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Short-lived mixed affective states in bipolar disorder

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Dear Editor,

People with bipolar disorder are known to have rapid alterations in mood states, and these changes in mood may occur within the course of days and weeks (Judd et al., 2003, 2002). Mood states lasting less than a day are hypothesized to exist but have been poorly studied and characterized (Kramlinger and Post, 1996; Tillman and Geller, 2003). Short-lived states of mixed mood have been studied even less so (Swann et al., 2013). This gap in literature is important to fill given association of mixed symptoms with suicidality and severity of mood episodes (Swann et al., 2013).

We used baseline data from an ongoing longitudinal study examining trajectories of cognitive and inflammatory response in individuals with bipolar disorder to study the prevalence, duration, and associations of subjectively reported mood states in which subjects rate themselves as feeling sad, happy, and energetic simultaneously. Our study design – which included self-reported affective ratings up to 3 times in a day – allowed us to explore the presence and duration of affective states on the scale of hours. Our sample included 50 participants with bipolar I and II disorder (BDs) and 91 healthy comparison participants (HCs). Bipolar disorder diagnosis was confirmed using the Structured Clinical Interview for DSM-IV. Inclusion criteria were diagnosis of Bipolar I or II disorder, age 25 years and greater, currently outpatient, and capable of providing informed consent. Exclusion criteria included acute illness or pregnancy, recent vaccination, history of dementia, seizures, Parkinson's, stroke, or head trauma, history of cancer treatment, uncontrolled diabetes/hypertension, among others.

The subjects' baseline evaluation data was obtained over three clinical visits during a 2-week period. BD subjects were administered Young Mania Rating Scale (YMRS), 28-item Hamilton Depression Rating Scale (HAM-D), Brief Psychiatric Rating Scale (BPRS), and self-reported 36-Item Short Form Health Survey (SF-36) at the start of the 2-week period. BDs were assessed for suicidal ideation (SI) and suicidal behavior (SB) using Columbia-Suicide Severity Rating Scale (C-SSRS) at baseline, middle and end of the 2-week period.

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Declaration of Competing Interest

All authors report no conflicts of interest.

The proportion of ratings in which SI or SB was reported (P-SI and P-SB respectively) was used as a measure of degree of SI and SB.

Both BDs and HCs were given a mobile phone and affective ratings were gathered 3 times per day at random intervals approximating morning, mid-day, and evening. Self-reported momentary ratings were made on 14 consecutive days for a total of 42 ratings. Each specific instance of affecting rating was assumed to represent a period of about 6–8 h. Affective ratings were made on a scale of 0–7 across domains such as sad/depressed, happy, energetic, productive, confident, etc. Average number of affective ratings was 31.5 (SD 8.9) in HCs and 29.5 (SD 10.1) in BDs with no significant difference ($p = 0.231$).

For the purpose of this analysis, Mixed Affective States (MAS) were operationally defined as instances of affective ratings where subjects provided ratings with simultaneously high sadness/depression (4), high happiness (4), and high energy (4). The proportion of total reported ratings with MAS (P-MAS) were calculated for all subjects. Since there were no precedents in literature for defining mixed symptoms with such self-report phone ratings, these criteria were pragmatically chosen based on the affective ratings available, using 4 as the median cut-off point on the 0–7 scale. We recognized that these criteria are not sufficient for a clinical diagnosis of mixed states; this was an operational, proxy definition so that available self-report data could be analyzed to potentially advance our understanding of mixed symptomatology.

Consecutive, uninterrupted affective ratings with MAS were considered a mixed affective “episode”. Maximum duration of mixed affective episodes (measured in spans of affective ratings) was determined for each subject. Short-Lived Mixed Affective States (SLMAS) were defined as mixed affective episodes with a duration of 3 ratings or less (corresponding to a period of less than 24 h). We examined statistical associations using Pearson correlations and differences using independent sample *t*-tests.

