

Introduction: Bipolar disorder (BD) is associated with premature death and ischemic heart disease is the main cause of excess mortality. The predictive power of heart rate variability (HRV) for mortality has been confirmed in patients with or without cardiovascular disease. While several studies have analyzed the association between HRV and BD, their results are incongruent; and none has analyzed the effect of the clinical factors characterizing illness burden on HRV.

Objectives: To assess the association between HRV and the following factors characterizing illness burden: illness duration, number and type of previous episode(s), duration of the most severe depressive or hypomanic/manic episode, severity of episodes, co-morbid psychiatric disorders, family history of BD or suicide, and duration and polarity of current episode in participants experiencing one.

Methods: We used a wearable device in 53 BD participants to assess the association between HRV using 4 measures (RMSSD, SDANN, SDNN and RR Triangular Index) and the abovementioned clinical factors characterizing illness burden. For each of the 4 HRV measures we ran 11 models, one for each burden of illness clinical factor as an independent variable.

Results: Longer illness duration, higher number of depressive episodes, and family history of suicide were negatively correlated with HRV; in the 14 participants experiencing a depressive episode, the MADRS score was negatively correlated with HRV

Conclusions: Our study analyzed the association between burden of illness and HRV in BD, while controlling for functional cardiovascular status, age, sex, BMI, education, and treatment. Our results showed that high illness burden is associated with reduced HRV.

Disclosure: No significant relationships.

Keywords: bipolar; heart rate variability; illness burden

O007

Bipolar disorder hospitalizations – a big data approach

M. Gonçalves-Pinho^{1*}, J.P. Ribeiro¹ and A. Freitas²

¹Department Of Psychiatry And Mental Health, Centro Hospitalar do Tâmega e Sousa, Penafiel, Portugal, Penafiel, Portugal and ²d4h, Center for Health Technology and Services Research (CINTESIS), Porto, Portugal

*Corresponding author.

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Introduction: Bipolar Disorder (BD) is a mental disorder characterized by long hospitalizations and frequent need for acute psychiatric care. Hospitalizations represent a valuable quality of care indicator in BD.

Objectives: The aim of this study was to describe a nationwide perspective of BD related hospitalizations and to use a BigData based approach in mental health research.

Methods: We performed a retrospective observational study using a nationwide hospitalization database containing all hospitalizations registered in Portuguese public hospitals from 2008 to 2015. Hospitalizations with a primary diagnosis of BD were selected based on International Classification of Diseases version 9, Clinical Modification (ICD-9-CM) codes of diagnosis 296.xx (excluding 296.2x; 296.3x and 296.9x).

Results: A total of 20,807 hospitalizations were registered belonging to 13,300 patients. 33.4% of the hospitalizations occurred in male patients and the median LoS was 16.0 days. Mean age was 47.9 years

and male patients were younger (46.6 vs. 48.6; $p < 0.001$). 59 hospitalizations had a deadly outcome (0.3%). The most common cause of hospitalization in BD was the diagnosis code 296.4x (Bipolar I disorder, most recent episode (or current) manic) representing 34.3% of all hospitalizations, followed by the code 296.5x (Bipolar I disorder, most recent episode (or current) depressed) with 21.4%. The mean hospitalization charges were 3,508.5€ per episode, with a total charge of 73M€ in the 8-year period of this study.

Conclusions: This is a nationwide study using BigData analysis giving a broad perspective of BD hospitalization panorama at a nationwide level. We found differences in hospitalization characteristics by gender, age and primary diagnosis.

Disclosure: No significant relationships.

Keywords: Hospitalization; Big Data; bipolar disorder; Administrative Database

O008

Game changer in the diagnosis of bipolar disorder using RNA editing-based blood biomarkers

J.-D. Abraham^{1*}, N. Salvetat¹, F. Checa-Robles¹, V. Patel¹, C. Cayzac¹, B. Dubuc¹, D. Vetter¹, J.-P. Lang², P. Courtet³, D. Kupfer⁴ and D. Weissmann¹

¹Neurology, ALCEDIAG/SYS2DIAG, MONTPELLIER, France;

²Center For Psychiatry And Psychotherapy, Les Toises, Lausanne,

Switzerland; ³Emergency Psychiatry And Acute Care, CHU

Montpellier / INSERM, Montpellier, France and ⁴Department Of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, United States of America

*Corresponding author.

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Introduction: In clinical practice, differentiating Bipolar Disorder (BD) from unipolar depression is challenging due to the depressive symptoms, which are the core presentations of both disorders. Patients with BD are often misdiagnosed during depressive episodes resulting in a delay in proper treatment and a poor management of their condition.

Objectives: The aim of the present study is to discriminate between unipolar depression and BD using a panel of RNA edited blood biomarkers.

Methods: Depressed patients were classified according to clinical scores in MADRS and IDSC-30 depression scales. After blood collection and RNA extraction, we used whole-transcriptome sequencing to identify differential A-to-I editing events, and Targeted Next Generation Sequencing to validate those biomarkers.

Results: We discovered 646 variants differentially edited between depressed patients and control in a discovery cohort of 57 participants. After using stringent criteria and biological pathway analysis, 6 biomarker candidates were singled out and tested in a validation cohort of 160 patients suffering from unipolar depression and 95 BD patients in a depressive episode, which allowed a differential diagnosis of BD with an AUC of 0.935 and high specificity (Sp=84.6%) and sensitivity (Se=90.9%).

