Use of Neuropsychological Test Battery for the Diagnosis of HIV-Associated Neurocognitive Disorders in Japan in 2013

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Objective: There is no exact data reporting prevalence of HIV-associated neurocognitive disorders (HAND) in Japan. In order to clarify the current status of HAND in Japan, we investigated the tests used to establish the diagnosis of HAND.

Method: We conducted a questionnaire survey to 12 major hospital registered for HIV treatment in Japan as of November 2013.

Results: The survey revealed no neuropsychological test battery used universally across Japan. Only three hospitals examined five or more domains of cognitive functions, while seven hospitals used neuropsychological tests without standardized score that could be used for assessment of severity of HAND, or making neuropsychological evaluation difficult.

Conclusions: The results of the survey did not allow accurate estimation of the prevalence of HAND in Japan. Establishment of a standardized battery of neuropsychological tests for accurate diagnosis of HAND is indispensable for future epidemiological studies.

Key words : HIV-associated neurocognitive disorders, neuropsychological test battery, cognitive domain, diagnosis

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Interest in HIV-associated neurocognitive disorders (HAND) has increased recently due to improvement in the prognosis of HIV-1 infected patients following the introduction of combination antiretroviral therapy^{1,2)}. The Frascati criteria endorsed by the American Academy of Neurology are regarded the gold standard for the diagnosis of HAND². However, contents of neuropsychological test batteries for the diagnosis are diversifying even in western countries, there has been little research which used the same neuropsychological test battery $^{3-5)}$. For this reason, the true prevalence of HAND remains unclear⁶. In Japan, several hospitals have applied comprehensive neuropsychological test batteries for the diagnosis of HAND depended upon decisions by the individual hospital⁷⁷. Unfortunately, this could inevitably create bias in the estimation of the true prevalence of HAND. Here we report the results of a nationwide survey of the neuropsychological tests applied by major hospitals in Japan involved in HIV treatment to establish the diagnosis

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The Japanese HIV Treatment Network System comprises the AIDS Clinical Center (ACC), which is located in Tokyo and is the major referral hospital, in addition to eight regional central hospitals located in eight geographic regions across Japan. In addition to the above nine institutions, three other hospitals were also included in this survey since they are also making an effort to diagnose HAND (the names of these 12 hospitals are listed in the Acknowledgment). The questionnaire survey was conducted from October through November 2013 and served to identify the neuropsychological tests used for the diagnosis of HAND across Japan, including cognitive functional tests. The questionnaire was answered by the clinical psychologist(s) at each hospital.

Cognitive functional tests were applied 338 times in the 12 hospitals during the preceding one year. One hospital had no experience in HAND evaluation. Among 11 hospitals, 10 developed their own battery of neuropsychological tests while the remaining hospital did not have a fixed test set. A total of 25 different neuropsychological tests were employed by 10 hospitals, and only two used the same test battery ; nine battery sets were used in 10 hospitals (Table 1). Small but comprehensive combinations of

Table 1 Neuropsychological tests and their corresponding domains used in 10 hospitals												
	Assessed cognitive domains	Neuropsychological test	A	В	C	D	E	F	G	Н	Ι	J
1	Information processing speed	Digit Symbol ¹ Trail Making Test A	0 0	0 0	0 0	0 0	0 0	0	0 0	\bigcirc^2 \bigcirc	0	0
2	Attention/Working Memory	Digit Span ¹ Tapping Span ³	0 0	0	0	0	0	0	0	\bigcirc^2	0	0
3	Verbal	Verbal Fluency Verbal Fluency ⁴ Verbal Fluency ⁵	0	0	0	0	0	0	0	0		0
4	Executive function	Similarities ¹ Similarities ⁵ Similarities ⁶ Trail Making Test B Stroop Test Behavioral Assessment of the Dysexecutive Syndrome	0	0	0	0	0		0 0	0 0 0	0	0
5	Visual-spatial construction	Block Design ¹ Cube drawing Draw a Clock test Rey-Osterrieth Complex Figure Test	0			0 0 0		0	0	\bigcirc^2 \bigcirc	0	0
6	Memory (Learning)	Rey-Osterrieth Complex Figure Test Story ⁷ Picture Recognition ⁷ Appointments ⁷	0	0	0		0	0	0			
7	Motor	Grooved Pegboard	0									
Number of domains covered using tests with standardized score			7	4	4	4	3	5	5	4	3	4

Among the 12 hospitals, 10 (A-J in Table) developed their own neuropsychological test batteries. Tests with standardized scores that could be used with standard deviation (SD) values are underlined. In addition to these tests, the combinations of brief tests such as the Mini-Mental State Examination (MMSE), Revised Hasegawa's Dementia Scale (HDS-R), Modified Mini-Mental State Examination (3MS), Frontal Assessment Battery (FAB), International HIV Dementia Scale, and Japanese HIV Dementia Scale, were used to screen severe cognitive impairment. Wechsler Adult Intelligence Scale Third Edition (WAIS-III) and Raven's Matrices Test were used to measure intelligence.

