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How does white matter microstructure differ between the vascular and amnesic mild cognitive impairment?

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ABSTRACT

Changes in white matter (WM) microstructure may relate to the pathophysiology of cognitive impairment. Whether WM microstructure differs in two common pre-dementia subtypes, vascular mild cognitive impairment (VaMCI) and amnesic mild cognitive impairment (aMCI), is largely unknown. This study included 28 VaMCI (12 men, age: 46 ~ 77 years) and 34 aMCI patients (14 men, age: 51 ~ 79 years). All patients underwent a battery of neuropsychological tests and structural and diffusion magnetic resonance imaging (MRI) scanning. WM microstructure was quantified using diffusion MRI parameters: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AxD) and radial diffusivity (RD). These parameters were compared between the two patient groups using tract-based spatial statistics (TBSS) after controlling for age, gender, and education. No significant differences in FA/MD/AxD/RD were observed between the VaMCI and aMCI groups, which suggests a similar pattern of WM microstructure in the early stage of cognitive impairment for different dementia types. However, the two groups exhibited significant differences in the relationship between FA and the Auditory Verbal Learning Test (AVLT), which were primarily located around the corona radiata and corpus callosum. Specifically, there were significant positive correlations ($R = 0.64$, $P < 0.001$) between the FA and AVLT in the VaMCI group, but the opposite trend was observed in the aMCI group ($R = -0.34$, $P = 0.047$). The differential relationship between WM and memory between VaMCI and aMCI indicates an independent neuropathology for specific memory deficits in different types of dementia.

INTRODUCTION

Vascular cognitive disorders (VCD) represent a wide spectrum of cognitive disorders associated with vascular causes, including vascular mild cognitive impairment (VaMCI) and vascular dementia (VD). VaMCI

common mild cognitive impairment (MCI) is amnesic MCI (aMCI), which represents the prodromal stage of

highly prevalent MCI subtypes, and both conditions are

Previous studies suggested that VaMCI patients exhibited more impairment in semantic memory and executive

White matter (WM) plays a critical role in normal

comparisons between VaMCI and aMCI were performed. Therefore, whether differences in WM impairments appear at very early stages of these two main dementia subtypes is not known.

The present study examined whether WM microstructure differed between VaMCI and aMCI by

and whether the relationships between WM and cognition differed between the two groups using diffusion magnetic

based spatial statistics (TBSS) method.

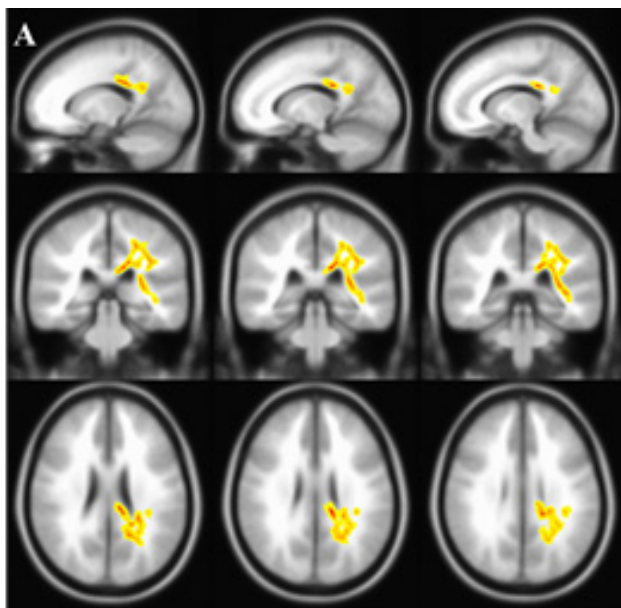


Figure 1: The “FA × Group” interaction effect on the AVLT_I

the cluster. Panel A

RESULTS

Demography and neuropsychological tests

observed for age, gender, or education between the two groups. There was a strong difference between the

the two groups (P scores between

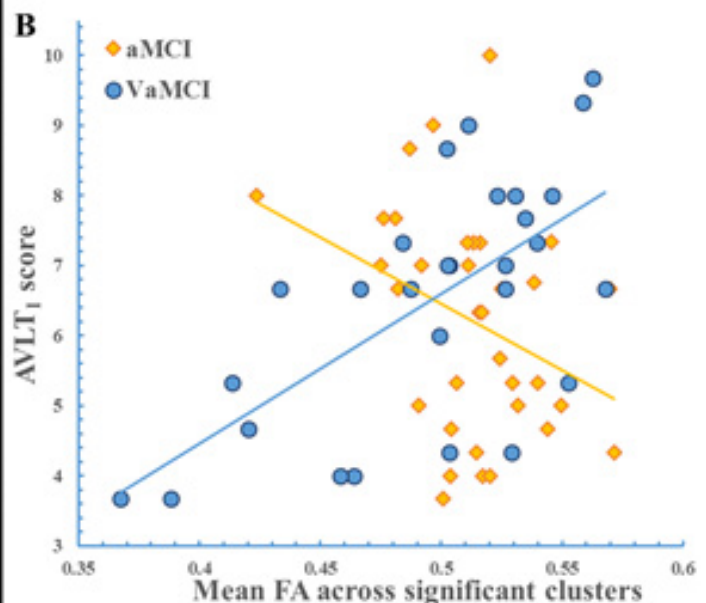
higher in the VaMCI group than the aMCI group. WM

to the VaMCI group (P distribution of abnormal regions for the two groups was P

The association between neuropsychological performance and FS score

effect for any of the neuropsychological scores, which suggests that the relationship between cognitive

two groups.



