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Visually-Rated Medial Temporal Lobe Atrophy with Lower Educational History as a Quick Indicator of Amnestic Cognitive Impairment after Stroke

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Abstract.
Background: Time and resource limitations prevent cognitive assessment in acute-to-subacute settings, even in comprehensive stroke centers.
Objective: To assess cognitive function in acute stroke patients undergoing routine clinical, laboratory, and radiological investigations, with a view to improving post-stroke care and treatment.
Methods: Sixty-nine patients (72.6 ± 11.1 years; 65% male) were prospectively enrolled within 14 days of acute ischemic stroke. Patients with altered consciousness, aphasia, or dysarthria were excluded. Clinical features including modified Rankin and NIH stroke scales, and vascular risk factors were assessed, as well as neuroimaging parameters by semi-quantitative evaluation of medial temporal lobe atrophy (MTLA) using MRA source images, FLAIR images for white matter changes (Fazekas scores), and T2* images for cerebral microbleeds. Neuropsychological screening was conducted using the Montreal Cognitive Assessment (MoCA) test. Univariate and multivariate analyses were used to evaluate the influence of variables on MoCA total and subscale scores.
Results: Lower MoCA scores of 22 or less were associated with MTLA [OR (95%CI), 5.3 (1.0–27.5); $p = 0.045$], education years [OR (95%CI), 0.71 (0.55–0.91); $p = 0.007$], and modified Rankin scale at discharge [OR (95%CI), 2.4 (1.3–4.5);

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$p = 0.007$]. The delayed recall MoCA score was correlated with MTLA ($r = -0.452$, $p < 0.001$), periventricular ($r = -0.273$, $p = 0.024$), and deep ($r = -0.242$, $p = 0.046$), white matter changes.
Conclusions: MTLA, together with lower educational history, are quick indicators of amnestic cognitive impairment after stroke. The association between cognitive impairment and physical disability at discharge may signify the importance of earlier cognitive assessment.

Keywords: Comprehensive stroke center, dementia, medial temporal lobe atrophy, Montreal Cognitive Assessment, post-stroke dementia, stroke

INTRODUCTION

Stroke is the leading cause of disability and mortality, with the number of estimated cases worldwide experiencing a significant shift within the next generation. In Europe, numbers are predicted to rise by a third by 2035 [1], and by an even greater proportion in the Asia-Pacific region [2]. Inevitably, the number of stroke survivors with post-stroke dementia (PSD) is also expected to rise, a factor associated with poor functional prognosis and early death [3–5]. In general, PSD refers to dementia occurring 3 months after the onset of stroke [6]. However, timely diagnosis should prompt early intervention [7]. 'How best to improve cognition after stroke' has been reported to be the highest priority research topic in a recent survey of patients with stroke [8] but with an increasing number of patients in a modern hospital setting, there is concern that neuropsychological assessment remains an afterthought, in part due to the overwhelming work burden in acute stroke care, as well as lack of resources, personnel, and infrastructure for cognitive evaluation.

The purpose of this study was to identify stroke survivors at higher risk of cognitive impairment, using routine clinical, laboratory, and radiological investigations, at a comprehensive stroke center. This study utilized the Montreal Cognitive Assessment (MoCA), which includes visuospatial and executive functional tasks, due to its effectiveness in evaluating PSD [9–11]. Hippocampal atrophy was semi-quantitatively assessed with MRA source images, due to sagittal or coronal T1-weighted images not usually being used in an acute clinical setting as a result of time constraints. In addition, the relationship between demographic, clinical, vascular, and neuroimaging, factors, and cognitive impairment was assessed. The features found to be associated with cognitive impairment may aid stroke physicians in the evaluation of post-stroke cognitive function, even in the acute to subacute phase.

METHODS

Subjects

Patients were prospectively enrolled in the period 2015–2016 within 14 days of acute ischemic stroke onset. We excluded patients with altered consciousness, delirium, aphasia, remarkable dysarthria or apparent clinical signs of major depression. Demographic characteristics, as well as clinical, vascular, and neuroimaging, factors were also assessed. This study was approved by the ethics committee of the National Cerebral and Cardiovascular Center. Each patient was informed of the research and an opt-out option was presented on a bulletin board in the hospital ward for the duration of hospital admission of patients. Patients were taken to the bulletin board in the ward and received an oral explanation of the research, including information about the project's aims, time requirements, and expectations between 5 and 14 days after stroke onset. Those who did not wish to participate in the study were given the opportunity to opt out. Patients were able to contact the research team if they had any concerns or wished not to participate via a telephone number provided. All patients' data were anonymized prior to analysis.

Neuropsychological evaluation

All subjects underwent a general physical, neurological, and neuropsychological, assessment with the Japanese version of MoCA [12, 13]. Only psychologists or medical doctors who had completed relevant training programs performed cognitive assessments in this study. All MoCA records were collected by

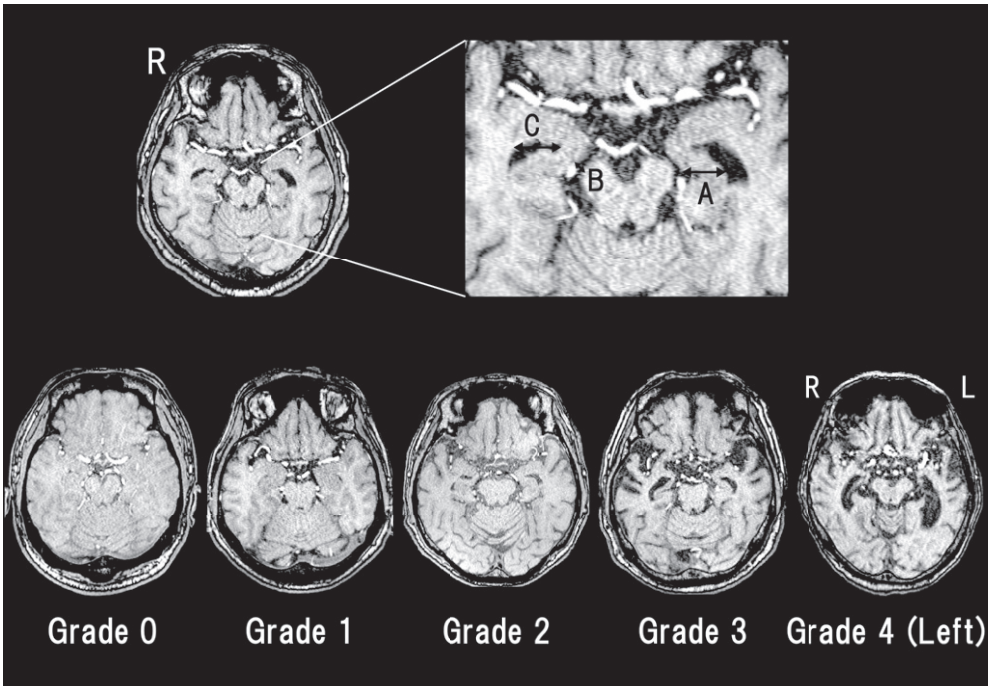

Fig. 1. Visual rating scale of hippocampal atrophy. Upper images show the area of measurement of (A) Width of the hippocampus, (B) Width of the perimesencephalic cistern, (C) Width of the anterior temporal horn. Lower images are representative for Grade 0–4. Please note that in the image to the right Grade 3 denotes the right hippocampus and Grade 4 the left hippocampus. R, right; L, left.

a central psychological review board. The board comprised of two neurologists and two neuropsychologists, and evaluation was confirmed through consensus of board members.

Visual rating scale (VRS) of hippocampal atrophy

The degree of hippocampal atrophy was semi-quantitatively defined according to published criteria [14, 15], with slight modifications using MRA source images. The width of the medial temporal lobe (A), perimesencephalic cistern gap (B), and anterior temporal horn of the lateral ventricle (C), were assessed. The MTA scale was graded on a scale of 0 (no atrophy) to 4 (severe atrophy) and averaged bilaterally (Fig. 1). (Details are available in the Supplementary Material). Hippocampal atrophy was rated by one neurologist (Y.T.) and independently by another (S.S.) and, if required, the joint assessment was further scrutinized by a third neurologist (M.I.). Inter-rater correlation coefficient between S.S. and Y.T. was 0.804 for hippocampal atrophy. Furthermore, external validation of MTLA was performed by a board-certified trained radiologist (G.S.). Inter-rater correlation coefficient between G.S. and Y.T. was 0.797.

