DEFINITION OF AN EADC-ADNI HARMONIZED PROTOCOL FOR HIPPOCAMPAL SEGMENTATION

Martina Bocchetta[1,2], Marina Boccardi[1], Liana G. Apostolova[3], Josephine Barnes[4], George Bartzokis[5], Richard Camicioli[6], John G. Csernansky[7], Charles deCarli[8], Mony J. de Leon[9], Leyla deToledo-Morrell[10], Michael Firbank[11], Rossana Ganzola[12], Lotte Gerritsen[13], Wouter Henneman[14], Ronald J. Killiany[15], Stéphane Lehéricy[16], Nikolai Malykhin[17], Johannes Pantel[18], Patrizio Pasqualetti[2], Gregory Preboske[19], Jens C. Pruessner[20], Alberto Redolfi[1], Nicolas Robitaille[12], Hilkka Soininen[21], Lei Wang[22], Craig Watson[8], Dominik Wolf[23], Henrike Wolf[24], Simon Duchesne[12], Clifford R. Jack[19] and Giovanni B. Frisoni[1], for the Harmonized Protocol group.

1LENITEM, IRCCS – S. Giovanni di Dio – Fatebenefratelli Brescia, IT; 2AFaR – Associazione Fatebenefratelli per la Ricerca, Rome, IT; 3Mary S. Easton Center for Alzheimer's Disease Research and Laby of NeuroImaging, David Geffen School of Medicine, Univ of California, Los Angeles; 4Dementia Research Centre, UCL Institute of Neurology, Univ College London, London, UK; 5Dept. of Psychiatry, David Geffen School of Medicine at UCLA, Los Angeles, CA; 6Dept of Biomedical Engineering, Univ of Alberta, Edmonton, AB, Canada; 7Dept of Psychiatry and Behavioral Sciences, Northwestern Univ Feinberg School of Medicine, Chicago, IL; 8Dept of Neurology, Univ of California, Davis, CA; 9Center for Brain Health, New York Univ School of Medicine, NY; 10Dept of Neurological Sciences, Rush Univ, Chicago, IL; 11Institute for Ageing and Health, Newcastle Univ, Wolfson Research Centre, Newcastle, UK; 12Université Laval and Centre de Recherche Université Laval – Robert Giffard, Quebec City, Canada; 13Karolinska Institute, Stockholm, SW; 14Dept of Radiology and Alzheimer Center, VU Univ Medical Center, Amsterdam, The Netherlands; 15Dept of Anatomy and Neurobiology, Boston Univ School of Medicine; 16Univ Pierre et Marie Curie-Paris 6, Groupe Hospitalier Pitié-Salpêtrière, Paris, FR; 17Dept of Biomedical Engineering, Centre for Neuroscience, Univ of Alberta, Edmonton, Alberta, Canada; 18Dept of Psychiatry and Psychoterapy, Univ of Frankfurt/Main, DE; 19Dept of Diagnostic Radiology, Mayo Clinic and Foundation, Rochester, MN; 20McGill Centre for Studies in Aging, Dept of Psychiatry, McGill Univ, Montreal, Quebec, Canada; 21Dept of Neurology, Univ of Eastern Finland and Kuopio Univ Hospital, Kuopio, FI; 22Northwestern Univ Feinberg School of Medicine, Dept of Psychiatry and Behavioral Sciences; 23Klinik für Psychiatrie und Psychotherapie, Johannes Gutenberg-Universität Mainz, DE; 24Psychiatric Univ Hospitals, Univ of Zurich, Zurich, CH
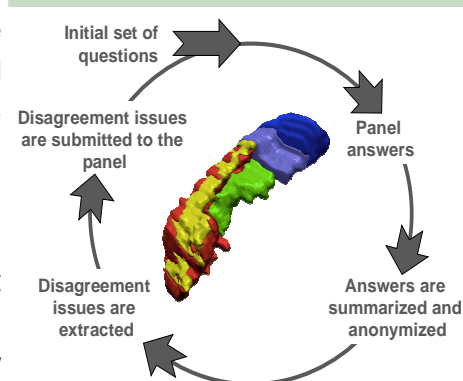
Background & Aim

Heterogeneity of protocols leads to different volume estimates, hampering comparison of studies and clinical use for Alzheimer's disease (AD). A Harmonized Protocol (HP) for manual hippocampal segmentation from magnetic resonance imaging is urgently needed.

