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Characteristics of cognitive function evaluation using the Montreal cognitive assessment in a cerebrospinal fluid tap test in patients with idiopathic normal pressure hydrocephalus

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ABSTRACT

Objectives: Though the Japanese version of the Montreal Cognitive Assessment (MoCA-J) scores change after a cerebrospinal fluid tap test (CSFTT), their characteristics remain unclear. To compare patient response rate to changes in cognitive function observed in the cerebrospinal fluid tap test, and to determine which group of patients were good responders.

Patients and methods: This study included 32 patients who were suspected of having idiopathic normal pressure hydrocephalus (iNPH) between May 2017 and October 2018. Cases were divided into, following a CSFTT, a gait responder group and a non-responder group. Scores of the MoCA-J were compared and examined before, one day after, and one week after the CSFTT.

Results: Significant changes in MoCA-J scores were observed 1 day and 1 week after the CSFTT in the gait responder group. The change in scores was larger, and had a larger effect size, one week after the CSFTT. On assessment, MoCA-J sub-items began to show changes in attention and abstract items one day after the CSFTT, and significant changes were noted in attention and abstract items in addition to executive functions and orientation one week after the CSFTT. The degree of cognitive function before the CSFTT was less closely related to the amount of change. Changes in cognitive function can be assessed at each time point after the CSFTT, and changes in cognitive function are measured regardless of the level of cognitive function.

Conclusion: These results suggest that evaluating patients with the MoCA-J may potentially support a more accurate iNPH diagnosis.

1. Introduction

Idiopathic normal pressure hydrocephalus (iNPH) does not follow any precedent diseases, such as subarachnoid hemorrhage or other, and is a pathological condition that causes disordered gait, cognition and urination as a result of enlarged brain ventricles. There are many individuals who may potentially be in asymptomatic phases of iNPH, which has been recognized in Japan as a common disease. [1]

The negative side effects of iNPH, including gait disorder, cognitive dysfunction and dysuria, can be improved by surgically installing a ventriculoperitoneal (VP) shunt or a lumboperitoneal (LP) shunt. [2] The diagnosis of iNPH is evaluated based on clinical symptoms such as gait disorder, cognitive dysfunction, urination disorder, alongside brain imaging results. Cerebrospinal fluid tap test (CSFTT) is performed in the diagnosis and medical treatment of INPH, and the necessity of shunt surgery is determined referring to the result of CSFTT. [3]

When performing a CSFTT in iNPH patients, a Mini Mental State Examination (MMSE) and a Frontal Assessment Battery (FAB) are generally used to evaluate cognitive function, and are recommended tests in the guidelines for the management of iNPH in Japan. [4] The Montreal Cognitive Assessment (MoCA) is used to assess cognitive function for iNPH. [5] In our hospital, as a support for patients who undergo a CSFTT, we evaluate cognitive function using a Japanese version of the Montreal Cognitive Assessment (MoCA-J).

The MoCA-J is used as a screening tool in the diagnosis of dementia, and the Mild Cognitive Impairment (MCI) test is said to have higher

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sensitivity than the MMSE in the detection of cognitive impairment. [6] MoCA-J derived scores correlate with Evans Index values in hydrocephalus [7], and, although it is known that the values change after a CSFTT, their underlying characteristics remain unknown.

The purpose of this study was to 1) compare patients' response rates to changes in cognitive function observed in the cerebrospinal fluid tap test, and to 2) determine which group of patients were good responders. In addition, we also sought to assess the desired evaluation time and specific items required for the identification of the pathology. In this study, it was hypothesized that those whose gait function improved also had improved cognitive function, and that the MoCA-J score would improve regardless of the severity of their pathology.

2. Materials and methods

Subjects consisted of 32 consecutively seen patients who were suspected of having iNPH, between May 1, 2017 and April 1, 2019, and had been referred by other hospitals. All patients underwent a CSFTT, and, based on the idiopathic normal pressure hydrocephalus treatment guidelines established in 2011, [4] were split into a gait function responder group, who showed improvements in their gait, and a non-responder group, who showed no such improvements. The gait function responder group was considered to probably have iNPH. Information on the improvement of cognitive function was entirely omitted from the assessment of which patients belonged to the gait function responder group or not.

