Research Article

iMedPub Journals
www.imedpub.com

Journal of Brain Behaviour and Cognitive Sciences

2018
Vol.1 No.3:14

Comparison of Cognitive, Affective, and Activities of Daily Living Functions in Patients with Parkinson's Disease and Progressive Supranuclear Palsy

Kenji Hinotsu, Nozomi Hishikawa, Yusuke Fukui, Kota Sato, Mami Takemoto, Toru Yamashita, Yasuyuki Ohta, Koji Abe*

Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

***Corresponding author:** Koji Abe

abekabek@cc.okayama-u.ac.jp

Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, 700-8558.

Tel: +81-86-235-7365

Citation: Hinotsu K, Hishikawa N, Fukui Y, Sato K, Takemoto M, et al. (2018) Comparison of Cognitive, Affective, and Activities of Daily Living Functions in Patients with Parkinson's Disease and Progressive Supranuclear Palsy. J Brain Behav Cogn Sci Vol.1 No.3:14

Abstract

Aim: The purpose of this study was to compare the cognitive/affective and Activities of Daily Living (ADL) functions of Parkinson's Disease (PD) and Progressive Supranuclear Palsy (PSP).

Methods: We retrospectively recruited 324 PD patients, 109 PSP patients, and 111 control subjects, and investigated their cognitive/affective and ADL functions, especially in PD patients when compared with PSP patients.

Results: Cognitive functional scores (MMSE, HDS-R, FAB, and MoCA) of total PD and PSP were lower than the control. In particular, recent and working memory, initiation, executive functions, and attention of PSP were significantly lower than total PD. Affective functional scores (geriatric depression scale, Apathy Score: AS, and Abe's BPSD score) of total PD and PSP were worse than the control, and AS of PSP was significantly worse than total PD. Within PD, cognitive/affective, and ADL functions were expressed in an H-Y stage-dependent manner.

Conclusion: Our results demonstrate that the PSP cognitive functions and AS were significantly worse than the PD. Moreover, the cognitive/affective and ADL functions of PD were similar to, or worse, than PSP in severe H-Y stages of PD, suggesting greater dysfunctions of both motor symptoms and cognitive/affective functions in an advanced stage of PD than PSP.

Keywords: Activities of daily living functions; Affective functions; Cognitive functions; Hoehn and Yahr stage; Parkinson's disease; Progressive supranuclear palsy

Received: December 10, 2018; **Accepted:** December 24, 2018; **Published:** December 31, 2018

Introduction

Parkinson's disease (PD) is considered as the second most prevalent neurodegenerative disease after Alzheimer's Disease (AD) [1] both of which are increasing worldwide due to rapid aging society [2]. PD is mainly characterized by motor symptoms such as resting tremor, bradykinesia, rigidity, and postural instability, and by non-motor symptoms including cognitive dysfunctions (executive, visual perception, attention), autonomic failure, sleep disorder, behavioural and psychiatric symptoms (e.g. depression, apathy, psychosis, hallucination) [3-5]. Their symptoms are related to the neuronal degeneration of mainly dopaminergic neurons associated with the accumulation of α-synuclein as Lewy bodies.

Progressive Supranuclear Palsy (PSP) is the second most extrapyramidal disorder after PD, [6] which is classically characterized by early postural instability, supranuclear gaze palsy, and parkinsonism, as well as cognitive and affective impairments [5,7-10]. The neuropathology of PSP includes degeneration of not only the subthalamic nucleus, globus pallidus, substantia nigra, ventral tegmentum of midbrain and pons, dentate nucleus, but also the precentral gyrus, and premotor and supplementary motor areas, accompanied by the accumulations of tau protein in the neuron and glial cells [11-14].

Although PD is neuropathologically different from PSP, they sometimes show similar clinical manifestations especially in cognitive and affective functions. Our previous studies showed the supplemental diagnostic method for distinguishing PD and PSP during the early stage by using the MRI, iodine-123 Meta-Iodobenzyl Guanidine (123I-MIBG) myocardial scintigraphy, Single Photon Emission Computed Tomography (SPECT), and MRI-based dynamic cerebrospinal fluid flow [15,16]. In the present clinic-based cross-sectional study, we compared the cognitive, affective, and Activities of Daily Living (ADL) functions of PD and PSP with age-matched control subjects for a possible different features.

Methods

Participants

In the present retrospective study, we recruited 324 patients with PD (178 males and 146 females; mean age: 73.9 ± 6.3 years) and 109 patients with PSP (66 males and 43 females; mean age: 73.7 ± 6.5 years) at the Department of Neurology Okayama University Hospital and its affiliated hospitals. Clinical diagnoses were based on the consensus criteria for probable PD [17] and the National Institute of Neurological Disorders and Stroke and the Society for PSP, Inc. (NINDS-SPSP) criteria [6]. In addition, PD patients were divided into 5 subgroups by Hoehn and Yahr (H-Y) stage, stage Ⅰ (6 males and 7 females; mean age: 71.8 ± 5.9 years), stage Ⅱ (28 males and 27 females; mean age: 72.9 ± 6.3 years), stage Ⅲ (54 males and 69 females; mean age: 73.6 ± 6.2 years), stage Ⅳ (83 males and 36 females; mean age: 74.8 ± 6.3 years), and stage Ⅴ (7 males and 7 females; mean age: 75.9 ± 6.3 years). Age- and gender- matched 111 control individuals were also included (66 males and 45 females; mean age: 74.1 ± 6.5 years) who underwent medical examinations and found no neurological nor psychiatric diseases. In the present study, their medical records were reviewed, and cognitive, affective and ADL functions have been assessed for the above 324 PD patients, 109 PSP patients, and 111 control subjects **(Table 1)**.

Ethical permission for this study was given by the Ethics Committee on Epidemiological Studies of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science (approval # 1603-031), and informed consents were obtained from participants in this study.

Assessments of cognitive, affective, and ADL functions

According to our previous reports, cognitive functions were assessed using Mini-Mental State Examination (MMSE), Hasegawa Dementia Score-Revised (HDS-R), Frontal Assessment Battery (FAB), and Montreal Cognitive Assessment (MoCA). As affective functions, depression, apathy and Behavioural and Psychological Symptoms of Dementia (BPSD) were evaluated using the Geriatric Depression Scale (GDS), Apathy Scale (AS) and the Abe's BPSD score (ABS), [18] respectively. Activities of Daily Living (ADL) of the patients were also assessed using the Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL).

Statistical analysis

Statistical analyses were performed using statistical software IBM SPSS Statistics for Windows, Version 22.0 (IBM Corporation, Armonk, N.Y., USA). After checking normality, we carried out the Kruskal-Wallis tests to compare each cognitive, affective and ADL functional assessments, subscales of cognitive, affective and ADL functional assessments with control, PD, and PSP groups. P-values less than 0.05 were considered significant.

Results

Demographic and characteristic data of participants (111 control subjects, 324 total PD patients, and 109 PSP patients) is presented in **Table 1**. Cognitive functional scores (MMSE, HDS-R, FAB, and MoCA) of total PD and PSP were significantly lower than control, and all of these scores of PSP were significantly lower than total PD **(Figures 1a-d)**. Affective functional scores (GDS, AS, and ABS) of total PD and PSP were significantly worser than control (**p<0.01) **(Figures 1e-g)**. AS of PSP were significantly worser than total PD (†† p<0.01) **(Figure 1f)**. The ADL score of total PD and PSP were also significantly lower than control (**p<0.01) **(Figure 1h)**, but no difference between PSP and PD. Within PD, cognitive, affective, and ADL functions were worser in an H-Y stage-dependent manner and cognitive and AS functions were worser in PSP than PD with H-Y stage Ⅱ and Ⅲ **(Figures 1a-h)**.

