Treating Comorbid Childhood Bipolar Disorder and ADHD

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Abstract

Objectives. Pediatric mania is difficult to distinguish from childhood hyperactivity. Both share common symptoms: distractibility, motoric hyperactivity, and talkativeness. Oftentimes, children are referred from their pediatrician due to a lack of appropriate response to stimulant medication. Pediatricians have learned that merely raising the dose or changing the stimulant does not work. A thorough neuropsychological evaluation often reveals bipolar mania. They may have comorbid bipolar disorder and ADHD. This paper will examine measures that can assist in this important differential diagnosis as well as offer treatment options, including medication management.

Methods. This case study includes three pediatric patients diagnosed with childhood bipolar disorder and ADHD. A comprehensive psychoeducational assessment was conducted for each of the patients, which resulted in this comorbid diagnosis.

Results. One of the most helpful measures was the TOVA (i.e., Test of Variables of Attention). When a child’s attention and impulsivity scores are normal, and response time and variability scores are abnormal, both on and off medication, that is an indication of a mood disorder. These children also performed poorly on measures of processing speed, and verbal learning and interference tasks. Measures of affect and personality were important diagnostically. A combination of amantadine and either clonidine HCL ER or propranolol, as prescribed by a medical psychologist, was found to be effective in controlling the symptoms of this comorbid diagnosis.

Conclusion. An evaluation of children’s intellectual, attentional, behavioral, mood, and personality functioning is crucial for a differential diagnosis. In cases of comorbidity, ADHD and childhood bipolar disorder, the sooner the child is on appropriate medications, the better. When just the surface diagnosis of ADHD is medicated, the outcome is often problematic. There may be a poor response to treatment and a higher rate of suicide.

Hospitalization Risk Among Adults with Bipolar I Disorder Treated with Oral Atypical Antipsychotics: A Long-Term Data Analysis of Medicaid Claims Data

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Abstract

Objective. To compare the risk of hospitalization for adult Medicaid beneficiaries with bipolar I disorder (BPD-I) when treated with lurasidone compared to other atypical antipsychotics (AAPs) as monotherapy.

Methods. Using IBM MarketScan Multi-State Medicaid Claims database, a retrospective cohort study was conducted on adult BPD-I patients who initiated an AAP (index date) between January 1, 2014 and June 30, 2019. Patients were required to be continuously enrolled during the 12-month pre- and 24-month post-index date. Marginal structural models were performed to estimate the risk of hospitalization (all-cause, BPD-I-related, and psychiatric-related) associated with each AAP and the average length of stay.

Results. The analysis included 8262 adult BPD-I patients, of whom AAP use was divided between lurasidone (14%), aripiprazole (17%), olanzapine (8%), quetiapine (29%), risperidone (10%), no/minimal (1%) or other (21%) during each month of post-index period. The adjusted odds ratios (aORs) for all-cause hospitalization were significantly higher for olanzapine (aOR=1.60, 95% CI=1.09–2.10) and quetiapine (aOR=1.54, 95% CI=1.18–1.89), compared to lurasidone. The aORs for BPD-I-related hospitalization were significantly higher for quetiapine (aOR=1.57, 95% CI=1.10–2.04) and risperidone (aOR=1.80, 95% CI=1.04–2.56) compared to lurasidone. The average length of hospital stay was more than twice as high for quetiapine compared to lurasidone (ARR=2.12, 95% CI=1.32–2.92). The risk of psychiatric-related hospitalization was numerically lower for lurasidone compared to all other AAPs.

Conclusion. Over a 24-month follow-up period, lurasidone-treated adult BPD-I patients had significantly lower risk of all-
cause hospitalization than those treated with olanzapine and quetiapine, lower risk of BPD-I-related hospitalization than quetia-pine and risperidone, and fewer hospital days than quetiapine in a Medicaid population.

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## Discovering Non-Invasive Biomarkers Predictive of Opioid Use Disorder Treatment Response

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### Abstract

**Background.** Opioid use disorder (OUD) continues to be the driving force behind drug overdoses in the United States, killing nearly 47,000 people in 2018 alone. The increasing presence of deadlier fentanyl analogues in the heroin drug supply are putting users at a greater risk for overdose than ever before. Admissions to treatment programs for OUD have also nearly doubled since 2006, yet relapse rates remain high. In response to these alarming statistics, developing approaches to reduce overdose deaths has become an area of high priority. As it is not yet known which patients are most likely to benefit from a specific treatment, there is a dire need to utilize new molecular tools to guide precision medicine approaches and improve treatment outcomes. Here we describe a proof-of-concept study evaluating plasma-derived extracellular vesicle (EV) signatures and how they differ in patients who responded to two pharmacologically contrasting treatments for OUD: the μOR agonist methadone, and the μOR antagonist naltrexone.

**Methods.** We obtained blood samples from patients with OUD who remained abstinent from illicit opioids for at least 3 months during treatment with methadone (n=5) and naltrexone (n=5), as well as matched healthy controls (n=5). EVs were isolated from plasma and histones were isolated from peripheral blood mononuclear cells (PBMCs). EVs were then analyzed for lipid and histone post-translational modification (PTM) content using liquid chromatography-mass spectrometry. EV miRNA cargo was determined by RNA sequencing.

**Results.** We found one lipid class and six miRNAs that differed significantly between the naltrexone group and the methadone and control groups. We also found that histone H3acK9acK14 was increasingly acetylated in PMBCs from both the methadone and naltrexone groups compared to controls.

**Discussion.** Naltrexone, which is used in treatment of OUD and other substance use disorders as well as disorders of impulse control, was found to have multiple potential corresponding molecular signatures that can be identified after long-term treatment. It remains to be seen if these markers can also be a good predictor for treatment response. In addition, significant gender differences in EV content are found between men and women with OUD, which supports the importance of examining changes in response to treatment in a gender informed way.

### Could Improved Microcirculation Reverse the Effects of Fetal Alcohol Syndrome? A Review

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### Abstract

Fetal alcohol spectrum disorders, (FASDs) are a spectrum of neurodevelopmental and cognitive conditions, caused by the consumption of alcohol in varying amounts in utero that affect an estimated 1 - 5% of the general population in the United States. The effects of the spectrum of disorders are lifelong, resulting in often significant learning difficulties, cognitive deficits, and behavioral issues. It is known that blood flow and microcirculation to the brain are affected by the consumption of alcohol in utero, and that microcirculation and neurology are intimately linked, with changes in the former having drastic effects on the latter. The purpose of the current review is to analyze whether improvement in microcirculation in the infant or child with FASDs could affect quality of clinical outcomes in the spectrum of disorders, or lead to the improvement of disorder-related symptoms. Scientific evidence from the literature suggests that, in theory, improving cerebral microcirculation in the infant or child with FASDs could affect quality of clinical outcomes in the spectrum of disorders, or lead to the improvement of disorder-related symptoms. Scientific evidence from the literature suggests that, in theory, improving cerebral microcirculation in the infant or child with FASDs could lead to a corresponding improvement in neurological health, and potentially an improvement in cerebral development, which may in theory lead to a lessening of symptoms. Further review into the connection between microcirculation and neurological health, and correspondingly, clinical outcomes in patients with neurological deficits, is warranted.