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Negative affect predicts social functioning across schizophrenia and bipolar disorder: Findings from an integrated data analysis

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Abstract

Most people with a serious mental illness experience significant functional impairment despite ongoing pharmacological treatment. Thus, in order to improve outcomes, a better understanding of functional predictors is needed. This study examined negative affect, a construct comprised of negative emotional experience, as a predictor of social functioning across serious mental illnesses. One hundred twenty-seven participants with schizophrenia, 113 with schizoaffective disorder, 22 with psychotic disorder not otherwise specified, 58 with bipolar disorder, and 84 healthy controls ($N=404$) completed self-report negative affect measures. Elevated levels of negative affect were observed in clinical participants compared with healthy controls. For both clinical and healthy control participants, negative affect measures were significantly correlated with social functioning, and consistently explained significant amounts of variance in functioning. For clinical participants, this relationship persisted even after accounting for cognition and positive/negative symptoms. The findings suggest that negative affect is a strong predictor of outcome across these populations and treatment of serious mental illnesses should target elevated negative affect in addition to cognition and positive/negative symptoms.

Keywords

Emotion; Serious mental illness; Transdiagnostic; Cognition; Social cognition; Positive symptoms; Negative symptoms

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1. Introduction

Serious mental illness such as schizophrenia (SZ) and bipolar disorder (BD) is associated with severe impairment in social functioning, as many who experience these disorders are unable to work, attend school, and maintain relationships. Treatments for these disorders often include antipsychotic medications, which are effective at controlling and reducing the positive symptoms of psychosis (e.g., delusions and hallucinations) and mania (Derry and Moore, 2007; Jablensky et al., 1999; Leucht et al., 2013). However, refractory symptoms along with broad cognitive deficits (e.g., cognitive deficits such as working memory and social cognitive deficits that include impaired Theory of Mind), and negative symptoms (e.g., lack of motivation) often remain (Abi-Dargham, 2014; Dodell-Feder et al., 2015). Impaired cognitive abilities and amotivation may lead to difficulties engaging in social roles (Lincoln et al., 2011) and substantial evidence indicates that these deficits and symptoms are predictive of poor social functioning in SZ and BD (Atre-Vaidya et al., 1998; Couture et al., 2006; Fett et al., 2011; Green et al., 2004; Palisoc et al., 2014; Simonsen et al., 2010; Strauss et al., 2012; Tabares-Seisdedos et al., 2008), even more so than psychotic (Strassnig et al., 2015) and manic symptoms (Bas et al., 2015; Tabares-Seisdedos et al., 2008). However, cognition and negative symptoms together account for a small portion of the variance in outcomes (Tabares-Seisdedos et al., 2008). Thus, there is a need for an exploration of additional factors that may impact functioning in serious mental illnesses.

1.1. Negative affect in serious mental illnesses

The construct of negative emotional experience or negative affect has been proposed as an important dimension of psychosis, cutting across the schizophrenia-bipolar diagnostic spectrum (van Rossum et al., 2011). People with SZ (Horan et al., 2008; Kring and Moran, 2008; Myin-Germeys et al., 2000; Oorschot et al., 2013) or BD (Gruber et al., 2011; Tso et al., 2014) report a higher frequency of negative emotions. This evidence is contrary to the longstanding reports of emotional abnormalities in SZ, which are largely based on the appearance of a lack of emotion in schizophrenia (e.g., flat affect and anhedonia, Bleuler, 1950; Kraepelin, 1919; Kring and Moran, 2008; Treméau, 2006). Yet recent research has shown that reduced emotional expression does not mean reduced emotional experience or capacity. For instance, SZ exhibit greater trait negative affect (Horan et al., 2008), are more likely to appraise stimuli with a neutral or positive valence as negative (Cohen and Minor, 2010), and react to even minor stressors with strong negative emotions (Myin-Germeys et al., 2005; Myin-Germeys et al., 2001). Negative affect also appears prior to the onset of psychotic symptoms in at risk populations (Phillips and Seidman, 2008). While these previous reports have focused on SZ, negative affects such as psychological stress, anxiety, and depression are heightened in both SZ and BD (Rowland et al., 2013). It has also been found that BD may be characterized by increased rumination about negative emotions (Green et al., 2011; Van der Gucht et al., 2009). Moreover, there is evidence that negative affect predicts social functioning in SZ (Tso et al., 2010, 2012) and BD (Gershon and Eidelman, 2014). However, few studies have evaluated if negative affect can predict social functioning above and beyond traditional predictors such as cognition, social cognition, and clinical symptoms in these disorders. Investigation of this research question will help

determine if negative affect should be routinely assessed for and targeted in treatment to further improve functional outcomes in serious mental illnesses.

1.2. The current study

The current study examined the relationship between negative affect and social functioning in serious mental illnesses using a large cross-sectional dataset integrated across multiple studies. The clinical sample included participants with schizophrenia, schizoaffective disorder, psychosis not otherwise specified, and bipolar disorder. This inclusive approach reflects the considerations of a lack of clear-cut genetic, biological, and clinical boundaries between these disorders (Cardno and Owen, 2014; Doherty and Owen, 2014; Frangou, 2014; Moller, 2003; Pearlson, 2015) and the dimensional and transdiagnostic nature of negative affect. Negative affect was assessed with multiple previously validated self-report measures. It was hypothesized that heightened negative affect would be observed in clinical participants relative to healthy controls and that measures of negative affect would predict social functioning independent of cognition, social cognition, positive symptoms, and negative symptoms in serious mental illnesses.

2. Method

2.1. Participants

Participants were part of four previous studies at the University of Michigan Departments of Psychology and Psychiatry, and College of Pharmacy. Inclusion criteria for clinical participants included: 1) The ability to give informed consent, 2) A DSM-IV diagnosis of schizophrenia, schizoaffective disorder, psychotic disorder not otherwise specified, bipolar I disorder, or bipolar II disorder using the Structured Clinical Interview for the DSM-IV (SCID; First et al., 1997) or the Diagnostic Interview for Genetic Studies (DIGS; Nurnberger et al., 1994), depending on the diagnostic instrument used in the previous study, 3) No current DSM-IV Axis I substance abuse/dependence diagnosis, and 4) Between the ages of 18-90. Participants with a documented dementia diagnosis were excluded from the current study. Inclusion criteria for healthy controls included: 1) No history of DSM-IV Axis-I disorders established using the non-patient version of the SCID, 2) No current psychotropic medications, and 3) No history of psychosis or mania for first-degree family members per participant's report. Trained clinical associates and graduate students under the supervision of psychiatrists and clinical psychologists conducted all diagnostic assessments. Additionally, to ensure that all self-report measures were completed according to instructions, research assistants were available to supervise and provide guidance to assist participants with the questionnaires if necessary. The study protocol was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Clinical samples and healthy controls

Data were pooled from four previous studies for a total of 404 participants. These participants included 320 clinical participants and 84 healthy controls (HC). The clinical participants consisted of individuals with schizophrenia (SZ; $n=127$), schizoaffective disorder (SA; $n=113$), psychotic disorder not otherwise specified (P-NOS; $n=22$), and

bipolar disorder (BD; $n=58$). The majority of BD participants were diagnosed with bipolar I disorder and only two were diagnosed with bipolar II disorder. Additionally, 36 BD participants with bipolar I disorder had experienced at least two manic episodes with psychotic features according to the DIGS assessment.

Due to variation of study protocols across these four previous studies and missing data, not all measures were completed by all participants. To capitalize on the high statistical power afforded by this large sample, the statistical analyses of this study were conducted based on organization of the clinical participants that provides the maximum number of participants and data. For the correlation analyses (Figure 1), clinical participants with available data for each particular pairwise correlation were included; the sample size thus varied across the pairwise analyses. For the hierarchical regression analyses (see details below), the clinical participants were organized into three overlapping subsamples based on available data as summarized in Table 1. Specifically, Clinical Sample 1 ($n=277$) consisted of clinical participants who had at least BACS, BDI-IA, PSI, and SAS-SR available. Clinical Sample 2 ($n=145$) is a subsample of Clinical Sample 1, consisting of clinical participants with additional measures (SANS, STAI-S) available. Similarly, Clinical Sample 3 ($n=75$) is a subsample of Clinical Sample 2, consisting of clinical participants with even more measures (MSCEIT, SAPS, DES-N) available.

2.3. Assessments

2.3.1. Demographics—Age, gender, level of participant and parental education, and familial SES were obtained (Table 2). For level of education, the number of years of education was converted to eight ordinal rankings based on the highest level of education completed: 1) grade 6 or less, 2) greater than grade 6, but less than graduating high school, 3) high school education or equivalent, 4) part college, 5) 2-year college degree, 6) 4-year college degree, 7) part graduate/professional school, and 8) graduate/professional school degree.

2.3.2. Cognition—The Brief Assessment of Cognition in Schizophrenia (BACS) was used to assess the cognitive domains of working memory, processing speed, and executive function (Keefe, 1999). Standardized scores (z -scores) for the BACS composite scores were calculated from the mean and standard deviation of the 84 healthy controls included in the current study.

2.3.3. Social cognition—The Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) is a performance-based test of social cognitive abilities, and includes four subscales: perceiving emotions, facilitating thought, understanding emotions, and managing emotions (Mayer et al., 1999). For ease of interpretation, uncorrected MSCEIT standard total scores (EQ) were used in the current analysis. Tasks from both the BACS and MSCEIT are recommended by the NIMH Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Committee to assess cognition and social cognitive skills (Green et al., 2005).

2.3.4. Clinical symptoms—The Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b) and Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a) were used to assess positive and negative symptoms in the last month, respectively. For SANS, global scores (averages) were calculated from the Affective flattening or blunting, Alogia, Avolition-apathy, and Anhedonia-asociality domain subscales. The Attention subscale was not included in the analysis due to conflicting findings regarding validity and reliability (Gonzalez-Blanch et al., 2012). Additionally, the Young Mania Rating Scale (YMRS) was used to assess manic symptoms (Young et al., 1978). Trained clinical psychology graduate students conducted all clinical ratings based on anchors provided by the SAPS and YMRS. Anchors for the SANS were developed by the researchers of this study in order to ensure reliability across clinicians. Since the YMRS was available for only the BD participants, it was not included in the regression analyses.

2.3.5. Social functioning—The Social Adjustment Scale – Self Report (SAS-SR) is a 54-item self-report measure designed to assess social functioning in the past two weeks across six specific domains: Work Role (i.e., Work for Pay, Unpaid Housework, or Student), Social and Leisure, Family Outside the Home, Primary Relationship, Parental, and Family Unit (Weissman, 1999). The scale has been validated for use in clinical populations (Weissman et al., 2001), and used to assess social functioning in SZ (Chen et al., 2012; Dodell-Feder et al., 2014; MacEwan and Athawes, 1997; Malchow et al., 2015) and BD (Blairy, 2004; Calabrese et al., 2004; Cusi et al., 2010; Shapira et al., 1999). The SAS-SR has demonstrated a strong relationship with other assessments of social functioning, including the performance-based Mayor-Salovey-Caruso Emotional Intelligence Test (Shamsi et al., 2011) and the clinician-rated Global Assessment of Functioning scale (Wittorf et al., 2008) in SZ. Higher scores indicate greater impairment.

2.3.6. Emotional frequency—The Differential Emotions Scale (DES) is a 20-item self-report questionnaire designed to assess overall frequency of emotions over the past two weeks and includes two subscales, the positive and negative emotion subscales (Izard, 1977). Considering that the focus of the current study was negative affect, only the negative subscale (DES-N) was used in the main analyses. Additionally, the current study used a modified version that appears in Fredrickson et al. (2003) and has been previously used in SZ (Johnson et al., 2011; Suslow et al., 2003).

2.3.7. Stress—The Psychological Stress Index (PSI) is an 18-item self-report measure designed to assess psychological stress over the last month in people with serious mental illness (Tso et al., 2012).

2.3.8. Anxiety—The state subscale of the State-Trait Anxiety Inventory (Form X-1; STAI-S) is a 20-item self-report measure designed to assess feelings of anxiety in the current moment within clinical populations (Spielberger et al., 1983). The STAI has been used in SZ (Bortolon and Raffard, 2015; Gelkopf et al., 2006; Ritsner et al., 2012) and demonstrates a strong relationship with negative affect measures such as the Beck Depression Inventory in a clinical population (Block, 1991; Nitschke et al., 2001). The current study used the state subscale only to match the time interval of the other negative affect measures.

2.3.9. Depression—The revised Beck Depression Inventory (BDI-IA) is a 21-item self-report measure designed to assess depressive symptoms within clinical populations (Beck and Steer, 1993). The current version was modified to assess depressive symptoms in the past few days compared with the standard time frame of one week for the purpose of our previous studies. The BDI-IA is highly correlated with revised version of the scale, the BDI-II (Beck et al., 1996) in clinical populations (Beck and Steer, 1993) and demonstrates a strong relationship with negative affect measures such as the STAI in a clinical population (Block, 1991; Nitschke et al., 2001).

2.3.10. Psychotropic medications—Medication information were obtained for all participants and verified via medical records when possible.

2.4. Data integration

All data were integrated from four studies conducted at the University of Michigan Departments of Psychiatry and Psychology, along with the University of Michigan College of Pharmacy between 2006 and 2015. All studies recruited clinical participants from community mental health facilities in the Michigan cities of Ann Arbor, Ypsilanti, and Detroit. Healthy controls were recruited primarily from Ann Arbor and Ypsilanti. Due to the collaborative efforts across departments, several participants completed more than one of the four studies. Participants who participated in more than one of these studies were only included in the current analysis once, resulting in data from each participant's most recent study participation only.

2.5. Statistical analyses

A one-way ANOVA or chi-square was used to determine if DSM-IV diagnostic groups were well matched for demographic and clinical characteristics. Tukey's HSD test, which accounts for all possible pairwise comparisons, was used for post-hoc analyses. Cronbach's alpha was used to evaluate the internal consistency of the self-report measures. Pearson correlational analyses (bivariate) were used to examine the relationship between BACS, SANS, MSCEIT, SAPS, YMRS, BDI-IA, PSI, STAI-S, DES-N, and SAS-SR scores. To minimize the effects of statistical anomalies on the results, 95% confidence intervals of the correlation estimates were also provided based on 1,000 bootstrapping samples (Carpenter and Bithell, 2000; Wood, 2004).