Subscale analysis of the above cognitive tests were significantly worser than control in the tasks of orientation of time and place (MMSE, HDS-R, MoCA), calculation (MMSE, HDS-R), recall (MMSE, HDS-R, MoCA), 3-stage commands (MMSE), digit span (HDS-R, MoCA), write a composition (MMSE), copy a **Figure** (MMSE, MoCA), visual retention (HDS-R), word fluency (HDS-R), letter fluency (FAB), conflict (FAB), go/no-go (inhibitory control) (FAB), Trail Making Test (TMT) (MoCA), clock drawing (MoCA), target tapping (MoCA), serial 7 subtraction (MoCA), and repeat sentences (MoCA) (*p<0.05, **p<0.01, total PD or PSP vs control)

Table 1: Demographic and characteristic data of control subjects, PD, and PSP patients. ¶¶ Data are represented as mean ± SD. † p<0.05, PSP **vs.** Total PD; ¶¶ p<0.01, PD with H-Y stage (Ⅰ - Ⅴ) **vs.** PSP. M/F: Male/Female; NA: Not Applicable; H-Y stage: Hoehn and Yahr stage; PD: Parkinson's Disease; PSP: Progressive Supranuclear Palsy.

	control	Total PD	PSP	H-Y stage of PD				
				Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅴ
Number	111	324	109	13	55	123	119	14
Gender (M/F)	66/45	178/146	66/43	6/7	28/27	54/69	83/36	7/7
age (years)	74.1 ± 6.5	73.9 ± 6.3	73.7 ± 6.5	71.8 ± 5.9	72.9 ± 6.3	73.6 ± 6.2	74.8 ± 6.3	75.9 ± 7.6
Duratoin (months)	NA	69.5 ± 58.9	31.3 ± 21.0†	16.4 ± 3.2	36.6 ± 32.6	61.5 ± 51.5	108.6 ± 58.7¶¶	142.4 ± 69.4¶¶

