Subcortical Nuclei Shrinkage in Mild Cognitive Impairment: a Volumetric Study

Xiaohua Chen[1], Wei Wen[1,2], Julian Trollor[1], Faisal Beg[4], Pradeep Kumar Reddy[4], Ali Khan[4], Nicole Kochan[1,2], Henry Brodaty[1,3], Perminder Sachdev[1,2]

School of Psychiatry[1], UNSW; Neuropsychiatric Institute[2], POWH; Aged Care Psychiatry[3], POWH, Sydney, Australia; Medical Image Analysis Laboratory[4], School of Engineering Science, Simon Fraser University, Canada

Introduction

Brain atrophy is part of the aging process and correlated with age-related cognitive impairment.

Subcortical nuclei have been reported to undergo degenerative changes with aging. However, the degree of change in these nuclei has not been quantified and their contribution is not known.

Mild cognitive impairment (MCI), considered to be a pre-dementia stage, can be predicted by several volumetric measurements, e.g. volumes of hippocampus[1].

We wished to examine whether volumetric data of subcortical nuclei make a contribution to MCI diagnosis.

Aim

The current study aimed to answer two questions:

1) Are subcortical nuclei shrinking with ageing?
2) Is there differential ageing in different subcortical nuclei?
3) Do MCI and normal participants differ in volumes of subcortical nuclei?
4) Do amnestic and non-amnestic MCI differ in the volumes of subcortical nuclei?

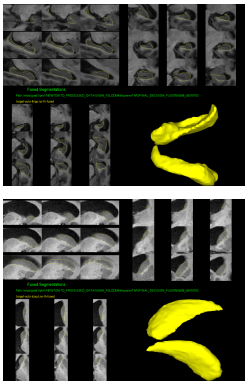
Subjects and Method

Subjects

▪Four hundred and fourteen community-dwelling individuals aged 70-90 were recruited randomly using electoral roll from two electorates in East Sydney, Australia.

▪Structural MRI images, comprehensive neuropsychiatric assessments and cognitive batteries were performed and mild cognitive impairment was defined based on international consensus criteria [2].

▪Template-based segmentation was applied using software (Free surfer) and Large deformation diffeomorphism and momentum (LDDMM) and these segments were fused using six cohort-specific templates [3]. Volumes of subcortical nuclei were obtained, including hippocampus, thalamus, caudate and putamen. Volumes of lateral ventricles were also calculated.



▪Volumes of subcortical nuclei were correlated to age in the whole sample to evaluate differential aging in subcortical grey matter.

▪A general linear model was applied to compare volumes of subcortical nuclei between MCI and normal participants, controlled for the effects of age, sex and intracranial volume.

▪Volumes of subcortical nuclei with significant difference between MCI and normal group were also compared in their associations with age.

▪Volumetric comparisons were also performed between amnestic and non-amnestic MCI participants.

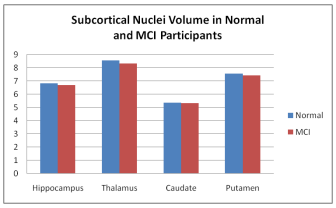
Results

Table 1 Demographic characteristics and volumetric data of the study sample

Variables	NC (N=230)	MCI (N=165)	Df	t/χ^2	*P* Value
Age (yrs)	77.86 (4.59)	78.70 (4.70)	393	1.769	0.078
Education (years)	11.78 (3.58)	11.78 (3.66)	393	-0.007	0.995
Sex (male, %)	96 (41.7)	80 (48.5)	1	1.770	0.183
ICV, litres	1.48 (1.83)	1.49 (1.82)	393	0.85	0.396
TLVV, mL	35.48 (15.05)	41.06 (18.91)	393	3.265	0.001
Left Hippocampus, mL	3.45 (0.39)	3.41 (0.46)	393	0.790	0.430
Right Hippocampus, mL	3.37 (0.38)	3.29 (0.48)	393	1.779	0.076
Hippocampus, mL	6.82 (0.74)	6.71 (0.88)	393	-1.356	0.176
Left Thalamus, mL	4.13 (0.43)	4.04 (0.43)	393	2.015	0.045
Right Thalamus, mL	4.44 (0.49)	4.29 (0.48)	393	3.009	0.003
Thalamus, mL	8.57 (0.89)	8.33 (0.86)	393	-2.650	0.008
Left Caudate, mL	2.61 (0.43)	2.59 (0.51)	393	0.422	0.673
Right Caudate, mL	2.74 (0.52)	2.76 (0.51)	393	-0.373	0.709
Caudate, mL	5.35 (0.92)	5.35 (0.98)	393	-0.005	0.996
Left Putamen, mL	3.87 (0.60)	3.79 (0.62)	393	1.333	0.183
Right Putamen, mL	3.68 (0.68)	3.65 (0.63)	393	0.431	0.667
Putamen, mL	7.55 (1.22)	7.44 (1.17)	393	-0.912	0.363

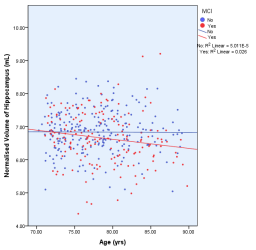
ICV, Intracranial volume; TLVV, Total lateral ventricle volume;
Note p-values are for t-tests of continuous variables and chi-square tests of discrete variables between men and women.

Negative correlation were found between age and volumes of total ventricle (β=0.365, p<0.001), total hippocampus (β=-0.242, p<0.001) and total thalamus (β=-0.214, p<0.001), corrected for intracranial volumes in the whole sample.



Participants with MCI had smaller hippocampus (F=4.726, p=0.030) and thalamus (F=9.452, p=0.002) compared to normal participants, corrected for age, sex and intracranial volume.

Age trajectories of hippocampus volume between normal and MCI participants



Age trajectories of hippocampus volume (Z=1.129, p>0.05) and thalamus volume (Z=0.581, p>0.05) did not differ between normal and MCI participants.

General linear model of four bilateral structure volumes with laterality as within-subjects factors and age, sex, and diagnosis of MCI as between-subjects factors, intracranial volumes as covariate, showed no interaction effect of laterality and age, laterality and sex, or laterality and MCI diagnosis.

There is no significant difference between amnestic and non-amnestic MCI in the volumes of hippocampus or thalamus.

Conclusion

The study suggested differential aging in subcortical nuclei where negative age trajectories were predominant in hippocampus and thalamus but not in caudate or putamen.

Smaller hippocampus and thalamus were found in participants with mild cognitive impairment compared with normal participants, although these two groups did not differ in the association between age and volumes of hippocampus or thalamus.

Amnestic MCI was not associated with significantly different volumes of hippocampus, suggesting the heterogeneity in the categories of MCI, which may explain their various outcomes.

Further longitudinal study to investigate volumetric change of MCI subjects who progressed to AD will benefit the understanding of the role of subcortical nuclei in aging and dementia.

References

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Acknowledgements

This research was supported by National Health and Medical Research Council (NHMRC Program Grant ID 350833, NHMRC Project Grant ID 510175) and Australian Research Council (ARC DP-0774213).

We wish to thank all the study participants and the Sydney Memory and Ageing Study team for their invaluable contribution.