Fast and Robust Quantification of Parahippocampal Atrophy via Temporal Horn Index

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Abstract. We propose a fast and robust method to obtain the temporal horn index (THI) as an indirect but sensitive regional measure for hippocampal and parahippocampal atrophy, based on MRI. The THI is defined as the temporal horn volume to lateral ventricular volume ratio. The proposed method relies on efficient 3D interactive segmentation and a fully automated histogram analysis. It provides consistent THI measurements within a few minutes even for extremely small temporal horns of less than 0.1 ml. The THI obtained by volumetric MRI analysis is sensitive to hippocampal and parahippocampal atrophy and is expected to provide an early marker for pathologic changes associated with Alzheimer's and Parkinson's disease.

1 Introduction

Diverse indications exist for the quantification of hippocampal volumes. One of the most important is to provide a quantitative marker in monitoring of pathologic changes associated with dementia in Alzheimer's (AD) and also Parkinson's diseases [1,2]. According to SILBERT et al., cerebral ventricular and hippocampal

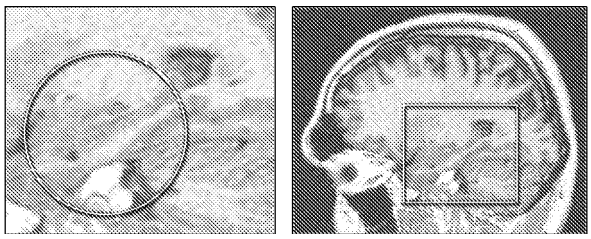
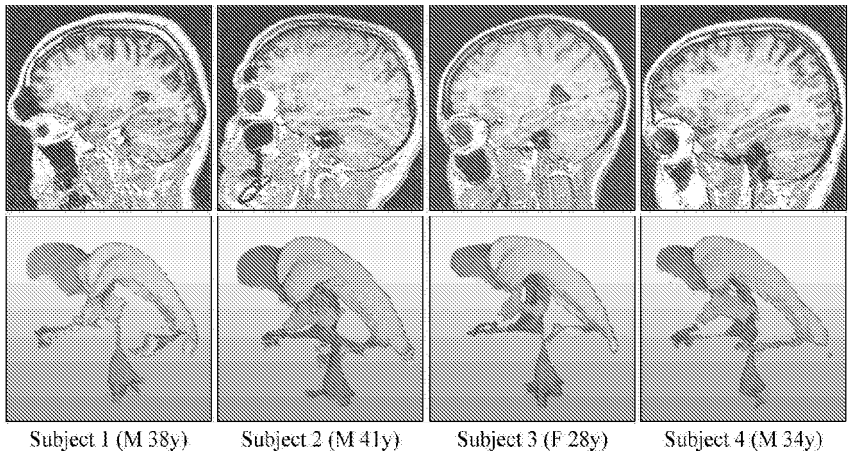


Fig. 1. Illustration of the hippocampus segmentation problem. To the left, a close-up of the MR image to the right is shown (box). In many cases, the hippocampal borders are not well defined (circle).

Fig. 2. Material used for the evaluation of the proposed method. T1 weighted MR images from four volunteers (top); five acquisitions each. Using the ILab platform (MeVis, Bremen), the volumes of the cerebral ventricles were measured (bottom).



volumes are sensitive to the accumulation of cortical neurofibrillary tangles and senile plaque, which are a key to judging the neuropathology of AD [2].

