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Treatment of social cognition in schizophrenia: Current status and future directions

William P. Horan *, Michael F. Green

VA Greater Los Angeles Healthcare System, United States
University of California, Los Angeles, United States

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ABSTRACT

Efforts to develop psychosocial interventions that specifically target social cognition in schizophrenia spectrum disorders began nearly two decades ago. The field has matured considerably since then and has engendered a great deal of optimism about this treatment approach. Indeed, the efficacy of social cognitive interventions, especially those that address multiple domains of social cognition, has received substantial support. This article critically evaluates the current evidence for social cognitive interventions, identifies limitations and open questions, and suggests priorities and directions for further research. Limitations of available studies include a frequent lack of methodological rigor, suboptimal selection of endpoints, and sparse evidence for generalization to functional improvements. We highlight several emerging psychosocial and non-psychosocial approaches that may enhance the efficacy of social cognitive interventions and promote generalization to improvements in real world functioning. We conclude that cautious optimism is warranted as the field moves forward into the next wave of social cognitive treatment studies.

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1. Introduction

Research on social cognition in schizophrenia spectrum disorders has expanded dramatically over the past two decades. A large accumulation of evidence indicates that people with schizophrenia show substantial impairments across social cognitive measures of emotion processing (particularly facial affect perception), social cue perception, attributional style, and mentalizing (aka "Theory of Mind") (Savla et al., 2013) throughout the course of illness. Social neuroscience studies of schizophrenia demonstrate functional and structural disturbances in brain areas associated with specific social cognitive domains (Green et al., 2015). Furthermore, these impairments are consistently associated with poor community functioning. In fact, in relation to non-social neurocognitive impairments, social cognitive impairments show even stronger relations to community functioning, account for incremental variance in functioning, and appear to be more proximal (i.e., act as a mediator) to functioning (Fett et al., 2011; Schmidt et al., 2011). The impressive body of evidence documenting substantial, wide-ranging, and functionally important impairments in social cognition has led to a great deal of enthusiasm about social cognition as a target for treatments to enhance the debilitating impairments in community functioning associated with schizophrenia.

Currently available antipsychotic medications do not lead to clinically significant improvements in social cognition in schizophrenia (Kucharska-Pietura and Mortimer, 2013; Penn et al., 2009). In contrast, a variety of psychosocial interventions approaches have been shown to improve several aspects of social cognition (Fiszdon and Reddy, 2012; Horan et al., 2008). About 20 years ago, pioneers such as G.E. Hogarty, H.D. Brenner, and V. Roder began incorporating social cognitive training exercises in "broad-based", multi-component treatment packages (e.g., Cognitive Enhancement Therapy [CET] (Hogarty et al., 2004), Integrated Psychological Therapy (Roder et al., 2006)). Although these early studies showed treatment benefits, it was not possible to determine any gains specifically from the social cognitive training exercises since they embedded among other treatment components that targeted neurocognition and social competence. This situation led to a number of small-scale "targeted" or proof-of-concept interventions that focused on only a single social cognitive domain, primarily facial affect perception, without other treatment components. These studies demonstrated that performance on social cognitive tasks was remediable through focused training interventions and they paved the way for a new generation of "comprehensive" intervention studies that more intensively targeted impairments in multiple social cognitive domains in the absence of other psychosocial interventions (e.g., cognitive remediation or social skills training).

In this article, we take a critical look at the current social cognitive interventions for schizophrenia spectrum disorders. We focus on "comprehensive" treatments since the field has clearly moved in the

* Corresponding author at: VA Greater Los Angeles Healthcare System, MIRECC 210A, Bldg. 210, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
E-mail address: horan@ucla.edu (W.P. Horan).

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direction of targeting multiple, rather than a single, social cognitive domains and, given the wide range of social cognitive impairments seen in people with psychosis, focusing on multiple domains would be expected to have a more robust impact on functioning. We begin with an overview of the generally encouraging results of comprehensive social cognitive intervention trials. We then consider this literature with a more critical eye and highlight key limitations of the existing database. We conclude by identifying open questions and describing promising new approaches to enhance efficacy and effectiveness in this rich area of treatment development.

2. Efficacy of social cognitive interventions: reasons for optimism

It is clear that a range of intervention approaches can improve at least one of the four main domains of social cognitive impairment in schizophrenia. Following an earlier meta-analysis of 19 broad-based, targeted, and comprehensive intervention studies (Kurtz and Richardson, 2012), Kurtz et al. (2016) recently conducted an effect size analysis that included 16 studies (313 participants) that specifically evaluated comprehensive treatment approaches. Fourteen of the studies were conducted with outpatients and two with inpatients. Over half of the studies used versions of the Social Cognition and Interaction Training ($n = 6$) or Social Cognitive Skills Training ($n = 3$) programs, which are both manualized, group-based interventions that target three or four of the main social cognitive domains, respectively, in either 20 or 24 sessions. The remaining seven studies targeted two social cognitive domains (in various combinations) using group-based treatments ranging from 12 to 52 sessions.