Preliminary Phase

Survey — Operationalization of differences into Segmentation Units (SUs) — Measurement of SUs
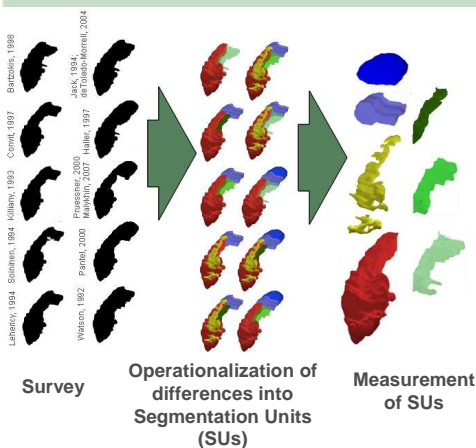
Landmark differences among the 12 most common protocols in the AD literature were extracted, operationalized, and quantitatively investigated. Results were used to run an evidence-based Delphi panel with 16 experts on hippocampus, asked to converge on a consensual protocol. Panelists converged on a most inclusive definition of hippocampus, including (besides the whole head, body and tail) all vestigial tissue and fimbria.

Delphi Panel

Initial set of questions → Panel answers → Answers are summarized and anonymized → Disagreement issues are extracted → Disagreement issues are submitted to the panel

Harmonized Protocol

1 - Hippocampus
2 - Amygdala
3 - Temporal Horn
4 - Entorhinal Cortex
5 - Parahippocampal White Matter
6 - Vertical Digitation
7 - Choroid Plexus
8 - Quadrigeminal Cistern
9 - Meninges/Tentorium Cerebelli
10 - Pulvinar
11 - Fornix
12 - Isthmus
13 - Corpus Callosum
14 - Retrosplenial Cortex

Based on this definition, the HP has been written, and benchmark images (40 hippocampi balanced for diagnosis, atrophy and magnet field strength) segmented by 5 expert tracers from different centers. Inter-rater agreement among the 5 tracers was over 0.94 (absolute method, 5 level ANOVA) for ICC, and > 0.73 for similarity (~Dice) coefficient among all 5 tracers.
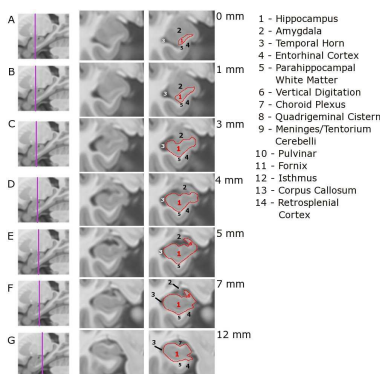
Benchmark Images
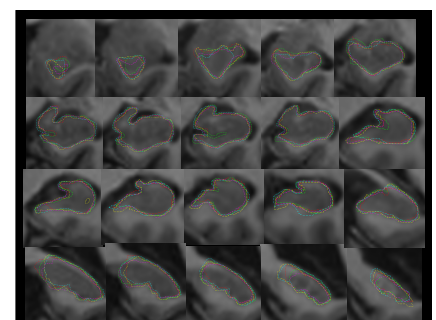
Qualification & Validation

Benchmark images have been uploaded in a web-based Certification Platform, where tracers from participating centers are qualifying as HP tracers. The platform provides visual and statistical feedback. The HP will be validated versus the most frequently used "local protocols", and with neuropathological data. Updated information on this ongoing step is available at:

www.hippocampal-protocol.net

Naive Tracers

C. Bauer, M. Blair, C. Boutet, E. Burton, E. Cavedo, A. Christensen, KS. Frederiksen, M. Grothe, M. Lanfredi, O. Martinez, M. Nishikawa, S. Pietrantonio, M. Portegies, G. Preboske, M. Pronk, T. Stoub, T. Swihart, C. Ward, L. Yawu