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Cognitive Training and Remediation in First-Episode Psychosis: A Literature Review

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Abstract

BACKGROUND: Neurocognitive and social cognitive impairments are core characteristics of psychotic disorders, which are present in the first episode of psychosis (FEP) and strongly predict poor social functioning. Addressing cognitive impairments through cognitive training and remediation (CTR) may be a crucial component of recovery-oriented treatment.

AIMS: The objectives of this review were to (1) evaluate the CTR theoretical basis and intervention components and (2) examine the effects of CTR on cognition and social functioning in FEP.

METHOD: A combined search of Ovid Medline, Embase, and Psych Info databases was conducted using keywords. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed. Quality and risk of bias were assessed using established instruments.

RESULTS: Ten randomized controlled trials were included in this review and had an overall fair to poor quality. CTR interventions in FEP utilize a range of theoretical backgrounds, with most including a focus on higher order cognitive processes. Varied doses and intervention components are used. All but one study found improvements in at least one cognitive domain. Global cognition, verbal learning, and memory and executive function were most commonly improved. Three studies found an effect on a range of functional outcomes.

CONCLUSIONS: A broad range of CTR interventions have promising effects for addressing cognitive impairments in FEP. Evidence of functional impact is less consistent. Further research is

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Supplemental Material

Supplemental material for this article is available online.

needed in FEP on CTR targeting sensory and perceptual processes, and to identify CTR intervention targets and treatment components that will lead to robust improvements in cognition and functioning.

Keywords

neurocognition; early intervention; recovery; functioning

Introduction

A first episode of psychosis (FEP) occurs in 100,000 adolescents and young adults annually in the United States (National Institute of Mental Health, n.d.; Simon et al., 2017). Psychotic disorders, such as schizophrenia, are associated with devastating disability in social functioning, defined as attainment of education, employment, and meaningful social relationships (Bromley & Brekke, 2010; Desai, Lawson, Barner, & Rascati, 2013; Wiersma et al., 2000). This disability places a significant burden on affected individuals, caregivers, and society. In 2013, the national cost of schizophrenia was \$155 billion, and nearly 75% of this cost was attributable to patients' unemployment and caregivers' lost productivity (Cloutier et al., 2016). Disability in social functioning is evident in the early stages of illness and is often not recovered with psychosis symptom remission (Henry et al., 2010; Norman et al., 2018). The FEP period, encompassing the first 5 years after the onset of psychosis, represents a critical treatment opportunity to alter an individual's functional trajectory (Birchwood, Todd, & Jackson, 1998; Crumlish et al., 2009; Norman et al., 2018). As a result, FEP specialty programs have grown substantially in recent years. However, such programs have failed to result in robust long-term improvements in social functioning (Bertelsen et al., 2008; Norman et al., 2018; Secher et al., 2015), suggesting that a critical treatment target may be missing.

Cognitive impairments are a core characteristic of psychotic disorders that are present before psychosis symptom onset and persist throughout the course of illness (Addington, Saeedi, & Addington, 2005; Bora & Murray, 2014; Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009). These impairments include both neurocognitive deficits (i.e., the domains of verbal learning and memory, executive functions, and attention) and social cognitive deficits, which refer to the processing and interpretation of social information, including emotion perception, inferring the mental states of others, and reading social cues (Fett et al., 2011). Both neurocognitive and social cognitive impairments have been strongly linked to poor social functioning in individuals with psychosis. Neurocognitive impairments have been found to account for up to 20% to 60% of the variance in functional outcomes (Fervaha, Foussias, Agid, & Remington, 2014; Fett et al., 2011; Green, Kern, Braff, & Mintz, 2000; Lepage, Bodnar, & Bowie, 2014; Najas-Garcia, Gómez-Benito, & Huedo-Medina, 2018). Social cognitive impairments are related to but distinct from neurocognitive impairments and may be more strongly linked to community functioning (Fett et al., 2011; Schmidt, Mueller, & Roder, 2011). Together, these impairments contribute more to functional decline than any other symptom domain (Fervaha et al., 2014; Fett et al., 2011; Lepage et al., 2014), and are one of the few consistent predictors of poor social functioning trajectories in FEP (Santesteban-Echarri et al., 2017).

As a result, remediating cognitive deficits may be a critical component of early intervention services. A large body of literature in chronic psychotic disorders suggests that cognitive training and remediation (CTR) interventions are effective at improving both cognitive and functional outcomes (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). A 2015 meta-analysis of CTR in early psychosis found small to moderate effects on cognition and functioning (Revell, Neill, Harte, Khan, & Drake, 2015). However, this analysis included patients who were high risk but had not yet developed a psychotic disorder, and due to its quantitative aims, was unable to provide a detailed analysis of the CTR theoretical basis and intervention components, which vary substantially between studies and may affect results. The current review sought to provide an updated narrative synthesis of the CTR literature in FEP. The objectives of this review were to (1) evaluate the theoretical basis and intervention components of CTR in FEP and (2) examine the effects of CTR on cognition and social functioning in FEP.

