Reviewer's report

Title: Diet quality and hippocampal volume in humans

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Reviewer: Martha Payne

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Manuscript Review
BMC Medicine
'Diet quality and hippocampal volume in humans'

This paper addresses the important issue of dietary influence on hippocampal aging, and examines whether dietary patterns (prudent vs. Western) are associated with hippocampal volume at two time points. The authors determined that the prudent diet was associated with greater left hippocampal volume, while a Western diet was associated with smaller left hippocampal volume. These findings suggest the potential for dietary interventions to promote hippocampal health, decrease age-related atrophy, and prevent negative health outcomes associated with hippocampal atrophy. A few revisions are warranted in order to clarify the research conducted and its interpretation.

Major Compulsory Revisions

1. It is unclear if dietary quality was used as a predictor of Yr4 hippocampal volume, or if only associations were examined between diet and overall volumes acquired at both time points. The abstract, introduction and discussion should clarify the exact longitudinal nature of research.

2. The use of two imaging protocols is not sufficiently addressed. Why were different protocols used for a longitudinal study, especially given that the same type of scanner was apparently available at both times. Adjustment for changes in ICV does not adequately control for the potential that different imaging protocols may have significantly altered hippocampal volume estimates, especially given that the ICV was derived using an automated process. The differing slice thickness and other acquisition parameters between the two times points may have altered the appearance of hippocampal and other anatomic boundaries – which could have substantially altered manual tracing, an effect which would not necessarily have been manifested in a systematically larger or smaller hippocampal volume between the two time points. As one expects the hippocampal volumes to decrease over time (in this older population), it is especially difficult to identify effects of protocol differences. Were any comparisons made between hippocampal tracings of individuals scanned with both protocols on the same day? Alternatively, mean hippocampal volumes could be compared between individuals who were age 64 at baseline with individuals who were age 64 at Yr4. Regarding ICV it would be helpful to include mean
volumes at both time points in order to demonstrate any systematic bias or lack thereof in intracranial vault size. In addition to more fully addressing the problem of two imaging protocols, the authors should highlight this problem as a study limitation in the Discussion.

Minor Essential Revisions

1. Figure 1 should identify N for each diet group given that many participants likely did not fit into any of the three categories (e.g., those + 1SD on prudent diet but average on Western).

2. How did the hippocampal atrophy – in either absolute terms or % change – compare with population norms? This information is important in terms of generalizability and because of the problem of two imaging protocols, identified above.

Discretionary Revisions

1. It would be helpful for authors to briefly address issues in comparing human with non-human studies. For example, a high sucrose diet is not an accurate approximation of a ‘Western’ diet, and human trials of vitamin supplementation (e.g., alpha-tocopherol) have failed to show benefits that would be expected based on animal studies.

2. Did authors consider handedness as a covariate? This factor is of potential importance given the laterality of findings.

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests