COGNITION DECLINE AND CORTICAL THICKNESS CHANGE IN CHRONIC KIDNEY DISEASE PATIENTS
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Purpose
The heavy burden of cognitive impairment in hemodialysis and ESRD patients has long been well recognized. Patients with chronic kidney disease (CKD) have a high prevalence of cognitive impairment and patients with end stage renal disease (ESRD) showed a high prevalence of leukoaraiosis, or white matter disease. Nevertheless, the relationship between cognitive impairment, leukoaraiosis, brain morphometric change and less advanced CKD was unknown. The aim of this study was to examine the relationship between brain morphometric change and cognitive decline in patients with CKD.

Method
We recruited CKD and non-CKD subjects with normal renal function and matched age, education and gender to the CKD patients for comparison from the Nephrology and Neurology out-patient clinics of Taipei Veterans General Hospital (VGH). All the subjects completed brain MRI scans and cognitive testing. The brain imaging was performed at, 3.0 T GE Discovery 750 imaging device at VGH. Two sequences were used: High-resolution 3D T1-weighted structural MRI data (BRAVO) and Fluid Attenuation Inversion Recovery (FLAIR) Turbo SE axial images. Each Subjects received a 30 minute battery of neuropsychological tests, consisting of: Mini-Mental State Examination (MMSE), Montreal Cognitive Test (MoCA), Wechsler Adult Intelligence Scale (WAIS) Digit span subtest, Verbal Fluency and 12-items word recall tests. Anatomical images were reconstructed using the FreeSurfer package (Martinos Imaging Centre, http://surfer.nmr.mgh.harvard.edu) to analyze brain structure. Processing each MR image involve removal of nonbrain tissue, Talairach transformation, segmentation of white and gray matter, intensity normalization, and parcellation of cerebral cortex. White matter hyperintensity (WMH) are defined as hyperintense changes on intermediate intensity/FLAIR and T2 weighted images with no corresponding T1 abnormality and the white matter hyperintensity volumes (WMHV) were determined by using SPM (http://www.fil.ion.ucl.ac.uk/spm/) and its extension toolbox, VBMtools (http://dbm.neuro.uni-jena.de/vbm/) on FLAIR images.

Result
Table 1 shows the comparisons of performance of cognitive tests and imaging characteristics of the study subjects between the CKD patients and control subjects. The 2 groups subjects are aged, gender and education matched. In battery of neuropsychological tests, the CKD groups showed lower score in MMSE (28.4±1.4) and digit span forward (11.1±2.1) compared with the normal control group significantly (24.7±4.6, 8.6±2.3). Brain morphometric comparison revealed CKD patients had smaller cerebral cortex volume and thinner cortical thickness than those in control group. The major differences of cortical thickness are located in the orbital frontal, lateral temporal and occipital regions (Fig. 1). No significant difference both in white matter volume and WMV between CKD and normal group.

Table 1. Summary of characteristics

<table>
<thead>
<tr>
<th></th>
<th>WMH volume, mm³</th>
<th>Gray matter volume, mm³</th>
<th>Cortical thickness, mm</th>
<th>MMSE</th>
<th>Digit span forward</th>
<th>eGFR mL/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>12.7±16.6</td>
<td>4.7 xE5±3.7xE4</td>
<td>2.51±0.15</td>
<td>28.4±1.4</td>
<td>11.1±2.1</td>
<td>82.0±14.3</td>
</tr>
<tr>
<td>CKD</td>
<td>16.8±19.3</td>
<td>4.2x E5±4.3xE4</td>
<td>2.25±0.14</td>
<td>25.1±4.1</td>
<td>8.9±2.2</td>
<td>34.1±18.0</td>
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<tr>
<td>P</td>
<td>0.41</td>
<td>&lt;0.001</td>
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Fig. 1 Cortical thickness maps identifying regions that have thinner cortical thickness in CKD

Conclusion
In this study, we found the cortical thickness are significantly reduced in CKD group and correlated with global cognition function (MMSE) decline. The major differences are located in orbital frontal, lateral temporal and occipital regions, which are regarded as being related to executive function and memory. There is no significant difference either on cognitive tests and the volume of WMV between CKD and control groups. However, the sample size of group is small, more subjects recruiting and further investigation such as connectivity study is necessary.

Reference
1. Pauline M., 'Coevolution of white matter hyperintensities and cognition in the elderly', Neurology 2012;79;442