Method

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed for the literature search and study selection (Moher, Liberati, Tetzlaff, & Altman, 2009). The search protocol included establishing eligibility criteria, an initial database search, abstract screening, full text review, and review of reference lists. A search strategy was developed as follows: ((early or first episode) AND (schiz* OR psychosis OR psychotic) AND cognit* AND (remediation OR rehabilit* OR train*)). The search was conducted as a multiplacement keyword search (searching the title, abstract, keyword, and subject heading fields) in Medline, Embase, and PsycINFO, all via the Ovid interface. Results were limited to journal articles only (i.e., conference abstracts were excluded). No other language or date limits were applied in the search. The search strategy can also be found in Supplemental Table 1, available online.

Inclusion and Exclusion Criteria

Studies were included if they met the following inclusion criteria: were a randomized controlled trial (RCT), tested a CTR intervention, included an FEP population, and reported on cognitive or functional outcomes. Studies were excluded if the sample included a nonpsychotic disorder diagnostic group (i.e., high risk for psychosis or nonpsychotic depression), were follow-up reports or secondary analysis from another study, or were conference abstracts only.

Data Extraction

A data extraction form was created to include relevant data from each study, including study identification (title, authors, and publication year), sample characteristics (sample size, gender, age, education level, and baseline symptoms), study characteristics (design, blinding, intervention description, treatment context, dose, and duration of CTR), main findings, and the risk of bias and quality assessment ratings.

Risk of Bias and Quality Assessment

Each study was appraised by one reviewer for risk of bias using the Cochrane Risk of Bias Tool for Randomized Controlled Trials (Higgins & Green, 2011). This tool consists of seven categories of potential bias, and each category was rated low, high, or unclear risk of bias (Table 1). Study quality was appraised using the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment of Controlled Intervention Studies tool (NHLBI, n.d.). This tool includes 14 criteria that may affect study quality. Overall quality for each study was rated as good, fair, or poor based on the criteria and guidelines in the NHLBI tool (Table 1).

Results

Study Selection

The initial database search returned 343 reports from Ovid Medline, 372 reports from PsychINFO, and 371 reports from Embase for a total of 1,086 reports. After removing duplicates, 409 studies were identified. Initial abstract review excluded 379 studies for failing to meet inclusion and exclusion criteria. Of the remaining 30 studies, five were excluded in full text review for not having an RCT design, three for including a non-psychotic diagnostic group in the sample, six for being follow up data from a primary report, four for lack of relevant outcomes reported, one for being a conference abstract, and one for not including a CTR intervention. Ten studies met the inclusion criteria for this review (Figure 1).

Risk of Bias and Quality Assessment

Table 1 details the risk of bias and quality assessment results. Areas of high or unclear risk of bias included blinding of outcome assessors (Eack et al., 2009; Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017) and incomplete outcome reporting (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017). Four studies received a poor quality rating (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017), four received a fair quality rating (Drake et al., 2014; Eack et al., 2009; Fisher et al., 2015; Puig et al., 2014), and two received a good quality rating (Østergaard Christensen et al., 2014; Wykes et al., 2007). Poor quality was largely due to a combination of insufficient or unclear blinding of outcome assessors (Eack et al., 2009; Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017), high or unreported overall attrition (Fernandez-Gonzalo et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017), and failing to include a power calculation or use intent to treat analysis (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004; Ventura et al., 2017).

Study Characteristics

Sample.—Sample characteristics are summarized in Table 2. Studies were conducted in the United States ($n = 3$), the United Kingdom ($n = 2$), Spain ($n = 2$), Denmark ($n = 1$), Canada ($n = 1$), and Norway ($n = 1$). Sample sizes ranged from 26 (Ueland & Rund, 2004) to 117 participants (Østergaard Christensen et al., 2014). The mean age ranged from 15 (Ueland & Rund, 2004) to 30 years (Fernandez-Gonzalo et al., 2015). All studies had more male than

female participants. Three studies reported race data, with one including 50% non-White participants (Ventura et al., 2017) and two including a majority of White participants (Drake et al., 2014; Eack et al., 2009). Participants had mild psychosis symptoms in all studies except one, where symptoms were moderate to marked (Ueland & Rund, 2004).

Treatment Context.

Five studies occurred within an FEP specialty service (Drake et al., 2014; Fisher et al., 2015; Mendella et al., 2015; Østergaard Christensen et al., 2014; Ventura et al., 2017), and two additional studies described services similar to an FEP specialty services and are considered “FEP-like” (Eack et al., 2009; Puig et al., 2014). One study occurred in an inpatient setting (Ueland & Rund, 2004) and two were unspecified (Fernandez-Gonzalo et al., 2015; Wykes et al., 2007; Table 2).

Intervention.

Intervention characteristics are detailed in Table 2, and a detailed description of each intervention is provided in Table 3.

Theoretical basis.

CTR interventions fall into two primary theoretical categories: “top-down” or broad neuropsychological rehabilitation approaches and “bottom-up” or targeted cognitive training approaches (Fisher, Herman, Stephens, & Vinogradov, 2016; Nuechterlein et al., 2014). The broad CTR approaches draw from fields of neuropsychology and educational psychology and focus on the higher order cognitive processes of memory, reasoning, executive functioning, and social cognition (Nuechterlein et al., 2014; Wykes & Reeder, 2005). The targeted cognitive training approach is rooted in neuroplasticity and cognitive neuroscience research and focuses on perceptual information and sensory processing. Training typically focuses on improving accuracy and efficiency of auditory and visual information processing, and then builds on the perceptual domain with more complex cognitive tasks in that domain (Nuechterlein et al., 2014; Vinogradov, Fisher, & De Villers-Sidani, 2012).

