an overall greater impairment on measures of capacity than bias in this sample. This is consistent with previous results in first-episode psychosis (Healey *et al*., 2016; Ludwig, 2017). These results and the positive correlation between the bias-based task and positive symptoms indicate that social-cognitive bias is not a general characteristic of schizophrenia, but specifically present in a subgroup characterized by more paranoid ideation and persecutory delusions, as has been previously suggested (Pinkham *et al*., 2016).

Study limitations

Replications of these results are needed, particularly given the limitations of the current study methods, which include a large number of analyses and, in the case of the cognitive variables, the use of norms derived from several different studies. Although we used multiple measures of functional outcome, we cannot rule out that some of the functional outcome measures used in this study were not ideal for early psychosis sufferers because they may not adequately capture impairments in functioning in this population. Future research should also include performance-based measures of functional capacity to enhance the ecological validity of the findings. Also, it is important to consider the methodological limitations of the social-cognitive measures when interpreting the results. The limitations in social-cognitive assessment are well known (Pinkham, Harvey & Penn, 2018), and the contrasting nature of some of our results in comparison with previous work highlights the need for a comprehensive social-cognitive battery for early psychosis.

Conclusions

Taken together, our results suggest that there is a common occurrence of cognitive impairments in this early psychosis sample, but also highlight the variability in clinical presentation. The distinction between social-cognitive capacity and deficit is further supported by our data. Emotion recognition and immediate verbal memory predicted variance in informant-reported community functioning, whereas attributional style emerged as the single cognitive predictor of variance in self-reported functional outcome. These findings provide continued support for addressing the role of social cognition as well as neurocognition in relation to functional outcomes in early psychosis. They also indicate that it does not suffice to examine how individual cognitive domains relate to different domains of functional outcomes one must also consider how different methods of functional assessment may affect these relationships. Future studies may need to consider other interacting variables because several pathways are probably involved in mediating the impact on functional outcomes.

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Integrative cognitive remediation for early psychosis: Results from a randomized controlled trial

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ABSTRACT

Early application of cognitive remediation may help prevent the development of long-term functional impairments that characterize psychotic disorders. Interventions that encompass both neurocognitive and social-cognitive training may work synergistically to bridge the gap between cognitive gains and functional outcomes in early psychosis. We integrated three cognitive remediation approaches: Neuropsychological Educational Approach to Remediation (NEAR), Compensatory Cognitive Training (CCT), and Social Cognition and Interaction Training (SCIT), and evaluated the effects on cognition, clinical symptoms, self-assessed and informant-assessed social functioning in early psychosis. A total of 49 patients diagnosed with primary psychotic disorder seeking service at an early-intervention service in Iceland were randomized to either a waiting-list control group (n = 24) or a 12-week group-based integrative cognitive remediation (n = 25). Neurocognition, social cognition, community functioning and clinical symptoms were assessed at baseline and post-treatment. The intervention group showed significant improvements in verbal memory, cognitive flexibility, working memory, ToM and a significant reduction in hostile attributions, compared to those receiving standard treatment alone, but there were no differences between groups on measures of social functioning or clinical symptoms. The intervention was well tolerated and received high treatment satisfaction ratings. Findings indicate that integrated cognitive remediation has potential to improve neurocognition and social cognition in early psychosis.

1. Introduction

Cognitive deficits are a core feature in psychotic disorders and have been found to explain anywhere from 20 to 60% of the variance in functional outcomes (Bilder et al., 2006; Fett et al., 2011; Green et al., 2000). One of the great challenges of treatment has been to develop effective treatment options for the functional impairments that characterize psychotic disorders. One prominent treatment is cognitive remediation, which effectively improves neurocognition, and when delivered within a comprehensive psychiatric rehabilitation program, functional outcomes in schizophrenia (McGurk et al., 2007; Wykes et al., 2011).

Cognitive remediation can be divided into three major intervention categories: Strategy-based/compensatory approaches, restorative approaches and social cognitive approaches. Regardless of training approach, cognitive remediation was defined by the Cognitive Remediation Expert Group in 2012 as “an intervention targeting cognitive deficit (attention, memory, executive function, social cognition or meta cognition) using scientific principles of learning with the ultimate goal of improving functional outcomes” (Cognitive Remediation Expert Working Group, 2012). Although the ultimate goal of cognitive remediation is to improve functional outcomes, generalization to everyday life remains a concern (Addington et al., 2005). In recent years, there has been growing interest in combining cognitive remediation and social-cognitive training. Social cognition, defined as the mental processes underlying people´s capacity to perceive, process and comprehend social information (Green et al., 2008), appears to have a stronger relationship to functional outcomes than does neurocognition

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(Allen et al., 2007; Fett et al., 2011) and mediate the relationship between the two constructs (Couture et al., 2006; Ludwig, 2017; Pinkham and Penn, 2006; Schmidt et al., 2011). Addressing social cognitive impairments may therefore increase the ability of patients to engage in and benefit from cognitive remediation as well as enhance the generalization of any cognitive gains acquired through the intervention to real-world functioning (Horan et al., 2016)

The existing interventions that combine cognitive remediation and social-cognitive training are effective in improving neurocognition and social cognition as well as psychosocial functioning in schizophrenia (Bell et al., 2001; Hogarty et al., 2004; Roder et al., 2011). However, most published trials on combined interventions include middle-aged chronically ill individuals with a confirmed diagnosis of schizophrenia, and although promising, the results in early psychosis remain preliminary (Boriello et al., 2015; Eack et al., 2009). Individuals early in the course of their psychotic disorder show, relatively stable, functionally relevant impairments in multiple domains of neurocognition and social cognition, but are also generally characterized by fluctuations in clinical presentation (Barder et al., 2013; Horan et al., 2011b; Mesholam-Gately et al., 2009; Williams et al., 2008). There is some evidence that early application of cognitive remediation may enhance the potential benefits on functional, social and cognitive outcomes (Bowie et al., 2014) and it has even been suggested that to achieve optimal functional response in these populations, it may be necessary to target both neurocognitive and social-cognitive deficits (Eack et al., 2011).

This study aimed to pilot-test a 12-week, group-based Integrative Cognitive Remediation (ICR) program that included three previously validated treatments: Social Cognition and Interaction Training (SCIT(Roberts et al., 2016); Neuropsychological Educational Approach to Remediation (NEAR(Medalia and Freilich, 2008), and Compensatory Cognitive Training (CCT(Mendella et al., 2015; Twamley et al., 2017, 2012) in a sample of patients early in the course of their psychotic illness. Integrating these three cognitive remediation approaches instead of using existing comprehensive interventions had several advantages.

First, we delivered three intervention approaches within 12-weeks, which is shorter than other combined neurocognitive and social-cognitive interventions and possibly more cost-effective and less of a burden to patients. In addition it gives room for more frequent treatment entry points, allowing earlier treatment in the course of first episode psychosis. Second, SCIT targets the full range of social-cognitive domains impaired in early psychosis and is flexible in its methods and activities to accommodate the full range of symptoms and characteristics of psychotic disorders. In addition, SCIT uses booster sessions in the form of “practice partners” to help with generalization. A practice partner can be an acquaintance or a close relative, which may be of value for younger patients who still live at home with their families. Third, the CCT approach targets cognitive domains (prospective memory, attention, learning/memory, and executive functioning) that have been found to be impaired in first-episode samples (Mesholam-Gately et al., 2009) and therefore it may be particularly valuable to include this approach. In addition, the goal of the CCT approach is to help patients learn and develop cognitive strategies to form long-term habits that are meaningful in the real world and patients early in the course or their illness may have greater brain plasticity and be especially receptive to developing new cognitive habits (Berger et al., 2007). Fourth, the intervention leaves room for personalized computer training tailored to baseline cognitive profiles, which has the potential to further enhance cognitive gains (Medalia and Saperstein, 2017). Most of the combined interventions use restorative methods (i.e., computer training) with a standard computer package where all participants work on the same exercises.

To our knowledge, there are no published studies that have integrated these three treatments. The current study will provide new information about the feasibility and effects of this brief, group-based intervention. It was hypothesized that, compared to a wait-list control group receiving treatment as usual, the ICR group would demonstrate improvements in neurocognition, social cognition, and social functioning at post-treatment.

2. Methods

2.1. Participants

Participants were recruited from an early intervention service for psychosis at Landspitali- The National University Hospital in Reykjavik, Iceland. Inclusion criteria were: duration of psychotic illness of five years or less; aged between 18–30 years; presence of cognitive performance greater than or equal to 0.5 standard deviations below norms on any of the neurocognitive or the social-cognitive measurements at baseline; Icelandic as first language; no evidence of intellectual disability (i.e. IQ < 70), or organic brain disorder.

The study was conducted from January 2016 to June 2017. Baseline assessments were performed on seventy-two patients up to eight months prior to the intervention, as part of a previous study by the current authors (Vidarsdottir et al., review). Forty nine participants that met the inclusion criteria were enrolled and randomized (see Fig. 1). Fifteen participants dropped out at different points in the study. Participants who attended less than one third of the sessions were considered as dropouts but included in the final intent-to-treat analysis. The study was approved by Landspitali, National University Hospital Ethics Committee (20/2015, ref.16; LSH 42–15) and written informed consent was obtained from all participants.

