Quantitative brain anatomy in a sample (n=93) of healthy elderly people

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Introduction

Modern MR scanners together with advanced brain image segmentation techniques, such as FreeSurfer [1-3], enable high quality 3D acquisitions followed by quantitative measures of the cortical sheet and estimation of subcortical volumes (Fig. 1a-c). There are an increasing number of applications and clinical problems that benefit from these technologies, such as developmental disorders, neuropsychiatric and neurodegenerative disorders, and assessment of mild cognitive impairment (MCI) and possible Alzheimer's disease. The aim of the present study was to investigate brain morphometric measures in normal aging, including hemispheric asymmetries [4], and relationships to age and gender, in a sample of healthy elderly people with normal cognitive function.

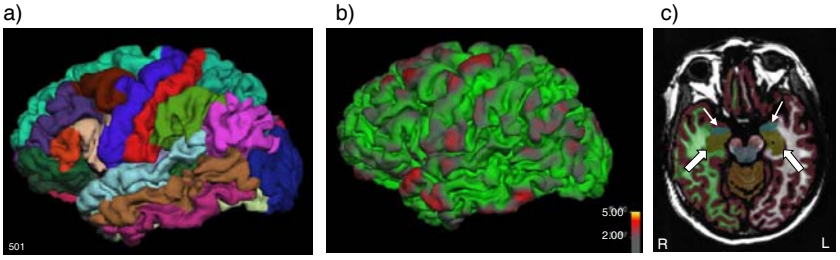

Fig 1. Cortical surface reconstruction and subcortical segmentation from dual volume T1-w MRI using FreeSurfer. (a) Cortical parcellation, (b) Cortical thickness map; (c) Color-coded subcortical segmentation depicting left and right *hippocampus* (fat arrows) and *amygdala* (thin arrows). [Data from subject 501.]

Materials and methods

The participants were part of a study of cognitive aging, brain function and genetic markers, where 330 subjects (180 in Bergen and 150 in Oslo) from 45 to 80 years were assessed by a set of neuropsychological tests. In Bergen, 109 of the participants were also examined on a 1.5 GE Signa Echospeed scanner with DTI and dual-volume SAG T1 3D FSPGR IR prepared acquisitions (TR/TE/TI/FA = 9.5/2.2/450/7°) at voxel-size 0.94x0.94x1.4 mm^3 using a standard 8-channel head coil. In the present study we included volumetric data from 93 subjects (27 males, 66 females) that were analyzed with FreeSurfer v.3.0x [1-3]. Mean age was 57.4 (SD 7.4; range 46-77), mean years of education was 14 (SD 3.1), and mean WASI IQ was 114 (SD 12.1). All except two subjects were APOE genotyped: 58 were APOE e4 non-carriers, 29 (4) were heterozygotic (homozygotic) for the APOE e4 allele. The participants were screened for previous and present neurological and psychiatric diseases, and history of substance abuse in an interview before invitation to the examination. All subjects gave their informed consent to participate, and the study was approved by the Regional Committee for Medical Research Ethics of Southern Norway.

Results

Table 1 shows a subset of the age and gender dependent morphometric results. For each of the three age intervals, and for males and females separately, the morphometric mean values are given for left hemisphere (ICV-normalized in brackets), followed by the ratio between left and right side, and the p-values from a two-sample t-test related to the following hypotheses: (i) no difference in sample means between left and right hemisphere across males and females, i.e. $p_{L/R}$ in the M-row, and (ii) no gender differences in total (left+right) mean values, i.e. $p_{M/F}$ in the F-row, where we in (ii) have normalized by total intracranial volume (ICV).

