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Research Paper

Differential improvement of negative-symptom subfactors after cognitive remediation in low-functioning individuals with schizophrenia

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ABSTRACT

Background: Negative symptoms and cognitive deficits have a substantial predictive value for functional deficits and recovery in schizophrenia. However, the relationship between negative symptoms and cognitive abnormalities is unclear possibly due to the heterogeneity of negative symptoms. This study used the model of expressive and experiential negative symptoms subfactors to decrease this heterogeneity. It examined these subfactors and cognition before and after treatment with computerized cognitive remediation training (CRT) in chronically-hospitalized individuals with psychosis and predominant negative symptoms.

Methods: Seventy-eight adult participants with a DSM-IV-TR diagnosis of schizophrenia or schizoaffective disorder were enrolled in a 12-week CRT program. Assessments of demographic and illness variables, baseline and endpoint assessments of psychopathology (Positive and Negative Syndrome Scale) and cognition (MATRICS Consensus Cognitive Battery - MCCB) were conducted.

Results: The baseline expressive negative subfactor was associated with Processing Speed ($r = -0.352$, $p \leq 0.001$) and Reasoning/Problem Solving ($r = -0.338$, $p \leq 0.001$). Following CRT, there was a significant decrease in the experiential negative subfactor ($p < 0.01$) but not of the expressive negative subfactor. Change in MCCB domains after CRT accounted for 51.1% and 50.2% of the variance of change in expressive and experiential negative subfactor scores, respectively. For both subfactors, Visual Learning was a significant predictor of change ($p < 0.05$).

Conclusion: Our findings suggest that CRT has benefits for negative symptoms in very low-functioning patients and that this change may be in part mediated by change in cognitive functions after CRT.

1. Introduction

Negative symptoms and cognitive deficits have a substantial predictive value for functional deficits and are important to recovery in schizophrenia (Green et al., 2012; Kahn and Keefe, 2013; Strassnig et al., 2015), but the relationship between specific cognitive abnormalities and negative symptoms is unclear. Although cross-sectional studies suggest an inverse correlation between negative symptoms and several cognitive domains, only a limited proportion of the variance of negative symptoms is explained by cognitive deficits (Bozikas et al., 2004; Nieuwenstein et al., 2001). This may be due to the heterogeneous nature of negative symptoms and their different neural underlying mechanisms. A better approach to study their variance with cognition may be to define more homogeneous subgroups of negative symptoms. Factor analyses with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) corroborate this approach by moving from a one-factor model to a two-factor structure of PANSS-measured negative symptoms. In exploratory and confirmatory factor analyses, Liemburg et al. (2013) found an “expressive deficit” (or expressive negative) subfactor that includes flat affect (N1 of the Negative PANSS items), poor rapport (N3), lack of spontaneity and flow of conversation (N6), mannerisms and posturing (G5), motor retardation (G7), and disturbance of volition (G13), and a “social amotivation” (or experiential negative) subfactor comprising emotional withdrawal (N2), passive/

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apathetic social withdrawal (N4), and active social avoidance (G16). This two-subfactor structure using PANSS negative item data from different patient samples was replicated by several other studies (Fervaha et al., 2014; Jang et al., 2016; Khan et al., 2017; Stiekema et al., 2016) confirming the same PANSS items for the social amotivation subfactor. For the expressive negative subfactor, PANSS items were the same across studies except for the PANSS disturbance of volition item (G13), which was included in only two studies (Liemburg et al., 2013; Stiekema et al., 2016), but not in the other three studies (Fervaha et al., 2014; Jang et al., 2016; Khan et al., 2017). Another negative symptom structure has been proposed more recently using different negative symptom scales. It suggests that a five-factor model may fit better than a two-factor model for negative symptoms rated with the Scale for the Assessment of Negative Symptoms (SANS), the Brief Negative Symptom Scale (BNSS), and the Clinical Assessment Interview for Negative Symptoms (CAINS) (Marder and Galderisi, 2017; Strauss et al., 2018). However, little is known about the association with cognitive symptoms of these five subfactors. Regarding the relationship of the two PANSS negative-symptom subfactors with cognitive symptoms, Jang et al. (2016) found that the expressive negative subfactor, but not the experiential negative subfactor, was correlated with poorer performance on the Trail Making Test – B, suggesting an association between the expressive negative subfactor and impaired executive function. This association suggests that treatment interventions targeting cognitive deficits could have an impact on the expressive negative subfactor. Recent studies also suggest that cognitive remediation can improve the experiential negative subfactor. Ventura et al. (2019) reported in first-episode-psychosis patients a positive effect of cognitive remediation training (CRT) on both the expressive and experiential negative symptoms of SANS-measured negative symptoms, while Cella et al. (2017) found in 309 subjects with schizophrenia and relatively low level of negative symptoms a beneficial effect of CRT on a subset of negative symptoms characterized by less expressive and more behavioral features immediately following therapy, but not retained at follow-up. To date, there are no studies assessing the effect of cognitive remediation on the PANSS two-subfactor negative symptom structure in individuals with chronic schizophrenia and severe psychopathology.

