Regional Gray Matter Atrophy in Vascular Mild Cognitive Impairment

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Background: The aim of this study was to explore the neuroanatomical bases of vascular mild cognitive impairment (VaMCI) with respect to attention/executive function, memory, language, and visuospatial function. *Methods:* We used voxel-based morphometric analysis to identify brain regions that significantly differed in terms of gray matter volumes (GMVs) between 43 patients with VaMCI and 55 healthy controls. Then, we compared the individual GMVs of the selected regions with the neuropsychological profiles of the VaMCI patients. *Results:* The delayed recall component of the Rey–Osterrieth Complex Figure Test (CFT) (74.4%), the Symbol Digit Modalities Test (74.4%), the Boston Naming Test (51.2%), and the CFT—copy (81.4%) shared the highest incidence of impairment in the 4 cognitive domains, respectively. Compared with controls, patients with VaMCI exhibited significantly reduced GMVs. This effect was mainly present in the frontal regions, including the bilateral dorsolateral prefrontal cortex (DLPFC), the orbital portion of the superior frontal gyrus (SFG), and the left supplemental motor area, and was also observed in the bilateral posterior cingulated cortex (PCC). GMVs were significantly correlated with performance in the Trail Making Test, part B, in the bilateral DLPFC and PCC, the clock drawing test in the right orbital portion of the SFG, and CFT—delayed recall in the right PCC. *Conclusions:* These results, from the perspective of brain morphology, uniquely explored the specific cerebral structural changes of VaMCI, thus providing a deeper understanding of the pathophysiology of the disease. **Key Words:** Vascular mild cognitive impairment—neuropsychology—magnetic resonance imaging—brain volume.

Vascular mild cognitive impairment (VaMCI) is the mild stage of vascular cognitive impairment, the diagnosis of which is based on 2 factors: demonstration of the presence of a cognitive disorder by neuropsychological testing and history of clinical stroke or presence of vascular disease by neuroimaging that suggests a link between the cognitive disorder and vascular disease.[1] Patients with VaMCI are commonly characterized by deficient attention/executive function but also show varying degrees of impairment in other cognitive domains, including memory, language, and visuospatial function.[2,3] Previous studies have indicated that VaMCI patients may regain normal cognition.[1,4] Thus, a deeper understanding of the pathological basis of VaMCI may facilitate the development of quantitative clinical-neuroimaging approaches to early detection.

Functional brain imaging data have revealed that cognitive constructs arise from collections of brain regions functioning together as intrinsic connectivity networks.[5-7]

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For instance, the executive control network (ECN), the default mode network (DMN), and the salience network are all associated with attention/executive function.[8,9] The ECN mainly includes the dorsolateral prefrontal cortex (DLPFC), the middle frontal gyrus/superior frontal gyrus (SFG), and the posterior parietal gyrus.[10,11] The key nodes of the DMN are the precuneus/posterior cingulated cortex (PCC), medial prefrontal gyrus, angular gyrus, and the medial temporal gyrus.[12] The salience network is primarily anchored in the ventrolateral prefrontal cortex, anterior insula, and anterior cingulated cortex.[13] In this complicated system, whether aberrant functioning of these brain regions corresponds to structural abnormalities in VaMCI patients is unclear.

In a preliminary study, we characterized neuropsychological and hemodynamic changes in VaMCI and its subtypes.[14] Chronic deficiencies in regional cerebral blood flow have been found to lead to regional gray matter (GM) atrophy.[15-17] Thus, the aim of the present study was to explore the neuroanatomical bases of VaMCI with respect to 4 cognitive domains: attention/executive function, memory, language, and visuospatial function. We used voxel-based morphometry (VBM) analysis to search for specific brain regions with reduced gray matter volumes (GMVs). Then, we tested for associations between the GMVs of the identified regions and the neuropsychological profiles of VaMCI patients. We hoped to gain a deeper understanding of VaMCI pathology from a morphological perspective.

Participants and Methods

Participants

We invited patients who had been admitted to our institution with cerebrovascular diseases to participate in

Table 1. *Demographic and neuropsychological variables in VaMCI patients and controls*

Variable	Patients (n = 43)	Controls (n = 55)	*P* value
Age (years)	43.5 ± 14.1	42.7 ± 12.1	.754
Male (%)	22 (51.2)	30 (54.5)	.739
Education (years)	9.0 ± 3.7	8.7 ± 3.2	.725
Treated hypertension (%)	15 (34.9)	17 (30.9)	.677
Treated hypercholesterolemia (%)	18 (41.9)	6 (10.9)	.000
Treated diabetes (%)	4 (9.3)	3 (5.5)	.696
Smoking (%)	19 (44.2)	25 (45.5)	.900
Screening test			
MMSE	26.5 ± 2.9	29.3 ± .9	<.001
MES	74.7 ± 10.2	95.3 ± 2.5	<.001
Memory			
AVLT-I	15.0 ± 4.2	21.1 ± 4.2	<.001
AVLT-II	3.4 ± 2.4	7.9 ± 1.6	<.001
CFT-delayed recall	11.1 ± 7.3	21.3 ± 5.9	<.001
SDMT—accidental memory	3.3 ± 2.8	4.5 ± 2.6	.135
Attention/executive function			
TMT-A (s)	74.4 ± 39.1	44.4 ± 9.9	<.001
SDMT	28.9 ± 11.1	47.6 ± 4.1	<.001
TMT-B (s)	166.8 ± 53.1	91.9 ± 16.7	<.001
SCWT-I	45.9 ± 6.6	48.7 ± 2.9	.036
SCWT-II (s)	102.0 ± 57.4	71.3 ± 27.5	.009
VFT—switching	11.8 ± 5.1	15.7 ± 3.7	.008
Language			
BNT	21.1 ± 4.0	25.0 ± 2.1	<.001
VFT—animal	13.0 ± 4.1	17.5 ± 3.4	<.001
VFT—city	13.1 ± 7.5	18.3 ± 5.3	.017
Similarity Test	12.6 ± 5.1	17.7 ± 3.7	.001
Visuospatial function			
CDT	18.2 ± 8.2	22.7 ± 4.0	.007
CFT—copy	29.4 ± 6.0	35.0 ± .7	<.001

Abbreviations: AVLT, Auditory Verbal Learning Test; AVLT-I, sum of the first 3 recalls of AVLT (immediate recall); AVLT-II, fifth recall of AVLT (delayed recall); BNT, Boston Naming Test (30-item version); CDT, clock drawing test; CFT, Rey–Osterrieth Complex Figure Test; MES, Memory and Executive Screening; MMSE, Mini-Mental State Examination; SCWT, Stroop Color–Word Test; SCWT-I, correct number of SCWT; SCWT-II (s), time of SCWT; SDMT, Symbol Digit Modalities Test; TMT, Trail Making Test; TMT-A, Trail Making Test, part A; TMT-B, Trail Making Test, part B; TMT-A (s), time of TMT-A; TMT-B (s), time of TMT-B; VaMCI, vascular mild cognitive impairment; VFT, verbal fluency test.