

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 31210

Title: Statin use and cognitive function in middle-aged adults with type 1 diabetes

Reviewer's code: 02446617

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-11-06 14:26

Date reviewed: 2016-11-17 05:23

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[] Accept
[] Grade B: Very good	[] Grade B: Minor language polishing	[] The same title	[] High priority for publication
[] Grade C: Good	[] Grade C: A great deal of language polishing	[] Duplicate publication	[] Rejection
[] Grade D: Fair	[] Grade D: Rejected	[Y] No	[Y] Minor revision
[] Grade E: Poor		BPG Search:	[] Major revision
		[] The same title	
		[] Duplicate publication	
		[] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The author's provides compelling evidence of correlation between statin use and cognitive impairment in patients with T1D. Robust statistical analysis has been utilized in order to rule out any confounding data that is limited by sample size. The author's analysis takes into account cardiovascular risks, gender differences and ApoE4 allele status, which is involved in both cardiovascular and Alzheimer's disease. The study also addresses the issue as to why their conclusion is different from the previous studies conducted including comparing and contrasting the reason for disparity between findings. Effect of statin was discussed well on the adverse effect it has on myelination however, compelling evidence also exist on statin effect on angiogenesis and vascular genesis. This becomes important in development of the brain as statin in a concentration dependent manner can either aid or disrupt angiogenesis. Shedding light on this in the discussion will strengthen the argument. Lastly the study in cooperates several major parameters affecting the patient's life that can affect the outcome of the results. However, the socio-economic impact such as employment and average household income has not been clearly addressed this study. If the data is readily available the author's should speculate the socio-economic impact on the outcome.



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Strengths: 1) Robust statistical analysis. 2) Takes into account major parameters such as BMI and cardiovascular risk effecting T1D. 3) Follows the patient from childhood to adulthood and provides a good time line for the correlation of statin use and cognitive impairment. Weakness: 1) If possible please indicate when the patients started taking statin and the dosage given to each patient. This can aid is the deciphering the onset of cognitive impairment. 2) Please discuss the effect of statin on angiogenesis in a developing brain.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 31210

Title: Statin use and cognitive function in middle-aged adults with type 1 diabetes

Reviewer's code: 01002592

Reviewer's country: Italy

Science editor: Fang-Fang Ji

Date sent for review: 2016-11-06 14:26

Date reviewed: 2016-11-18 17:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The present version of this report must be amended in some parts. It needs at first to be more attractive for readers being rather difficult to follow in the present version. Major points: -data presentation is a key point and in this article they are rather confusing and without accompanying graphs easy to understand. The Tables are plenty of numbers: albeit they are needed, focused graphs must help readers; -the whole article needs to be better written either in English (an extensive editing is necessary) and in its content because the presentation lacks of consequentiality and must be less dispersive; -type 1 diabetes and the related problems are not presented and discussed at the beginning of the discussion whose first sentences are unsound. Discussion cannot start as in this paper. I suggest to look at the main syndrome that is type 1 diabetes and start on two or three main research questions such as the role of islet beta cell apoptosis (see J Cell Physiol. 2005 204:124-30 regarding the apoptosis of beta cells and the role of NF-KappaB transcription factor and IL-18 in K. Bendtzen studies Eur J Immunol. 2003 33:2278-86 and some two or three other articles in 2015/6 of other authors). Then you must start with the relationship between statins and brain injuries. At the end, the Conclusions must be also shown in a figure containing the main results of the study,



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attracting the reader on that has been found and demonstrated: a figure and not Table or only words. Please revise completely the references either deleting the redundant ones and checking them because they are written in a casual manner: no one seems to be the same of the other. Moreover you reported the dog while the volume and pages are present. In some cases only the dog is present, etc. Please check all carefully.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 31210

Title: Statin use and cognitive function in middle-aged adults with type 1 diabetes

Reviewer's code: 00646289

Reviewer's country: Turkey

Science editor: Fang-Fang Ji

Date sent for review: 2016-11-06 14:26

Date reviewed: 2016-11-21 02:29

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

ESPS Manuscript No: 31210 Reviewer's Code: 00646289 This paper aims to test the correlation between statin use and cognitive impairment in adults with childhood-onset Type 1 Diabetes (T1D), as a group of patients with chronic exposure to metabolic dysregulation. It is a valuable study, and the results are well analyzed. It should be published for utilization of both clinicians and basic researchers. Although statin has already been correlated to cognitive impairment to some extent in different disorders, there is only one study reported on the situation in T1D patients, which is referred and discussed in the paper by the authors. It is a significant issue, considering that FDA has recently expanded advice on statin risks. The points that need to be considered are; - The Introduction section will be improved if the authors add statements giving brief information on why and when statins are prescribed in T1D patients. -Do the authors have information on the exact ages of patients when statin use has started? -Authors state that patients used mostly lipophilic statins. Do they have the information regarding the intensity of the statin treatments that these patients received (high/moderate/mild)? Such a correlation would be informative. -Introductory sentences should be added to the Discussion section that summarizes the study before going on to



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the discussion of the results. -The manuscript should be over-read for minor mistakes in language, such as: Page 11, Line 8 from the bottom: "with an higher prevalence" should be "with a higher prevalence" Page 16, Line 5 from top: "adult ages 60 years and older.." should be "adults of ages 60 years and older.." Page 16, Line 7 from top: the statement "although at least one examined participants with 10+ years of statin use.." may be better as; "although at least one examined participant was on statins for 10+ years.."

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 31210

Title: Statin use and cognitive function in middle-aged adults with type 1 diabetes

Reviewer's code: 02459030

Reviewer's country: China

Science editor: Fang-Fang Ji

Date sent for review: 2016-11-06 14:26

Date reviewed: 2016-11-22 18:27

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This study indicated that statin use was associated with cognitive impairment, particularly affecting memory, in these middle-aged adults with childhood-onset T1D. Logistic and linear regression models tested the association between three-level degree of statin use (covariate of interest) and cognitive impairment or cognitive domain z-scores (outcomes). The statistical methods were used properly. Importantly, the authors take into account of confounding data, including age, education, CAD, LDL-c and apo E4 allele status. There is one question needed to be answered. We have known that statin could decreased TCH and LDL, and delayed the development of atherosclerosis in brain vessels. Thus, why does statin lead to cognitive impairment? Please discussed the possible potential mechanisms.