The most commonly assessed social cognitive domains in this review were facial affect identification (assessed in 12/16) and mentalizing (in 13/16). The weighted effect sizes were large ($d = 0.84$) for affect identification and medium-to-large ($d = 0.70$) for mentalizing. Fewer studies included measures of social perception (4/16) and attributional bias (7/16). Effect sizes were large ($d = 1.29$) for social perception and small-to-medium across three indexes of attributional bias ($d = 0.30$–0.52). It is worth noting that several of these studies included assessments of social cognitive domains that were not directly targeted in their social cognitive interventions. On secondary symptom outcome measures, there was a non-significant effect for positive symptoms ($d = 0.27$ in 7/16 studies), a marginally significant, small effect for negative symptoms ($d = 0.32$ in 10/16 studies), and a significant, small-to-medium effect for general symptoms ($d = 0.40$ in 4/16 studies).

In addition to these generally optimistic effect sizes, the evidence overwhelmingly indicates that social cognitive interventions are well tolerated, with high levels of subjective satisfaction and generally low levels of attrition across studies. In addition, there is preliminary evidence for the portability of social cognitive interventions outside of the academic settings in which they were developed. Both SCIT and SCST have been translated into foreign languages and successfully implemented in markedly different cultures, including China, Egypt, Israel, and Turkey (Gohar et al., 2013; Hasson-Ohayon et al., 2014; Tas et al., 2012b; Wang et al., 2013). Along these lines, SCIT has been implemented in a community mental health setting (Roberts et al., 2010), providing initial feasibility data for more widespread dissemination.

Another question that has been considered is whether improvements in basic non-social neurocognition are prerequisites for improvements in social cognition. Two studies directly addressed this issue by comparing both social cognitive and neurocognitive outcomes in participants randomized to either social cognitive or cognitive remediation (Horan et al., 2011; Wölwer et al., 2005). Both studies found that social cognitive gains among these who received social cognitive treatment did not depend on neurocognitive changes. Further, those receiving cognitive remediation did not show significant improvements in social cognition. These findings suggest that neurocognitive changes are not necessary "building blocks" for social cognitive improvements, and that improvement in social cognition will not necessarily follow non-social cognitive improvements. Similarly, Kurtz et al. reported that improvements in social cognition were not accompanied by improvements in neurocognition in three studies that addressed this issue. In fact, performance on overall neurocognitive measures actually got worse over the course of treatment ($d = -0.31$). Thus, neurocognitive improvements do not appear to be necessary for social cognitive changes.

Aside from improving performance on social cognition tasks, there is also preliminary evidence that social cognitive interventions can impact the neural systems that underlie social cognitive difficulties. Campos et al. (2016) recently reviewed what they referred to as "neuroplastic effects" of social cognitive interventions. They found 11 studies (representing eight distinct data collections) that used a variety of neuroscientific approaches, including structural and functional magnetic resonance imaging (MRI), electroencephalography (EEG), and magnetoecephalography (MEG). Despite relatively small sample sizes and highly diverse approaches to intervention, the majority of the studies reported some neural changes (e.g., reduced grey matter loss, increased regional brain activity, decreases in alpha range EEG activity). Overall, this collection of positive findings bodes well for our ability to map neural changes onto performance-based enhancements that occur with training. However, the sheer number of different brain regions reported to be affected (e.g., left middle frontal gyrus, inferior parietal lobe, superior temporal gyrus, hippocampus, amygdala, etc.) raises basic questions about the consistency and replicability of the findings.

To summarize, there are several reasons to be optimistic about the value of social cognitive interventions. Indeed, the medium to large improvements in several social cognitive domains seen in the Kurtz review are impressive compared with relatively modest effect sizes found for other psychosocial treatments for schizophrenia (e.g., cognitive remediation; (Wykes et al., 2011)). Further, emerging evidence supports the portability and specificity of social cognitive interventions, as well as their potential impact on neural systems involved in social cognition. However, we have areas of concern as described in the next section.

3. Critical evaluation of the literature: reasons for caution

While acknowledging the encouraging initial findings reviewed above, it is informative to look deeper when assessing the current status of this area. Kurtz et al. noted several methodological limitations of the studies that evaluated comprehensive social cognitive treatments, as well as a few limitations of their own approach to conducting the review. We highlight and expand upon these limitations in the next section. We also consider a number of important open questions.

