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Clinical Assessment for Attention Test in adult with Attention-Deficit/ Hyperactivity Disorder for Evaluation of symptoms and medication effects

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ABSTRACT

Purpose: Although attention-deficit/hyperactivity disorder (ADHD) has historically been thought to be predominantly a childhood disorder, many cases of ADHD persist into adulthood. Therefore, it is necessary to assess the symptoms and efficacy of medication using objective assessment tools in adults with ADHD. The aim of this study was to assess usefulness of the Clinical Assessment for Attention Test (CAT) comprising Span, Cancellation and Detection Test, Symbol Digit Modalities Test, memory updating test, paced auditory serial addition test, position Stroop test, and continuous performance test (CPT) for adults with ADHD.

Methods: ADHD outpatients without intellectual disorders (IQ ≥ 80) with age range of 20-39 years were recruited (15 males and 10 females; mean age 27.7 ± 5.5). The participants did not receive any psychopharmacological treatment and were assessed with CAT at baseline.

Results: The patients showed significantly decreased attention scores in Cancellation and Detection Test (Visual Cancellation Task and Auditory Detection Task) and CPT, although this decrease was not correlated to age or intelligence quotient. The effect of psychopharmacological treatment was assessed in two participants using CAT.

Discussion: Cancellation and Detection Test and CPT are useful tools to support the diagnosis of adults with ADHD as well as evaluation of the efficacy of psychopharmacological treatment.

Keywords: Attention-deficit hyperactivity disorder, Clinical Assessment for Attention Test, Continuous performance test, Extended-release methylphenidate, Atomoxetine

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by a persistent pattern of inattention and/or hyperactivity/impulsivity. According to the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5), ADHD interferes with functioning or development in multiple settings [1]. The worldwide prevalence of childhood ADHD was estimated to be 3.4% (CI 95% 2.6-4.5) in a meta-analysis [2]. Historically, ADHD has predominantly been thought to be a childhood disorder that can remit through adolescence. However, recent studies indicate that ADHD is conceptualized as a neurodevelopmental disorder that continues into adulthood in approxi-

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mately 50%-65% of diagnosed cases [3, 4]. The main symptoms in children with ADHD are inattention and hyperactivity, although the most common symptoms in adults with ADHD is inattention [5]. The prevalence of adulthood ADHD was 2.5% (95% CI 2.1-3.1) in a meta-regression analysis [5]. In Japan, the prevalence of adulthood ADHD has been estimated to be 1.65% [6].

In children with ADHD, diagnosis is made and psychopharmacological efficacy is evaluated on the basis of clinical symptoms observed by parents at home or by teachers at school. Pharmacological treatment is an important part of ADHD management both in children and adults. Dysregulation of the monoaminergic neurotransmitters, primarily norepinephrine and dopamine, has been hypothesized to play a central role in ADHD pathophysiology [7]. ADHD is likely attributable to the impairment of executive functions in the frontal lobe, specifically in the pre-frontal cortex [8]. Osmotic release oral system-methylphenidate (OROS-MPH), atomoxetine (ATX), guanfacine, and lisdexamfetamine have been approved for the treatment of children with ADHD in Japan. Three of these four drugs (OROS-MPH, ATX, and guanfacine) have also been approved for the treatment of adults with ADHD in Japan. In adults, ADHD is typically diagnosed according to various criteria such as DSM-5. Moreover, the efficacy of medication for adults with ADHD is assessed based on their subjective or objective symptoms or using rating scales such as the Conners' Adult ADHD Rating Scales (CAARS). It is important to precisely determine of treatment effectiveness using objective assessment tools. The continuous performance test (CPT) is a computer-administered neuropsychological test, and it is widely used worldwide for measuring sustained attention [9]. CPT aids clinical assessment and medication management of ADHD [10]. As a standardized CPT, the Clinical Assessment for Attention Test (CAT) was developed and is available in Japan [11]. CAT is a multiple objective assessment neuropsychologic test battery including CPT. CAT has been standardized with Japanese healthy adolescents and adults and is a useful and validated tool for measuring attention in patients with brain injury; however, it has not been well validated for adults with ADHD [12].

