

A Novel Psychosocial Intervention for Motivational Negative Symptoms in Schizophrenia: Combined Motivational Interviewing and CBT

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Objective: Negative symptoms are a primary cause of disability in schizophrenia for which there are no established pharmacotherapies. This study evaluated a novel psychosocial intervention that combined two evidence-based practices—motivational interviewing and cognitive-behavioral therapy (MI-CBT)—for the treatment of motivational negative symptoms.

Methods: Seventy-nine participants with schizophrenia and moderate to severe negative symptoms were included in a randomized controlled trial comparing the 12-session MI-CBT treatment with a mindfulness control condition. Participants were assessed at three time points through the study period, which included 12 weeks of active treatment and 12 weeks of follow-up. The primary outcome measures were motivational negative symptoms and community functioning; the secondary outcomes included a posited biomarker of negative symptoms: pupillometric response to cognitive effort.

Results: Compared with the control group, participants in the MI-CBT group showed significantly greater improvements in motivational negative symptoms over the acute treatment period. Their gains relative to baseline were maintained at follow-up, although the differential benefit relative to control subjects was attenuated. There were nonsignificant effects toward improvements in community functioning and differential change in the pupillometric markers of cognitive effort.

Conclusions: The results show that combining motivational interviewing with CBT yields improvements in negative symptoms, a feature of schizophrenia generally thought of as resistant to intervention. Motivational negative symptoms not only responded to the novel treatment, but the gains were maintained over the follow-up period. Implications for future studies and for improving the generalization of the negative symptom gains to daily functioning domains are discussed.

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Schizophrenia is associated with a high rate of disability, and it is one of the most expensive per-patient psychiatric conditions (1). While there have been advances in pharmacological interventions for positive symptoms, they have had a minimal impact on daily functional outcomes for those living with the illness. Motivational factors, commonly conceptualized and measured as negative symptoms, are a primary determinant of functional disability in schizophrenia (2, 3).

Negative symptoms generally refer to the absence or diminution of normal functions such as emotional expression and goal-oriented activities. An important distinction exists between expressive negative symptoms, that is, reduced display of affect and speech, and motivational negative symptoms, that is, lowered volition, drive, and capacity for pleasure (4). The motivational negative symptoms have the greatest impact on outcomes and are consistently predictive of poorer future social and occupational outcomes (2, 3).

Despite their importance in predicting outcomes, negative symptoms are less frequently a target for psychopharmacological studies and are more difficult to treat than positive symptoms. Apart from pharmacological studies, recent research indicates that psychosocial treatments may have promise for motivational deficits.

Cognitive-behavioral therapy (CBT) is a structured, action-oriented approach to changing maladaptive thoughts and problematic behaviors that interfere with functioning. According to a cognitive-behavioral model of schizophrenia, motivational negative symptoms are influenced by two component processes: defeatist beliefs (e.g., “Why bother trying if I won’t be perfect”) and avoidant behavior (e.g., social withdrawal) (2, 6, 7). Preliminary studies support the efficacy of CBT for negative symptoms (e.g., 6, 8–10); however, these interventions are typically time and resource intensive. Moreover, a potential barrier to delivering therapies such as

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CBT is that individuals may have low motivation to engage with and adhere to treatment. Recognition of the importance of motivation for effective CBT has led to integrating motivational interviewing and CBT (MI-CBT), which has shown positive results for a variety of disorders, including substance use, depression, anxiety, and physical health-related behaviors (12). Motivational interviewing is a well-established, evidence-based approach, effective for initiating and maintaining behavioral changes across a range of clinical populations (5). It is an ideal companion to systemized therapies such as CBT because it provides an effective framework from which a clinician can work to augment intrinsic motivation and encourage the client to view the treatment benefits as worth the “cost.” In serious mental illness, motivational interviewing has been used in brief applications that precede other interventions to enhance treatment engagement (13) and improve outcomes for targets, including substance misuse and psychiatric symptoms (14–16). However, integrated MI-CBT has not, to our knowledge, been tested as an approach for treating motivational negative symptoms or improving functioning in schizophrenia.

Beyond treatment of negative symptoms, a secondary goal is to identify accurate and sensitive tools to measure motivation deficits in psychiatric research. Neurophysiological indicators may provide objective clinical trial endpoints to facilitate treatment development. One such indicator is pupil dilation. The variation in the size of the pupil in response to psychological stimuli is a reliable index of attentional effort (17). We selected pupillometry as the preferred neurophysiological approach for this study because of the extensive pupillometric research in schizophrenia for assessing attention, cognitive control, and, more recently, task-based motivation (e.g., 18–22). A notable gap in this literature is that pupil size has not been evaluated in relation to motivational negative symptoms in a randomized controlled trial for schizophrenia.

We report here a controlled study of a novel group-based psychosocial intervention for the motivational negative symptoms of schizophrenia. The primary outcomes consisted of one proximal measure, motivational negative symptoms, and one more distal measure, community functioning. We expected significantly greater gains in the treatment condition during the 12-week acute intervention period compared with the active control. We also examined a physiological secondary outcome measure: pupillary response, as a biological marker of motivated effort on a cognitive task. Expressive negative, depressive, positive, and agitation symptoms were examined to evaluate specificity of effects. Durability was assessed at 12 weeks posttreatment.

METHODS

Participants

Ninety-nine participants were recruited from outpatient clinics at the Veterans Affairs Greater Los Angeles Healthcare System. Selection criteria included DSM-5 (23) diagnosis of schizophrenia; age 18–65 years; no clinically significant neurological

disease; no history of serious head injury; no evidence of moderate or greater current substance use disorder; no history of intellectual or developmental disability; clinical stability (i.e., no inpatient hospitalizations during the 3 months prior to enrollment, not meeting criteria for a major depressive episode in the 8 weeks prior to enrollment, and no changes in antipsychotic medication type in the 4 weeks prior to enrollment); and moderate to severe levels of motivational negative symptoms (defined as a score ≥ 15 out of 36 on the motivation and pleasure subscale of the Clinical Assessment Interview for Negative Symptoms [CAINS MAP] [4, 24] in the 4 weeks preceding study entry). Baseline data from this sample have been reported previously (21, 22).

Design

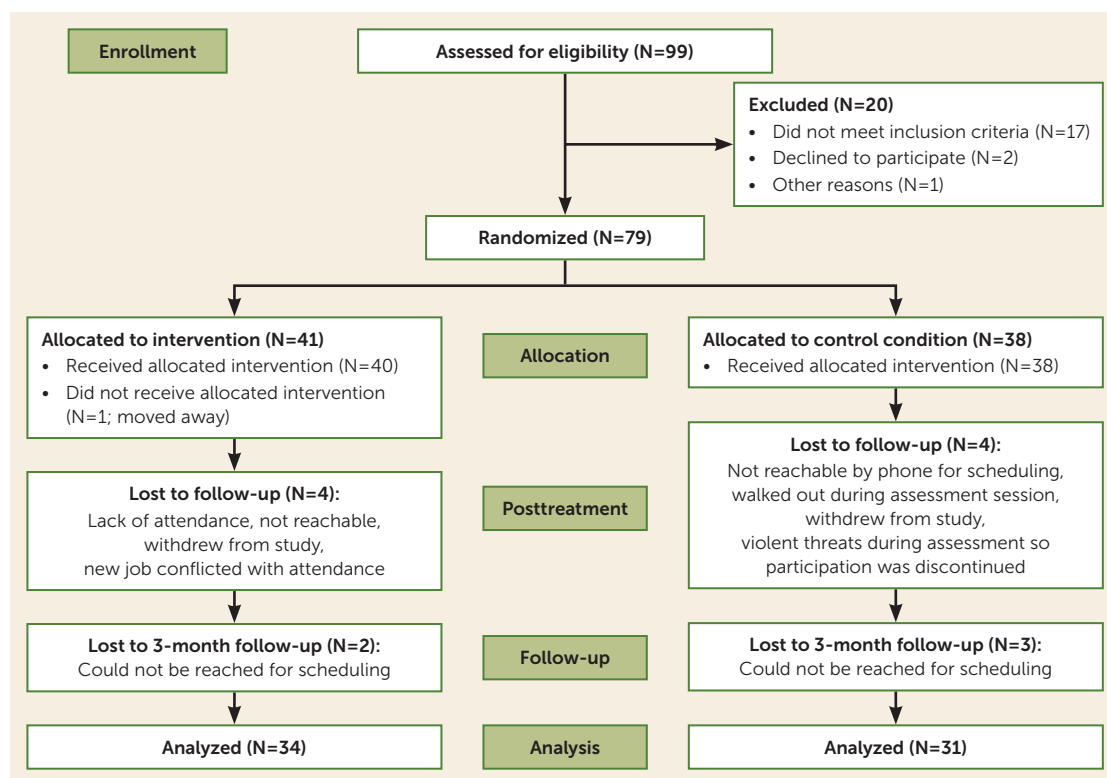
This study was approved by the Institutional Review Board at the Veterans Affairs Greater Los Angeles Healthcare System. Written informed consent was obtained from all participants after they were provided a complete description of study procedures. Of the 99 potential participants who gave initial consent, 79 individuals with schizophrenia and moderate to severe negative symptoms met inclusion criteria and agreed to participate in the trial (Figure 1). Participants were randomized in cohorts to either the treatment or active control; cohort sizes were allowed to range from five to eight to allow good group dynamics while minimizing delays in treatment initiation, and a block procedure was used to maintain balance of the arms throughout the study. Participants were assessed at baseline, at end of treatment (12 weeks), and at end of follow-up (24 weeks). The diagnostic interview and cognitive assessment were performed only at baseline; all three assessment points included pupillometry and measures of clinical symptoms and community functioning. Assessors were blind to treatment condition.