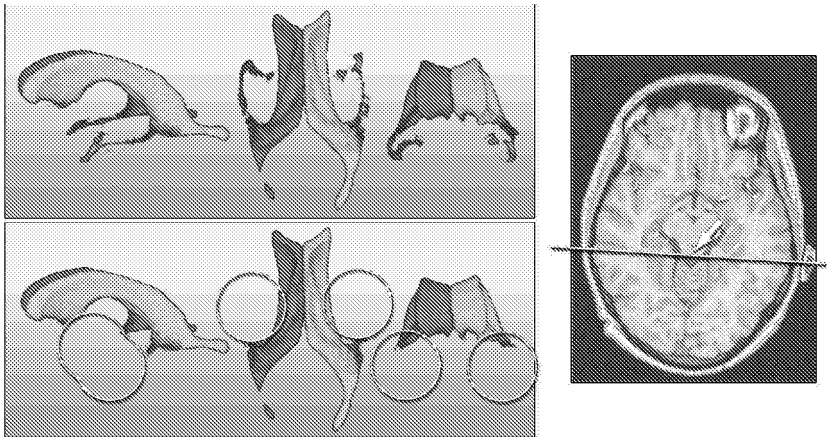
Currently, no fast and sensitive method for direct hippocampus volumetry is available for clinical use. To our knowledge, current segmentation methods are either time consuming or unreliable. Direct hippocampus segmentation is a challenging task, since parts of its border are poorly differentiated in clinical images ([3], cf. Fig. 1). Purely manual processing with total interaction times of about one hour per dataset is frequent. Even highly advanced segmentation methods based on deformable shape models and atlases are reported to require at least 10–30 minutes per dataset for manual landmark placement [3,4] with a performance comparable to manual segmentation. In addition, systematic volumetric errors are often related to partial volume effects, which are crucial for any thin and elongated object.

Since the temporal horns of the cerebral ventricles are adjacent to the hippocampal formation, we propose to use the temporal horn volume (THV) as an indirect and sensitive regional measure for hippocampal and parahippocampal atrophy. Furthermore, we propose to consider THI in order to obtain a specific and normalized measure. Moreover, special emphasis was placed on both reproducibility and speed of the proposed image analysis method.

2 Methods and Material

In four healthy volunteers (age 28–41 y, cf. Fig. 2), 20 thin-slice T1 weighted MRI datasets (Siemens Magnetom Quantum 1.5 T, MPRAGE, 256×256 matrix, 1.0 mm isotropic voxel size, 160 contiguous sagittal sections, acquisition

Fig. 3. Definition of the THV by subtraction of the LVV with (top, images from Subject 3) and without temporal horns (bottom, circles); the latter is denominated LVV*. To the right, a coronal plane (straight line) defined by the posterior tip of the inferior colliculus (arrow) is shown on an axial section.



time approx. 9 min) were acquired, five acquisitions on the same day each. The volunteers were repositioned in the scanner between acquisitions.

Segmentation of lateral ventricles including frontal horn, trigone, posterior horn, and temporal horn was performed applying an Interactive Watershed Transform (IWT) to the original images. The IWT, which has been described previously [5], fully works in 3D; only a few landmarks (approximately two to six) suffice to segment both lateral ventricles. This segmentation was performed twice for every dataset, once with and once without the temporal horns, resulting in two volumes for each side, which are denominated LVV (lateral ventricular volume) and LVV*, respectively. The coronal plane defined by the posterior tip of the inferior colliculus and perpendicular to the AC-PC line was used as posterior boundary of the temporal horn (cf. Fig. 3 right).

A fully automated analysis of over-inclusive regional histograms, as described in [6], was applied to both segmentations (each containing two objects, left and right lateral ventricle) in order to robustly estimate LVV(L/R) and LVV*(L/R). The analysis is based on a trimodal Gaussian model (cerebro-spinal fluid, white, and gray matter) that explicitly includes partial volume terms, so-called Mixed Gaussians. Assuming equally distributed partial volume effects, Mixed Gaussians take the form of plateau curves. The model is fitted to the histogram data by minimizing squared errors using a LEVENBERG-MARQUARDT method.

3 Results

Individual left and right LVV and THV were successfully obtained in all datasets using the landmark-driven IWT within less than four minutes. No preprocessing

Table 1. Lateral ventricular volumes for five independent acquisitions, four volunteers, two sides (L/R), with (LVV) and without temporal horns (LVV*), resulting in $5 \times 8 \times 2 = 80$ measurements, given in ml. To assess inter-examination reproducibility, mean values are given besides standard deviations (SD in ml) and variation coefficients (VC = SD/Mean, in %).