Conclusions: We have shown that a combination of 6 blood RNA editing-related biomarkers allows to discriminate unipolar and bipolar depression This 6 BMKs panel may be crucial to improve BD diagnosis and orientate the treatment therefore addressing the needs of millions of patients suffering from misdiagnosis and

incorrect treatment for their diseases. This will change the game for the management of patients.

Disclosure: No significant relationships.

Keywords: RNA editing; Blood biomarker; diagnosis; bipolar disorder

O009

Lithium treatment and estimate glomerular filtration rate in bipolar disorder patients: A cross-sectional study

S. Fernandes^{*}, T. Cerqueira-Silva, A. Pinto and Â. Miranda-Scippa
Faculdade De Medicina Da Bahia, Universidade Federal da Bahia (UFBA), Salvador, Brazil

^{*}Corresponding author.

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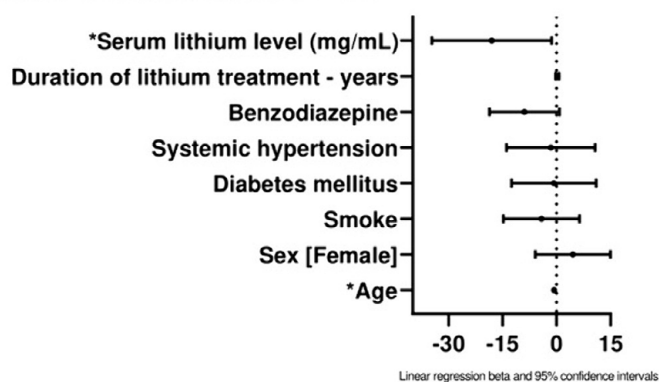
Introduction: Lithium has been the mainstay therapy for bipolar disorder (BD) for decades, but there is little consensus regarding its possible effects on kidney function and the rate of change in estimated glomerular flow rate (eGFR) over time.

Objectives: To describe patients with BD regarding their renal function and their sociodemographic and clinical characteristics potentially related to eGFR.

Methods: This is a cross-sectional study with an initial sample of 95 patients with BD. Multiple linear regression analysis was applied to investigate the association of lithium serum levels and their duration of treatment with eGFR, independent of confounding factors. We excluded patients without data regarding any of the variables from the final model.

Results: In the multivariate analysis, the model was composed of eight variables (Figure 1). The mean duration of treatment was 10 years (Figure 2). Serum lithium level was associated with low levels of eGFR ($\beta = -18.06$ [-34.70 - -1.42], $p = 0.03$); among the other variables, only age remained associated with it ($\beta = -0.72$ [-1.10 - -0.33], $p = <0.01$).

Figure 1 – Forest plot of multivariate analysis



Note: ^{*}P<0.05

Figure 2: Description of the study sample

Age (years) - median (IIQ)	49.0 (37.0— 57.5)
Female - n (%)	76 (80.0)
Race	
White	20 (21.1%)
Black	75 (78.9%)
BMI - median (IIQ)	28.4 (24.2—32.8)
Smoke - n (%)	20 (21.1)
Systemic hypertension - n (%)	11 (11.6)
Diabetes Mellitus - n (%)	14 (14.7)
Dyslipidemia - n (%)	10 (10.5)
Antipsychotic use - n (%)	67 (70.5)
Anticonvulsant use - n (%)	53 (55.8)
Benzodiazepine use - n (%)	21 (22.1)
BD Types	
BD type I	85 (89.5%)
BD type II	10 (10.5%)
Serum lithium levels (mg/ml)* - median (IIQ)	0.7 (0.6—0.9)
Lithium treatment duration - years	10.0 (6.0—16.0)
Daily lithium dosis	900.0 (900.0— 1200.0)
Serum urea	25.0 (21.0—29.5)
Serum creatinine	0.8 (0.7— 1.0)

^{*}Only 83 patients

Conclusions: We replicated the correlation between serum lithium levels and eGFR. Our results contradict the claim that duration of treatment with lithium correlates with lower levels of eGFR, while suggesting serum lithium level could be a possible early marker of lithium nephrotoxicity.

Disclosure: No significant relationships.

Keywords: bipolar disorder; serum lithium level; lithium; nephrotoxicity

O010

Prospective early warning signals to detect transitions to manic and depressive episodes in bipolar disorder

F. Bos^{1*}, M. Schreuder², B. Doornbos³, E. Snippe¹, R. Bruggeman¹, L. Van Der Krieke², B. Haarman², M. Wichers¹ and S. George¹

¹Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen, Netherlands; ²Psychiatry, University Medical Center Groningen, Groningen, Netherlands and ³Bipolar Disorders, GGZ Drenthe, Assen, Netherlands

^{*}Corresponding author.

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Introduction: For patients with bipolar disorder, early recognition of impending mood episodes is crucial to enable timely intervention. Longitudinal digital mood monitoring using ecological momentary assessment (EMA) enable prospective study of early warning signals (EWS) in momentary affective states prior to symptom transitions.

Objectives: The present study examined in a unique longitudinal EMA data set whether EWS prospectively signal transitions to manic or depressive episodes.

Methods: Twenty bipolar type I/II patients completed EMA questionnaires five times a day for four months (average 491 observations per person), as well as weekly symptom questionnaires concerning depressive (Quick Inventory for Depressive