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Modeling the role of negative symptoms in determining social functioning in individuals at clinical high risk of psychosis

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ABSTRACT

A priority for improving outcome in individuals at clinical high risk (CHR) is enhancing our understanding of predictors of psychosis as well as psychosocial functioning. Social functioning, in particular, is a unique indicator of risk as well as an important outcome in itself. Negative symptoms are a significant determinant of social functioning in CHR individuals; yet, it is unclear which specific negative symptoms drive functional outcome and how these symptoms function relative to other predictors, such as neurocognition and mood/anxiety symptoms. In a sample of 85 CHR individuals, we examined whether a two-factor negative symptom structure that is found in schizophrenia (experiential vs expressive symptoms) would be replicated in a CHR sample; and tested the degree to which specific negative symptoms predict social functioning, relative to neurocognition and mood/anxiety symptoms, which are known to predict functioning. The two-factor negative symptom solution was replicated in this CHR sample. Negative symptom severity was found to be uniquely predictive of social functioning, above and beyond depression/anxiety and neurocognition. Experiential symptoms were more strongly associated with social functioning, relative to expression symptoms. In addition, experiential symptoms mediated the relationship between expressive negative symptoms and social functioning. These results suggest that experiences of motivational impairment are more important in determining social functioning, relative to affective flattening and alogia, in CHR individuals, thereby informing the development of more precise therapeutic targets. Developing novel interventions that stimulate goal-directed behavior and reinforce rewarding experiences in social contexts are recommended.

1. Introduction

An emerging priority in the clinical high risk (CHR) field is improving our understanding of factors that lead to transition to a psychotic disorder as well as improving outcomes for those who may not transition, yet remain functionally impaired. Above and beyond attenuated psychotic symptoms, social functioning is a significant predictor of whether an individual may develop psychosis (Cannon et al., 2008; Cornblatt et al., 2012; Fusar-Poli et al., 2012). Further, for those who are ascertained to be at-risk, but do not develop psychosis over the follow-up period, at least half remain socially impaired (Addington et al., 2011; Schlosser et al., 2012). By improving our understanding of social functioning in this population, therapeutic targets may be developed to significantly improve outcome and possibly even prevent the onset of psychosis.

Current research into the determinants of social functioning impairments in CHR individuals highlights the role of negative symptoms, mood, and cognitive deficits (Carrión et al., 2011; Cornblatt et al., 2007; Fulford et al., 2013; Meyer et al., 2014).While depressive symptoms may be associated with poorer global and social functioning in CHR individuals (Fulford et al., 2013), the largest study conducted to date ($n = 167$) found that negative symptom severity was substantially predictive of baseline and longitudinal social functioning, above and beyond neurocognition and other symptom domains. Further, negative symptoms were shown to mediate the relationship between global neurocognition and social functioning (Meyer et al., 2014). Prior studies have tended to focus on identifying the specific *cognitive* impairments that are uniquely predictive of social functioning, such as deficits in executive functioning and processing speed (Carrión et al., 2011; Eslami et al., 2011). However, it is unclear what *negative symptoms* drive functional impairment in this population.

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Recent research investigating the structure of negative symptoms in schizophrenia has shown that these symptoms are most parsimoniously explained by a solution consisting of two independent factors: experience and expression (Blanchard and Cohen, 2006; Foussias and Remington, 2010; Kring et al., 2013). The experiential negative symptom factor encompasses avolition (decreased motivation), anhedonia (decreased experience of pleasure) and asociality (decreased value for social contact). The expressive factor, on the other hand, captures both emotional expressivity and alogia, or poverty of thought as evidenced by decreased speech output. In individuals with schizophrenia, experiential symptoms more robustly predict functional outcome than expressive deficits (Green et al., 2012; Rassovsky et al., 2011). No studies to our knowledge have been conducted on the influence of specific negative symptoms on functioning in CHR individuals, nor have any studies replicated whether the two-factor solution is applicable in this population. By improving our understanding of the relative influence of experiential vs expressive symptoms on social functioning, we may be able to refine treatment strategies and intervene with a higher degree of precision. For instance, experiential symptoms appear to be more modifiable than expressive symptoms, using adapted cognitive behavioral therapy (CBT) (Velthorst et al., 2014), and emerging data suggests that emotional expressivity in schizophrenia may be improved via intranasal oxytocin (Woolley et al., 2015).