The first aim of this study was to assess the usefulness of CAT as an objective assessment tool for adults with ADHD. The second aim was to demonstrate the usefulness of CAT for detecting the effectiveness of psychopharmacological treatment in adults with ADHD.

Subjects and Methods

Subjects

The subjects of this study were outpatients in the Department of Neuropsychiatry, Ehime University Hospital. The study period was from January 2013 to December 2018. The inclusion criteria were as follows: (1) adults aged 20-39 years; (2) who were diagnosed with ADHD based on the DSM-5 criteria; (3) who visited our hospital for the first time during the study period; (4) who were not treated with any psychotropic, and (5) who signed informed consent forms. Patients with a full scale intelligence quotient (FSIQ) lower than 80 using Wechsler Adult Intelligence Scale III (WAIS-III) were excluded. The present study included 25 patients with ADHD (15 males and 10 females; mean age 27.7 ± 5.5; range, 20-38 years).

Instruments

Assessments were made using the Adult ADHD Self-Report Scale (ASRS) 1.1 [13] and CAARS [14]. ASRS was developed in conjunction with the World Health Organization and is widely used in clinical settings in Japan. ASRS comprises two parts: A (6 items) and B (12 items). ASRS Part A is recommended as a screening tool for adults with ADHD. Frequency of symptom occurrence was rated on a 5-point Likert scale (0 = never; 1 = rarely; 2 = sometimes; 3 = often; 4 = very often). Items 1, 2, 3, and 4 represent symptoms of inattention and items 5 and 6 represent symptoms of hyperactivity and impulsivity. When four or more items are more frequent than the cut-off (>2 points for Q1-Q3 and >3 points for Q4-Q6), the respondents are considered to present with clinical symptoms of ADHD.

CAARS is a 66-item self-administered questionnaire for adults with ADHD. Each item is rated on a scale from 0 to 3, and the total scores range from 0 to 198. CAARS comprises four factor-derived subscales (inattention/memory, hyperactivity/irritability, impulsivity/emotional lability, and self-concept), two ADHD symptom subscales (inattentive symptoms and hyperactive-impulsive symptoms), and one ADHD index consisting of items that distinguish between patients with ADHD and normal individuals. Conners et al [14] suggested

that those with T scores of >65 on the ADHD index of CAARS are likely to be diagnosed with ADHD. The reliability and validity of the Japanese version of CAARS have been proven [15].

CAT

CAT is a standardized test battery for assessing generalized attention. It comprises seven sub-tasks, with standardized, age-appropriate values for each task established by the Japan Society for Higher Brain Dysfunction [12]. CAT includes Span (Digit Span and Tapping Span), Cancellation and Detection Test (Visual Cancellation Task and Auditory Detection Task), Symbol Digit Modalities Test (SDMT), memory updating test, paced auditory serial addition test (PASAT), position Stroop test, and CPT.

Span

Span consists of forward and backward spans. Digit Span uses auditory stimuli, and Tapping Span uses visual stimuli.

Cancellation and Detection Test

Cancellation and Detection Test consists of a Visual Cancellation Task, which involves visual stimuli, and an Auditory Detection Task, which involves auditory stimuli. The contents of Visual Cancellation Task are to cross out a target stimulus dispersed within rows of random interfering stimuli displayed on a sheet as soon as possible using a pencil. Two sets of the stimulus sequence were used: digits (part I) and kana-letters (part II). The time required to complete all tasks and the ratio of correct answers to the total number of stimuli were assessed. The contents of Auditory Detection Task are to respond to the target sound among five different sounds of kana-letters read at the rate of one letter per second on a compact disc. Subjects are asked to tap their finger each time they hear the target letter. The proportion of correct answers and their accuracy (the number of accurate answers compared to the number of total responses) were assessed.

SDMT

Subjects are given a sheet of paper at the top of which is printed the key (9 abstract symbols and 9 corresponding numbers). A sequence of 110 symbols, each printed in a square, is presented below the key. Empty squares are located below the squares containing the symbols. Subjects are asked to make as many associations as possible within 90 seconds.

