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ABSTRACT

Poor treatment engagement is an enduring problem in the care of patients with schizophrenia. Evidence suggests that targeted cognitive training (TCT) improves cognition and functional outcomes, but this time-consuming intervention might reduce patients' engagement in other treatment activities when implemented in real-world settings. This is especially true of residential care programs which encourage patients to engage in group therapies, self-care, and a wide variety of structured social, work, and other rehabilitation activities. This study aimed to determine whether TCT negatively impacts engagement in other psychosocial treatments. Patients with schizophrenia were recruited from a community-based residential care program and randomized to one of two intervention arms: treatment as usual (TAU; $n = 22$) or TAU augmented with TCT ($n = 24$). Psychosocial treatment engagement was tracked over 20 weeks. Treatment groups did not significantly differ on baseline variables or psychosocial treatment engagement in the 5 weeks prior to randomization. TCT had a positive effect on engagement ($\beta = 0.112$, $p = 0.003$), but there was no treatment-by-time interaction ($\beta = -0.029$, $p = 0.672$). Participants in TCT engaged in an average of 1.34 additional group therapies, 0.58 additional activities of daily living, and 0.84 additional rehabilitation activities per week in comparison to TAU participants. Baseline cognition was also a significant predictor of psychosocial treatment engagement. Overall, results suggest that TCT can be implemented in real-world settings without negatively impacting engagement in other psychosocial treatments. Additional studies are needed to determine what role nonspecific factors play in the positive impact of TCT.

1. Introduction

Cognitive training improves cognition and functional outcomes for patients diagnosed with schizophrenia (SZ) (Fisher et al., 2009; Keshavan et al., 2014; Wykes et al., 2011). However, with the recommended course of treatment typically involving hour-long trainings, multiple times per week, lasting several months (Fisher et al., 2015), the intervention might be difficult to implement in community-based treatment settings. Moreover, although several randomized controlled trials have demonstrated the efficacy of cognitive training in SZ (Hogarty et al., 2004; Wykes et al., 2007), less is known about implementing the treatment in real-world care settings (but see Tsapekos et al., 2017; Vita et al., 2011), and whether participating in such a time-intensive intervention negatively impacts patient engagement with established psychosocial treatment activities.

Comprehensive treatments for chronic SZ are often complex and demanding, including medication management, individual therapy, skills training, supported education/employment, and family counseling (Spaulding et al., 2016). This is especially true of long-term residential care. While the overall rate of hospitalizations for patients with SZ has declined, occasional acute and transitional inpatient care is still common (Chi et al., 2016; Fakhoury and Priebe, 2007; Messias et al., 2007; Whitehorn et al., 2004). Such stays are critical periods of treatment where clinicians seek to stabilize and then reintegrate patients into the community. Residential rehabilitation programs for SZ now commonly offer a day-long menu of interventions including skill groups, process groups, art therapy, and music therapy.

Poor treatment engagement (i.e., participation in offerings; Kreyenbuhl et al., 2009), however, undermines the collective effectiveness of these interventions. Unfortunately, treatment engagement in SZ patients is low (Leucht and Heres, 2006) with deleterious consequences

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including symptom exacerbation, relapse, homelessness, and suicide (Dixon et al., 2016; Fischer et al., 2008). Identifying possible barriers and predictors of engagement and methods to maximize engagement is therefore essential.

Although implementing cognitive training into residential care settings is appealing, adding a time-intensive intervention to an existing treatment program risks exhausting patients' motivational and energy resources, and may therefore reduce patients' engagement in other important treatment activities (Heckman et al., 2015). However, there is some evidence that cognitive training may actually increase, rather than decrease rates of treatment utilization (e.g., Wykes et al., 2003). Whether such results generalize to residential care settings is unknown. Lindenmayer et al. (2008) implemented a cognitive training program in a long-term inpatient setting and found that patients randomized to receive one form of cognitive training completed a greater number of hours in a work program. However, to our knowledge, no study has directly examined the impact of cognitive training on psychosocial treatment engagement within a community-based residential care setting.