In across-sectional analysis, we initially examined whether the two-factor negative symptom structure would be replicated in a CHR sample. We then applied path analysis to evaluate theoretically driven models to examine the negative symptom determinants of social functioning in CHRs. Based on prior research, we also included neurocognition and depressed mood into our analyses as predictors of functioning. We hypothesized that 1) both expressive and experiential negative symptoms would be robust predictors of social functioning, above and beyond mood symptoms or neurocognition, and 2) consistent with findings in schizophrenia, experiential symptoms would be more strongly associated with social functioning than expressive symptoms.

2. Methods

2.1. Participants

The study included 85 CHR participants who were recruited from the Prodrome Assessment, Research and Treatment (PART) program at the University of California, San Francisco. Participants were recruited from community mental health centers, outpatient clinics, local schools, and universities. CHR status was ascertained using the Structured Interview for Prodromal States (SIPS, version 4.0; Miller et al., 2002). Participants were included in the study if one or more of the following criteria were met: 1) the presence of attenuated positive, psychotic symptoms, occurring at least weekly with onset or worsening in the past year, 2) brief intermittent psychotic symptoms, with an onset in the prior three months, or 3) a 30% decline in global functioning (GAF) score over the past year, plus either a diagnosis of schizotypal personality disorder or a first degree relative with a psychotic disorder. Inclusion criteria were: 1) clinically stable (no hospitalization within the past 3 months and, if on medication, stable dose over the past month); 2) good general health; 3) fluent and proficient in English; 4) IQ ≥ 70 (WASI, 1st edition, 2 subtest version: Vocabulary and Matric Reasoning); 5) no substance dependence or significant use that would interfere with study participation; and 6) between the ages of 12 and 35.

2.2. Procedure

All participants provided written informed consent or assent for the study and were compensated for their participation. Parental informed consent for minors was also obtained. Once an intake evaluation determined study eligibility, participants underwent a series of structured clinical assessments, symptom and functioning measures, and neurocognitive testing. Advanced graduate students, predoctoral interns, and postdoctoral fellows administered the study-related assessments.

2.3. Measures

Symptom severity was assessed using the SIPS and the accompanying Scale of Prodromal Symptoms (SOPS), the Scale for the Assessment of Positive Symptoms (SAPS), the Scale for the Assessment of Negative Symptoms (SANS), and the Brief Psychiatric Rating Scale (BPRS). The SANS includes global ratings of four negative symptoms: affective flattening, alogia, anhedonia/asociality, and avolition/apathy. A depression–anxiety composite score was computed from the BPRS, which is based on a recent factor analysis (Kopelozicz et al., 2008) that included the following scale items: anxiety, depression, suicidality, and guilt. Social functioning was measured using the Global Functioning: Social Scale (GF-S; Cornblatt et al., 2007).Cognitive functioning was measured using the abbreviated battery of Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS). The abbreviated battery included the assessment of the following domains: speed of processing (Trail Making Test Part A; category fluency animal naming); working memory (letter–number span; WMS-III spatial span); verbal learning and verbal memory (HVLT-R immediate and delayed recall); visual learning and visual memory (BVMT-R immediate and delayed recall); and problem solving (D-KEFS Tower Test). We used the global cognition composite score from the MATRICS battery as a measure of overall cognitive functioning.

2.4. Data analysis plan

First, the data were examined for normality and we examined whether demographic characteristics were associated with social functioning. Second, we computed zero-order correlations to investigate possible associations between social functioning, experiential and expressive negative symptoms, depression–anxiety, and global cognition composite scores. Third, we sought to replicate the two-factor solution of negative symptoms commonly found in people with schizophrenia (Blanchard and Cohen, 2006; Kring et al., 2013; Foussias and Remington, 2010) in a CHR sample. To do this, we conducted a principal component analysis with an Oblimin rotation on all items comprising the Scale for the Assessment of Negative Symptoms, with the global items removed. Fourth, to investigate whether experiential and expression negative symptoms were predictive of social functioning, we estimated and tested a hierarchical linear regression model. Given previous research showing a relationship between symptoms of depression and social functioning (Fulford et al., 2013), we entered the BPRS depression–anxiety composite score as a first level predictor of social functioning. At the second level, we added the expression negative symptom composite, followed by the experiential negative symptom composite at the third level. For the hierarchical linear regression model, we report unstandardized regression coefficient estimates, standard errors, and F-values for the changes in R-squared. Based on these regression models, we then estimated and tested mediated path models to better understand the relationship between the significant predictors and social functioning.

