ESPS PEER-REVIEW REPORT

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

COMMENTS TO AUTHORS

The manuscript entitled "Therapeutic Targets and Delivery Challenges for Alzheimer's Disease" by Desai and colleagues reviews the pathophysiology and pharmacotherapy of Alzheimer's disease (AD). Although the topic of the review it timely and relevant to the field, there are a few issues listed below that lessen my enthusiasm for the paper. 1) Many of the paragraphs in the manuscript read as a collection of related facts without a clear and coherent theme. This leaves the reader with information, but without a clear context in which to understand that information. I think many readers will find this material hard to follow in part because it is often not clear why individual paragraphs are included and what the take away message of that paragraph should be. This is a consistent issue throughout the manuscript. 2) Related to item 1 above; Paragraphs often are not focused on a single main point. Instead, many paragraphs lump tangentially related information together into a single paragraph. This style may leave readers confused about the main points the authors intend to highlight. I suggest the authors only include the material that is most directly related to the points they want the reader to understand. 3) Although neuroanatomy does not appear to be the primary focus of this review, the authors do include a limited amount of information about

neuroanatomy associated with AD. Unfortunately, the neuroanatomical description is quite vague, does not connect AD symptoms to neuroanatomy well, and leaves the reader feeling like this is an area the authors are somewhat less comfortable/familiar with. This material is largely limited to a few sentences on page 7. This certainly seems like relevant information, but I believe a stronger connection between symptoms (e.g., memory dysfunction) and brain regions (e.g., hippocampus) is warranted. 4) Figure captions are little more than titles for figures. I believe the captions would be improved by including a more thorough description of the figure so that readers better understand the message they depict. 5) Citations: The manuscript needs significant work in regard to citations. 1) There are paragraphs that do not include citations at all; 2) There are sentences that describe prior work that are not cited; 3) the sole citation for some paragraphs is a prior review paper. I would encourage these authors to cite and sentences that are based on prior work and focus more on the original research rather than prior review papers. 6) There are a number of spelling, grammar, punctuation issues throughout the manuscript that interfere with the ease of reading this material. 7) A relatively minor issue is that the authors seem to be fond of the use of "viz". As a reader, I found it to be overused and distracting. I certainly think its limited use is appropriate, but would suggest the authors consider alternative wording as well.

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		[Y] No	

COMMENTS TO AUTHORS

The manuscript summarizes the pathophysiology and new approaches for the treatment of Alzheimer's Disease. In particular, drug delivery systems across blood-brain barrier are discussed and characterized. Article needs revision as follows. 1) The article seems too long and redundant in some parts: the sections should be divided in available treatments and prospective therapies, or, alternatively, linked to the pathologic mechanisms, as reported in tables. 2) The environmental factors are just mentioned in "4.3 Mitochondrial Dysfunction Cascade Hypothesis": a discussion on them should be expanded. 3) The figures 4-8 should be better connected to figure 3. 4) The English language should be ameliorated.