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Original article

Gender-based differences in oxidative stress parameters do not underlie the differences in mood disorders susceptibility between sexes

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ABSTRACT

The present study aimed to determine whether any gender-related difference exists concerning oxidative stress parameters in a population of 231 subjects, and if these changes might be related to gender-associated differences in major depressive disorder (MDD) or bipolar disorder (BD) vulnerability. This is a case-control nested in a population-based study. The initial psychopathology screen was performed with the Mini-International Neuropsychiatric Interview and the diagnostic was further confirmed with the Structured Clinical Interview for DSM-IV. Blood samples were obtained after the interview and the oxidative stress parameters such as uric acid, advanced oxidation protein product (PCC) and lipid hydroperoxides (TBARS) were determined. Our results indicated a higher prevalence of MDD and BD in women when compared to men. In addition, significant gender differences were found in the levels of PCC (0.27 ± 0.27 vs. 0.40 ± 0.31 nmol CO/mg protein, men vs. women, respectively; $P = 0.02$) and uric acid (4.88 ± 1.39 mg/dL vs. 3.53 ± 1.02 mg/dL, men vs. women, respectively; $P = 0.0001$), but not in TBARS (0.013 ± 0.01 nmol/mg of protein vs. 0.017 ± 0.02 nmol/mg of protein, men vs. women respectively; $P = 0.243$). After sample stratification by gender, no association was found between oxidative stress parameters and clinical diagnosis of MDD and BD for women ($P = 0.516$ for PCC; $P = 0.620$ for TBARS $P = 0.727$ for uric acid) and men ($P = 0.367$ for PCC; $P = 0.372$ for TBARS $P = 0.664$ for uric acid). In this study, women seem more susceptible to oxidative stress than male. However, these gender-based differences do not seem to provide a biochemical basis for the epidemiologic differences in mood disorders susceptibility between sexes.

1. Highlights

Gender-based differences in oxidative stress parameters.

Oxidative stress parameters were not associated with gender-related mood disorders.

2. Introduction

It is well established that the brain consumes up to 20% of the total oxygen requirement of the organism. As a consequence of aerobic metabolism, large amounts of redox active molecules derived from molecular oxygen are formed [10]. Under physiological conditions, these reactive oxygen species (ROS) can act as cell-signaling molecules, capable to regulate vascular function and modulate several biochemical pathways [44]. However, an imbalance between production of ROS or even their insufficient decomposition by the endogenous antioxidant system causes a condition called oxidative stress [28,39].

Oxidative damage threatens the overall functionality of several tissues, but the brain is especially vulnerable due to the high amounts of polyunsaturated fatty acids, which are prone to oxidation, high amounts of iron and low activity of antioxidant enzymes [10]. Studies have consistently shown that oxidative stress is a common feature across major psychiatric disorders, including major depressive disorder (MDD) and bipolar disorder (BD) [14,22,26,32,40]. Nevertheless, little is known about specific targets of oxidation in the brain, and especially if this neurodegeneration associated with psychiatry disorders might be different according to gender.

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Considerable differences are found in the prevalence and presentation of psychiatry disorders in men and women. Beginning at puberty and persisting through adult life, the prevalence and incidence of MDD are higher in females than in males [36]. Epidemiological studies showed that women are more than twice as likely to be diagnosed with depression as men [35]. BD exhibits less obvious gender specificity. BD type I has an equal prevalence in men and women, whereas many studies have shown that there are more women than men with BD type II [6,15,16]. Despite the prevalence data, the clinical features, phenomena and evolution of MDD and BD greatly differ between men and women, especially the course of illness, quality of life and psychosocial functioning of patients [23,31,34].

The exact mechanism responsible for the gender-dependent differences is not fully understood. Biological factors such as hormones, and psychosocial factors have been postulated to explain these differences [24]. Some findings suggest that sexual hormones might underlie some differences in oxidative stress parameters observed in women with vascular disease [32,37]. However, gender effects on oxidative stress status addressed in clinical studies are very limited and often with controversial results [32]. In the present study, we aimed to determine whether gender-related difference concerning oxidative stress parameters might be related to differences in mood disorders vulnerability.

3. Methods

3.1. Subjects

This report consists in a case-control nested in a population-based study including 1560 individuals 18 to 24 years old living in the urban area of Pelotas, RS (Brazil). Full details on the larger study have been previously published [20]. Briefly, the sample selection was performed by clusters, between August 2007 and December 2008 in the 448 census sectors defined by the Brazilian Institute of Geography and Estatistics (IBGE) in the city of Pelotas and considering 39,667 individuals in this age range. In order to ensure the necessary sample inclusion, 89 census-based sectors were systematically drawn. All participants gave written informed consent before entering the study, which was approved by the local ethics committee.

This study is nested in a population-based study and the instruments were applied by trained interviewers during a home visit. As an initial psychopathology screen, the whole population underwent the Mini-International Neuropsychiatric Interview [38]. For the purposes of the current study, we attempted to recruit every person with past or current history of mania/hypomania from the population-based study. Two additional groups were recruited, people without history of mood disorders (control sample) and people with current depression but no past history of mania/hypomania (93 subjects in each group). These additional groups were randomly selected and matched for sex and age. Importantly, we did not exclude people on account of any other mental disorder. In order to improve diagnosis reliability, we further used the used the Structured Clinical Interview for DSM-IV (SCID) [9]. Some subjects were reclassified after this interview, which was used as the group-defining criterion for the present study. After reclassifications, our final sample consisted of 94 control subjects, 82 participants with major depression and 55 with bipolar disorder (33 type I and 22 type II) (Fig. 1). Of all 231 subjects, 16 were making use of psychiatric medication including antidepressants, benzodiazepines or mood stabilizers. Of these individuals, two were control, nine MDD and five BD.

3.2. Instruments

To assess depressive symptoms, the validated versions of the Hamilton Depression Rating Scale (HDRS) [12] and the Young Mania Rating Scale (YMRS) were used [40]. Information on drug misuse was obtained with the Alcohol, Smoking and Substance Screening Test (ASSIST) [17], and undertaken by two psychologists who had intensive training in the specialist outpatient facilities at

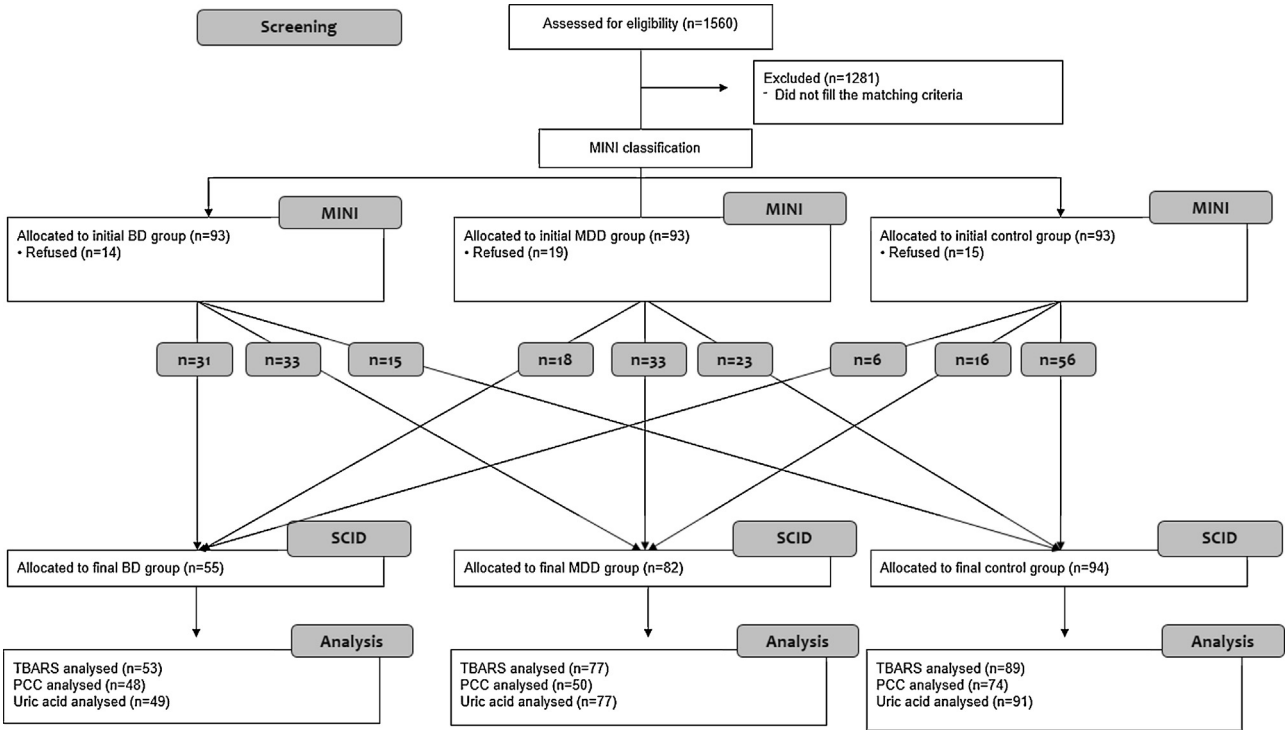

Fig. 1. Flow-chart of the processing of participants from since enrollment to cross-section study until biological sample collection.