The hypothesized paths were estimated using Mplus (Mplus 7.3). The relationship between the measured variables was estimated using the sample covariance matrix. The hypothesized latent structure was then tested by fitting the measurement model, linking the latent variables to their indicators. Path coefficients displayed in the figure represent the impact of changes in a single predictor variable on a dependent variable, while holding other variables in the model constant. Direct effects indicate the impact of the independent variable (X) on the dependent variable (Y); specific indirect effects denote the product of the relationship between X and the mediator (M) and the relationship between M and Y. We report direct and specific indirect effects for the

two competing models. For each path, the standardized regression coefficient β, the standard error estimates and the *p*-value are reported. Model fit results are also reported: χ^2, the Root Mean Square Residual (RMR scores close to 0 indicate good model fit); and the Akaike Information Criterion (AIC, a comparative measure of model fit in which lower values suggest a better fit). Analyses were performed with an alpha level of 0.05.

3. Results

Demographic and clinical data are reported in Table 1. Participant age, gender, education, and global cognition scores were not associated with social functioning, experiential, or expression negative symptoms. We found no gender differences in any demographic or clinical variables.

Although the sample size was not ideal for a factor analysis, Kaiser–Meyer–Olkin measure of sampling adequacy was .77, and Bartlett's Test of Sphericity was significant, $\chi^2\,(171) = 798.97$, $p < .001$, indicating that a factor analysis was appropriate for these data. Consistent with findings in people with schizophrenia (Blanchard and Cohen, 2006; Kring et al., 2013; Foussias and Remington, 2010), we replicated the two-factor solution of negative symptoms in our CHR sample, which explained a total of 42.89% of the variance. All individual experiential items loaded between .35 and .66 on the experiential factor, and all expressive items loaded between .39 and .88 (see Table 2). No items cross-loaded higher on the other factor. Consistent with previous research in schizophrenia, two attention items did not load on either factor (Blanchard and Cohen, 2006). We then used the two independent factors (experience and expression) in our subsequent analyses.

Table 3 includes the results of the bivariate correlations between social functioning, experiential and expression negative symptoms, global cognition and depression–anxiety scores. We found significant negative correlations between social functioning and experiential ($r = -.61$, $p < .01$) and expression($r = -.30$, $p < .01$) negative symptoms. Social functioning was not related to global cognition ($p = .73$) or depression–anxiety ($p = .22$). More severe symptoms of depression–anxiety, however, were associated with greater experiential ($r = .31$, $p < .01$), but not expression negative symptoms, ($r = -.02$, $p = .88$) and experiential symptoms were significantly associated with expressive symptoms ($r = .38$, $p = .01$).

The results of the hierarchical linear regression model are reported in Table 3. Given the significant correlation between experiential negative symptoms and symptoms of depression–anxiety, this composite variable was entered as a first level predictor, followed by expression symptoms at level two and experiential symptoms at level three. Depression scores did not uniquely predict social functioning. Expression negative symptoms were a significant predictor of social functioning, with the combination of these two predictors accounting for about 10% of the variance. When experiential negative symptoms were added to the model, however, experiential negative symptoms emerged as the only significant predictor, with the full model accounting for 39% of the variance in social functioning (Table 4).

Given the observed relationships between experiential and expressive negative symptoms to social functioning, we tested two competing mediation models to see which fit the data better. In the first model, we tested whether experiential negative symptoms mediated the relationship between expressive negative symptoms and social functioning. In the second model, we tested whether expressive symptoms mediated the relationship between experience and social functioning. In the first model ($\chi^2 = 43.146$, df = 3; RMSEA = 0.00: AIC 466, 29), we found a significant, specific indirect mediation effect for experiential negative symptoms (B = −0.247, S.E. = 0.086, $p = .004$) and a non-significant direct relationship between expressive negative symptoms and social functioning (B = −0.116, S.E. = 0.132, $p = 0.381$). Fig. 1 depicts the mediated path model with experiential negative symptoms (M) fully mediating the relationship between expressive negative symptoms and social functioning. In other words, expressive symptoms influence experiential symptoms, which thereby determine the level of social functioning. See Fig. 1 for a summary of the standardized beta weights and error terms. In the second model ($\chi^2 = 43.146$, df = 3; RMSEA = 0.00: AIC 472, 56), expressive symptoms were examined as a potential mediator between experiential and social functioning. We found a non-significant specific indirect mediation effect for expressive negative symptoms (β = .−0.041, S.E. = 0.048, $p = 0.397$, β = −0.030) and a significant direct relationship between

Table 1
Demographic and clinical characteristics.

	Clinical high risk ($n = 85$)
	Mean (SD)
Age (years)	18.67 (4.5)
% male	58%
Education (years)	11.83 (3.0)
Racial background	
White	52%
Asian	22%
African American	5%
More the one race	15%
Other	6%
% Hispanic	20%
SOPS positive symptom total	10.39 (4.2)
SOPS negative symptom total	12.62 (5.8)
SANS global rating	7.82 (3.4)
Global cognition composite (z-score)	−.59 (.67)
BPRS depression–anxiety composite	2.72 (1.1)
Global Functioning — Social	5.76 (1.3)
SANS	
Experiential symptoms	2.13 (1.1)
Expression symptoms	.82 (.94)

SOPS = Scale of Prodromal Symptoms; BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms.

Table 2
Results of factor analysis using the Scale for the Assessment of Negative Symptoms.

	Expression	Experience
Paucity of expressive gestures	.876	.244
Affective nonresponsivity	.809	.363
Vocal inflections	.794	.380
Decreased spontaneous movement	.757	.208
Poverty of speech	.748	
Unchanging facial expression	.737	.394
Poor eye contact	.693	
Latency of response	.671	.129
Blocking	.399	.204
Inattentiveness during mental status	−.105	
Social inattentiveness		
Relationships with friends/peers	.379	.656
Self neglect	−.119	.653
Grooming/hygiene	−.221	.619
Ability to feel intimacy/closeness	.466	.616
Physical anergia	.289	.568
Recreational interest/activity	.440	.563
Sexual activity	.304	.405
Impersistence at work/school	.119	.350

Note: Extraction method: principal component analysis. Rotation method: Oblimin with Kaiser Normalization.

Table 3
Correlations between social functioning and experiential and expression negative symptoms, global cognition, and depression–anxiety.

	Global Functioning — Social
Experiential negative symptoms	−.61**
Expression negative symptoms	−.30**
Global cognition	.04
Depression–anxiety	−.14

** $p < .01$.

Table 4
Hierarchical linear regression models predicting social functioning.

	B	SE	R^2	Change in R^2	F change in R^2
Step 1					
Depression–anxiety	−.14	.13	.02	–	
Step 2					
Depression–anxiety	−.14	.12	.10	.09	7.97**
Expression symptoms**	−.42	.15			
Step 3					
Depression–anxiety	.10	.11	.39	.28	37.94**
Expression symptoms	−.08	.14			
Experiential symptoms**	−.76	.12			

** $p < .01$.

experiential negative symptoms and social functioning ($\beta = -0.756$, S.E. = 0.134, $p = .000$). The second model was not as good of a fit, relative to the first model, and does not support a mediation effect. Taken together, the results demonstrate that the influence of expressive symptoms on social functioning is best explained when considering their influence on experiential symptoms and the subsequent influence of experiential symptoms on social functioning.

4. Discussion

The results of the analyses support our hypotheses and provide further information on the role that specific negative symptoms may play in predicting social functioning in CHR individuals. First, negative symptom severity was found to be a robust predictor of social functioning, above and beyond depressed mood and neurocognition. Although depression–anxiety was related to experiential symptoms, it did not influence functioning and experiential symptoms were found to be an independent, and unique predictor of functioning, above and beyond mood symptoms. This is in line with prior studies with CHR, recent-onset, and chronic schizophrenia samples, which consistently demonstrate the critical role of negative symptoms in determining level of functioning (Foussias et al., 2011; Foussias and Remington, 2010; Gard et al., 2009; Meyer et al., 2014; Perivoliotis et al., 2009). Notably, the two, independent factor solution of negative symptoms (experiential vs. expressive symptoms) was replicated, to our knowledge, for the first time in a CHR sample. Second, we found support for our hypothesis that experiential negative symptoms were more predictive of social functioning, relative to expressive symptoms, suggesting that avolition and anhedonia are more important in determining level of social functioning than affective flattening and alogia. Further, the mediated path analysis demonstrated that experiential negative symptoms mediated the relationship between expressive negative symptoms and social functioning. Thus, expressive symptoms may influence social functioning via their effect on experiential symptoms.

