

Dear Editor,

We sincerely thank you and the reviewers for the constructive feedback on our manuscript entitled, "**Alcohol and Alcoholism Associated Neurological Disorders: Current Updates in a Global Perspective and Recent Recommendations.**" We appreciate the reviewers' insightful comments, which have strengthened our work significantly.

In our revised submission, we have thoroughly addressed all comments to enhance the depth and clarity of our manuscript. Specifically, we have included additional references on the genetic and neurobiological mechanisms underpinning alcohol dependence and its impact on neurological health. We have expanded sections discussing serotonin's role in alcohol use disorder and added descriptions of key terms related to alcohol dependence to better define our subject matter. reviewer's point has been addressed in the rebuttal document for clarity.

Thank you again for your guidance and the opportunity to improve our work. We look forward to your feedback on our revised manuscript and hope it meets the standards for publication in WJEM.

Sincerely,

Reviewer comments

The paper provided a detailed overview of the neurobiology of alcohol addiction, followed by recent studies published in the genetics of alcohol addiction, molecular mechanism and detailed information on the various acute and chronic neurological manifestations of alcoholism for the Future research. The article is well written. I have some suggestions for this paper.

Alcoholism appears to be a complex genetic disorder, with variations in many genes influencing risk. Some of these genes have been identified, including two alcohol metabolism genes, ADH1B and ALDH2, which have the most potent known effects on the risk of alcoholism. The author should provide more references to reveal the related mechanisms.

Answer: Thank you very much for this valuable comment. we incorporate additional references to clarify the genetic mechanisms underlying alcoholism risk.

2) Signs that might be battling with alcohol dependence include: Unit of alcohol, Hazardous drinking, Alcohol dependence, Alcohol Tolerance, Reverse tolerance to alcohol, Alcohol

Withdrawal Alcohol abuse, Alcohol Addiction. The author should provide a brief description of these concepts.

Answer: Thank you very much for this insightful comment. We have provided brief descriptions of these concepts to clarify their distinctions and relevance to alcohol dependence on page 4 (Alcohol definition section)

3) Brain plasticity events contribute to the development of AUD and result in cravings and habitual alcohol-seeking behavior. Furthermore, chronic or high-dose alcohol intake causes adverse or adaptive reactions in the central nervous system (CNS) as well as in nearly every organ system. The author should focus on the relationship between alcoholism and the nervous system, provide more information.

Answer: Thank you very much for this important comment. we expanded on the relationship between alcoholism and the nervous system to highlight the neurobiological mechanisms involved in the manuscript.

4) Serotonin is an inhibitory neurotransmitter produced by neurons in the raphe nuclei. It is also known as 5-hydroxytryptamine or 5-HT. Reduced serotonin neurotransmission has been linked to higher alcohol use and susceptibility to alcoholism. There is an increase in extracellular 5-HT levels after acute alcohol intake. Chronic alcohol consumption, on the other hand, causes a general decrease in 5-HT neurotransmission, as demonstrated by reduced levels of 5-hydroxyindoleacetic acid (5-HIAA), the major metabolite of 5-HT, in heavy drinkers' cerebrospinal fluid. This decrease in extracellular 5-HT in the context of chronic alcohol exposure could be attributed to either increased reuptake of 5-HT from the extracellular space via the serotonin transporter (5-HTT) or defective 5-HT release in the raphe nuclei. The author should provide more references to reveal the related mechanisms.

Answer: Thank you very much for this insightful comment. we added more references to detail the mechanisms linking serotonin to alcohol use and susceptibility in the manuscript.