B, the scatterplot.

Table 1: Demographic information and cognitive testing of the cohorts

| | aMCI (n = 34) | VaMCI (n = 28) | Group Comparison (p value) |
|---|------------------|-------------------|-------------------------------|
| Gender (Male/Female) | | | |
| Age (yrs) | | | |
| Education (yrs) | | | |
| Auditory Verbal Learning Test (AVLT) | | | |
| <i>Immediately recall</i> | | | |
| <i>Delayed recall</i> | | | |
| <i>Delayed recognition</i> | | | |
| MMSE | | | |
| MoCA | | | |
| Fazekas score | | | |

p

Group comparison of diffusion MRI parameters

r_1 scores for the two groups, similar to

the VaMCI and aMCI groups in any of the diffusion parameters (AD, RD, MD, and FA).
diffusivity (RD).

r_1 effects for the other cognitive scores.

The association between diffusion MRI parameters and neuropsychological performance

The association between diffusion MRI parameters and FS score

r_1 corrected P values were significant for the left posterior corona radiata (PCR), superior corona radiate (SCR), posterior thalamic radiation, and internal capsule (including the inferior longitudinal fasciculus and

$P =$

P

P score in the VaMCI group but a negative correlation in the aMCI group ($R = -0.45$, $P = 0.03$).
 P revealed a very similar pattern for the relationship between

DISCUSSION

The present study demonstrated that WM the VaMCI and aMCI groups, which are the very early stages of two main types of clinical dementia, VD and and memory performance in this prodromal stage was progress of various dementia types.

with WM microstructure differences between the VaMCI and aMCI groups. To the best of our knowledge, our compared WM microstructure between VaMCI and aMCI, which are the prodromal stages of two common dementia types. Our present negative results are compatible with previous studies that demonstrated that WM regions with

hypothesis to interpret the cognitive impairments in VaMCI patients is that brain dysfunction results from

hypothesis that abnormal connectivity was a pathological studies demonstrated WM microstructure differences

divergence of WM impairments between the two types

of dementia does not exist at the origin, but it gradually becomes obvious during the development and progression of dementia. This intriguing notion provides valuable insights into WM pathology and the relevant mechanisms underlying different types of dementia.

widely used to successfully detect WM microstructural cannot exclude the possibility that these imaging indices differences at the microscopic level. Therefore, other imaging measures for WM are encouraged to validate our currently observed negative results between the VaMCI and aMCI patients.

different between the two groups, but the relationship

Vascular diseases likely interrupt large WM tracts of with more severe WM damage likely performed worse in and vice versa. In contrast, the aMCI patients stronger WM connectivity was likely associated with a compensation mechanism that underlies the memory

