leukocytosis and hyperproteinorrhea. Analytical evaluations showed thrombocytopenia, anemia, acute kidney injury, hyperbilirubinemia and rhabdomyolysis. Empirical treatment with intravenous antibiotics was initiated. During hospitalisation, all cultural tests were negative, but Leptospira DNA was detected in urine and blood samples. The patient completed the antibiotics, continued daily Risperidone 6mg and was discharged without psychotic symptoms.
Results and Discussion, This is the case of a patient with severe leptospirosis whose clinical presentation symptoms were psychotic and preceded by weeks the appearance of more typical ones.
The diagnosis was established after the identification of Leptospira DNA in product samples. Although the patient had previously experienced psychotic symptoms induced by cannabinoids, he was abstinent and asymptomatic for 15 years. Indeed, delusions and hallucinations did not improve after isolated titration of antipsychotics, but subsided with antibiotic add-on, suggesting infectious causality.
A systematic literature review was conducted, but only 4 eligible articles were found. From these, only one focused psychotic symptoms. This article concluded that psychotic symptoms tend to occur after the diagnosis of Leptospirosis and usually do not remit with antibiotherapy, but with the institution of antipsychotic therapy. These data are contrary to those that, in a medical reasoning (cause-effect) are expected, as well as those presented in this article.
Conclusions: The paucity of data available makes the presentation of this clinical case pertinent. Further studies are needed to establish the pathophysiological mechanisms of the neuropsychiatric manifestations associated with leptospirosis, their clinical evolution and therapeutic guidelines.
No conflict of interest

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EFFECT OF GLUTAMATE MODULATOR JNJ-46356479 AND CLOZAPINE ON GLUTAMATE AND GABA BRAIN-LEVELS IN A POSTNATAL KETAMINE MOUSE MODEL OF SCHIZOPHRENIA

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Background: Alterations in glutamatergic neurotransmission have been postulated to be a key pathophysiologic mechanism of schizophrenia (SZ) [1]. Given the lack of efficacy of antipsychotics on treating negative and cognitive symptoms, glutamate (GLU) inhibitors could be a good pharmacological strategy to improve these symptoms. Positive allosteric modulators (PAM) of the mGLU receptor 2, such as JNJ-46356479 (JNJ), inhibit the presynaptic release of GLU. We have previously reported that JNJ treatment during a critical period of neurodevelopment mitigate neuropathological impairments in a postnatal ketamine (KET) mouse model [2]. Dealing with GLU storm during early stages of SZ may be particularly effective to prevent the disease appearance or slow the progression and the clinical deterioration of patients.
Aim: To evaluate the efficacy of an early JNJ treatment in reversing neuropathological deficits induced in a postnatal KET mouse model of schizophrenia. We investigated the immunofluorescence-based quantification of vesicles labeled with GLU transporter (VGLUT) and GABA transporter (GAD65/67) as markers of glutamatergic and GABAergic neurotransmission, respectively.
Methods: A total of 36 C57BL/6J pups were exposed to KET (30mg/kg) on postnatal days (PND) 7, 9, and 11 to disrupt NMDAR function. Then, mice were daily treated subcutaneously with 10mg/kg of JNJ-46356479 (JNJ) or clozapine (CLZ), as a clinical antipsychotic of reference, during the adolescent period (PND 35-60). Mice were perfused on PND 120 with phosphate buffer saline 1X followed by 4% paraformaldehyde. Coronal sections of prefrontal cortex (PFC) and hippocampus (HPC) were prepared for immunofluorescent double labeling with antibodies for Vglut1 and GAD65-67. Confocal images were automatically analyzed using ImageJ software to quantify the number of GLU and GABA vesicles.
Results: Due to sex differences in immunofluorescence-based quantification of GLU and GABA vesicular transporter, we conducted a multivariate analysis of variance. The analysis revealed significant differences in the number of GLU vesicles among the HPC subregions across treatment groups (CA1 ($F(11,36) = 5,39$, $p < 0.001$), CA2 ($F(11,36) = 2,23$, $p = 0.049$ and CA3 ($F(11,36) = 5,39$, $p < 0.001$)). Post-hoc test indicated a significant increase in the number of GLU vesicles between the KET group and vehicle (VEH) group, particularly in the CA3 region ($p = 0.012$). Although the difference between the groups in GLU levels in CA1 did not reach statistical significance ($p = 0.056$), a notable trend was observed. The administration of JNJ treatment in the KET mice model significantly reduced the levels of GLU in both CA1 and CA3 regions ($p = 0.004$ and $p = 0.000$, respectively), whereas no effect was observed with CLZ treatment. While we observed differences in GABA levels in the CA3 region, these differences did not reach statistical significance according to the post-hoc test. No significant differences were found in GLU and GABA vesicular levels in the dentate gyrus and PFC regions.
Conclusion: These findings indicate the effectiveness of JNJ treatment in attenuating GLU dysregulation in both CA1 and CA3, suggesting its potential as a therapeutic approach for mitigating GLU-related pathology in SZ. Comparatively, JNJ appears to exert a more pronounced effect than clozapine.
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POSTPARTUM PSYCHOSIS PRESENTING WITH CATATONIA AND RESPONSIVE TO THIAMINE TREATMENT

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Postpartum psychosis is an acute illness of multifactorial origin and is considered a psychiatric emergency. With an estimated global prevalence of 0.089 to 2.6 per 1000 births, postpartum psychosis classifies as an illness with a low incidence rate. However, it carries the potential for serious medical and social consequences, including the risk of suicide and filicide, if not promptly detected and treated. The clinical picture of postpartum psychosis includes a wide variety of rapid-onset psychotic symptoms such as hallucinations and delusions, strange behavior, confusion, delirium-like disorganization and catatonia [1].In this article we present a case of postpartum psychosis presenting with catatonia and responsive to thiamine treatment.
A 30-year-old female patient who was 6 weeks postpartum with no previous history of psychiatric illness and no significant family history admitted to psychiatry clinic with loss of apetite, decreased speech amount, psychomotor retardation, auditory hallucinations and thought disorder (''this is not my baby, my marriage is fake.''). At her physical examination she had immobility, mutism, staring, posturing, echopraxia, rigidity, withdrawal, autonomic obedience and proximal muscle weakness in upper and lower limbs. The Bush-Francis Catatonia rating scale was 14 points. Additionally in her psychiatric evaluation she had short-term memory impairment, confusion and confabulation. Initially, lorazepam was added 7,5 mg/day to treatment for her catatonia, rapid response to lorazepam was observed. However, no remarkable response was observed to olanzapine 10 mg/day, her psychotic symptoms and cognitive impairment remained. Lumbar puncture, brain MRI, PET-MRI, and EEG investigations were performed for differential diagnosis. Any abnormal finding was not observed except slightly high protein level in cerebrospinal fluid (CSF). Also screening of antibodies for autoimmune etiology in CSF and serum resulted negative. Consideration of postpartum period, poor nutritional intake before hospital admission due to the catatonic symptoms, cognitive impairment and high serum lactate level (31,73 mg/dL) and pyruvate level (1,51 mg/dL) with slight acidosis (pH:7,301), empirical intravenous (IV) thiamine 1500 mg/day infusion was

added to treatment for 8 days. During the IV thiamine administrations, her short-term memory impairment, confusion and confabulation significantly improved at fourth day, serum lactate and pyruvate levels turned the normal level at the end of admissions. With 5 mg/day olanzapine and 500 mg/day oral thiamine treatment, her psychotic symptoms and proximal muscle weakness in upper and lower limbs ameliorated. The patient was discharged to be followed up in outpatient clinic.

When evaluating for thiamine deficiency, the typical history may include poor nutritional intake, excessive alcohol intake, or the patient belonging to the special populations (pregnant women, recipients of bariatric surgery, anyone with poor overall nutritional status, etc.) [2].The present patient indicates that the possibility of thiamine deficiency should be considered in cases of psychosis and cognitive impairment especially in peripartum period without classical neurological disturbance (nystagmus, opthalmoplegia, paresthesias etc.) and high-intensity T2 MRI lesions [3].

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SHORT- AND LONG-TERM EFFECTS OF BREXPIPRAZOLE ON FUNCTIONING IN ADULTS WITH SCHIZOPHRENIA WITH OR WITHOUT AGITATION/HOSTILITY: POST HOC ANALYSIS

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Background: Patients with schizophrenia often experience symptoms of agitation and hostility [1,2], which are associated with a negative impact on functional outcomes [3,4]. In a previous post hoc analysis, brexpiprazole demonstrated potential to be an efficacious and well-tolerated treatment for agitation and hostility in patients with schizophrenia [5]. This post hoc analysis evaluated the short- and long-term effects of brexpiprazole on functioning in adult patients with schizophrenia, analysed by improvement in agitation and hostility symptoms.

Methods: Data were analysed from three Phase 3, 6-week, randomised, double-blind, placebo-controlled studies (ClinicalTrials.gov identifiers: NCT01396421, NCT01393613, NCT01810380), and two Phase 3, long-term (up to 52 weeks) open-label extension (OLE) studies (NCT01397786, NCT01810783). In the short-term studies, eligible patients (aged 18–65 years) were randomised to placebo or brexpiprazole (fixed-dose 0.25, 1, 2 or 4 mg/day, or flexible-dose 2–4 mg/day, depending on the study), or to quetiapine extended-release in one study (active reference; not included in this analysis). In each study, the primary endpoint was change from baseline in Positive and Negative Syndrome Scale (PANSS) Total score. Functioning was assessed as a secondary endpoint, using the Personal and Social Performance scale (PSP). In the OLE studies, patients were treated with flexible-dose brexpiprazole 1–4 mg/day. In this pooled post hoc analysis, agitation response was defined as ≥1-point improvement from baseline to Week 6 in PANSS Excited Component (PANSS-EC) score ("agitation responders" subgroup), and hostility response was defined as ≥1-point improvement from baseline to Week 6 in PANSS P7 (hostility) item score ("hostility responders" subgroup). Short-term data were compared between brexpiprazole 2–4 mg/day and placebo. Long-term data were evaluated by prior treatment group (prior brexpiprazole, or prior placebo). Outcomes were assessed using descriptive statistics, and least squares (LS) mean changes from baseline.

Results: In the pooled short-term sample, baseline PSP scores were comparable between treatment groups. In the brexpiprazole group, 76.5% (664/868) of patients met the criterion for agitation response at Week 6, compared with 66.9% (346/517) in the placebo group. In the brexpiprazole group, 83.1% (717/863) of patients met the criterion for hostility response at Week 6, compared with 76.7% (395/515) in the placebo group. Short-term improvement in functioning was greater in the subgroups of agitation or hostility responders, compared with non-responders, regardless of treatment group. There was a greater improvement in functioning from baseline to Week 6 with brexpiprazole versus placebo in the subgroup of agitation responders ($p<0.01$), and in the subgroup of hostility responders ($p<0.01$). In the pooled OLE sample (n=607), 92.4% of patients had previously shown agitation response, and 92.6% had previously shown hostility response; in those prior response subgroups, improvement in functioning was maintained throughout the OLE studies, regardless of prior treatment.

Conclusion: In adults with schizophrenia, improvements in functioning were greater in patients who showed improvement in agitation or hostility symptoms, regardless of treatment; in these subgroups, brexpiprazole was associated with greater improvement in functioning versus placebo. Improvements in functioning were maintained throughout long-term treatment with brexpiprazole, regardless of prior treatment.

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Conflict of interest:

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SHORT- AND LONG-TERM EFFECTS OF BREXPIPRAZOLE ON FUNCTIONING IN ADULTS WITH SCHIZOPHRENIA ANALYSED BY IMPROVEMENT IN ANXIETY: POST HOC ANALYSIS

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Background: In patients with schizophrenia, symptoms of anxiety contribute to impaired functioning and quality of life [1]. Treatment guidelines emphasise that maintaining or improving patients' functioning should be one of the major goals of schizophrenia management [2]. In previous analyses, brexpiprazole was associated with clinically relevant improvement in functioning in patients with schizophrenia, in the short- and long-term [3]. This post hoc analysis evaluated the short- and long-term effect of brexpiprazole on functioning in adult patients with schizophrenia, analysed by improvement in anxiety symptoms.

Methods: Data were analysed from three Phase 3, 6-week, randomised, double-blind, placebo-controlled studies (ClinicalTrials.gov identifiers: NCT01396421, NCT01393613, NCT01810380), and two Phase 3, long-term (up to 52 weeks) open-label extension (OLE) studies (NCT01397786, NCT01810783). In the short-term studies, eligible patients (aged 18–65 years) were randomised to placebo or brexpiprazole (fixed-dose 0.25, 1, 2 or 4 mg/day, or flexible-dose 2–4 mg/day, depending on the study), or to quetiapine extended-release in one study (active reference; not included in this analysis). In each study, the primary endpoint was