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Simultaneous assessment of cognitive and affective functions in multiple system atrophy and cortical cerebellar atrophy in relation to computerized touch-panel screening tests

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ABSTRACT

Cognitive impairment and affective dysfunction of multiple system atrophy (MSA) and cortical cerebellar atrophy (CCA) have not been simultaneously examined comparing standard test batteries and a sensitive tool to detect subtle cognitive decline in patients. In the present study, we simultaneously examined cognitive and affective ability in MSA with predominant cerebellar ataxia (MSA-C, n = 25), MSA with predominant parkinsonism (MSA-P, n = 8), and CCA (n = 14) patients using computerized touch panel screening tests. Mini-mental state examination (MMSE), Hasegawa dementia scale-revised (HDS-R), frontal assessment battery (FAB), and Montreal cognitive assessment (MoCA) scores were significantly lower in MSA-C patients than in age-and gender-matched normal controls. One MSA-C patient showed a decrease in the regional cerebral blood flow (rCBF) of the frontal lobe. MSA-P patients showed no such cognitive decline. Only FAB and MoCA scores were significantly lower in the CCA patients. MSA and CCA patients also showed a mild to moderate depressive state. Touch-panel screening tests demonstrated a significant decline of beating devils game in all three disease groups including MSA-P patients, and a significant extension of the flipping cards game only in MSA-C patients. The present study demonstrated different cognitive and affective functions among MSA-C, MSA-P, and CCA patients, and a sensitive screening method for cognitive assessment using touch-panel tests.

1. Introduction

Multiple system atrophy (MSA) is an adult-onset, sporadic, progressive neurodegenerative disease characterized by cerebellar ataxia, parkinsonian features, autonomic failure, urogenital dysfunction, and corticospinal disorders [1]. The neuropathological findings include widespread and abundant central nerve system (CNS)-synuclein-positive glial cytoplasmic inclusions (Papp–Lantos inclusions) in association with neurodegenerative changes in striatonigral or olivopontocerebellar structures [2]. On the other hand, cortical cerebellar atrophy (CCA) has been considered as a disease entity that develops cerebellar cortical lesions mainly in the cerebellar vermis, but a collective view on the distribution of idiopathic CCA has not yet been established [3].

Recent reports [4–10] suggested that cognitive impairment of MSA is more frequent than previous reports. However, few studies compared MSA with predominant cerebellar ataxia (MSA-C) to MSA with predominant parkinsonism (MSA-P) in relation to cognitive assessment. Only one study reported significant declines of the mini-mental state examination (MMSE) score, verbal memory, visuospatial functions, and speech and language ability in MSA-C patients than in normal controls, and significant declines of verbal memory and executive function in MSA-C patients than in MSA-P patients [11]. A previous report showed a frontal dysfunction in CCA [12]. As for affective functions, MSA and CCA patients were reported to be depressive [13,14], but no report simultaneously compared cognitive and affective functions between MSA and CCA.

We have reported a computerized touch panel-type screening test for early detection of ischemic stroke (IS), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) [15–17]. However, such a computerized touch panel test has never been applied to MSA-C, MSA-P, and CCA patients. The aim of the present study was, therefore, to simultaneously

Abbreviations: AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; ANOVA, analysis of variance; CCA, cortical cerebellar atrophy; CNS, central nerve system; DSM-IV, diagnostic and statistical manual of mental disorders, 4th edition; eZIS, easy Z-score imaging system; FAB, frontal assessment battery; GDS, geriatric depression scale; HDS-R, Hasegawa dementia scale-revised; IS, ischemic stroke; MMSE, mini-mental state examination; MoCA, Montreal cognitive assessment; MRI, magnetic resonance imaging; MSA, multiple system atrophy; MSA-C, MSA with predominant cerebellar ataxia; MSA-P, MSA with predominant parkinsonism; NC, normal controls; PD, Parkinson's disease; rCBF, regional cerebral blood flow; SD, standard deviation; SPECT, single-photon emission tomography; ^{99m}Tc-ECD, ^{99m}Tc labeled ethyl cysteinate dimer; VI, vitality index.

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Table 1
Demographic data of participants in this study.

	Control	MSA-C	MSA-P	CCA
No. of cases	106	25	8	14
Gender (M/F)	50/56	12/13	1/7	6/8
Age at onset (y)	–	60.4 ± 8.2	62.4 ± 5.7	50.9 ± 21.2
Duration of disease (y)	–	2.9 ± 1.8	4.1 ± 3.6	14.4 ± 15.4
Age at exam. (y)	64.6 ± 6.6	63.2 ± 7.2	66.4 ± 4.7	65.3 ± 12.6
SARA	–	17.6 ± 5.7	–	15.2 ± 6.8
UMSARS-II	–	–	25.5 ± 6.4	–

examine cognitive and affective functions in MSA-C, MSA-P, and CCA patients in relation to the computerized touch panel screening test.