		V_1	V_2	V_3	V_4	V_5	Mean	SD	VC
Subject 1	LVV(L)	13.66	13.44	13.79	14.07	13.87	13.77	± 0.23	(1.7 %)
	LVV*(L)	13.17	12.89	13.38	13.36	13.30	13.22	± 0.20	(1.5 %)
	LVV(R)	9.34	9.33	8.88	9.45	8.75	9.15	± 0.31	(3.4 %)
	LVV*(R)	8.94	8.92	8.52	8.95	8.44	8.75	± 0.25	(2.9 %)
Subject 2	LVV(L)	14.39	14.32	14.01	14.84	14.30	14.37	± 0.29	(2.1 %)
	LVV*(L)	14.22	14.12	13.83	14.59	14.07	14.16	± 0.28	(2.0 %)
	LVV(R)	17.93	17.70	17.70	17.82	17.67	17.76	± 0.11	(0.6 %)
	LVV*(R)	17.55	17.42	17.41	17.46	17.28	17.42	± 0.10	(0.6 %)
Subject 3	LVV(L)	13.93	14.02	14.16	14.06	14.42	14.11	± 0.19	(1.3 %)
	LVV*(L)	13.86	13.85	14.05	13.97	14.39	14.02	± 0.22	(1.6 %)
	LVV(R)	11.82	11.86	11.88	11.96	11.93	11.89	± 0.06	(0.5 %)
	LVV*(R)	11.59	11.62	11.75	11.71	11.67	11.67	± 0.07	(0.6 %)
Subject 4	LVV(L)	11.36	11.84	11.82	11.39	11.47	11.58	± 0.24	(2.0 %)
	LVV*(L)	11.18	11.45	11.45	11.10	11.28	11.29	± 0.16	(1.4 %)
	LVV(R)	10.25	10.45	10.97	10.69	10.35	10.54	± 0.29	(2.8 %)
	LVV*(R)	9.88	10.06	10.37	10.09	9.95	10.07	± 0.19	(1.9 %)

of the image data was required, such as denoising or intensity homogenization. From the histograms, object volumes could be quantified highly reproducible for all twenty image acquisitions (cf. Table 1). The temporal horn index is defined by THI = THV / LVV, while temporal horn volumes are calculated by subtraction THV = LVV– LVV*.

Grand means were recorded for LVV: 12.90 ml (range min–max: 9.15–17.76 ml), THV: 0.32 ml (0.09–0.55 ml), and THI: 2.63 % (0.67–4.46 %). In order to assess inter-examination reproducibility for these three measures, mean standard deviations were evaluated for LVV: 0.22 ml (range min–max: 0.06–0.31 ml), THV: 0.07 ml (0.03–0.12 ml), and THI: 0.56 % (0.21–0.99 %); n=5×8.

4 Discussion and Conclusion

The inter-examination variation coefficients for the lateral ventricular volumes are around two percent throughout (cf. Table 1), which is excellent, taking into account the small object volumes as well as their elongated and complex shapes. Measuring THV by subtraction rather than directly has a twofold motivation. First, note that reproducibility is better for THV than for LVV, reflecting the fact that variations of LVV and LVV* are positively correlated. Second, regional histograms of solely the tiny temporal horns are extremely sparse. In comparison, the histograms for the two larger objects yield a higher robustness and reproducibility. From the user perspective, however, it is equivalent whether to

directly segment the temporal horns or to exclude them from a previous lateral ventricle segmentation.

As shown in a previous study [6], cerebral ventricular segmentation and volumetry based on the IWT and histogram analysis are largely independent of the landmark positions, such that both intra and inter-observer variations are very small. Therefore, we concentrated on inter-examination characteristics, which are vital for longitudinal and follow-up studies. A mean THV standard deviation of only 0.07 ml, corresponding to a mean THI standard deviation of 0.56 %, provides a solid basis for reliably quantifying volumetric changes in the parahippocampal region. The mean THV in our four volunteers was small with only 0.32 ml. Yet, increased THV is observed in patients with mild or severe hippocampal atrophy. Given that the absolute precision of our method remains constant, which we expect for the subtraction method, the relative precision for patients will be superior in comparison to healthy volunteers.

In a study comprising 192 subjects with probable AD, who underwent two MRI examinations with an interval of one year, correlations between image based volumetric change and change in behavioral and cognitive measures were found to be even greater for the temporal horn than for the hippocampus [1]. This further supports the suitability of THV/THI as a reliable biomarker in AD. JACK et al. demonstrated the technical feasibility of using "structural MRI measures as a surrogate endpoint of disease progression in therapeutic trials", resulting in "markedly lower estimated sample size requirements for clinical trials [1]."Our method is appropriate to be used in trials, which benefit from quantification of hippocampal or parahippocampal atrophy, and has the potential to replace direct hippocampus volumetry in many cases.

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