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Anxiety symptoms across twenty-years in schizoaffective disorder, bipolar disorder, and major depressive disorder

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ABSTRACT

Anxiety symptoms and anxiety disorders are common in both mood and psychotic disorders. However, limited comparative information exists regarding the long-term course of anxiety in schizoaffective disorder, bipolar disorder, and major depressive disorder. Prospective evaluation of the 20-year trajectory of self-reported anxiety and somatic-related anxiety in three major diagnostic groups, 43 schizoaffective patients, 47 bipolar patients, and 109 major depression patients was conducted. The patients were recruited at an index phase of hospitalization, and then reassessed longitudinally at six subsequent follow-ups over 20-years. The sample was well characterized with symptom, recovery and functioning data being available. This study found that in the earlier years of illness, self-reported anxiety was greater in schizoaffective and major depression patients than bipolar patients. The three groups were similar for anxiety symptoms during the 20-year course of their illness. Last, we found in all patients, self-reported anxiety in the early years predicted having a period of recovery and lower global functioning in the future. Our data provides unique information regarding the comparative course of anxiety in related mood and psychotic disorders. Both clinicians and researchers should focus on assessing, diagnosing, and treating anxiety in mood and psychotic disorders, as a means to improve outcomes and quality of life in these individuals.

1. Introduction

Anxiety disorders are highly comorbid with mood and psychotic disorders. Research suggests that more than 50% of patients with a primary mood or anxiety disorders have an additional current anxiety or depressive disorder and the number goes up to 75% of patients when lifetime diagnoses are considered (Brown and Barlow, 2009). Similarly, in schizoaffective disorder, rates of anxiety disorders are notable at approximately 30–45% (Ciapparelli et al., 2007; Cosoff and Hafner, 1998). Moreover, significant evidence exists that the presence of anxiety within mood and psychotic disorders influences the manifestation, course, and outcome of the disorders. However, limited information exists on the longitudinal course of anxiety in these disorders and how the longitudinal trajectory compares in the different mood and psychotic disorders. Therefore, in this study, we investigated the prospective longitudinal 20-year trajectory of self-reported anxiety in three major affective disorders, schizoaffective disorder, bipolar disorder, and major depression.

The presence of anxiety in mood and psychotic disorders is associated with a more complex clinical manifestation. In psychosis more generally, anxiety disorders are associated with increased suicide attempts (Nepon et al., 2010; Pallanti et al., 2004), have an impact on symptom presentation (Tibbo et al., 2003), and worsen functioning (Pallanti et al., 2004). A limited number of investigations have independently assessed schizoaffective disorder. Specifically, in schizoaffective disorder, along with schizophrenia and bipolar disorder with psychotic features, a diagnosis of panic disorder has been found to be associated with a four year earlier age of onset (Ongur et al., 2009). The impact of anxiety on bipolar disorder and depression has been more widely studied. In bipolar disorder, the presence of anxiety symptoms or disorders is associated with an earlier age of onset, increased symptomology, worse outcomes over the long term, more suicidal ideation and suicide attempts, and increased healthcare utilization (reviewed in Goes, 2015; Goldberg and Fawcett, 2012; Schaffer et al., 2012). Of note, the role of anxiety in decreased quality of life and functioning appears to be independent of other symptoms or comorbidities (Schaffer et al., 2012). Comparable to bipolar disorder, comorbid anxiety has a similar effect on morbidity in depression (reviewed in Goldberg and Fawcett, 2012; Schaffer et al., 2012).

Although, individual studies tend to demonstrate a higher rate of

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anxiety disorders in mood disorders than schizoaffective disorder, this is not a wholly consistent finding. For example, a study including 157 schizoaffective patients and 304 bipolar I patients found schizoaffective patients (30%) had a significantly greater rate of comorbidity with anxiety disorders than bipolar I patients (22%) (Young et al., 2013). Similarly, although studies tend to suggest higher rates of anxiety comorbidity for major depression than bipolar disorder (e.g., Kessler et al., 2005), this is not a wholly consistent finding. For example, one study including 286 major depression patients, and 65 bipolar I and 33 bipolar II disorder patients found bipolar I (55%) and II (59%) patients had a greater rate of comorbidity with anxiety disorder than major depression patients (45%) (Zimmermann et al., 2009). Possible reasons for discrepancies across individual studies could be due to small sample sizes, type of sample studied, and/or inconsistencies in the definition and tools used to measure the disorders. These factors make comparing rates across studies more difficult. Given the vast majority of studies investigate one diagnostic group cross-sectionally, there is a need to research the presence of anxiety trans-diagnostically and longitudinally.

The few reports that have investigated multiple diagnostic groups longitudinally have significantly added to our knowledge. Two studies investigating community-based samples, demonstrated over a 15–25-year period, comorbid anxiety with depression was more enduring over time then either disorders alone; and lead to worse outcomes and lower functioning then individuals with either syndrome alone (Fichter et al., 2010; Merikangas et al., 2003). Furthermore, one study demonstrated that it is nature of the baseline anxiety symptoms themselves, rather than having a diagnosis of an anxiety disorder that predicted the amount of time spent in later depressive episodes in both bipolar and depressive disorders over 17-years (Coryell et al., 2012).

In summary, anxiety symptoms and anxiety disorders are present in mood and psychotic disorders. A better understanding of this association could clarify not only the phenomenology and trajectory of the disorders, but could also elucidate underlying transdiagnostic and unique features to the disorders. Given, the emphasis on dimensions rather than diagnosis, we focused on self-reported anxiety symptoms. Therefore, the overall goal was to determine anxiety levels in three disorders with a mood and psychosis component, schizoaffective disorder, bipolar disorder, and major depressive disorder, over the course of 20-years. An additional goal was to assess whether anxiety symptoms early in the course of the disorders predicted later outcome.

2. Methods

2.1. Participants and measures

The present study includes data from the Chicago Follow-up Study. The Chicago Follow-up Study is a prospectively designed, longitudinal research initiative, studying psychopathology and recovery in psychological disorders (Harrow et al., 2004; Harrow and Jobe, 2005). The study population consisted of individuals with a mental illness whose symptoms were severe enough to require hospitalization. All of the participants were hospitalized in adult wards of private and/or state psychiatric facilities during their illness. To increase both the generalizability of the sample and the sample size, no set exclusion criteria were used, when participants were first enrolled. However, some participants were excluded on an ad hoc basis as deemed necessary to allow for completion of the study (e.g., due to low intelligence quotient or age). All but a few patients were under 35-years of age at admission. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Institutional Review Board approval was obtained from the University of Illinois-Chicago and written informed consent was obtained from all participants.

One hundred and ninety-nine participants were included in the present sample. The bipolar and depression samples had anxiety data available at an index phase of hospitalization and bipolar, depression, and schizoaffective samples had data available at six follow-up periods over 20-years. Within the bipolar sample, 70.2% of patients were psychotic at the index phase of hospitalization and in the depression sample, 15.6% of participants were psychotic. Participants were included for analysis if they had anxiety data available for at least four out of the six follow-up periods. Given all participants in this study had anxiety data for the first follow-up, we determined there were 125 participants who had the first follow-up who were not included in this sample; therefore, the sample presented in the article constitutes 61% of the larger sample. The majority of participants included had five or more follow-ups (157 of 199; 79%). Of importance, the sample included did not differ from the larger sample with regards to age, sex distribution, number of previous admissions, and education level at index hospitalization. Research diagnoses were confirmed using at least one of two structured interviews: (1) the Schedule for Affective Disorders and Schizophrenia (SADS; Endicott and Spitzer, 1978) and/or (2) the Schizophrenic State Inventory (Grinker and Harrow, 1987). Groups were diagnosed using the Research Diagnostic Criteria (Spitzer et al., 1978) based on research diagnoses at the index hospitalization, resulting in 43 schizoaffective (37 schizoaffective-depressed and 6 schizoaffective-manic), 47 bipolar, and 109 unipolar depression patients. Satisfactory inter-rater reliability was established for the diagnoses. The follow-up evaluations involved structured interviews on symptoms and functioning. These interviews were conducted by trained raters who were blind to the diagnoses.

Anxiety and anxiety-related somatic symptoms over the last few weeks were measured using items from the Symptom Discomfort Scale (S1) of the Katz Adjustment Scales (Katz and Lyerly, 1963). The KAS S1 is a 55-item self-report instrument based on the Hopkins Symptom Checklist (Derogatis et al., 1974), which was the precursor to the SCL-90. From the KAS S1, 10 items were extracted based on theory to include in an anxiety and anxiety-related somatic symptom scale developed by one of the authors (MH). The items were rated on a four-point scale from “have not had this complaint” to “bothers me almost all the time”: (1) feeling keyed up and jittery, (2) feeling you were not functioning as well as you could, feeling blocked, or feeling unable to get things done, (3) headaches, (4) pains in the heart or chest, (5) heart pounding or racing, (6) trouble getting your breath, (7) faintness or dizziness, (8) difficulty falling asleep or staying asleep, (9) bad dreams, and (10) loss of appetite. The Chronbach's alpha for the scale was 0.76. Alpha coefficients above 0.7 are considered adequate (Cortina, 1993). Additionally, point biserial correlations investigated the relationship between the presence of psychotic symptomology and the anxiety scale. The correlation between the anxiety symptoms with the presence of hallucinations was a small effect ($r = 0.17$), with the presence of delusions was a medium effect ($r = 0.40$), and with the presence of overall psychotic symptomology was a medium effect ($r = 0.34$). This analysis demonstrates a differentiation between ratings on the anxiety scale and other psychotic symptomatology. Last, this anxiety scale was used in previous publications investigating schizophrenia patients with notable findings demonstrating the utility of this anxiety construct (Harrow et al., 2009, 2012).

Overall functioning was measured using the Global Assessment Scale (GAS), which was also completed at every follow-up, rated for the past year (Endicott et al., 1976). Recovery status was also coded for every follow-up period. A period of “recovery” during a follow-up year was defined operationally as the absence of positive or negative symptoms and no re-hospitalizations during the follow-up year. Recovery also required partially adequate (or better) work and social functioning (scores of “2 ” “employed half-time or greater” on the Strauss-Carpenter scales (1972)).

Table 1
Participant characteristics.

	Schizoaffective	Bipolar	Depression
N	43	47	109
Age at index	22.30 (3.28)	24.28 (5.496)	23.16 (4.17)
Gender (% male)	51	43	37
Education - years completed (sd)	13.60 (2.17)	13.53 (2.38)	13.68 (2.10)
2-year follow-up GAS	50.48 (19.09)	57.30 (20.73)	60.25 (19.07)
Period of recovery (%)	54	70	75
Number of prior hospitalizations	1.33 (2.02)	1.81 (2.64)	0.71 (1.29)
Median (range)	1.00 (0–10)	1.00 (0–12)	0 (0–7)
Medications (% on)			
Anti-psychotics	56	17	12
Anti-depressants	12	17	11
Lithium	20	67	11
Any other medication	66	63	32

Mean (standard deviation) unless otherwise noted.
GAS = Global Assessment Scale.

2.2. Statistical analyses

All data were analyzed using IBM SPSS Statistic version 24. Demographics were analyzed using analyses of variance (ANOVA) and chi-square tests. Baseline and follow-up data were individually analyzed using a between groups ANOVA. Partial-eta squared effect sizes are provided. In addition, follow-up anxiety data were analyzed using Generalized Estimation Equation (GEE), which allowed for an investigation of whether groups differed in their longitudinal trajectory for anxiety symptoms. A logistic regression, combining across data from all patient groups, was used to analyze the relationship between anxiety scores and recovery status. Similarly, a regression was used to analyze the relationship between anxiety scores and global functioning.

3. Results

3.1. Participant characteristics

Table 1 documents the participant characteristics. Overall, groups did not differ for age at index hospitalization ($F(2, 196) = 2.35$, $p = 0.098$), though bipolar patients were older than schizoaffective patients ($p = 0.03$). Groups did not differ for sex distribution ($X^2(1) = 2.71$, $p = 0.26$) or level of education achieved ($F(1, 190) = 0.08$, $p = 0.93$). Groups differed for number of previous hospitalizations ($F(2, 196) = 6.21$, $p = 0.002$), with bipolar patients having a greater number than depression patients ($p = 0.001$) and schizoaffective patients having marginally more hospitalizations than depression patients ($p = 0.07$). In the overall ANOVA, groups did not differ for global functioning at the two-year follow-up ($F(2, 119) = 2.395$, $p = 0.096$), though schizoaffective patients had worse functioning compared to depression patients ($p = 0.03$). Percentage of patients on anti-psychotics, anti-depressants, lithium, and other medications is provided in Table 1.

3.2. Anxiety at index hospitalization

Data at index hospitalization were unavailable for the schizoaffective group. An ANOVA demonstrated that depression patients had greater anxiety than bipolar patients at the index hospitalization phase ($F(1, 82) = 4.94$, $p = 0.03$, partial eta-squared = 0.06).