2. Patients and methods

2.1. Participants

Twenty-five MSA-C patients (12 male, 13 female; age at exam., 63.2 ± 7.2 years; age at onset 60.4 ± 8.2 years), 8 MSA-P patients (1 male and 7 female; age at exam., 66.4 ± 4.7 years; age at onset, 62.4 ± 5.7 years), and 14 CCA patients (6 male, 8 female; age at exam., 65.3 ± 12.6 years; age at onset, 50.9 ± 21.2 years), who obtained medical care in Okayama University Hospital from April 2010 to May 2012 participated in this study. The MSA patients were divided into cerebellar (MSA-C) or parkinsonian (MSA-P) type based on the diagnostic criteria for MSA [1]. The CCA patients were diagnosed by clinical symptoms and exclusion diagnosis [18]. One hundred and six age- and gender-matched individuals who lacked any history of neurological or psychiatric disorders were included as normal controls (NC) (50 male, 56 female; age at exam., 64.6 ± 6.6 years) in this study. Clinical details for each group are shown in Table 1.

2.2. Cognitive and affective assessments

Cognitive functions were assessed using the MMSE [19], Hasegawa dementia scale-revised (HDS-R) [20], frontal assessment battery (FAB) [21], and Montreal cognitive assessment (MoCA) [22] scores. Affective functions such as depression and vitality were assessed using the geriatric depression scale (GDS) [23,24] and the vitality index (VI) [25].

MMSE evaluates seven aspects of cognition such as orientation, registration, attention and calculation, recall, comprehension of spoken language (naming objects, spoken language ability, following commands), writing, and construction drawing [19]. HDS-R evaluates orientation, immediate recall, serial subtraction, backward digit recitation, recall of three words, recall of five objects, and verbal fluency (generating names of vegetables) [20]. FAB is a six-item scale designed to evaluate frontal deficits, including conceptualization (similarities test), mental flexibility (lexical fluency), motor programming (Luria's "fist-edge-palm" test, conflicting instructions, and Go–No go tests), and environmental autonomy (prehension behavior) [21]. MoCA evaluates visuospatial and executive ability, naming, memory, attention, language, abstraction, delayed recall, and orientation with a maximum of 30 points and a cutoff score of 26 (25 or below indicating impairment). This has superior sensitivity for detecting patients with MCI and also reflects frontal function including attention, concentration, working memory and abstract thinking [22,26]. GDS involves a screening questionnaire for depression and anxiety. Total scores range from 0 to 15, with higher scores indicating more symptoms of depression [23,24]. VI is composed of five subscales relating to common basic activities of inpatients with long-term care, with a maximum performance score of 10 [25].

2.3. Touch-panel screening test

A touch-panel screening test for the early diagnosis of dementia (the Ryokansan, Ohtsu Computer Corp, Ohtsu, Japan) was administered to all subjects. The touch panel was large and the test did not include tasks such as writing that require fine manual dexterity. The screening test consisted of the following four games: beating devils, flipping cards, arranging pictures, and finding mistakes. We recorded accuracy (percent correct) in the beating devils game and the time to complete the game for the other three games. In the beating devils game, patients were instructed to distinguish between the emergence of heroes and devils, and we measured their accuracy in exterminating only the devils during a 30-sec period (Fig. 1a). In the flipping cards game, we measured the time (sec) to turn over all pairs of matching picture

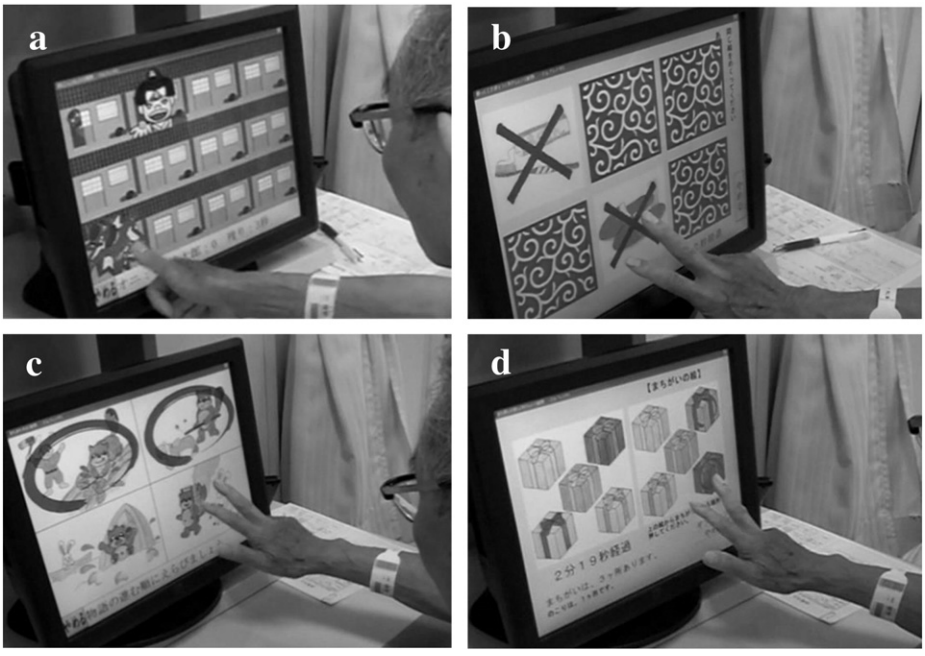

Fig. 1. Examples of computerized touch panel screen for (a) beating devils, (b) flipping cards, (c) arranging pictures, and (d) finding mistakes games.