Sodium MRI enhancement of the medial temporal lobe in mild Alzheimer's Disease

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Objective

The objective of this study is to investigate the differences in sodium concentration in the brains of patients with Alzheimer's disease (AD) versus non-demented elderly controls.

Background

Alzheimer's disease is a devastating and relatively common dementia resulting in loss of memory and mental faculties in elderly individuals. Over 2 million Americans suffer from AD and the progressive loss of memory and ability to care for themselves results in a total health care cost of >$50 billion dollars annually[1]. There is significant interest in the diagnostic imaging of AD with the goal of improved diagnosis, prognosis, and monitoring of therapeutic responses to treatment. Pathologically, AD is marked in part by a loss of neural cells and formation of β–amyloid plaques, primarily in the frontal and temporal lobes. We hypothesize that these changes would lead to an increase in sodium signal by two mechanisms. First, an expansion of the sodium-rich extracellular space due to cell death would lead to an increased amount of sodium in affected areas[2,3]. Second, β–amyloid is known to create channels in cell membranes[4] that leads to deregulation of sodium ions which may contribute to the increased singal in sodium MR. To investigate these hypotheses, we first found that sodium was elevated in a small cohort of formalin fixed post-mortem AD brains over controls (unpublished data) and this led us to investigate whether sodium is increased in the brains of AD patients *in vivo*. Here we show ^{23}Na imaging on the brains of 4 patients diagnosed by a board certified neurologist as having mild AD as well as 5 age-matched controls.

Methods

This study was approved by the Institutional Review Board of the University of Pennsylvania. Each volunteer was imaged in a broadband-enabled Siemens 3T Trio clinical scanner. The study began in a vendor-supplied proton 8 channel head array coil. A series of scout images were obtained and used to position a 3 minute T_1-weighted whole volume sequence (MP-RAGE) run at 1.28mm isotropic resolution for anatomical localization and later co-registration of images. The patient was then placed into a home-built 25cm diameter, 20cm length quadrature birdcage head coil with a detached RF endcap[5]. This coil was interfaced to the scanner with a custom T/R switch including a high gain, narrowly tuned pre-amplifier. A low resolution, 12 second, 3 plane sodium GRE localizer was performed for slice positioning. From this, the ventricles are clearly visible and an outline of the head is seen which is used to position the coronal sodium head scan. For both the MP-RAGE and the following sodium head scan, the Anterior to Posterior angle of the lateral ventricle was used to roughly prescribe the same axis tilt for the coronal scans in all volunteers. A .146cm^3 voxel size, 20 minute coronal sodium spoiled GRE scan was then performed with the following parameters: TR/TE 9.13/2.96ms, 60° flip angle, Slice Thickness 10mm, non-selective excitation by a 1ms hard pulse, FoV 245mm^2, 64x64 matrix size, 6/8 Partial Fourier (phase and slice), elliptical scanning, 130Hz/Px, 210 averages. The resulting images were then normalized to the sodium concentration of the highest 10th percentile of pixels, typically found in the CSF and in the slices used in table 1, found in the lateral ventricles. Region of interest analyses were drawn to compare the sodium levels in the medial temporal lobes.

Results and Discussion

Figure 1 shows representative proton and sodium MR images taken in this study from control AD participants within a year of age. In the overlaid images, the green circles represent the regions of interest (ROI) for these two subjects. A small amount of asymmetry is seen in the ROI due to the different sizes of the brains and due to the fact that segmentation was performed with images that are not interpolated. The scale on the right represents percentage of enhancement, where the average of the highest 10th percentile (lateral ventricles) is 100. Note that while the control subject shows enlarged ventricles, the sodium level measured from the medial temporal lobes are higher in the AD brain. Table 1 shows the results of the ROI analyses of controls and AD patients. The values reported for LMTL and RMTL (left and right medial temporal lobes) are reported as percent enhancement compared to ventricle along with the signal standard deviations (SD) within the ROI. A Student's two-tailed t-test reveals a significant difference between the control and AD subjects. At this time the mechanism for this sodium enhancement in the medial temporal lobe of AD brains is not known. Studies are underway to investigate whether the intracellular or extracellular sodium concentrations or relaxation properties are changed and to compare these findings to other dementias. In conclusion, we have demonstrated ~12% sodium MR enhancement in AD brains in comparison to age-matched controls. To our knowledge this is the first investigation using sodium MR in the setting of AD.

Figure 1

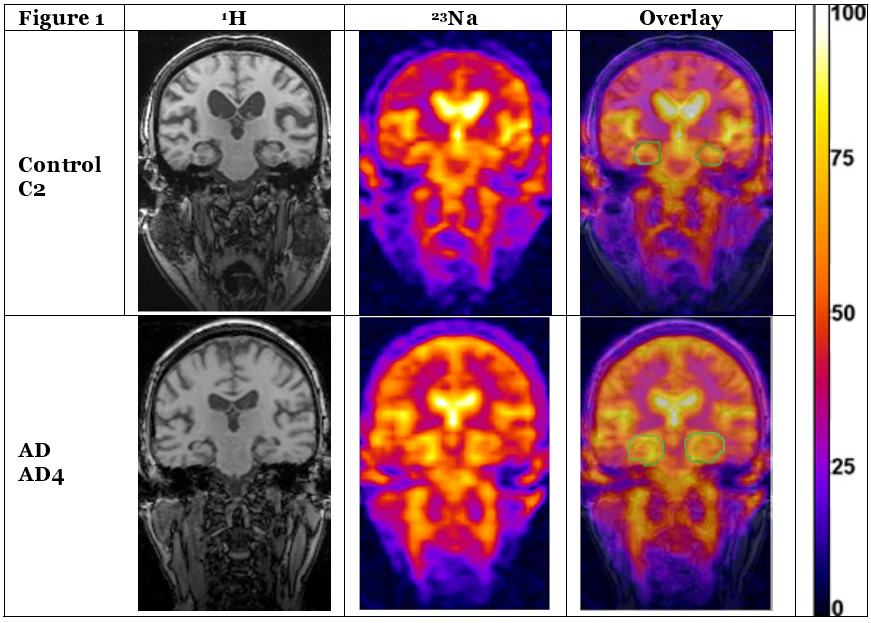

Table 1

Patient	Sex	Age	LMTL	SD	RMTL	SD
C1	F	75	.42	.07	.40	.07
C2	M	76	.58	.08	.58	.10
C3	M	74	.46	.04	.46	.05
C4	M	81	.53	.11	.53	.09
C5	F	66	.60	.10	.60	.07
Average			.52*	.08	.51*	.08
AD1	F	75	.62	.10	.65	.14
AD2	M	75	.64	.13	.65	.10
AD3	M	64	.65	.10	.61	.12
AD4	F	77	.66	.12	.64	.08
Average			.64*	.01	.64*	.02

* $p < .001$ for combined L and R data

References **1.**Bird TD and Miller BL in *Harrison's Principles of Internal Medicine, 16th edition* Chap. 350, Sec. 2 **2.**Hilal SK, et al. J Comput Assist Tomogr 1985;9:1-7 **3.**Thulborn KR, et al. Magn Reson Med 1999;41:351-9 **4.** Arispe N, et al. Proc Natl Acad Sci 1993;90:567-71 **5.** Alecci M, et al. Magn Reson Med 2003;49:363-70