Six of the 10 studies used broad interventions (Drake et al., 2014; Eack et al., 2009; Fernandez-Gonzalo et al., 2015; Østergaard Christensen et al., 2014; Puig et al., 2014; Wykes et al., 2007), and two broad interventions also incorporated social cognition training (Eack et al., 2009; Fernandez-Gonzalo et al., 2015); however, the specific cognitive domains trained varied between studies (Table 3). One study used a purely targeted training approach of auditory information processing and verbal working memory (Fisher et al., 2015). Two used a hybrid intervention that combined targeted and broad components, with one focusing on visual information processing for the targeted training (Ventura et al., 2017) and one using a cognitive differentiation module to “improve basic cognitive skills” prior to advancing to complex tasks of memory and social perception (Ueland & Rund, 2004). One study used a compensatory training-only approach (Mendella et al., 2015), in which strategies to work around cognitive deficits were used, as opposed to training these domains directly.

Dosing and delivery.

There was a high degree of heterogeneity in intervention dosing and duration. Dosing ranged from 24 hours (Mendella et al., 2015) to 127.5 hours (Eack et al., 2009) and from a duration of 8 weeks (Fisher et al., 2015) to 2 years (Eack et al., 2009). Most studies ($n = 7/10$) dosed the intervention between 30 and 40 hours, however, one study had 24 hours (Mendella et al., 2015) and two studies had over 100 hours of CTR (Eack et al., 2009; Ventura et al., 2017). Training typically occurred for 1 hour per session. Frequency of CTR varied from one (Mendella et al., 2015) to five times per week (Fisher et al., 2015).

Five interventions were delivered by a therapist on a one-to-one basis (Drake et al., 2014; Østergaard Christensen et al., 2014; Puig et al., 2014; Ueland & Rund, 2004; Wykes et al., 2007), one was delivered in a therapist led group (Mendella et al., 2015), one was self-delivered by participants at home without therapist involvement (Fisher et al., 2015), one was delivered in small groups with each participant training individually and a therapist present (Fernandez-Gonzalo et al., 2015), and two used a combination of small groups with a therapist and larger therapist-lead groups (Eack et al., 2009; Ventura et al., 2017).

Adherence.

Three studies reported adherence data. There was a completion of 32.9 ($SD = 10.5$) hours of 40 hours in Fisher et al. (2015), 28.7 hours ($SD = 11.2$) of 32 hours in Østergaard Christensen et al. (2014), and 30.7 ($SD = 8.8$) of 32 to 40 hours in Fernandez-Gonzalo et al. (2015).

Effects of CTR on Cognitive and Functional Outcomes

Cognition.—All studies except Ventura et al. (2017) reported on cognitive outcomes. A wide range of cognitive improvements were found across the studies, with eight of nine studies finding improved cognition in at least one domain. Ueland and Rund (2004) found no effect on any cognitive outcomes and was the only study to occur in an inpatient setting, had the smallest sample size, and was rated low quality. Global cognition, verbal learning and memory, and executive functioning were most commonly improved.

Global cognition.—Seven studies reported on global cognition, with four studies finding an effect in the moderate (Eack et al., 2009; Fisher et al., 2015) to large (Mendella et al., 2015; Puig et al., 2014) range and three failing to find an effect (Drake et al., 2014; Østergaard Christensen et al., 2014; Ueland & Rund, 2004). Each study finding an effect was from a different theoretical base, with a dosing range from 24 to 127.5 hours. One study finding a large effect received a poor quality rating (Mendella et al., 2015). All of the interventions finding no effect on global cognition were broad interventions and each had a different quality rating.

Verbal learning and memory.—Seven studies reported on verbal learning and memory, with four finding a significant effect (Eack et al., 2009; Fisher et al., 2015; Østergaard Christensen et al., 2014; Puig et al., 2014) and three finding no effect (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004). There was a wide range of theoretical base and dosing represented in both the group of studies that found an effect and

the group that did not. All studies failing to find an effect were rated poor quality and two had the smallest sample sizes of all studies (Mendella et al., 2015; Ueland & Rund, 2004).

Executive functioning.—Nine studies reported on executive functioning, with five finding a significant effect (Drake et al., 2014; Eack et al., 2009; Fisher et al., 2015; Puig et al., 2014; Wykes et al., 2007) and four finding no effect (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Østergaard Christensen et al., 2014; Ueland & Rund, 2004). Studies finding an effect had a dose of at least 40 hours, while those failing to find an effect tended to have a dose of 32 hours or less of CTR. Theoretical basis and delivery were varied in both the group of studies that found an effect and the group that did not. Most studies failing to find an effect were poor quality (Fernandez-Gonzalo et al., 2015; Mendella et al., 2015; Ueland & Rund, 2004), whereas no studies finding an effect were poor quality.

Social cognition.—Three studies targeted social cognition with two showing large effects in varied social cognitive domains (Eack et al., 2009; Fernandez-Gonzalo et al., 2015) and one showing no effect (Ueland & Rund, 2004).

Durability of cognitive effects.—Four studies included a follow up assessment ranging from 3 to 12 months post-treatment. Cognitive effects were durable in three studies in at least one domain (Østergaard Christensen et al., 2014; Puig et al., 2014; Wykes et al., 2007). The study failing to show durability had a very high rate of attrition at follow-up (Drake et al., 2014). All studies assessing durability used a broad CTR, delivered one-to-one, and a dose of between 32 and 40 hours.

Social Functioning.—All studies assessed a range of functional outcomes, and the majority failed to find differences between CTR and control groups (Drake et al., 2014; Fernandez-Gonzalo et al., 2015; Fisher et al., 2015; Mendella et al., 2015; Østergaard Christensen et al., 2014; Ueland & Rund, 2004; Wykes et al., 2007). Three studies found an effect on functioning, including engaging in social relationships and work attainment (Eack et al., 2009), participation in meaningful activities and platonic and romantic relationships (Ventura et al., 2017), and overall functioning from communication to daily living skills (Puig et al., 2014). All studies finding functional improvement included some degree of broad CTR, occurred in an FEP or FEP-like treatment context, and incorporated one-to-one coaching as part of the delivery method. Two also incorporated group delivery and had the largest doses of training (Eack et al., 2009; Ventura et al., 2017). One included a bridging group to practice applying cognitive skills to real-world situations (Ventura et al., 2017). Functional improvements were observed more often in studies lacking blinded outcome assessors (Eack et al., 2009; Ventura et al., 2017). One additional study failed to find group effects in functional outcomes; however, it was found that improved cognition in any domain was associated with improved social behavior (Wykes et al., 2007). Four studies included a follow-up assessment of functioning (Drake et al., 2014; Østergaard Christensen et al., 2014; Puig et al., 2014; Wykes et al., 2007), and none found an effect on functioning at this time point.

Discussion

The findings from this review indicate that CTR interventions incorporating a broad theoretical approach are most commonly studied in the FEP population, and due to a limited number of studies from a targeted theoretical approach, the relative efficacy of each approach cannot be determined. The majority of studies dosed CTR between 32 and 40 hours, which appears to be sufficient to induce cognitive improvements. Overall, findings support CTR's efficacy for improving cognition in individuals with FEP in a manner that may persist after intervention completion, with common improvements in global cognition, verbal learning and memory, executive functioning, and social cognition. However, the evidence for an effect on social functioning is mixed. These results must be considered in the context of the overall fair quality of included studies, with several risks of bias due to insufficient blinding of participants and outcome assessors, high rates of attrition, lack of adherence reporting, and insufficient use of power and intent to treat analysis. In addition, interpretations of the results are limited by the high degree of heterogeneity in CTR intervention components, dosing and delivery, and by the variety of instruments used for cognitive and functional assessment, which presented barriers to comparing results across studies.

The results from this review highlight the tremendous variability in CTR theoretical approaches and intervention components used in FEP. Across just 10 studies, four different theoretical approaches were identified, and further variability exists within each approach related to the specific cognitive domains trained. The two dominant theoretical paradigms, broad versus targeted CTR, each have particular strengths, which may be expected to lead to different patterns of results. For example, broad CTR approaches are based upon evidence that it is possible to improve higher order cognition by explicitly training these domains (Nuechterlein et al., 2014; Wykes & Reeder, 2005). These programs typically strive for transfer of cognitive skills to tasks important for everyday living, and many teach strategies to more efficiently learn cognitive skills (Nuechterlein et al., 2014). However, broad CTR lacks a focus on improving perceptual and sensory information processing, which is known to be impaired in psychotic disorders in a manner that affects effective higher order cognitive processing (Javitt, 2009; Silverstein & Keane, 2011; Vinogradov et al., 2012). In contrast, the targeted cognitive training approach emphasizes that successful CTR must start by improving the efficiency and accuracy of information processing at the sensory and perceptual phase of the information processing pathway before building to more complex cognitive tasks (Nahum, Lee, & Merzenich, 2013; Vinogradov et al., 2012). This approach recognizes that psychotic disorders are characterized by impairments in neural systems distributed throughout the brain, versus discrete impairments in neurocognitive domains, and that these distributed systems must interact together to process sensory information (Vinogradov et al., 2012). Targeted approaches emphasize massed practice in one cognitive domain to promote neuroplasticity and are designed to leverage implicit learning mechanisms by gradually adapting in difficulty level (Fisher et al., 2016). Due to the variability in intervention design and treatment targets arising from the theoretical basis, it is difficult to combine results of the varied CTR interventions for meta-analytic study. There is a need for a greater volume of research on each approach so that comparative effectiveness

analyses can be completed. Until then, it is difficult to compare the efficacy of CTR interventions in FEP given the heterogeneity of interventions from and within different theoretical approaches.

While there was a high degree of heterogeneity in cognitive domains improved across studies, the results from this review paint an overall optimistic picture of the ability to improve cognitive impairments in FEP with CTR regardless of theoretical basis. Common cognitive improvements were observed in global cognition, verbal learning and memory, and executive functioning. Improvements in verbal learning and memory may be especially promising, as this has been found to be the most impaired cognitive domain in FEP (Aas et al., 2014; Mesholam-Gately et al., 2009). Given the broad range of cognitive improvements, it is difficult to determine whether patient characteristics or the theoretical basis, dosing or delivery of the intervention affected cognitive results. Our findings suggest that 32 to 40 hours of training are sufficient to induce at least moderate cognitive changes, regardless of how the doses were distributed (i.e., 2 vs. 5 months). It may be that the effective dose is domain-specific, as improvements in executive functioning were more common with doses of at least 40 hours versus 32 hours or less. However, in the absence of adherence data the exact training threshold needed to produce cognitive gains is unknown.

The only study to find no cognitive effect was conducted in an inpatient setting with participants who had elevated psychotic symptoms (Ueland & Rund, 2004), suggesting that the optimal window for CTR may require psychosis symptoms to be well controlled. However, the null results may also be attributed to the small sample size. Indeed, several studies in this review may have been underpowered to detect differences between groups (Lewandowski, 2016). Alternatively, the null results of this study could be related to the adolescent age-group of participants, which represented the youngest mean age of all studies. It has been shown that earlier onset of psychosis in the adolescent years is associated with more severe symptoms and worse treatment outcomes, which may have reduced the responsiveness to CTR interventions (Vyas, Kumra, & Puri, 2010). However, adolescence may also be a time of heightened neuroplasticity, allowing for greater gains from CTR interventions (Fuhrmann, Knoll, & Blakemore, 2015; Vyas et al., 2010). Another study also included an adolescent sample (Puig et al., 2014) and this study found improvements in cognition and functioning, suggesting that CTR can be effective for adolescents as well as young adults with FEP. This is consistent with a null finding of a moderating effect of age on CTR outcomes in FEP found in a recent meta-analysis (Revell et al., 2015). As only three studies reported race demographics of their participants (Drake et al., 2014; Eack et al., 2009; Ventura et al., 2017), with only one including a racially diverse sample (Ventura et al., 2017), the generalization of outcomes to diverse populations representative of those affected by FEP is limited.

The case for CTR to improve the social functioning of individuals in the FEP period is developing but is less robust. The lack of far transfer effects from cognitive gains to improved everyday functioning is likely attributable to several factors, including an incomplete understanding of the cognitive, behavioral and neural targets of social functioning, potentially insufficient dosing, lack of concurrent psychiatric rehabilitation interventions, limitations of assessing only group effects, lack of post-trial follow-up

periods, and inconsistent operationalization of social functioning. As all studies finding functional improvement used some degree of broad CTR, it may be that training of higher order cognitive processes, such as reasoning and executive functions, is needed in order to transfer cognitive skills to improved daily functioning (Wykes & Reeder, 2005). However, the necessary cognitive domains that must improve to drive improved functioning cannot be determined from this review due to the varied cognitive improvements across studies.

Previous research has indicated that changes in verbal learning, executive functioning, and social cognition may contribute most to improved functioning after CTR in FEP, suggesting that targeting these domains holds the greatest promise for restoring functioning (Eack, Pogue-Geile, Greenwald, Hogarty, & Keshavan, 2011). Social cognition may be a critical treatment target as it is more strongly linked to social functioning than neurocognition (Fett et al., 2011). In addition, impairments in social cognition may be linked to poor motivation, which has additional impact on functioning (Gard, Fisher, Garrett, Genevsky, & Vinogradov, 2009; Najas-Garcia et al., 2018). Early evidence suggests that social cognition training may lead to improved reward processing related to motivation in schizophrenia (Fisher et al., 2017). Thus, CTR interventions that combine neurocognitive and social cognitive training may be capable of improving functioning through three pathways—neurocognition, social cognition, and motivation—which all have unique contributions to functional outcome (Fisher et al., 2017; Najas-Garcia et al., 2018); however, more research is needed to test this hypothesis.

The effects of combined interventions on social functioning should also be explored. For example, meta-cognition, or the ability to form an integrated and complex understanding of the self and others, has been associated with social functioning and insight in psychotic disorders (Lysaker et al., 2019). No studies in this review incorporated metacognitive approaches, and addressing metacognition may lead to improved insight into cognitive impairments and treatment needs, thus promoting engagement in CTR interventions (Vohs et al., 2018). Finally, little is known about the neural mechanisms supporting social functioning in FEP. A recent meta-analysis points to a link between whole brain volume and structural and functional integrity of fronto-limbic brain areas and functional outcome in schizophrenia (Wojtalik, Smith, Keshavan, & Eack, 2018). However, little is known about such relationships in FEP, and importantly, no studies in FEP have investigated whether these areas are malleable in response to CTR in a manner that is associated with improvements in social functioning.

Two studies finding functional improvement were unique in their intensive dosing and long treatment periods (Eack et al., 2009; Ventura et al., 2017). These studies also included a high degree of social contact with peers and therapists, and one included a bridging group to apply cognitive skills to real-world situations (Ventura et al., 2017). Thus, it is difficult to ascertain whether the high dose of CTR or the nonspecific effects of these intervention components contributes most to functional improvement (Fisher et al., 2016). A recent secondary analysis found that among the “active ingredients” of a CTR intervention, only therapeutic alliance was associated with improvements in social functioning (Cella & Wykes, 2019). Thus, it is possible that the intensive nature of Eack et al (2009) and Ventura et al. (2017) facilitated a stronger therapeutic alliance, which translated to improved

functioning. The Cella and Wykes (2019) findings may have important implications for the design of CTR interventions if the ultimate goal is to improve individuals' everyday functioning; however, resource- and time-intensive interventions may come at the expense of limited scalability and practicality in real world settings.

The treatment context in which functional gains occur following CTR has clinical relevance, as FEP specialty services share a goal of functional recovery. The lack of cognitive interventions included in such services has been suggested as a contributor to suboptimal results (Breitborde, Moe, Ered, Ellman, & Bell, 2017). This review found mixed evidence that addition of CTR to early intervention services improves functional outcomes, warranting further research. Research in chronic schizophrenia has found that functional gains are largest when CTR is provided in the context of psychiatric rehabilitation programs, such as those explicitly targeting vocational rehabilitation (Wykes et al., 2011). No studies in this review provided such services.

Finally, lack of consensus for best practices in measurement of social functioning in FEP complicates evaluation of far transfer effects from cognitive gains to improved functioning. Due to the complex nature of social functioning, such improvements likely should not be expected immediately after CTR (Fisher et al., 2016). The optimal length of follow-up needed to accurately assess gains in functioning is not known; however, the low number of studies including a follow-up assessment may have contributed to negative results. Due to the heterogeneity of cognitive impairments in FEP, assessing individual differences, that is, whether improvements in cognition are associated with improvements in social functioning—as opposed to only group differences in social functioning—may also be needed to assess the effects of CTR on functional outcomes.

Strengths and Limitations

This is the first known review of CTR in FEP to incorporate a descriptive analysis of the theoretical basis, intervention components, and treatment context of included studies and to select a homogeneous FEP sample. This review is limited by searching only major databases and performing the quality assessment with only one reviewer. Limiting the search to major databases may prevent inclusion of negative studies published in the grey literature, resulting in biased conclusions. The lack of two reviewers for the quality and risk of bias assessments may result in a biased assessment of study quality, and thus these results should be interpreted with caution. The authors minimized this bias by utilizing well-validated quality and risk of bias assessment tools.

Conclusion

A broad range of CTR interventions are promising for improving cognitive impairment in FEP, but their effects on social functioning are mixed. Broad and targeted CTR likely affect cognition and social functioning via different pathways. The wide heterogeneity of CTR intervention components, coupled with limitations of overall study quality, presents barriers to identifying which particular CTR protocols may be most useful in clinical practice. However, when considered together with meta-analyses demonstrating efficacy of CTR for a range of cognitive outcomes in both FEP and chronic schizophrenia (Revell et al., 2015;

Wykes et al., 2011), results from this review suggest that CTR, regardless of theoretical background, may be beneficial for improving cognition in FEP. Future studies must continue to identify the necessary treatment targets, intervention components, and doses needed to drive robust and durable improvements in cognition and functioning. Together, these research initiatives hold promise for filling a critical treatment gap in early psychosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

PRISMA flowchart.

Note. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT = randomized controlled trial. From Moher, Liberati, Tetzlaff, and Altman (2009).

Table 1.

Risk of Bias and Quality Assessment.

Tool	Drake	Eack	Fernandez-Gonzalo	Fisher	Mendella	Østergaard Christensen	Puig	Ueland	Ventura	Wykes
Cochrane Risk Of Bias rating										
Random sequence generation	+	+	+	?	+	+	+	+	?	+
Allocation concealment	+	+	+	?	+	+	+	?	?	+
Blinding of participants and personnel	-	-	-	+	-	-	-	-	-	-
Blinding of outcome assessors	+	-	-	+	-	+	+	?	?	+
Incomplete outcome data	+	+	-	+	-	+	+	-	-	+
Selective reporting	+	+	+	+	+	+	+	+	+	+
Other bias	+	+	+	+	+	+	+	+	+	+
National Heart, Lung, and Blood Institute Quality Assessment										
RCT design	+	+	+	+	+	+	+	+	+	+
Randomization method	+	+	+	?	+	+	+	+	?	+
Allocation concealment	+	+	+	?	+	+	+	?	?	+
Blinding of participants and personnel	-	-	-	+	-	-	-	-	-	-
Blinding of outcome assessors	+	-	-	+	-	+	+	?	?	+
Baseline characteristics	+	+	+	+	+	+	+	?	+	+
Overall attrition	-	+	-	-	+	+	-	?	?	+
Differential attrition	-	+	+	+	+	+	+	?	?	+
Adherence	?	?	+	+	?	+	?	?	?	?
Background treatments	+	+	+	+	+	+	+	+	+	+
Validity of outcome assessment	+	+	+	+	+	+	+	+	+	+
Sample size calculation included	+	-	-	-	-	+	-	-	-	+
Prespecified outcomes and analysis	+	+	+	+	+	+	+	+	+	+
Intent to treat analysis	+	+	-	+	-	+	+	-	-	+
Overall Quality	Fair	Fair	Poor	Fair	Poor	Good	Fair	Poor	Poor	Good

Note. (+) = criteria met/low risk of bias; (-) = criteria not met/high risk of bias; (?) = unclear if criteria met/unclear risk of bias.

Table 2.

Study Sample, Intervention Characteristics, and Outcomes.

Study	Sample (T, C)	Treatment context	Control (total h)	Delivery, dosing (total h) and adherence+	Theory	Attrition ± %, T, C	Cognitive and functional outcomes (T > C)
Drake et al. (2014)	Size: 61 (31, 30) mean age: (24.7, 23.4); % male (68, 53); race (%): 79 White, 5 African/African Caribbean, 13 South Asian, 3 East Asian; country: United Kingdom	FEP specialty program	Social contact group (40)	One-to-one, 1 h, 3–5× per week for 12 weeks (40)	Broad	48, 26	Cognition: Completion of more WCST categories ($p = .012$, effect size NR); 42-week FU: none; function: posttraining and FU: none on Social and Occupational Functioning Assessment Scale
Eack et al. (2009)	Size: 58 (31, 27); mean age: 25.92; % male: 69; race (%): 69 White, 19 African American, 10 Asian, 2 others; country: United States	FEP-like: individual supportive therapy, psychoeducation, relapse prevention and stress/emotion management	Enriched supportive therapy (NR)	60 h of neurocognitive training with one therapist per two participants + 45, 1.5 h social cognitive training groups, over 24 months; training frequency NR (127.5)	Broad	18, 19	Cognition: neurocognition composite ($d = 0.46$, $p = .023$), social cognition ($d = 1.55$, $p < .001$); function: social adjustment ($d = 1.53$, $p < .001$) including social and global functioning
Fernandez-Gonzalo et al. (2015)	Size: 53 (28, 25); mean age: (30.9, 30.2); % male (60.7, 68); race (%): NR; country: Spain	NR	Computer games and training (32–40)	Trained on individual computers in groups up to 6 with 1 therapist, 1 h, 2× per week for 4–5 months (32–40); adherence: mean 30.7 h ($SD = 8.8$)	Broad	11, 24	Cognition: visual attention ($\eta^2 = 0.18$, $p = .006$), visuospatial working memory ($\eta^2 = 0.1$, $p = .049$), immediate logical memory ($\eta^2 = 0.114$, $p = .03$), delayed logical memory ($\eta^2 = 0.17$, $p = .009$), emotion processing ($\eta^2 = 0.167$, $p = 0.09$); function: none on Social Functioning Scale or Quality of Life Inventory
Fisher et al. (2015)	Size: 86 (43, 43); mean age: (21.7, 20.7); % male (72, 77); race (%): NR; country: United States	FEP specialty program	Computer games (40)	Self-administered, 1 h, 5× per week × 8 weeks (40); adherence: Mean 32.9 h ($SD = 10.45$)	Targeted	32, 26	Cognition: Global cognition ($d = 0.73$, $p < .01$), verbal memory ($d = 0.69$, $p < .01$), problem solving ($d = 0.46$, $p = .03$); function: none on Strauss Carpenter Quality of Life scale or Global Functioning Role and Social scales
Mendella et al. (2015)	Size: 27 (16, 11); mean age: (25, 24.8); % male (68.8, 81.8); race (%): NR; country: Canada	FEP specialty program	TAU	Therapist-led group, 2 h, 1× per week × 12 weeks (24)	Compensatory	13 (total)	Cognition: Global cognition ($\eta^2 = 0.35$; $p = .002$), visual attention ($\eta^2 = 0.178$, $p = .032$), social cognition (MSCEIT; $\eta^2 = 0.17$, $p = .041$); function: none on UPSA
Østergaard Christensen et al. (2014)	Size: 117 (T: 60, C: 57); mean age: (25, 24.9); % male: (68, 53); race: NR; country: Denmark	FEP specialty program including social skills training	TAU	One-to-one, 1 h, 2× per week for 16 weeks (32); adherence: mean 28.7 h ($SD = 11.2$)	Broad	15, 17.5	Cognition: posttraining: verbal memory ($d = 0.46$), 1-year FU: Working memory ($d = 0.56$), verbal memory ($d = 0.58$). All $p < .05$; function: posttraining and FU: None on UPSA
Puig et al. (2014)	Size: 50 (25, 25); mean age: (16.7, 16.8); % male (52, 52); race (%): NR; country: Spain	FEP-like: psychoeducation, case management	TAU	One-to-one, 1 h, 2× per week × 20 weeks (40)	Broad	40, 44	Cognition: posttraining: verbal memory ($\eta^2 = 0.17$, $p = .003$), working memory ($\eta^2 = 0.08$, $p = .04$), executive functions ($\eta^2 = 0.11$, $p = .019$), 3-month FU: gains maintained (effect sizes NR); function: posttraining: Life Skills Profile ($\eta^2 = 0.09$,