2.2. Design

The study had a randomized wait-list control design which allowed all individuals to be treated eventually. It allowed for a comparison between ICR and treatment as usual (TAU) as well as measurement of change in performance before and after treatment. It also allowed for double-baseline assessment in a subset of participants ($n = 12$), which allowed for an informal check of the test-retest reliability of the social-cognitive measures in this sample. Following baseline assessment, participants were randomized by an independent research assistant in blocks of four and five into ICR group ($n = 25$) or wait-list control group ($n = 24$). Cognitive assessments were completed by trained psychologists who were blind to treatment assignment. After treatment, each participant was re-administered the outcome measures and, if in the ICR group, asked to complete a feedback questionnaire.

2.3. Measures

2.3.1. Neurocognition

Participants were administered a comprehensive neuropsychological test battery including measures previously used in Icelandic populations (Guðmundsson, 2015; Stefansson et al., 2014). Processing speed was assessed using the Digit Symbol Coding subtest from the Wechsler Adult Intelligence Scale, 4th edition (WAIS-IV; (Wechsler, 2008) and Trails A (Reitan, 1958). Verbal memory was assessed using the Wechsler Memory Scale, 3rd edition (WMS-III) Logical Memory immediate recall total score (LMI), delayed recall total score (LMII), immediate theme total score (LMI theme) and delayed theme total score (LMII theme(Wechsler, 1997). Logical reasoning was assessed using the Wechsler Abbreviated Scale of Intelligence ($WASI^{is}$) Matrix Reasoning total score, Icelandic standardization (Guðmundsson, 2015; Wechsler, 1999). Attention and working memory were assessed using the WAIS-IV Digit Span forward and Digit Span working memory span (Digit Span backwards + Digit Span in a row)/2; (Wechsler, 2008). Planning was assessed using the Delis-Kaplan Executive Function System (D-KEFS) Tower subtest (Delis, 2001). Inhibition was assessed using the Stroop Color-Word Interference score

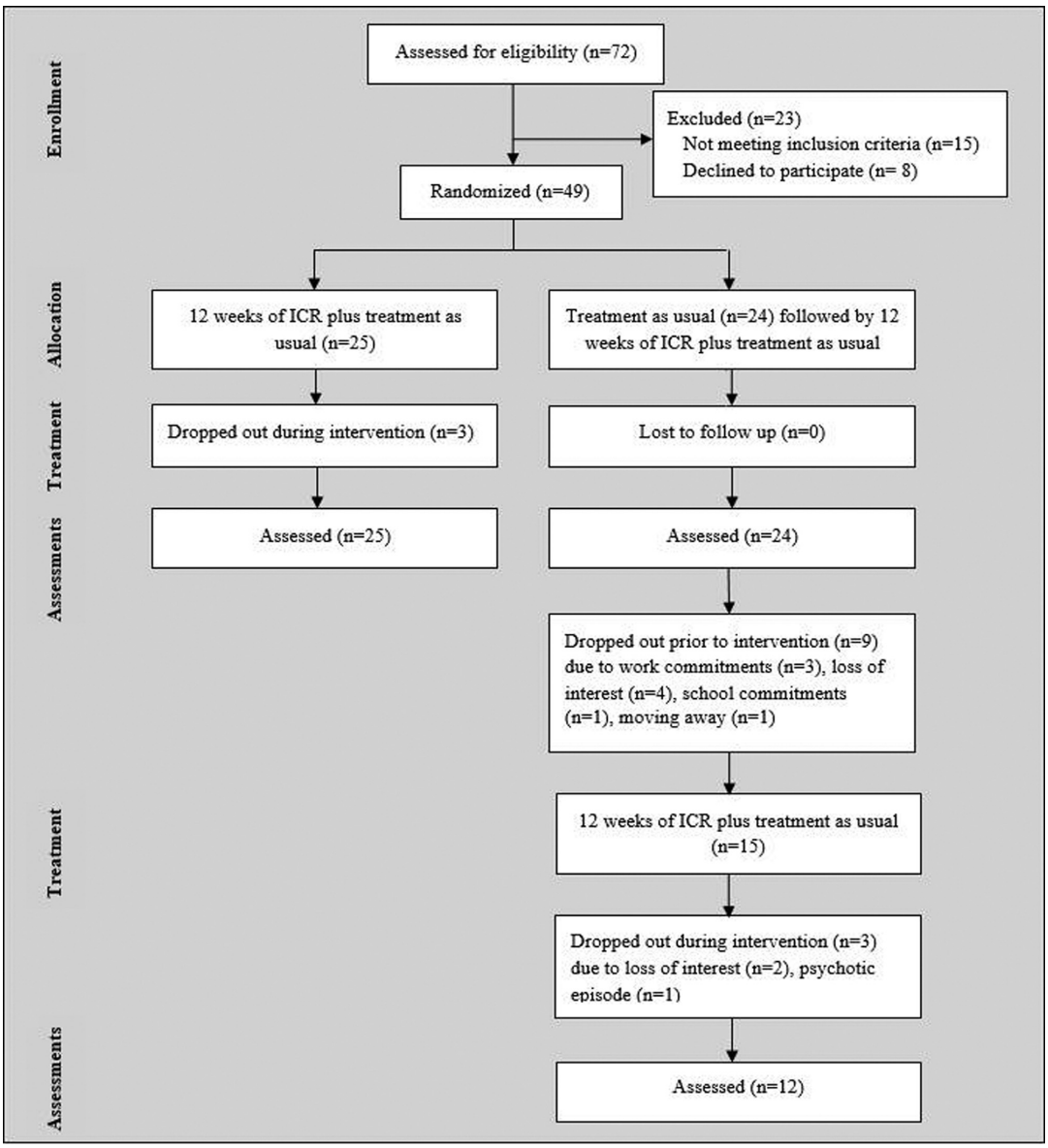

Fig. 1. Consort diagram.

(Golden, 1978; Stroop, 1935). Cognitive flexibility was assessed using Trails B (Reitan, 1958).

2.3.2. Social cognition and cognitive insight

Social cognition was assessed with three widely used social-cognitive measures that are sensitive to social-cognitive training effects. ToM was assessed using the Hinting task (range 0–20) (Corcoran et al., 1995). Attributional bias was assessed using the Ambiguous Intentions Hostility Questionnaire-Ambiguous items (AIHQ-A; Combs et al., 2007b). The scale yields scores for hostility bias, aggression bias and a blame score. The hostility and aggression scales range from 5 to 25 and the blame scale ranges from 15 to 80. Emotion recognition was assessed using the Facial Emotion Identification Task (range 0–19) (FEIT; (Kerr, 1993). A metacognitive measure of confidence was added to the standard administration of the FEIT by asking participants to indicate how confident they were that their answer was correct using Likert-type anchors ranging from *100% sure* (4) to *guessed* (1). We then calculated average confidence ratings for trials where participants correctly identified an emotion with higher score indicating more confidence in correct answers, and confidence ratings for trials where participants incorrectly identified an emotion with higher score indicating more confidence in incorrect answers. The Beck Cognitive Insight Scale (Beck et al., 2004) was used to assess cognitive insight (range −18–27).

The test-retest reliability of the social-cognitive measures for those participants with a double baseline (n = 12) were as following: Hinting task (r = 0.720, p = 0.000), FEIT (r = 0.525, p = 0.000), confidence in

FEIT correct answers ($r = 0.488$, $p = 0.001$), confidence in FEIT incorrect answers ($r = 0.507$, $p = 0.000$), AIHQ hostility bias ($r = 0.416$, $p = 0.008$), AIHQ blame score ($r = 0.583$, $p = 0.000$), and AIHQ aggression bias ($r = 0.191$, $p = 0.271$).

2.3.3. Social functioning

Social functioning was assessed with three self-report measures and two informant-report measures. The informant-based measures completed by family members, partners, or high-contact clinicians and included the Life Skills Profile-39 (range 38–156) (LSP-39; (Rosen et al., 1989) and the informant-report version of the Behavior Rating Inventory of Executive Function-Adult Version (range 72–225) (BRIEF-A; (Roth et al., 2005). Self-assessed social functioning included the self-report version of the Behavior Rating Inventory of Executive Function-Adult Version (range 72–225) (BRIEF-A; (Roth et al., 2005), the Quality of Life Scale (range 16–112) (QOLS; (Flanagan, 1978) and the Occupational Self Assessment (range 21–84) (OSA; (Baron et al., 2006).

2.3.4. Clinical symptoms

Symptomatology was assessed with the Positive and Negative Syndrome Scale (PANSS; (Stanley et al., 1987) and the Depression Anxiety Stress Scale 21-item (DASS-21; Lovibond and Lovibond, 1995). PANSS raters were experienced clinicians who knew the participants well. They routinely use the measure and had received training in its use prior to the study.

2.3.5. Participant feedback

The feedback questionnaire included ratings of treatment intensity (length of the intervention and length of each session) and usefulness of specific treatment components (SCIT, CCT and NEAR).

2.4. Treatment conditions

Both groups received TAU during the study which differed across participants based on their individual treatment plan. All participants received case-management and supportive counseling at least one times per week in addition to one or more of the following treatment components: medication management, socialization at the early intervention service (lunch, board games, all girl groups) occupational therapy, education about psychosis, individual or group-based exercise, and/or family support. Some participants were enrolled in school or had part-time employment but no participants received other organized cognitively oriented therapies.

ICR was conducted twice per week over a 12-week period, with each session lasting up to 120 min and consisted of 10–12 participants and four therapists. The lead author (OGV) was the leading therapist, trained and supervised by the second and third co-authors (DR and EWT, respectively). Other co-therapists included an occupational therapist, a clinical psychologist, and a staff member from the early intervention center.

Each session started with SCIT, a manual based group psychotherapy targeting several domains of social cognition including emotion recognition, ToM and attributions as well as metacognitive overconfidence and interaction skills to improve social functioning. A break was provided after SCIT, followed by a combined session of CCT, a strategy-based compensatory approach designed to target prospective memory, attention, learning/memory, and executive functioning, and NEAR, which utilizes commercially available educational software in a manner that is intrinsically motivating and rewarding. It used computer based exercises and games from BrainHQ (Posit Science, Inc., San Francisco, CA), Lumosity (www.lumosity.com) and Games for the Brain (www.gamesforthebrain.com). The CCT manual was edited by EWT and OGV to fit this study. For a summary of session content, treatment strategies, and modifications applied, see Table 1. To enhance motivation, each participant received their cognitive profile from the baseline measures and had an interview with one of the therapists about which cognitive domains they viewed as most important to improve and why. To support generalization to everyday life, all group members were assigned a practice partner who was a staff member at the early intervention service. All sessions were audiotaped and rated by an independent rater for fidelity to the SCIT and CCT programs separately. No material was edited out of the SCIT program and the fidelity to the manual was 86.6%. The main domains targeted by the CCT program were targeted in the intervention and most of the strategies were introduced. However the time spent on practicing each strategy was shorter than in the original CCT manual and a new fidelity scale was developed by the authors for this study. Fidelity to the modified CCT treatment manual was 83.3%.

2.5. Data analysis

Raw scores were used for all measures. Measures of distribution were calculated and inspected to assess normality and potential outliers. Skewed data were handled using Log transformations. Chi-square and *t*-tests were used to compare individuals who received the intervention to those who were in the wait-list control group on demographic, clinical, and cognitive variables. Chi-square and *t*-tests were also used to compare individuals who dropped out of the study to those who completed the study.

Analysis of covariance (ANCOVA) was used to test change over time between the two conditions post-treatment while controlling for pre-treatment levels. Paired sample *t* tests were used to compare baseline with post-training assessments for all subjects who received the intervention ($n = 37$). The number of improvers on the cognitive measures was calculated using the Standard Deviation Index (Duff, 2012). The 68% confidence interval was used to determine reliable change (improvement >1 SD).

3. Results

3.1. Baseline analysis

Demographic and clinical characteristics are shown in Table 2. Comparisons revealed significant differences on years of education between the ICR group and the TAU group at baseline. Education correlated with Matrix ($r = 0.381$, $p = 0.007$), Digit Span backward ($r = 0.392$, $p = 0.006$), LMI ($r = 0.288$, $p = 0.045$), LMII ($r = 0.302$, $p = 0.035$), and the AIHQ blame scale ($r = 0.304$, $p = 0.044$) and was therefore entered as a covariate with the baseline performance in the ANCOVA for those variables only.

No other significant differences were found on other demographic, clinical, or cognitive variables. No significant differences were found between those who dropped out of the study ($n = 12$) and those who were included in the intent-to-treat analysis on any demographic, clinical or cognitive variables ($n = 37$).

3.2. Between-group comparisons

For the ANCOVA, the data met assumptions of equality of error variances and homogeneity of regression. There were significant between-group effects on the LMI theme, LMII theme, Digit Span working memory span, Trails B, Hinting task and the AIHQ hostility bias (see Table 3). All other group differences in outcomes at post-treatment were non-significant. However, medium effect sizes in favor of ICR were noted on the BRIEF-A self-report. The post-treatment completion rate for the cognitive measures was 100% (49 out of 49) and 95% (47 out of 49) for the self-report measures. The post-treatment completion rate for the PANSS was 69% (34 out of 49) and 75% (37 out of 49) for the informant-based social functioning measures. For outcome variables that were correlated with education, there were no group differences whether or not we controlled for education.

Table 1
Session content, treatment strategies and modifications.

	SCIT	CCT	NEAR
Session content	Review of the agenda for the session, check-ins, and activities specific to the session topic	Introduction of a strategy, discussion on how participants could use the strategy in everyday life	Strategy practice iPad training
Treatment strategy	*Sessions 1–6* *Phase I – Emotions* Introduce ICR and establish group alliance. Address emotion perception, emotion self-awareness and overconfidence by defining emotions as a group, emotion mimicry training, and understanding paranoia *Sessions 7–15* *Phase II-Figuring out situations* Address theory of mind, social perception, attributional bias and overconfidence by learning to think up other guesses, separating social facts from guesses, and gathering more evidence about a situation *Sessions 16–24* *Phase III – Checking it out* Integrate skills learned in the group to real life events and focus on generalization to day-to-day life	*Sessions 1–6* *Prospective memory* Goal setting, calendar use and weekly planning *Session 7–12* *Conversational and task vigilance* Goals revisited, "self-talk" to stay focused during tasks *Sessions 13–18* *Verbal learning and memory* Goals revisited, reducing information, making information meaningful, writing things down and name-learning skills *Sessions 19–24* *Executive functioning/ cognitive flexibility* Goals revisited, brainstorming and 6-step problem solving method	*Sessions 1–24* *Individualized iPad training using commercial programs* Training programs tailored to each participants baseline cognitive profile CCT strategy practice on iPads Participants select exercises that are fun and easy to build confidence Therapists use verbal encouragement and reinforcement Therapists guided the training using questions to enhance metacognition and information processing
Modifications	Discussion about homework eliminated No homework assigned other than meeting with the practice partner Practice partner exercises reduced to include CCT strategy training as well	Manual reduced to twelve 15–20 min sessions using iPad training for practice instead of paper-pencil No discussion about homework	Strategies from the CCT manual were practiced on iPads when appropriate

Note. SCIT: Social Cognition and Interaction Training; CCT: Compensatory Cognitive Training; NEAR: Neuropsychological Educational Approach to Remediation.

3.3. Within-group comparisons

Among all ICR recipients, the neurocognitive variables that significantly improved from baseline to post ICR treatment included all the verbal memory measures (LMI, LMI theme, LMII, and LMII theme), Stroop Interference, Tower, and Matrix (see Table 4). Significant changes were also observed in performance on the Hinting Task and the AIHQ hostility bias. The only social functioning measure that significantly improved was the BRIEF-A self-report. Significant change was seen on the PANSS negative symptom scale with negative symptoms reducing. Thirty-three of the 37 participants improved on at least one of the neurocognitive measures and 29 improved on at least one of the social-cognitive measures. No one improved on all outcome measures.The post-treatment completion rate for the cognitive measures was 92% (34 out of 37) and 97% (36 out of 37) for the self-report measures. The post-treatment completion rate for the PANSS was 84% (31 out of 37) and 76% (28 out of 37) for the informant-based social functioning measures.

3.4. Feasibility

Group attendance levels were good (77.6%; range 33.3–100%). Satisfaction ratings revealed that participants found the SCIT component most useful (44.2%) followed by the iPad training (37.8%) and CCT strategies (18.0%). Most rated the length of ICR (12 weeks) being appropriate (79.1%) and the length of each session (two hours) also being appropriate (93.5%). The practice partner exercises were completed 63.3% of the time and took on average 17.4 min (SD 2.2).

3.5. Post-hoc analysis

We conducted linear regression analysis among ICR participants to evaluate the effects of attendance and the number of completed practice partner exercises on post-treatment outcomes. Attendance significantly predicted outcome for the following measures at post-treatment: LMII theme ($p = 0.038$), Digit Span working memory span ($p = 0.046$), Trails A ($p = 0.043$), and predicted at trend-level outcome for LMI theme ($p = 0.063$), and LMII ($p = 0.087$). The number of practice

Table 2
Demographic and clinical characteristics for study participants.