3.1. Methodological limitations

Existing treatment studies have a number of basic methodological limitations that warrant caution when interpreting the findings in this area. A few limitations of the Kurtz et al. review itself are also worth noting. These include the following:

1. The overall number of studies ($n = 16$) was relatively small.
2. Sample sizes were generally small, with 12/16 studies including 24 or fewer participants per group (8/16 included 19 or fewer and the smallest study included 7 per group).
3. 5/16 studies used quasi-experimental designs rather than randomized controlled trial designs.
4. 7/16 studies used treatment as usual as the comparison condition rather than an active control condition.
5. For 9/16 studies, the people conducting the assessments were not blinded to treatment condition.
6. 12/16 studies did not address treatment fidelity.

7. Effect sizes (d) were computed by subtracting the post-treatment control condition from the post-treatment experimental condition, and dividing this difference by the pooled standard deviation across conditions. While this effect size estimate has some strengths (e.g., less potential for inflated within-group effects relative to between group comparisons), it does not take into account any pre-treatment between-group differences. In fact, three of the 11 studies that reported baseline comparisons found statistically significant differences (and others found trends) on social cognition outcome measures between the experimental and control conditions.
8. Regarding the social perception domain, two studies that used the half-Profile of Non-Verbal Sensitivity (PONS), which is typically considered a measure of social perception, were not included in the effect size analysis. Both studies found negligible differences between the experimental and control conditions. Inclusion of these studies would have reduced the effect size for this domain, which was based on only four studies.
9. A remarkably diverse range of social cognition outcome measures was employed in these studies, and many of the measures have poor or unknown psychometric properties and validity in this population.

We believe this last point about instrumentation for clinical trials is particularly important. Results can vary considerably depending on the specific outcome measure employed. For example, the majority of studies that found treatment effects in the domain of mentalizing used relatively simple questionnaire or picture sorting tasks, with largely unknown psychometric properties in schizophrenia. However, the three studies that used The Awareness of Social Inference Test (TASIT), a more challenging and ecologically valid measure that shows relatively good psychometrics, failed to find treatment effects (also see (Fiszdon et al., 2016) for a recent study showing treatment effects on a questionnaire but not on the TASIT). Similarly, for the domain of social perception, the four studies reporting treatment effects used either unpublished tasks or variants of a picture-sorting task designed to assess intelligence in children. In contrast, studies using the more challenging PONS failed to show treatment effects. The use of relatively simple mentalizing and social perception tests may lead to inflated effect sizes estimates. Alternatively, it is possible that overly simple tests could show diminished sensitivity to change (due to ceiling effects) in higher functioning patients and lead to underestimates of effect sizes. Overall, the consistent negative findings with more challenging and psychometrically acceptable measures of mentalizing and social perception raise concerns about the robustness of the effect size estimates for social cognitive interventions in these domains.

Attributional bias presents a different measurement issue. All nine studies that assessed this domain used a single measure, the Ambiguous Intentions Hostility Questionnaire. Despite the significant effect size estimate for this domain overall, only four of the nine studies reported significant treatment benefits. Further, the scale does not have strong psychometric properties, it sometimes fails to distinguish schizophrenia from healthy controls, and it may be narrowly relevant only to patients with paranoid symptomatology (Mancuso et al., 2011; Pinkham et al., 2016). Unfortunately, the few other measures available to assess this domain have similar problems.

In summary, the existing database on comprehensive social cognitive treatments is relatively small and the overall methodological quality of these studies is variable and generally modest. Although evidence for efficacy is relatively consistent across studies using different measures of facial affect perception, results appear more closely tied to the particular outcome measures that are selected for the other three domains. The extant literature clearly has a number of important methodological limitations that necessitate caution when interpreting the overall effect sizes.

3.2. Open questions

There are also a number of important open questions that need to be addressed to make meaningful progress in social cognitive treatment development. We focus on six of these questions.

1. What are appropriate social cognitive outcome measures for use in clinical trials?

There is currently no consensus in the field about an optimal set of outcome measures for clinical trials. Currently available instruments for clinical trials have relatively poor or unknown psychometric properties and validity (Davidson et al., in press; Green et al., 2008b). As a result, two recent NIMH-sponsored initiatives sought to identify or develop measures that are suitable for clinical trials.

The Social Cognition Psychometric Evaluation (SCOPE) project followed a process analogous to that of MATRICS and attempted to evaluate existing measures that might be suitable for clinical trials (Pinkham et al., 2014; Pinkham et al., 2016). The RAND expert panel consensus building method was used to identify the most promising eight measures, two for each of the four main social cognitive domains. In a large-scale psychometric and validity study, one measure for the domains of emotion processing (Bell-Lysaker Emotion Recognition Test [BLERT]) and mentalizing (Hinting Task) showed adequate properties for clinical trial use. The remaining tasks showed weaker properties requiring further development or poor overall properties.

