



# Higher cardio-respiratory fitness is associated with increased mental and physical quality of life in people with bipolar disorder: A controlled pilot study

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## ABSTRACT

The aim of this study was to investigate whether cardiorespiratory fitness among outpatients with bipolar disorder is associated with health related quality of life (HRQL) and explore differences versus healthy controls. Outpatients with bipolar disorder and healthy controls matched for age, sex and body mass index completed the 36-item Short Form Health Survey, the Positive-and-Negative-Affect-Schedule (PANAS), a maximal cardiorespiratory fitness test, and wore a Sensewear Armband to measure physical activity and sedentary behavior for eight days. Unpaired *t*-tests, Pearson correlations and backward regression analyses were performed. Outpatients with bipolar disorder ( $n = 20$ ; 14♀;  $47.9 \pm 7.9$  years) had a significantly lower physical and mental HRQL than healthy controls ( $n = 20$ ; 14♀;  $47.8 \pm 7.6$  years), a lower maximum oxygen uptake ( $VO_{2max}$ ) and were more sedentary. While no significant correlates were found for HRQL in controls, higher  $VO_{2max}$  values and lower PANAS negative affect scores predicted better physical and mental HRQL in people with bipolar disorder. The final regression model explained 68% and 58% of the variability in physical and mental HRQL respectively. Cardiorespiratory fitness is associated with mental and physical HRQL among people with bipolar disorder. The current study offers novel targets for scientific investigation and clinical interventions to increase HRQL in people with bipolar disorder.

## 1. Introduction

Bipolar disorder (BD) is a chronic and severe mental illness with a life-time prevalence of approximately 2% (Stubbs et al., 2016). According to the World Health Organization global burden of disease study, BD ranks within the top 20 causes of disability among all medical conditions worldwide and 6th among all mental disorders (Whiteford et al., 2010). Of particular concern is the 10-year lower life expectancy as compared to the general population (Kessing et al., 2015a). Although the underlying causes for the increased risk for premature mortality are multi-factorial, it is well established that a higher risk for cardio-metabolic diseases plays a major role (Kessing et al., 2015b). Cardio-

metabolic co-morbidity is increased in people with BD (Vancampfort et al., 2015a, 2016a) with psychotropic medication use (Correll et al., 2015) and unhealthy lifestyle behaviours (Bly et al., 2014; Martin et al., 2016; Vancampfort et al., 2016b, 2016c) key contributing factors.

Unsurprisingly, the chronic nature, the recurrence of manic and/or depressive symptoms and the high prevalence of somatic co-morbidities have a major impact on the physical and psychological domains of health related quality of life (HRQL) of a person with BD (Bernstein et al., 2016; Jansen et al., 2013; Martín-Subero et al., 2014). HRQL is an important patient-rated outcome and is a measure of the impact an illness has upon the functional health status as perceived by the patients themselves (IsHak et al., 2012). It is therefore an important target of

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interventions aiming to achieve functional recovery and identifying determinants of HRQL in people with BD is essential and may help improve the focus of multidisciplinary treatment. Previous research indicated that the presence of depressive symptoms (Michalak et al., 2013; Piccinni et al., 2007), somatic (Fenn et al., 2005; Kilbourne et al., 2009; Kolotkin et al., 2008) and psychiatric (e.g., the presence of anxiety) (Albert et al., 2008) co-morbidity, cognitive problems (Anaya et al., 2016), illicit drug use (Kilbourne et al., 2009), nicotine dependence and a lack of social support (Gutiérrez-Rojas et al., 2008) all have a profound negative impact on HRQL in people with BD.

There is a growing interest in the association between cardiorespiratory fitness and health and well-being among people with BD (Vancampfort and Stubbs, 2016), yet to date, the impact of cardiorespiratory fitness on the HRQL of people with BD has not been investigated. This is surprising given the fact that people with BD have significantly reduced cardiorespiratory fitness levels ((Vancampfort et al., 2015b, 2016d), and that lower fitness levels are associated with difficulties in undertaking activities of daily life (Vancampfort et al., 2016e). Although the relationship between cardiorespiratory fitness and general health perceptions has been found in population-based studies (Sloan et al., 2009), research investigating this relationship among people with BD is lacking.

The aim of the current study was to examine the relationship between cardiorespiratory fitness and HRQL among people with BD and determine if this relationship differed compared to healthy controls. To this end, we first assessed the mental and physical HRQL, cardiorespiratory fitness and physical activity participation of people with BD compared with an age, gender and body mass index matched healthy population.

