QyScore® MRI markers diagnostic accuracy in the clinical spectrum of Alzheimer's Disease

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INTRODUCTION
BACKGROUND

In Alzheimer's disease (AD) the spread of neurodegeneration, especially tau pathology and synapse loss detectable by quantitative magnetic resonance (MR) techniques, is the most important pathological substrate of clinical symptoms[1]

Diagnostic criteria for AD acknowledge the key role of imaging markers of medial temporal lobe structures, such as hippocampus and amygdala, for early diagnosis [2,3,4]

Non-invasive and automated MR brain imaging methods can support the quantitative characterization of AD, and its prodromal stages, increasing the objectivity in the disease assessment [5]

Objectives

To assess the diagnostic accuracy of **QyScore®** medial temporal lobe atrophy markers in distinguishing AD dementia and Mild Cognitive Impairment (MCI) from cognitively healthy controls (HC) individuals

To assess the consistency of their diagnostic accuracy between two large open access datasets: ADNI and OASIS

[1] DeTure MA et al., 2019, [2] Albert MS et al. 2011, [3] McKhann GM et al., 2011, [4] Dubois B et al., 2014, [5] Ledig C et al., 2018

MATERIALS & METHODS

Data description: ADNI (1, 2, GO, 3) and OASIS datasets

Total	HC	sMCI	pMCI	AD	p-value	p-value post-hoc comparisons					
N = 2012	N = 643	N=583	N=319	N=467		**HC vs sMCI**	**HC vs pMCI**	**HC vs AD**	**sMCI vs pMCI**	**sMCI vs AD**	**pMCI vs AD**
Age	74±5	72±7.8	74±6.9	74±7.8	**<.0001**	**<.0001**	0.999	0.387	**0.007**	**<.0001**	0.645
Sex F/M (% F)	344 / 299 (54%)	240 / 343 (41%)	127 / 192 (39%)	221 / 246 (47%)	**<.0001**	--	--	--	--	--	--
MMSE	29±1.1	27±1.7	27±1.7	23±2.7	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
FAQ	1±3.3	2±3.2	5±4.8	13±7.6	**<.0001**	**0.009**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
APOE ε4 carriers (n/%)	158 / 570 (27%)	230 / 550 (41%)	207 / 318 (65%)	295 / 456 (64%)	**<.0001**	--	--	--	--	--	--

Values are reported in mean ± standard deviation for continuous variables or frequencies (percentage) for categorical variables;
Abbreviations: HC = cognitively healthy controls; sMCI = stable Mild Cognitive Impairment; pMCI = progressor Mild Cognitive Impairment; AD = Alzheimer's Disease; F/M = Female/Male; MMSE = Mini-Mental Status Examination; FAQ = Functional Activities Questionnaire; APOE = ApolipoproteineE

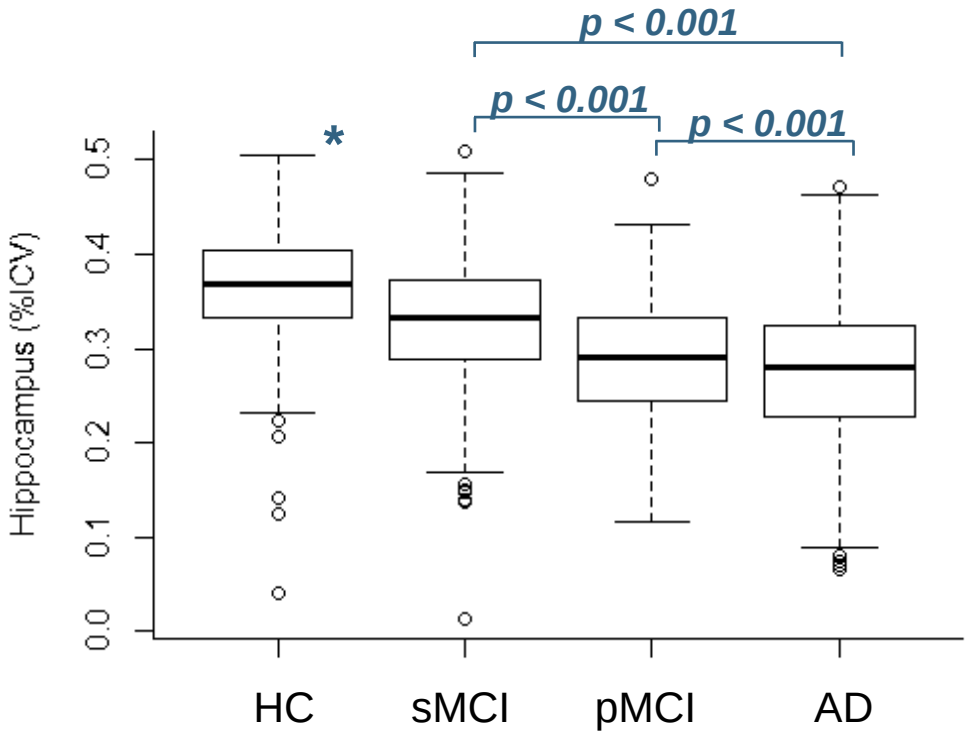
Segmentation methods

- Hippocampus and Amygdala volumes segmented by QyScore®
- Volumes normalized by intracranial volume (%ICV)

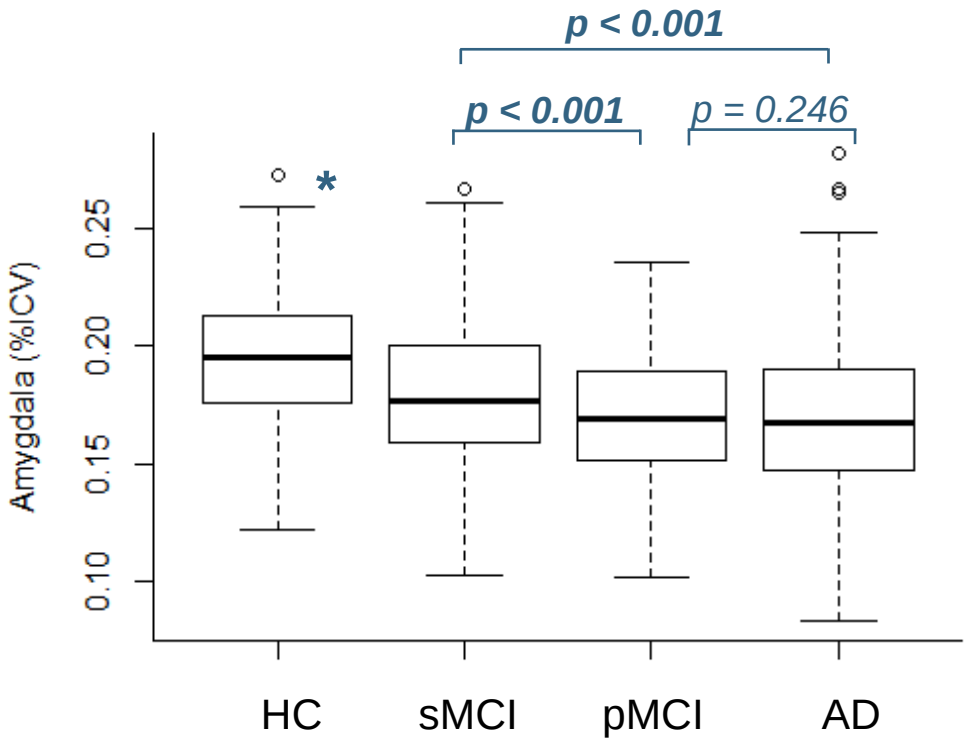
Statistical analysis

- Chi-Square test for categorical variables
- For sociodemographic and clinical variables: ANOVA with post hoc Tukey's test
- For imaging variables: ANCOVA (Age, Sex, Datasets as covariates) with post hoc Tukey's test
- Area under the curves (AUCs) of receiver operating characteristics (ROC) curves were calculated for volumetric measurements

RESULTS



* HC volumes significantly differed from all other groups $p < 0.001$



* HC volumes significantly differed from all other groups $p < 0.001$

Significant difference of hippocampal volumes among all groups

Amygdala volumes significantly differed among all groups, except between pMCI and AD

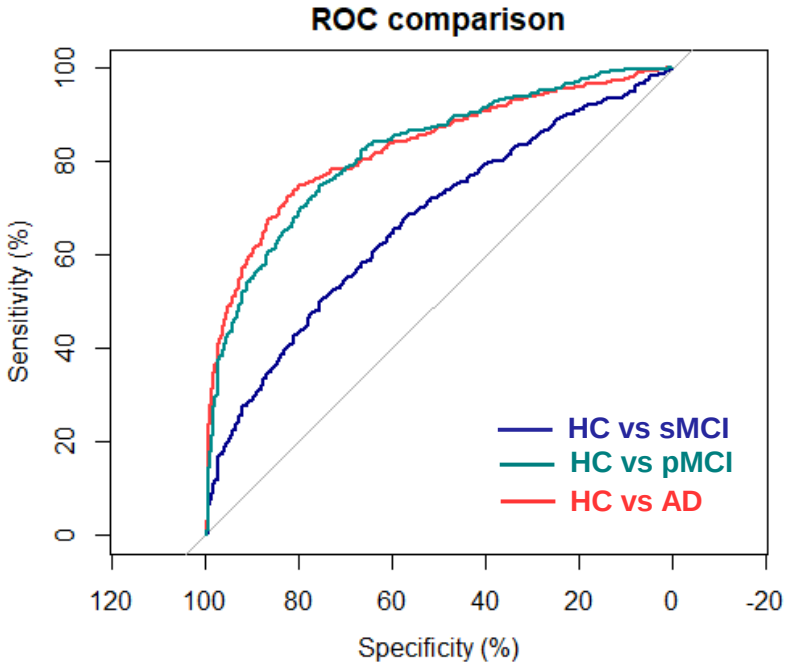
Abbreviations: HC = cognitively healthy controls; sMCI = stable Mild Cognitive Impairment; pMCI = progressor Mild Cognitive Impairment; AD = Alzheimer's Disease

RESULTS

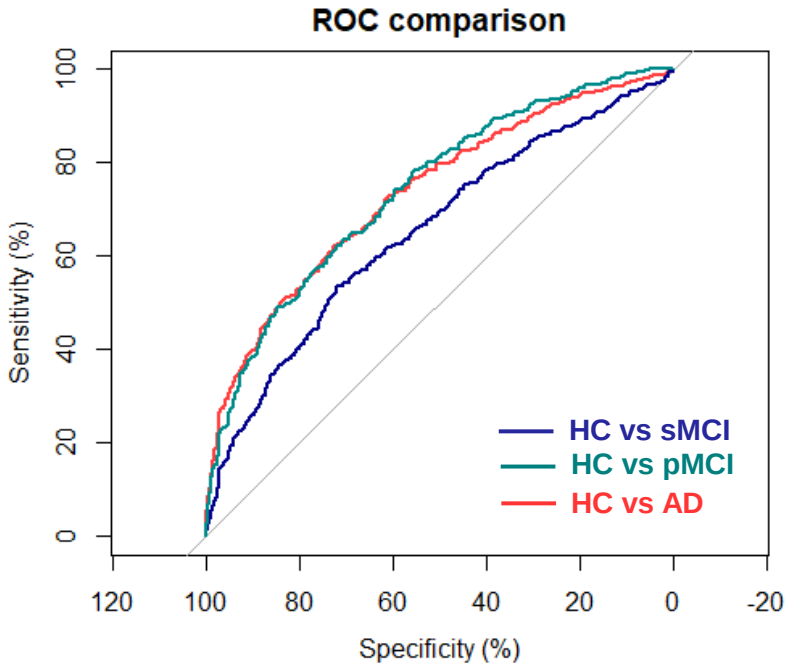
Hippocampal volume showed the highest diagnostic accuracy in discriminating AD dementia patients and pMCI from HC

Both markers show consistent results between ADNI and OASIS datasets

Hippocampus



Amygdala



		HC vs sMCI		HC vs pMCI		HC vs AD	
		AUC 95% CI	AUC	AUC 95% CI	AUC	AUC 95% CI	AUC
Hippocampus	**Whole Sample**	0.640-0.699	0.669	0.793-0.850	**0.821**	0.804-0.854	**0.828**
	ADNI	0.591-0.658	0.623	0.755-0.820	**0.789**	0.81-0.877	**0.849**
	OASIS	0.426-0.793	0.612	0.507-0.963	**0.775**	0.733-0.837	**0.787**
Amygdala	**Whole Sample**	0.621-0.683	0.652	0.793-0.850	0.741	0.704-0.765	0.735
	ADNI	0.573-0.641	0.606	0.658-0.733	0.696	0.710-0.780	0.745
	OASIS	0.354-0.755	0.553	0.669-0.919	0.797	0.657-0.769	0.715

Abbreviations: HC = cognitively healthy controls; sMCI = stable Mild Cognitive Impairment; pMCI = progressor Mild Cognitive Impairment; AD = Alzheimer's Disease

CONCLUSIONS

Our results suggest that Hippocampus volumes accurately discriminated between clinical diagnostic groups associated with AD dementia (HC vs AD, HC vs pMCI)

Results are consistent between cohorts suggesting a good stability of the diagnostic performance of QyScore® markers

Hippocampus and Amygdala volumes measured with a fully automated tool (**QyScore®**) support the diagnostic work-up of AD, particularly in distinguishing HC vs AD, and HC vs pMCI

Those MRI markers could therefore be used to define the clinical spectrum of AD more accurately, and to track the clinical progression of the disease

Abbreviations: HC = cognitively healthy controls; pMCI = progressor Mild Cognitive Impairment; AD = Alzheimer's Disease