Cognitive remediation has shown significant gains in addressing changes in cognition in schizophrenia. A meta-analysis of 26 CRT outcome studies showed improvement of cognition with a medium effect size of 0.41 (McGurk et al., 2007; Wykes et al., 2011). Cognitive remediation has been known to be most effective when combined with comprehensive psychiatric rehabilitation (Choi and Medalia, 2005). Hence, it is important to examine the effect of CRT on specific negative-symptom subfactors in very established and low-functioning patients as this may further help in elucidating more precise treatment targets for CRT.

We previously reported that treatment with computerized cognitive remediation improved cognitive performance in specific cognitive domains based on 12-week randomized trials of patients with chronic schizophrenia (Lindenmayer et al., 2008; Lindenmayer et al., 2017; Lindenmayer et al., 2018). The objective of the present post hoc analysis was to explore the association between cognitive performance and negative-symptom subfactors with the aims to (1) examine the cognitive correlates of the expressive and experiential negative subfactors at baseline; and (2) to assess the effect of CRT on these subfactors in a sample of chronically-hospitalized individuals with schizophrenia characterized by predominant negative symptoms. Based on the results of previous studies, we hypothesized (1) an association between the expressive negative subfactor and executive function; and (2) an improvement in experiential negative subfactor following CRT.

2. Material and methods

We conducted a post hoc analysis based on data from a previously reported randomized, 12-week study with CRT (Lindenmayer et al., 2018). Study conduct was consistent with the Declaration of Helsinki and in accordance with Good Clinical Practices as required by the International Conference on Harmonization guidelines. All subjects provided written informed consent prior to study enrollment, and were enrolled from November 2012 to April 2017. The trial protocol was approved by the institutional review board at Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY (ClinicalTrials.gov: NCT01036282).

2.1. Subjects

Subjects participating in this study were age 18 to 60, predominantly inpatients in a long-term tertiary care psychiatric center, diagnosed with schizophrenia or schizoaffective disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV-TR) (American Psychiatric Association, 2000), on a stable dose of antipsychotic medication for at least 4 weeks prior to enrollment, and a Mini-Mental State Exam (MMSE) score of 24 or higher. Participants were assessed by trained clinical and cognitive raters at baseline and after 12 weeks for neurocognition, social cognition, psychopathology, and functioning.

2.2. CRT program

CRT consisted of approximately 36 sessions of computerized cognitive remediation exercises utilizing COGPACK (Geibel-Jakobs and Olbrich, 1998) or BrainHQ (Fisher et al., 2009). The COGPACK (COGPACK, version 6.0, Marker Software, Ladenburg, Germany, http://www.cogpack.de/) computer program facilitates practice across a broad range of cognitive functions, including attention and concentration, psychomotor speed, learning and memory, and executive functioning. The curriculum for the COGPACK exercises was manualized with a general progression from easier to more difficult tasks and through cognitive domains in the order described above. BrainHQ targets cognitive ability hierarchically in an adaptive design, with repeated exercises aimed at lower cognitive levels (e.g., auditory perception) then advances to more complex cognitive constructs, such as verbal memory (Mahncke et al., 2006). All subjects received performance scores on their accuracy and speed after completing each exercise, which were recorded in the computer and used to reinforce participants to further progress on their performance. For BrainHQ, performance was rewarded using visual and auditory enhancements, animated graphics, and an accretion of points for each trial that was successfully completed. For both COGPACK and BrainHQ, there was flexibility in the curriculum allowing for individualized instruction and support. COGPACK and BrainHQ sessions were co-facilitated by a Clinical Psychologist and an MA-level Psychology graduate student, and were held in groups of 5–8 participants to facilitate individualized feedback. Sessions were 40 minutes long and held three times a week. Half of the group also received once per week an augmentation of CRT using the Mind Reading program (Baron-Cohen et al., 2004), which is an interactive, computerized social cognition program practicing the recognition of emotions. All participants engaged in weekly discussion groups (Bridging Groups). The Bridging Groups were structured with detailed manuals and the goals were to review with subjects how to apply newly-acquired cognitive skills to everyday tasks and to promote socialization (McGurk et al., 2009; McGurk et al., 2017). All participants were concurrently involved in a weekly 20-hour rehabilitation program as part of their in- and outpatient treatment. There was no formal integration of this concomitant rehabilitation program with the study intervention beyond the customary interdisciplinary staff communications (for more details see Lindenmayer et al., 2008).

2.3. Assessments

Symptom assessments were conducted at baseline and endpoint by trained raters with good inter-rater reliability for the PANSS (Intraclass Correlation Coefficient, ICC > 0.80). PANSS is a widely-used instrument for the clinical assessment of symptoms in schizophrenia. We used the results of the factor analysis described by Khan et al. (2017), which found a negative-symptom factor consisting of an expressive negative subfactor (PANSS items N1, N3, N6, and G7), and an experiential negative subfactor (N2, N4, and G16). We did not use the model of Liemburg et al. (2013), which includes disturbance of volition (PANSS G13 item) in the expressive negative subfactor. G13 item is defined as "disturbance in the willful initiation, sustenance and control of one's thoughts, behavior, movements and speech", and was not endorsed by our participants with a high frequency. In contrast to our study, Liemburg et al. (2013) included subjects with recent onset of psychosis and did not rule out secondary negative symptoms. It has been suggested that disturbance of volition is more prevalent in the early stages of schizophrenia (Fervaha et al., 2017) and associated with depression (Krynicki et al., 2018).

Cognition was assessed with the Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery (MATRICS Consensus Cognitive Battery - MCCB) (Nuechterlein et al., 2008; Kern et al., 2008). The MCCB subtests are organized into the following 7 domains: (1) Speed of Processing: Trail Making Test, Brief Assessment of Cognition Symbol Coding, and Category Fluency; (2) Attention/Vigilance: Continuous Performance Test-Identical Pairs; (3) Working Memory: Wechsler Memory Scale–III Spatial Span and Letter-Number Span; (4) Verbal Learning: Hopkins Verbal Learning Test-Revised; (5) Visual Learning: Brief Visuospatial Memory Test-Revised; (6) Reasoning and Problem Solving: Neuropsychological Assessment Battery Mazes; and (7) Social Cognition: Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) Managing Emotions. T-scores were created for each of the seven cognitive domains and an overall composite score, which was the primary efficacy outcome, and a neurocognitive composite score, which included T-scores for 6 domains, excluding the social cognition domain.

2.4. Data analyses

Analyses were performed for subjects who completed both baseline and endpoint MCCB and PANSS evaluations, regardless of the number of CRT sessions completed. Descriptive statistics were computed as mean and standard deviation (SD) or median and interquartile range for continuous variables, and as absolute and relative frequencies for categorical variables. Data were examined for normality and univariate outliers before analyses. The distributions of the MCCB Visual Learning, and Reasoning and Problem-Solving domains were skewed toward more impairment. Reflected log transformations improved the distributions and were used in further analyses of comparisons. All statistical tests were conducted using SPSS 21.0 (IBM Corporation, 2012) and R (R Development Core Team, 2013).

2.4.1. Correlations

The association between PANSS expressive and experiential negative subfactors, and cognitive domains and composite scores was computed using a correlational analysis. A partial correlation was determined to control the potential influence of education level on the relationship between the subfactor scores and cognitive scores. To avoid erroneous inferences due to multiple testing, an association between variables was considered substantive if the correlation coefficient was at least 0.3 (Hinkle et al., 1988) with a significance level of 0.001.

2.4.2. Paired t-tests

Paired *t*-tests were calculated to assess changes in negative-symptom subfactor scores between baseline and end of study. Post hoc *t*-tests were performed to compare differences between expressive and experiential negative subfactor scores from baseline to endpoint. Cohen's d was used as the appropriate effect size measure since baseline and end-of-study scores had similar standard deviations and were of the same sample size. Cohen's d was determined by calculating the mean difference between baseline and end-of-study scores, and then dividing the result by the pooled standard deviation: Cohen's d = $(M2 - M1) / SD_{pooled}$, where $SD_{pooled} = \sqrt{((SD_1^2 + SD_2^2) / 2)}$.

2.4.3. Stepwise regression analysis

Stepwise multiple linear regressions were performed based on change in each MCCB domain T-Score to determine the role of these variables in explaining the change scores (endpoint score minus baseline score) of the two negative-symptom subfactors. Change scores of the two negative-symptom subfactors were considered dependent variables. MCCB domains were ordered based on results of a prior study, which assessed the same population of subjects and showed that Processing Speed, Attention/Vigilance and Working Memory were predictors of improvement following cognitive remediation therapy (Lindenmayer et al., 2017). MCCB domains were entered as Speed of Processing (step 1), Attention/Vigilance (step 2), Working Memory (step 3), Verbal Learning (step 4), Visual Learning (step 5), Reasoning/Problem Solving (step 6), and Social Cognition (step 7). A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Subjects

One-hundred-thirty-one subjects were enrolled in the study, and 53 participants did not have endpoint evaluations due to the following reasons: 22 were discharged to the outpatient clinic and did not attend the CRT program in the outpatient clinic, 6 were hospitalized for medical reasons, 18 withdrew from treatment (14 completed only partial baseline assessments, and 4 were screened and randomized but did not begin treatment), 3 were arrested, and 4 subjects were transferred to another inpatient facility. Seventy-eight subjects (56 men and 22 women) completed baseline and endpoint MCCB and PANSS evaluations. Average age of study participants was 40.33 (SD = 12.74, range = 18–55) with an average duration of illness of 14.78 years (SD = 9.10). All subjects were on stable antipsychotic medication with a mean chlorpromazine equivalent dose of 496.56 mg (SD = 116.78) and their extrapyramidal symptoms were low (mean at baseline = 2.75; mean at endpoint = 3.11). The mean of participants' Personal and Social Performance Scale (PSP) total scores was 54.13 (SD = 13.55). Other demographic characteristics are reported in Table 1.

3.2. Associations between negative-symptom subfactors and cognition

At baseline, there were significant negative correlations between the

Table 1
Demographic characteristics.

	Mean (SD)
Age (years)	40.33 (12.74)
Length of stay (LOS, months)	12.55 (4.53)
Education (years)	9.01 (2.55)
Total antipsychotic dose (chlorpromazine equivalents)	496.56 (116.78)
	N
Sex (M/F)	56/22
PANSS (total)	74.50 (8.93)
PANSS (negative)	19.76 (3.05)
PSP (total)	54.13 (13.55)
Treatment sessions completed	
Completed 36 sessions:	54
Completed < 36 sessions:	24
Diagnosis (schizophrenia/schizoaffective)	81%/19%

PANSS = Positive and Negative Syndrome Scale; PSP = Personal and Social Performance Scale.

Table 2
Baseline correlations between negative symptom subfactors and MCCB domain T-Scores and overall composite T-Scores.

		SoP	A/V	WM	VL	ViL	R/PS	SC	COMPOSITE
Expressive negative subfactor	Pearson correlation	−0.352*	−0.190	−0.155	−0.144	−0.152	−0.338*	−0.124	−0.253
	Sig. (2-tailed)	≤0.001	0.043	0.094	0.119	0.101	≤0.001	0.183	0.007
	N	118	114	117	118	118	117	117	113
Experiential negative subfactor	Pearson correlation	−0.134	−0.174	−0.067	−0.066	0.083	−0.197	−0.056	−0.106
	Sig. (2-tailed)	0.147	0.065	0.475	0.478	0.369	0.033	0.545	0.263
	N	118	114	117	118	118	117	117	113

SoP = Speed of Processing; A/V = Attention/Vigilance; WM = Working Memory; VL = Verbal Learning; ViL = Visual Learning; R/PS = Reasoning/Problem Solving; SC = Social Cognition.

* Correlation is significant at the 0.001 level (2-tailed).

expressive negative subfactor score and Processing Speed (r = −0.352, p = 0.001), and Reasoning/Problem Solving (r = −0.338, p = 0.001). There were no significant correlations between the experiential negative subfactor and any cognitive domains (see Table 2).

3.3. Changes in negative-symptom factor and subfactor scores following cognitive remediation

Change in the negative-symptom factor score was significant (t = 2.524, p = 0.014) from baseline (mean = 17.79, SD = 3.73) to endpoint (mean = 16.68, SD = 3.68); effect size, Cohen's d = 0.29. There was a significant change between baseline (mean = 8.36, SD = 1.96) and end of the study (mean = 7.73, SD = 1.89) of the experiential negative subfactor Score (t = 2.695, p = 0.009); effect size, Cohen's d = 0.51. There was no significant change in the expressive negative subfactor Score (t = 1.276, p = 0.206) from baseline (mean = 9.43, SD = 2.42) to endpoint (mean = 8.99, SD = 2.28); effect size, Cohen's d = 0.19.

3.4. Stepwise regression analysis

Changes from baseline to endpoint of each MCCB domain were included as predictors in the stepwise regression model and changes from baseline to endpoint of the two negative-symptom subfactors were the dependent variable. The regression model of the expressive negative subfactor accounted for 51.1% of the variance (Table 3) and the regression model of the experiential negative subfactor accounted for 50.2% of the variance (Table 4). The results of the stepwise regression analysis of Speed of Processing (step 1), Attention/Vigilance (step 2), Working Memory (step 3), Verbal Learning (step 4), Visual Learning (step 5), Reasoning/Problem Solving (step 6), and Social Cognition (step 7) are presented in Tables 3 and 4. For both negative-symptom subfactors, only Visual Learning was a significant predictor of change ($p < 0.05$).

4. Discussion

In this hospital-based study, individuals with chronic schizophrenia

Table 3
Stepwise regression analysis of MCCB domain T-Scores associated with change in expressive negative subfactor score in individuals with schizophrenia.

Factor	β	SE	Beta	t	p-Value
Speed of Processing	−0.020	0.085	−0.188	−0.056	0.190
Attention/Vigilance	−0.10	0.086	−0.355	−0.178	0.187
Working Memory	1.67	0.971	−1.001	−1.090	0.099
Verbal Learning	0.23	0.022	0.377	1.001	0.100
Visual Learning	3.78	0.927	1.367	2.663	0.020
Reasoning/Problem Solving	0.16	0.087	0.187	0.066	0.176
Social Cognition	0.07	0.070	0.145	0.057	0.199

Notes: Standardized regression coefficient: Beta; $R^2 = 0.511$, $F = 3.220$, $P = 0.022$.

Table 4
Stepwise regression analysis of MCCB domain T-Scores associated with change in experiential negative subfactor score in individuals with schizophrenia.

Factor	β	SE	Beta	t	p-Value
Speed of Processing	−0.043	0.099	−0.19	−0.065	0.201
Attention/Vigilance	−0.21	0.101	−0.379	−0.199	0.145
Working Memory	1.89	0.991	0.98	1.908	0.090
Verbal Learning	0.34	0.029	0.39	0.980	0.111
Visual Learning	3.19	0.909	1.56	2.561	0.029
Reasoning/Problem Solving	0.21	0.099	0.199	0.099	0.154
Social Cognition	0.10	0.064	0.135	0.076	0.178

Notes: Standardized regression coefficient: Beta; $R^2 = 0.502$, $F = 3.12$, $P = 0.025$.

undergoing CRT experienced improvement in both the negative-symptom factor and the experiential negative subfactor. In addition, we found at baseline that the expressive negative subfactor correlated with specific cognitive domains suggesting that affective flattening and alogia, but not emotional and social withdrawal, are associated with executive function. While there was a significant improvement of the experiential negative subfactor after CRT, there was no change of the expressive negative subfactor. Finally, a specific cognitive domain (Visual Learning) predicted some of the variance of change in both expressive and experiential negative subfactors.

Our findings are supported by the results of the meta-analysis by Cella et al. (2017), which reported a significant effect of CRT on negative symptoms with an overall effect size of 0.39 (Hedges g). Our slightly lower effect size of 0.29 is most likely due to the marked chronicity and low-level functioning of our participants. In contrast to our observed significant improvement of only the experiential negative subfactor, Ventura et al. (2019) found that both expressive and experiential domains significantly improved after CRT. However, participants in their study were much younger and had a recent first-episode of psychosis compared to our older and more chronic participants, which may explain this discrepancy.

The association between the baseline expressive negative subfactor and concurrent deficits in specific cognitive domains (Speed of Processing and Reasoning/Problem Solving) corroborate previous findings of an association between PANSS expressive negative symptoms and Speed of Processing suggesting that expressive negative symptoms are related to impaired executive function (Jang et al., 2016). Studies with the Scale for the Assessment of Negative Symptoms (Andreasen, 1989) also reported an association between expressive negative symptoms and cognitive deficits (Hartmann-Riemer et al., 2015), as well as Working Memory and executive functioning (Ergül and Üçok, 2015). In contrast to studies using the SANS, we did not find an association between experiential negative symptoms and cognitive deficits.

Following CRT, there was a significant decrease in negative-symptom factor and experiential negative subfactor scores. The latter two constructs include emotional withdrawal (PANSS N2 item) and it has been suggested that improved socialization is associated with less emotional withdrawal (Siegrist et al., 2015). Subjects participated in a weekly Bridging Group, which facilitated transfer of cognitive practice into everyday activities. It took place in a group-format, which offered and stimulated interactions between participants. In addition, CRT was embedded in a regular rehabilitative setting as described by Lindenmayer et al. (2008). Finally, all CRT sessions were facilitated by trained facilitators who actively interacted with all participants to support their progression with the CRT exercises, did troubleshooting, and spent time with participants on difficult exercises. Our results also corroborate a previous report that social skills training improved SANS-measured diminished motivation but not diminished expression (Granholm et al., 2014).

We found that change in the Visual Learning domain after CRT was a significant predictor of change in both negative subfactors. This relationship may have been mediated by our social cognition program. Participants practiced visual recognition of facial emotions. Importantly, all CRT and social cognition exercises included a variety of visual aids such as vignettes or videos of social situations with reward stimuli. Furthermore, visual presentations and explanations by the group facilitator about the goal of CRT together with discussion of how to transfer CRT practices to everyday situations were always done in group settings. Thus, Visual Learning may be a promising moderator and treatment target for improving negative symptoms in future CRT interventions.

Our study has some limitations. Our sample size was small and this was a post hoc analysis which carries the risk of erroneous inferences due to multiple testing. To minimize this risk, we used a significance level of < 0.001 to identify significant correlations. It included participants with chronic illness and did not have a comparison sample with acute participants. Therefore, our results only apply to subjects with a chronic course. PANSS negative symptoms items may not include all the dimensions of negative symptoms (Blanchard and Cohen, 2006), and are mostly based on observed behavior and not on subjective accounts by subjects of negative symptoms (Fervaha et al., 2014). The two-factor model may be an artifact because of different rating methods between the two factors: the rating of expressive negative symptoms is based on direct observation during the interview, while the rating of the experiential negative symptoms is based in part on reports of social activities outside of the interview. This results in correlated errors among items leading to an overestimation of the reliability of these factors (Liemburg et al., 2013).

Within these limitations, our study confirms the two-factor structure of negative symptoms assessed with the PANSS consisting of expressive and experiential negative symptoms in individuals with severe and extensive psychopathology. In these chronically-hospitalized participants characterized by predominant negative symptoms, we found a significant decrease in experiential negative symptoms following CRT but not in the expressive deficit. Visual Learning predicted some of the variance in change of the expressive and experiential negative symptoms and may therefore serve as an important target for CRT. Our results point out the strength of CRT in ameliorating not only cognitive deficits, but also negative symptoms, particularly when applied within an inpatient rehabilitation setting for patients with low levels of functioning. It remains to be explored whether more active and more intensive social cognition interventions could also ameliorate the expressive deficits. Such techniques may lead to novel therapeutic approaches for the treatment of both the expressive and experiential negative symptoms in schizophrenia.

Contributors

SS, JPL, and AK designed the study, oversaw data collection and data analyses, contributed to data interpretation and manuscript preparation. IL facilitated the CRT sessions and OJ prepared the database. MKCK contributed to the manuscript preparation. All authors have approved the final manuscript.

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None.

Conflicts of interest statement

None.

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