Separate hierarchical regressions were performed to determine if each of the available measures of negative affect was predictive of social functioning in the clinical samples, independent of available known predictors (cognition, positive and negative symptoms, and/or social cognition). For Clinical Sample 1, BACS was entered in Step 1, and then BDI-IA (Model A) or PSI (Model B) was entered in Step 2 to determine if either of these negative affect measures accounted for additional variance in social functioning. Similarly, for Clinical Sample 2, BACS and SANS were entered in Step 1, and then BDI-IA (Model A), PSI (Model B), or STAI-S (Model C) was entered in Step 2. For Clinical Sample 3, BACS, SANS, MSCEIT, and SAPS were entered in Step 1, and then BDI-IA (Model A), PSI (Model B), STAI-S (Model C), or DES-N (Model D) was entered in Step 2.

Previous reports have indicated a possible association between levels of negative affect and use of atypical antipsychotics (Lataster et al., 2011), mood stabilizing medications (Mula and Sander, 2007), antidepressants (Barge-Schaapveld et al., 1995; Wichers et al., 2009), and benzodiazepines (Ritsner and Gibel, 2006) in clinical populations. To evaluate the relationship between psychotropic medications and self-report measures of negative affect in this study, all psychotropic medications were classified into types and dummy coded for each type. Five types of psychotropic medications were identified: atypical antipsychotics, typical antipsychotics, mood stabilizers, antidepressants, and benzodiazepines. All of the five dummy variables were entered as predictor variables into separate regression models predicting BDI-IA, PSI, STAI-S, or DES-N, respectively. This procedure was repeated for each of the three clinical samples.

All analyses were conducted using SPSS version 22 (IBM). An alpha less than 0.05 was considered significant. Bonferroni correction was not used due to the strong a priori grounds for predictions.

3. Results

Overall, the three clinical samples were very similar in terms of demographic characteristics (Table 2). Demographic and clinical information according to DSM-IV diagnosis is available in the supplemental materials (see Supplemental Tables 1 and 2, respectively). All self-report measures demonstrated good to excellent internal consistency ($\alpha = 0.85$ to 0.94). Negative affect measures were significantly correlated with one another within each clinical sample ($r = 0.33$ to 0.73 , $p < 0.01$ for all). Negative affect measures (BDI-IA and STAI-S) and were also significantly correlated with SAPS and SANS ($r = 0.23$ to 0.40 , $p < 0.05$, respectively) but not BACS or MSCEIT in Clinical Sample 3 (the only sample with MSCEIT data available).

3.1. Elevated negative affect in serious mental illnesses

Descriptive statistics of PSI, STAI-S, DES-N, and SAS-SR for the clinical samples and HC are summarized in Table 2. All three clinical samples reported significantly higher levels of negative affect across the measures, along with poorer social functioning (SAS-SR), than HC. See Supplemental Table 2 for these comparisons by DSM-IV diagnostic groups.

3.2. Negative affect measures as predictors of social functioning

As expected, cognition (BACS), social cognition (MSCEIT), and clinical symptoms (SANS, SAPS, and YMRS) were associated with social functioning (SAS-SR) in serious mental illnesses. Additionally, all measures of the negative affect (BDI-IA, PSI, STAI-S, and DES-N) were also significantly correlated with SAS-SR among clinical participants (Figure 1). For healthy controls, “traditional” predictors of social functioning (BACS and MSCEIT) were not correlated with SAS-SR ($r = -0.05$ and 0.02 ; $p > 0.05$, respectively); all measures of negative affect were correlated with SAS-SR ($r = 0.39$ to 0.55 ; all p 's < 0.001) except DES-N ($r = 0.11$, $p > 0.05$).

Results of the hierarchical regression analyses are shown in Table 3. In Clinical Sample 1, PSI and BDI-IA each predicted a significant amount of variance in SAS-SR independent of

BACS (Table 3 first column, Models A and B). In Clinical Sample 2, BDI-IA, PSI, and STAI-S each predicted a significant amount of variance in SAS-SR independent of BACS and SANS (Table 3 second column, Models A to C). In Clinical Sample 3, BDI-IA, PSI, STAI-S, and DES-N each predicted a significant amount of variance in SAS-SR independent of BACS, SANS, MSCEIT, and SAPS (Table 3 third column, Models A to D). Additional analyses based on clinical participants organized into independent samples (i.e., 132 participants exclusive to Clinical Sample 1; 70 clinical participants exclusive to Clinical Sample 2; and 75 clinical participants exclusive to Clinical Sample 3; Supplemental Table 3), as well as by diagnostic group (Supplemental Table 4), yielded similar results.

3.3. Relationship between psychotropic medications, negative affect, and social functioning

Frequencies of psychotropic medications for the three clinical samples and each DSM-IV diagnostic group are presented in Supplemental Table 5. Regression analyses showed that taking antidepressant medications significantly predicted lower BDI-IA and lower PSI in Clinical Sample 1 (see Supplemental Table 6 first column, Models A and B), and PSI in Clinical Sample 2 (see Supplemental Table 6 second column, Model C).

4. Discussion

The current study examined the relationship between self-reported negative affect and social functioning in three clinical samples consisting of people with various forms of serious mental illness: schizophrenia, schizoaffective disorder, psychotic disorder not otherwise specified, or bipolar disorder. Our primary analyses showed that negative affect: 1) was elevated in serious mental illness compared with healthy controls, 2) was significantly correlated with social functioning in clinical participants as well as healthy participants, and 3) explained significant amounts (15% to 51%) of variance in social functioning in clinical participants even after accounting for traditional predictors such as cognition, positive symptoms, and negative symptoms. Previous reports have found that negative affect predicts functional outcomes in SZ (Blanchard et al., 1998; Horan et al., 2008; Kiwanuka et al., 2014). The current study expands this finding to other diagnostic groups commonly regarded as serious mental illness, including SA, P-NOS, and BD. Although the main analyses of this study used a transdiagnostic approach combining all of these diagnostic groups into overlapping samples, the additional analyses broken down by diagnosis and independent samples showed the same patterns of results—that negative affect was elevated in each of these DSM-IV diagnostic groups and samples when compared with healthy controls (despite some differences between some of the clinical groups), and that each of the negative affect measures significantly predicted social functioning. Thus, the association between elevated negative affect and social functioning impairment may exist as a dimension across these populations. Overall, these findings indicate that elevated negative affect is not only prevalent across common serious mental illnesses, it also has a robust and important association with social functioning that deserves further research and clinical attention.

It remains to be addressed what precipitates increased negative affect in serious mental illnesses and through what mechanisms does negative affect lead to social dysfunction. The

origin of heightened negative affect in serious mental illness may be explained by the documented phenomenon of heightened stress sensitivity—a reduced ability to tolerate minor, everyday stressors—which often results in the experience of increased negative emotions (Myin-Germeys et al., 2003). Previous reports have linked stress sensitivity to the pathophysiology of schizophrenia [i.e., blunted hypothalamic-pituitary-adrenal (HPA) axis corticosterone response] using animal models (Zimmerman et al., 2013), along with reduced hippocampal volume serving as a marker of stress sensitivity in psychotic disorders (Collip et al., 2013). Similar findings have been observed in bipolar disorders, such as reduced cortisol metabolism (Steen et al., 2014; Steen et al., 2011) and glucocorticoid receptor hyporesponsiveness (Fries et al., 2014). Stress sensitivity via HPA axis function may also play a role in the development of psychotic symptoms in at-risk populations (Corcoran et al., 2012) and has been implicated in the onset of bipolar spectrum disorders (Alloy et al., 2006). In addition, it has been shown that people with SZ report more aversion from viewing neutral and positive stimuli than healthy controls (Cohen and Minor, 2010) and people with BD report higher levels of negative affect and exhibit increased cardiovascular reactivity to stressful situations (Muhtadie and Johnson, 2015), suggesting that even benign events could add to the experience of negative emotions in people with serious mental illness. In addition, “traditional” predictors of social functioning (e.g., social cognition and negative symptoms) may also contribute to negative affect and related social functioning deficits in serious mental illness. For example, one may misinterpret a neutral or ambiguous facial expression of a co-worker as angry due to social cognitive impairments and thus feel stressed about having to interact with a seemingly upset co-worker. Although this would normally be considered a minor or negligible stressor for most people, this could elicit strong negative emotions in people with serious mental illness, consequently making it difficult to perform work-related tasks and engage socially, especially in the presence of negative symptoms (e.g., amotivation) and/or positive symptoms (both were related to negative affect in the current study). Future investigations should attempt to understand how negative affect interacts with cognition, social cognition, and psychotic/bipolar symptoms to compromise social functioning. There is evidence of reduced cognitive regulation of negative affect and an association between emotion dysregulation and negative affect in SZ and BD (Perry et al., 2012; Rowland et al., 2013). Therefore, it may prove beneficial to provide psychosocial interventions such as cognitive behavioral therapy and cognitive remediation in addition to psychotropic medications, in order to help patients build sustainable skills in effective reappraisal and coping of distressing symptoms and emotional events (Smith et al., 2003). It is noteworthy that while healthy controls showed reduced levels of negative affect compared with clinical participants, the correlations between negative affect measures and social functioning were observed not just among clinical participants, but also healthy individuals. This suggests that negative affect may be a critical determinant of socioemotional functioning and supports previous work emphasizing the relationship between negative affect and outcomes across psychiatric and non-psychiatric populations (Pilkonis et al., 2013; Wilson and Cleary, 1995). Future investigations of the neurobiological and psychosocial mechanisms of negative affect as a functional dimension across normal functioning and psychopathology would further advance our understanding of mental health and various mental disorders.

