

Harmonization of protocols for manual tracing of the hippocampus

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GBF: meeting introduction and summary.

Rationale for this EADC-ADNI joint effort: necessity to provide standardized measures of hippocampal volumetry in clinical and experimental settings. Different clinical trials do use hippo volumetry as an outcome, but results can not be straightforward compared.

Involved partners in the project.

SLIDES ARE AVAILABLE AT:

http://centroalzheimer.it/public/MB/SOPs/AAN/01_SOPsAAN_intro.ppt

CDC comments that the Framingham study is not mentioned, and that it collected a very rich archive of hippocampi.

CRJ comments that this effort is necessary, not only *per se* but within the wider standardization of the diagnosis including the other parameters (es CSF). He underlines possible commercial interest by pharma industry.

MB: methods

Description of the steps of the whole project, and of the specific steps carried out so far.

Operationalization procedure carried out to turn the differences among tracing protocols into a limited number of well defined and measurable units, that can undergo quantitative investigation. Decisions about which features should be included and which excluded in the harmonized protocol will be helped by the quantitative evidence gathered in this phase.

Criteria for protocols selection. Features extraction: landmarks for most anterior and most posterior slice, and for superior, inferior, lateral and medial borders at the level of head, body and tail. Correspondent prototypical tracings carried out on a control and an AD ADNI subjects, representing each protocol. Web-meetings with the corresponding Authors, carried out to correct the tracing and obtain their final certification by the author for each protocol. Tabulation of all features by all protocols. Language harmonization. Reduction of redundancy. *Differences extraction*.

The extracted differences are thus operationalized into few and measurable *tracing units*.

Measurements: contribution of each tracing unit to total hippo volume, to re-test variability, to the differences between AD and ctrl. Possible ways to use this info in taking decisions for the definition of a harmonized protocol. Need for validation and implementation of a harmonized protocol as last stage of the project.

SLIDES ARE AVAILABLE AT:

http://centroalzheimer.it/public/MB/SOPs/AAN/02_SOPsAAN_methods.ppt

MB: preliminary results

Tables with landmark extraction for each protocol and the prototypical tracings, both corrected with the corresponding authors, are available at: <http://www.hippocampal-protocol.net> . At this link, the survey table of protocols features and of the differences among protocols are also available.

Extracted differences consist in image orientation, most posterior slice, superior boundary, separation from parahippo ctx in the hippo body, (most anterior slice, no more relevant with 3D navigation).

Operationalized tracing units: minimum hippo body (common to all protocols), hippo WM (alveus/fimbria, can only be included or excluded); Tail (4 different criteria), “subiculum” (rough overlapping with histology) (5 different criteria for separating hippo from parahippo ctx). These tracing units have been modelled in 3D and measured in the two exemplar subjects. Measurements are ongoing (samples of AD and ct). 3D models give an idea of the reconstructed shape of the hippocampus based on the different protocols, or based on maximally inclusive tracing criteria.

Conclusions:

In this stage the differences among tracing protocols have been operationalized, and preliminary results have been obtained on their impact on total hippocampal volume and on their contribution to the AD atrophy detected in the hippocampus by manual tracing.

NEXT: these measures, taken so far on 1 control and 1 AD prototypical subjects, will be gathered from a *sample* of subjects, characterized by different degrees of hippocampal atrophy. Moreover, measures will be taken on the contribution of each tracing unit to the re-test variability of manual tracings.

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CDC proposes to trace our prototypical hippocampi with the method used in his lab (modified from Jack 1994) and see differences in 3D shape. Wish to share their p maps and resources.

Asks: What about longitudinal stability of tracing (same question from Jo Barnes participating in remoto)? MB: the final steps of the implementation of the harmonized protocol includes *periodical* certification of the tracers.

CRJ: request to have masks/templates, available online, that people may download and use on their own images (SD: purpose to do that). Commercial interest. Need to provide material for both 1.5 and 3 Tesla images.

Enrike Wolf: asks whether a standardized software has been considered

CDC asks free software

GBF: this will be considered in the next step.

Next presentations/meetings relating to this project will be at AIC/ICAD, July 2010.