Study	Sample (T, C)	Treatment context	Control (total h)	Delivery, dosing (total h) and adherence+	Theory	Attrition ‡ %, T, C	Cognitive and functional outcomes (T > C)
Ueland and Rund (2004)	Size: 26 (14, 12); mean age: (15.2, 15.5); % male (57, 50); race (%): NR; country: Norway	Inpatient	TAU	One-to-one, frequency NR (30)	Targeted + Broad	0, 12	$p = .04$ and VABS ($\eta^2 = 0.13$, $p = .03$), FU: None
Ventura et al. (2017)	Size: 80 (39, 41); Mean Age: (21.5, 21.5); % male (74, 83); race (%): 50 White, 29 African American, 11 Asian, 9 Native American, 1 Pacific Islander; country: United States	FEP specialty program + individual case management focused on work/school recovery	Health Behaviors Group (108)	Trained on individual computers in groups with 1 therapist: 1 h, 2× per week × 6 months, then 1 h, 1× per week × 3 months, then 1 h every other week × 3 months; concurrent bridging group 1 h/week × 9 months, then 1× every other week × 3 months; total duration 12 months (108)	Targeted + Broad	NR	Cognition: Cognitive results NR; function: Social Attainment Survey ($p = .05$, effect size NR)
Wykes et al. (2007)	Size: 40 (21, 19); mean age: (18.8, 17.5); % male (62, 68); race (%): NR; country: United Kingdom	NR	TAU	One-to-one, 1 h, approximately 3× per week × 12 weeks (40)	Broad	19, 21	Cognition: posttraining and 3-month FU: WCST—increase in 1,1 categories ($d = 0.55$, $p = .04$); function: posttraining and FU: none on Quality of Life Scale or Social Behavior Scale

Note. T = cognitive training and remediation group; C = control group; h = hours; + = adherence given if reported; ‡ = attrition from baseline to posttraining; FEP = first episode psychosis; FU = follow-up; NR = not reported; WCST = Wisconsin Card Sorting Test; TAU = treatment as usual; VABS = Vineland Adaptive Behavior Scale; MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test; UPSA = UCSD Performance-Based Skills Assessment. Partial η^2 effect sizes: small > 0.01, medium > 0.06, large > 0.1.

Table 3.

Intervention Description.

Study	Description of cognitive intervention
Drake et al. (2014)	CIRCUITS: Tasks requiring a mixture of cognitive skills, including attention, working memory, registration and recall, and planning are practiced in a computerized environment designed to provide social context. Trainers coached and supported participants 1:1 and could enter into training environment to adjust task difficulty.
Eack et al. (2009)	CET: Computerized cognitive training in domains of attention, memory, and problem solving, completed in pairs with a coach. Group social cognitive training focused on perspective taking, social context appraisal, and emotion management.
Fernandez-Gonzalo et al. (2015)	NPH-MH: Each session included 30 minutes of cognitive exercises followed by 30 minutes of social cognitive exercises. Cognitive exercises included attention, memory and executive functions. Social cognition exercises included emotion processing, theory of mind, and cognitive bias. Training was individualized based on baseline and previous-session performance and difficulty level was adaptive.
Fisher et al. (2015)	Posit Science Auditory Training: This included computerized exercises that seek to improve the speed and accuracy of auditory information processing, while also targeting verbal working memory. Difficulty level was adaptive. Training is self-administered without therapist support; however, participants were contacted once or twice per week by telephone to discuss progress and set training goals if needed.
Mendella et al. (2015)	Compensatory Cognitive Training: Two hours of group-based intervention teaching compensatory strategies for prospective memory, attention and vigilance, learning and memory, and executive functions were conducted. Strategies were incorporated into game-like scenarios. Goal setting was used to enhance motivation, and homework provides practice with strategies in the real world.
Østergaard Christensen et al. (2014)	NEUROCOM: Computerized training was delivered in four modules. Modules 1 to 3 focused on domains of attention, executive functions, and learning/memory. The fourth module was individualized. Training included attention, planning, strategy learning and problem solving, working memory, verbal and visual recall, and recognition memory. Approximately half of training was drill and practice and half strategy learning and compensatory. Difficulty level was adaptive. Bridge sessions focused on work, social, and cognitive competencies.
Puig et al. (2014)	CRT: 1:1 training was conducted with a focus on improving flexibility in thinking and information set-maintenance, executive functions for memory and planning, set/schema manipulation and formation, and strategy learning. Difficulty level was adaptive.
Ueland and Rund (2004)	1:1 training included four modules: cognitive differentiation, attention, memory, and social perception. Cognitive differentiation targeted basic cognitive skills as a base for enhancing social interaction and problem-solving skills.
Ventura et al. (2017)	Computerized cognitive training first focused on basic cognition in the visual domain and built to more complex tasks and virtual scenarios. Difficulty level was adaptive. Participants trained on individual computers in groups in a computer lab with a cognitive coach. Bridging groups were used for goal setting and applying cognitive skills to daily life and occurred weekly to biweekly. Strategy learning was included.
Wykes et al. (2007)	CRT was used as described above in Puig et al.

Note. CIRCUITS = Computerized Interactive Remediation of Cognition–Interactive Training for Schizophrenia; 1:1 = one-to-one training; CET = cognitive enhancement therapy; NPH-MH = neuro personal trainer–mental health; CRT = cognitive remediation therapy.