3.3. Anxiety at follow-up periods

Figure 1 depicts the anxiety scores for the three groups across the 20-year follow-up period. Differences between groups were found just for the 2-year follow-up with schizoaffective ($F(1, 80) = 6.22$, $p = 0.02$, partial eta-squared = 0.07) and depression ($F(1, 134) = 3.55$, $p = 0.06$, partial eta-squared = 0.03) patients having greater anxiety scores than bipolar patients. No differences were found for the other follow-up periods.

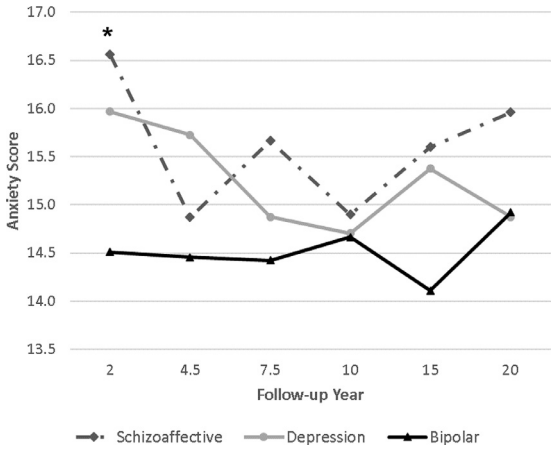

Fig. 1. Longitudinal trajectory of self-reported anxiety in patients with schizoaffective disorder, bipolar disorder, and major depressive disorder over a 20-year period.
Maximum anxiety scale score out of 40.
* Denotes significant difference between groups, which were derived from the individual analyses of variances on the follow-up data.

3.4. Longitudinal trajectory of anxiety over 20-years

A Generalized Estimating Equation Model evaluated for differences between the three patient groups over the six follow-up periods after the index hospitalization phase. There was no significant main effect of group (*Wald Chi-square*(2) = 2.98, $p = 0.23$), follow-up period (*Wald Chi-square*(5) = 6.76, $p = 0.24$) or group by follow-up period interaction (*Wald Chi-square*(10) = 14.79, $p = 0.14$).

3.5. Relationship between initial anxiety and later recovery and global functioning

The relationship between anxiety scores at the two-year follow-up and having a period of recovery over the next 18-years was investigated in all groups combined to ensure a sufficient sample size using a logistic regression. Anxiety scores significantly predicted having a future period of recovery ($\beta = -0.14$, *Wald Chi-square*(1) = 10.07, $p = 0.002$). Anxiety scores also explained a significant proportion of variance in experiencing a future period of recovery, $R^2 = 0.09$.

Second, the relationship between self-reported anxiety at the two-year follow-up and functioning scores at the 20-year follow-up were investigated in all groups. Anxiety scores significantly predicted future functioning ($\beta = -1.75$, $t = -4.096$, $p < 0.001$). Anxiety scores also explained a significant proportion of variance in future functioning scores, $R^2 = 0.14$, $F(1, 106) = 16.78$, $p < 0.001$).

4. Discussion

Anxiety commonly co-occurs in mood and psychotic disorders. In this study, we prospectively examined self-reported anxiety and anxiety-related somatic symptoms in three major groups with an affective diagnosis, schizoaffective, bipolar, and depression patients, over a 20-year follow-up period. Additionally, the relationships between anxiety early in the illness and later recovery and functioning were investigated.

In the early years of the illness (i.e., at the two-year follow-up) we found that schizoaffective and major depression patients reported greater anxiety than bipolar patients. Our results fit into a mixed literature. A study by Young et al. (2013) demonstrated 153 schizoaffective patients had greater rates of anxiety comorbidity then 304 bipolar I disorder patient; whereas, Cosoff and Hafner (1998) investigating 20 schizoaffective and 20 bipolar inpatients found similar rates of anxiety disorder comorbidity in the two disorders. Our findings coincide with the majority of the literature which finds higher rates of anxiety comorbidity for major depression than bipolar disorder, including the National Comorbity Survey Replication (e.g., Kessler et al., 2005). However, a study by Zimmerman et al. (2009) including 286 major depression patients, and 65 bipolar I and 33 bipolar II disorder patients found bipolar patients had a greater rate of comorbidity with anxiety disorder than major depression patients. Our study may help explain differences in cross-sectional data, in that patients at different trajectories of their illness may report different rates of anxiety, which could result in discrepant results across studies. Second, this study used self-reported anxiety items on an inventory as opposed to comparing rates of anxiety comordity, and may potentially explain differences between our findings and other studies. Last, these findings underscore the importance of measuring anxiety in schizoaffective disorder. Anxiety disorders in psychosis have been underevaluated, underdiagnosed, and undertreated due to more restrictive hierarchical diagnostic rules in earlier versions of the Diagnostic and Statistical Manual of Mental Disorders. Of note, studies show cognitive behavioral therapy can be effective in the treatment for anxiety disorders in psychosis (Frueh et al., 2009; Halperin et al., 2000) and given the negative impact of anxiety on functioning in psychosis (Achim et al., 2011), this could be of great impact in improving outcomes and quality of life for individuals with schizoaffective disorder.

Of interest, 37 of our 43 schizoaffective patients were of the depressed subtype at index hospitalization. This suggests that perhaps the schizoaffective patients and major depression patients showed a similar pattern of anxiety symptoms due shared depressive phenomenology. Given our sample size, these findings should be replicated in other longitudinal cohorts. Theoretically, this suggests that transdiagnostic similarities in the anxiety pattern associated in schizoaffective depressed subtype and major depression.

After the 2-year follow-up, we did not find significant differences in self-reported anxiety between the groups, nor did we find a difference in the course of anxiety over the 20-year follow-up period. We have investigated hallucinations in similar sample to that presented in this paper from the Chicago Follow-up Study, which included 25 schizoaffective patients, 25 bipolar with psychosis patients, and 49 depression patients (Goghari et al., 2013). That study demonstrated group differences over the 20-year follow-up period. Schizoaffective patients had more hallucinations than bipolar with psychosis patients at the 2-year follow-up, and depression patients at most follow-ups. Bipolar with psychosis patients did not differ from depression patients at any of the follow-ups. This pattern of differences over the longitudinal course of hallucinations, one key psychotic symptom, in a similar sample, suggests the pattern of no group differences in self-reported anxiety symptoms over the 20-year course of these three disorders might be unique to the phenomenology of anxiety.

We found that self-reported anxiety at the two-year follow-up predicted having a period of recovery over the subsequent 18-years in all patients. Consistent with this finding, anxiety at two-year follow-up predicted global functioning 18-years later in all patients. This suggests the importance of anxiety in mood and psychotic disorders in influencing overall outcome. Our findings are consistent with a body of literature that suggests in both bipolar disorder and major depression, early anxiety predicts the potential for later recovery and functioning (reviewed in Goes, 2015; Goldberg and Fawcett, 2012; Schaffer et al., 2012). Additionally, as treatments exist for anxiety in both mood and psychotic disorders, improving patients' anxiety levels, could be a feasible way to improve outcomes and day-to-day functioning in these disorders (Frueh et al., 2009; Halperin et al., 2000; Kedzior et al., 2015; Wright et al., 2014).

Limitations of this investigation include sample size. Our study could have benefitted from a larger sample size, which would have allowed us to differentially investigate the role of early anxiety on later outcomes within each group separately rather than all patients combined. We also did not have index anxiety data for the schizoaffective group, though we had data from the 2–20-year follow-up period. Additionally, it would have been beneficial to have information on rates of anxiety disorders, in addition to self-reported anxiety for comparison to the previous literature. Last, as we did not use a clinical inventory of anxiety, determining whether changes in this inventory relates to changes in clinically-relevant symptoms cannot be done. However, as we were able to determine that the anxiety symptoms at the 2-year follow-up predicted outcome after 18-years, this suggests that this anxiety scale did relate to clinical phenomenology of interest. This study, however, also has a number of strengths, which is the inclusion of multiple diagnostic groups, including schizoaffective disorder, which is understudied; multiple follow-ups over 20-year period; and a well-characterized sample with measures of symptoms, recovery, and functioning.

In summary, this article further argues for the importance of assessment and diagnosis, and treatment of anxiety symptoms and disorders in psychotic and mood disorders given their presence over the longitudinal trajectory of the disorders and the long term effects of anxiety on outcome. This paper also underscores the necessity of both clinical and research investigations of anxiety in schizoaffective disorder, which has been relatively understudied compared to other mood and psychotic disorders. Furthermore, by comparing three mood and psychotic disorders, this study suggests that the longitudinal pattern of self-reported anxiety could be one way to understand transdiagnostic comorbidities in different disorders. Future longitudinal studies should confirm and extend these findings in larger samples and other disorders.

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Conflict of interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.03.050.

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