The other project, Social Cognition and Functioning (SCAF) in schizophrenia (Green and Penn, 2013), took an alternative approach. Clinical scientists teamed with basic researchers to identify key constructs and well-validated performance measures for these constructs from social cognitive neuroscience that showed promise for adaptation as clinical trial endpoints. This project is conceptually related to the CNTRCS project for neurocognition, which attempted to adapt measures from the cognitive neuroscience literature for use in clinical trials in schizophrenia. Out of four adapted paradigms, only one, the empathic accuracy task, demonstrated adequate properties for clinical trial use, while the others showed a variety of problems that would require substantial additional development work to address.

Thus, while there has been some progress on instrumentation much work remains. There have been promising candidate measures for two social cognitive domains within the SCOPE project. However, even these two measures could be improved upon. For example, the multimodal BLERT includes only one model, a white male actor, and would benefit from greater diversity. In addition, the Hinting Task is a simple questionnaire-based measure that has fairly limited ecological validity and sometimes shows ceiling effects in schizophrenia (e.g., (Roberts and Penn, 2009)). Instrumentation in social perception and attributional bias is particularly limited. Further, there are other important domains of social cognition, such as empathy, that have thus far received limited attention in the social cognitive intervention literature. Although funding agencies often do not prioritize method development studies, new social cognition outcome measures are a critical treatment development need.

Aside from the social cognitive tasks that have been identified as promising in the SCAF and SCOPE projects, the Mayer-Salovey-Caruso Emotion Intelligence Test (MSCEIT (Mayer et al., 2002)) is a well-validated and extensively normed emotional intelligence test that is suitable for clinical trials in schizophrenia. Because of the substantial data base behind the MSCEIT it was intentionally omitted from consideration by the SCOPE project. The task is divided into four branches and the 4th branch, Managing Emotions, was selected for inclusion in the MATRICS Consensus Cognitive Battery (MCCB) based on extensive psychometric evaluation in schizophrenia (Nuechterlein et al., 2008). Because it is part of the MCCB, this branch is frequently used in clinical trials of social cognitive training (e.g., (Horan et al., 2011)). The MSCEIT as a whole captures some of the key social cognitive domains for schizophrenia

research, including facial affect perception and emotion regulation, but it misses others, such as social perception, mentalizing, and attributional bias. Given those considerations, plus the length of administering all four branches, this psychometrically sound battery is rarely used in its entirety in clinical trials of schizophrenia.

2. Do social cognitive interventions produce enduring changes in social cognition?

It is not at all clear whether social cognitive interventions lead to any enduring improvements in social cognition. Only two of the 16 studies reviewed above considered post-treatment durability of treatment effects and the results were mixed. One reported retention of gains at six months post-treatment in an inpatient forensic sample (Combs et al., 2007) whereas the other included a thee-month follow up in an outpatient sample but did not find social cognitive gains at either the end of treatment or follow up (Roberts and Penn, 2009). Moving forward, it will be critical to demonstrate that treatment benefits last beyond the conclusion of treatment.

3. Do social cognitive interventions generalize to improvements in functional outcome?

Although the ultimate goal of social cognitive interventions is to enhance daily life functioning, we know very little about the generalizability of these treatments. Kurtz and Richardson (2012) reported on functional outcome in their earlier meta-analysis, but did not consider generalization to functioning in their recent review of comprehensive treatment studies. Table 1 lists the relevant studies. As shown in Section A, only three studies used performance-based measures of functional capacity, which assess one's ability to perform instrumental tasks or use social skills in a controlled research setting. All three studies used fairly similar variants of performance based measures of social skill (MASC, SSPA) with two reporting treatment benefits and the third reporting a non-significant trend in this direction. No improvement was found on a measure of instrumental daily life skills (UPSA), which assesses skills (e.g., dealing with finances, generating shopping lists) that are less directly linked to social cognitive treatments.

As shown in Section B, the picture is considerably more complicated for the more ambitious goal of generalizability to real-world functioning. It is encouraging that 6/9 studies report at least some evidence for a social cognitive treatment benefit. However, several factors warrant caution at this early stage. First, as described above, the methodological limitations of most studies (e.g., small samples, quasi-experimental designs, lack of active control conditions) undermine efforts to establish convincing evidence of generalizability. Second, many different measures are used and there is wide variability in which aspect(s) of functional outcome are assessed (social relations, family relations, finances, independent living and self-care, physical health, leisure activities, vocational activities). Even when the same scale is used across multiple studies (e.g., the Birchwood Social Functioning Scale), some studies focus on particular subscales while others consider global summary scores. Finally, several studies used scales that were created by the study team and/or have unknown psychometric properties. Greater precision in how functional outcome is defined and more standardized, psychometrically sound assessment tools are needed establish a corpus of convergent evidence of generalizability. Similar challenges in defining and assessing functional outcome have emerged in the context of treatment development for non-social cognition in schizophrenia (Brown and Velligan, 2016; Green et al., 2008a; Harvey et al., 2011; Harvey and Velligan, 2011).