Characteristics	*Whole samplen = 49*		*ICRn = 25*		*TAUn = 24*				
	n	Mean (SD)/%	*n*	Mean (SD)/%	*n*	Mean (SD)/%	t/x^2	*df*	*p*
Age (years)	49	24.2 (3.2)	25	23.6 (3.4)	24	24.8 (2.9)	−1.31	47	0.196
Education (years)	49	11.3 (1.6)	25	10.7 (1.2)	24	11.9 (1.7)	−3.00	42	0.006*
Gender,% male	43	86.0%	23	92.0%	20	83.3%	0.86	1	0.417
Diagnosis									
Schizophrenia	34	68.0%	16	64.0%	18	75.0%	0.70	1	0.404
Psychosis NOS	14	28.0%	8	32.0%	6	25.0%	0.29	1	0.588
Bipolar with psychotic features	1	2.0%	1	4.0%	0	0.0%	0.98	1	1.000
Age of onset (years)	49	22.3 (3.1)	25	21.6 (3.4)	24	23.0 (2.6)	−1.62	47	0.112
Duration of illness (months)	49	28.7 (22.0)	25	30.4 (26.5)	24	26.8 (16.4)	0.57	47	0.571
Number of hospitalizations	49	2.73 (1.9)	25	3.0 (2.2)	24	2.5 (1.6)	0.85	47	0.397
Atypical antipsychotics	44	89.8%	22	88.0%	22	91.7%	0.18	1	1.000
Typical antipsychotics	5	10.2%	4	16.0%	1	4.2%	1.87	1	0.349
No antipsychotics	3	6.0%	1	4.0%	2	8.3%	0.40	1	0.609

Note. ICR: integrated cognitive remediation; TAU: Treatment as Usual: Psychosis NOS: Psychosis not otherwise specified.
* Significant difference between groups.

Table 3
Analysis of covariance results comparing conditions at post-treatment and controlling for baseline scores.

Measures	Baseline Mean (SD) TAU	Post-treatment Mean (SD) TAU	Baseline Mean (SD) ICR	Post-treatment Mean (SD) ICR	*F*	*p*	N^2 *effect size*
Neurocognition							
Symbol Coding	65.5 (14.8)	64.5 (11.5)	59.2 (14.4)	62.6 (13.6)	0.22	0.644	0.01
Trails A[a]	29.8 (8.7)	30.9 (11.3)	28.6 (10.9)	27.9 (12.0)	0.82	0.371	0.02
Digit Span forward	8.3 (1.9)	8.3 (1.5)	8.1 (1.8)	8.5 (1.7)	0.18	0.678	0.01
Digit Span WM	8.0 (1.4)	7.6 (1.3)	7.7 (1.5)	8.2 (1.4)	6.63	**0.014**	0.13
LMI	31.2 (8.7)	33.3 (10.3)	29.8 (10.5)	35.1 (12.4)	1.09	0.301	0.03
LMI theme	12.3 (2.7)	12.2 (3.3)	11.7 (3.2)	14.4 (4.6)	6.10	**0.018**	0.13
LMII	20.0 (8.2)	20.2 (8.4)	16.6 (9.4)	22.1 (9.5)	3.93	0.054	0.09
LMII theme	8.4 (2.7)	8.4 (3.0)	7.4 (3.4)	9.4 (3.1)	4.81	**0.034**	0.11
Matrix Reasoning	27.2 (4.5)	28.6 (3.8)	26.8 (4.8)	28.0 (5.2)	0.29	0.593	0.01
Stroop Interference[a]	29.2 (11.7)	29.6 (9.2)	30.4 (9.3)	27.0 (7.5)	1.87	0.179	0.04
Tower	16.7 (3.5)	18.3 (4.1)	16.1 (2.6)	17.1 (4.4)	0.15	0.697	0.01
Trails B[a]	77.6 (28.7)	86.9 (32.1)	73.1 (20.4)	70.6 (14.2)	9.53	**0.004**	0.19
Social cognition							
Hinting Task	14.8 (2.9)	15.8 (3.0)	14.0 (2.7)	16.5 (2.6)	4.76	**0.035**	0.10
AIHQ Hostility[a]	10.3 (3.0)	8.4 (2.7)	9.2 (2.8)	6.2 (1.9)	6.21	**0.025**	0.13
AIHQ Blame[a]	34.0 (9.5)	33.1 (9.7)	34.4 (10.9)	29.8 (10.1)	0.49	0.488	0.01
AIHQ Aggression[a]	8.6 (1.8)	7.9 (1.3)	7.9 (1.8)	7.7 (1.9)	0.00	0.997	0.01
FEIT	12.9 (2.2)	13.1 (2.7)	12.7 (2.7)	13.6 (2.4)	0.57	0.456	0.01
FEIT confidence in correct answers	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	2.0 (0.5)	2.59	0.115	0.05
FEIT confidence in incorrect answers[a]	1.2 (0.8)	1.1 (0.8)	1.2 (0.7)	1.0 (0.6)	0.14	0.714	0.01
BCIS total	8.8 (6.8)	8.8 (65)	8.5 (6.5)	7.7 (5.9)	0.245	0.624	0.01
Social functioning							
LSP-39	124.7 (13.8)	128.6 (8.6)	127.5 (15.1)	127.6 (14.5)	0.19	0.670	0.01
BRIEF-A informant-report[a]	127.8 (32.2)	130.3 (30.3)	130.4 (27.2)	129.9 (23.1)	0.13	0.718	0.01
BRIEF-A self-report[a]	127.0 (22.8)	128.2 (22.2)	124.9 (25.1)	119.0 (23.3)	2.73	0.110	0.06
OSA	49.2 (8.9)	47.6 (9.4)	52.06 (12.0)	49.8 (7.8)	0.41	0.526	0.01
QOLS	73.0 (13.3)	69.1 (10.2)	77.1 (14.4)	70.1 (13.6)	0.26	0.616	0.01
Clinical symptoms[a]							
PANSS positive	11.9 (4.0)	11.1 (3.8)	13.7 (5.2)	12.9 (4.9)	1.30	0.264	0.04
PANSS negative	15.6 (4.9)	13.0 (3.7)	15.6 (6.2)	14.2 (5.0)	0.89	0.354	0.03
DASS-21 depression	6.3 (5.2)	9.7 (5.9)	7.7 (6.8)	7.4 (5.4)	2.25	0.141	0.05
DASS-21 anxiety	4.2 (4.2)	6.3 (5.0)	4.8 (4.2)	4.3 (4.3)	1.37	0.249	0.03
DASS-21 stress	5.7 (4.7)	7.2 (5.5)	5.7 (4.9)	6.7 (5.1)	0.05	0.829	0.01

Note. TAU; Treatment as Usual; ICR: integrated cognitive remediation; Digit Span WM: Digit Span working memory span; LMI and LMII: Logical Memory part I and II; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task; BCIS: Becks Cognitive Insight Scale; LSP-39: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self Assessment; QOLS: Quality of Life Scale; PANSS: Positive and Negative Syndrome Scale; DASS-21: Depression, Anxiety and Stress Scale.
Bolded significant values indicate those significant at $p < 0.05$.
[a] Higher scores reflect greater pathology.

partner meetings predicted at trend-level outcome for LMI theme ($p = 0.096$). In all instances, greater ICR treatment intensity was associated with more positive outcome on the dependent variable.

4. Discussion

This study examined the effectiveness of ICR on neurocognition, social cognition, social functioning, and clinical symptoms compared with TAU, in patients engaged with the services of an early intervention service for psychosis in Iceland. ICR, compared to TAU, was associated with small to medium effect size improvements on both neurocognitive and social-cognitive measures, including immediate and delayed verbal memory (LMI theme and LMII theme), cognitive flexibility (Trails B), working memory (Digit Span working memory span), ToM (Hinting Task), and hostile attributions (AIHQ hostility bias). Other comparable integrated therapy approaches have yielded similar results (Eack et al., 2009; Roder et al., 2011).

The effects on immediate and delayed verbal memory add to the extensive findings from similar studies in early schizophrenia (Revell et al., 2015). The relative contribution of each subprogram to outcomes is uncertain. The CCT approach specifically targets verbal memory and executive functioning but previous research on CCT in early psychosis did not find specific effects on executive functions or verbal memory post-treatment (Mendella et al., 2015). The significant effects found in this study may indicate that we were more efficient in teaching specific CCT training content related to verbal memory and executive functions, or that other components of the intervention may contribute to these gains. Cognitive remediation using NEAR has demonstrated significant effects on cognitive flexibility and verbal memory (Hodge et al., 2010) and previous research on SCIT has also reported improvements in cognitive flexibility (Combs et al., 2007a). In addition to the between-group effects, The ICR group obtained significant within-group effects on inhibition, planning and logic reasoning. Since this is an initial study with limited power to detect between-group differences, it may be useful to interpret within-group effects to evaluate whether ICR should be evaluated in a large-scale study. In contrast to numerous studies on cognitive remediation in schizophrenia (Mendella et al., 2015; Wykes et al., 2011) we did not observe improvements in processing speed (Digit Symbol Coding) which may reflect that the baseline performance was within 0.5 standard deviations of the usual reference age group, leaving little room for improvement (Twamley et al., 2011; Wechsler, 2008). However, these results are in line with a previous study on the effects of a combined neurocognitive and social-cognitive intervention in early course schizophrenia (Eack et al., 2009) and highlight the importance of investigating the potential benefits of these interventions in early psychosis samples.

