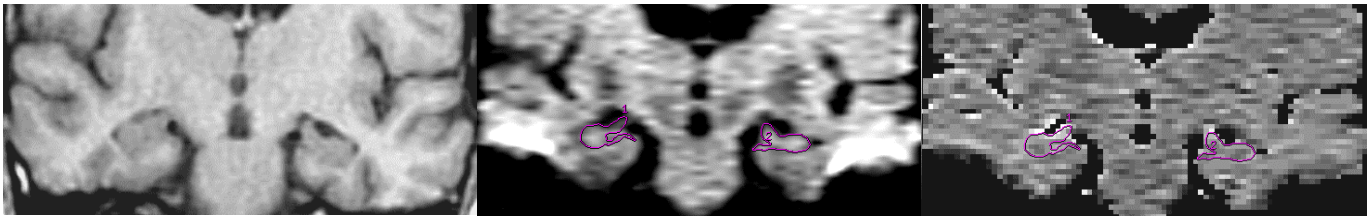
DWI Predicts Future Progression to Alzheimer's Disease in People with Amnestic Mild Cognitive Impairment

K. Kantarci[1], R. C. Petersen [1], B. F. Boeve [1], D. S. Knopman[1], G. E. Smith[1], R. J. Ivnik[1], E. G. Tangalos[1], C. R. Jack[1]
[1]Mayo Clinic, Rochester, MN, United States

Background and objective: Non-invasive markers to identify people with pre-clinical or prodromal Alzheimer's disease (AD), and predict their rate of progression to AD are needed for early interventions. An important group in identifying early markers for AD are people with amnestic mild cognitive impairment (aMCI). People with aMCI are at an elevated risk for developing AD compared to cognitively normal elderly, and most of them have prodromal AD (1). Hippocampal apparent diffusion coefficients (ADC) on diffusion weighted MRI (DWI) are elevated in people with AD with respect to normal elderly. In a previous study, we identified elevated hippocampal ADC also in people with aMCI (2). Our objective in this study is to determine if baseline hippocampal ADC can predict future progression to AD in cognitively normal elderly and people with aMCI.

Methods: We studied 67 cognitively normal elderly controls and 22 patients with aMCI who underwent DWI at baseline. Clinical group membership was determined through a comprehensive clinical examination in each subject at baseline and every year during the follow-up period, creating four possible clinical groups after longitudinal assessment: Control-stable, control-converter to aMCI or AD, aMCI-stable, and aMCI-converter to AD. Single shot echo planar - fluid attenuated inversion recovery (EPI-FLAIR) DWI was performed in a coronal plane with TR=9999ms, TE=93ms, TI= 2200 ms, slice thickness 5 mm, slice spacing 2.5 mm, and FOV= 40x20 cm to cover whole head. A FLAIR image with b=0 s/mm^2, and DWI with b=1000 s/mm^2 in three orthogonal directions were acquired from each slice. With the image analysis software FuncTool (General Electric Medical Systems, Milwaukee, WI), average ADC maps were computed pixel by pixel with the Stejskal and Tanner equation. ROIs were manually traced over the right and left hippocampal heads on the EPI- FLAIR images that concurrently appeared on the ADC maps as shown in the figure. We compared right + left hippocampal ADC values of the stable and converter groups using rank sum tests.



Results: Five of the 67 controls converted to aMCI and AD, and 12 of the 22 aMCI patients converted to AD during longitudinal assessment (table). All subjects were followed for at least one year with an average period of 40±12 months. There was no difference between the follow-up periods of stable and converter groups (rank-sum tests p>0.05). Baseline hippocampal ADC of aMCI-converters were higher than aMCI stables (rank-sum tests p=0.011). In people with aMCI, baseline hippocampal ADC predicted future progression to AD with a sensitivity of 70% at 75% specificity on ROC analysis.

Table: Baseline hippocampal ADC (median and range x10^{-6} mm^2/sec) in the stable and converter groups

	Control stable	Control converter to amnestic MCI or AD	Amnestic MCI stable	Amnestic MCI converter to AD
N	62	5	10	12
Right + left hippocampal ADC	1720 (1519-1902)	1713 (1597-1927)	1712 (1472-1862)*	1815 (1679-2130)*

**Difference between stable and converter groups are statistically significant (rank-sum tests; p<0.05)*

Conclusion: Elevation of hippocampal ADC in people with aMCI who progressed to AD (within the average follow-up period of 40 months) demonstrates early ultrastructural changes during the progression of Alzheimer's pathology. Hippocampal ADC may be useful in identifying patients with aMCI who will progress to AD in the future for preventive therapies.

References:

1)Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment clinical characterization and outcome Arch Neurol. 1999; 56: 303-308.
2)Kantarci K, Jack CR, Xu YC, et al. Mild Cognitive impairment and Alzheimer's disease: Regional diffusivity of water. Radiology 2001; 219:101-107.