In this study, we observed strong intercorrelations between the measures of depression, anxiety, psychological stress, and frequency of negative emotions. Additionally, each of these measures consistently predicted social functioning independent of “traditional” predictors (including cognition, social cognition, positive symptoms, and negative symptoms) in clinical participants. Taken together, these findings support the conclusion that measures of depression, anxiety, psychological stress, and frequency of negative emotions included in this study may be conceptualized as observed variables driven by an underlying construct best described as negative affect. This is consistent with previous reports of strong correlations between similar measures of negative affect such as the STAI or BDI (Block, 1991; Nitschke et al., 2001) and a latent variable of negative affect derived using the BDI and Beck Anxiety Inventory (Clark et al., 1994) in clinical populations. Future confirmatory factor analysis using a comprehensive battery of negative affect measures on a large clinical sample and incorporation of longitudinal data would offer more insight into the factor structure of negative affect and its relationship with clinical and functional outcomes in serious mental illness.

In terms of psychotropic medications, whether or not a patient was taking antipsychotics, mood stabilizers, and benzodiazepines showed no relationship with negative affect. However, taking an antidepressant was associated with less negative affect, as suggested by lower BDI-IA and PSI in clinical participants taking an antidepressant medication (although further statistical inference was not possible due to the unavailability of dosage information for many participants). This relationship may be explained by the influence of antidepressant medications on stress sensitivity and the HPA axis. If stress sensitivity is a precipitant of heightened negative affect in SZ and BD, as supported by findings mentioned previously (Alloy et al., 2006; Collip et al., 2013; Corcoran et al., 2012; Fries et al., 2014; Steen et al., 2014; Steen et al., 2011; Zimmerman et al., 2013), it is possible that antidepressants may ameliorate stress reactivity via physiological mechanisms that reduce HPA dysfunction (Jacobson, 2014), which may consequently reduce negative affect. For instance, antidepressants may promote hippocampal neurogenesis, which could improve stress response via modulation of HPA axis function (Surget et al., 2011; Wang et al., 2012). More generally, it may be the case that just as antidepressants reduce negative affect in depression, they also reduce negative affect in psychosis and bipolar disorder.

This study relied heavily on self-report measures, which should be interpreted with caution. Verbal and working memory deficits have been reported in SZ and BD (Kuswanto et al., 2013) and may influence the accuracy of self-reports. SZ may overestimate the intensity of retrospective ratings of affect in self-report measures (Ben-Zeev et al., 2012), which may be due to cognitive biases to negative emotions (Strauss and Gold, 2012). Considering that the time interval for the self-report measures used in this study ranged from the current moment (STAI-S), the past few days (BDI-IA), the past two weeks (DES-N), to the past month (PSI), measures with a longer time interval may be subject to an overestimated frequency of emotions by participants. Accordingly, measures with a more recent time interval, BDI-IA and STAI-S, showed stronger correlations and higher prediction of social functioning in the current study, suggesting that measures with a reduced reliance on memory may be better suited to assess negative affect.

In spite of these short-comings, self-report measures of social functioning and negative affect similar to those used in this study have demonstrated reliability in numerous studies of SZ and BD (Baumstarck et al., 2013; Bell et al., 2007; Leidy et al., 1998; Lloyd et al., 2010; Ma et al., 2014; Trivedi et al., 2004; Whitty et al., 2004). Self-report measures of quality of life in clinically compliant and stable patients with schizophrenia are highly correlated with clinician estimates (Voruganti et al., 1998), and demonstrate excellent suitability indices of reliability and validity despite cognitive impairments in schizophrenia (Baumstarck et al., 2014; Whitty et al., 2004). Thus, self-reports provide critical, reliable, and valid assessment of negative affect and social functioning (Bellack et al., 2007).

Some other potential limitations of the study exist. The similarity in epochs between all self-report measures (most were less than one month) compared with the one-month epoch of the clinical assessments may confound the results. Further, the results may be complicated by the different requirements placed on participants (e.g., differences in study duration) between studies, thus introducing confounds such as differential levels of fatigue and emotional states. The correlational and cross-sectional nature of the study prohibits any causal inferences. Longitudinal study designs with similar requirements placed on participants, along with consistent measurement epochs for clinical assessments and self-report measures, would help to determine the causal relationships between negative affect and social functioning in serious mental illness after accounting for “traditional” predictors. Another concern lies in the variable ratios of participants diagnosed with bipolar disorder (21% to 45%) and those with schizophrenia/schizoaffective disorder (35% to 72%) in the clinical samples, which may limit the generalizability of the current findings. However, as mentioned above, additional regression analyses limited to participants with bipolar disorder only showed the same results as those based on the entire clinical samples or participants with schizophrenia or schizoaffective disorder only (Supplemental Table 4). This suggests that the current findings are unlikely to be driven by participants with schizophrenia or schizoaffective disorder alone.