1. A subtest of WAIS-III⁸⁾. 2. A subtest of the Revised Wechsler Adult Intelligence Scale⁹⁾. 3. A subtest of the Revised Wechsler Memory Scale¹²⁾. 4. A subtest of the HDS-R, with no standardized score¹³⁾. 5. A subtest of FAB with no standardized score¹⁴⁾. 6. A subtest of the 3MS with no standardized score¹⁵⁾. 7. A subtest of the Rivermead Behavioral Memory Test¹⁶⁾.

neuropsychological subtests were used in seven hospitals. The Wechsler Adult Intelligence Scale Third Edition (WAIS-III)⁸⁾, which was designed to measure intelligence, was applied by two hospitals. The Mini-Mental State Examination (MMSE) was used in all 12 hospitals, while the Digit Symbol and Digit Span were used in 10 hospitals, and the Verbal Fluency test was used by nine hospitals. The Trail Making Test A (TMT-A) and Similarities were used in eight and seven hospitals, respectively.

We extracted subtests that used the standard deviation (SD) as a standardization index for the diagnosis of HAND. The most frequently used subtest was the Digit

Symbol and Digit Span, followed by the TMT-A, Trail Making Test B (TMT-B) and Block Design. One hospital used the Digit Span and Digit Symbol tests, which were based on the Wechsler Adult Intelligence Scale-Revised version⁹⁾, as well as from WAIS-III. The Verbal Fluency and Similarities were also cited from various sources by those hospitals. The above findings resulted in variability in clinical practice and scoring. Although the clinical psychologists in all hospitals were aware of the HAND diagnostic criteria, 10 (83%) hospitals did not determine the severity of HAND for the following reasons ; a) difficulties in determining whether or not the neurocognitive impairment is due to HAND, b) test reading and interpretation of cognitive domains are non-specific, and c) the use of subtests without normative data convertible to SDs.

Although a definitive diagnosis of HAND requires assessment of five or more cognitive domains using tests with demographically adjusted scores²⁾, only four out of 10 hospitals used a fixed battery of tests, and assessed their corresponding cognitive domains. The information processing speed was assessed by the Digit Symbol and TMT-A in four of four hospitals. The Digit Span and Story were used for evaluation of attention/working memory and memory, respectively. The other cognitive domains were assessed by different tests in each of the 12 hospitals.

Our survey clarified the current inadequacy in the diagnosis of HAND in Japan. The participating hospitals used different batteries, and one hospital varied the content of the battery according to the patients studied. Some batteries were commonly used by several hospitals and the trend was based on previous studies, suggesting that each hospital independently adopted tests that had been applied overseas. The diverse batteries of neuropsychological tests used in Japan are similar to those described in previous studies in other countries⁵⁾. Interestingly, Kamminga et al.⁵⁾ found that only three subtests were mutually used across 19 international studies and that no universal battery was used in these studies.

Previous studies assessed cognitive domains using various subtests⁵; including the Digit Span for attention/ working memory, TMT-A for information processing speed, TMT-B for executive function, Verbal Fluency for verbal, and Rey-Osterrieth Complex Figure Test for visual-spatial construction. The majority of currently used neuropsychological tests share several cognitive domains. Understandably, no fixed domains in any of the tests is universally appropriate for all patients¹⁰. For these reasons, a neuropsychological test battery should comprise different subtests suited to the patient's cognitive dysfunction¹¹⁾. Thus, a trained psychometrist is required to be selective in administering the most suitable neuropsychological test battery when assessing cognitive function, and interpret the characteristic of the disorder in the individual patient. Based on this, the value of neuropsychological evaluation is sometimes limited, although the criteria for the diagnosis of HAND require assessment of five or more cognitive domains using specific neuropsychological tests.

In conclusion, the exact prevalence of HAND in Japan remains difficult to determine under the current clinical practice. Establishment of a standardized battery of neuropsychological tests with defined scores that cover five or more cognitive domains is indispensable for accurate diagnosis of HAND and future epidemiological studies.

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Author Disclosure Statement

The authors declare no conflict of interest.

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日本における HIV-associated neurocognitive disorders の 神経心理検査バッテリーによる診断の現況

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目的:本邦における HIV-associated Neurocognitive Disorders (HAND)の有病率は報告されていない。本邦の HANDの神経心理学的診断の実態を調査し、有病率把握に関する課題を明らかにした。 対象および方法:HANDの評価を行っている 12 施設(ACC, 8 ブロック拠点病院および3 中核拠点病院)を対象に神経心理検査バッテリーの内容、および HANDの判定状況についてアンケート方式で調査を行った。

結果:7 施設で HAND の判定が行われていなかった。判定を行わない理由として,標準値を算 出するためのデータが不足した神経心理検査を使用していることと神経心理検査結果の解釈が難し いことがあげられた。また,HAND の判定基準を満たす5つ以上の認知領域を評価しているのは3 施設であった。

結論:本邦において HAND の有病率を把握することは困難な状況にある。今後,疫学的研究のために,HAND を診断できる神経心理検査バッテリーの確立が望まれる。

キーワード:HIV 関連神経認知障害,神経心理検査バッテリー,認知領域,診断