Tissue Cell Fraction (TCF) from Quantitative Sodium MR Imaging Does Not Change with Age in Cognitively Normal Subjects

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Purpose:

The loss of brain volume with increasing age is a normal process seen in all individuals, even those who are cognitively normal. Sodium ion homeostasis, a highly conserved metabolic process that consumes about 60% of the aerobically derived energy of the brain, is essential to maintain the resting membrane potential that supports the action potentials that underlie brain function. The intimately linked sodium and potassium concentration gradients across the semi-permeable cell membrane require constant volumes for the intra-and extra-cellular compartments if the resting membrane potential is to be maintained at the same energy demand. Expansion of the extracellular volume in the setting of cell loss will alter this resting potential unless more ions are pumped to maintain the same concentrations, given the larger volume. Cell loss with expansion of the extracellular volume would thus be expected to increase metabolic demand of remaining cells to increase the flux of the Na/K ion pumps or, in the face of no increase in energy supply, function would be expected to be compromised as the resting membrane potential declines. Alternatively, cell loss with aging may be compensated by brain shrinkage so that the cell density is unchanged, thereby conserving the energy demands and function. We have used quantitative sodium MR imaging (qNaMRI) [1] at both 3.0 and 9.4 Tesla and the two-compartment model of tissue sodium concentration (TSC) to measure TSC and its derived quantity of tissue cell fraction TCF, to investigate the change in TCF as a function of age in cognitively normal subjects.

Methods:

Under an IRB approved protocol with signed consent, qNaMRI [2] using 3-D flexible twisted projection imaging, with B0 and B1 corrections and a separate signal calibration using the same protocol on a phantom, was performed at 9.4 Tesla (T) on 14 normal individuals. The adult ambulatory subjects (aged 20-65 years) were cognitively normal with no known medical or neuropsychiatric problems. Anatomical imaging showed the expected variation in brain anatomy with age with increasing cerebrospinal fluid spaces but no evidence of other anatomical abnormalities. The acquisition parameters (T_E/T_R = 0.26/160 ms, 3760 projections, 90° tip angle, radial fraction = 0.31, gradient strength = 5.47 G/cm, 1 average) provided a nominal 3.5 mm isotropic spatial resolutions in 10 minute. The sodium images were used to calculate TSC and TCF maps. The maps were then analyzed across 34 selected regions of interest for TCF values, which were then plotted as a histogram (Figure 1) and as a function of age (Figure 2).

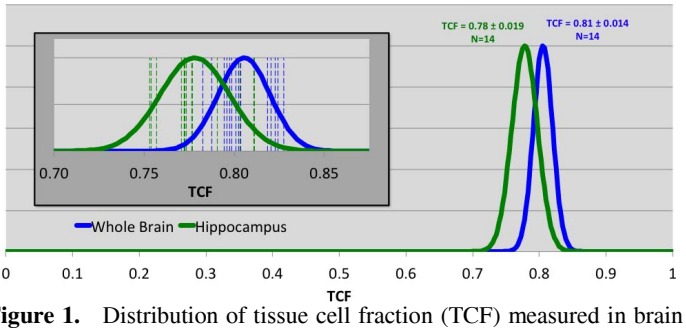

Figure 1. Distribution of tissue cell fraction (TCF) measured in brain parenchyma for whole brain including gray and white matter (blue, 0.81±0.014) and hippocampus that is primarily gray matter (green, 0.78±0.019) for cognitively normal individuals (N=14). The inset shows the individual measurements (vertical dashed lines) of each individual for the two distributions. The standard deviations of these distributions of cell density are less than 2% of the total range of possible cell densities.

Results:

The distribution of TCF measured at 9.4T in the whole brain (Figure 1, blue) including gray and white matter shows a very narrow distribution as well as in selected regions of gray matter such as the hippocampus (Figure 1, green). The convoluted cortex at the spatial resolution available results in partial volume averaging of values between gray and white matter but the distribution still only shows a variance of less than 2%. The plots of TCF measured at 9.4T with age for whole brain (Figure 2, blue) and hippocampus (Figure 2, green) show no significant age dependence. A similar result was previously obtained at 3.0 Tesla on a smaller number of elderly subjects [2].

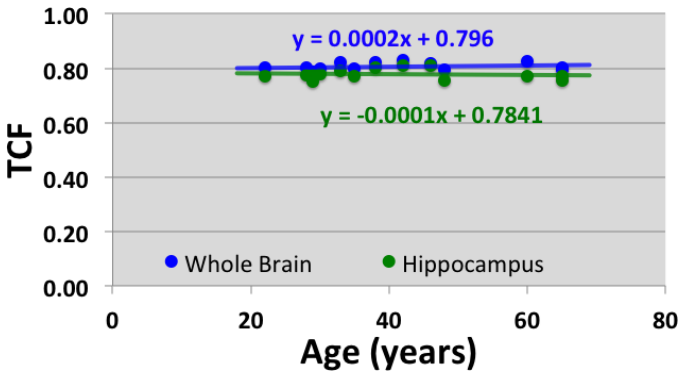

Figure 2. TCF as a function of age (years) in the group of subjects in Figure 1. The fitted lines have near zero gradient indicating that there is no age dependence for TCF in whole brain and in regional values such as hippocampus in cognitively normal individuals.

Conclusion:

TCF measured by qNaMRI shows that cell density is maintained with age in cognitively normal individuals despite decreases in brain volume. This result is consistent with the concept that a constant cell density is required for normal function and the brain shrinkage observed with age is a normal morphological process and should not be construed as indicative of pathology. Previous results at 3 Tesla showed that TCF decreased in patients with mild cognitive impairment and mild probably Alzheimer's disease [2].

References: [1] Magn Reson Med 2010 63:1583–1593, [2] Paper 106, 49th Annual Meeting ASNR Seattle, WA, June 6th.-