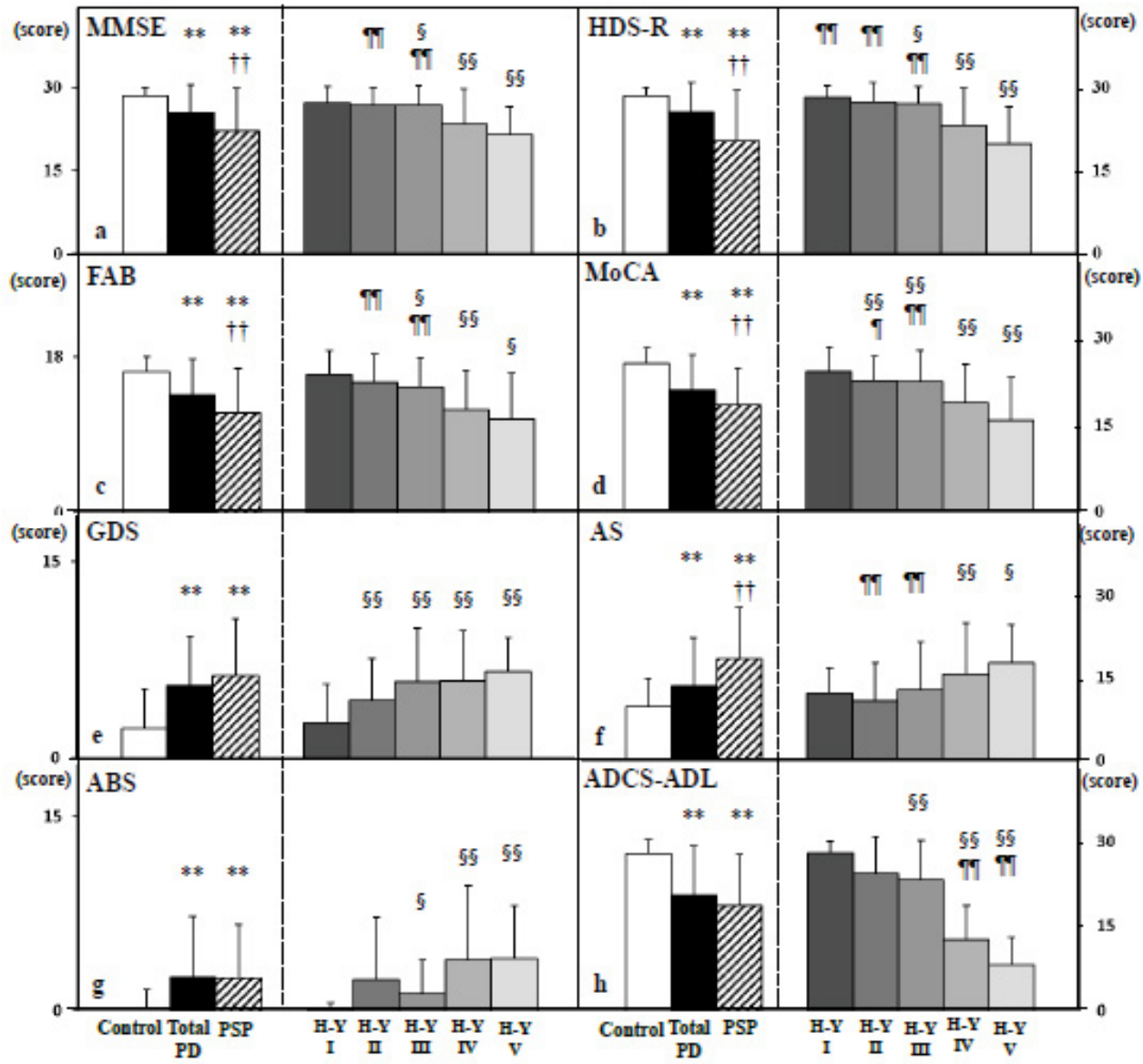

Figure 1 (a-h left side) Comparison of cognitive, affective and ADL functional scores among the three groups; control: white bars, total PD: black bars, and PSP: striped bars. The results are expressed as full scores (*p<0.05, **p<0.01: Total PD or PSP **vs.** control, † p<0.05, †† p<0.01: Total PD **vs.** PSP). (a-h right side) Comparison of cognitive, affective and ADL functional scores among the six groups; PSP: striped bars, and PD with Hoehn and Yahr (H-Y) stage Ⅰ-Ⅴ (gray bars). The results are expressed as full scores (§ p<0.05, §§ p<0.01: PD with H-Y stage (Ⅰ-Ⅴ) **vs.** control, ¶ p<0.05, ¶¶ p<0.01: PD with H-Y stage (Ⅰ-Ⅴ) **vs.** PSP).

(Table 2). Furthermore, these cognitive tests of PSP showed significant decreases than those of PD, and a tend to worse with progression of H-Y stage from Ⅰ to Ⅴ in orientation of time, place and age (MMSE, HDS-R), registration (MMSE, HDS-R), calculation (MMSE, HDS-R), recall (HDS-R, MoCA), repeat sentence (MMSE), obey a written command (MMSE), copy a **Figure** (MMSE, MoCA), digit span (HDS-R, MoCA), visual retention (HDS-R), word fluency (HDS-R), conceptualization (FAB), letter fluency (FAB), programming (FAB), conflict (FAB), and verbal abstraction (MoCA) († p<0.05, †† p<0.01, total PD **vs.** PSP) **(Table 2)**.

Most GDS subscales showed that total PD and PSP were significantly worser than control (*p<0.05, **p<0.01), especially in H-Y stage Ⅲ and Ⅳ (# p<0.05, ## p<0.01). The subscale of "problems in memory" in total PD was significantly worser than PSP († p<0.05) **(Table 3)**.

Most subscales of AS were significantly worser in total PD than control for plans for future (*p<0.05), and have some interest, no idea what about to do, indifference, unconcern, need a push to get started, apathy, and spiritless (respectively, **p<0.01). PSP declined in the following subscales comparing with control; have some interest, engrossed in something's, looking for something to do, plans for future, motivations, energy for daily activities,

Table 2: Cognitive function (MMSE, HDS-R, FAB, MoCA) subscale analysis data of control, PD, and PSP. Data are represented as mean ± SD Kruskal-Wallis test was performed respectively *p<0.05 and **p<0.01, Total PD or PSP versus control; † p<0.05 and †† p<0.01, PSP **vs.** Total PD; § p<0.05 and §§ p<0.01, PD with H-Y stage (Ⅰ-Ⅴ) **vs.** control; ¶ p<0.05 and ¶¶ p<0.01, PD with H-Y stage (Ⅰ-Ⅴ) **vs.** PSP. FAB: Frontal Assessment Battery; GDS: Geriatric Depression Scale; HDS-R: Hasegawa Dementia Scale-Revised; H-Y stage: Hoehn and Yahr stage; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; PD: Parkinson's Disease; PSP: Progressive Supranuclear Palsy.

	Control	Total PD	PSP	PD with H-Y stage				
				Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅴ
MMSE subscale								
orientation(time)	4.9±0.4	4.3±1.2**	3.6±1.6**,††	4.8±0.6	4.7±0.9¶¶	4.6±0.9¶¶	3.8±1.3§§	3.5±1.3§§
orientation(place)	4.9±0.3	4.6±0.9*	4.1±1.5**,†	4.8±0.4	4.8±0.5¶	4.7±0.7¶¶	4.2±1.2§§	4.7±0.6
registration	3.0±0.0	2.9±0.4	2.8±0.8**,†	3.0±0.0	3.0±0.0¶	3.0±0.1¶	2.8±0.6§§	2.8±0.6
calculation	4.5±1.1	3.4±1.8**	2.4±1.9**,††	3.7±1.7	3.9±1.6¶¶	3.6±1.8§,¶	3.6±1.8§,¶¶	2.1±2.0§§
recall	2.5±1.1	2.2±1.0*	2.0±1.1**	2.2±1.0	2.5±0.7¶	2.4±0.8	1.9±1.1§§	1.5±1.0§
naming	2.0±0.0	2.0±0.2	1.9±0.5*	2.0±0.0	2.0±0.0	2.0±0.0¶	1.9±0.4	2.0±0.0
repeat sentence	0.9±0.3	0.9±0.3	0.8±0.4†	1.0±0.0	0.8±0.4	1.0±0.2¶¶	0.9±0.3	0.8±0.4
3-stage commands	2.9±0.3	2.6±0.8**	2.5±0.9*	3.0±0.0	2.6±0.7	2.7±0.6	2.4±0.9§§	1.9±0.8§§,¶
obey a written command	1.0±0.0	1.0±0.2	0.9±0.3**,††	1.0±0.0	1.0±0.0¶	1.0±0.0¶¶	0.9±0.2	1.1±0.3¶
write a composition	1.0±0.2	0.8±0.4**	0.7±0.4**	0.9±0.3	0.8±0.4	0.9±0.3§	0.7±0.4¶¶	0.5±0.5¶¶
copy a figure	1.0±0.1	0.8±0.4**	0.7±0.5**,†	1.0±0.0	0.8±0.4§	1.0±0.2¶¶	0.7±0.5§§	0.5±0.5§§
HDS-R subscale								
orientation(age)	1.0±0.0	1.0±0.2	0.9±0.3**,††	1.0±0.0	1.0±0.0¶¶	1.0±0.2¶¶	0.9±0.3	0.9±0.3
