Brain Expansion Capacity: measuring brain volume adaptation to water loading in the human brain

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Introduction: The ability of brain cells to modulate osmolality locally in response to variations in the serum osmotic load is crucial to the maintenance of normal neuronal activity (1-5). This ability is compromised with senescence, leading to impaired water regulation in brain tissue, electrolyte disorders, increased metabolic disturbances in the hospital setting, and increased morbidity and mortality among the elderly. Animal studies suggest that one aspect of this regulatory dysfunction manifests itself as an age-related reduction in the capability of brain tissue to expand (6-8) in response to water perturbations. Since one of the primary functions of the osmotic regulatory system is to limit variations in cell size in the central nervous system (CNS) (9), changes in the expansion capability of brain tissue could be indicative of changes in the biochemical and biomechanical properties of brain tissue. Unfortunately, our limited ability to measure volume changes in brain tissue *in vivo* means that there is little understanding of the genesis or etiology of this volume regulatory dysfunction in the aging brain. Here we examine the use of water loading to study basics mechanisms of volume regulation.

Theory: We hypothesized that in the healthy normal adult brain, the brain's capacity to expand is a well-regulated system related to tissue biochemistry as well as tissue biomechanics and thus, similar to the concept of Bulk modulus has a fixed expansion capacity, $\xi_B(r)$, defined in Eq. [1], where $\Delta V(r)$ is the local change in the water volume in a specific volume of tissue $V(r)$ in a specific region r in response to a change in the local osmotic pressure, $\Delta\pi(r)$. Brain tissue osmotic pressure cannot be noninvasively measured, however, because serum osmotic pressure and brain tissue osmotic pressure rapidly equilibrate, we can substitute tissue changes in osmotic pressure with serum changes in osmotic pressure. In addition, if we employ van t'Hoff's equation to relate serum osmolality and serum osmotic pressure, then we can examine the ratio of local changes in tissue volume with serum osmolality. As this represents a correlation rather than a tissue property, we define this new metric, Eq. [2], as the correlative expansion capacity, $\xi_C(r)$. $\xi_C(r)$ should also be relatively constant in a normal functioning system. Under mild water loading, we can expect changes in volume to be reflected in changes in the tissue water signal in MRI, as CSF space yields to tissue expansion, Eq. [3]. This ratio of relative tissue water signal change to serum osmolality can be defined as the MR expansion capacity, $\xi_W(r)$, Eq. [4], that when multiplied by the MR water content $\beta_W(r)$, results in an approximation of $\xi_C(r)$. Because the MR water content is relatively insensitive to mild water shifts and has a maximum limit of one, changes in $\xi_C(r)$ should be dominated by $\xi_W(r)$.

$$\xi_B(r) \equiv \frac{\Delta V(r)/V(r)}{\Delta\pi(r)} \quad [1]$$

$$\xi_C(r) \equiv \frac{\Delta V(r)/V(r)}{\Delta[Osm]} \quad [2]$$

$$\frac{\Delta V(r)}{V(r)} \approx \frac{\Delta S_{BW}(r)}{S_{BW}(r)}\beta_W(r) \quad [3]$$

$$\xi_C(r) \approx \frac{\Delta S(r)/S(r)}{\Delta[Osm]}\beta_W(r) \equiv \xi_W(r)\beta_W(r) \quad [4]$$

Methods: To test the theory that the correlative expansion capacity is constant, we measured $\xi_W(r)$, the MR correlative expansion capacity in 4 healthy adults (2 females, 2 males, age range 18-22 yrs, mean: 20.0 ± 1.6 yrs) from a previous water load study (10). Details of the experiment are described elsewhere (10-11). The ROI was located primarily in gray matter along the Sylvian fissure. As a quick proof of principle that $\xi_W(r)$ is age dependent we also measured $\xi_W(r)$ in this same region in a 32 year old participant. Finally, to test that white matter, because of its relatively larger amounts of astrocytes – compared to gray matter - would have a greater capacity, we examined a region dominated by white matter containing the supramargina gyrus in a 26 year old female participant, and a region containing only white matter in the centrum semiovale in a 20 year old female participant. Subjects' change in their tissue water signal was measured through a 16-point T_2 relaxometry experiment using single voxel spectroscopy (6 cm^3, TM/TR=10-ms/12-s) before and after a 3-hour water load. Blood draws were taken every 20 minutes to monitor serum sodium levels and serum osmolality. Changes in serum osmolality was calculated from beginning of water load to cessation, i.e., immediately before the 2nd spectroscopy examination.

Results and Discussion: The variation in the expansion capacity in the Sylvian fissure region for the four participants were smaller than their age variation, in spite of large variances in the relative signal change and serum osmolality (Table I). As expected, $\xi_W(r)$, was lower in the older participant, and greatest in the pure white matter region. White matter contains a great amount of astroglia, compared to gray matter, and so we expected white matter to have a larger expansion capacity than gray matter. Water is known to shunt into the astrocytes during the initial stages of edema; a process thought to preserve and protect neuronal cell volume (12). Both regions dominated by white matter show much larger signal gain. This study was not specifically designed to test for age-related differences; nonetheless, the Sylvian fissure differences are provocative. Results presented here suggest that volume regulatory processes can be presented and quantified as a biomechanical process.

Table I. Regional Differences in the Brain Expansion Capacity, ξ_W

Sylvian Fissure, Group 1 (n=4)				
	Age (yrs)	$\Delta S_{BW}/S_{BW}$	Δ[mOsm]/kg	ξ_W (kg/Osm)
	18	0.1036	14	7.40
	20	0.1117	14	7.98
	20	0.0610	9	6.78
	22	0.0305	4	7.62
Mean	20	0.0767	10.3	7.44
Std	1.6	0.0380	4.8	0.50
CV	8.2%	46.5%	46.7%	6.7%
Group 2 (n=1)				
	32	0.0469	12	3.91
Supramarginal Gyrus (mixed white/gray) Group 3 (n=1)				
	26	0.0764	6	13.07
Centrum Semiovale (white matter) Group 4 (n=1)				
	20	0.18701	4	45.17

References

(1) Dóczi T, Acta Neurochir 1993; 121: 1-8.
(2) Zs.-Nagy I. J Molecular Med 1997; 75: 703-714.
(3) Mrak RE et al, J Neuropath & Exper Neurology 1997; 56(12): 1269-1275.
(4) Rogers J et al, Neurobio Aging 1988; 9: 601-605
(5) Raichle ME Adv Biochem Psychopharmacology 1981; 28: 329-336.
(6) Weed LH et al, Am J of Phys; 3-19-1919; 48: 531-558.
(7) Cohadon F et al, Gerontology 1986; 32 Suppl 1: 46-49.
(8) Desbordes P et al, J Gerontology 1987; 42(6): 655-659.
(9) Klatzo I, J of Neuropath & Exper Neurology 1967; 26(1): 1-14.
(10) Rossmiller SR et al, Proc ISMRM, 10th Mtg 2002, p 968.
(11) Knight-Scott J, Proc ISMRM, 14th Mtg 2006, p 3142.
(12) Ayus et al, J Am J Physiol Renal Physiol 2008; 295: 619-624.