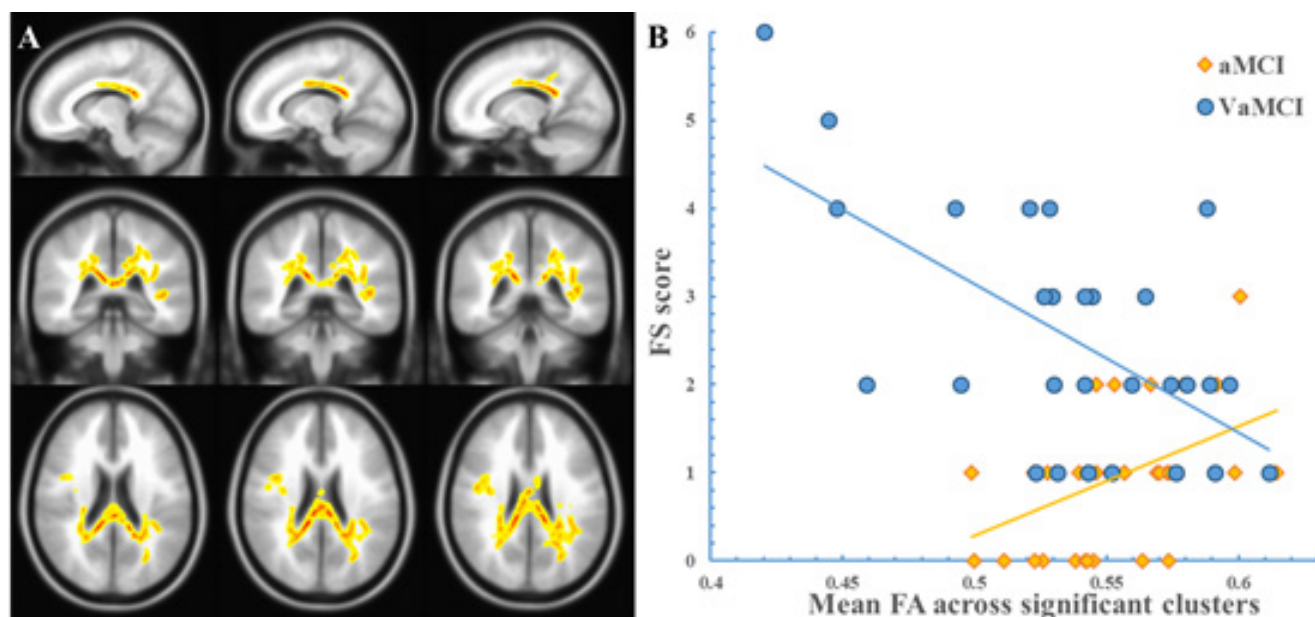


Figure 2: The “FA × Group” interaction effect on the FS score

value of the cluster. Panel A

B, the scatterplot.

observed interaction indicates that the neuropathological differences in the early stage of dementia between different

relationships rather than different brain phenotypes per se. The differences in brain phenotypes become obvious with the progression of dementia. Widely distributed

temporal lobe, cingulate and lingual gyri, CC, and bilateral

cingulum bundle, sagittal stratum and fornix, internal

interactions that were largely compatible with these previously reported regions.

in clinical and research studies, and this rating method

rating system only offers a rough and global index of

WM impairment in patients with VaMCI than aMCI, which was unlike diffusion MRI parameters. We also

score relationship differed between the VaMCI and aMCI

the VaMCI group may be associated with an increase in the

at the macrostructural level, which is represented by

not that obvious in the aMCI group. This result was likely

whether their effects are the result of some unmeasured risk factors or one factor is in the etiological pathway of

changes from complete axonal degeneration to relatively benign pathology.

LIMITATIONS AND FUTURE WORKS

primary focus on the cognitive domain of memory. Other cognitive domains, such as executive functions, should be included in the future. Second, the diagnoses for each group primarily relied on clinical diagnoses but lacked suggestive amyloid imaging or histopathological data for

compared the two most common subtypes of MCI but did not include the healthy control groups and other types of

MATERIALS AND METHODS

matched in gender, age, and education. The recruited patients were outpatients who were registered at the

evaluations, including complete sociodemographic and clinical (cognitive, behavioral, neurological, functional, and physical) data collection. Patient histories were collected from informants, generally spouses or children. Two experienced neurologists performed the diagnoses for the two groups. The medical research ethics committee

this study. The study was conducted in accordance with approved guidelines, and written informed consent was obtained from all participants.

Inclusion criteria

Criteria for aMCI

Diagnosis of aMCI was made based on recent international consensus criteria, which were adapted

impairments that did not meet the Diagnostic and

performance of general cognitive functioning and no

abnormal memory function, documented by extensive

neuropsychological evaluation; normal general cognitive function, Clinical Dementia Rating Scale (CDR) score

) and
) was

Criteria for VaMCI

Diagnosis of VaMCI depended on the following

cognitive impairment due to subcortical ischemic vessel

Exclusion criteria

Participants were excluded if they exhibited any

or auditory abnormalities that made clinical assessments

Mandarin language abilities to complete the assessment;

The exclusive criteria for VaMCI also included the following conditions: signs of large vascular disease, such territorial infarcts and watershed infarcts or hemorrhages.

Neuropsychological evaluations

neuropsychological tests to assess general mental status and other cognitive domains. These tests included CDR

Two attending neurologists performed all evaluations.

Scanning parameters

WMH/lacunar infarct rating

signal surrounding the ventricles and deep WM according

The rater was blinded to the clinical data of participants.

Diffusion MRI preprocessing

onto the same skeleton.

Statistical analysis

Statistics for demographics were calculated using Statistical comparisons of the spatial distributions of

two groups.

method applies statistical analyses throughout the entire

reliable alignment of the WM tracts and overcomes prior

voxel were statistically compared between the aMCI and gender, and education were included as covariates. We

of data, make the diagnosis and neuropsychological evaluations, study supervision, obtaining funding

REFERENCES

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ahead of print.

cognitive impairment due to cerebral small vessel disease

CONFLICTS OF INTEREST

Author contributions

drafting the manuscript

drafting the manuscript

manuscript for content

of data, study supervision, obtaining funding
Gaolang Gong, study concept and design,

intellectual content, obtaining funding

B and Chetelat G. Brain structural, functional, and cognitive correlates of recent versus remote autobiographical memories in amnesic Mild Cognitive Impairment.

imaging in patients with subcortical vascular cognitive

cognitive impairment detected by diffusion tensor imaging.

normal appearing white matter in patients who are aging, or

amnesic mild cognitive impairment and various dementias.

Divergent Structural Connectivity Patterns between Patients

of diffusion tensor imaging in the differential diagnosis of
disease in patients with only mild white matter alterations

and functional connectivity and the progression of

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White matter hyperintensities in mild cognitive impairment:
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enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference.