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The effect of mood phases on balance control in bipolar disorder

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ABSTRACT

The aim of this study was to investigate balance control during gait and sit-to-walk in individuals with bipolar disorder and healthy controls by examining the inclination angles between the whole-body center-of-mass (COM) and ankle in the sagittal plane. Twenty-one individuals with bipolar disorder in the euthymic (i.e., asymptomatic; n = 11) and depressed (n = 10) phases and 7 healthy controls (ages between 18 and 45) performed gait and sit-to-walk at self-selected comfortable speed. Mood phases for individuals with bipolar disorder were measured using the Patient Health Questionnaire and Altman Self-Rating Mania Scale. We collected motion data using a 16-camera motion capture technology. We found smaller COM-ankle inclination angles at seat-off during sit-to-walk for the bipolar-depressed group compared to the bipolar-euthymic and healthy groups, indicating poorly controlled balance for the bipolar-depressed group in sit-to-walk. However, we found larger COM-ankle inclination angles at beginning of single stance phase of gait for the bipolar-euthymic group compared to the healthy group, indicating well controlled balance for the bipolar-euthymic group in gait. Our results suggest an association between the depressed phase and balance impairment during daily movements in relatively young adults (ages $\leq$ 45 years). Our results also suggest that the depressed phase may be as detrimental to balance control as the effect of age-related neuromuscular weakness.

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1. Introduction

Over 10% of U.S. adults aged 39 years and younger have a lifetime history of mood disorders (Jonas et al., 2003), and mood disorders are the largest contributor to disability in adults aged 45 years and younger (United States Burden of Disease Collaborators, 2013). Bipolar disorder is a disabling mood disorder that is characterized by periods of depressed and manic/hypomanic phases, with periods of euthymic (asymptomatic) phase (American Psychiatric Association, 2013). Statistics show that lifetime and 12-month prevalence of bipolar disorder is 4.4 and 2.8%, respectively, among adults in the United States, with mean age of onset at approximately 20 years old (Merikangas et al., 2007). Individuals with bipolar disorder are known to spend a major part of their life either in the depressed phase (approximately 30%) or the euthymic phase (approximately 50%) (Judd et al., 2002).

A growing body of literature demonstrates that mood disorders are accompanied by abnormalities in motor behavior. For example, individuals with bipolar disorder have unsteady gait pattern (Hausdorff et al. 2004) and poor performance in upper body extremity tasks (Lohr and Caligiuri, 2006; Lage et al., 2013) compared to healthy individuals. In addition, our recent study found that the hypomanic phase in bipolar disorder is associated with fast movement speed (Kang et al., 2018). Furthermore, individuals with major depressive disorder have slower gait velocity (Lemke et al., 2000; Michalak et al., 2009; Radovanović et al., 2014) and poorer performance in upper extremity tasks (Lohr et al., 2013) compared to healthy individuals.

Recent evidence also suggests that impairment in balance control is an important motor symptom in mood disorders. It was reported that individuals with bipolar disorder in the euthymic phase (Bolbecker et al., 2011) and individuals with major depressive disorder (Doumas et al., 2012; Deschamps et al., 2015) have significantly larger sway area during quiet standing, compared to healthy individuals. Additionally, balance control during quiet standing in individuals with major depressive disorder was improved after a repetitive transcranial magnetic stimulation treatment (Deschamps et al., 2016; Thomas-Ollivier et al., 2016).

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Taken together, these findings about abnormal motor behavior with mood disorders and impaired balance control during quiet standing in bipolar disorder (the euthymic phase) and major depressive disorder suggest that individuals with bipolar disorder in the euthymic and depressed phases may also have impaired balance control during motor behavior tasks. However, the association between mood disorders and balance control during tasks of daily living is not yet known.

