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Precisely-Measured Hydration Status Correlates with Hippocampal Volume in Healthy Older Adults

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Dehydration is a well-known cause of reversible cognitive impairment in older people, especially those with pre-existing cognitive deficits. The standard practice is to treat any older person with confusion arriving in an emergency room with intravenous fluid. Typically, these patients are seen to “perk right up” and are quickly discharged. Surprisingly, this near universal clinical practice has motivated few mechanistic studies, and it remains uncertain why cognition in older people is so sensitive to hydration status.[1]

To address this issue, we used deuterium/bromide dilution to measure hydration status precisely in 11 cognitively and medically healthy older adults (7 women; mean age: 63.2; range: 50.3—71.5) and related this to magnetic resonance imaging (MRI)- measured brain structure. In deuterium/bromide dilution studies, subjects ingest a known quantity of deuterium (D_2O), which distributes throughout the total body water (TBW) pool, and sodium bromide, which distributes throughout the extracellular water (ECW) pool, which includes plasma, interstitial fluid, and lymph. Deuterium and bromide blood concentrations are measured at baseline and 3 hours postingestion to measure TBW and ECW. Intracellular water (ICW), which is found predominantly in lean tissue, is calculated by subtracting ECW from TBW. Decreased ICW is considered the physiological basis of dehydration.[2]

The hydration outcome measure was the ECW:ICW (E:I) ratio that is insensitive to body size and has been shown to be increased in elderly subjects.[2] MRI measures of interest were hippocampal volume, which closely tracks cognition in neuro-degenerative disease,[3] and total ventricular and gray matter volumes, which correlate with age and cognitive function, and have previously demonstrated reversible volume changes in situations of frank dehydration.[4-8]

Subjects underwent dilution studies and 3T MRI on a single day. Dilution study laboratory analyses were performed at the Columbia University Body Composition Unit using standard methods.[9] Regional and total intracranial brain volumes were obtained with FreeSurfer (http://surfer.nmr.mgh.harvard.edu/). Partial correlation analysis, controlling for age and total intracranial volumes, was used to assess the relation between the E:I ratio and hippocampal, total gray, and ventricular volume. Results were Bonferroni corrected for three comparisons and considered significant at $p < 0.017$.

The E:l ratio, a measure of subtle dehydration, correlated inversely with hippocampal volume ($r = -0.925$; $p < 0.0001$) but not with total gray volume or total ventricular volume. To gauge the specificity of the hippocampal result, we examined the E:l ratio correlation

with two similarly sized structures (globus pallidus and amygdala.) Results were not significant.

Our finding of an apparent anatomically specific correlation between hippocampal volume and subtle variations in hydration status is novel. Prior studies have shown reversible global brain changes (ventricular enlargement, decreased gray matter) without regional specificity in response to water restriction and intense exercise in younger subjects.[4-8] We did not find such global changes. Additional studies are needed to determine if the finding of a specific association between hippocampal volume and hydration status is limited to older subjects, or whether it is also present in younger subjects but was obscured in prior studies[4-8] by global changes induced by severe dehydration.

The hippocampus is well known to be especially vulnerable to toxic insults such as hypoxia. Our results, and results from one rodent study,[10] suggests the hippocampus may be similarly sensitive to hydration status. If confirmed, the finding of an association between subtle dehydration and hippocampal structure could provide a neuroanatomic explanation for the prominent cognitive effects of dehydration commonly seen in older people.

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References

1. Lieberman HR: Hydration and cognition: a critical review and recommendations for future research. J Am Coll Nutr 2007;26(suppl 5):555S–561S [PubMed: 17921465]
2. Steen B: Body water in the elderly–a review. J Nutr Health Aging 1997; 1:142–145 [PubMed: 10995081]
3. De Leon M, George A, Stylopoulos L, et al.: Early marker for Alzheimer's disease: the atrophic hippocampus. Lancet 1989; 334:672–673
4. Kempton MJ, Ettinger U, Foster R, et al.: Dehydration affects brain structure and function in healthy adolescents. Hum Brain Mapp 2011; 32:71–79 [PubMed: 20336685]
5. Cian C, Barraud P, Melin B, et al.: Effects of fluid ingestion on cognitive function after heat stress or exercise-induced dehydralion. Int J Psychophysiol 2001; 42:243–251 [PubMed: 11812391]
6. Streitbürger D-P, Möller HE, Tittge-meyer M, et al.: Investigating structural brain changes of dehydration using voxel-based morphometry. PloS One 2012; 7:e44l95
7. Nakamura K, Brown RA, Araujo D, et al.: Correlation between brain volume change and T2 relaxation time induced by dehydration and rehydration: implications for monitoring atrophy in clinical studies. Neuroimage Clin 2014; 6:166–170 [PubMed: 25379428]
8. Duning T, Kloska S, Steinsträter O, et al.: Dehydration confounds the assessment of brain atrophy. Neurology 2005; 64:548–550 [PubMed: 15699394]
9. Lukaski HC, Johnson PE: A simple, inexpensive method of determining total body water using a tracer dose of D20 and infrared absorption of biological fluids. Am J Clin Nutr 1985; 41: 363–370 [PubMed: 2982253]
10. Shin D-M, Kim C-S, Chun WY: Hippocampal Transcriptional Networks Altered by Dehydration in Mice (#195). Victoria, Australia: Lorne Genome, 2017