

COVID (Johnston et al. *Neuropsychopharmacology*. 2024; 49(1): 23-40).

Objectives: Our objective was to examine two patient cases to identify patterns, explore potential treatment options, and contribute insights to clinical practice in psychiatry.

Methods: This case series reports the clinical histories, demographic information, diagnostic findings, and treatment details of two long COVID patients who were treated in analogy to the well-established guideline for treatment-resistant depression.

Results: A 33-year-old female patient, who failed to respond to phytotherapy and conventional psychopharmacological treatments, including two trials of antidepressants and augmentation with an atypical antipsychotic agent received 10 intravenous esketamine treatments, administered at doses of up to 50 mg (0.86 mg/kg/hour). She experienced substantial clinical improvement without any adverse effects within 8 weeks. A 34-year-old non-responding female patient received 9 sessions of intranasal esketamine, targeting a dosage of 84 mg, resulting in complete remission without significant adverse effects within 6 weeks.

Conclusions: There is an urgent need for effective and sustainable treatment options that address the debilitating neuropsychiatric symptoms of long COVID. This condition disproportionately affects young women, a group that is frequently underrepresented in research and insufficiently recognized in clinical practice. In this case series, we report on two female patients with severe physical and social impairment from long COVID, who showed significant clinical improvement following add-on esketamine administration.

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EPV1566

Is there enough evidence to stop using available and accessible antipsychotics such as haloperidol and promote the use of newer and more expensive drugs? What is the hope for populations that cannot afford them

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Introduction: Doctors Without Borders works in humanitarian settings. In these settings, we have observed a notable movement away from first generation medications such as haloperidol towards second-generation antipsychotics, where these medications are available. We began to question whether the evidence clearly justified this and decided to contribute to the evidence.

Objectives: To assess the clinical benefits and harms of haloperidol compared to olanzapine for people with schizophrenia and schizophreniaspectrum disorders.

Methods: Searched the Cochrane Schizophrenia study-based register of trials, screened the references of all included studies. We contacted relevant authors of trials for additional information where clarification was required or where data were incomplete. The register was last searched on 14 January 2023.

Results: We didn't find a statistically significant difference between haloperidol and olanzapine in global state (RR 0.84, 95% CI 0.69 to 1.02), nor in relapse (RR 1.42, 95% CI 1.00 to 2.02). Haloperidol resulted in an increase of extrapyramidal side effects compared to olanzapine (RR 3.38, 95% CI 2.28 to 5.02). For weight gain, there may be a large reduction in the risk with haloperidol compared to olanzapine (RR 0.47, 95% CI 0.35 to 0.61). Haloperidol may result in an increase of leaving the study early compared to olanzapine (RR 1.99, 95% CI 1.60 to 2.47).

Conclusions: Overall, the certainty of the evidence was low to very low for the main outcomes in this review, making it difficult to draw reliable conclusions. There is no clear difference between haloperidol and olanzapine in terms of global state and relapse. Different side effect profiles were noted. These findings should contribute to continue using haloperidol and olanzapine.

Many studies did not use equivalent doses of the two medications when they were compared. Most studies used comparatively higher doses of haloperidol compared to olanzapine.

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EPV1568

Depression and Fitness: The Role of Psychopharmacology

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Introduction: The use of antidepressants is becoming more prevalent among athletes due to the growing awareness of mental health issues in sports. However, the impact of these medications, especially selective serotonin reuptake inhibitors (SSRIs), on physical performance remains uncertain. Studies on psychotropic drugs' effects on athletic capabilities raises concerns about their use in sports, particularly under anti-doping regulations.

Objectives: This review aims to assess the impact of antidepressants on physical exercise performance and muscle metabolism, in order to clarify how they influence physical capabilities.

Methods: A literature search was conducted on PubMed in September 2024 using search terms such as "sports" AND "antidepressants," "physical activity" AND "antidepressants," "exercise" AND "selective serotonin reuptake inhibitors," among others. Only systematic reviews and meta-analyses were included, without restrictions on language or year. Three articles met the scope of this work.

Results: The effects of antidepressants on athletes are inconsistent, with some studies indicating no significant change in performance, while others report reduced endurance. Paroxetine and fluoxetine, commonly prescribed SSRIs, may impair endurance due to increased serotonin levels, which can exacerbate fatigue, known as central fatigue hypothesis. It is also emphasized that SSRIs may reduce athletic performance, especially under thermal stress, by affecting thermoregulation, alongside its interference in serotonin pathways. Potential metabolic impact of these drugs was found, as chronic exposure to SSRIs showed modulation of glucose uptake, mitochondrial respiration, and muscle mass. Furthermore, SSRIs also induced changes in electrical muscle activity.

Conclusions: The evidence on the effects of antidepressants, particularly SSRIs, on physical performance and muscle function remains inconclusive. Athletes and healthcare providers must weigh these risks carefully, considering both the clinical and ethical implications of psychotropic drug use in competitive sports. Therefore, future research should focus on more consistent study protocols and explore the long-term metabolic consequences of SSRIs in physically active populations.

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EPV1569

Evolutionary History and Phylogeny of Biochemical Functions of Hypericin and Hyperforin in *Hypericum* spp

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Introduction: *Hypericum* spp., particularly *Hypericum perforatum* (such as St. John's Wort), produce hypericin and hyperforin, secondary metabolites that play critical roles in the plant's defense mechanisms. These compounds, characterized by their polycyclic and lipophilic properties, have evolved to deter herbivores and protect against pathogens. Understanding the evolutionary pressures that shaped these compounds enhances our knowledge of their biochemical roles.

Objectives: This review aims to synthesize current knowledge on the evolutionary development of hypericin and hyperforin within the *Hypericum* genus, focusing on how these metabolites evolved to fulfill defensive ecological functions.

Methods: A comprehensive literature review was conducted, examining phylogenomic studies, structural analyses, and biochemical research related to the biosynthesis of hypericin and hyperforin. We reviewed relevant phylogenetic data to understand the diversification of these compounds across *Hypericum* spp.

Results: The literature supports that hypericin and hyperforin evolved in response to selective pressures during the Cretaceous-Paleogene boundary, with their complex polycyclic aromatic structures optimized for defense. These structures, which include conjugated π -systems, are central to the compounds' ability to deter herbivores and resist pathogens, reflecting an evolutionary adaptation that is conserved across the genus.

Conclusions: The evolution of hypericin and hyperforin within *Hypericum* spp. is a prime example of how secondary metabolites serve dual purposes in nature and human use. The phylogenetic and

biochemical insights reviewed highlight the importance of these compounds as both ecological defenses and pharmacologically active agents.

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EPV1570

Perspectives of the use of Perampanel in Psychiatric Symptoms

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Introduction: Perampanel is a selective antagonist of the AMPA receptor for glutamate, primarily approved for the treatment of certain types of epilepsy. With the evolving understanding of psychiatric disorders' neurobiology, it's hypothesized that targeting the glutamatergic system could offer substantial therapeutic benefits (Perversi F, Costa C, Labate A, Lattanzi S, Liguori C, Maschio M, et al. The broad-spectrum activity of perampanel: state of the art and future perspective of AMPA antagonism beyond epilepsy. *Front Neurol* [Internet]. 2023 [cited 2024 Sep 2];14:1182304).

Objectives: The purpose of this study is to evaluate the effectiveness of perampanel in managing psychiatric symptoms such as sleep disturbances, depression, anxiety, and irritability.

Methods: A comprehensive review of scientific studies was carried out, centering on clinical trials and observational research that explored the application of perampanel in individuals exhibiting psychiatric symptoms. The review included articles published between 2013 and 2024, utilizing databases like PubMed, Scopus, and PsycINFO for sourcing. The inclusion criteria covered studies that assessed the impact of perampanel on psychiatric conditions, detailing both the clinical results and any side effects.

Results: Findings indicate that perampanel may have beneficial effects in reducing symptoms of insomnia (Abenza-Abildúa MJ, Suárez-Gisbert E, Thuissard-Vasallo IJ, Andreu-Vazquez C. Perampanel in chronic insomnia. *Clin Neurol Neurosurg*. 2020 May 1;192), depression and anxiety (Scorrano G, Lattanzi S, Salpietro V, Giannini C, Chiarelli F, Matricardi S. The Cognitive and Behavioural Effects of Perampanel in Children with Neurodevelopmental Disorders: A Systematic Review. *J Clin Med* [Internet]. 2024 Jan 10 [cited 2024 Sep 3];13(2)) in certain patient groups. However, significant adverse effects were also reported, including behavioural changes and increased aggression in some cases, necessitating careful monitoring during treatment.

Conclusions: Numerous antiepileptic medications have been effectively utilized in treating psychiatric conditions. Perampanel, in particular, has demonstrated effectiveness in managing nocturnal seizures, preserving sleep architecture, and treating restless legs syndrome. A study conducted in Spain revealed that combining perampanel with either an antidepressant or an anxiolytic significantly enhances sleep quality after three months in patients without epilepsy (Abenza-Abildúa MJ, Suárez-Gisbert E, Thuissard-Vasallo IJ, Andreu-Vazquez C. Perampanel in chronic insomnia. *Clin Neurol Neurosurg*. 2020 May 1;192).