White matter changes and cerebral microbleeds

White matter changes (Fazekas scale) and cerebral microbleeds (CMBs) were evaluated according to published criteria [16–18]. The details are available in the Supplemental Material.

Statistical analysis

Univariate statistical (Mann-Whitney U test and Chi-square test), and multivariate (multivariate logistic analysis and multiple regression analysis), analyses were used to evaluate the influence of demographic, clinical, and neuroimaging variables on MoCA total and subscale scores. Variables were selected for further multivariate analysis if they revealed a p value <0.20 in univariate analysis. Correlations of neuroimaging parameters with total and subtest scores of MoCA were assessed using Pearson's correlation coefficient analysis. All analyses were performed in SPSS version 23.

Table 1
Clinical features and demographic data

	Total ($n=69$)	MoCA $\leqq$ 22 ($n=39$)	MoCA $\geqq$ 23 ($n=30$)	p value
Demographic factors				
Age, y, mean ± SD	72.6 ± 11.1	75.2 ± 10.6	69.1 ± 11.0	0.018*
Males, *n* (%)	45 (65.2)	24 (70.0)	21 (61.5)	0.464
Education, y, mean ± SD	12.2 ± 3.0	11.2 ± 2.8	13.6 ± 2.8	0.002*
Clinical features				
mRS (premorbid), mean ± SD	0.2 ± 0.7	0.3 ± 0.8	0.1 ± 0.3	0.147
mRS (at discharge), mean ± SD	1.3 ± 1.2	1.7 ± 1.2	0.8 ± 1.0	0.001*
NIHSS (on admission), mean ± SD	3.6 ± 3.8	3.4 ± 2.6	3.8 ± 4.9	0.341
NIHSS (at discharge), mean ± SD	1.0 ± 1.5	1.6 ± 1.3	1.2 ± 0.6	0.011*
Vascular risk factors				
Hypertension, *n* (%)	62 (89.9)	38 (97.4)	24 (80.0)	0.038*
Diabetes mellitus, *n* (%)	19 (27.5)	9 (23.1)	10 (33.3)	0.344
Previous cerebrovascular disease, *n* (%)	16 (23.2)	11 (28.2)	5 (16.7)	0.26
Neuroimaging factors				
Supratentorial lesion, *n* (%)	51 (73.9)	25 (64.1)	26 (86.7)	0.034*
Left supratentorial lesion, *n* (%)	22 (31.9)	9 (23.1)	13 (43.3)	0.073
Infratentorial lesion, *n* (%)	17 (24.6)	14 (35.9)	3 (10.0)	0.013*
Fazekas PVH, mean ± SD	1.8 ± 0.6	1.9 ± 0.6	1.6 ± 0.2	0.036*
Fazekas DSWMH, mean ± SD	2.0 ± 0.8	2.1 ± 0.8	1.7 ± 0.8	0.04*
MTLA (VRS), mean ± SD	1.9 ± 0.5	2.1 ± 0.4	1.8 ± 0.5	0.003*
Microbleeds, *n* (%)	19 (28.4)	14 (36.8)	5 (17.2)	0.078
Microbleeds (lobar), mean ± SD	1.0 ± 3.9	1.6 ± 5.1	0.2 ± 0.6	0.178

mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; Fazekas PVH, periventricular hyperintensity scale; Fazekas DSWMH, deep white matter hyperintense scale; MTLA, medial temporal lobe atrophy; VRS, visual rating scale; and SD, standard deviation. *$p<0.05$.

RESULTS

Total and subscale scores of MoCA

Of 522 patients admitted to the stroke center with acute ischemic stroke between August 1, 2015 and April 20, 2016, 453 patients did not fulfill inclusion criteria due to altered consciousness, aphasia, remarkable dysarthria, visual impairment, severe hearing impairment, or severe hemiparesis of upper limb extremities. Those with even a slight disturbance of consciousness were excluded. The demographic characteristics of the 69 patients are provided in Table 1. Stroke subtypes included cardioembolic stroke ($n=20$), atherothrombotic brain ($n=12$), and lacunar ($n=20$), infarction, and stroke of unknown etiology ($n=17$). MoCA score was 22.0 ± 3.8 (mean ± standard deviation) and was conducted at 7.9 days on average after stroke onset. Subjects were divided into two groups, low ($n=39$) and, high ($n=30$), MoCA score (Table 1), according to total MoCA score cut-off (22/23) [18, 19].

