Reviewer 2

The title of this review indicates it will cover the effects of physical activity (PA) on biomarkers of Alzheimer's disease. The content of the review in this regard is extremely superficial and not well organized.

The introduction is appropriate and leads the reader to anticipate a thorough discussion of the effect of physical activity on AD risk.

The authors then move into a section titled AD risk factors which is very limited in this regard. Only the first two small paragraphs and the large Figure 1 of this section are are dedicated to risk factors. The majority of this section (paragraphs 3-5) describe the amyloid cascade hypothesis of AD and do so in a very superficial and limited manner. This discussion does not belong in a section titled Risk Factors as it is not a risk factor. There are several misstatements in this discussion as well, such as "abeta production and deposition by APP" (l. 69). Abeta is derived from APP, not deposited by APP. Also, "abeta 42, the most common type" (l. 72) is not correct. Abeta 40 is the most common type.

I fail to see the relationship of Section 3 to the topic of this review as outlined in the title. It, again, is a rather superficial discussion, but if it were not included I would have not noticed it's absence. If it is left in, the authors should somehow reveal its relevance to the overall discussion of the topic. I'm not sure how this could be done.

Sections 4 and 5, the main topic of the review, I again find to be very superficial and very under referenced. For example, a recent review of this topic by Yuede et al., (Neurobiology of Stress 8:158-171, 2018) references far more studies of PA effects on markers of AD than are covered here and there have been several more studies on this topic published since the Yuede review was published. I also found this section of the review very difficult to follow. There are many layers to the effect of physical activity on AD onset and progression. The type of physical activity matters, wheel running, treadmill running, swimming, etc. Intensity matters, as does age at which PA begins, and how long it continues. All these parameters are intermixed in this section in short, declarative sentences which leaves the reader confused as to the role of PA on AD.

Respons to Reviewer 2:

We have included a new paragraph in the Risk Factors section including below references:

BMJ Open 2017 Mar 24;7(3):e011843. doi: 10.1136/bmjopen-2016-011843.

Daviglus ML, et al. National Institutes of Health State-of-the-Science Conference statement: preventing Alzheimer disease and cognitive decline. Ann Intern Med. 2010;153(3):176–81.

We have also included Aetology of Alzheimer’s disease in section 3 .