orientation(place)	2.0±0.1	1.9±0.4*	1.7±0.7**,††	2.0±0.0	2.0±0.3¶¶	2.0 0.1¶¶	1.8±0.5§§	1.9±0.3
orientation(time)	3.9±0.3	3.3±1.0**	2.9±1.4**,†	3.9±0.3	3.6±0.9¶¶	3.6±0.7¶¶	2.9±1.2§§	2.6±1.3§§
registration	3.0±0.0	2.9±0.4	2.7±0.9**,†	3.0±0.0	3.0±0.3¶	3.0±0.1¶¶	2.8±0.6§§	2.7±0.7
calculation	1.9±0.3	1.6±0.7**	1.3±0.8**,†	1.8±0.4	1.7±0.5¶	1.7±0.6¶¶	1.4±0.9§§	1.1±0.9§§
recall	5.3±1.0	4.8±1.6*	4.0±2.1**,††	5.0±1.4	5.4±1.1¶¶	5.1±1.3¶¶	4.2±1.9§§	3.8±1.9
digit span	1.7±0.6	1.4±0.8**	1.0±0.8**,††	1.8±0.4	1.5±0.8¶	1.5±0.8¶¶	1.3±0.8§§	0.6±0.8§§
visual retention	4.8±0.5	4.3±1.1**	3.6±1.7**,††	4.9±0.3¶	4.6±0.8¶¶	4.6±0.7¶¶	4.0±1.3§§	3.3±1.6§
word fluency	4.9±0.6	4.3±1.5**	2.8±2.2**,††	4.8±0.6¶	4.6±1.2¶¶	4.6±1.1¶¶	3.9±1.8§§,¶¶	2.8±2.3§
FAB subscale								
conceptualization	2.7±0.6	2.4±0.9	2.1±1.2**,†	2.5±1.0	2.4±1.0	2.6±0.7¶	2.3±1.0	1.9±1.2
letter fluency	2.6±0.7	2.0±1.0**	1.6±1.1**,†	2.5±0.7	2.3±0.8¶¶	2.1±1.0§§	1.8±1.0§§	1.6±1.2
programming	2.7±0.5	2.5±0.9	1.9±1.3**,††	2.7±0.7	2.8±0.6¶¶	2.7±0.6¶¶	2.1±1.1§§	2.2±1.3
conflict	2.9±0.3	2.3±1.1**	1.7±1.4**,††	2.7±0.9	2.5±1.0¶	2.5±0.9¶¶	2.1±1.3§§	1.8±1.5
go/no-go	2.2±1.0	1.5±1.4**	1.4±1.3**	2.5±1.0	2.0±1.2	1.7±1.3	1.0±1.3§§	0.7±1.1§
forced grasping	3.0±0.1	2.8±0.6*	2.8±0.7	3.0±0.0	3.0±0.1	2.9±0.4	2.6±0.9§§	2.7±1.0
MoCA subscale								
trail making test	0.8±0.4	0.4±0.5**	0.3±0.5**	0.9±0.4	0.4±0.5§§	0.5±0.5§§	0.4±0.5§§	0.0±0.0§§
copy a figure	0.9±0.3	0.7±0.5**	0.5±0.5**,††	1.0±0.0	0.7±0.4	0.8±0.4¶¶	0.5±0.5§§	0.4±0.5§
clock drawing	2.6±0.6	2.1±0.9**	1.9±1.1**	2.7±0.5	2.2±0.9	2.3±0.8	1.9±1.0§§	1.4±1.1§§
naming	2.9±0.4	2.7±0.7	2.7±0.6	3.0±0.0	2.8±0.5	2.8±0.5	2.6±0.9	2.1±1.1§
digit span	1.8±0.5	1.5±0.7*	1.3±0.7**,††	2.0±0.0	1.7±0.5¶	1.6±0.6¶¶	1.3±0.8§§	1.4±0.7
target tapping	1.0±0.2	0.7±0.4**	0.6±0.5**	0.9±0.4	0.8±0.4	0.8±0.4¶	0.6±0.5§§	0.6±0.5
serial 7 subtraction	2.8±0.6	2.2±1.0**	2.0±1.0**	2.4±1.0	2.4±0.9	2.4±0.9	1.9±1.0§§	1.5±1.2§§
repeat sentences	1.3±0.6	0.9±0.6**	0.8±0.7**	1.0±0.0	1.2±0.7	0.8±0.6§§	0.8±0.5§§	0.6±0.7
phonemic fluency	0.6±0.5	0.5±0.5	0.4±0.5*	0.6±0.5	0.7±0.5	0.5±0.5	0.5±0.5	0.3±0.5
verbal abstraction	1.9±0.3	1.8±0.5	1.6±0.7**,†	2.0±0.0	1.9±0.3	1.9±0.4¶	1.6±0.6§	1.5±0.5
recall	3.2±1.5	2.4±1.8**	1.5±1.5**,††	2.0±1.8	2.5±1.6	2.8±1.8¶¶	2.0±1.§§	1.4±1.8
orientation(time, place)	5.9±0.3	5.3±1.2**	4.8±1.6**	5.9±0.4	5.4±1.0	5.5±0.9§	5.0±1.5§§	4.6±1.6