Memory updating test

In memory updating Test, sequences of numbers are presented orally. Subjects listen to strings of digits of unknown length from their perspective and are asked to recall the 3 or 4 most recently presented numbers in memory.

PASAT

In PASAT, subjects listen to a digital recording of digits presented one at a time and are then asked to add the number they just heard with the number they heard before it. For example, if the numbers "3," "1," and "2" were presented, the participant should answer "4" and then "3." As for the interval between each number, 1- and 2-second intervals were tested. The proportion of correct answers was assessed in each test.

Position Stroop test

Position Stroop test uses a Japanese-kanji version of the High-Mid-Low format developed by Sohlberg [16]. Subjects are asked to call out the position of kanji that means high, mid, or low, instead of their meaning. Completion time and proportion of correct answers were assessed.

CPT

CPT is a computerized vigilance test that presents stimuli briefly and provides reaction times as well as accuracy data. In the simple version, subjects respond to the digit "7" that appeared briefly in the center of the screen at random intervals. In the X version, digits appear in a random order, and subjects are asked to respond to every "7." In the more difficult (AX) version, subjects are asked to respond to "7" only if it follows "3." Each subject's reaction time (RT), proportion of correct answers, and accuracy were assessed for each version. CAT took approximately 120 minutes to complete.

Procedure

The patients who were enrolled in this study completed ASRS Part A and CAARS; they also completed WAIS-III at the first and second hospital visits. The study protocol was explained to the subjects who were diagnosed with ADHD, and they were asked to complete their first CAT. All subjects completed CAT in the medication-off condition, and two participants (a 21-year-old female treated with 100 mg ATX for 126 days and a 26-year-old

male treated with 27 mg OROS-MPH for 308 days) were assessed using CAT again in the maintenance medication condition. To rank the degree of attention deficits, standardized data of each assessment in the CAT manual were employed [12].

Statistical analyses

Scores of some tasks of CAT are associated with age and intelligence. Spearman's rank correlation coefficient was used to assess the association of score of each task in CAT with age or FSIQ in WAIS-III. The present study included subjects in their twenties; thus, we used the normal value of the corresponding twenties age group (abnormal score <−1.0 SD). The significance level was 5%. All data were analyzed using SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA).

Ethics

This study was approved by the institutional review board of Ehime University Graduate School of Medicine (#1206008). All subjects agreed to participate and provided written informed consent.

Results

CAT

At baseline, no patient was treated with any antipsychotic. Characteristics of patients with ADHD and their FSIQ are presented in Table 1. Average ASRS score was >4. Inattention scores and ADHD symptoms/index scores of CAARS were >65. Results of individual assessment items of CAT are summarized in Table 2. In this study, the mean (SD) scores of healthy controls from the CAT manual were used as reference [12]. Attention scores in the Cancellation and Detection Test (Visual Cancellation Task and Auditory Detection Task), SDMT, memory updating test, PASAT, and CPT were lower patients with ADHD than in standardized controls. Scores of Span, SDMT, PASAT, and position Stroop test were correlated to FSIQ. The score of memory updating test was correlated to age. There was no correlation of scores of Cancellation and Detection Test (Visual Cancellation Task and Auditory Detection Task) and CPT with age or FSIQ.

Psychopharmacological treatment

Two patients treated with ATX or OROS-MPH were assessed using CAT. In the Cancellation and Detection Test, there were significant improvements in completion time and the proportion of correct answers (Figure 1). In addition, there were improvements in RT and the proportion of correct answer in CPT, except in the X version in case #2 (Figure 2).

Table 1. Demographic characteristics of subjects

Characteristic	Subjects (N = 25)
Age, years	27.7 (5.5)
Sex (male:female)	15:10
Specify of ADHD, n (male: female)	
Combined presentation	12 (7:5)
Predominantly inattentive presentation	13 (8:5)
WAIS-III summary scores	
FSIQ	104.5 (14.8)
Verbal IQ	105.9 (13.0)
Performance IQ	101.3 (17.0)
WAIS-III index scores	
Verbal Comprehension	109.2 (13.4)
Perceptual Organization	101.1 (17.1)
Working Memory	94.5 (17.5)
Processing Speed	93.8 (16.4)
ASRS	4.63 (1.1)
CAARS	
Inattention/memory	73.3 (10.2)
Hyperactivity/irritability	62.1 (12.0)
Impulsivity/emotional lability	63.7 (13.3)
Self-concept	62.0 (8.4)
Inattentive symptoms	74.2 (11.0)
Hyperactive-impulsive symptoms	64.8 (12.6)
ADHD symptoms	72.5 (10.7)
ADHD index	68.8 (10.3)

Values are presented as mean (standard deviation)

WAIS, Wechsler Adult Intelligence Scale; IQ, intelligence quotient; ASRS, Adult ADHD Self-Report Scale; CAARS, Conners' Adult ADHD Rating Scale; ADHD, attention-deficit/hyperactivity disorder

Discussion

The aim of this study was to explore the use of CAT in Japanese adults with ADHD and evaluate its effectiveness in this population. This study yielded two novel findings. First, although CAT was developed and standardized for Japanese adults with brain injuries, this research proved the usability of Cancellation and Detection Test and CPT in CAT for assessing attention impairment in Japanese adults with ADHD. Second, Cancellation and Detection Test and CPT in CAT are useful for assessing the effectiveness of pharmacological treatment, even considering the limitation of the small study sample (two 2 participants) treated with medica-

Table 2. Results of clinical assessment for attention

Task	Assessment	Subjects (N = 25)	Standardized data	Significant difference	FSIQ, r	Age, r
Span						
Digit, forward	Span	6.7 (1.1)	7.5 (0.9)	n.s.	0.60**	0.10
Digit, backward	Span	5.3 (0.8)	5.4 (0.7)	n.s.	0.37	0.31
Tapping, forward	Span	6.3 (1.1)	6.9 (1.1)	n.s.	0.34	−0.12
Tapping, backward	Span	6.2 (1.3)	6.2 (1.3)	n.s.	0.13	−0.17
Cancellation and Detection Test						
Visual cancellation						
Part A, “3”	Completion time	90.0 (23.5)	67.0 (10.3)	2SD	−0.01	0.02
	% correct answer	99.1 (1.7)	99.6 (0.7)	n.s.	−0.03	−0.10
Part B, “kana”	Completion time	103.5 (21.6)	81.9 (13.0)	1SD	0.11	−0.17
	% correct answer	99.8 (0.6)	98.3 (1.8)	n.s.	0.01	0.15
Auditory detection	% correct answer	94.2 (6.6)	98.8 (1.5)	2SD	0.24	0.12
	Accuracy	96.8 (5.9)	99.0 (1.2)	1SD	0.15	−0.03
SDMT	Achievement rate	53.3 (8.1)	67.9 (10.5)	1SD	0.42*	0.24
Memory updating test						
Three digits	% correct answer	90.8 (8.9)	96.4 (4.6)	1SD	0.01	0.26
Four digits	% correct answer	74.1 (14.0)	85.0 (13.3)	n.s.	0.36	0.51**
PASAT						
2 s	% correct answer	67.7 (21.7)	86.9 (10.4)	1SD	0.51**	−0.21
1 s	% correct answer	42.3 (14.0)	57.7 (14.7)	1SD	0.36	−0.21
Position Stroop test	Completion time	69.0 (13.9)	63.6 (11.7)	n.s.	−0.15	0.23
	% correct answer	97.9 (2.6)	99.0 (1.2)	n.s.	−0.50*	−0.16
CPT						
Simple version	Reaction time	325.1 (79.5)	283.5 (37.7)	1SD	0.22	0.02
	% correct answer	97.9 (2.6)	98.9 (1.7)	n.s.	0.20	−0.01
X version	Reaction time	507.2 (69.0)	439.6 (55.0)	1SD	0.16	−0.11
	% correct answer	95.4 (8.8)	99.1 (3.7)	n.s.	0.08	0.07
AX version	Reaction time	482.2 (63.9)	415.7 (60.3)	1SD	−0.07	−0.28
	% correct answer	86.3 (18.0)	96.9 (9.6)	1SD	0.00	0.30

Scores between 1 SD and 2 SD or below and scores > 2 SD than the average of the healthy controls are indicated (1SD, 2SD)
SDMT, Symbol Digit Modalities Test; PASAT, paced auditory serial addition test; CPT, continuous performance test
Spearman’s rank correlation coefficient, *$P < 0.05$, **$P < 0.01$

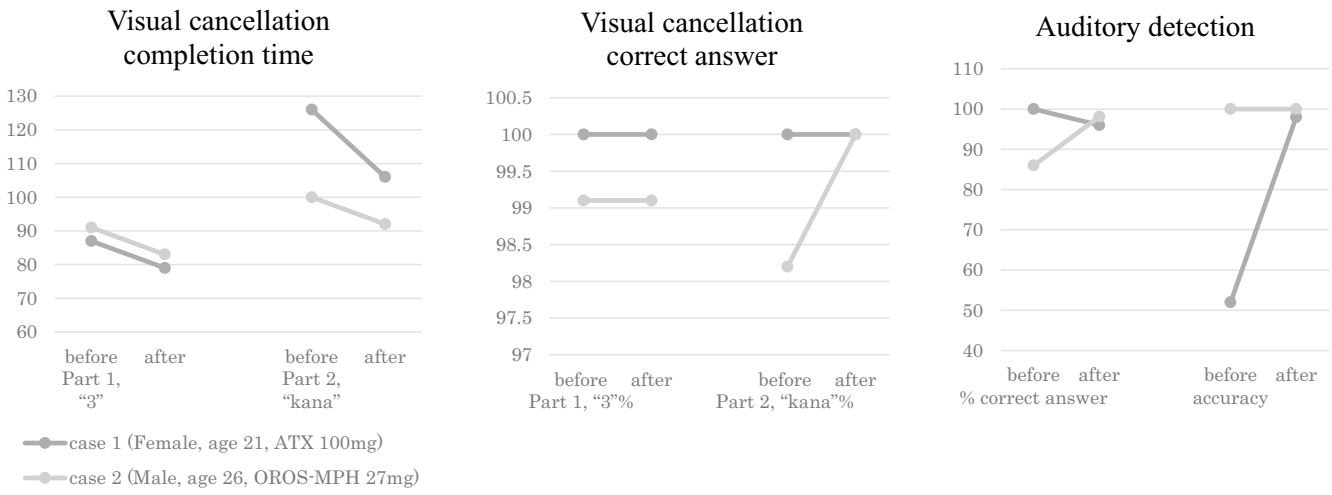

Figure 1. Changes in Cancellation and Detection Test scores
ATX, atomoxetine; MPH, methylphenidate