The improvement in ToM is in line with previous findings on the social-cognitive gains from social-cognitive interventions (Kurtz et al., 2016). These results are promising since ToM has been identified as the social-cognitive domain with the strongest associations to community outcomes and interpersonal skills (Fett et al., 2011). A significant effect

Table 4
Pre- to post-treatment change in ICR intent-to-treat sample (n = 37).

Measures	Baseline Mean (SD)	Post-treatment Mean (SD)	Paired t-test	Cohen´s D_{av}	Number and percentage of improvers based on SDI
Neurocognition					
Digit Symbol Coding	61.4 (15.4)	64.4 (12.7)	−1.48, p = 0.149	0.06	4/34, 12%
Trails A[a]	28.9 (10.3)	28.0 (11.8)	0.68, p = 0.500	0.01	8/33, 24%
Digit Span Forward	8.1 (1.8)	8.3 (1.6)	−1.53, p = 0.135	0.07	11/35, 31%
Digit Span WM	7.6 (1.4)	8.0 (1.4)	−2.56, p = 0.015	0.17	8/34, 24%
LMI	29.5 (10.6)	35.5 (12.3)	−3.62, p = 0.001	0.29	12/33, 36%
LMI theme	11.7 (3.2)	14.2 (4.5)	−3.70, p = 0.001	0.37	15/33, 45%
LMII	17.5 (9.5)	23.8 (10.0)	−5.07, p = 0.001	0.45	9/32, 28%
LMII theme	7.6 (3.3)	9.7 (2.9)	−4.20, p = 0.001	0.36	9/32, 28%
Matrix Reasoning	26.6 (4.9)	28.1 (5.0)	−2.33, p = 0.026	0.14	4/34, 12%
Stroop Interference[a]	30.6 (10.9)	25.6 (9.1)	2.98, p = 0.005	0.21	12/34, 35%
Tower	16.6 (2.8)	17.9 (3.9)	−2.08, p = 0.047	0.13	10/30, 30%
Trails B[a]	72.3 (18.6)	69.4 (16.5)	1.11, p = 0.274	0.04	3/31, 10%
Social cognition					
Hinting Task	14.3 (2.8)	16.3 (2.8)	−5.92, p = 0.001	0.54	15/31, 48%
AIHQ Hostility[a]	9.7 (2.9)	7.0 (2.3)	5.74, p = 0.001	0.52	13/31, 42%
AIHQ Blame[a]	30.6 (9.9)	30.7 (9.9)	−0.07, p = 0.947	0.00	3/32, 9%
AIHQ Aggression[a]	8.0 (1.8)	8.1 (1.9)	−0.08, p = 0.938	0.00	7/30, 23%
FEIT	12.9 (2.6)	13.6 (2.4)	−1.85, p = 0.073	0.09	7/34, 21%
FEIT confidence in correct answers	1.8 (0.4)	1.9 (0.3)	−1.45, p = 0.158	0.06	6/32, 19%
FEIT confidence in incorrect answers[a]	1.1 (0.7)	1.0 (0.6)	0.67, p = 0.508	0.01	6/33,18%
BCIS total	8.0 (6.5)	7.7 (5.6)	−0.28, p = 0.779	0.06	1/30, 3%
Social functioning					
LSP-39	124.0 (15.0)	127.8 (12.7)	−1.62, p = 0.118	0.10	6/25, 24%
BRIEF-A informant-report[a]	130.4 (30.8)	127.1 (25.5)	0.69, p = 0.497	0.02	2/26, 8%
BRIEF-A self-report[a]	127.6 (22.9)	120.3 (22.7)	2.07, p = 0.047	0.12	6/32, 19%
OSA competence	49.58 (11.4)	51.5 (9.8)	−1.05, p = 0.303	0.05	4/24, 17%
QOLS	76.9 (13.9)	73.3 (12.8)	1.88, p = 0.071	0.11	0/31, 0%
Clinical symptoms[a]					
PANSS positive	12.2 (4.7)	12.6 (4.5)	−0.39, p = 0.700	0.00	6/26, 23%
PANSS negative	16.2 (5.6)	14.0 (4.6)	2.47, p = 0.020	0.18	6/26, 23%
DASS-21 depression	6.6 (6.0)	6.6 (5.0)	0.00, p = 1.00	0.00	6/31, 19%
DASS-21 anxiety	4.3 (4.0)	4.3 (4.3)	−0.05, p = 0.964	0.00	6/31, 19%
DASS-21 stress	5.0 (4.1)	6.0 (4.7)	−1.55, p = 0.133	0.07	2/31, 6%

Note. SDI: Standard Deviation Index; Digit Span WM: Digit Span working memory span; LMI and LMII: Logical Memory part I and II; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task; BCIS: Becks Cognitive Insight Scale; LSP-39: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self Assessment; QOLS: Quality of Life Scale; PANSS: Positive and Negative Syndrome Scale; DASS-21: Depression, Anxiety and Stress Scale.

[a] Higher scores reflect greater pathology.

was not found for emotion recognition, which contradicts some previous studies on social-cognitive interventions (Bartholomeusz et al., 2013; Grant et al., 2017; Horan et al., 2011a). Results on SCIT´s effect on emotion recognition have been inconsistent, with some studies reporting significant effects (Combs et al., 2007a; Roberts and Penn, 2009) but others not (Roberts et al., 2014). One explanation may be that emotion recognition training was only a small part of the intervention and only addressed in the first month of treatment, when two months remained until the post-treatment assessments were done. As suggested by (Roberts et al., 2014) it may be beneficial to increase emotion recognition training throughout the latter half of the intervention. The improvements in hostile attributional style should be interpreted with caution, due to the low test-retest reliability of the measures. However, these findings add valuable information to the previous inconsistent results of the small number of studies conducted on the effects of social-cognitive interventions on attributional style (Grant et al., 2017). Given the correlation between attributional style and executive functioning (Mehta et al., 2014), and SCIT´s previous success in remediating both domains, improvements in cognitive flexibility may enhance improvements in attributional style, and vice versa.

We did not find ICR associated improvements in informant-assessed social functioning or clinical symptoms which was also reported in a recent short-term trial on CCT for first-episode subjects (Mendella et al., 2015). Generally, smaller effect sizes have been found for functioning in early psychosis samples than chronic schizophrenia (Revell et al., 2015). It may be that observable changes in functioning are not detected at post-treatment, but rather at longer follow-up and a 12-month follow-up study is currently underway. Although we did find a small within-group effect on self-assessed problems related to exectutive functioning in every-day life, the results may reflect the need for more appropriate measures of social functioning in early psychosis focusing on social relationships and self-esteem. It is plausible that some of the measures of social functioning used in this study did not capture impairments in functioning in this sample, since baseline functioning was relatively high. In addition, the post-treatment completion rate for the informant-based social functioning measures (BRIEF-A informant-report and LSP-39) and the clinician-rated measure of symptomatology (PANSS) was relatively low, and the results may in part reflect reduced power. However, we did find a small within-group effect on negative symptoms for participants who completed the ICR but it may be that a more symptom-focused intervention is needed to improve psychiatric symptoms severity (Eack et al., 2009).

Regarding the feasibility, ICR was well received by participants, with good attendance and little drop-out. Most found the intervention to be useful and tolerable, in line with previous research on SCIT (Parker et al., 2013; Roberts et al., 2010). A greater dosage of ICR might lead to stronger outcomes, consistent with dose-response effects observed in other psychosocial interventions for schizophrenia (Medalia and Richardson, 2005; Roberts et al., 2014). When asked which treatment approach they found most beneficial the participants varied in their answers, suggesting it may be highly valuable to offer participants personalized approaches to meet the rehabilitation needs of each individual.

This study had several methodological limitations. First, the sample

size is modest, which may have reduced power to detect smaller treatment effects. Second, the average time between the baseline assessments and start of treatment was 3.7 months (SD 3.6). During this time, patients received treatment at the early intervention service and therefore the effects may be due to other factors than the ICR. However none of the participants received any other group psychotherapy or cognitive training, and cognitive test findings have been reported to be highly stable over many years in first-episode and schizophrenia patients (Haatveit, 2015; Horan et al., 2011a; Kurtz et al., 2005). Third, PANSS raters were not blind to group assignment. Fourth, we did not correct for multiple comparisons due to our small sample size, and it is possible that some of our results reflect Type I error. The results should therefore be regarded as preliminary until replicated. Fifth, test-retest reliability for some of the social-cognitive measures was low. However, limitations in social-cognitive assessment are a well-known methodological issue and recently, the Hinting Task has been identified as the only social-cognitive measure recommended for use in clinical research in early psychosis (Ludwig et al., 2017).

We conclude that ICR is a time-effective and feasible program for early psychosis patients. It appears to yield clinical benefits, particularly in the areas of verbal memory, cognitive flexibility, working memory, ToM, and hostile attributional biases. More training of the acquired skills in everyday life may be necessary for the effects to generalize to social functioning and a follow-up study is needed to determine the durability of the effects. Future research should clarify the relative contribution of each subprogram to its impact on outcomes and replication of the study in a larger sample is needed.

Conflict of interest

None.

