

Cognitive Function of Patients with Adult Moyamoya Disease

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Background: Neurocognitive impairment is one of several unsolved social issues faced by patients with moyamoya disease. Although efforts have been made to investigate cognitive function using neuropsychologic tasks, generalizability has been limited. Here, in a preliminary study, we used structured neuropsychologic tasks to establish a standardized neuropsychologic assessment for adult moyamoya patients with and without difficulty in social independence. *Methods:* Ten patients with neuroradiologically confirmed adult moyamoya disease (3 male, 7 female) participated. Half of all subjects did not have difficulty with social independence (group 1) and the others had (group 2). Group differences were evaluated after basic cognitive abilities and frontal lobe function were tested. *Results:* Although the mean age of group 1 was substantially higher than that of group 2, disease duration did not differ significantly between groups. Means scores for intelligence functions including all subtests for basic cognitive abilities were higher in group 1 compared with group 2. Scores from only 2 frontal lobe evaluation tasks (Trail Making Test B and Theory of Mind) were significantly different between groups. *Conclusions:* This preliminary study provides a profile of neurocognitive dysfunction in adult patients with moyamoya disease using structured neuropsychologic tasks. A broad range of cognitive functions was disrupted particularly in the patients who had difficulty with social independence. To obtain stronger evidence regarding neurocognitive dysfunction in patients with moyamoya disease, a multicenter prospective study is essential. **Key Words:** Moyamoya disease—cognitive impairment—neuropsychologic tests—adult.

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Moyamoya disease is an uncommon cerebrovascular condition characterized by progressive occlusion of bilateral internal carotid arteries and is known to cause strokes

in relatively younger people.^{1,2} Several efforts to identify its pathogenesis have recently detected gene mutations and deletions that make people susceptible to the familial form of the disease, and further investigation might clarify the direct mechanisms underlying the disease.³⁻⁶ Extracranial-intracranial bypass surgery has been established as an effective neurosurgical intervention that increases cerebral blood flow (CBF) and guards against ischemic attacks. However, difficulty with social independence accompanied by cognitive impairment has recently been recognized as an important unsolved social issue faced by patients with adult moyamoya disease.⁷ These patients are physically independent in daily life, but economically dependent because cognitive impairment leads to difficulty obtaining vocational skills. Here, we define the status of

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these patients as “difficulty with social independence.” Generally, cognitive impairment has been described as a neuropsychologic sequela occurring after strokes that manifest as disturbances in memory, attention, performance, and social behavior in pediatric cases.^{8,9} However, recent reports have focused on adult cases with neurocognitive impairment even without radiological evidence of major stroke.^{7,10} Nakagawara et al⁷ indicated that even if infarction has not yet occurred, brain dysfunction was associated with persistent hemodynamic compromise in the medial frontal lobes that can be visualized using [¹²³I]iomazenil (IMZ)-single photon emission computed tomography (SPECT). This technique has the potential to become a tool for diagnosing cognitive impairment in adult moyamoya patients who do not show major abnormalities on computed tomography scans or magnetic resonance imaging. In contrast, a common methodology for neuropsychologic evaluation of these patients is yet to be determined, even to the extent that which questions to include remains undecided. Because previous studies have selected considerably different tasks for this evaluation, results have been unsurprisingly inconsistent.¹⁰⁻¹² Therefore, we address this concern by administering structured tests to 2 groups of adult moyamoya patients, 1 with difficulty in social independence and the other without.

Materials and Methods

Participants

Ten patients with neuroradiologically confirmed adult moyamoya disease (3 men and 7 women; mean age, 34.2 years; range, 19-51 years) participated in this study. Because this survey was formed by completely anonymous retrospective information, this study did not have the ethics committee approval. All subjects were proficient in Japanese. To identify specifics regarding neuropsychologic assessment in moyamoya patients who have difficulty with social independence, the 10 patients were divided into 2 groups. Group 1 comprised 5 patients without difficulty in social independence. The subjects in this group had a higher educational background without need for special education programs, better socioeconomic status, and did not need public support. Group 2 comprised 5 patients who had difficulty with social independence. Two of the 5 patients required a special education program, and all were socioeconomically disadvantaged and needed public support. The mean duration of the disease was 9.1 years. Only 1 patient had a history of small intracerebral hemorrhage (periventricular region) at onset. Other patients had histories of transient ischemic attacks or minor ischemic strokes. Magnetic resonance imaging revealed these minor strokes in 4 patients, whereas the remaining subjects showed no abnormalities in the radiological assessment. No subjects

showed radiological abnormality evidenced by an ischemic lesion affected by more than 2 cortical arteries. [¹²³I]iodoamphetamine-SPECT showed 1 case of resting-state CBF impairment in group 1 and 3 cases in group 2. Cerebrovascular reserve impairment was found in 9 of the 10 cases. Revascularization surgery comprising superficial temporal artery–middle cerebral artery bypass was performed in 9 of the 10 patients and their preoperative symptoms were relieved. All patients were physically independent, with modified Rankin Scale scores no greater than 2 at the time of study inclusion. Table 1 and Table 2 summarize the clinical characteristics and radiological features of each patient group.

Neuropsychologic Assessment

Basic cognitive ability was evaluated using the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) to assess intelligence, the Wechsler Memory Scale-Revised (WMS-R) to assess memory,^{13,14} and supplemental subtests for each task. Several frontal functioning tests were also administered to detect specific neuropsychologic deficits associated with adult moyamoya disease that co-occurs with difficulty in social independence. The Frontal Assessment Battery tested general frontal cognitive ability. The Trail Making Test Part A assessed speed of information processing,^{15,16} and the Trail Making Test Part B (TMT-B) and the Wisconsin Card Sorting Test assessed executive ability.^{16,17} The Go/No-Go and No-Go/Go tasks were used to measure response inhibition,¹⁸ and the Apathy Scale measured the extent of apathy. The Reading the Mind in the Eyes (Eyes) task is a theory-of-mind task that was given to examine the ability to infer the mental status of others.¹⁹

Data Analysis

To identify group differences regarding clinical profiles and neuropsychologic tasks, a univariate analysis was performed. *P* values were calculated based on the 2-tailed *t* test for parametric data and the Mann-Whitney *U* test for nonparametric data. Next, to determine which factors contributed to the differentiation between groups, a discriminate analysis was applied to the data set. A predictive model was then constructed after a stepwise variable selection procedure. Finally, the contribution rate that discriminated between the groups and the expected classification rate were calculated along with their *F* and *P* values. These statistical data were generated using JMP software, Version 10.0.2 (SAS Institute Inc, Cary, NC). A *P* value less than .05 was considered statistically significant.

Results

The mean scores for clinical variables and neuropsychologic assessments of each patient group are given in

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