The present study was designed, in part, to determine whether participation in a targeted cognitive training program (TCT; Fisher et al., 2009; Fisher et al., 2015) delivered in the context of a real-world transitional care center, negatively impacted engagement with other psychosocial groups and activities. Secondarily, we aimed to explore whether individual differences in demographic, clinical, and cognitive variables predict psychosocial treatment engagement. In outpatient settings treating adults with serious mental illness, age, gender, and cognition have all been shown to impact engagement for people with SZ (Agarwal et al., 1998; Axelrod and Wetzler, 1989; Fuentes et al., 2016; Kreyenbuhl et al., 2009; O'Brien et al., 2009). Findings are mixed regarding symptoms (MacBeth et al., 2013; Nose et al., 2003) and illness duration (Agarwal et al., 1998; Axelrod and Wetzler, 1989). We sought to determine whether the demographic, cognitive, and illness severity findings observed in outpatient settings would replicate within a residential treatment program. Based on the prior literature, we hypothesized that older age, female gender, better cognition, and fewer clinical symptoms would all be positively associated with treatment engagement.

2. Methods

2.1. Participants and design

Participants were 46 psychiatric patients recruited from a community-based residential care program following 1-month of stabilization. Study participants were administered baseline measures of cognition and clinical symptoms and then randomized to one of two arms using stratified random assignment by gender, age, and ethnicity. The study was a parallel design with participants assigned to either treatment as usual (TAU; $n = 22$) or TAU augmented with TCT ($n = 24$). The primary inclusion criterion was meeting formal diagnostic criteria for schizophrenia or schizoaffective disorder verified using the Structured Clinical Interview for DSM-IV-TR (First et al., 2002). Exclusion criteria included inability to assent, not being fluent in English, previous significant head injury, neurological illness, severe systemic illness, or current mania. The Institutional Review Board of the University of California, San Diego approved all experimental procedures (IRB#130874).

2.2. Intervention

Participants randomized to TCT were scheduled 3–5 days per week to complete 1 h of training per day (i.e., 1 h engaged with the computer software performing exercises). Training was delivered over a period of approximately 12–15 weeks. TCT was administered in a dedicated classroom in groups of up to 5 participants (although typically 2 or fewer participated at one time) using individual laptop computers with headphones. Participants worked individually, with little participant-to-participant interaction during computerized training itself. Although group interaction was not explicitly encouraged, participants did interact during weekly social events and graduation parties for each participant, which were designed to provide incentive and reward. Study staff monitored training, ensured task instructions were understood, and provided encouragement. For example, staff used motivational interviewing techniques to facilitate participation, and reinforced progress to a new level within a task. Six modules of auditory processing exercises supplied by PositScience were administered (Sound Sweeps, Fine Tuning, Syllable Stacks, Memory Grid, To-Do List, and Rhythm Recall). Our focus was auditory training due to robust previous findings in this domain (Fisher et al., 2016). We provide a description of each exercise below:

Sound Sweeps (targets auditory processing speed): Two successive frequency-modulated tone sweeps are presented and participants indicate whether the frequency increased or decreased within each tone. *Fine Tuning* (targets auditory perception and processing speed): Participants indicate which one of two confusable syllables were presented. *Syllable Stacks* (targets auditory memory): Users report the order of presented syllables in a serial memory span task. *Memory Grid* (targets auditory memory): Participants match identical cards representing syllables. *To-Do List Training* (targets auditory memory): Participants see a grid of everyday items (e.g., plant, carrots, shovel) and select the items in accordance with spoken instructions. *Rhythm Recall* (target auditory memory): Participants recreate auditory melodies.

2.3. Measures

Psychosocial treatment engagement was operationally defined by the number of hours of attended group therapies, number of completed activities of daily living (quantified as 1 credit per full day of completed activities of daily living plus 1 additional credit for showering), and number of hours of structured social or vocational rehabilitation activities (quantified as 1 credit per hour of activity attended) tracked weekly over a maximum of 20 weeks (5 weeks prior to and up to 15 weeks after treatment randomization). Activities were recorded by clinical staff working in the facility unaffiliated with the study and who were blind to participants' treatment condition. We examined outcomes operationalized both as the average of the standardized activities, and as each unstandardized activity individually.

Clinical symptoms were assessed with the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b). SANS global ratings of affective flattening or blunting, alogia, avolition-apathy, anhedonia-asociality, and attention were summed to create a general measure of negative symptoms for each participant. (The SANS Impersistence at Work or School item was adapted to reflect activities at the inpatient center in order to avoid ceiling effects; thus, SANS total scores are not comparable to those reported in the extant literature). SAPS global ratings of hallucinations, delusions, bizarre behavior, and formal positive thought disorder were summed to create a general measure of positive symptoms for each participant. Cognition was assessed using the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein et al., 2008). Cognitive outcomes were operationalized as age and gender corrected T-scores for the Neurocognitive Composite (MCCB-NC). Participants were administered all clinical and cognitive measures prior to treatment randomization.

2.4. Analyses

Data were analyzed using linear mixed models (Hox, 2010) and the lme4 package for *R* (Bates et al., 2014). All models included random intercepts and random slopes for time. To address our first aim, psychosocial treatment engagement was regressed onto a time-varying treatment status variable (i.e., coded 0 for TAU participants at all time

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points, 0 for TCT participants from weeks −4 to 0 [i.e., pre-treatment], and 1 for TCT participants from weeks 1 through 15), and the interaction of week by treatment status. To address our second aim, psychosocial treatment engagement was regressed onto fixed effects of age, gender, illness duration, positive symptoms, negative symptoms, and cognition. These variables were analyzed in separate models. We used the Šidák-Holm method with an initial significance level of 0.05 to counter the familywise error rate due to multiple comparisons. All available data were analyzed regardless of dropout (see Supplemental Fig. 1).

3. Results

Demographic characteristics, clinical symptoms, chlorpromazine equivalent doses, days to follow-up assessment, and training hours completed by TCT participants are all reported in Table 1. Participants did not differ on any of the baseline demographic variables or outcome measures.

A CONSORT flow diagram with enrollment, exclusion, and discontinuation totals is reported in supplemental material. Three patients assigned to TCT and 1 assigned to TAU chose to stop participating in the study after being randomized. An additional 5 participants assigned to TCT and 1 assigned to TAU were excluded from continued participation by facility staff due to issues such as suicidality, aggression, or other behavioral problems unrelated to treatment assignment. Combining both participant and staff initiated reasons for discontinuation, the dropout rate was higher for patients randomized to TCT (33%) compared to patients randomized to TAU (9%); however, the difference was not statistically significant ($\chi^2(1) = 2.668$, $p = 0.10$).

TCT treatment status had a significant positive effect on psychosocial treatment engagement ($b = 0.290$; $SE = 0.101$; $p = 0.004$; $CI_{95\%} = [0.09, 0.49]$; $\beta = 0.104$). The interaction of week-by-treatment status was non-significant ($b = -0.012$; $SE = 0.021$; $p = 0.547$; $CI_{95\%} = [-0.05, 0.03]$; $\beta = -0.038$). To determine whether the main effect of treatment status was due to differences between TAU and TCT participants prior to randomization, we next added a treatment group variable to the model (i.e., dummy coded 0 for TAU participants and 1 for TCT participants *at all time points*, including those prior to randomization). While the main effect of treatment status remained significant ($p = 0.008$), treatment group did not have a significant effect on psychosocial treatment engagement ($p = 0.328$). We also fitted a model where treatment engagement from weeks −4 through 0 (i.e., pre-treatment) was regressed onto the treatment group variable alone. The results indicated that treatment group was not significantly related to psychosocial treatment engagement prior to randomization ($p = 0.322$). Thus, groups did not differ in the frequency of their psychosocial treatments received prior to randomization. Finally, we examined whether the number of cognitive training hours completed among TCT participants significantly predicted treatment engagement, and found the relationship was positive but non-significant ($p = 0.694$).

We further explored the positive effects of TCT treatment status by running additional linear mixed models replacing the psychosocial treatment composite variable in each with the number of attended group therapies, self-care, or structured socials and rehabilitation activities; the average number of these activities completed per week by group is reported in Table 3. Regression parameter estimates suggested that relative to TAU, TCT participants were expected to engage in an average of 1.34 additional group therapies ($CI_{95\%} = [0.22, 2.46]$), 0.58 additional activities of daily living ($CI_{95\%} = [0.08, 0.94]$), and 0.84 additional rehabilitation activities ($CI_{95\%} = [-0.16, 1.84]$) per week.

Parameter estimates for the fixed effects of age, gender, illness duration, positive symptoms, negative symptoms, and cognition are reported in Table 2. Only the fixed effect of cognition was significant. Many of the effects, however, were non-negligible in size, especially the effects of age and negative symptoms. For every additional MCCB-NC T-score in cognitive ability, patients completed 0.12 additional group therapies ($CI_{95\%} = [0.03, 0.22]$), 0.05 additional activities of daily living ($CI_{95\%} = [0.02, 0.08]$), and 0.08 additional rehabilitation activities ($CI_{95\%} = [0.01, 0.15]$) per week. A clinically-relevant presentation of the results, shown in Fig. 1, indicates that patients with MCCB-NC T-scores in the upper third of the sample (T-scores > 31; range = 32 to 53) accumulated nearly 100 additional psychosocial treatment activities over 15 weeks of stay relative to patients with severely impaired cognition, defined as patients with MCCB-NC T-scores in the lower third of the sample (T-scores < 18; range = −3 to 16).

Table 1
Demographic and clinical characteristics.

	Treatment as usual	Targeted cognitive training	*p*
Sample size	22	24	
Age	35.73 (13.00)	34.54 (12.13)	0.75
Gender: Male	9 (41%)	13 (54%)	0.55
Hispanic	6 (27%)	4 (17%)	0.61
Race			0.51
African American	3 (14%)	5 (21%)	
Asian	2 (9%)	1 (4%)	
Caucasian	12 (55%)	13 (54%)	
More than one race	5 (23%)	3 (12%)	
Native American	0 (0%)	2 (8%)	
Education	11.95 (2.17)	11.71 (1.99)	0.69
Chlorpromazine equivalents	982.54 (758.10)	1329.42 (972.78)	0.82
Illness duration	15.23 (12.78)	16.12 (13.67)	0.82
SAPS	4.45 (5.14)	5.12 (4.00)	0.62
SANS	6.18 (3.97)	7.75 (4.50)	0.22
MCCB-NC	23.95 (13.71)	23.12 (12.14)	0.83
Days to follow-up	99.30 (24.26)	89.44 (19.79)	0.20
Hours of training		27.94 (10.20)	

Note. Means and standard deviations are reported for continuous variables. Counts and percentages are reported for discrete variables. Groups were compared using regression for continuous variables and χ^2 tests for categorical variables. Education is in years completed. SAPS = Scale for the Assessment of Positive Symptoms reported as total global rating scores; SANS = Scale for the Assessment of Negative Symptoms reported as total global rating scores; MCCB-NC = MATRICS Consensus Cognitive Battery Neurocognitive Composite age and gender corrected T-scores. Hours of training reflects number of hours engaged with the computer software. The SANS Impersistence at Work or School item was adapted to reflect activities at the inpatient center in order to avoid ceiling effects.

4. Discussion

Results of this study demonstrate that a time- and resource-intensive course of computerized cognitive training, TCT (Fisher et al., 2009, 2015), is associated with increased, rather than decreased, engagement in existing psychosocial treatment activities. That is, contrary to concerns that the heavy time requirements of TCT might interfere with existing psychosocial treatments, TCT actually had a positive impact on engagement, especially the number of group therapies attended. Our results support and extend the literature by showing that the previously reported positive association between cognitive training and treatment engagement (e.g., Wykes et al., 2003) observed among SZ outpatients also extends to patients in community based residential care settings. This effect was not, however, dependent on the

Table 2
Parameter estimates for fixed effect predictors of treatment engagement.

	b	*SE*	$CI_{95\%}$	β	$p_{\cdot SH}$
Age	0.015	0.009	[−0.003, 0.033]	0.187	0.362
Gender (Male)	−0.223	0.232	[−0.676, 0.231]	−0.111	0.342
Illness duration	0.010	0.009	[−0.008, 0.027]	0.128	0.475
Positive symptoms	−0.031	0.025	[−0.081, 0.018]	−0.141	0.528
Negative symptoms	−0.048	0.027	[−0.102, 0.006]	−0.203	0.370
Cognition	0.024	0.009	[0.007, 0.041]	0.306	0.044

Note. Fixed main effects for each predictor—age, gender, illness duration, positive symptoms, negative symptoms, and cognition—were fitted in separate models. *b* = estimate of regression coefficient; *SE* = standard error of estimate; $CI_{95\%}$ = 95% confidence interval; β = standardized estimate of regression coefficient; $p_{\cdot SH}$ = Šidák-Holm adjusted *p*-value.

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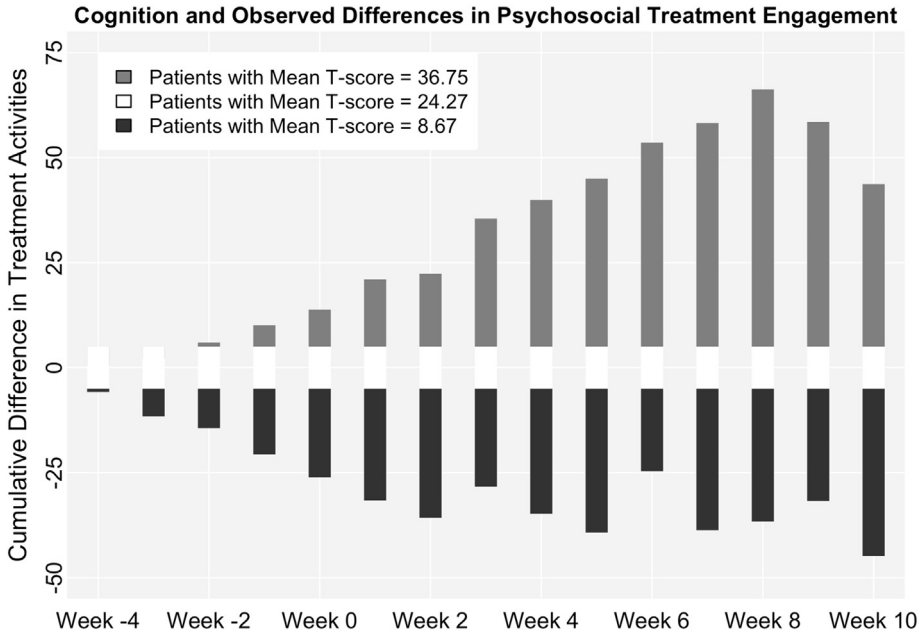

Fig. 1. Difference in psychosocial treatment activities accumulated over several weeks of residential care. Patients were divided into groups based on thirds (lower, mid, and upper tertiles of the observed MCCB-NC T-score distribution). Patients with relatively high MCCB-NC T-scores nearly 100 additional psychosocial treatment activities over 15 weeks of stay relative to patients with severely impaired cognition. Weeks −4 to 0 were measured pre-treatment.

