Collaboration for a Systematic Comparison of Different Techniques to Measure Subfield Volumes: Announcement and First Results

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Background: The hippocampus consists of several histologically and functionally distinct subfields that are differently affected by neurodegenerative processes. Particularly in the early stages subfield-specific atrophy measurements often provide superior diagnostic information compared to global hippocampal atrophy measurements. Consequently several approaches to investigate subfield specific atrophy using in vivo MR imaging have been developed and have been successfully used in small populations. However a systematic performance comparison in a common, large, and well defined data set with different degrees of hippocampal atrophy has yet to be done. The overall goal of this study is therefore to compare the performance of six representative manual and automated T1 and T2 based subfield labeling techniques in a sub-set of the ADNI2 population with mild hippocampal atrophy (MCI, eMCI, amyloid-pos and amyloid-neg controls).

Methods: The project has two phases: 1. Preparation: High resolution hippocampal T2 sequence harmonization and implementation at 20 3T Siemens ADNI2 sites. 2. Comparison of the performance of the following approaches: a. T1-based Freesurfer+Large-Diffeomorphic Metric Mapping in combination with shape analysis (NW shape subfields,1). b. T1-based deformation-based morphometry using a high resolution, high field ex vivo reference atlas (UPenn Def subfields, 2). c. T2-based Model based subfield segmentation using Bayesian Inference (MGH subfields3). d. T2-based automated multi-atlas segmentation combined with similarity-weighted voting (UPenn ASHS subfields 4). e. Manual subfield parcellation (CIND subfields, 5). e. Routines for total hippocampal volume and hippocampal subfield volumes as implemented in the Freesurfer 5.1. release (FS hippo, subfields) . (cf Figure 1 for labeling schemes)

Results: The first phase of the project has been completed and a sequence with the following parameters has been implemented: TR/TE 8020/50 ms 0.4x0.4x2.0 mm resolution, min 24 slices, acquisition time: 8.1 min. Project-specific data acquisition started late in December 2012 . As of the end of June 2013, 204 high resolution data sets have been acquired and undergone quality control. Of those 204, 30 cases (15 cognitively intact controls and 15 eMCI) cases with T2 high resolution hippocampal image and whole brain T1 image were selected and were processed with all methods. Linear regression analyses with subfield/hippocampus as dependent and group (controls, eMCI), age and intracranial volume were used to test for group effects and to determine power and minimal sample sizes for each method. The subfield with the highest power and smallest sample size are listed in Table 1

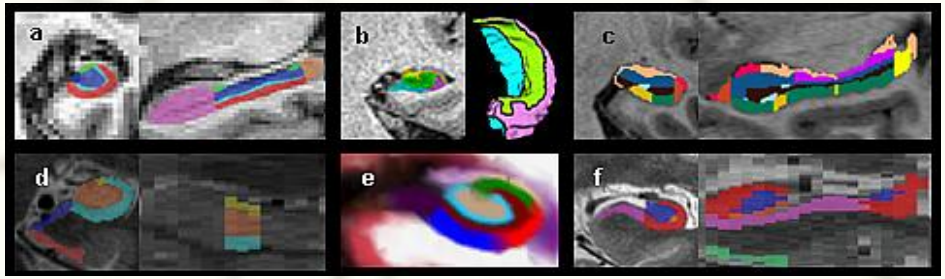

Figure 1. a. Parcellation UPenn Deformattion subfields. b. Parcellation NW shape subfields. .c Freesurfer 5.1. subfields. d. CIND manual subfields. e. MGH subfields. f. U Penn ASHS subfields.

Method	CIND	MGH	UPenn ASHS	UPenn Def	NW Shape	FS Hippo	FS subfield
	man	auto	auto	auto	auto	auto	auto
Image	hr T2	hr T2	hr T2	wb T1	wb T1	wb T1	wb T1
Subfield	CA1	Fimbria	CA1-3	CA2-3	CA1	Hippo	Fimbria
Power	**0.945**	**0.616**	**0.987**	0.22	0.258	0.27	0.418
Sample Size	**11**	**23**	**10**	76	62	60	32

Table 1. Bold, significant effect for group, man, manual parcellation; auto, automated parcellation

Conclusions:

The overall goal of this project is to highlight the particular strengths and limitations of the different approaches and so to provide guidance for the selection of the appropriate approach for different research questions. The findings in this small pilot sample seem to indicate that methods using a dedicated high resolution T2 hippocampal image are more sensitive to the milder hippocampal volume losses in eMCI than methods using whole brain T1 images. T1 based methods however have the advantage that that they use a sequence that is routinely acquired in clinical setting and that they are less sensitive to motion than the high resolution T2 which might give them an advantage in more cognitively impaired subjects. The findings in this small data set will help to further refine the automated techniques which will then be applied to a representative sample of the ADNI data set that encompasses the whole range of hippocampal atrophy seen in AD.

All high resolution images acquired for this project are available to the research community for download on the ADNI website.

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1. Hippocampus 2009:19:541-548,2. Neuroimage 2009;44:385-398, 3. Hippocampus 2009;19:1658-1661, 4. Neuroimage 2010;53:1208-1224, 5. Neurobiol Aging 2007;28:719-726