All subscale scores, namely visuoexecutive function (VE) (0–5), naming (0–3), attention (0–6), language (0–3), abstraction (0–2), delayed recall (DR) (0–5), and orientation (0–5), were significantly different between the two groups. DR showed the clearest intergroup difference between the two groups, with the score 3.1 times higher in the high- than the low-scored group (2.7 versus 0.9). DR ($\beta=0.376$, $p<0.001$), VE ($\beta=0.324$, $p<0.001$), and attention ($\beta=0.309$, $p<0.001$) significantly contributed to total MoCA scores ($R=0.993$, $R^2=0.986$, adjusted $R^2=0.984$, analysis of variance $p<0.001$) using multiple regression analysis.

Factors associated with low MoCA score

In univariate analysis, age, educational history, mRS and NIHSS, at discharge, hypertension, supratentorial and infratentorial lesion, Fazekas PVH and DSWMH, and MTLA were significantly different between the high- and low-scored groups (Table 1). There was no significant difference between the two groups for premorbid mRS. The multivariate logistic regression analysis revealed a strong relationship between lower MoCA score and MTLA [OR (95%CI), 5.3 (1.0–27.5); $p=0.045$], mRS at discharge [OR (95%CI), 2.4 (1.3–4.5); $p=0.007$], and education years [OR (95%CI), 0.71 (0.55–0.91); $p=0.007$] (Table 2).

Table 2
Odds ratios for factors associated with lower MoCA score

	odds ratio (95%CI)	*p* value
MTLA (VRS)	5.3 (1.0–27.5)	0.045*
mRS (at discharge)	2.4 (1.3–4.5)	0.007*
Education, y	0.71 (0.55–0.91)	0.007*
Hypertension	12.4 (0.6–268.9)	0.109
History of stroke	3.4 (0.6–18.8)	0.161
Age ≧ 75	0.4 (0.1–1.9)	0.244
Left supratentorial lesion	0.57 (0.1–2.2)	0.42
Fazekas PVH	1.4 (0.4–5.1)	0.578

MTLA indicates medial temporal lobe atrophy; VRS, visual rating scale; and Fazekas PVH, periventricular hyperintensity scale.
*$p < 0.05$.

Factors associated with low delayed recall score

Since DR most strongly contributed to the low MoCA score, we also explored factors associated with low DR score. According to the DR score, the subjects were divided into low ($n = 33$; scored ≤1) and high ($n = 36$; scored ≥2) groups. In univariate analysis, age ($p = 0.033$) and MTLA ($p = 0.038$) showed significant differences between the two groups (Table 3). The multiple regression analysis showed lower DR score correlated with MTLA ($\beta = -0.331$, $p = 0.017$) but not with PVH ($p = 0.656$), scale ($R = 0.537$, $R^2 = 0.289$, adjusted $R^2 = 0.219$, analysis of variance $p = 0.002$).

Factors associated with low visuoexecutive function score

We also explored factors associated with low VE score (Table 4). In multiple regression analysis, lower VE score correlated with education years ($\beta = 0.360$, $p = 0.004$), mRS at discharge ($\beta = -0.257$, $p = 0.026$), MTLA (≤2 or ≥2.5) ($\beta = -0.249$, $p = 0.037$), and microbleeds ($\beta = -0.244$, $p = 0.039$), but not with the PVH scale ($p = 0.612$) ($R = 0.608$, $R^2 = 0.370$, adjusted $R^2 = 0.283$, analysis of variance $p < 0.001$).

