

## Hippocampal subfield atrophies in converted and not-converted Mild Cognitive Impairments patients by a Markov random fields algorithm

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**Introduction:** Although measurement of total hippocampal volume is considered as an important hallmark of Alzheimer's disease (AD) [1], recent evidence demonstrated that atrophies of hippocampal subregions might be more sensitive in predicting this neurodegenerative disease [2]. The vast majority of neuroimaging papers investigating this topic are focused on the difference between AD and patients with mild cognitive impairment (MCI), not considering the impact of MCI patients who will or not convert in AD. For this reason, the aim of this study was to determine if measurements of hippocampal subfields provide advantages over total hippocampal volume for discriminating these groups

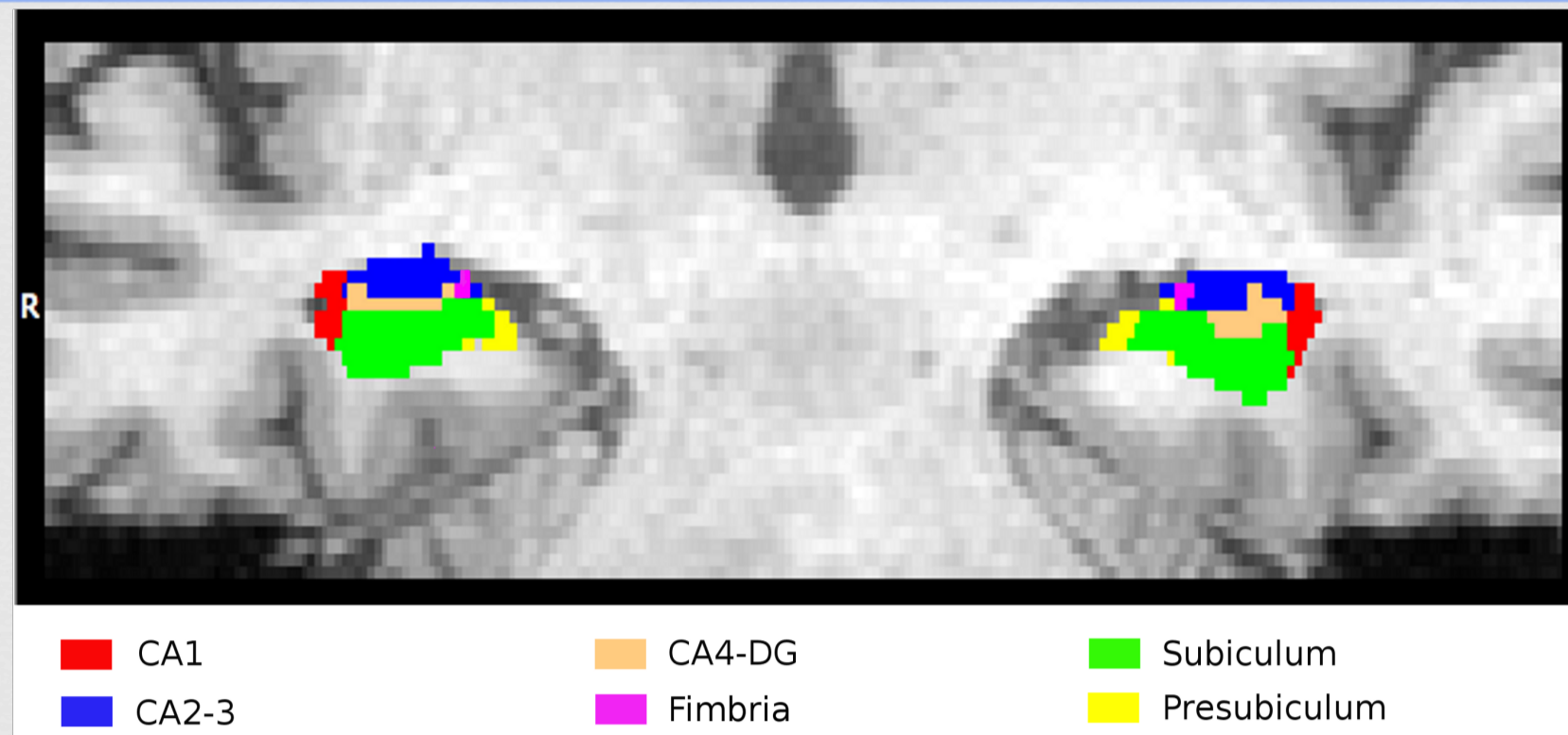


Figure 1: Example of hippocampal subfield segmentation obtained by Freesurfer.