4. When during the course of schizophrenia are social cognitive interventions most useful to implement?

All of the comprehensive treatment studies in the Kurtz et al. (2016) review were conducted with chronically ill participants. However, it is now well-established that wide-ranging, functionally relevant social cognitive impairments are present during the early post-onset phase of psychotic disorders (McCleery et al., 2014). Individuals with a recent-onset of psychosis therefore also stand to benefit from social cognitive interventions; in fact, interventions at this stage could have stronger and more generalizable effects before chronic patterns of social dysfunction are entrenched.

A few early studies supported the promise of intervention during the recent onset period. Studies using the broad-based, multi-component CET approach in early course patients have shown improvements in social cognition and functioning, as well as protective effects against neural degeneration (Eack et al., 2007; Eack et al., 2011). Two pilot studies targeting only social cognition, using either group-based SCIT or a novel individually administered computerized social cognitive intervention, have shown promising results in early phase participants (Bartholomeusz et al., 2013; Nahum et al., 2014). This area therefore appears ripe for treatment development.

Social cognitive interventions could be useful even earlier in the course of psychotic disorders. There is rapidly accumulating evidence that social cognitive difficulties are present in high-risk individuals with prodromal syndromes (Lee et al., 2015), and may predict conversion to psychosis (Healey et al., 2013; Kim et al., 2011). A few studies have shown the feasibility of computerized cognitive remediation in prodromal subjects and one of these incorporated social cognitive training exercises (Hooker et al., 2014). It is possible that social cognitive interventions could be a safe, low-risk tool in helping to prevent conversion to psychosis.

5. Who benefits, and does not benefit, from social cognitive intervention?

It is quite clear that not all participants benefit from social cognitive interventions. Emerging evidence also suggests there are likely different profiles of social cognitive impairment among people with psychosis (Karpouzian et al., 2016; Rocca et al., 2016). It would be valuable to be able to identify those who are most likely to benefit from different types of social cognitive intervention to provide a more personalized treatment approach and optimally allocate resources. Data on this topic is scarce. The earlier Kurtz and Richardson (2012) meta-analysis of all types of social cognitive interventions considered general sample characteristics of age, sex, gender distribution, duration of illness, in- vs. out-patient status, education, and neuroleptic dosage. Only illness duration was found to moderate treatment gains in that longer duration of illness was associated with greater improvements.

The literature on cognitive remediation can provide some guidance for efforts to address this question. A recent review by Medalia et al. (2016) identified three categories of variables that have been examined as predictors of treatment response in cognitive remediation: cognitive (baseline neurocognitive profile); psychological (e.g., clinical stability, motivation); biological (genetic variability [e.g., single nucleotide polymorphisms], medications). We are aware of one comprehensive treatment study that examined the potential impact of cognition and found that baseline neurocognition did not significantly relate to the amount of improvement in a comprehensive social cognitive treatment (Fiszdon et al., 2016). Further research on such factors will be useful.

6. What are the optimal parameters for and active ingredients of social cognitive intervention?

As the field progresses, it will be useful to identify the optimal parameters for social cognitive intervention. For example, the comprehensive studies have differed in duration of training (2.5–6 months), frequency of training (1 vs. 2 times per week), and group size (3–12 members). Further, all of the studies used a group format, though it is possible that individual sessions may be more useful for some participants (e.g., (Nahum et al., 2014)). We also understand very little about the active ingredients of these interventions. A diverse range of training techniques and materials have been employed, including

Table 1
Comprehensive social cognitive treatment studies that examined generalization to functional outcomes.

