Definition of Harmonized Protocol for Manual Hippocampal Volumetry: an EADC-ADNI project

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Background

Heterogeneity of landmarks among protocols leads to different volume estimates, hampering comparison of studies and clinical use. There is an urgent need to define a harmonized protocol for manual hippocampal segmentation from magnetic resonance scans. Landmark differences among the twelve most common protocols were extracted, operationalized, and quantitatively investigated. The results were presented to the Delphi panel, consisting of sixteen researchers with substantial expertise in hippocampal segmentation, in order to reach an evidence-based consensus on segmentation landmarks.

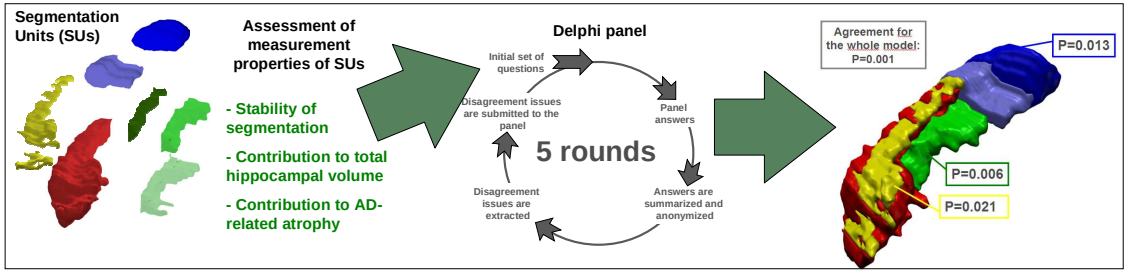

Figure 2: Evidence-based Delphi method
In the Delphi voting sessions quantitative evidence on SUs (representing landmark variability) was provided to help panelists taking decision on harmonized landmarks. Anonymized feedback and reasons for panelists' choices were provided in subsequent rounds, until convergence was achieved. Five rounds were required to converge on all issues.

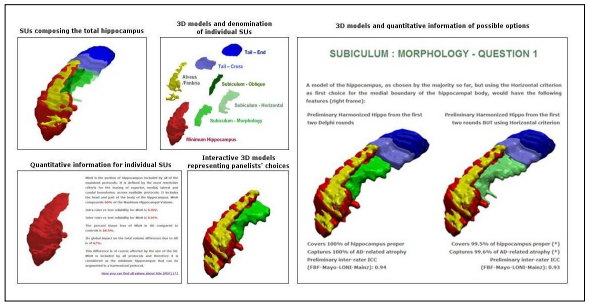

Figure 1. Examples of information provided to panelists in the Delphi rounds

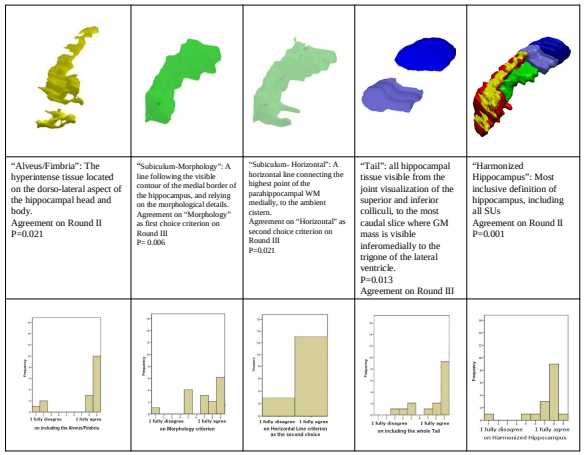

Figure 3. Modeling (upper line), Definition of SUs and panelists' answers distribution (bottom line)

Methods

The Delphi panel participated in iterative anonymous voting sessions where feedback from previous rounds was utilized to progressively facilitate panelists' convergence on agreement. Panelists were presented with segmentation alternatives, each associated with quantitative data relating: (i) reliability, (ii) impact on whole hippocampal volume, and (iii) correlation with Alzheimer's disease (AD)-related atrophy (**Figure 1**). Panelists were asked to choose among alternatives and provide justification, comments and level of agreement with the proposed solution. Anonymous votes and comments, and voting statistics of each round were fed into the following Delphi round. Exact probability on binomial tests of panelists' preferences was computed.

Results

Sixteen panelists completed five Delphi rounds. Agreement was significant on inclusion of alveus/fimbria (p=0.021); inclusion of the whole hippocampal tail (p=0.013); segmentation of the medial border of the body following visible morphology as the first choice (p=0.006) and following a horizontal line in the absence of morphological cues (p=0.021); inclusion of the minimum hippocampus (comprising head and body) (p=0.001); inclusion of vestigial tissue in the segmentation of the tail (p=0.022) (**Figures 2-3**). Significant agreement was also achieved for exclusion of internal cerebrospinal fluid pools (p=0.004), and use of AC-PC orientation (p=0.006). Based on previous quantitative investigation, the hippocampus so defined covers 100% of hippocampal tissue, captures 100% of AD-related atrophy, and has good intra-rater (0.99) and inter-rater (0.94) reliability.

Conclusions

A Harmonized Protocol for Manual Segmentation has been agreed among an international panel of experts. The protocol will be validated with neuropathological data and its accuracy will be compared with protocols currently used in AD research.