duration of TCT, nor the number of training hours completed, suggesting that non-specific factors rather than changes in cognition that are targeted by the intervention itself may contribute to increased engagement in other foreground psychosocial groups/activities. That is, there was no "treatment-time-response" relationship between cognitive training and psychosocial treatment engagement. Nonetheless, over the course of the study, TCT participants accumulated an average of an additional 20 group therapies, 13 rehabilitation activities, and 9 activities of daily living. This amounts to an extra week of treatment defined in these terms.

Results of the current study should be interpreted in light of certain limitations. First, the dropout rate was higher for patients randomized to TCT (33%) compared to patients randomized to TAU (9%). Although this discrepancy is not statistically significant, and our dropout rate is comparable to similar studies (Tsapekos et al., 2017), it is possible that missing outcome data were associated with scores on the outcomes themselves (missing not at random). That is, patients who dropped out of TCT may have also engaged in fewer psychosocial treatment activities. We should note, however, that the positive effect associated with TCT was not time dependent, suggesting that dropout cannot entirely explain the results. Second, although clinical staff who recorded psychosocial treatment engagement outcomes were not directly informed of participants' treatment status and efforts were made to ensure their blinding, residential staff may have nonetheless been able to guess status from the additional time TCT participants spent with study staff or been informed by participants. We cannot rule out the expectancy effect as a contributor to the positive association between TCT and engagement in psychosocial treatment activities. Similarly, since the participants were not blind to their treatment assignment, we cannot rule out the possibility that participant expectations may have influenced their engagement with other activities. Future studies are needed to replicate these findings comparing TCT to an active control group. Finally, although we did not find a significant difference in psychosocial treatment engagement between TAU and TCT participants prior to randomization (weeks −4 through 0), the groups were not entirely equal, and thus stratifying assignment over psychosocial treatment levels would have strengthened the methodological rigor of our study.

It is also noteworthy that the present cohort of patients was more impaired relative to samples from other cognitive training studies. For example, the mean MCCB-NC T-score of 23 is approximately 5 to10 points lower than means obtained in more typical outpatient samples (e.g., August et al., 2012). This suggests the possibility that some of the present results may not fully generalize to outpatient settings with higher functioning patients. On the other hand, this difference further highlights the significance of the present findings: even among patients with significantly impaired cognition, and who therefore are more likely to have poor treatment engagement, TCT has a positive and significant impact on engagement. Finally, psychosocial treatment engagement in the present study was only defined in terms of patients' attendance or completion, not their level of active participation in group therapies and activities. Results may therefore not fully speak to patients' actual quality of engagement in their treatments.

Notwithstanding these limitations, the finding of a significant increase in engagement in other psychosocial treatments raises this question: what are the primary versus secondary "ingredients" of therapeutic gains with TCT? Bottom-up models suggest that changes in basic information processing should precede changes in cognition, and that improved cognition should precede changes in functional outcomes (Green et al., 2012; Javitt, 2009; Thomas et al., 2017). Moreover, TCT, a neuroplasticity-based intervention, is thought to require dozens of hours of training to be effective (Fisher et al., 2016). We have previously reported that TCT significantly improved verbal learning and auditory perception in this sample (Joshi et al., 2017; Thomas et al., submitted). However, psychosocial treatment engagement was independent of both the interaction of treatment and time, and the number of TCT hours completed. That is, gains in psychosocial treatment engagement were not dependent on completing TCT or on accumulating hours of training. This could suggest—but certainly does not prove—

Table 3
Average number of group therapies, activities of daily living, and rehabilitation activities completed per week by group.

	Treatment as usual	Targeted cognitive training
Group therapies	16.97	18.54
Activities of daily living	12.89	13.78
Rehabilitation activities	11.49	12.54

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that changes in psychosocial treatment engagement were due to non-specific factors (cf. Wykes and Spaulding, 2011). Unfortunately, a further limitation of this study is that we lacked an active control group that would have allowed us to distinguish between specific and non-specific treatment effects. Future studies are needed that can distinguish between the effects of improved cognition due to TCT, on the one hand, and changes in factors such as motivation, self-efficacy, and feelings of social support, on the other.

Nonetheless, it is plausible that non-specific factors might have cascading benefits on treatment engagement. Participants might feel successful at TCT due to positive and motivational feedback, both interpersonal and computer-driven, activating greater treatment-related self-efficacy. Improved self-efficacy might then lead to greater willingness to engage in other activities and, ideally, better overall treatment outcomes. This might explain why cognitive training has been found to be more beneficial when implemented in the context of a comprehensive rehabilitation program (McGurk et al., 2007).

It is important to note that the broader research literature on cognitive training suggests that the success of the intervention and psychosocial interactions are not independent. For example, Sandoval et al. (2017) compared cognitive training in conditions without peer interaction or where participants were asked to track each other's progress and provide encouragement. Results indicated that peer interaction significantly improved cognitive performance during training. Moreover, Medalia and Richardson (2005) found that therapists' qualifications (degree) predicted a positive response to certain forms of cognitive training. It is possible that a therapists' ability to motivate and reinforce training has benefits both in terms of training itself, and in terms of engagement with other psychosocial treatments. Finally, there is evidence that encouraging patients to use their newly improved cognitive skills in complex and demanding situations can better prepare them to translate their cognitive gains into improved real-world functioning (Medalia and Choi, 2009; Medalia and Richardson, 2005).

Future research is necessary to elucidate relationships among TCT and psychosocial treatment engagement, but our findings offer cause for optimism regarding the capability of patients with SZ to engage in, and benefit from, time demanding cognitive training interventions without apparent interference with other important activities.

Analyses conducted to explore demographic and clinical predictors of psychosocial treatment engagement revealed that only baseline cognition had a significant positive relationship. Patients with severely impaired cognition were less likely to attend additional group therapies and rehabilitation programming, and complete additional activities of daily living in comparison to patients with higher cognition. These results present an interesting paradox: patients with the greatest apparent need of functional enhancement appear to engage the least in important psychosocial treatment activities. This finding suggests that patients with lower cognition may benefit from additional supportive contacts or interventions designed to increase participation in psychosocial activities.

Age, gender, illness duration, positive symptoms, and negative symptoms were all non-significantly related to psychosocial treatment engagement. However, the effect sizes for these variables suggest that non-significance may be a function of sample size. Overall, the results are consistent with the literature suggesting that younger male patients with greater symptom severity are more likely to disengage from treatment.

Future studies will explore whether changes in psychosocial treatment engagement relate to changes in cognition associated with TCT, and whether demographic, clinical, and cognitive variables moderate these relationships. Nonetheless, our results suggest that engagement begets engagement, and that people with SZ can successfully participate in complex and time-intensive treatment activities regardless of their constellation of clinical symptoms. Treatment programs should not avoid time-intensive treatment packages, and instead should increase expectations, reinforce effort, and apply motivational interventions to augment treatment success.

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Contributors

Michael Thomas, Ph.D. was a co-principal investigator for this study, obtained extramural funding for research, completed all statistical analyses, and wrote the first draft of this manuscript. Gregory Light, Ph.D. was the principal investigator for this study, obtained extramural funding for research, and contributed to manuscript preparation and editing. All other authors participated in aspects of study design, including subject recruitment and data collection. All authors were responsible for reviewing and approving the final manuscript.

Conflict of interest

Dr. Light reports having been a consultant to Astellas, Boehringer-Ingelheim, Dart Neuroscience, Heptares, Lundbeck, Merck, NeuroSig, Neuroverse, and Takeda.

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