

# EADC-ADNI Definition of Harmonized Protocol for Manual Hippocampal Segmentation on MRI



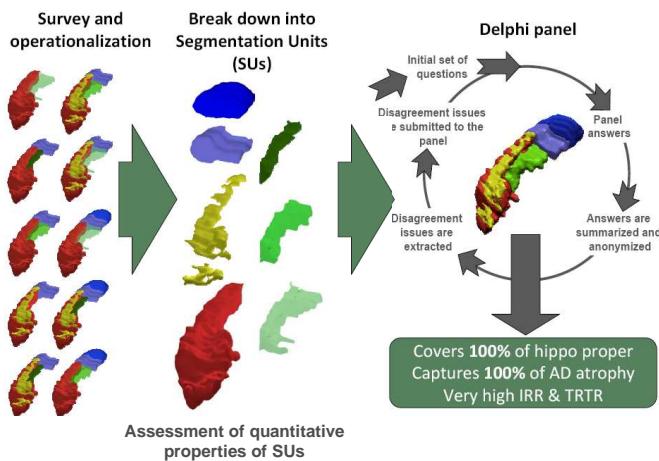
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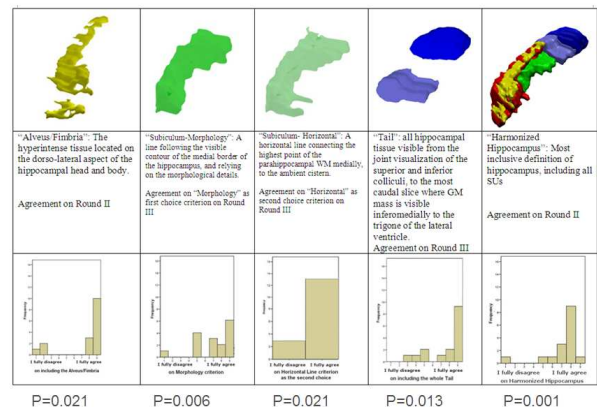
**Objective** Heterogeneity of landmarks among protocols leads to different volume estimates, hampering comparison of studies and clinical use for diagnosis and tracking of Alzheimer's disease (AD). There is an urgent need to define a harmonized protocol for manual hippocampal segmentation from magnetic resonance scans (MRI).

**Methods** Landmark differences among the 12 most common protocols were extracted (Fig. 1, 2), operationalized, and quantitatively investigated. Results were used in an evidence-based convergence technique, a Delphi panel of sixteen experts on hippocampus, participating in iterative anonymous voting sessions with feedback from previous rounds. The panel chose among segmentation alternatives, associated with quantitative data relating reliability, impact on whole hippocampal volume, and correlation with AD-related atrophy. Exact probability on binomial tests of panelists' preferences was computed.

**Figure 1. Steps from operationalization of landmark differences to the definition of the Harmonized Protocol.**



**Figure 2. Consensus on landmarks through the five Delphi panel voting rounds.**



**Results** After 5 Delphi rounds, agreement was significant on (Figure 2): inclusion of alveus/fimbria ( $p=0.021$ ), 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 vestigial tissue in the segmentation of the tail (63% agreement,  $p=n.s.$ ), and for the whole set of landmarks ( $p=0.001$ ). Segmentation modalities (internal CSF, orientation) were also defined. 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** This consensual protocol will be validated with neuropathological data and its accuracy will be compared with protocols currently used in AD research. Updated information is available at [www.hippocampal-protocol.net](http://www.hippocampal-protocol.net).