

Journal Name:	<u>International Journal of Biochemistry Research & Review</u>
Manuscript Number:	2013_IJBcRR_6380
Title of the Manuscript:	ALCOHOL EXACEBATES DYSLIPIDEMIA IN THE PREFRONTAL CORTEX OF DIABETIC RATS
Type of the Article	Research Paper

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PART 1: Review Comments

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Compulsory REVISION comments	1. Go through the whole article thoroughly for punctuation and grammar, there are substantial typing errors where a space should be in between two words. 2. Change type II diabetes to type 2 diabetes in the whole paper. It should be "<i>aspartate aminotransferase (AST)</i>" for the whole article. Not Aspertate. 3. In experimental design, clarify the number of rats in each group. It should be six according to abstract and methods.. line 59 4. In sample preparation section, include the unit for standard supernatant in HDL estimation. I assume that ddH2O mean distilled water. Please indicate for abbreviations. It would be better if the abbreviations are put in a separate list. 5. For figures and tables, use the same short form for the four experimental groups so that it is uniform, eg. CON, DIA, DLA, DHA for all. 6. Correct grammar errors: just a few to mention; the brain "was" removed.... "centrifuged"... in line 14 and 15, remove " on the other" in line19, line 32 , ..understand the effects of alcohol rather than alcohol's effects. witnessed a consistent "drop" in line 161, should be compares the "triglyceride" levels in line 168, the level "of" triglycerides in line 169,	Noted, the corrections have effected The corrections have been effected The number is 6, the correction is effected USP units/ml Noted, the observations have been effected The errors in lines 14, 15, 19, 32, 161, 168, 169, 170, 271, 276 and others alike have been corrected.