To characterize each group's demographics, we examined patients' age, gender, Evans Index, and presence or absence of disproportionately enlarged subarachnoid-space hydrocephalus (DESH). Patients underwent a lumbar puncture performed by a neurologist or neurosurgeon on the day of admission, from which 30 ml of cerebrospinal fluid was obtained.

Evaluation of cognitive function by the MoCA-J was performed before, 1 day after, and 1 week after the CSFTT. Assessments of gait function and cognitive function were performed by occupational therapists. To ensure inter-rater reliability in the cognitive function evaluation, the same occupational therapist consistently evaluated all the patients undergoing CSFTT.

This was a retrospective study.

Clinical information from each time point of the MoCA-J was retrospectively acquired from patients' electronic medical records.

The information obtained by the CSFTT was statistically analyzed to examine the rate of change of the MoCA-J scores at each evaluation time point after the CSFTT and the characteristics of the subordinate items in the MoCA-J predicting these changes. In addition, we decided to examine whether the improvement rates were biased depending on patients' baseline level of cognitive function.

3. Statistical analysis

Demographic differences between the gait responder group and the non-responder group were compared using a Fisher's exact test and unpaired *t*-test Patient cognitive function evaluation before the CSFTT was used as a baseline for comparison, and comparisons were carried out using a paired t at 1 day and 1 week after the CSFTT. Differences between baseline and reevaluation values were assessed to calculate the effect size. A one-way analysis of variance was used to analyze differences in cognitive function between the gait responder group and the non-responder group throughout the entire evaluation period.

When analyzing differences in MoCA-J scores at each evaluation time point, a Bonferroni correction was performed to prevent errors associated with multiple comparisons. A regression curve was drawn and analyzed to assess whether the amount of improvement differed for each baseline cognitive function score. The regression curve represents a 95% confidence interval, and the inflection point is determined by detecting, using a third-order polynomial, the point at which the rate of improvement changes. Regression curves were analyzed at 1 day and 1 week after the CSFTT. Records were collected retrospectively from patients' electronic medical records. The level for statistical significance was set at $P < 0.05$. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) (version 22.0 for Windows, IBM Japan, Tokyo, Japan).

This study was reviewed and approved by the Institutional Review Board of Nara Prefecture General Medical Center (Approval no. 454), who waived the requirement for informed consent due to the retrospective nature of the study.

Table 1
Relationships between demographic characteristics of CSFTT gait responders and non-responders.

	n	Gait responders	n	Non-responses	*P*-value Non responders *vs.* gait responders
Age (years)	24	78.2 ± 6.2	8	77.9 ± 8.1	0.904[b]
Sex	24		8		> 0.999[a]
male		16		5	
female		8		3	
Evans index,	22	0.33 ± 0.03	6	0.32 ± 0.02	0.773[b]
DESH	23		6		> 0.999[a]
-		4		1	
+		19		5	

n, % ; mean ± sd ; . P-value : a, Fisher's exact test; b, unpaired *t*-test.
CSFTT = cerebrospinal fluid tap test; DESH = disproportionately enlarged subarachnoid-space hydrocephalus.

4. Results

In the demographics analyses, the Evans index had four unreliable data points, and DESH was treated as a missing value because of discrepancies in the data corresponding to three people.

There was no statistically significant difference between age, gender, Evans index values and DESH status between the gait responder and non-responder groups (Table 1). MoCA-J scores showed significant improvements at both 1 day after and 1 week after the CSFTT in the gait responder group. In the non-responder group, there were no significant improvements at any of the CSFTT time periods or across the entire period (Fig. 1).

Assessment of variations in the sub-items of the MoCA-J and variations in the effect sizes revealed changes in the Attention and Abstraction items at 1 day and 1 week after the CSFTT. In addition, changes were also observed in visuospatial and executive functioning and orientation. The total scores of MoCA-J increased by an average of 2 points one day after the CSFTT, and an average of 3 points one week after the CSFTT (Table 2).

The relationship between baseline MoCA-J scores before the CSFTT and the amount of change in the scores revealed a significant change in the baseline score, from 5 to 20 points, 1 day after the CSFTT. The inflection point, as determined by the third-order polynomial, occurred 1 day after the CSFTT, and corresponded to a score of 18 points (Fig. 2A). One week after the CSFTT, the score increased regardless of the baseline score. Although a score of 14 points is shown 1 week after the CSFTT, the regression curve around the inflection point was nearly flat (Fig. 2B).

5. Discussion

So far, re-evaluation of cognitive function using the MoCA has been conducted several different time points, such as immediately after or within 3 days after the CSFTT, with no consistent measurement time point. [5,8,9] In this study, improvements in MoCA-J scores were observed from 1 day to 1 week after the CSFTT, and the amount of change tended to be especially significant 1 week after the CSFTT. Consistently,

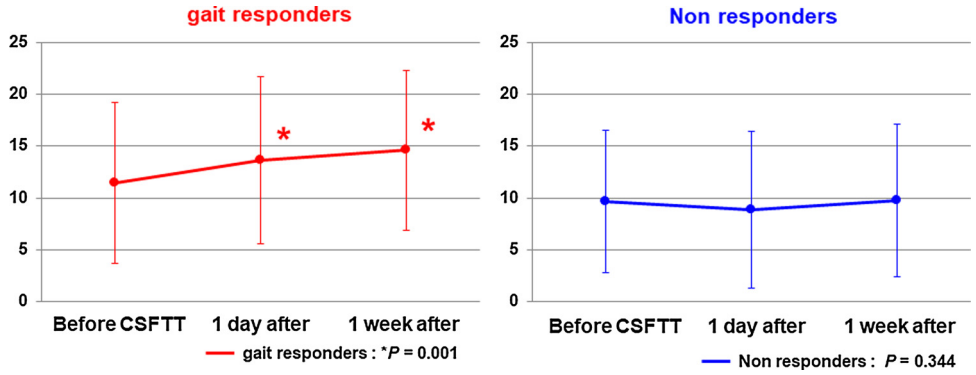

Fig. 1. Transition of MoCA-J scores of gait responders and non-responders. Gait responders showed significant changes 1 day and 1 week following the CSFTT onwards, but there were no significant differences in non-responders.

a recent study that observed cognitive function assessment by MMSE after a CSFTT in iNPH patients has reported that cognitive function improved one week after [10].

Patient evaluations using the MoCA-J, as well as MMSE evaluations, may be performed up to one week after a CSFTT. For evaluation after 1 week following a CSFTT, sub-items reflecting visuospatial functioning, executive functioning, and capacity for attention, abstraction, and orientation, are beginning to significantly change. It is therefore beneficial to not only evaluate the total MoCA-J scores but also these sub-items, as the capacities of which they are reflective are easy to improve.

Among the scores of the MoCA-J sub-items with particularly large effect sizes, attention and abstraction are items which are closely related to frontal lobe function and showed changes at early stages following the CSFTT. Many reports suggest that cognitive functional symptoms in iNPH are related to frontal lobe functional symptoms [11]. This study strongly suggests improvement in frontal lobe function. Though the MoCA-J has many sub-items adopted by the MMSE and FAB, based on our previous research, the FAB tends to show change from day 1 onwards following a CSFTT [10]. Since frontal lobe function is improved by a CSFTT from an early stage, we consider that items of visuospatial and executive functioning and capacity for attention and abstraction tend to improve from an early stage.

Our previous study revealed that characteristics of the MMSE assessment are more likely to be different in patients with severe cognitive impairments at baseline and tend to be reduced in severity in patients with scores of 22 or more [10]. This may be related to reports that the decline in frontal lobe-dependent functions is noticeable in iNPH patients who score 24 points or more on the MMSE [12]. Evaluation using the MMSE is likely to produce a ceiling effect, which is less likely to be a problem using the MoCA-J due to its inherent difficulty. Based on this study and the results of previous studies, if their baseline cognitive function score is 22 or more on the MMSE, a patient should be evaluated using the MoCA or FAB. Because this study observed changes regardless of the degree of cognitive function at baseline, the MoCA-J can be used to evaluate cognitive function after a CSFTT, regardless of the level of cognitive function. However, it must be kept in mind that, given the difficulty of these assessment, floor effects need to be considered as well.

When studying cognitive function, it is often challenging to evaluate changes in learning ability. Studies have shown that the effects on learning are difficult to observe in neuropsychological tests on patients with iNPH [14]. Therefore, we think that the improvement in cognitive function presented in this study is not largely due to changes in learning ability.

The following may be helpful when applying this study to the clinical practice. Both the MoCA-J score and the walking function were significantly improved in the same cases; this co-incidence indicates a possible relationship between the walking function and the MoCA-J.

Table 2
Comparison of MoCA-J scores before, 1 day after, and 1 week after the CSFTT in the gait responders and non-responders.

					P-value		Effect size (r)	
	n	Before CSFTT	1 Day After CSFTT	1 weak After CSFTT	*P*-value for all	1 Day After	1 weak After	1 Day After	1 weak After
Gait responders									
Visuospatial/Executive	24	1.8 ± 1.5	2.0 ± 1.6	2.3 ± 1.7	**0.030**[a]	0.219	**0.009**[b]	0.328	0.548
Naming	24	2.1 ± 1.2	2.5 ± 1.1	2.5 ± 0.8	0.091[a]	0.115	0.176[b]	0.385	0.349
Attention	24	2.8 ± 2.3	3.4 ± 2.3	3.5 ± 2.0	**0.004**[a]	**0.025**	**0.008**[b]	0.493	0.556
Language	24	0.8 ± 0.8	0.9 ± 0.8	1.0 ± 0.8	0.376[a]	0.834	0.520[b]	0.170	0.235
Abstraction	24	1.0 ± 0.9	1.4 ± 0.8	1.4 ± 0.8	**0.001**[a]	**0.010**	**0.010**[b]	0.546	0.546
Delayed recall	24	0.3 ± 0.7	0.5 ± 1.1	0.6 ± 1.1	0.259[a]	0.490	0.142[b]	0.242	0.368
Orientation	24	2.6 ± 2.1	2.8 ± 2.1	3.3 ± 2.4	**0.021**[a]	0.819	**0.020**[b]	0.173	0.504
Total	24	11.4 ± 7.8	13.6 ± 8.1	14.6 ± 7.7	**0.000**a	**0.001**	**0.000**[b]	0.648	0.782
Non-responders									
Visuospatial/Executive	8	1.9 ± 1.4	1.9 ± 1.6	1.5 ± 1.4	0.531[a]	> 0.999	0.885[c]	0.000	0.295
Naming	8	1.8 ± 1.3	1.5 ± 1.2	2.0 ± 1.3	**0.037**[a]	0.341	0.341[c]	0.500	0.500
Attention	8	2.3 ± 1.6	2.3 ± 2.0	2.3 ± 2.1	> 0.999[a]	> 0.999	> 0.999[c]	0.000	0.000
Language	8	0.6 ± 0.5	0.3 ± 0.5	0.6 ± 0.5	0.099[a]	0.159	> 0.999[c]	0.613	0.000
Abstraction	8	1.1 ± 1.0	0.8 ± 0.9	0.9 ± 0.8	0.089[a]	0.159	0.341[c]	0.613	0.500
Delayed recall	8	0.1 ± 0.4	0.1 ± 0.4	0.4 ± 0.7	0.133[a]	No change	0.170[c]	No change	0.500
Orientation	8	1.9 ± 1.8	2.1 ± 2.2	2.1 ± 2.1	0.670[a]	0.701	> 0.999[c]	0.354	0.250
Total	8	9.6 ± 6.9	8.9 ± 7.5	9.8 ± 7.4	0.344[a]	0.701	> 0.999[c]	0.354	0.099

Data are represented as mean ± sd. .
P-value : a, One-way ANOVA; b, paired *t*-test (Bonferroni correction).
CSFTT = cerebrospinal fluid tap test.

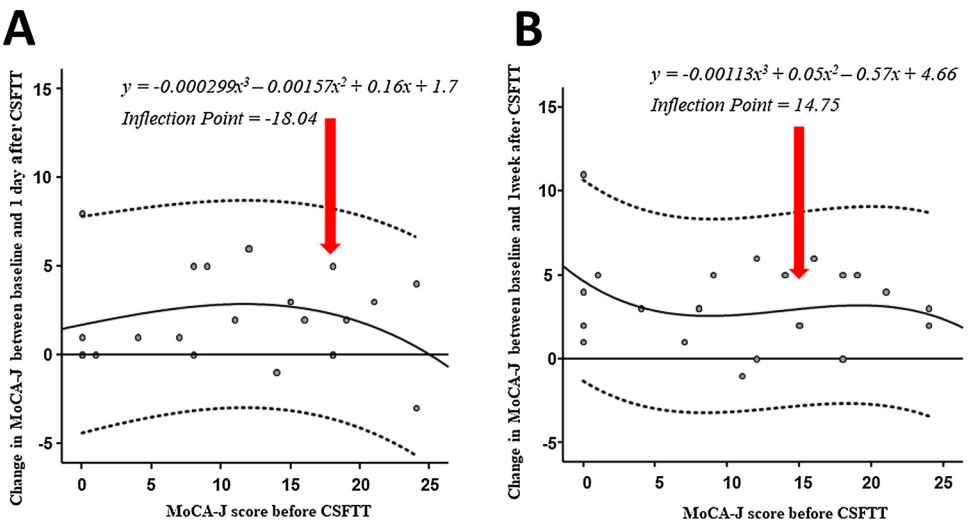

Fig. 2. Improvement in MoCA-J scores and regression curve representing the influence of baseline scores on MoCA-J scores in gait responders. Figure A shows the improvement rate 1 day after the CSFTT, and Figure B shows the improvement rate 1 week after the CSFTT. Inflection points are represented by arrows, indicating that the change in MoCA-J scores is reduced at the inflection points. Figure B shows that the regression curve is flat and can be improved without being influenced by baseline scores (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

Thus, it may be useful to evaluate cognitive function by MoCA-J in patients who have a walking difficulty. The cognitive function characteristics that show a large change in the MoCA-J sub-item score may be the main focus of observation in patients during the CSFTT period.

Although the exact numerical values obtained in this study cannot be used in the decision-making process on whether to perform shunt treatment on a new patient, it is important to explain to the patient both its potential for improving cognitive ability as seen in this study, as well as the limitations of the study. Once the patient can understand how this treatment can improve their ability, they may be more willing to agree to proceed with the treatment.

6. Limitations

Although a CSFTT is highly specific, its sensitivity is considered to be somewhat low [8,13] and there may be false negative cases within the non-responder group. In addition, because this study does not target patients undergoing a shunt surgery, there is also a possibility that false positives may be included in the gait responder group. It remains unclear at this time whether the properties obtained in a CSFTT predict abilities following shunt treatment, for which future studies involving shunt treatment groups would be warranted. The change in the scores of the MoCA-J after a CSFTT averaged out to approximately 2 points on the first day following a CSFTT, and 3 points 1 week following a CSFTT. However, these cannot be used as strict cut-off points; it is necessary to examine the diagnostic performance of the MoCA-J by analyzing the cases in which it was used.

Although the reliability of the MCI assessment by MoCA-J has been verified [6], the universality among ethnic groups in the evaluation of iNPH patients has not been verified, so it is necessary to conduct future research in other countries.

7. Conclusion

It is possible to perform evaluations using the MoCA-J from one day to one week following the CSFTT. It is also possible to better assess accuracy by focusing on the sub-items of executive functioning, capacity for attention and abstraction, and orientation.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare for this article

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