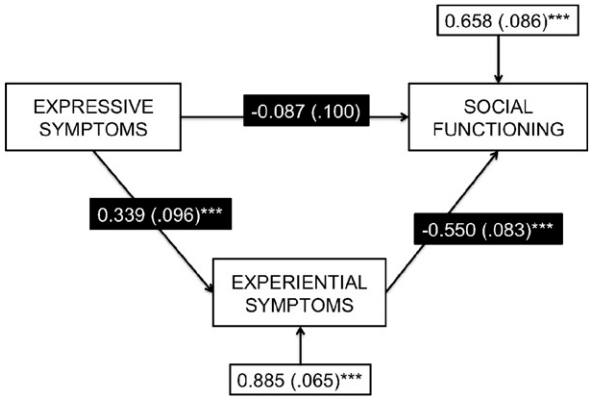

Fig. 1. Experiential negative symptoms mediate the relationship between expressive negative symptoms and social functioning. Standardized regression coefficients and standard error estimates are reported for each path. ***p-value ≤ .001.

To the best of our knowledge, this is the first such report in a CHR sample, and is consistent with published studies in persistent schizophrenia (Green et al., 2012; Rassovsky et al., 2011). Indeed, a growing body of evidence indicates that subjective experiences of interest in engagement, drive to pursue goal-directed behavior, and experiences of anticipatory and consummatory pleasure are critical determinants of healthy social functioning in schizophrenia (Cohen and Minor, 2010; Green et al., 2012). Avolition and anhedonia, especially anticipatory anhedonia, may reflect the behavioral correlate of reward system deficits, which are now considered core features of the pathophysiology of schizophrenia (Barch and Dowd, 2010; Barch, 2005; Dowd and Barch, 2012; Schlosser et al., 2014; Wotruba et al., 2014). As such, it is not surprising that the presence of these deficits are significantly predictive of poorer social functioning in CHR individuals, and may explain why previous studies have shown that the presence of more severe negative symptoms predicts the future development of psychosis (Fusar-Poli et al., 2012; Nelson et al., 2013; Piskulic et al., 2012).

The limitations of this study should be noted. First, the results presented in this study were cross sectional and, as such, we cannot draw any conclusions about the longitudinal influence of negative symptoms on outcome. Path analysis may only test theoretically driven relationships between variables and do not prove causality; a longitudinal design would need to be applied to determine the directionality of these relationships. Secondly, there may be concern regarding the content overlap between specific negative symptom items and the measurement of social functioning. A benefit of our approach in this study, was the use of the two factor solution, which was comprised of many items in the SANS, rather than relying on single items in the model. Nonetheless, this issue is not a unique limitation to this study, and indeed, it has spurred an interest in developing new negative symptom measures to emphasize the importance of distinguishing the unique and independent components of negative symptoms (Kring et al., 2013). Additionally, while this study did not support the role of neurocognition and mood/anxiety symptoms as robust predictors of functioning, prior studies have shown these factors to be predictive of outcome in the CHR population (Carrión et al., 2011; Fulford et al., 2013; Meyer et al., 2014). It is possible that we were underpowered to fully account for the role of neurocognition, given that the largest study conducted on this topic to date did indeed show a modest influence of neurocognition on social functioning (Meyer et al., 2014). Another explanation may be that the relationship between cognition and real-world outcomes is indirect and likely mediated by other variables, such as motivation (Fervaha et al., 2015; Gard et al., 2009). The absence of a relationship between mood symptoms and social functioning may possibly be due to our larger sample size and our measure of mood symptoms. In our study, we used a validated composite measure of depression/anxiety, rather than relying on a single item construct. Lastly, we may have observed a more robust influence of expressive symptoms on social functioning if there was a greater range of severity. However, the stronger relationship between experiential symptoms and social functioning, relative to expressive symptoms, is consistent with findings in schizophrenia.

The results from this study support an emerging literature, which is highlighting the important role of the internal experiences of negative symptoms, such as difficulty with expending effort to engage in motivated behavior and social anhedonia. As such, it is important that we develop interventions to target the experiential component of motivation across the course of illness. While cognitive behavior therapy (CBT) might be able to target some aspects that influence negative symptoms and functioning, such as defeatist beliefs, the results on improving functioning have been mixed (Carbon and Correll, 2014; Velthorst et al., 2014; Wykes et al., 2008). Given these findings, it is likely that we need a new approach that can overcome the challenges inherent to treating a population that struggles with motivation. As

such, taking advantage of digital health technologies, which may deliver interventions in real-time with relatively less effort for individuals than engaging in more traditional psychotherapy approaches, may hold tremendous potential. Interventions aimed at promoting better outcomes for individuals across the psychosis spectrum may benefit from focusing on strategies to enhance engagement in one's life, increasing goal-directed behavior, supporting greater effort expenditure, and harnessing intact consummatory pleasure to improve quality of life.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Contributors

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

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