Author's Reply: Regarding issues with article on hippocampal volumetry

Sir,
We appreciate the interest in our article and the incisive comments brought forward by the authors. We would like to reply to the concerns raised by them.

There is evidence in literature pointing to hippocampal atrophy correlating with Alzheimer's dementia (AD) and quantitative analysis of hippocampus has been used as a method (if not as popular as in mesial temporal sclerosis (MTS)) in diagnosis and prognostication in dementia of Alzheimer's type.[1,2] The main talking point in this paper is on hippocampal volumetry irrespective of the cause (MTS/AD) and can be directly applied to patients with MTS as the age range of our study population is appropriate for this disease. We have commented on the possibility of there being a difference in hippocampal volume in the elderly and we accept that this data may not be useful above this age range. There is a need for further studies in elderly age group to see if the difference in hippocampal volumes (HV) is reflected here as well.

Imaging was done on 200 healthy volunteers at our institution as part of a wider study dedicated to cognitive mapping of the human brain funded by the Department of Science and Technology. We based our sample size from this study group. As indicated by smaller sample sizes in similar studies done previously, it is challenging to be able to put together a study that involves imaging essentially normal individuals, due to the costs involved. We agree that large population-based studies focusing on hippocampal volumetry in healthy individuals with appropriate sampling methods will add to the body of evidence.

As mentioned in our paper, volumetry in MTS can aid in lateralization, predicting postoperative outcome, and help in selecting patients for invasive preoperative monitoring.[3] There is also a strong correlation between atrophy detected by volumetry and histologically identified cell loss.

While it is unclear as to why there is a difference in HV between the Indian and Western population, we believe that it may be a reflection of the fundamental difference between the two populations in terms of their physical characteristics.

As already mentioned in the results section of the paper, using 2 standard deviations (95% confidence interval), the normal HV based on our study would be 1.813-3.009 cm^3.

While assessing intraobserver variability, since the same subject HV were being compared to see if there was a significant difference, we felt a paired t-test was appropriate. We chose 20 subjects from the total 200 in a randomized manner. We felt reassessing 20 would prove sufficient to point to intraobserver consistency of findings.

The review article by Konrad et al.,[4] elaborates different ways and methods of segmenting different parts of the hippocampus. Using this article as a reference we developed a protocol for segmenting the hippocampus in our study. This protocol along with the anatomical landmarks used has been explained in the methods section of the study. We have also dedicated a paragraph discussing contentious aspects of hippocampal segmentation. After using this protocol to segment the hippocampus; we used software in the Siemens Syngo workstation, which is regularly used by radiologists to calculate the area in each slice and then the volume. We hope that this method, as it is available as standard with all magnetic resonance imaging (MRI) machines, will facilitate its wider use.

We have not extrapolated the data into elder age group. We have only stated that as we have found differences in younger adults, it is possible that there could be similar differences even in the elderly age group. As mentioned in point a), we agree with you and do stress the need for studies to be done in the elderly age group.

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References

1. Apostolova LG, Mosconi L, Thompson PM, Green AE, Hwang KS, Ramirez A, et al. Subregional hippocampal atrophy predicts Alzheimer's dementia in the cognitively normal. Neurobiol Aging 2010;31:1077-88.
2. Jack CR Jr, Wiste HJ, Vemuri P, Weigand SD, Senjem ML, Zeng G, et al. Alzheimer's Disease Neuroimaging Initiative. Brain beta-amyloid measures and magnetic resonance imaging atrophy both predict time-to-progression from

mild cognitive impairment to Alzheimer's disease. Brain 2010;133:3336-48.

3. Coan AC, Kubota B, Bergo FP, Campos BM, Cendes F. 3T MRI Quantification of hippocampal volume and signal in mesial temporal lobe epilepsy improves detection of hippocampal sclerosis. AJNR Am J Neuroradiol 2014;35:77-83.

4. Konrad, C., *et al.*, Defining the human hippocampus in cerebral magnetic resonance images — an overview of current segmentation protocols. Neuroimage, 2009. 47: p. 1185-95.