Cell Volume Fraction ("cell density") is Stable despite Cerebral Volume Loss in Normal Human Ageing as Measured by Quantitative Sodium MR Imaging at 9.4Tesla

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Target audience: Researchers in ageing, Clinical neuroradiologists

Purpose: To determine the age dependence of the relationship between cell volume fraction (CVF) and cerebral hemispheric volume (CHV) across cognitively normal human ageing, given that the recent neuropathology literature reports that neuronal number and density remain stable with normal aging[1].

Methods: Normal subjects (N=48, age 22-80, 49±19 years, 23 male) gave consent for this IRB approved protocol. Quantitative sodium MR imaging was performed on a customized 9.4T human scanner[2] using a birdcage radiofrequency transmit/receive coil and the flexible twisted projection imaging (TPI) sequence under conditions of full T1 relaxation and minimal T2 relaxation (TR=160ms, TE=0.26ms, FA=90^o, nominal voxel size=3.5x3.5x3.5mm^3). B0 and B1 mapping were used to correct inhomogeneities across the field of view. Signal intensities were converted to concentrations using a 3-point calibration phantom (30, 70 and 110mM NaCl in 3% agarose gel) that matched the coil loading of a human head.[3] Descriptive statistics (mean+/-SD/maximum/minimum, median, and voxel number) were obtained using a regions of interest (ROI) analysis applied to axial tissue sodium concentration (TSC) maps. Fixed criteria using easily identifiable landmarks defined ROI in the frontal, parietal, occipital and temporal lobes, basal ganglia, thalamus and brainstem. The volumes of the cerebrum and cerebral spinal fluid (CSF) space were determined from voxel counts of ROI placed over the cerebrum and calvarium. With no significant laterality differences, right and left values were combined for analysis. The CHV was calculated from the number of voxels of CSF (TSC>70) and the total number of all intracranial voxels. CVF was derived from TSC using the two-compartment model equation: CVF=(TSC – Ce)/(Ci - Ce) where Ci and Ce are intracellular and extracellular sodium concentration, respectively[3]. Linear correlation analysis was made for CVF and TSC with subject age and for CSF volume with subject age. Significance was defined $p<0.05$.

Results: Whole brain CVF and TSC (mean+/-SD) are 0.82+/-0.01 and 36.2+/-1.7mmol/L, respectively. Although this is a cross-sectional experimental design, the expected from well-established literature relationship of decreasing CHV with advancing age is found to be significant ($p<0.0001$). No significant ($p=0.22$) relationship was found between age and CVF (**Figure 1**) for the entire brain or for brain regions with only a trend towards significance ($p=0.05$) for frontal and parietal regions (**Table I**).

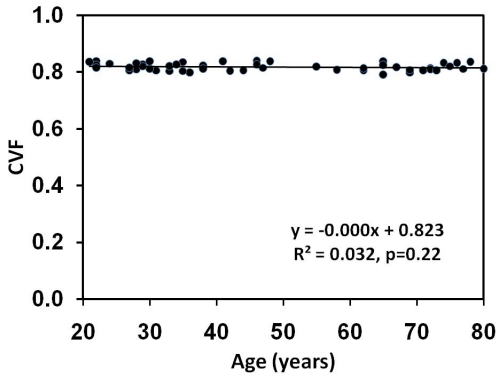

Figure 1. Cell volume fraction (CVF) as a function of age for cognitively normal subjects.

Table I. Regional CVF and TSC values (mean±SD) of cognitively normal subjects along with the Pearson correlation coefficients and p-values for age dependence.

	N	CVF Mean (SD)	TSC (mmol/L) Mean (SD)	r (TSC vs Age)	p-value
Frontal	48	0.82 (0.02)	36.3 (2.1)	0.258	0.05
Parietal	48	0.82 (0.01)	36.0 (1.8)	0.282	0.05
Temporal	48	0.81 (0.01)	37.0 (1.7)	0.035	0.34
Occipital	48	0.83 (0.01)	34.8 (1.8)	0.145	0.81
Cerebellum	48	0.83 (0.01)	35.3 (1.4)	0.124	0.40
Brainstem	48	0.82 (0.01)	36.2 (1.5)	0.157	0.28
Thalamus	48	0.81 (0.02)	37.0 (2.4)	0.146	0.31
Basal Ganglia	48	0.81 (0.02)	37.4 (2.2)	0.084	0.40
Whole Brain	48	0.82 (0.01)	36.2 (1.7)	0.165	0.22

Discussion/Conclusion: Stable CVF and TSC values despite volume loss with normal aging extends the neuropathology in vitro result to in vivo in that cell density does not change in normal ageing in all regions of the brain examined. This parameter may therefore be useful in the detection and monitoring of neurodegenerative diseases that are associated with cell loss.

References:

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