TABLE 1

Brain structure		46-56 yrs (9 M, 23 F)			56-60 yrs (9 M, 18 F)			61-77 yrs (9 M, 25 F)		
		Left (nor)	Left/Right	$p_{L/R}$ | $p_{M/F}$	Left (nor)	Left/Right	$p_{L/R}$ | $p_{M/F}$	Left (nor)	Left/Right	$p_{L/R}$ | $p_{M/F}$
Gray matter [cm^3]	M	209.5 (0.095)	0.996	0.9579	205.0 (0.101)	1.011	0.9585	199.2 (0.101)	0.987	0.6553
	F	188.3 (0.106)	1.000	0.0938	179.2 (0.104)	0.997	0.5773	186.2 (0.113)	0.994	0.2568
White matter [cm^3]	M	611.2 (0.277)	1.000	1.0000	582.5 (0.285)	1.000	1.0000	551.4 (0.276)	1.000	1.0000
	F	503.1 (0.280)	1.000	0.7192	484.8 (0.278)	1.000	0.6053	477.8 (0.285)	1.000	0.5085
Lateral ventricles [cm^3]	M	13.6 (0.006)	1.125	0.4696	17.4 (0.008)	1.180	0.2878	21.2 (0.011)	1.095	0.7874
	F	9.3 (0.005)	1.063	0.2884	10.6 (0.006)	1.160	0.1183	16.5 (0.010)	1.002	0.7063
Mean cortical thickness [mm]	M	1.84 (SD = .07)	1.006	0.6361	1.86 (SD = .07)	1.012	0.2989	1.87 (SD = .09)	1.005	0.9870
	F	1.86 (SD = .10)	1.006	0.6320	1.88 (SD = .08)	1.013	0.5710	1.90 (SD = .11)	0.999	0.2954
Thalamus [mm^3]	M	6708 (0.0030)	1.003	0.9553	6563 (0.0032)	1.063	0.5289	5904 (0.0030)	0.964	0.9837
	F	6071 (0.0034)	1.006	0.1034	5822 (0.0034)	1.006	0.1308	5433 (0.0033)	1.024	0.5920
Hippocampus [mm^3]	M	3835 (0.0017)	0.951	0.0165*	3477 (0.0017)	0.907	0.0157*	3371 (0.0017)	0.944	0.1704
	F	3612 (0.0020)	0.937	0.0052*	3467 (0.0020)	0.937	0.0011*	3333 (0.0020)	0.956	0.0877
Amygdala [mm^3]	M	1426 (0.0006)	0.935	0.0571	1291 (0.0006)	0.887	0.0062*	1371 (0.0007)	0.941	0.1717
	F	1339 (0.0007)	0.951	0.0229*	1215 (0.0007)	0.884	0.1930	1234 (0.0007)	0.944	0.5224

Conclusion & Discussion

There was no age-dependent variation in ICV. However, mean ICV in females was smaller than in males (1755 cm^3 vs 2151 cm^3). We observed little change in gray matter along the age groups. A small, but significant reduction (10%) in total white matter from age group 1 to 3 was found for males (p=0.035) . The 5% WM reduction in females was not significant (p=0.111). The volume increase of the lateral ventricles from age group 1 to 3 was 63% in males (p=0.0062) and 81% in females (p<0.0001). Mean cortical thickness showed little variation across age, gender, or hemispheres. A significant 10% decrease of the thalamus volume was found between age group 1 and 3 in both men and women. For subjects less than 61 years the ICV-normalized hippocampus and amygdala volumes were both significantly smaller in woman than in men. Moreover, hippocampus and amygdala in the right hemisphere were significantly larger than in the left hemisphere ($p < 0.02$). According to the large meta-analytic study in [4], it seems that FreeSurfer overestimates the hippocampus (HC) and underestimates the neighbouring amygdala (AMYG), i.e. overall mean HC_{left} = 3494 (2779 in [4]) , HC_{right} = 3717 (3060), $AMYG_{left}$ = 1294 (1883), $AMYG_{right}$ = 1406 (1926) . A next step will be to investigate brain-behaviour relationships in the sample using results from the extensive neuropsychological testing, and also study the linkage between brain morphometry and APOE-, BDNF-, and CHRNA4 genotypes (cf. [5]).

References

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