Treatment and Control Procedures

Both groups received 12 1-hour weekly group treatment sessions. The treatment and control conditions were matched for location, format, duration, peer interaction, didactic instruction, worksheets, and homework. All sessions were led by two cofacilitators. Participants received compensation after each session and each assessment (\$15/hour).

MI-CBT condition. The treatment manual was adapted from published motivational interviewing and CBT texts, as well as the dual-diagnosis motivational interviewing manual (25), which was designed for use in people with substance use and psychotic disorders. The sessions integrate a motivational interviewing approach focused on building motivation for goals, establishing a commitment to change, and resolving ambivalence with CBT-based behavioral activation, problem solving, and cognitive restructuring exercises. Each session followed the same structure: 1) weekly check-in: review of homework to share past-week progress and identify behavioral and cognitive facilitators and impediments to successful completion; 2) skills training: role-playing

FIGURE 1. CONSORT flowchart for a controlled trial of combined motivational interviewing and cognitive-behavioral therapy



and problem-solving exercises to address behavioral challenges, and, if applicable, cognitive restructuring exercises to identify and modify unhelpful cognitions (e.g., defeatist performance beliefs); and 3) goal setting: collaborative development of an individualized homework assignment of behavioral steps for the upcoming week. See Table S1 in the online supplement for a detailed description of the sessions.

Control condition. An adapted mindfulness-based stress reduction protocol was utilized as an active control. Session content included short videos, didactics, and experiential practice. Participants employed a variety of types of mindfulness in sessions that followed the same format as the treatment condition: 1) weekly check-in: review homework to share daily progress with practicing mindfulness; 2) skills training: introduction of new mindfulness techniques and group practice, using recorded audio or scripts read by facilitators; and 3) goal setting: collaborative development of individualized homework assignments of mindfulness techniques to practice in various settings throughout the week. Participants in this condition completed weekly mindfulness logs to record daily practice.

Treatment Quality Control and Fidelity Monitoring

The study principal investigator (PI) (L.F.R.) was the primary facilitator for 88% of the treatment and control cohorts. Facilitators, including the PI, did not conduct assessments, which were performed blind to condition. For the two

cohorts not run by the PI (one treatment and one control), the trained doctoral-level cofacilitators met with the PI weekly for supervision. Two sessions of each cohort were observed and assessed for fidelity by a senior clinical psychologist (S.G.) for those led by the PI, or by the PI for the other two; session leaders were rated on adherence to specific motivational interviewing and CBT components, as well as general group facilitation skills. The ratings were uniformly high for both conditions (>90 out of 100) across all 16 cohorts, indicating excellent mastery of the therapeutic techniques and fidelity to the protocols.

ASSESSMENTS

Symptoms

Clinical symptoms were evaluated at all three time points using the Clinical Assessment Interview for Negative Symptoms (CAINS) (4) and the expanded UCLA version of the Brief Psychiatric Rating Scale (BPRS) (26). The CAINS is a 13-item instrument that yields two subscales measuring negative symptom factors: the motivation and pleasure (MAP) subscale (one of our primary outcomes), which measures motivational negative symptoms, and the expression subscale, which measures experiential negative symptoms. The BPRS is a 24-item instrument with multiple subscales. We used the CAINS expression subscale and the BPRS subscales for positive symptoms, depression, and agitation to characterize the sample and examine the specificity of treatment effects.