### Material and Methods

Hippocampal subfields volumetry was extracted in 55 AD, 32 converted and 89 not-converted MCI (c/nc-MCI) and 47 healthy controls from ADNI database, using an atlas-based automatic algorithm embedded in the Freesurfer framework [3]. To evaluate the impact of hippocampal atrophy in discriminating the insurgence of AD-like phenotypes we used three classification methods: Support Vector Machine, Naive Bayesian Classifier and Neural Networks Classifier.

**Results:** Taking into account only the total hippocampal volume, all classification models reached a sensitivity of about 66% in discriminating between c-MCI and nc-MCI. Otherwise, classification analysis considering all segmenting subfields increased accuracy to diagnose c-MCI from 68% to 72%. Statistical comparisons among subfields suggested that subiculum and presubiculum are more informative than the other hippocampal subregions in discriminating between nc-MCI and c-MCI, with AUC values of 0.76 and 0.77 respectively.

	CTR	nc-MCI	c-MCI	AD	F/p level (ANOVA)	Post-hoc t-test (cMCI vs ncMCI)
N°	47	89	32	55		
Age	78.19±4.40	75.42±7.18	75.53±7.38	75.89±6.35	F=2.04/ p=0.109	p=0.938
Gender (n°, % male)	31; 65.96	58; 65.17	22; 59.46	35; 63.64	p=0.970	p=0.714
MMSE	28.96±1.14	27.20±1.71	26.81±1.96	19.11±5.73	F=68.68/ p<0.0001	p=0.290
Global CDR	0.09±0.22	0.50±0.00	0.50±0.00	1.09±0.69	F=103.07/ p<0.0001	p=0.999
GDSCALE	1.19±1.61	1.72±1.51	1.53±1.50	1.85±1.61	F=1.75/ p=0.16	p=0.548

Table 1: Clinical characteristics of subjects

A)

Mode	Accuracy	Sensitivity	Specificity
SVM	0.6612	0.6404	0.7188
NN	0.6694	0.6517	0.7188
NB	0.6529	0.6292	0.7188

B)

Mode	Accuracy	Sensitivity	Specificity
SVM	0.7107	0.6966	0.7500
NN	0.7273	0.6966	0.8125
NB	0.6860	0.6742	0.7188

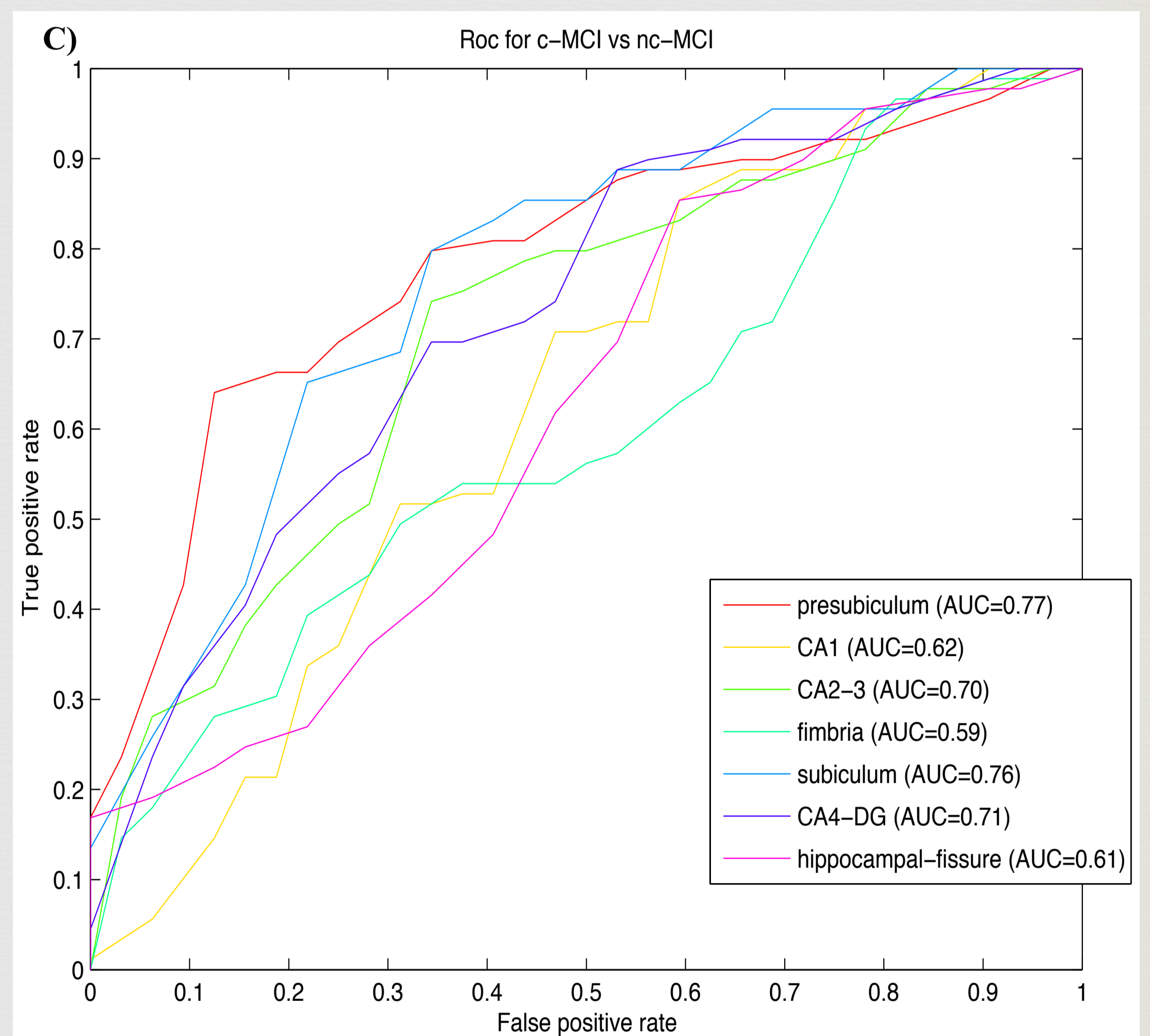


Figure 2: Comparison of performances of three classification methods (SVM, NBC and NNC) in discriminating between c-MCI and nc-MCI, obtained by using A) the whole Normalized Hippocampal Volume or B) the Normalized Hippocampal Subfield Volumes. C) ROC curve showing the individual discriminant power of each hippocampal subregion in classify the insurgence of AD-like phenotypes

### Discussion:

Our work is one of the first multivariate neuroimaging study which addresses the potential of hippocampal subfield volumetry in improving the diagnostic accuracy for distinguishing early AD from nc-MCI. The obtained accuracy improvement confirmed the hypothesis that microstructural changes in the hippocampal subregions may have a higher specificity, thus reinforcing a better identification of MCI-related neurodegenerative processes. In particular, among all hippocampal subfields, subiculum and presubiculum demonstrated the greatest discriminant power in distinguishing nc-MCI from c-MCI. This pattern of hippocampal subfield loss is in agreement with previous post-mortem and neuroimaging studies, highlighting the role of the subicular region in AD-related neurodegenerative processes.

### References:

- [1] Frisoni GB, Fox NC, Jack CR Jr, Scheltens P, Thompson PM. The clinical use of structural MRI in Alzheimer disease. *Nat Rev Neurol* 2010, 6(2):67-77
- [2] La Joie R, Perrotin A, de La Sayette V, Egret S, Doeuve L, Belliard S, et al. Hippocampal subfield volumetry in mild cognitive impairment, Alzheimer's disease and semantic dementia. *NeuroImage: clinical* 2013, 3: 155-162
- [3] Van Leemput K., Bakkour A., Benner T., Wiggins G., Wald L.L., Augustinack J. Automated segmentation of hippocampal subfields from ultra-high resolution in vivo MRI. *Hippocampus* 2009, 19:549-557