

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

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Background: To define a Harmonized Protocol for hippocampal segmentation, landmark differences among the twelve most common protocols were extracted, operationalized, and quantitatively investigated. The results were presented to the Delphi panel (sixteen researchers with substantial expertise in hippocampal segmentation), through a consensus facilitating technique, in order to reach an evidence-based consensus on harmonized landmarks (Figure 1).

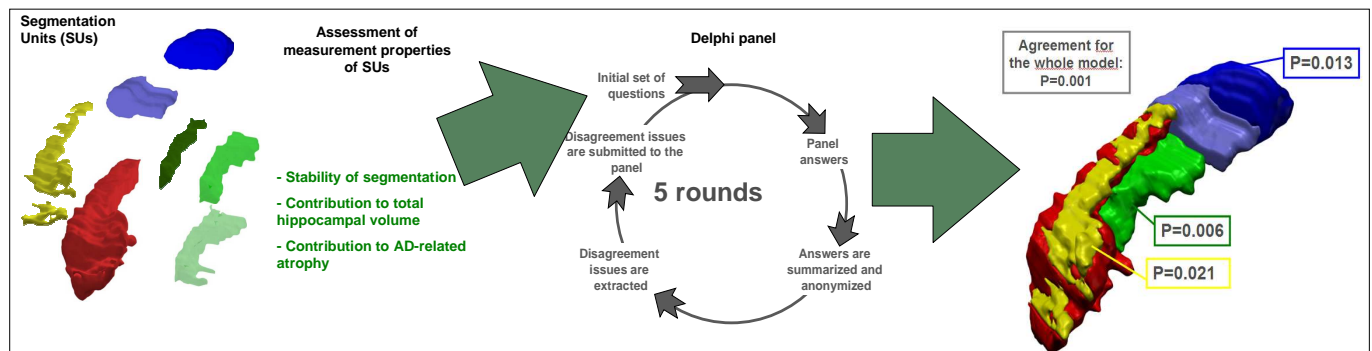


Figure 1: Evidence-based Delphi method. In the Delphi voting sessions quantitative evidence on SUs (representing landmark variability) was provided to help panelists taking decision on harmonized landmarks. Anonymized feedback and reasons for panelists' choices were provided in subsequent rounds, until convergence was achieved. Five rounds were required to converge on all issues.

Methods: 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.

Figure 2. Modeling (upper line), Definition of SUs and panelists' answers distribution (bottom line)

<p>"Alveus/Fimbria": The hyperintense tissue located on the dorso-lateral aspect of the hippocampal head and body. Agreement on Round II P=0.021</p>	<p>"Subiculum-Morphology": A line following the visible contour of the medial border of the hippocampus, and relying on the morphological details. Agreement on "Morphology" as first choice criterion on Round III P= 0.006</p>	<p>"Subiculum-Horizontal": A horizontal line connecting the highest point of the parahippocampal WM medially, to the ambient cistern. Agreement on "Horizontal" as second choice criterion on Round III P=0.021</p>	<p>"Tail": all hippocampal tissue visible from the joint visualization of the superior and inferior colliculi, to the most caudal slice where GM mass is visible inferomedially to the trigone of the lateral ventricle. P=0.013 Agreement on Round III</p>	<p>"Harmonized Hippocampus": Most inclusive definition of hippocampus, including all SUs Agreement on Round II P=0.001</p>

Results: Sixteen panelists completed five Delphi rounds. Agreement was significant for inclusion of all Segmentation Units, and the majority (63%) agreed on inclusion of vestigial tissue in the segmentation of the tail (Figure 3). Significant agreement was also achieved for exclusion of internal cerebrospinal fluid pools ($p=0.004$), and use of AC-PC orientation ($p=0.006$).

Conclusions: A Harmonized Protocol for Manual Segmentation has been agreed among an international panel of experts. The hippocampus so defined covers 100% of hippocampal tissue, captures 100% of AD-related atrophy, and has good ICCs (>0.94). The protocol will be validated with neuropathological data and its accuracy will be compared with protocols currently used in AD research.