Although investigating balance impairment during activities of daily living is common in older adults with and without clinical conditions (ages $\geq$ 65 years), reports by Bolbecker et al. (2011) and Doumas et al. (2012) suggest balance impairment in mood disorders may be observed in relatively young adults much less than 65 years old. Moreover, high prevalence of mood disorders, which accounts for the largest cause of disability, in relatively young adults (ages $\leq$ 45 years) suggest that it may be even more important to investigate motor symptoms such as balance impairment in mood disorders in this age group. Since this younger adult age group is less likely to have age-related confounders in motor symptoms, investigation of their motor behavior may lead to a better understanding of the association between mood disorders and balance control during activities of daily living.

Gait and sit-to-walk are functional daily movements that require complex control of balance during postural transitions in adults across all ages (Kang and Dingwell, 2008; Magnan et al., 1996). Several studies have assessed balance control in gait and sit-to-walk by examining the relative position of the whole-body center-of-mass (COM) to the ankle or the center-of-pressure (COP), and have shown that COM-ankle or COM-COP inclination angles are affected by age and risk of falling (Chen and Chou, 2010; Chen and Chou, 2013; Chen and Chou, 2017; Hahn and Chou, 2004; Lee and Chou, 2006; MacKinnon and Winter, 1993; Sawers and Hahn, 2012). For example, Lee and Chou (2006) reported that COM-COP inclination angles in the sagittal plane were significantly smaller for older adults at risk for falls compared to healthy older adults. In another study, Chen and Chou (2013) reported that, during sit-to-walk, COM-ankle inclination angles in the sagittal plane at seat-off were significantly more posterior for healthy older adults compared to older adults with a history of falling. Although previous studies report impaired balance control in individuals with mood disorders during standing tasks and in older adults during dynamic tasks, it is not known how balance control might be impaired in individuals with bipolar disorder during dynamic tasks like gait and sit-to-walk.

The aim of this study was to investigate COM-ankle inclination angles in the sagittal plane during gait and sit-to-walk in individuals with bipolar disorder in the euthymic and depressed phases and healthy individuals aged 45 years or younger. It is widely recognized that balance control during dynamic movement is disturbed by central nervous system dysfunction (Winter, 1995), which is a major feature of bipolar disorder (Manji et al., 2003). Therefore, we hypothesized that bipolar-depressed and bipolar-euthymic individuals would have smaller COM-ankle inclination angles in the sagittal plane compared to healthy individuals. Between bipolar-depressed and bipolar-euthymic individuals, we hypothesized that COM-ankle inclination angles in the sagittal plane would be similar.

2. Methods

The current study represents an additional analysis of data from a subset of participants collected in a larger study that was reported elsewhere (Kang et al., 2018). The previous analysis focused on mood phase effects on spatiotemporal and kinetic gait parameters of gait and sit-to-walk, and the current analysis focuses on mood phase effects on balance control. In the previous study, participants were identified from the Heinz C. Prechter Longitudinal Study of Bipolar Disorder Cohort (McInnis et al., 2018), and a total of 53 adult participants (39 bipolar; 14 healthy) consented to the experimental protocol approved by the University of Michigan Institutional Review Board. Mood phase on the day of testing for the 53 participants was measured using two self-report questionnaires: the 9-item Patient Health Questionnaire (PHQ-9; depressive symptomatology; score from 0 to 3 per item) (Kroenke et al., 2001) and the 5-item Altman Self-Rating Mania Scale (ASRM; manic symptomatology; score from 0 to 4 per item) (Altman et al., 1997). We included 21 bipolar participants who were in the euthymic phase (n = 11; PHQ-9 < 6; ASRM < 6) or the depressed phase (n = 10; PHQ-9 $\geq$ 6; ASRM < 6) (Saunders et al., 2014), and 7 healthy participants. All participants were 45 years old or younger. Bipolar participants had a diagnosis of bipolar disorder meeting clinical criteria in the fourth edition Diagnostic and Statistical Manual of Mental Disorder (American Psychiatric Association, 2000) and had no active substance abuse in the past 3 months. Healthy participants had no personal diagnosis of any mental disorder. All participants were free from neurological or orthopedic disorder that might affect gait and sit-to-walk.

Participants performed gait trials on an 8-meter walkway and sit-to-walk trials from an armless and backless chair (height 42 cm) at self-selected comfortable speed. We collected data from a total of 5 trials for each movement. We used a 16-camera optoelectronic motion capture system (Motion Analysis Corp., Santa Rosa, CA), and collected movement data from 54 reflective markers attached on each participant's whole-body: bilaterally on the forehead and posterior head, acromion process of the scapula, upper arm, lateral humeral epicondyle, forearm, radial and ulnar styloids, the second and fifth metacarpal heads, anterior superior iliac spine, posterior superior iliac spine, thigh, lateral femoral epicondyle, shank, lateral malleolus, the first and fifth metatarsal heads, cuboid and heel, and unilaterally on jugular notch, xiphoid process, C7, T10, right scapula and sacrum. Additionally, 8 reflective markers (bilaterally on the medial humeral epicondyle, greater trochanter, medial femoral epicondyle and medial malleolus) were attached during a static reference trial prior to movement trials; the markers on the lateral and medial malleoli were used to estimate the position of ankle joint center (i.e., midpoint between lateral and medial malleoli). Due to technical issues, the marker number and placement (the fifth metacarpal head and cuboid) were slightly modified for one bipolar participant. We also collected ground reaction force data using a force plate (Advanced Mechanical Technology Inc., Watertown, MA) embedded in the floor to detect several gait and sit-to-walk events. The marker data were sampled at 120 Hz, and were filtered at 6 Hz using a fourth-order Butterworth low-pass filter. The ground reaction force data were sampled at 1200 Hz, and were filtered at 50 Hz using a fourth-order Butterworth low-pass filter.

Visual3D (C-Motion Inc., Germantown, MD) was used for data analysis. The whole-body COM was calculated using the weighted sum of a 15-segment biomechanical model (Kang and Gross, 2015; Kang and Gross, 2016). We calculated gait velocity during one gait cycle and sit-to-walk duration (i.e., time interval between onset and stance leg toe-off). Onset was identified using the initial COM movement in the forward direction (Kerr et al., 2004) and stance leg toe-off was identified using the ground reaction force data. Additionally, we identified seat-off using the pelvis movement in the vertical direction, and swing leg toe-off using the shank angular velocity (Greene et al., 2010).

We followed previously validated methods to calculate COM-ankle inclination angles in the sagittal plane (Chen and Chou, 2010). Briefly, two lines were created, one that connected the COM and the ankle joint center of the stance foot and another vertical line that passed through the ankle joint center. The COM-ankle inclination angle was calculated as the angle between the two lines in the sagittal plane. We investigated COM-ankle inclination angles for the stance foot at contralateral toe-off (i.e., beginning of the single stance phase) and contralateral heel strike for gait trials (end of single stance phase) (Fig. 1) (Chen and Chou, 2010). For sit-to-walk trials, COM-ankle inclination angles for the initial stance foot at the instant of seat-off and for the initial swing foot at the instant of stance leg toe-off were investigated (Fig. 1) (Chen and Chou, 2013).

Age, age of onset, year of illness, gait velocity, stride length, sit-to-walk duration and length of the first step during sit-to-walk passed the normality test using Shapiro-Wilk test. Thus, mean values in such variables were compared among the bipolar-euthymic, bipolar-depressed and healthy groups using one-way analysis of variance (ANOVA) with Tukey correction. Body mass index, PHQ-9 and ASRM did not pass the normality test, thus mean differences were compared using Kruskal-Wallis test. COM-ankle inclination angles were compared using a linear mixed model with random effects of participant and fixed effects of gait velocity/sit-to-walk duration (i.e., covariate) and group to control for potential effects of gait velocity/sit-to-walk duration (Chen and Chou, 2013). A p-value less than 0.05 was considered significant when testing differences among the bipolar-euthymic, bipolar-depressed and healthy groups for all statistical analyses. We estimated effect size using Cohen's d, which was denoted as d in the results section ($0.2 \leq d < 0.5$ as a small effect; $0.5 \leq d < 0.8$ as a medium effect; $0.8 \leq d < 1.3$ as a large effect) (Cohen, 1988).