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Paper III

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Integrative cognitive remediation for early psychosis: A 12-month follow-up

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ABSTRACT

In recent years, a growing number of studies have attempted to treat social-cognitive impairment within neurocognitive remediation as means of improving outcome in psychotic disorders with promising results. However, the durability of the effects is still under debate and little is known about the long-term efficacy of integrated neuro- and social-cognitive remediation in early psychosis. The purpose of this study was to examine long-term effects of a 12-week integrative cognitive remediation (ICR) for early psychosis. Thirty-seven patients diagnosed with primary psychotic disorder and previously treated with ICR as part of their standard treatment were assessed on cognitive performance, psychopathology, and functional outcome at baseline, 3 months (posttest) and 12 months (follow-up). After participating in ICT, individuals showed significant improvements on most neurocognitive and social cognitive domains. A significant increase in number of participants employed was found at 12-month. The study suggests ICR may have favorable effect on long-term cognitive improvements and functional gains in early psychosis.

1. Introduction

Deficits in neurocognition and social cognition are evident in schizophrenia at all stages of the illness and affect multiple domains of functioning (Bilder et al., 2006; Green et al., 2012; Horan et al., 2012; Keefe and Harvey, 2012; Savla et al., 2013; Schaefer et al., 2013). The consistent relationship between social cognition and functional outcomes (Fett et al., 2011) and the possible role of social cognition as a mediator between neurocognition and functional outcomes (Couture et al., 2006; Schmidt et al., 2011) has sparked interest in combined neurocognitive and social-cognitive interventions. Existing research suggests that broad-based multi-component interventions, where social cognition is addressed as well as neurocognition, may produce durable cognitive and functional improvements (Hogarty et al., 2006; Mueller et al., 2015; Roder et al., 2011; Wykes et al., 2011). Although numerous randomized controlled trials have been conducted on the effectiveness of combined interventions within schizophrenia, only a handful of studies have explored these effects in early psychosis. There appear to be several benefits of early application of such integrated interventions. Targeting cognition early may have protective effects against neural degeneration (Eack et al., 2010a) and help reverse the functional decline associated with psychotic disorders (Horan et al., 2012). Integrated neurocognitive and social-cognitive interventions appear to effectively improve neurocognition, social cognition, and social functioning in patients who are within five years of their first psychotic episode (Boriello et al., 2015; Eack et al., 2009, 2010b; Lewandowski et al., 2011; Vidarsdottir et al., 2019a), with greater improvements than achieved in chronic schizophrenia (Boriello et al., 2015; Bowie et al., 2014; Deste et al., 2019). Furthermore, improvements in neurocognition and social cognition that result from integrated treatments may mediate functional improvement in early course schizophrenia (Eack et al., 2011) that may persist up to one year after cessation of treatment (Eack, 2010b). However, there is still a need for more evidence on the durability and generalizability of these interventions before they can be recommended as part of routine treatment at early intervention in psychosis (EIP) services. This includes assessing how sustainable gains may be over time as well as examining whether improvements are greater for those who receive integrated

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cognitive remediation as part of their standard care at an EIP service as opposed to those who do not.

We recently integrated three evidence-based neurocognitive and social-cognitive approaches and, with a wait-list randomized controlled trial, evaluated the effects of Integrative Cognitive Remediation (ICR) on cognition, functional outcome and clinical symptoms in the same population (Vidarsdottir et al., 2019a). In this report, we aim to examine changes in cognition, psychiatric symptom severity and functional outcome from baseline to 12-month follow-up for all participants who received the intervention (n = 37). In addition, we evaluated the stability of outcomes from posttreatment to 12-month follow-up.

2. Methods

2.1. Participants

The participants initially enrolled in the study were 49 patients from an EIP service at Landspitali-The National University Hospital in Iceland (Reykjavik). Because the original study was a wait-list randomized control trial, all participants were eventually offered the intervention. A total of 37 participants received the ICR intervention in addition to their standard treatment and were included in the current sample. Inclusion criteria were as follows: 18 to 30 years of age, an ICD-10 diagnosis of schizophrenia or schizoaffective disorder, acute and transient psychotic disorder, schizotypal disorder, delusional disorder or other non-unipolar or non-bipolar psychotic disorders (World Health Organization, 2008), duration of psychotic illness of five years or less, baseline impairment in at least one cognitive domain greater than 1 SD, Icelandic speaking, and no evidence of an intellectual disability or organic brain disorder (i.e. IQ < 70).

We also examined work and school outcomes for a group of patients (n = 30) who were seeking treatment at the EIP service during the RCT trial, and had been assessed at baseline as part of a previous study (Vidarsdottir et al., 2019b). Nine of these participants were enrolled in the RCT study but did not want to receive the integrated intervention, and 21 patients were never enrolled in the RCT study (see consort flowchart). These patients continued their standard treatment and are included in this study as a historical control group. The study was approved by appropriate institutional review boards and all participants provided informed consent.

2.2. Procedure

Participants were reassessed 12-months after the end of treatment with the same cognitive, clinical and functional outcome measures that had been administered at baseline and posttreatment. Assessments were administered by clinical psychologists and case-managers external to the treatment teams.

2.3. Measures

The psychometric properties of the measures have been reported elsewhere (Vidarsdottir et al., 2019a, 2019b). According to the original protocol (Vidarsdottir et al., 2019a), psychopathology was assessed with Positive and Negative Syndrome Scale (PANSS STanley, 1987) and the Depression Anxiety and Stress Scale 21-item (DASS-21; Lovibond, 1995). The Beck Cognitive Insight Scale (BCIS; Beck et al., 2004) was used to assess cognitive insight. Neurocognitive tests included those listed below by cognitive domain:

1 Processing speed: Symbol Coding subtest from the Wechsler Adult Intelligence Scale 4th edition (WAIS-IV) (Wechsler, 2008) and the total time for the Trail Making Test A (TMT A; Reitan, 1958).
2 Attention: Digit Span forward subtest from the WAIS-IV (Wechsler, 2008).
3 Working memory: Digit Span working memory span from the WAIS-IV (digit span backwards + digit span in a row)/2; Wechsler, 2008).
4 Cognitive flexibility: Trail Making Test B total time (TMT B; Reitan, 1958).
5 Verbal memory: Wechsler Memory Scale 3rd edition Logical memory (WMS-III; Wechsler, 1997). Total scores for immediate recall (LMI), immediate recall theme (LMI theme), delayed recall (LMII) and delayed recall theme (LMII theme).
6 Visual reasoning: Wechsler Abbreviated Scale of Intelligence Matrix Reasoning (WASI-IS; Guðmundsson, 2015; Wechsler, 1999).
7 Planning: Tower Test from the Delis-Kaplan Executive Function System (D-KEFS) total achievement score (Delis, 2001).
8 Inhibition: Stroop Color-Word interference score (Golden, 1978; Stroop, 1935).

Social-cognitive tests included those listed below by social-cognitive domains:

1 Theory of mind: Hinting task total score (Corcoran et al., 1995).
2 Attributional style: The Ambiguous Intentions Hostility Questionnaire-Ambiguous items (AIHQ-A; Combs et al., 2007). Total scores were calculated for hostility, blame and aggression separately.
3 Emotion recognition: The Facial Emotion Identification Task total score (FEIT; Kerr and Neale, 1993).
4 Metacognitive overconfidence was assessed by adding a metacognitive measure of confidence to the standard administration of the FEIT (confidence in correct FEIT answers and confidence in incorrect FEIT answers).

Functional outcome was assessed with three self-report measures and two informant-report measures, listed below. Informants were high-contact clinicians, family members or partners. Information on employment rates and school enrollment were gathered from the participants and their case-managers.

1. Informant-reported community functioning: Life Skills Profile (LSP; Rosen et al., 1989).
2. Informant-reported and self-reported executive dysfunction: The Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A; Roth, 2005).
3. Subjective quality of life: The Quality of Life Scale (QOLS; Flanagan, 1978).
4. Self-reported occupational competence: The Occupational Self Assessment (OSA; Baron, 2006).

2.4. Intervention

All participants received a 12-week integrated cognitive remediation intervention plus standard treatment. The intervention is extensively described in a previous report (Vidarsdottir et al., 2019a). In summary, the intervention was delivered over 24 2-hour-long sessions according to treatment manuals and was based on the following three cognitive remediation approaches: Neuropsychological Educational Approach to Remediation (NEAR; Medalia and Freilich, 2008), Compensatory Cognitive Training (CCT; Mendella et al., 2015; Twamley et al., 2019, 2012) and Social Cognition and Interaction Training (SCIT; Roberts et al., 2016).

During the active treatment phase and follow-up, each participant continued to receive standard care based on an individualized treatment plan. All participants received case-management or supportive counseling at least once per week.

2.5. Statistical analyses

All variables were assessed for normality. Cognitive, clinical, and functional outcome data were collected during the active phases of this

treatment trial to examine baseline to posttreatment gains of the intervention group. These data are included in this durability study to examine the overall change from baseline to 12-month follow-up assessments. Independent *t*-tests and chi square tests (for dichotomous variables) were performed on demographic and clinical variables to evaluate differences between groups (Intervention group vs. historical control group) at baseline. Between-group differences in the number of participants employed, as well as the number of participants enrolled in school at baseline, posttreatment and 12-month follow-up were analyzed with a Chi-square test.