To conclude, negative affect was elevated and highly predictive of social functioning in common serious mental illnesses including schizophrenia, schizoaffective disorder, psychotic disorder not otherwise specified, and bipolar disorder. The findings suggest that negative affect should be routinely assessed in clinical settings and targeted with empirically-supported treatments, especially psychosocial interventions, in order to improve social functioning in those who experience serious mental illness.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Large sample size ($N=404$) used to investigate negative affect transdiagnostically.
- Negative affect explains outcome variance independent of traditional predictors.
- Negative affect may be a critical treatment target across serious mental illnesses.

Figure 1.

Pearson correlations between all measures and the social adjustment scale (SAS-SR) across all clinical participants. Variables are listed according to the size of the Pearson correlations. Note that all available data were used in these correlational analyses, resulting in different sample sizes for each measure. 95% confidence intervals (95% CI) are listed below the effect sizes (r) at the top of the figure and were derived from bootstrapping with 1,000 samples. Higher SAS-SR indicates poorer functional outcomes. BACS = Brief Assessment of Cognition in Schizophrenia. MSCEIT = Mayer-Salovey-Caruso Emotional Intelligence Test. SAPS = Scale for the Assessment of Positive Symptoms. SANS = Scale for the Assessment of Negative Symptoms. YMRS = Young Mania Rating Scale. DES-N = negative emotion subscale of the modified version of the Differential Emotions Scale. PSI = Psychological Stress Index. STAI-S = state subscale of the State-Trait Anxiety Index. BDI-IA = revised version of the Beck Depression Inventory. SAS-SR = Social Adjustment Scale – Self-Report. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1

Composition of clinical samples by DSM-IV diagnoses and measures available

	Clinical Sample 1 (n=277)	Clinical Sample 2 (n=145)	Clinical Sample 3 (n=75)
(a) <i>Diagnostic composition</i>			
Schizophrenia	103 (37.2%)	55 (37.9%)	26 (34.7%)
Schizoaffective disorder	96 (34.7%)	32 (22.1%)	15 (20.0%)
Psychosis NOS	20 (7.2%)	NA	NA
Bipolar disorder	58 (20.9%)	58 (40.0%)	34 (45.3%)
(b) <i>Measures</i>			
Cognition (BACS)	✓	✓	✓
Negative sx (SANS)		✓	✓
Social cognition (MSCEIT)			✓
Positive sx (SAPS)			✓
Negative affect			
BDI-IA	✓	✓	✓
PSI	✓	✓	✓
STAI-S		✓	✓
DES-N			✓
Social functioning (SAS-SR)	✓	✓	✓

Note. All Clinical Samples are overlapping; Clinical Sample 1 includes all of Clinical Sample 2 and Clinical Sample 2 includes all of Clinical Sample 3. DSM-IV = Diagnostic and Statistical Manual on Mental Disorders – Fourth Edition. NOS = not otherwise specified. sx = symptoms. NA = data not available. BACS = Brief Assessment of Cognition in Schizophrenia. SANS = Scale for the Assessment of Negative Symptoms. MSCEIT = Mayer-Salovey-Caruso Emotional Intelligence Test. SAPS = Scale for the Assessment of Positive Symptoms. DES-N = negative emotion subscale of the modified version of the Differential Emotions Scale. PSI = Psychological Stress Index. STAI-S = state subscale of the State-Trait Anxiety Index. BDI-IA = revised version of the Beck Depression Inventory.

Table 2

Demographic, cognitive, clinical, and functional characteristics of the clinical samples and healthy controls

		HC (<i>n</i> =84)	Clinical Sample 1 (<i>n</i> =277)		Clinical Sample 2 (<i>n</i> =145)		Clinical Sample 3 (<i>n</i> =75)	
	Scale range	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	χ^2 , <i>t</i> , or <i>U</i>	<i>M</i> (<i>SD</i>)	χ^2 , <i>t</i> , or <i>U</i>	<i>M</i> (<i>SD</i>)	χ^2 , <i>t</i> , or <i>U</i>
Age		42.0 (12.2)	43.4 (11.2)	-1.08	42.3 (10.9)	-0.31	42.2 (11.2)	-0.19
Gender (number of males)		51 (60.7%)	150 (54.2%)	0.90	78 (53.8%)	0.84	39 (52.0%)	1.04
Education ^a	1-8	6.0 (1.7)	4.4 (1.7)	5740.50 ***	4.7 (1.7)	3682.50 ***	4.9 (1.7)	2072.50 ***
Parental education ^{a, b}	1-8	5.1 (1.9)	5.5 (2.1)	4919.50	5.5 (2.1)	4385.00	5.4 (2.1)	2197.50
Family SES ^{a, b}	1-4	2.7 (0.7)	2.7 (0.8)	4138.00	2.7 (0.8)	3563.00	2.7 (0.8)	1303.50
BACS		0.0 (1.0)	-1.6 (1.3)	12.17 ***	-1.3 (1.2)	8.73 ***	-0.9 (1.0)	-5.79 ***
MSCEIT ^b		102.6 (18.0)					97.1 (18.4)	-1.44
Age of onset (years) ^a			21.9 (9.7)		18.1 (7.3)		17.9 (7.3)	
Illness duration (years)			21.6 (12.5)		24.3 (12.3)		24.4 (12.9)	
SANS	0-5				5.4 (4.1)		3.7 (3.6)	
SAPS	0-5						2.6 (3.1)	
YMRS ^a	0-4						2.6 (3.5)	
BDI-IA ^b	0-54	1.9 (3.5)	13.3 (11.0)	-14.48 ***	12.9 (11.4)	-10.59 ***	10.8 (9.1)	-7.74 ***
PSI ^b	0-4	1.2 (0.5)	2.2 (0.7)	-14.30 ***	2.2 (0.6)	-13.18 ***	2.2 (0.6)	-11.15 ***
STAI-S ^{a, b}	1-4	27.6 (6.9)			41.6 (13.3)	-10.48 ***	39.0 (12.8)	-6.81 ***
DES-N ^{a, b}	1-5	1.3 (0.7)					2.4 (0.6)	-9.70 ***
SAS-SR ^b	0-5	1.5 (0.3)	2.2 (0.5)	-14.80 ***	2.2 (0.5)	-11.68 ***	2.1 (0.5)	-9.03 ***

Note.

* $p < 0.05$,** $p < 0.01$,^aData not collected for all clinical participants.

^bData not collected for all health control participants. Each clinical sample was not an independent sample and therefore only Pearson chi-square tests (χ^2), *t*-tests, or Mann-Whitney tests (*U*) were used to compare each clinical sample with the healthy controls. For the education variables, an ordinal ranking was created, with a higher level of education signified by a higher ranking. HC = healthy control. SES = socioeconomic status. BACS = Brief Assessment of Cognition in Schizophrenia. MSCEIT = Mayer-Salovey-Caruso Emotional Intelligence Test. SANS = Scale for the Assessment of Negative Symptoms. SAPS = Scale for the Assessment of Positive Symptoms. YMRS = Young Mania Rating Scale. BDI-IA = revised version of the Beck Depression Inventory. PSI = Psychological Stress Index. STAI-S = state subscale of the State-Trait Anxiety Index.

DES-N = negative emotion subscale of the modified version of the Differential Emotions Scale. SAS-SR = Social Adjustment Scale – Self-Report.
M = mean. SD = standard deviation.

 $p < 0.001$.

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Table 3

Hierarchical regression analyses of negative affect measures as predictors of social functioning after controlling for cognition and symptoms

Clinical Sample 1 (n=277)				Clinical Sample 2 (n=145)				Clinical Sample 3 (n=75)			
Variable statistics		Model statistics		Variable statistics		Model statistics		Variable statistics		Model statistics	
<i>b</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>b</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>b</i>	<i>p</i>	<i>R</i> ²	<i>F</i>
Step 1 (all models)											
BAC	–	0.00	0.00	–	0.49	0.0	6.68	–	0.17	0.1	3.3
S	0.1	3	4	0.0	4	9	2	0.1	6	6	3
	7			6				8		5	
SAN				0.2	0.00			0.2	0.07		
S				6	6			5	4		
MSC								0.0	0.81		
EIT								3	9		
SAP								0.1	0.41		
S								0	4		
Step 2 (Model A)											
BDI-IA	0.7	<0.0	0.5	0.7	<0.0	0.4	138.	0.6	<0.0	0.3	57.
	2	01	1	0	01	5	82	9	01	8	41
											01
Step 2 (Model B)											
PSI	0.5	<0.0	0.2	0.5	<0.0	0.2	56.2	0.4	<0.0	0.1	15.
	4	01	9	1	01	6	0	0	01	5	01
Step 2 (Model C)											
STAI-S				0.5	<0.0	0.2	62.4	0.6	<0.0	0.3	46.
				5	01	8	3	2	01	4	65
											01
Step 2 (Model D)											
DES-N								0.4	<0.0	0.1	18.
								3	01	8	23
											01

Note. Only standardized betas are reported. NA = data not available. BACS = Brief Assessment of Cognition in Schizophrenia. SANS = Scale for the Assessment of Negative Symptoms. MSCEIT = Mayer-Salovey-Caruso Emotional Intelligence Test. SAPS = Scale for the Assessment of Positive Symptoms. BDI-IA = revised version of the Beck Depression Inventory. PSI = Psychological Stress Index. STAI-S = state subscale of the State-Trait Anxiety Index. DES-N = negative emotion subscale of the modified version of the Differential Emotions Scale. SAS-SR = Social Adjustment Scale – Self-Report. 95% CI = 95% confidence interval.

* $p < 0.05$.

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$d > 0.001$ ***
 $d > 0.1$ ***