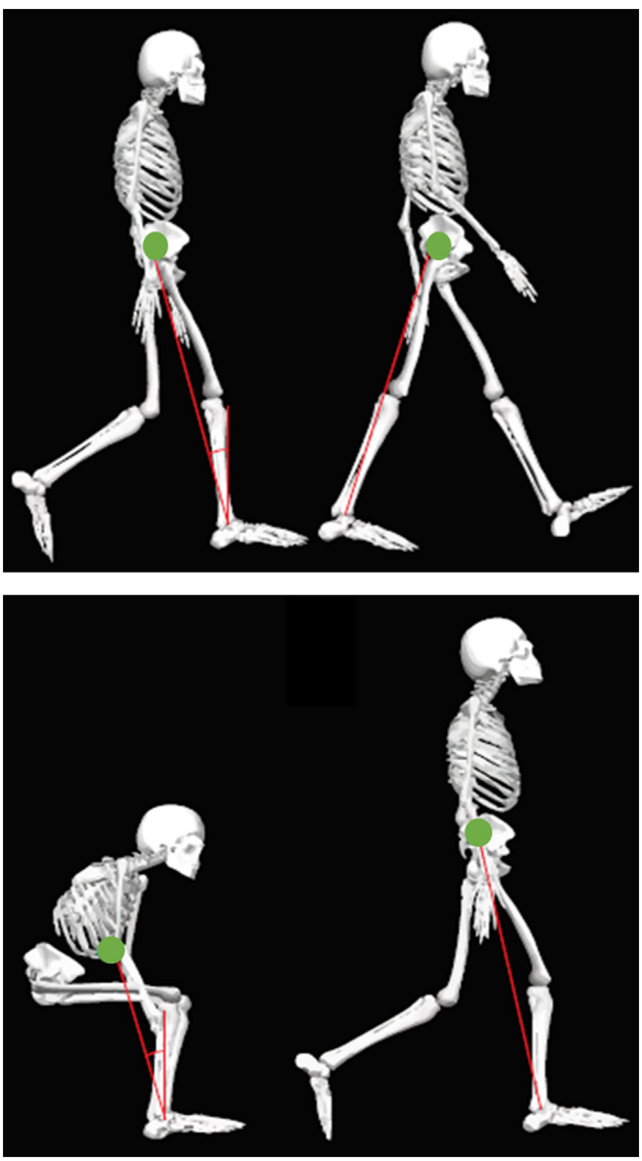

Fig. 1. COM-ankle inclination angles in the sagittal plane. Dots represent the whole-body center-of-mass. COM-ankle inclination angles were calculated at the instants of contralateral toe-off (top left) and contralateral heel strike (top right) for gait trials, and the instants of seat-off (bottom left) and stance leg toe-off (bottom right) for sit-to-walk trials.

3. Results

Age and body mass index were not different among the bipolar-euthymic (34.5 ± 7.0 years; 26.0 ± 4.0 kg/m^2), bipolar-depressed (35.4 ± 6.6 years; 27.4 ± 7.5 kg/m^2) and healthy groups (30.9 ± 4.0 years; 25.0 ± 4.1 kg/m^2) ($p = 0.328$ and 0.624, respectively). Total score on PHQ-9 was greater for the bipolar-depressed group (14.7 ± 6.5) than for the bipolar-euthymic (2.3 ± 1.5) and healthy (0.0 ± 0.0) groups ($p < 0.001$), and total score on ASRM was similar among the bipolar-euthymic (2.1 ± 1.6), bipolar-depressed (1.3 ± 1.6) and healthy (1.1 ± 3.0) groups ($p = 0.104$). Age of onset and years of illness were similar between the bipolar-euthymic (15.6 ± 4.3 years; 20.7 ± 9.1 years) and bipolar-depressed groups (15.5 ± 6.1 years; 19.7 ± 7.5 years) ($p = 0.633$ and 0.844, respectively). Most of the bipolar participants were taking multiple psychiatric medications: lithium (n = 8), anticonvulsants (n = 11), antipsychotics (n = 9), antidepressants (n = 11) and sedative-hypnotics (n = 4).

Mean gait velocity, stride length, sit-to-walk duration and length of the first step during sit-to-walk were not different among the bipolar-euthymic, bipolar-depressed and healthy groups ($p = 0.735$, 0.320, 0.920 and 0.901, respectively) (Table 1). When the effect of gait velocity and sit-to-walk duration were separated using the linear mixed model, significant effects of group on COM-ankle inclination angles emerged with large effect size (Table 2). During gait, COM-ankle inclination angles at contralateral toe-off for the bipolar-euthymic group were 1.9° and 1.6° larger compared to the bipolar-depressed and healthy groups, respectively ($p = 0.016$ and $d = 0.97$; $p = 0.012$ and $d = 0.89$, respectively). COM-ankle inclination angles at contralateral heel strike were not affected by group ($p = 0.459$). During sit-to-walk, COM-ankle inclination angles at seat-off were 2.9° and 3.7° smaller for the bipolar-depressed group compared to the bipolar-euthymic and healthy groups, respectively ($p = 0.007$ and $d = 0.94$; $p = 0.006$ and $d = 1.36$, respectively). There was no group effect on COM-inclination angles at stance leg toe-off ($p = 0.433$).

4. Discussion

The aim of this study was to assess balance control during gait and sit-to-walk in individuals with bipolar disorder and healthy individuals, who were 45 years or younger, by examining COM-

Table 1
Mean gait velocity and sit-to-walk duration for the bipolar-euthymic, bipolar-depressed and healthy groups for the comfortable speed condition.

	Euthymic	Depressed	Healthy
Gait velocity (m/s)	1.20 (0.14)	1.16 (0.28)	1.24 (0.12)
Stride length (m)	1.41 (0.11)	1.31 (0.17)	1.39 (0.13)
Sit-to-walk duration (s)	1.92 (0.26)	1.92 (0.22)	1.88 (0.16)
Step length (m)	0.70 (0.09)	0.70 (0.10)	0.68 (0.08)

Note: Values in parentheses are standard deviations.
There were no significant differences in gait velocity, stride length, sit-to-walk duration and step length among the three groups when compared using one-way ANOVA with Tukey correction (all $p > 0.05$).

Table 2
Mean COM-ankle inclination angles in the sagittal plane for the bipolar-euthymic, bipolar-depressed and healthy groups for the comfortable speed condition.

COM-ankle inclination angles (°)	Euthymic	Depressed	Healthy
Gait			
Contralateral toe-off	−12.7 (1.9)	−10.8 (2.0)*	−11.1 (1.7)*
Contralateral heel strike	17.0 (2.4)	16.9 (3.0)	17.7 (1.7)
Sit-to-walk			
Seat-off	−12.2 (2.7)†	−9.3 (3.4)	−13.0 (1.8)†
Stance toe-off	−8.9 (2.3)	−8.4 (1.5)	−7.9 (1.2)

Note: Values in parentheses are standard deviations.
* Significant differences ($p < 0.05$) compared to the bipolar-euthymic group using the linear mixed model with random effects of participant and fixed effects of gait velocity and group.
† Significant differences ($p < 0.05$) compared to the bipolar-depressed group using the linear mixed model with random effects of participant and fixed effects of sit-to-walk duration and group.

ankle inclination angles in the sagittal plane. The primary finding was that balance control was diminished in the bipolar-depressed group during sit-to-walk, as evidenced by smaller COM-ankle inclination angles during the standing phase compared to the healthy and bipolar-euthymic groups. In contrast, balance control in the bipolar-euthymic group was similar to or even better than the healthy and bipolar-depressed groups during gait and sit-to-walk. This study investigates the effects of bipolar disorder on balance control during dynamic motor tasks, and demonstrates a vulnerability of individuals with bipolar disorder in the depressed phase for risk of instability.