Study	In/outpatient	Sample size	Design	Measure(s)	Result
(A) Studies examining functional capacity					
(Horan et al., 2011)	Outpatient	Experimental: 16 Active control: 19	Group randomization	UCSD Performance-based Skills Assessment (Patterson et al., 2001): total score. Maryland Assessment of Social Competence (MASC) (Bellack et al., 1994): Overall effectiveness rating.	No significant treatment effect (trend for MASC).
(Roberts and Penn, 2009)	Outpatient	Experimental: 20 TAU: 11	Quasi-experimental	Social Skills Performance Assessment (SSPA) (Patterson et al., 2001): Total score. Data were analyzed with change scores in total psychiatric symptoms as a covariate in completer and intention to treat analyses.	Significant treatment effect on SSPA for completer analyses. No significant treatment effect for intention to treat analyses.
(Roberts et al., 2014)	Outpatient	Experimental: 33 TAU: 33	Group randomization	Social Skills Performance Assessment (SSPA) (Patterson et al., 2001): Total score.	Significant treatment effect for SSPA.
(B) Studies examining real-world functioning					
(Combs et al., 2007)	Forensic inpatients	Experimental: 18 Active control: 10	Quasi-experimental	Social Functioning Scale (SFS) (Birchwood et al., 1990): 2 subscales including social engagement and interaction subscales. Also examined number of aggressive incidents (physical and verbal) on the treatment ward for the 3 months prior to and following treatment.	Significant treatment effect on both SFS subscales. Also significant decrease in number of aggressive incidents.
(Gil Sanz et al., 2009)	Outpatient	Experimental: 7 TAU: 7	Group randomization	World Health Organization Disability Scale (WHO-DAS-II) - Spanish version (Vazquez-Barquero et al., 2006): 6 subscales including comprehension and communication, capacity to move, personal care, the capacity to relate to others, daily activities, social participation.	Treatment (i.e., between-group) effects not examined. Significant within-group treatment group improvements on 2/6 WHO-DAS-II subscales: personal care, daily activities.
(Hasson-Ohayon et al., 2014)	Outpatient	Experimental + Social Mentoring: 34 Social mentoring alone: 21		Social Functioning Scale (SFS) (Birchwood et al., 1990): 2 subscales including social engagement and interpersonal-communication subscales	Significant treatment effect on 1/2 SFS subscales: social engagement.
(Mazza et al., 2010)	Outpatient	Experimental: 16 Active control: 17	Group randomization	Personal and Social Performance Scale (PSPS) (developed by authors for this study): 4 subscales including socially useful activities, personal and social relationships, self-care, disturbing and aggressive behavior. A global score on 100-point scale is reported.	No significant treatment effect. Effect went in the unexpected direction: PSPS got worse in experiential group and better in control group.
(Roberts et al., 2014)	Outpatient	Experimental: 33 TAU: 33	Group randomization	Global Social Functioning Scale (GSFS) (Cornblatt et al., 2007); Quality of Life Scale (QOL) (Heinrichs et al., 1984): 2 subscales including social and work.	No significant treatment effect for GSFS and QOL.
(Roncone et al., 2004)	Inpatient	Experimental: 10 TAU: 10	Group randomization	Italian version of the Disability Assessment Schedule (DAS) (Morosini et al., 1988): Total score.	Significant treatment effect for DAS.
(Tas et al., 2012a)	Outpatient	Experimental: 19 Active control: 26	Group randomization	Social Functioning Scale (SFS) (Birchwood et al., 1990): 7 subscales including social withdrawal, interpersonal communication, prosocial activities, recreation, independence/performance, employment/occupation. Quality of Life Scale (QOL) (Heinrichs et al., 1984): 5 subscales including interpersonal relations, instrumental role, intrapsychic function, common objects and activities, total score.	Significant treatment effect for 5/7 SFS subscales and for 5/5 QOL scores.
(Wang et al., 2013)	Outpatient	Experimental: 22 TAU wait-list control: 17	Quasi-experimental	Chinese version of the Personal and Social Performance Scale (PSPS) (Tianmei et al., 2011): Total score.	Significant treatment effect for PSPS.
(Rocha and Queiros, 2013)	Outpatient	Experimental: 19 TAU: 16	Quasi-experimental	Life Skills Profile (LSP) (Rosen et al., 1989): 5 subscales including self-care, non-turbulance, social contact, communication and responsibility; total score	Significant treatment effect on 3/5 LSP subscales: social contact, communication, and total score. (Note: within group effect sizes were small, and TAU scores decreased more than experimental group scores increased).

didactic presentations with audiovisual stimuli, drill-and-practice exercises, modeling, corrective feedback, brain-storming exercises, interactive games, role play exercises, and homework assignments. A better understanding of the most effective techniques can guide efforts to refine these interventions.

4. Promising approaches to enhance efficacy and generalizability

It is clear from the previous section that there is ample room for improvement of social cognitive interventions. Several lines of research point to novel approaches that might be usefully incorporated into

these interventions to enhance efficacy and generalizability. These include psychosocial and psychopharmacological approaches.

4.1. Psychosocial approaches

Promising psychosocial approaches include bridging activities, new technologies, and combination treatments.

4.1.1. Bridging activities

Bridging activities in psychiatric rehabilitation are specifically designed to help participants apply skills learned in the clinic to their daily life. These activities have been found to play a key role in generalization of treatment benefits from psychosocial skills training and cognitive remediation (Glynn et al., 2002; Wykes et al., 2011). Similar activities could also be used to enhance the generalizability of social cognitive interventions. In a recently completed RCT of the SCST program we developed, we built on an established In-Vivo amplified social skills training manual (Glynn et al., 2002) and examined whether adding six in vivo training sessions in community settings would facilitate generalization (Horan et al., 2016a). The sessions occurred in prespecified locations (e.g., coffee shop, cafeteria, mall) and followed a structured set of activities with corresponding worksheets that were designed to provide participants with the opportunity to practice social cognitive skills in familiar community settings with a trainer to guide them. Although participants enjoyed the sessions and said they were useful, the in vivo components did not lead to differential gains in functional capacity or real-world functioning compared to a matched SCST group that received additional training activities in the clinic.