Groups were well-matched on age and sex. Mean age for HCs and BDs was 48 (SD 7.6) and 49 (SD 7.9). 57% of HCs and 62% of BDs were female. Mean HAM-D score among BDs was 19.17 (SD 10.85) and mean YMRS was 6.51 (SD 5.30). While both groups had low P-MAS overall, BDs had significantly higher P-MAS compared to HCs: 7.7% (SD 12.6%) vs 3.1% (SD 7.1%), $t = 2.75$, $df = 139$, mean difference = 4.5%, 95% CI 1.3–7.8%, $p = 0.007$. In the BD group, P-MAS was significantly correlated with BPRS total score ($r = 0.375$, $p = 0.011$), HAM-D total score ($r = 0.390$, $p = 0.007$), and SF-36 mental component score ($r = -0.403$, $p = 0.018$), while no significant correlation was found with YMRS total score ($r = 0.087$, $p = 0.561$). These significant correlations remained significant on linear regression even when proportion of ratings with high sadness, high happiness, and high energy as separate variables were controlled for in a general linear model (Table 1), indicating that these significant associations with P-MAS are not being driven by high sadness, high happiness, or high energy individually but rather by their simultaneous experience. In subjects with at least one MAS, a significant correlation was noted between P-MAS and P-SI ($r = 0.614$, $p = 0.004$), while the correlation with P-SB was not significant ($r = 0.342$, $p = 0.094$). Similar significant correlation for P-SI was noted with mean maximum episode duration ($r = 0.810$, $p < 0.001$). Except for two BDs and one control subject, all other

subjects had a maximum episode duration of three ratings or less (Table 1), indicating that these episodes would be considered as short-lived per our definition.

Several limitations need to be pointed out. We utilized an operational, proxy definition of MAS based on self-report only. It is possible that the increased prevalence of SLMAS in BDs may reflect an association with psychiatric comorbidities such as borderline personality disorder or ADHD. We did not have data on comorbidities available for our subjects at the time of analysis, and therefore this possibility remains unexamined. Clinical rating scales were administered at the beginning of the study, while self-reported affective ratings were recorded during the subsequent 2-week burst. Small sample size may also limit generalization, and these findings require replication in larger samples.

In conclusion, our analysis shows that self-reported states of being sad, happy and energy simultaneously are reported with greater frequency in BDs compared to HCs, and that the overwhelming majority of these states have a duration of less than a day. These states are associated with greater depression, worse functioning, and greater suicidal ideation, in congruence with previous literature on traditionally defined mixed states (Swann et al., 2013). Future work will seek to better characterize SLMAS and examine its relationship with psychiatric comorbidities and treatment response.

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Table 1

Associations and duration of self-reported mixed affective states in study subjects.

Pearson correlation of variables with P-MAS in BDs				
	<i>N</i>	<i>r</i>	<i>p</i> -value	<i>p</i> -value adjusted
HAM-D 28 score	47	0.39	0.007	0.008
BPRS-24 score	45	0.375	0.011	0.012
SF-36 mental component	34	−0.403	0.018	<0.001
YMRS	47	0.087	0.561	0.524

Pearson correlation of MAS characteristics with P-SI and P-SB in BDs (restricted to subjects with MAS)						
	P-SI			P-SB		
	<i>R</i>	<i>p</i> -value	<i>N</i>	<i>R</i>	<i>p</i> -value	<i>N</i>
P-MAS	0.614	0.004	20	0.342	0.094	25
Maximum episode duration	0.810	<0.001	20	0.270	0.1917	25

Maximum duration of episodes of MAS (measured in the span of affective ratings)			
	Maximum episode duration	<i>N</i> of subjects	Percentage
Healthy controls	1	29	90.6
	2	2	6.3
	3	0	0.0
	4	1	3.1
	Total	32	100
Individuals with bipolar disorder	1	18	69.2
	2	4	15.4
	3	2	7.7
	4	1	3.8
	5	1	3.8
	Total	26	100

BPRS – Brief Psychiatric Rating Scale; HAM-D – 28-item Hamilton Depression Rating Scale; MAS – Mixed Affective States; P-MAS – Proportion of total ratings with mixed affective states; P-SI – Proportion of ratings in which suicidal ideation was reported; P-SB – Proportion of ratings in which suicidal behavior was reported; SF-36 – 36-Item Short Form Health Survey (SF-36); YMRS – Young Mania Rating Scale.