Difference between those who had been discharged from the EIP service by the time of follow-up and those who had not were assessed across all clinical, cognitive and functional measures with *t*-tests. The Mann-Whitney U test or the Friedman test was used for skewed variables. A repeated measures ANOVA with a Greenhouse-Geisser correction was conducted to compare scores on cognitive, clinical, and functional outcome measures at baseline, posttreatment, and 12-month follow-up for the intervention group. Change scores (follow-up minus baseline) were calculated for variables demonstrating significant improvement from baseline to 12-month follow-up. Correlates of these change scores and PANSS positive and PANSS negative symptom severity at baseline were examined were examined with Pearson correlations. Post-hoc tests were applied to all significant findings to investigate whether the effects seen at posttreatment persisted at 12-month follow-up. To control for Type I error associated with multiple comparisons, alpha was set to 0.01 for significance testing. Effect sizes for ANOVA analyses was computed with partial η^2 in which medium (>0.06) and large (>0.14) effects were considered clinically meaningful.

3. Results

Table 1 summarizes demographics, clinical characteristics, rate of employment, and rate of school enrollment for the intervention and the historical control group at baseline. No significant differences were found between the two groups at baseline. At 12-month follow-up, 12 (32.4%) of the intervention group and 16 (53.3%) of the historical control group had been discharged from the EIP service. No significant differences were found between those who were discharged and those who were still in treatment at 12-month follow-up on any of the outcome variables.

3.1. Stability and change in cognitive functioning from baseline to 12-month follow-up

Performance at 12-month follow-up was significantly better than performance at baseline for several neurocognitive and social-cognitive measures (see Table 2) including Symbol Coding, Digit Span forward, LMI, LMI theme, LMII, LMII theme, Matrix Reasoning, Stroop interference, Tower, Hinting Task and AIHQ hostility bias. The effect sizes for these changes ranged from 0.163 (Digit Span forward) to 0.506 (LMII). None of the change scores for these variables were associated with PANSS positive or PANSS negative symptom severity at baseline.

Post-hoc tests demonstrated a significant level of continued improvement from posttreatment to 12-month follow-up in performance on LMI ($p = 0.011$), LMII ($p = 0.009$), LMII theme ($p = 0.034$) and Symbol Coding ($p = 0.039$). None of the social-cognitive domains statistically improved from posttreatment to 12-month follow-up. Although scores on AIHQ hostility bias and TMT B were elevated at 12-month follow-up compared to posttreatment, post-hoc tests demonstrated that the difference was non-significant.

3.2. Change in functional outcomes and clinical symptom severity from baseline to 12-month follow-up

No significant changes were found on measures of functional outcome (Table 2). Effect sizes of informant-reported improvement in functional outcome were 0.150 for community functioning (LSP), and 0.081 for executive dysfunction (BRIEF-A informant report). Effect sizes range from small to large on the three self-report measures of functioning (OSA, BRIEF-A self-report and QOLS) with effect sizes of 0.136, 0.100 and 0.097, respectively. There were no between group differences in occupational or educational status at any assessment point. However, the number of participants working increased significantly between baseline and 12-month follow-up in the ICR group ($t(36) = -3.97$, $p < 0.001$), but not in the historical control group. At baseline, 21.6% were working in the ICR group and 33.3% in the historical control group; these percentages increased to 37.8% and 39.2%, respectively, at posttreatment and 56.8% and 46.7% at 12-month follow-up (seeFig. 2). The number of participants enrolled in school increased from 5 (13.5%) to 7 (18.9%) in the ICR group and from 3 (10%) to 6 (20%) in the control group, but the difference was not significant in either group. Regarding clinical symptoms, a large effect size was observed in negative symptoms although the change was nonsignificant.

4. Discussion

This study provides preliminary data on the immediate and long-term effects of ICR in a sample of young adult early psychosis patients. ICR participants showed significant improvements in multiple neurocognitive and social-cognitive domains from baseline to 12-month

Table. 1
Demographics and clinical characteristics for the intervention group ($n = 37$) and the historical control group ($n = 30$).

Characteristics	*n*	Intervention group% /Mean (SD)	*n*	Historical control group% /Mean (SD)	*T or* X^2	df	*p*
Age (years)	37	24.0 (3.3)	30	24.4 (3.9)	−0.427	65	0.671
Education (years)	37	11.0 (1.4)	30	11.7 (1.9)	−1.770	65	0.081
Age of onset (years)	37	22.0 (3.1)	30	22.6 (2.8)	−0.818	64	0.417
Duration of illness (months)	37	31.5 (24.1)	30	24.2 (18.4)	1.353	64	0.181
Number of hospitalizations	37	2.9 (1.9)	30	3.3 (2.3)	−0.769	65	0.445
Gender,% male	33	89.2%	25	83.3%	0.115	1	0.500
Diagnosis							
Schizophrenia	26	70.3%	25	83.3%	0.920	1	0.338
Psychosis NOS	10	27.0%	4	13.3%	1.142	1	0.285
Schizoaffective disorder	1	2.7%	1	3.3%	0.011	1	0.916
Atypical antipsychotics	33	89.2%	22	73.3%	1.857	1	0.173
Typical antipsychotics	5	13.5%	1	3.3%	1.042	1	0.307
No antipsychotics	2	6.3%	7	23.3%	3.167	1	0.075
Work	8	21.6%	10	33.3%	0.637	1	0.425
School enrollment	5	13.5%	3	10.0%	0.004	1	0.950

Note. NOS: Not otherwise specified.

Table. 2
Results of Analyses of Variance for cognitive, functional outcome and clinical measures, baseline compared with 12-month follow-up for intervention completers.

Measures	Baseline Mean (SD)	Posttreatment Mean (SD)	12-month Mean (SD)	*F(df), p*	$\eta^{2,}$ effect size
Neurocognition					
Symbol Coding	61.0 (14.0)	64.8 (13.2)	68.5 (14.3)	**9.15(1.5), $p = 0.001$**	0.234, large
TMT A[a]	29.0 (10.6)	27.7 (12.1)	26.4 (10.5)	1.84(1.9), $p = 0.171$	0.060, small
Digit Span forward	7.9 (1.7)	8.4 (1.6)	8.6 (1.7)	**5.63(1.7), $p = 0.009$**	0.163, large
Digit Span WM	7.6 (1.4)	8.2 (1.4)	8.4 (1.6)	3.33(1.7), $p = 0.049$	0.100, medium
LMI	30.9 (10.3)	36.3 (12.3)	41.3 (11.3)	**19.21(1.9), $p = 0.000$**	0.407, large
LMI theme	12.1 (3.0)	14.5 (4.6)	15.3 (3.4)	**14.96(1.7), $p = 0.000$**	0.348, large
LMII	18.1 (9.0)	23.7 (10.1)	27.9 (8.1)	**28.71(2), $p = 0.000$**	0.506, large
LMII theme	8.1 (3.0)	9.7 (3.0)	10.7 (2.5)	**19.51(1.8), $p = 0.000$**	0.411, large
Matrix Reasoning	26.6 (5.1)	28.2 (5.3)	28.5 (4.4)	**5.56(1.9), $p = 0.007$**	0.171, large
Stroop Interference	31.3 (11.1)	26.5 (9.3)	26.1 (7.9)	**5.95(1.8), $p = 0.006$**	0.170, large
Tower	16.7 (3.0)	17.8 (4.1)	19.4 (3.7)	**8.062(2), $p = 0.001$**	0.244, large
TMT B[a]	75.1 (24.1)	68.3 (16.5)	75.8 (28.9)	1.89(1.6), $p = 0.180$	0.063, medium
Social cognition					
Hinting Task	14.0 (2.9)	16.0 (2.8)	16.2 (2.8)	**17.25(1.8), $p = 0.000$**	0.373, large
AIHQ HB[a]	9.6 (3.0)	7.0 (2.4)	8.3 (2.7)	**11.96(1.9), $p = 0.000$**	0.315, large
AIHQ BS[a]	31.2 (10.1)	31.4 (10.2)	30.1 (9.3)	0.26(1.6), $p = 0.728$	0.009, small
AIHQ AB[a]	8.3 (1.6)	8.2 (2.0)	8.5 (1.8)	0.40(2), $p = 0.675$	0.015, small
FEIT	13.1 (2.5)	13.8 (2.4)	13.2 (2.5)	1.34(1.9), $p = 0.269$	0.044, small
FEIT conf. correct	1.8 (0.4)	1.9 (0.4)	1.8 (0.4)	1.09(2), $p = 0.344$	0.036, small
FEIT conf. incorrect[a]	1.1 (0.7)	1.0 (0.6)	1.1 (0.7)	0.69(1), $p = 0.414$	0.023, small
BCIS	−5.9 (8,3)	−5.5 (6.7)	−6.4 (6.1)	0.21(1.6), $p = 0.762$	0.008, small
Functional outcome					
LSP	123.3 (14.7)	127.3 (13.5)	130.0 (13.6)	3.54 (1.9), $p = 0.040$	0.150, large
BRIEF-A informant[a]	130.4 (29.7)	127.2 (27.2)	120.6 (28.1)	1.86(2), $p = 0.169$	0.081, medium
BRIEF-A self-report[a]	125.4 (22.8)	118.8 (22.8)	116.0 (25.1)	2.89(1.8), $p = 0.072$	0.100, small
OSA	52.6 (13.4)	54.4 (11.8)	58.0 (12.8)	3.45 (1.8), $p = 0.047$	0.136, medium
QOLS	77.6 (12.8)	74.3 (12.7)	78.6 (14.2)	2.79(1.9), $p = 0.073$	0.097, medium
Clinical symptoms					
PANSS positive[a]	11.9 (4.4)	12.2 (4.6)	11.6 (5.4)	0.17(1.5), $p = 0.788$	0.008, small
PANSS negative[a]	15.2 (5.6)	14.3 (4.9)	12.5 (4.4)	3.54(1.6), $p = 0.049$	0.150, large
DASS-21 depression[a]	6.6 (6.4)	6.5 (5.1)	6.0 (5.6)	0.27(2), $p = 0.756$	0.010, small
DASS-21 anxiety[a]	4.2 (4.2)	4.6 (4.5)	4.1 (4.0)	0.19(1.9), $p = 0.816$	0.007, small
DASS-21 stress[a]	5.3 (4.3)	6.2 (5.0)	5.2 (4.9)	1.07(1.9), $p = 0.348$	0.040, small