In this study, COM-ankle inclination angles at seat-off were 3-4° smaller for bipolar-depressed young adults than for bipolar-euthymic and healthy young adults, which was comparable to the report by Chen and Chou (2013). The decrease in COM-ankle inclination angles during sit-to-walk indicates balance impairment in the bipolar-depressed group were similar to the decrease in inclination angle reported by Chen and Chou (2013) for healthy older adults and older adults with a history of falling compared to healthy young adults. These results suggest that the effect of depressed mood on balance control during sit-to-walk in young adults may be as detrimental to balance control as the effect of age-related neuromuscular weakness. Our results were in line with previous reports for balance impairment during quiet standing in individuals with major depressive disorder (Deschamps et al., 2015; Deschamps et al., 2016; Doumas et al., 2012; Thomas-Ollivier et al., 2016), and provides further evidence of the association between mood disorders and balance deficits. Importantly, impaired balance control during motor behavior tasks is related to instability in performing daily movements (e.g., gait) (Dingwell et al., 2001), suggesting that the depressed phase may be associated with instability outside of the laboratory.

Although it was expected that the bipolar-euthymic group would have smaller COM-ankle inclination angles (i.e., poorer balance control) during movements compared to the healthy group, COM-ankle inclination angles were actually the largest for the bipolar-euthymic group at the instant of contralateral toe-off (i.e., beginning of single stance phase). Larger COM-ankle inclination angles (approximately 3°) in the sagittal plane during gait have been reported for healthy older adults relative to older adults with gait impairment (Lee and Chou, 2006). Although the difference in our results between the bipolar-euthymic and healthy groups (1.6°) was less than differences reported by Lee and Chou (2006), our results indicate that balance control for the bipolar-euthymic group was at least comparable to, if not better than, the healthy group.

Our results for the bipolar-euthymic group for gait were opposite to a previous study reporting poor balance control during quiet standing in euthymic individuals with bipolar disorder compared to healthy individuals (Bolbecker et al., 2011). One possible reason for the apparently conflicting results is the difference in tasks: dynamic movement and quiet standing. Balance control during dynamic movement such as gait and that during static posture impose two distinct requirements for the central nervous system (Winter, 1995). Additionally, previous evidence suggests that static and dynamic balance control are different in individuals with balance impairment. For example, the increase in postural sway in individuals with balance impairment from standing on a static platform to a dynamic platform was not as large as in healthy controls (Nardone et al., 2006). Although it was not possible to directly compare static and dynamic balance control in our dataset, it may be that mood phase affects balance control differently for static and dynamic motor tasks. Alternatively, the use of antidepressants may explain the differences. It has been reported that, in older adults, some antidepressants worsen balance control during quiet standing (Laghrissi-Thode et al., 1995) but increase gait velocity (Draganich et al., 2001; Paleacu et al., 2007), and increased gait velocity may lead to increase in COM-ankle inclination angles as shown in this study. Since the participants tested in this study performed dynamic movements only, however, it is still unclear if these postulated explanations account for the greater stability in gait for the bipolar-euthymic group than for the healthy group.

In conclusion, bipolar disorder is associated with alterations in balance control in young adults during daily movements. Instability in sit-to-walk (i.e., smaller COM-ankle inclination angles) was manifested in the depressed phase, and more stable gait (i.e., larger COM-ankle inclination angles) was manifested in the euthymic phase. Our findings also suggest that clinicians and researchers should consider balance impairment as an important motor symptom for the depressed phase.

Conflict of interest

Drs. Kang, Mickey and Gross, and Mr. Krembs have no conflict of interest. Dr. McInnis has consulted for Janssen and Otsuka Pharmaceuticals.

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