Correlation between Regional Cerebral Volumes and Markers of Renal Function in Chronic Kidney Disease Patients

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Introduction: Chronic Kidney Disease (CKD) is highly prevalent among the elderly, and individuals with CKD suffer disproportionate risk of cognitive dysfunction (1) and dementia (2). CKD is also associated with a number of factors implicated in structural and functional changes in the brain, including traditional risk factors of cardiovascular disease (3). However, there has been little research to quantitatively assess the relation of brain structure to markers of renal functioning and cardiovascular health. Examining the role of renal function in the acceleration of structural changes related to aging is crucial to understanding the processes by which CKD contributes to premature cognitive aging. Here we examined measures of regional brain morphometry in relation to laboratory measures of renal disease and vascular risk among older stroke-free adults with CKD.

Methods: All images were obtained on a Siemens 1.5 Tesla Avanto system. Volumetric 3D-FLASH images (3D T1-weighted volumetric scan: TE/TR/flip angle=4.76ms/11ms/20o, in-plane resolution 1mmx1mm over a 256 mm FOV, a total of 192 1mm slices were acquired to cover the entire brain) were obtained from 14 CKD patients. Images were processed using MIPAV Brain-Extraction Tool (BET) followed by Brainstrip to remove extraneous tissue. The skull-stripped image was then segmented using the FANTASM plug-in (4). The skull-stripped images were then aligned using the Talairach Transform (5). Once aligned to Talairach space, volumes of interest (VOI) were created on the image. The VOIs drawn in the Talairach space were then reverse-transformed to give VOIs defined in the original image space. Segmentation of the skull-stripped images was performed using FANTASM (6). The segmented images were used to calculate regional volumes (7). Regional volumes of each segmentation class were normalized by the total regional volume, giving a regional ratio for grey matter (GM), white matter (WM), and cerebrospinal fluid (CSF). Laboratory markers of renal and cardiovascular health were measured within 90 days of the MRI exam, and included estimated glomerular filtration rate (eGFR), creatinine, urine protein: creatinine ratio (UPr: Cr), hemoglobin, uric acid, and fibrinogen. Pearson correlation coefficients were estimated between a subject's GM, WM, and CSF ratios and these laboratory markers of renal function and cardiovascular health.

Results: Age was related to higher whole-brain CSF ratio, (r =.795, p=0.003). Age was significantly related to lower GM ratios in the anterior (r=-.783), occipital (r=-.904), and posterior lobes (r=-.864), ($p < .01$ for all correlations). Age was related to lower WM ratios in the limbic lobe (r=-.793) and sub-lobar space (r=-.830) ($p < .01$ for all correlations)

After correcting for age, eGFR was associated with higher CSF ratio in the occipital lobe (r=.806) and lower GM ratio in the posterior lobe (r=-.801) ($p < .01$ for all correlations), as well as lower WM ratios in the occipital (r=-.669) and parietal lobes (r=-.713), ($p < .05$ for all correlations). Uric acid was associated with higher CSF ratios in the frontal lobe (r=.671), the midbrain (r=.697), and pons (r=.813) ($p < .05$ for all correlations). Uric acid was also associated with lower WM ratio in the pons (r=-.681), decreased GM ratios in the frontal (r=-.726) and temporal lobes(r=-.75), and lower whole-brain GM ratio (r=-.731), ($p < .05$ for all correlations). Fibrinogen was related to lower WM ratios in the posterior lobe (r=-.751, p< 0.01). Hemoglobin was related to higher CSF ratio in the midbrain (r=.713), higher GM ratio in the pons (r=.697), and lower WM ratio in the midbrain (r=-.74), ($p < .05$ for all correlations). Urinary protein to Creatinine ratio was related to higher GM ratio in the anterior lobe (r=.675), posterior lobe (r=.677), as well as lower WM ratio in the posterior Lobe (r=-.667), ($p \leq 0.05$ for all correlations).

Conclusions: To our knowledge this is the first study to look at the correlation of regional brain volumes to cardiovascular and renal function markers in CKD patients, a population with high cardiovascular risk and a greater risk of cognitive dysfunction. Our study indicates that after accounting for structural change in the brain due to age, markers of renal function and cardiovascular health were related to both global and regional structural changes. In general, lower renal function and greater CV risk was related to increased CSF volumes and decreased GM and WM volumes. Region specific effects were found in the frontal, temporal, occipital, and parietal lobes of the cortex, the anterior and posterior lobes of the cerebellum, the midbrain, and the pons. A general reduction of white matter was observed in most of these regions. Further research is needed into the functional correlates of these differences in brain structure in CKD patients.

References

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