Survey of Protocols for Manual Hippocampal Volumetry: Preparatory Steps for an EADC-ADNI Harmonized Protocol

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Objective

Uniformity of hippocampal measurement is required for the use of its volume as a standardized diagnostic index, a surrogate measure in clinical trials for AD drugs and a gold standard for automated segmentation algorithms.

Background

Hippocampal atrophy is a key diagnostic marker for early- preclinical Alzheimer's disease (AD), but manual tracing on magnetic resonance (MR) images (present gold standard procedure) result in heterogeneous volumetric estimates (2 to 5.3 cm^3) depending on the adopted segmentation protocol.

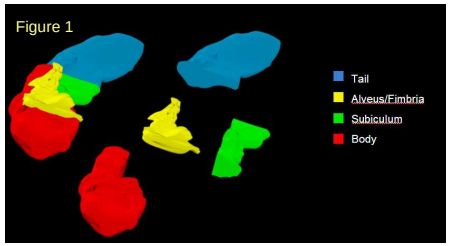
Methods

We selected 10 most used tracing protocols in the AD literature for evaluation. The same rater carried out complete tracings on two MR scans (one control, one matched AD ADNI subjects) on 1.2 mm slices, using each of the 10 protocols. We arranged individual interactive web conferences with the primary author of each protocol, to check the appropriate execution of the tracing, and correct it when necessary. We extracted the differences among the author-certified protocols, quantified their impact on total hippocampal volume, and operationalised them in order to compute their influence on reliability measures in the next steps.

Results

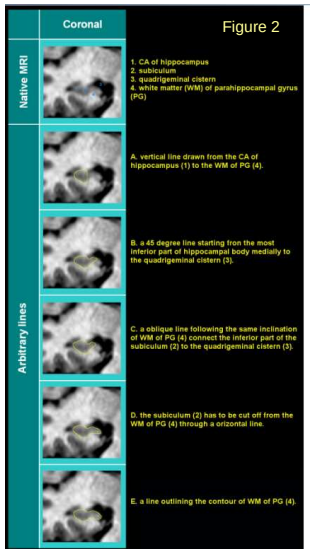
The relevant differences regarded the definition of the medial border (subiculum), of the last slice (tail), and the inclusion of hippocampal white matter (alveus/fimbria) (Figure 1).

Figure 1



The 5 different ways to trace the medial border of the hippocampus, separating it from the rest of the parahippocampal gyrus, lead to a maximum difference amounting to the 10% of the total hippocampal volume (Figure 2), while the inclusion/exclusion of alveus and fimbria lead to a 6% difference (Figure 3).

Figure 2



The different definitions of the last slice lead to a maximum difference amounting to the 27% of the total hippocampal volume (Figure 4). Instead, heterogeneities in the definition of the first slice are no longer an issue due to the currently available 3D navigation software.

Figure 3

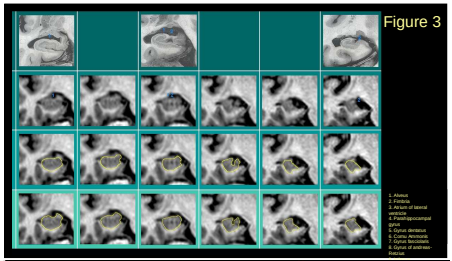
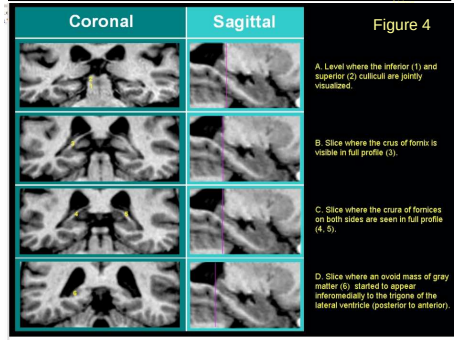


Figure 4



Conclusions

These results are preparatory to an international consensus for a harmonized protocol for the manual tracing of the hippocampus.