Correlation of imaging parameters with MoCA score

The distribution of average MTLA was 1.0 ($n = 9$), 1.5 ($n = 8$), 2.0 ($n = 36$), 2.5 ($n = 13$), and 3.0 ($n = 3$). MTLA grade correlated with DR ($r = -0.452$, $p < 0.001$) and MoCA total score ($r = -0.288$, $p = 0.016$), but not with other subscale scores. Fazekas PVH scale score correlated, though

Table 3
Factors associated with low delayed recall score

	Total ($n = 69$)	Recall ≦ 1 ($n = 33$)	Recall ≧ 2 ($n = 36$)	*p* value
Demographic factors				
Age, y, mean ± SD	72.6 ± 11.1	75.8 ± 9.1	69.6 ± 12.0	0.033*
Males, *n* (%)	45 (65.2)	22 (66.7)	23 (63.9)	0.809
Education, y, mean ± SD	12.2 ± 3.0	11.5 ± 2.9	12.9 ± 3.0	0.061
Clinical features				
mRS (premorbid), mean ± SD	0.2 ± 0.7	0.3 ± 0.8	0.2 ± 0.5	0.622
mRS (at discharge), mean ± SD	1.3 ± 1.2	1.6 ± 1.2	1.1 ± 1.1	0.052
NIHSS (on admission), mean ± SD	3.6 ± 3.8	3.9 ± 3.6	3.3 ± 3.9	0.272
NIHSS (at discharge), mean ± SD	1.0 ± 1.5	1.0 ± 1.3	0.9 ± 1.7	0.241
Vascular risk factors				
Hypertension, *n* (%)	62 (89.9)	32 (97.0)	30 (83.3)	0.108
Diabetes mellitus, *n* (%)	19 (27.5)	7 (21.2)	12 (33.3)	0.26
Atrial Fibrillation, *n* (%)	16 (23.2)	11 (33.3)	5 (13.9)	0.056
Previous cerebrovascular disease, *n* (%)	16 (23.2)	8 (24.2)	8 (22.2)	0.843
Neuroimaging factors				
Supratentorial lesion, *n* (%)	51 (73.9)	22 (66.7)	29 (80.6)	0.189
Left supratentorial lesion, *n* (%)	22 (31.9)	9 (27.3)	13 (36.1)	0.431
Infratentorial lesion, *n* (%)	17 (24.6)	10 (30.3)	7 (19.4)	0.296
Fazekas PVH, mean ± SD	1.8 ± 0.6	1.8 ± 0.6	1.7 ± 0.6	0.278
Fazekas DSWMH, mean ± SD	2.0 ± 0.8	2.1 ± 0.8	1.8 ± 0.8	0.217
MTLA (VRS), mean ± SD	1.9 ± 0.5	2.1 ± 0.4	1.8 ± 0.5	0.038*
Microbleeds, *n* (%)	19 (28.4)	9 (28.1)	10 (28.6)	0.968
Microbleeds (lobar), mean ± SD	1.0 ± 3.9	1.8 ± 5.5	0.3 ± 0.6	0.504

mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; Fazekas PVH, periventricular hyperintensity scale; Fazekas DSWMH, deep white matter hyperintense scale; MTLA, medial temporal lobe atrophy; VRS, visual rating scale; and SD, standard deviation.
*$p < 0.05$.

Table 4
Factors associated with low visuoexecutive score

	Total ($n=69$)	VE $\leqq 3$ ($n=26$)	VE $\geqq 4$ ($n=43$)	p value
Demographic factors				
Age, y, mean ± SD	72.6 ± 11.1	74.7 ± 11.3	71.3 ± 10.9	0.167
Males, *n* (%)	45 (65.2)	15 (57.7)	30 (69.8)	0.307
Education, y, mean ± SD	12.2 ± 3.0	11.0 ± 2.6	13.0 ± 3.1	0.014*
Clinical features				
mRS (premorbid), mean ± SD	0.2 ± 0.7	0.4 ± 1.0	0.1 ± 0.3	0.179
mRS (at discharge), mean ± SD	1.3 ± 1.2	1.6 ± 1.2	1.1 ± 1.2	0.102
NIHSS (on admission), mean ± SD	3.6 ± 3.8	3.5 ± 3.0	3.6 ± 4.2	0.731
NIHSS (at discharge), mean ± SD	1.0 ± 1.5	1.1 ± 1.4	0.9 ± 1.6	0.292
Vascular risk factors				
Hypertension, *n* (%)	62 (89.9)	25 (96.2)	37 (86.0)	0.242
Diabetes mellitus, *n* (%)	19 (27.5)	7 (26.9)	12 (27.9)	0.929
Atrial Fibrillation, *n* (%)	16 (23.2)	7 (26.9)	9 (20.9)	0.568
Previous cerebrovascular disease, *n* (%)	16 (23.2)	9 (34.6)	7 (16.3)	0.08
Neuroimaging factors				
Supratentorial lesion, *n* (%)	51 (73.9)	15 (57.7)	36 (83.7)	0.017*
Left supratentorial lesion, *n* (%)	22 (31.9)	5 (19.2)	17 (39.5)	0.079
Infratentorial lesion, *n* (%)	17 (24.6)	10 (38.5)	7 (16.3)	0.038*
Fazekas PVH, mean ± SD	1.8 ± 0.6	1.9 ± 0.6	1.7 ± 0.6	0.227
Fazekas DSWMH, mean ± SD	2.0 ± 0.8	2.0 ± 0.9	1.9 ± 0.8	0.463
MTLA (VRS), mean ± SD	1.9 ± 0.5	2.1 ± 0.5	1.9 ± 0.5	0.079
Microbleeds, *n* (%)	19 (28.4)	10 (40.0)	9 (21.4)	0.103
Microbleeds (lobar), mean ± SD	1.0 ± 3.9	2.0 ± 6.1	0.4 ± 1.2	0.158

VE, visuoexecutive score of MoCA; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; Fazekas PVH, periventricular hyperintensity scale; Fazekas DSWMH, deep white matter hyperintense scale; MTLA, medial temporal lobe atrophy; VRS, visual rating scale; and SD, standard deviation. *$p<0.05$.

only weakly, with MoCA total score ($r=-0.245$, $p=0.044$) and with DR ($r=-0.273$, $p=0.024$). Fazekas DSWMH scale score correlated with DR ($r=-0.242$, $p=0.046$), and showed a trend toward lower MoCA total score ($r=-0.235$, $p=0.053$). BOMBS score did not correlate with MoCA total, or subscale, score ($p>0.05$).

Intercorrelations between imaging parameters

MTLA was weakly associated with Fazekas PVH ($r=0.476$, $p<0.001$) and with Fazekas DSWMH ($r=0.348$, $p=0.004$).

DISCUSSION

This study, which was conducted at a single comprehensive stroke center on prospectively-enrolled patients with ischemic stroke, found that MTLA, education years, and mRS at discharge were associated with cognitive impairment. Using the established MoCA cut-off score of 22/23 in post-stroke cognitive impairment [19, 20], patients were divided into the lower and higher MoCA score groups, demonstrating a clear difference in the MTLA grade between groups. The source images of time-of-flight MRA are T1-weighted, and we utilized them to conveniently assess MTLA without repeated axial or coronal T1-weighted images. As MRA images, but not T1-weighted images, are routinely taken in comprehensive stroke centers, the presence of MTLA in MRA source images could conveniently inform the physician of co-existing cognitive impairment in the presence of short education-years. Moreover, the source images of MRA are T1-weighted with thin slices, which is useful in finding the most appropriate slice in the assessment of hippocampal atrophy.

In an era of increasing endovascular therapy in stroke patients, routine and detailed assessment of cognitive impairment, together with MR volumetry, such as Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD) and PET/SPECT, may be difficult to implement due to limited time and resources. The increasing number of stroke survivors, however, necessitates accurate and earlier diagnosis of PSD to provide earlier intervention and focused management. PSD is associated with poor functional prognosis and early death [5]. Indeed, the current study showed lower MoCA scores were associated with higher mRS at discharge, suggesting

physical frailty is associated with cognitive impairment, which could cumulatively be described as 'mental frailty'. In support of our findings, a UK study showed that physical function was positively associated with processing-speed and executive function [21]. The association between physical and mental frailty may need more attention in stroke patients as physical disability is routinely assessed with NIHSS, Barthel index, and mRS. However, such assessment may not apply for cognitive impairment, which can greatly influence the activity of daily living and quality of life. Indeed, another recent study has shown that more than half of stroke patients with significant functional recovery measured by mRS continued to have cognitive impairment when assessed with MoCA [22]. The impact of a stroke extends far beyond physical disability, and a 'good outcome' may not in reality describe a satisfactory consequence. Therefore, greater attention to the multiple levels of recovery, in combination with physical and cognitive assessment, should be considered. Comprehensive stroke care should also include earlier cognitive assessment.