Cognition

The MATRICS Consensus Cognitive Battery (MCCB) (27) was used to assess baseline cognitive functioning. It includes 10 tests measuring seven domains: speed of processing, attention/vigilance, working memory, verbal memory, visual memory, reasoning and problem solving, and social cognition. Standardized *t* scores were computed for each of the seven domains, correcting for age and gender. The composite score was based on the average *t* score from each of the domains and was used to characterize the sample.

Community Functioning

The Specific Level of Functioning Scale (SLOF) (28) assessed community functioning at the three time points. The SLOF is a 43-item report of daily behavior and functioning across a range of domains; the primary outcome variable was obtained by summing the interpersonal relationships and work skills subscales.

Pupillometry

The cognitive Deck Choice Effort Task–Pupillometry Version has been described in detail elsewhere (21, 22). Briefly, participants respond rapidly to a series of yellow or blue digits by indicating either whether the number is odd or even or whether it is lesser than or greater than five (with the question being determined by the color). There are two conditions: “easy,” in which 90% of the digits are a single color, and “hard,” in which the color changes for 90% of the trials, thereby requiring frequent switching between odd/even and lesser/greater-than decisions. Participants completed nine blocks of each condition type (easy, hard). Throughout the task, pupillometry data were acquired continuously at 220 Hz via a Viewpoint head-fixed infrared eye tracker (Arrington Research, Scottsdale, Ariz.). Periods of invalid data (e.g., during eyeblinks or saccades) were identified algorithmically and replaced with interpolated data (for additional details, see reference 22). A pupil dilation ratio trajectory was calculated for each task block by dividing pupil size at each time point during the block by the mean pupil size across the 1-second period just prior to block onset (29, 30). We then calculated an overall trajectory for each task condition by taking the median pupil ratio for each time point across all blocks in that condition. Finally, we calculated the mean pupil dilation ratio by averaging the values from the median trajectories across time, excluding the period corresponding to the first digit, to yield two dependent measures indicating pupil ratios for the easy and hard conditions.

Data Analysis

Preliminary analyses examined the two groups for baseline differences in demographic characteristics, cognition, symptoms, attendance, and the outcome measures.

We then examined the efficacy and durability of treatment effects by testing for group differences in the longitudinal trajectories of the primary outcome measures using generalized linear mixed models (GLMMs) with group (MI-CBT, control) as the between-subject factor, time (0, 12, 24 weeks)

as the within-subject factor, and a group-by-time interaction, along with subject-level random intercepts. GLMMs properly account for the correlations induced by repeated measurements within subjects and automatically handle missing data, producing unbiased parameter estimates as long as incomplete observations are missing at random (31). We fitted a single model to each outcome, encompassing both the acute treatment and follow-up periods, to maximize power and obtain consistent estimates across time points. Our aims correspond to particular contrasts within those models. Specifically, our primary efficacy hypotheses concern the group-by-time interactions from 0 to 12 weeks, corresponding to differential effects of MI-CBT compared with the control condition over the acute treatment period. Our secondary durability hypotheses, evaluated for outcomes showing acute treatment effects, involve two contrasts: the 0- to 24-week interaction, which, if significant, would imply a continued advantage of MI-CBT relative to the control condition at the end of the follow-up period, and the 12- to 24-week interaction, which would indicate whether there was a significant attenuation of that treatment benefit. Post hoc within-group contrasts provide estimates of the change in each treatment arm over the acute intervention and follow-up periods. Following current guidelines (32), the primary models were fitted without covariate adjustments.

The same GLMM approach was used to examine 1) the efficacy and durability of treatment for the secondary outcome measures related to pupillometry, and 2) the specificity of treatment effects by looking at tertiary outcomes, including experiential negative symptoms from the CAINS and the BPRS subscales. Finally, tolerability ratings were examined with one-way analyses of variance. Analyses for the two primary outcome variables were corrected for multiple comparisons using a Bonferroni adjustment (at an alpha of 0.025); all other analyses were considered exploratory. Effect sizes for the mixed models are reported as Cohen's f^2 , which indexes explained versus unexplained variability; values of 0.02, 0.15, and 0.35 are generally considered small, medium, and large, respectively (33).

RESULTS

Preliminary Analyses

There were no significant differences between the groups at baseline in demographic characteristics, symptoms, cognition, or the primary and secondary outcome variables (Table 1). The groups also did not differ significantly in treatment session attendance (average of about 9.7 out of 12 sessions in each arm).

Analyses of Treatment Efficacy and Durability

Estimated marginal means, tests of the key efficacy and durability contrasts, and corresponding effect sizes are summarized in Table 2 for all primary and secondary variables. Figure 2 shows the outcome trajectories for outcome measures that showed significant or near-significant acute

treatment effects. Figure S1 in the online supplement shows the raw means for the primary outcome variable that showed significant effects.

Primary Outcome Measures

On the CAINS MAP, there was an acute treatment effect (0- to 12-week interaction: $F=10.50$, $df=1,111$, $p=0.0016$, $f^2=0.10$) whereby the MI-CBT group showed a significant improvement ($F=26.02$, $df=1,111$, $p<0.0001$, $f^2=0.23$) but the control group did not ($F=0.16$, $df=1,111$, $p=0.6855$, $f^2=0.001$). In terms of durability, at follow-up the MI-CBT group still showed substantial (albeit somewhat reduced) gains relative to baseline ($F=15.02$, $df=1,111$, $p=0.0002$, $f^2=0.14$). However, the benefit of MI-CBT relative to the control condition was attenuated (12- to 24-week interaction: $F=5.42$, $df=1,111$, $p=0.0217$, $f^2=0.049$; 0- to 24-week interaction: $F=0.59$, $df=1,111$, $p=0.445$, no longer significant), as the control group was also somewhat improved by 24 weeks ($F=6.6$, $df=1,111$, $p=0.0111$, $f^2=0.06$). On the SLOF, there was an acute treatment effect for the 0- to 12-week interaction favoring MI-CBT, although it fell short of significance ($F=1.81$, $df=1,119$, $p=0.0722$, $f^2=0.015$). There were no other significant effects.

Secondary Outcomes and Specificity Analyses

As shown in Table 2, on the easy trials of the pupillometry task, there was a significant differential treatment effect during the acute period, such that the MI-CBT group showed an increase in average pupil dilation from baseline to post-treatment assessment, whereas the control group did not (0- to 12-week interaction: $F=5.20$, $df=1,00$, $p=0.0248$, $f^2=0.052$; MI-CBT group change: $F=7.70$, $df=1,00$, $p=0.0066$, $f^2=0.077$; control group change: $F=0.24$, $df=1,00$, $p=0.6274$, $f^2=0.024$). However, these effects did not persist over follow-up. On the hard trials, there were effects that fell short of significance suggesting differential change over the acute treatment period (0- to 12-week interaction: $F=3.26$, $df=1,00$, $p=0.0742$, $f^2=0.033$), such that dilation diameter increased from baseline to posttreatment assessment in the treatment group but not in the control group.

To examine the specificity of the MI-CBT effect on motivational negative symptoms, we fitted parallel models for the CAINS expressive negative symptoms and BPRS positive, depression, and agitation symptoms. There was no evidence of differential treatment effects on any of these measures.

Tolerability Ratings

Participants reported uniformly high tolerability ratings (rated on scales from 0 to 10). Across groups, there were high mean ratings for how much they liked the groups (mean=9.2, $SD=1.1$), how enthusiastic they considered the trainers (mean=8.9, $SD=1.4$), how well the trainers knew the material (mean=9.4, $SD=1.1$), how much the treatment helped their daily lives (mean=8.6, $SD=1.7$), and how much the treatment helped with symptoms (mean=8.6, $SD=1.8$). There were no significant between-group differences.

TABLE 1. Demographic and attendance data for participants in a controlled trial of combined motivational interviewing and cognitive-behavioral therapy^a

Characteristic or Measure	MI-CBT Group (N=41)		Control Group (N=38)	
	N	%	N	%
Male	39	95	36	95
Hispanic	4	10	5	13
Race				
Asian	2	5	1	3
Black	23	56	20	53
White	13	32	14	37
Other	1	3	2	5
	Mean	SD	Mean	SD
Age (years)	54.8	8.8	54.1	8.2
Education (years)	12.7	1.7	13.1	1.2
Sessions (0–12)	9.3	3.1	10.0	2.2
Homework (0–10)	5.8	3.7	6.7	3.6
MCCB score	32.9	12.8	33.3	9.6
UPSA-2 score	36.8	6.6	36.3	5.7

^a There were no significant differences between groups on any variable. MCCB=MATRICES Consensus Cognitive Battery; MI-CBT=motivational interviewing and cognitive-behavioral therapy; UPSA-2=UCSD Performance-Based Skills Assessment.

DISCUSSION

In this examination of a novel application of MI-CBT for motivational negative symptoms in schizophrenia, the treatment was well tolerated and feasible to administer. Participants attended the majority of sessions, completed the majority of homework assignments, and reported enjoying and benefiting from the intervention. Attrition was low and fidelity ratings were uniformly high. We found a robust treatment effect for MI-CBT that was partially maintained at follow-up for the proximal primary outcome, motivational negative symptoms. For the distal primary outcome, community functioning, we found an acute treatment effect showing improvement in the expected direction, although it did not reach statistical significance. For the pupillary biomarker measures, in one condition we found a significant interaction during the acute treatment phase, and in the other an effect that fell short of significance, suggesting that participants who received the MI-CBT intervention more effectively modulated their effort exertion on the task than those in the control condition. This study provides initial evidence, for the efficacy of motivational interviewing and CBT integrated into one cohesive treatment and applied in a group format to remediate motivational negative symptoms in schizophrenia. Our results are encouraging for psychosocial interventions aiming to improve quality of life for people with schizophrenia and indicate specific directions for future clinical research.

Our findings are consistent with recent pharmacological and neuromodulation studies showing that negative symptoms may be malleable (34, 35). Notably, this study shows significant

TABLE 2. Treatment effects for primary, secondary, and specificity measures across baseline, endpoint, and follow-up assessments in a controlled trial of combined motivational interviewing and cognitive-behavioral therapy^a

Measure and Group	Estimated Marginal Means					
	Baseline		Endpoint		Follow-Up	
	Mean	SE	Mean	SE	Mean	SD
MAP						
Control	2.11	0.12	2.05	0.13	1.75	0.13
MI-CBT	2.09	0.11	1.42	0.13	1.59	0.13
SLOF						
Control	46.9	1.47	45.90	1.61	47.63	1.63
MI-CBT	45.7	1.44	48.37	1.49	47.35	1.56
Pupil-easy						
Control	0.993	0.008	0.988	0.008	0.991	0.009
MI-CBT	0.982	0.007	1.01	0.008	0.988	0.008
Pupil-hard						
Control	1.01	0.008	0.99	0.009	1.003	0.010
MI-CBT	0.99	0.008	1.02	0.009	1.008	0.009
DAS						
Control	47.7	2.8	47.6	2.9	48.49	3.0
MI-CBT	50.2	2.7	49.6	2.8	46.99	2.8
EXP Neg						
Control	1.47	0.16	1.21	0.17	1.21	0.18
MI-CBT	1.51	0.16	0.97	0.16	0.98	0.17
BPRS						
Positive						
Control	2.13	0.14	2.03	0.15	1.92	0.15
MI-CBT	2.33	0.14	1.99	0.14	1.91	0.15
Depression						
Control	2.01	0.12	1.95	0.13	2.06	0.14
MI-CBT	2.02	0.12	1.89	0.13	1.67	0.13
Agitation						
Control	1.23	0.07	1.29	0.08	1.24	0.08
MI-CBT	1.33	0.07	1.35	0.07	1.30	0.08

^a For F statistics, degrees of freedom range from 1, 100 to 1, 125. BPRS= Brief Psychiatric Rating Scale; DAS= Defeatist Attitude Scale; EXP Neg= expression subscale of the Clinical Assessment Instrument for Negative Symptoms; MAP= motivation and pleasure subscale of the Clinical Assessment Instrument for Negative Symptoms; MI-CBT= motivational interviewing and cognitive-behavioral therapy; SLOF= Specific Level of Functioning Scale.

gains from a psychosocial intervention that is highly resource efficient. Other recent psychosocial modalities have been more demanding. For example, they may require 36–52 sessions (8, 9); rely on individual rather than group format (8); require handheld digital technology (9, 11, 36); involve home visits and in vivo trainings (37); or primarily target neurophysiology without bridges to daily functioning (34, 38). The present intervention is one that can be replicated and disseminated generally without excessive staff or equipment.

Although MI-CBT was effective in improving motivational negative symptoms, the treatment effect was less substantial on functioning. There are two possible explanations for this pattern of findings. First, the theoretical model of motivational change that underlies motivational interviewing posits a stage-like cycle of increasing motivation and activating behavior change (5, 25). Our results indicate that the intervention supports participants through early stages (i.e., attitudes about the worthiness of making changes) but

less so in later stages (i.e., sustained lifestyle and behavioral changes). Twelve weeks is a relatively short time to actualize significant alterations in domains like social connectedness or work status, and the improvements in these areas might have been more robust with a longer follow-up. Relatedly, the intervention may serve a catalytic effect within a critical window. That is, it is possible to have a treatment effect window during the weeks of active intervention and the months immediately following, in which participants are more likely to engage in other important intervention modalities that could facilitate enhanced functioning (e.g., social skills training, occupational interventions). Future studies should examine variable treatment length, with a focus on a longer intervention that incorporates booster sessions.

Second, the SLOF may be a suboptimal measure to evaluate gradual improvements in functioning. Daily functioning is a complex construct, and a measure that detects small improvements may be more appropriate for assessing meaningful change than one designed to assess global outcomes. Many

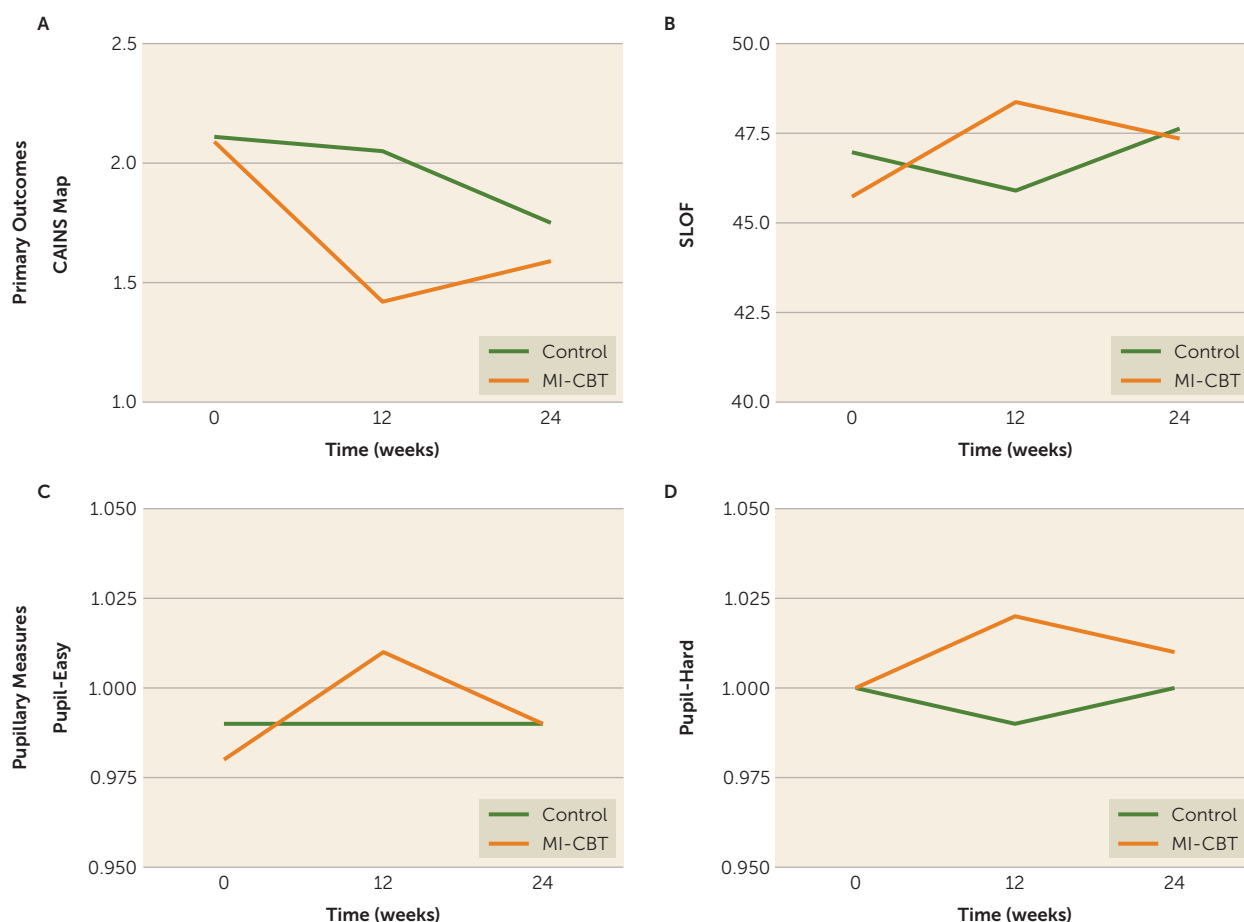
Statistics								
Acute Treatment Effect (0–12 weeks)			Durability of Treatment Effect (12–24 weeks)			Durability of Treatment Effect (0–24 weeks)		
F	p	f ²	F	p	f ²	F	p	f ²
10.5	0.001	0.10	5.42	0.02	0.05	0.59	0.45	0.01
1.81	0.072	0.02	1.26	0.21	0.01	0.45	0.65	0.01
5.20	0.025	0.05	2.57	0.11	0.03	0.30	0.59	0.00
3.26	0.074	0.03	1.02	0.32	0.01	0.49	0.49	0.01
0.02	0.882	0.00	1.07	0.30	0.01	1.47	0.23	0.01
1.41	0.238	0.01	0.00	0.96	0	0.18	0.28	0.01
1.56	0.215	0.01	0.01	0.91	0	1.22	0.27	0.01
0.14	0.712	0.001	2.41	0.12	0.02	3.8	0.05	0.03
0.17	0.680	0.001	0.01	0.92	0	0.09	0.77	0.00