## 2. Methods

### 2.1. Participants and procedure

Over a 10-month period, consecutive adult (18–65 years) outpatients with a DSM 5 diagnosis of BD I or II (American Psychiatric Association, 2013) of the UPC KU Leuven, campus Kortenberg, in Belgium were invited to participate. Acutely psychotic patients and those with a DSM 5 diagnosis of substance use disorder during the previous 6 months were excluded. Somatic exclusion criteria included evidence of severe cardiovascular, neuromuscular and endocrine disorders, which, according to the American College of Sports Medicine (2013), prevented participants of being physically active as per usual. Healthy control subjects were recruited among acquaintances of the wider research team. These researchers were however unaware of the specific aims of this research (i.e. comparison of data with BD patients) and blinded from the test results of the patient population. All healthy controls were volunteers who received a general physical examination and were free of significant cardiovascular, neuromuscular and endocrine disorders that might hinder safe participation. An independent statistician performed the matching for age, gender and body mass index (BMI). The study procedure was approved by the Scientific and Ethical Committee of the UPC KU Leuven, campus Kortenberg, Belgium and conducted in accordance with the principles of the Declaration of Helsinki. All participants gave their informed written consent. There was no compensation for participation in the study.

### 2.2. Anthropometric assessments

Anthropometric measurements included body weight and height. Body weight was measured in light clothing to the nearest 0.1 kg using a SECA beam balance scale, and height to the nearest 0.1 cm using a wall-mounted stadiometer.

### 2.3. Medication use

Data on current use of antidepressants, mood stabilizers and antipsychotics was collected from the medical records. Daily dosage of each antipsychotic was converted into a daily equivalent dosage of chlorpromazine following the consensus of Gardner et al. (2010). If patients were treated with a combination of antipsychotics, all obtained equivalent dosages of chlorpromazine were summed together. We did not include the daily dosage of mood stabilizers in the statistical analyses if the same mood stabilizer was not present in at least 10 participants.

### 2.4. Cardiorespiratory fitness testing

Graded exercise tests were conducted to measure cardiorespiratory fitness. All tests were performed on a cycle ergometer (Siemens-Elema 380B; Ergometrics 800S, Ergometrics, Bitz, Germany) in an air-conditioned laboratory where the room temperature was regulated at 18–22 °C. Tests were supervised by an experienced physiotherapist (PhD) blinded for the patient status and for other test results. Patients were asked to cycle at a constant rate of 60 rates per minute. The initial workload of 20 W was increased by 20 W every minute. Blood pressure was measured at rest, with the patient sitting on the bicycle, and every 2 min during the graded exercise test. Heart rate and a 12-lead electrocardiogram (Max Personal Exercise Testing®, Marquette, WI, USA) were registered continuously. In- and expired gasses were analyzed breath-by-breath by means of the Oxycon Pro (Jaeger, Mijndhardt, The Netherlands). In order to define a maximal oxygen uptake ( $\text{VO}_{2\text{max}}$ ) (ml/kg/min) we followed the criteria described by the European Association for Cardiovascular Prevention and Rehabilitation (Mezzani et al., 2009). A maximal effort was assumed if the cardiopulmonary exercise testing was terminated by the patient due to exhaustion, dyspnea, pain or tiredness in the legs and if (1) a peak respiratory exchange ratio (RER)  $\geq 1.10$  and/or (2) a rating of perceived exertion  $\geq 16$  on the Borg Scale (Borg, 1998).

### 2.5. Health related quality of life: the 36-item Short Form Health Survey (SF-36)

The SF-36 health related quality of life questionnaire (Ware et al., 1993) assessed eight domains of functioning during the previous four weeks, including: physical functioning, role limitations due to physical problems, vitality, bodily pain, social functioning, role limitations due to emotional problems, in addition to mental and general health. Scores for the SF-36 range from 0 to 100, with higher scores indicating a better health related quality of life. The four domains: physical functioning, role limitations due to physical problems, bodily pain and general health were summarised into a physical component score, whereas the four domains energy/vitality, social functioning, role limitations due to emotional problems and mental health were summarised into a mental component score.

### 2.6. The Positive-and-Negative-Affect-Schedule (PANAS)

The PANAS (Watson et al., 1988) is a 20-item questionnaire assessing positive and negative affect and was chosen as a measure of usual daily mood. Ten items measure positive affect (e.g., excited, inspired) and 10 items measuring negative affect (e.g., upset, afraid). Each item is rated on a five-point Likert Scale, ranging from 1 = very slightly or not at all to 5 = extremely, to measure the extent to which the affect is experienced in general.

### 2.7. Objective physical activity assessment: Sensewear Armband (SWA)

The SWA was worn over the right arm triceps muscle and assessed minute to minute movement through multiple sensors, namely a two-

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