A recent study has shown that MTLA is the only radiological feature independently associated with cognitive impairment 1 year after stroke onset [23, 24]. In this context, studies examining CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) subjects [25], and animal models of chronic hypoperfusion [26], have also suggested hippocampal atrophy is induced by white matter lesions caused by chronic hypoperfusion via disruption of neuronal networks. There is a close functional and structural connection between the hippocampus and neocortical areas through the medial temporal lobe. Such cortico-subcortical connections can be damaged by white matter lesions [24]. Furthermore, another recent study in minor stroke patients has shown early cognitive impairment detected with MoCA is independently associated with white matter damage [27]. Such findings align with the associations between hippocampal atrophy, ischemic white matter changes, and memory (delayed recall) impairment in the current study, further implicating an interaction between chronic hypoperfusion and hippocampal damage in stroke patients.

The lack of association between Fazekas and MoCA scores by multivariate analysis suggests chronic hypoperfusion is not the sole factor underlying cognitive impairment with hippocampal atrophy in stroke patients. MTLA is increasingly seen as a key biomarker of AD; ischemic vascular lesions and neurodegeneration frequently overlap, which together contribute to PSD pathology [28, 29]. According to previous reviews, the prevalence of pre-stroke dementia is about 10% [6]. In the current study, therefore, pre-stroke dementia due to neurodegeneration, such as AD, may have contributed to MTLA in the MoCA $\leq$22 group. Thus, close monitoring of clinical course after stroke may facilitate diagnosis of co-existing AD in stroke survivors.

We acknowledge the limitations of this study. Firstly, this study did not include detailed neuropsychological assessment. In comprehensive stroke centers, detailed neuropsychological assessment may not be available in acute to subacute settings. Therefore, MoCA is preferable for rapid screening for cognitive impairment in the acute-to-subacute phase after stroke, which can be related to the detailed cognitive assessment in the chronic phase. Secondly, recently available amyloid imaging such as Pittsburgh compound B (PiB)-PET was not performed in this study. If amyloid imaging had been performed, the presence or absence, of overlapping Alzheimer's disease pathology may have been identified. Nevertheless, the pathological role of amyloid remains unclear, particularly in regard to atrophy in the medial temporal regions, which may be affected by tau, prior to amyloid, pathology. In addition, approximately 30% of cognitively normal elderly are reported to be PiB-positive [30]. Thirdly, this study used a visual rating scale for MTLA. Volumetric MRI, such as VSRAD, is a more sensitive method in the detection of hippocampal atrophy. T1-weighted sagittal images are recommended for the method but is not always available in an acute setting. This study aimed to evaluate hippocampal atrophy with MRA source images normally taken in the regular clinical practice, and proved that they are still useful in predicting presence of cognitive impairment in patients with ischemic stroke. The interrater agreement was 80.4% recorded, rated 'strong' in relation to previous reports [31]. Furthermore, external validation by a trained radiologist was also performed, which agreement was 79.7%. Fourthly, the inclusion criteria is an inherent limitation to this study. This study was designed to only enroll patients who would be assessed properly for their cognitive status; in other words, stroke patients with less severity and fewer comorbidities. Indeed, the NIHSS of patients enrolled in this study was mostly less than 10. Despite potential selection biases, the inclusion criteria enabled the performing of this pilot study of cognitive assessment, even in

the acute phase of stroke. The reasoning behind the cognitive assessment of acute stroke patients was to start earlier intervention against dementia, as well as its co-existing comorbidities [7].

In conclusion, MTLA identified on MRA source images, together with lower educational history, can be a quick indicator of cognitive impairment after stroke. In addition, the association of cognitive impairment with physical disability at discharge may demonstrate the importance of cognitive assessment in the earlier phase after stroke.

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Authors' disclosures available online (https://www.j-alz.com/manuscript-disclosures/18-0976).

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: http://dx.doi.org/10.3233/JAD-180976.

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