	alcohol lowered the level more significantly in the low alcohol intake “group” in line 170, line 271.. not only ~~to~~ reverse... line 276.. due to the increased~~d~~in lipid peroxidation,..... process, <i>which</i> is an Please go through the whole article again to prevent grammar mistakes. 7. For tables of results, make sure the values are in the correct cells with no overlap or mal-alignment. Advisable to use the superscripts eg. * or # to show the significant values more obvious. (current version has many mis-alignments) 8. In abstract, line 17 to 19. I guess the authors would like to say the TG levels are higher in diabetes group compared to the normal control group (92.01+/-0.18 versus 72.62+/-0.52) whereas the total cholesterol and HDL levels are found to be lower in the diabetes group compared to normal control group (..... values). Current meaning is the levels increase/decrease from to; sounds like change in value from baseline to higher/lower value in the same group. Rewrite to give a clear description of the results. 9. In conclusion portion in the abstract, line 20 and 21, clarify whether alcohol either high or low intake exacerbated the adverse effect of diabetes neuronal dyslipidaemia in all aspects (i.e. triglyceride, cholesterol and HDL). According to the results, cholesterol and HDL levels are further reduced by alcohol. For TG, TG is higher in the diabetes group compared to control, however alcohol has protective effect by lowering TG: 72.62 in control, 92.01 in diabetes, 65.14 in diabetes plus low alcohol, 67.53 in diabetes plus high alcohol. MUST revise this conclusion.	Done Superscripts added The abstract has been re-written in line with your suggestions The conclusion has been re-written to read “Our findings showed that, both low and high chronic alcohol intake in diabetes lead to dyslipidemia in the prefrontal cortex, probably by lowering ALT and AST levels or via the mechanism that suppresses the enzymes of lipid syntheses in the prefrontal cortex”
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	10. Line 37, the diabetic dyslipidemia is associated with “moderate elevation of TG, low HDL and increase in small dense LDL particles”. It is not low HDL and small dense LDL particles. 11. The reference 7 is not relevant with the text. The reference research paper did not mention the cited information. Recheck for the proper correct reference. 12. In methods portion, the authors described the research was according to NIH publication on laboratory animal use and care with reference no 11. BUT the reference is again not correct and relevant one. Mention correct reference for that statement. 13. In the section 3, RESULTS portion, description of the findings with reference tables and figures in parathesis, with incorporation of relevant figures and tables in the paragraph is better than current listing down of the tables line by line and description. Eg: Instead of Fig 2 shows that both diabetes and alcohol lowered high density lipoprotein (HDL) total cholesterol significantly at ($P= 0.05$), while triglycerides level was significantly increased by diabetes. Alcohol intake exacerbates the effect of diabetes.	This correction has been effected Ref 7 is now: James Best, George Jerums, Harvey Newnham, Richard O'Brien. Diabetic Dyslipidemia. Dept Medicine, St Vincent's Hospital; Endocrine Unit, Austin Hospital; Dept Medicine, Box Hill Hospital; Diabetes Unit, Monash Medical Centre, Victori ADS Position Statements. 1994 Ref 11 is now: Zimmermann M: Ethical guidelines for investigations of experimental pain in conscious animals. Pain 1983;16:109-110
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	Table 1: Compares the triglycerides levels in all experimental groups. Diabetes increased significantly ($P < 0.05$) the level triglycerides in the prefrontal cortex; while alcohol lowered the level with more significantly decrease in the low alcohol intake. Table 2: Compares the cholesterol levels in all experimental groups. Diabetes significantly ($P < 0.05$) lowered the total cholesterol level in the prefrontal cortex; while low alcohol intake lowered the cholesterol level more than in high alcohol intake group. The following style is preferable: Both diabetes and alcohol lowered high density lipoprotein (HDL) and total cholesterol significantly ($P = 0.05$), while triglyceride level was significantly increased by diabetes. Alcohol intake exacerbates the effect of diabetes. (Figure 1) Put the figure 1 Diabetes increased the level of triglycerides significantly ($P < 0.05$) in the prefrontal cortex; while alcohol lowered the level more significantly especially in the low alcohol intake group. (Table 1) Show the table 1 Diabetes significantly ($P < 0.05$) lowered the total cholesterol level in the prefrontal cortex; while low alcohol intake lowered the cholesterol level more than in high alcohol intake group (Table 2) Etc, for all the tables and figures. 14. The authors mention about lipid peroxidation in the methods section, but there is no result for that parameter in the results section.	The style has been changed to reflect the suggested one
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	15. There is no evidence to say alcohol decreases serum ALT level. Consider revising the statement in line 271 to 273. (It is only the finding of this study that ALT levels in diabetes and alcohol group are lower than the control and diabetes group. Do not generalize this finding. Evidence does not exist for humans) 16. Line 275. It should be “the finding of hypertriglyceridemia in the diabetic group is consistent with the previous reports [13,14,15]” 17. Line 285 and 286, do the authors want to mention about “Our results showed the triglyceride levels are significantly higher in the prefrontal cortex”? Because that whole paragraph is discussion about triglyceride. 18. For conclusion, the authors have concluded that alcohol intake (either low or high) exacerbates the adverse effects of diabetes neuronal dyslipidaemia (this statement needs revision; refer to comment 9 for this statement) by lowering ALT and AST levels or via the mechanism..... What is the supporting evidence for saying the effect of alcohol on brain dyslipidaemia is through the lowering of ALT and AST according to your study. This conclusion should be made only with evidence and extreme precaution.	This portion has been removed from the methods section The ALT and AST in this study were measured in the serum and tables 4 and 5 show that the levels were lowered by both high and low alcohol intake in diabetes. Diabetes increased the levels according to our results. The statement in lines 271-273 was a suggestive possibility and hence the term probably. This suggestion has also been effected The statement “Our results also showed that the total cholesterol level was significantly decreased in the prefrontal cortex”In lines 285 and 286 is correct. The sentence has been pushed down to join the discussion on cholesterol. The conclusion now reads “Our findings showed that, both low and high chronic alcohol intake in diabetes lead to dyslipidemia in the prefrontal cortex, probably by lowering ALT and AST levels or via the mechanism that suppresses the enzymes of lipid syntheses in the prefrontal cortex, leading to reduction in synaptosomal membrane cholesterol, and altered neuronal and physiological function.”
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Minor REVISION comments	Can the authors give any special reasons why the lipid levels are measured in the prefrontal cortex rather than the serum? The importance and possible clinical significance on human brain as well. Consult with a native speaker for language to prevent unnecessary misinterpretation and information conveyed to the readers.	Lipids constitutes at least 60% of the brain tissue and hence any change in its level would have direct impact on the brain function
Optional/General comments	Abstract needs major revision. Introduction is fair. Materials and method is acceptable and reproducible, description is clear apart from minor changes. Results section needs revision. Discussion portion must be changed. Conclusion must be revised. Missing and non corresponding references must be amended.	All suggestions have been comply with.