conducted an umbrella review of meta-analyses of randomized placebo-controlled trials investigating drugs repurposed as add-on treatments for mania and bipolar depression.
Methods: We performed a systematic search and screening of the existing literature looking for the most up-to-date or comprehensive meta-analyses of randomized controlled trials (RCTs) on adults suffering from BD during an acute mood episode (mania or depression) which compared a repurposed drug and placebo as adjunctive treatments. We performed a critical appraisal according to "A MeaSurement Tool to Assess systematic Reviews" Version 2 (AMSTAR 2). We synthesized meta-analytic findings regarding efficacy, tolerability, and safety, also assessing the quality of evidence using the "Grading of Recommendations, Assessment, Development and Evaluations" (GRADE) approach.
Results: In nine eligible meta-analyses investigating 12 drugs (four for mania and eight for bipolar depression) we observed a heterogeneous quality of reporting was according to AMSTAR 2.
In mania, allopurinol (for symptoms reduction and remission at 4-8 weeks) and tamoxifen (for response and symptoms reduction at 4-6 weeks) showed higher efficacy than placebo, with evidence of low and very low quality, respectively.
In bipolar depression, modafinil/armodafinil (for response, remission, and symptoms reduction at 6-8 weeks) and pramipexole (for response and symptoms reductionat 6 weeks) were superior to placebo, with low-quality evidence. Results on celecoxib and N-acetylcysteine were of low quality and limited to certain outcomes.
Conclusions: Overall, the lack of evidence of high and moderate quality does not allow firm conclusions on the clinical utility of repurposed drugs as adjunctive treatments for mania and bipolar depression, limiting recommendations for their use in clinical practice. However, since some lines of evidence seem to hold some potential, and standard treatments for mania and bipolar depression remain not entirely satisfactory, the search for novel therapeutic targets and strategies for the management of BD warrants further research in the field.

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EPP0555

Cognitive reserve in Older Adults with Bipolar Disorder and its relationship with cognitive performance and psychosocial functioning

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Introduction: Cognitive reserve (CR) refers to the ability of the brain to cope with damage or pathology. In bipolar disorder (BD), it has been seen that the effects of the disease may potentially reduce CR, thus compromising cognitive outcomes. This concept takes on special relevance in late life in BD, due to the increased risk of cognitive decline because of the accumulative effects of the disease and the potential effects of aging. Therefore, we believe that CR may be a protective factor against cognitive decline in older adults with bipolar disorder (OABD).
Objectives: The aim of this study was to study the CR in OABD compared with healthy controls (HC) and to analyze its association with psychosocial functioning and cognitive performance.
Methods: A sample of euthymic OABD, defined as patients over 50 years old, and HC were included. CR was assessed using the CRASH scale. Differences in demographic, clinical, and cognitive variables between patients and HC were analyzed by t-test or X2 as appropriated. Lineal simple and multiple regressions analyses were used to study the association of CR and several clinical variables with functional and cognitive performance.
Results: A total of 83 participants (42 OABD and 41 HC) were included. Compared to HC, OABD exhibited poorer cognitive performance ($p<0.001$), psychosocial functioning ($p<0.001$) and lower CR ($p<0.001$). Within the patient's group, the linear simple regression analysis revealed that CR was associated with psychosocial functioning ($\beta=-2.16$; $p=0.037$), attention ($\beta= 3.03$; $p=0.005$) and working memory ($\beta = 2.98$; $p=0.005$) while no clinical factors were associated. Age and CR were associated with processing speed and verbal memory, but after applying multiple regression model, only the effect of age remained significant ($\beta =-2.26$; $p= 0.030$, and $\beta =-2.23$; $p= 0.032$ respectively). CR, age, and number of episodes were related to visual memory, but the multiple regression showed that only age ($\beta = -2.37$; $p= 0.023$) and CR ($\beta = 3.99$; $p<0.001$) were associated. Regarding executive functions only the number of manic episodes were significant. CR and age at onset were associated with visuospatial ability, but multiple regression only showed association of CR ($\beta =2.23$; $p=0.032$). Other clinical factors such as number of depressive or hypomanic episodes, illness duration, admissions, type of BD, and psychotic symptoms were not associated.
Conclusions: To the best of our knowledge, this is the first report that studies the CR in a sample of OABD. We demonstrated that OABD had lower CR than HC. Importantly, we observed that CR was associated with cognitive and psychosocial functioning in OABD, even more than disease-related factors. These results suggest the potential protector effect of CR against cognitive impairment, supporting that improving modifiable factors associated with the enhancement of CR can prevent cognitive decline.

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EPP0556

Lithium management around delivery: a retrospective observational cohort study

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Introduction: During the perinatal period lithium is proven effective as maintenance therapy and to prevent postpartum psychosis. Pregnancy affects all aspects of kidney physiology altering the pharmacokinetics of lithium. To minimize the risk of both maternal and neonatal complications around delivery, several authors have provided clinical advice on lithium dosing around delivery: decreasing dose by 30-50%, suspend lithium therapy 24-48 hours before scheduled cesarean section or induced delivery or even discontinuing lithium after first signs of labour.
Objectives: To evaluate the validity of these recommendations by investigating 1) maternal lithium serum concentrations changes around delivery, 2) the lithium trasplacental passage at delivery and 3) the association between neonatal lithium serum concentration at delivery and neonatal outcomes.
Methods: Psychopathologically stable women with a singleton pregnancy (n=66) who used lithium around delivery, were included in this retrospective observational cohort study (HCB/2020/1305). All women were advised to suspend lithium administration at the onset of labour in the event spontaneous deliveries. Study date: demographic, psychiatric, obstetric and neonatal outcomes for each mother-infant pair obtained from the hospital medical records.Lithium serum concentrations were determined by means of an AVL 9180 electrolyte analyzer based on the ion- selective electrode (ISE) measurement principle. Limit of quantification (LoQ) was 0.20 mEq/L.
Results: The most common psychiatric diagnosis was a bipolar disorder type I (n=54, 90%). Forty mothers (61%) were on lithium monotherapy. Mean (SD) umbilical cord and intrapartum maternal lithium serum concentration was 0.59 (0.13) mEq/L and 0.55 (0.13) mEq/L respectively. There was a strong positive correlation between umbilical cord and maternal lithium serum concentrations (Pearson correlation coefficient 0.95 (95%IC: 0.91,0.97). In a subsample (N=22) a paired t test indicates that the maternal serum lithium concentrations at delivery were significantly lower (mean difference=0.19 mEq/L, 95%CI=0.13-0.25) than those during obtained the day before delivery hospitalization, after a mean (SD) of 31.29 (±11.92) hours (SD=11.92) have elapsed since the taking the last dose of lithium prior to delivery. Four women (6%) relapsed early postpartum.There were no significant differences between lithium monotherapy (N=18/40) and polytherapy (N=11/26) groups with regard to acute neonatal complications (p>0.05). The only acute neonatal complication associated to umbilical cord lithium serum concentration was hypotonia [0.712 (0.298) vs. 0.534 (0.214) (F=5.065; df=1,60; p=0.028)].
Conclusions: When lithium is used around delivery, maternal and neonatal well-being can be maximized by maintaining maternal serum lithium concentrations at the minimal effective level and discontinuing briefly when presenting to hospital for delivery.

Disclosure of Interest: None Declared

EPP0557

Cortisol awakening response in bipolar patients with comorbid type 2 diabetes mellitus

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Introduction: Bipolar Disorder (BD) is a severely debilitating psychiatric disorder with high rates of morbidity and mortality, and patients with BD have a 10-year reduction in their life expectancy. Bipolar disorder (BD) is frequently associated with type 2 diabetes mellitus (T2DM). BD patients with comorbid T2DM have been shown to have three times higher odds of a chronic course and rapid cycling and are more likely to present worse outcomes to treatment with lithium and/or other mood stabilisers when compared to BD patients without IGM (impaired glucose metabolism).
Objectives: The functioning of the hypothalamic-pituitary-adrenal (HPA) axis has been never investigated in BD with respect to the glucose metabolic status. Therefore, we assessed the cortisol awakening response (CAR) in bipolar patients with or without comorbid T2DM.
Methods: Twenty euglycemic bipolar patients [12 males and eight females; mean age (±SD): 47.4 ± 14.4 years; mean (±SD) duration of illness: 18.3 ± 12.1 years], 16 BD patients with T2DM [11 males and five females; mean age (±SD): 63.6 ± 12.8 years; mean (±SD) duration of bipolar illness: 17.1 ± 10.8 years; mean (±SD) duration of T2DM: 5.2 ± 5.3 years], 18 healthy subjects [seven males and 11 females; mean age (±SD): 45.0 ± 12.1 years] and 12 non-psychiatric subjects with T2DM [eight males and four females; mean age (±SD): 56.7 ± 11.2 years; mean (±SD) duration of