Note. P-values in bold indicate $p < 0.01$. Effect sizes, partial η^2, indicate small > 0.01, medium > 0.06, and large > 0.14 effects. [a]Higher scores reflect greater pathology. TMT: Trail Making Test; Digit Span WM: Digit Span working memory span; LMI and LMII: Logical Memory part I and II; AIHQ: Ambiguous Intentions Hostility Questionnaire; FEIT: Facial Emotion Identification Task; BCIS: Becks Cognitive Insight Scale; LSP: Life Skills Profile; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; OSA: Occupational Self Assessment; QOLS: Quality of Life Scale; PANSS: Positive and Negative Syndrome Scale; DASS-21: Depression, Anxiety and Stress Scale.

follow-up with medium to large effect sizes. In analyzing the maintenance of these improvements, our data supports previous findings suggesting that cognitive improvements seen immediately posttreatment on the neurocognitive domains of verbal memory and processing speed are at lease durable up to 12 months later (Buonocore et al., 2018; Eack, 2010b). The continued significant improvement observed on three out of the four verbal memory measures is particularly promising as previous studies have found that verbal memory deficits continue to deteriorate over the long term (Bozikas and Andreou, 2011), and improvements in verbal memory may be the most reliable neurocognitive predictor of functional improvement (Eack et al., 2011; Green et al., 2000).

Previous findings on the stability and durability of social-cognitive improvements have been somewhat mixed (Combs et al., 2009; Roberts et al., 2014), and the available studies are too few to allow any firm conclusions to be drawn. The importance of social cognition in predicting functional outcomes has been widely demonstrated (Couture et al., 2006) but further research on the long-term stability of social-cognitive performance following integrated interventions is warranted. However, despite this, some recommendations can be made on the basis of previous studies and the current results. To maintain and increase social cognitive gains, it may help to recommend continued practice of social cognition, possibly in the form of booster sessions. In addition, findings on attributional style should be interpreted with caution, as the test-retest reliability of the AIHQ-A is low in early psychosis samples ((Ludwig et al., 2017; Vidarsdottir et al., 2019a). Further developments of psychometrically sound measures of attributional style are needed.

Although not statistically significant, it is notable that there were improvements from baseline to 12-month follow-up on both self-reported and informant-reported functional outcomes. In addition, there was a large significant increase in employment rates found only the ICR group at follow-up. These results are particularly encouraging and may suggests that ICR may be a contributing factor in the increase in patients' competitive employment rates one year after treatment. However, because we could not differentiate between the ICR group and the historical control group regarding employment rates, these results should be interpreted with caution.

Overall, the major implication of these findings is that the 12-week integrated neuro- and social-cognitive intervention used in our previous trial may yield clinically significant long-term functional benefits, supporting the efficacy of this intervention. The delay between intervention-associated effects on neuro- and social cognition and benefits in functional outcomes highlights the need for longitudinal studies. Although the long-term functional gains may have been independent of cognitive improvement, it may also be that meaningful functional change may take longer than 12-weeks to emerge.

Limitations

First, measures of cognition, clinical symptoms, self-reported and informant reported functional outcome were not administered to the historical control group at 12-month follow-up. Second, it is not apparent from the results of our study which elements of ICR are most

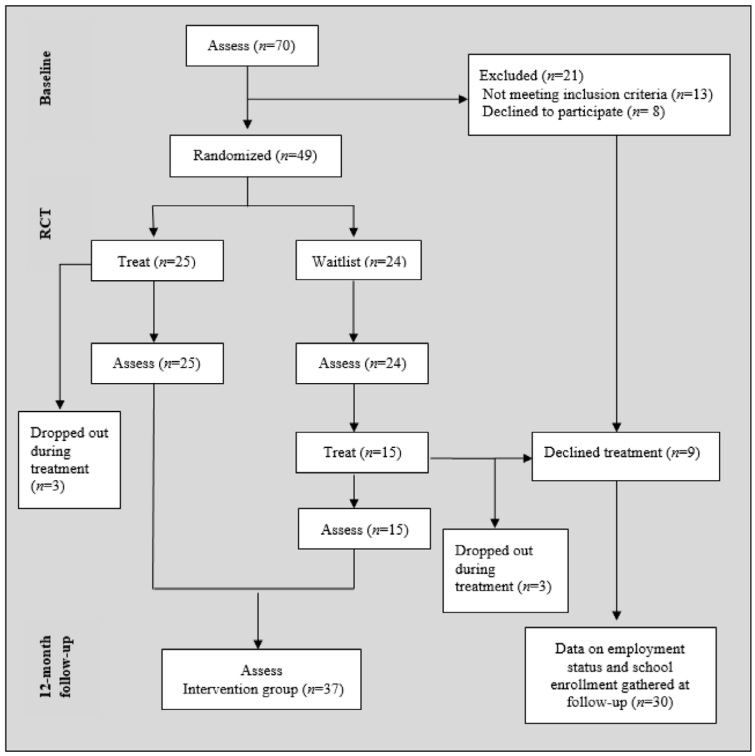

Fig. 1. Consort diagram.

predictive of the durability of gains at 12-month follow-up. Further research is warranted to provide more informative data about the longitudinal maintenance of the various observed improvements. Third, because of the repeated measurements, some of the results could reflect practice effects. Practice effects were minimized by retesting one year after treatment ended, which may be considered a long test-retest interval. The observed improvements were greater than observed gains of a half a standard deviation found in multiple retesting (Scharfen et al., 2018). This is further supported by results from our previous study showing that changes seen in those treated were greater than those made by individuals who received no ICR treatment between two separate testing occasions. However, it is important to investigate between-group differences over the long-term before any firm conclusions can be made. Fourth, functional outcome and clinical symptoms were not assessed blindly because they were based on self-reports and informant-reports completed by a close-contact caregiver, spouse or a family member. However, we used diverse multiple methods to assess functional outcomes, including three self-reports, two informant-reports as well as performance-based measures .

Conclusion

Despite these limitations, this study addresses a very important issue in the treatment of cognition in early psychosis, as relatively little is known about the efficacy and durability of combined neuro- and social-cognitive interventions in this population. The results are encouraging and suggest that ICR may produce lasting effects on cognition, negative symptoms, and functional outcome. However, a further investigation of

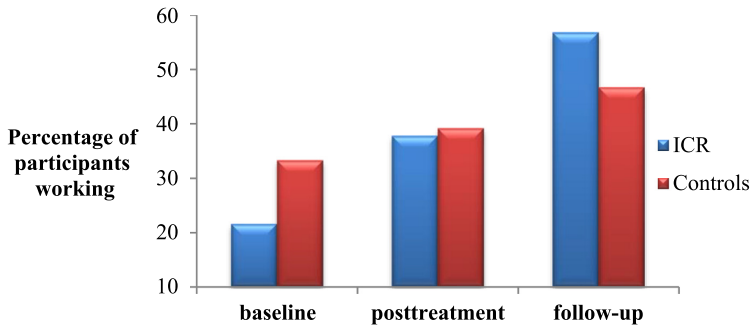

Fig. 2. Longitudinal course of participants working in the ICR and historical control groups.

the long-term efficacy of the intervention, with a randomized controlled trial is warranted.

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Contributors

OGV was involved in the study design, writing the manuscript, and was responsible for the data analysis. BBM, BG, and EWT were involved in the study design, data analysis, and editing the manuscript. DLR and ES were involved in the design and in editing the manuscript. All authors contributed to and approved the final manuscript.

Declaration of Competing Interest

None

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