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## Brief report

# Exercise tolerance is reduced in bipolar illness

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#### Abstract

*Background:* Cardiovascular and cerebrovascular disease is 2–3 times more common in bipolar patients than the general population. Asymptomatic bipolar patients have electrocardiogram abnormalities at high rates. The question of heart function in asymptomatic bipolar subjects arises.

Methods: This study examined the impact of exhaustive exercise on cardiac function in untrained euthymic bipolar and control subjects. Twenty-four non-athletic adults, 10 controls and 14 with bipolar type I, exercised on a treadmill at 70% of maximal oxygen consumption until physical exhaustion. Two-dimensional and Doppler echocardiography were performed before and immediately after exercise.

Results: Bipolar subjects had significantly reduced exercise duration (75.9 $\pm$ 40.5min for bipolar and 95.0 $\pm$ 40.1 min for control, P<0.01). There were no statistical differences between bipolar illness and normal controls in echocardiographic variables either at rest or after exhaustive exercise.

Conclusion: Medically asymptomatic, euthymic bipolar subjects appear to have reduced exercise tolerance but normal cardiac function

Limitations: More bipolar patients smoked (28.6% vs. 0% controls) and patients tended to be heavier (189.1 $\pm$ 29.3 vs. 165.0 $\pm$ 29.5 lb, t=2.0, P=0.06). None of the normal controls were taking any medications. These variables could have impacted the reduced exercise tolerance.

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#### 1. Introduction

Bipolar illness is a severe psychiatric condition that is characterized by extensive comorbidity. Psychiatric comorbidity of anxiety disorders and substance abuse

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is quite high (Kessler et al., 2005). Medical comorbidity is less well studied, but recent surveys have found that bipolar patients suffer from chronic medical problems at two to three times the rate of the general population. For example over 35%–50% of bipolar patients are obese (Fagiolini et al., 2002, 2003; Shah et al., in press), compared with some 22% of the general population (Ferri, 2005). Cardiovascular disease is particularly more prevalent in bipolar subjects compared to the

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general population, with hypertension affecting 34.8% of bipolar subjects (Kilbourne et al., 2004) and only about 15% of the general population, and congestive heart failure diagnosed in 3.2% of bipolar subjects (Kilbourne et al., 2004) compared with 1.6% of the general population (Ferri, 2005). Similarly, the standardized mortality ratios (SMRs) for non-suicide deaths in bipolar subjects are nearly twice that of the general population (Osby et al., 2001). Over 26% of bipolar subjects admitted to an inpatient unit for treatment of a mood episode have abnormal electrocardiograms (El-Mallakh et al., 1996).

There may be many reasons for the higher rates of medical problems. For example, some two-thirds of bipolar patients smoke and a larger fraction has a history of smoking (de Leon et al., 2002; Corvin et al., 2001). Medications may contribute to weight gain, and higher rates of obesity (McElroy et al., 2002; Fagiolini et al., 2003). These factors can increase the risk of cardiovascular and cerebrovascular disease. To examine this question, we performed echocardiographs in untrained, medically asymptomatic bipolar subjects and matched normal controls at baseline and after exhaustive exercise.

#### 2. Methods

The study was approved by the Human Studies committee at our institution. Written informed consent was obtained from all participants.

#### 2.1. Participant characteristics

Twenty-four (14 males and 10 females) healthy adults were enrolled in the study. Inclusion criteria included age ≥ 18 years, able to give consent, and ambulatory with normal pulmonary function test. Exclusion criteria are competitive athletes, or history of heart or lung disease. None were diagnosed nor received medications for chronic medical conditions. All patients were clinically euthymic (mood scales were not performed). Control subjects denied any history of mood disorders or psychotic illness, but did not undergo a structured diagnostic interview.

#### 2.2. Pulmonary and metabolic measurements

Pulmonary function test and the rate of oxygen consumption  $(VO_2)$  measurements were performed using routine methods with a Sensormedics (V Max series. 229, Yorba Linda, CA) system. Pulmonary function testing and  $VO_2$  were measured at baseline, and were monitored throughout the exercise duration.

#### 2.3. Echocardiography

Two-dimensional and Doppler echocardiography were performed at baseline, and immediately after exercise. Echocardiography was performed using ATL Ultrasound system (HDI 5000 [2–4 MHz transducer]) and HP (Hewlett-Packard) 2500 (2.5–3.5 MHz transducer) systems. Standard views were obtained with the patient in the left decubitus position. Pulse wave Doppler was performed as previously described (American Society of Echocardiography, 2002). Left ventricular volumes and ejection fraction were calculated using Biplane Simpson's method (Schiller et al., 1989), while cardiac output was measured using Doppler methods of the left ventricular outflow tract (LVOT) (McLean et al., 1997). Images were recorded on SVHS tapes, which were subsequently analyzed using the TomTec system.

#### 2.4. Exercise protocol

All subjects exercised at an initial speed of 1.7 mph with 10% grade. The incline and the speed of the treadmill were increased progressively according to the subject's oxygen consumption (VO<sub>2</sub>), until it reached 70% of the maximum predicted value. Then, the treadmill's speed and incline were maintained to keep VO<sub>2</sub> consumption at that level until the subject reached physical exhaustion. Subjects were paid \$1.00/min of exercise as an incentive to maintain exercise level until true exhaustion.

#### 2.5. Statistical analysis

Results are presented as mean+standard deviation (SD). Comparison of all measurements were made using paired Student's *t*-test with correction for multiple comparisons using Bonferroni's method. Correlations utilized simple and multiple linear regression analysis. A test for examining proportional criteria was used to assess the relative fractions of subjects exceeding 60 min of exercise (El-Mallakh et al., 1994).

#### 3. Results

Demographics of study participants are presented in Table 1. The average age of bipolar subjects was  $41.3\pm \text{SD}$  11.9 years and for the control population it was  $37.7\pm11.5$  years (t=0.74, P=0.47). Four bipolar subjects smoked, but none of the controls smoked. Bipolar patients tended to be heavier than psychiatrically normal controls (189.1 $\pm$ 29.3 vs. 165.0 $\pm$ 29.5 lb, t=2.0, P=0.06). Six bipolar subjects were obese while

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