However, two studies of SCIT used bridging strategies in considerably larger doses and found improvements in functioning. Tas et al. (2012a) engaged a family member or close friend in separate social cognitive training sessions so they could serve as "social cognition partners", and found that patients showed larger improvements in real-world functioning compared to a matched control condition. Roberts et al. (2014) had each participant identify a "practice partner" with whom to complete homework assignments; although the frequency of practice partner engagement was quite variable, patients showed a small improvement in functional capacity (though not real-world functioning) compared to treatment as usual. Neither study was designed to test whether bridging activities had any added benefit beyond regular treatment. However, these do support continued development of bridging strategies to enhance generalization.

4.1.2. New technologies

Incorporation of new technological innovations into social cognitive interventions may also help enhance treatment benefits. Three potential approaches include computerized interventions, virtual reality applications, and portable devices.

Although computerized interventions are extensively used in cognitive remediation, there have been only a few efforts to investigate them for social cognition. This may partly reflect a belief that interacting with a computer is not "social" and is therefore incapable of developing skills required to navigate the complexities of real world social situations. This assumption remains untested. There are certain advantages to using computerized programs. For example, complex social cognitive processes can be broken down into simpler components and the difficulty of training exercises can be individually titrated to personal skill levels, thereby providing an opportunity to gradually increase the difficulty and integrative complexity of their training exercises. Theoretically, this could be an efficient avenue for tapping into the neuroplasticity of social cognitive circuits and thereby enhance the real-world experience of social encounters. Fortifying these neural circuits could benefit social cognition during actual social interactions, thereby boosting motivation to engage in further social experiences, and creating a positive, self-sustaining interplay between brain function and behavioral experience (Dodell-Feder et al., 2015). This is also a highly scalable intervention that can be administered to large numbers of people through computer programs installed on computers or over the Internet. Computerized approaches may also be particularly useful for individuals who are unable or unwilling to come into a clinic for treatment.

Perhaps the most prominent social cognitive computerized intervention currently is SocialVille, which has been used in a series of studies by S. Vinogradov and colleagues. The program incorporates 27 training exercises that target lower-level affect perception and social cue perception, as well as higher level mentalizing, self-referential style, and empathy. The user is required to make hundreds of increasingly more challenging discriminations of socially-relevant information (e.g., emotional faces, eye gazes, prosody, social situations) that gradually involve more complex, multi-modal, and ecologically-valid stimuli. The program showed some promise when used alone in a recent-onset sample (Nahum et al., 2014) and in combination with standard cognitive remediation in an at risk sample (Hooker et al., 2014). SocialVille is currently being evaluated in a large, multi-site RCT (Rose et al., 2015).

Aside from computerized programs, virtual reality simulators could provide useful opportunities to experience a wide variety of complex, dynamic, and interactive situations, and to practice social cognitive skills in a safe environment without any negative repercussions. This technology has been increasingly used for psychiatric rehabilitation in autism and schizophrenia spectrum disorders (e.g., Bekele et al., 2014; Smith et al., 2015). A few studies in schizophrenia have shown positive results in social skills training (Park et al., 2011; Rus-Calafell et al., 2014), and one group has conducted promising early work with a virtual reality intervention focused specifically on social cognitive skills ranging from emotion perception to mentalizing (Peyroux and Franck, 2014).

Mobile devices provide promising tools to enhance generalization of benefits. Mobile devices, via smartphone apps (self-initiated or automated), text messaging to prompt adaptive behaviors or homework, and experience monitoring (e.g., mood or mood or symptom monitoring with associated prompts for adaptive coping behaviors), are increasingly used to deliver services outside the clinic for SMI (Depp et al., 2016). In addition to positive benefits for self-management of psychiatric symptoms and medication adherence, a few studies found that these methods can enhance socialization (Ben-Zeev et al., 2014; Granholm et al., 2012). This technology could be adapted to in vivo exercises that focus more specifically on social cognitive skills.

4.1.3. Combination treatments

Finally, although a concerted effort was made about two decades ago to separate social cognitive skills training from other treatment components, it may be that it is most effective when used in combination with other interventions. There is considerable interest in whether the combination of cognitive remediation plus social cognitive intervention has synergistic effects that enhance outcomes (Horan et al., 2016b). Although some studies have not found such synergistic effects, other more recent studies suggest benefits, although these studies were not designed to test the separate and combined effects of cognitive versus social cognitive training (Fernandez-Gonzalo et al., 2015; Fisher et al., 2017; Lindenmayer et al., 2013; Sacks et al., 2013).

In our lab, we have adapted the SCST program for use in combination with vocational rehabilitation. In two RCTs, we are evaluating this combination in chronically ill participants with schizophrenia participating in Supported Employment and in recently housed Veterans participating in a work therapy program. Several other combination treatment approaches may be useful. For example, aerobic exercise has been found to have pro-social cognitive effects (Firth et al., 2017) and might be usefully combined with social cognitive interventions. In addition, administering social cognitive interventions with recovery-oriented cognitive therapy that targets dysfunctional socialization attitudes (e.g., "interacting with others it too much effort", "others will think I'm not smart", "people don't like me" (Beck et al., 2009)) could

address motivational issues that prevent participants from using new social cognitive skills during the course of their daily lives.

4.2. Combining psychopharmacology with social cognitive training

As mentioned above, not all participants benefit from social cognitive training programs, even though we see effects at the group level. This heterogeneity in treatment response has raised the question of whether it would be beneficial to combine social cognitive training with psychopharmacology, specifically with oxytocin (OT). OT is thought to enhance the salience of social information, and single-dose OT has shown encouraging, though mixed, results as a stand-alone approach to enhance social cognition in schizophrenia (Davis et al., 2013). Two intervention studies, using very different methods, examined whether it can augment social cognitive training.

In a study from our team, we randomly assigned 27 schizophrenia subjects to receive either 40 international units (IU) of OT or placebo 30 min prior to each training session (Davis et al., 2014). This study used a shortened 6-week, 12-session, version of SCST. OT-treated subjects demonstrated greater improvements on a measure of empathic accuracy compared with placebo following the training program. This advantage of OT was sustained one week and one month following the last dose of drug. Scores on facial affect identification improved in both groups, indicating that social cue identification responded well to training whether or not the subject has OT. These findings suggested that individuals with an impaired ability for processing social information can use OT to enhance the salience of social information. This increase in salience, in turn, increases the ability of subjects to learn higher-level social cognitive skills.

In contrast to this generally encouraging finding, another group failed to find a benefit of administering OT during social cognitive training (Cacciotti-Saija et al., 2015). This study considered chronic administration of OT (24 IU twice daily) in 52 individuals with early psychosis. This social cognitive training for this study was also 12 sessions over 6-weeks. No benefits of OT were observed on any of the primary outcome measures, which included one measure of social processing (i.e., Reading the Mind in the Eyes Test), along with symptoms and social functioning. Aside from the differences in patient samples (chronic schizophrenia versus early psychosis), a key difference between the two studies is that ours used only acute administration of OT before training, while Cacciotti-Saija, et al. had ongoing, twice-daily administration. A caution from preclinical studies is that increases in social behaviors following acute administration of OT can be lost with chronic administration (Bales et al., 2013).

Overall, we consider the combination of psychopharmacology with social cognitive training to be a promising direction and one that justifies more exploration. However, basic scientific questions remain. For example, it is challenging to demonstrate that OT is having central, versus peripheral, effects. Also, there have been no basic dose-finding studies to determine the correct dose of OT for social cognitive effects. Other non-psychosocial combination approaches also appear worth exploring. For example, neurostimulation (e.g., transcranial direct current stimulation [tDCS]) has shown potential additive value in combination with cognitive remediation (Nienow et al., 2016), and might also be usefully combined with social cognitive treatments (Rassovsky et al., 2015).

5. Conclusions: proceeding with cautious optimism

Given the number and seriousness of the limitations of prior work, one could interpret the literature on comprehensive treatments for social cognition in a more pessimistic light (e.g., “because of the limitations of studies in this area we can't trust any of the previous results”) or a more optimistic light (e.g., “despite the limitations of studies in this area we are seeing treatment benefits”). We believe the evidence supports a cautiously optimistic interpretation, particularly in light of the consistency of improvements in some areas (e.g., facial affect identification) and the fact that the more well-controlled studies are finding treatment benefits. However, it is clear that much work remains before widespread efforts to disseminate and implement social cognitive interventions in community mental health settings are justified.

As we move forward into the next wave of studies, further small-scale pilot studies of existing intervention approaches are not needed. Instead, research priorities include developing new psychosocial and non-psychosocial intervention approaches to further enhance efficacy across multiple social cognitive domains, validating new social cognitive endpoints that are appropriate for clinical trials, identifying personal predictors of treatment outcome, and conducting larger (ideally multi-site) studies using rigorous RCT methods. The substantial challenge of generalizability also remains. Creative new approaches are needed to help link the benefits of social cognitive treatments to meaningful improvements in community functioning.

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