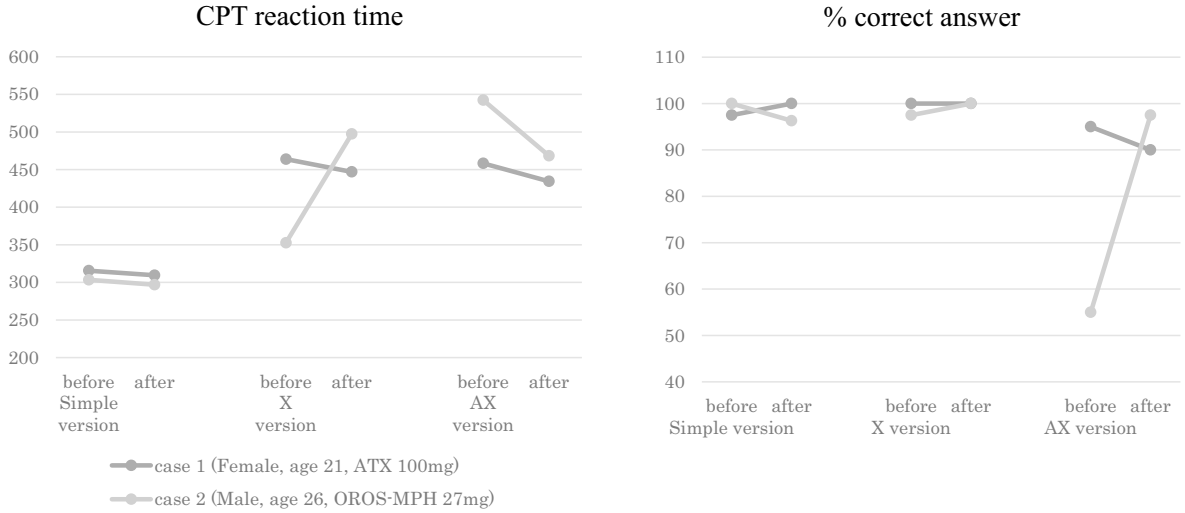

Figure 2. Changes in CPT scores
ATX, atomoxetine; MPH, methylphenidate

tions.

Previous research has revealed significant correlations between age and scores of PASAT and position Stroop test, and also between FSIQ and score of PASAT [17, 18]. Therefore, the present study excluded participants aged >40 years as well as those with intellectual disabilities (FSIQ < 80). Nonetheless, some tasks were statistically associated with age and FSIQ. Digit Span in CAT is the same task as Digit Span in WAIS-III. SDMT in CAT is similar to SDMT in WAIS-III with minor differences, in terms of time limit and subject of associations. Obviously, our results indicated a correlation of FSIQ score with both Digit Span ($r = 0.60$, $P < 0.01$) and SDMT ($r = 0.42$, $P < 0.05$). In addition, scores of position Stroop test ($r = -0.50$, $P < 0.05$) and PASAT ($r = 0.51$, $P < 0.01$) were correlated with FSIQ in this study. These results were consistent with those of previous studies [17, 18]. The present study suggested that Cancellation and Detection Test and CPT in CAT are useful for assessing the characteristics of adults with ADHD because these tests do not consider age and FSIQ.

Several previous studies have reported that certain deficits in visual and auditory information processing exist in ADHD [19-21]. Cancellation and Detection Test is associated with visual and auditory selective attention and may be helpful in detecting ADHD symptoms in adults. CPT is considered a well-validated tool for measuring sustained attention and has been used for objective assessment of neurocognitive function in ADHD as well as response to pharmacological treatment [22]. A previous study indicated that CPT shows greater sensitivity than self-reported scales in patients with ADHD also in individuals with malingering [23]. Two participants who showed improvements with medication were assessed with Cancellation and Detection Test and CPT. The results suggested that these tasks were useful to support ADHD diagnosis and to evaluate the effectiveness of psychopharmacological treatment. However, RT of the X version of CPT in case #2 was considerably extended after treatment. One of the possibilities is that because CPT required approximately 40 minutes for completion, some participants might have experienced sleepiness and/or felt difficulty in concentrating during CPT. Other CPTs such as Test of Variables of Attention (TOVA) and the third edition of Conners' Continuous Performance Test (Conners' CPT-III) are available to evaluate attention function. TOVA takes 21.8 minutes to complete, while its shorter version takes 10.9 minutes. Conners' CPT-III takes 14 minutes. The usefulness of TOVA and Conners' CPT-III in adults with ADHD has been evaluated [24-26]. However, to the best of our knowledge, the Japanese version of TOVA or Conners' CPT-III cannot be used at this point. In future studies, it is necessary to focus on cases that use CPT sensitivity and specificity to detect impairments in adults with ADHD in Japan.

Our study has several limitations. The first limitation is that only two patients were enrolled in the longitudinal study with or without medication. We did not perform a statistical analysis of the efficacy of psychopharmacological treatment. In addition, the test-retest reliability of CAT has been indicated

for patients with brain damage in a 1-week period [12]; however, the practice effect may have influenced the results of this study. As the second limitation, our study only assessed impairment in attention although the triple pathway model of ADHD dealt with more comprehensive deficits in neurocognition, including delay-related processing and impaired temporal processing as well as deficits in inhibitory control [27]. Other limitations include the small number of participants, absence of sex differences, and lack of a control group. Despite these limitations, CAT can help psychiatrists assess symptoms and diagnose ADHD in adults.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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