participants reported meaningful and positive behavioral changes in their exit interviews. For instance, one participant reported decreasing from 30 to 15 cigarettes per day; another received a delayed eye surgery after setting the goal to improve their health; and another attained sobriety. One participant identified physical health and weight loss as her goal and established a support network, began exercising, and improved self-care and mood. A participant who had smoking cessation as a goal and cited friends who still smoked as a barrier established a new social support group of like-minded residents at his supported-living facility. Thus, it appears that meaningful changes in daily functioning were occurring for many participants, and a more granular assessment may detect intervention-related changes.

Pupillary response is a well-established indicator of effort allocation on cognitive tasks; thus, we explored its potential as a biomarker of clinical change in the treatment of motivational negative symptoms. The results suggest that it may be sensitive to treatment-related changes. Importantly, participants who received MI-CBT modulated their physiological effort exertion more effectively following the 12-week intervention than at baseline compared with control participants. This finding is encouraging given the

dearth of meaningful biomarkers and objective indices of negative symptoms. While this is the first study, to our knowledge, to examine changes in pupillary response on an effort task over a psychosocial motivational intervention for schizophrenia, other studies have shown change in pupil response to stimulation following cognitive control training, when combined with pharmacological intervention (39).

In summary, this was a rigorously controlled treatment study using an innovative and accessible intervention, and the results support the efficacy of MI-CBT for improving motivational negative symptoms. As mentioned, study limitations include the relatively short follow-up period and a potentially insufficient measurement of community functioning. In addition, the generalizability of findings from this chronically ill, predominantly male sample of veterans is unclear. The lack of an extrapyramidal side effect scale to assess primary versus secondary negative symptoms is a potential limitation. That participants were paid for attendance in the sessions also limits generalizability of feasibility to clinical settings, and the comparison with an active intervention may underestimate the treatment effect. Evidence for the efficacy of negative symptom interventions is growing, and our results provide additional support. A critical direction for future research is to translate these gains to lasting improvements in daily functioning.

FIGURE 2. Overall mixed models for primary outcomes and pupillary measures in a controlled trial of combined motivational interviewing and cognitive-behavioral therapy^a

^a CAINS MAP=motivation and pleasure subscale of the Clinical Assessment Instrument for Negative Symptoms; MI-CBT=motivational interviewing and cognitive-behavioral therapy; SLOF=Specific Level of Functioning Scale.

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**Examination Questions for A Novel Psychosocial Intervention for
Motivational Negative Symptoms in Schizophrenia:
Combined Motivational Interviewing and CBT**

- 1. Motivational Interviewing can enhance the efficacy of CBT for psychosis by:**
 - A. Improving the speed at which it works
 - B. Changing the therapeutic focus of the CBT intervention
 - C. Augmenting intrinsic motivation for engaging in the therapy itself
 - D. Motivating the therapist
- 2. Negative symptoms are considered an unmet treatment need because:**
 - A. They are a primary determinant of poor functional outcomes
 - B. They interfere with the drugs targeting positive symptoms
 - C. They are treatment resistant
 - D. No efforts have been made to intervene at the level of negative symptoms
- 3. During cognitive tasks, pupillary response is a well-established indicator of:**
 - A. Cardiorespiratory fitness
 - B. Processing speed
 - C. Cognitive control
 - D. Effort allocation