no idea what about to do, indifference, unconcern, need a push to get started, apathy, and spiritless (respectively, **p<0.01). Similarly, 8 subscales of PSP were significantly worser than total PD in motivations († p<0.05), learning new thing, engrossed in somethings, indifference, unconcern, need a push to get started, apathy, and spiritless (respectively, †† p<0.01) **(Table 3)**.

Subscales analysis of ABS were significantly worser in total PD than control in offensive and abusive words, and apathy and

Table 3: Affective function (GDS, AS, ABS) subscale analysis data of control, PD, and PSP. Data are represented as mean ± SD. Kruskal-Wallis test was performed respectively. *p<0.05, **p<0.01; Total PD or PSP **vs.** control, † p<0.05, †† p<0.01; PSP **vs.** Total PD, § p<0.05, §§ p<0.01; PD with H-Y stage (Ⅰ-Ⅴ) **vs.** control, ¶ p<0.05, ¶¶ p<0.01 PD with H-Y stage (Ⅰ-Ⅴ) **vs.** PSP. ABS, Abe's behavioural and psychological symptoms of dementia score; ADCS-ADL: Alzheimer's Disease Cooperative Study-Activities of Daily Living; AS: Apathy Scale; GDS: Geriatric Depression Scale; H-Y stage: Hoehn and Yahr Stage; PD: Parkinson's Disease; PSP: Progressive Supranuclear Palsy.

	Control	Total PD	PSP	PD with H-Y stage				
				Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅴ
GDS subscale								
satisfied with life	0.1±0.3	0.2±0.4**	0.4±0.5**	0.1±0.3	0.1±0.3	0.3±0.5§§	0.3±0.5§§	0.1±0.3
feel happy	0.2±0.4	0.4±0.5*	0.4±0.5**	0.2±0.4	0.3±0.5¶	0.3±0.5	0.4±0.5§	0.5±0.5
good mood	0.3±0.5	0.5±0.5**	0.6±0.5**	0.2±0.4	0.5±0.5§§	0.5±0.5§	0.6±0.5§§	0.8±0.4§
worth living	0.1±0.2	0.2±0.4**	0.2±0.4**	0.0±0.0	0.2±0.4	0.3±0.5§§	0.2±0.4	0.0±0.0
filled with energy	0.3±0.5	0.5±0.5**	0.6±0.5**	0.1±0.3¶	0.4±0.5	0.4±0.5	0.5±0.5§	0.8±0.4§
less activity	0.4±0.5	0.6±0.5**	0.7±0.5**	0.3±0.5	0.5±0.5§§	0.6±0.5§	0.7±0.5§§	0.6±0.5
better to be inside	0.2±0.4	0.5±0.5**	0.5±0.5**	0.5±0.5	0.5±0.5§§	0.6±0.5§§	0.4±0.5§§	0.6±0.5
feel empty	0.0±0.2	0.2±0.4**	0.2±0.4**	0.0±0.0	0.2±0.4	0.3±0.5§§	0.2±0.4§	0.4±0.5
bored	0.1±0.3	0.2±0.4*	0.3±0.5**	0.2±0.4	0.1±0.3	0.2±0.4	0.3±0.4§	0.5±0.5
anticipatory anxiety	0.1±0.3	0.3±0.5**	0.3±0.5**	0.2±0.4	0.3±0.5	0.3±0.5§§	0.4±0.5§§	0.5±0.5§
powerlessness	0.1±0.3	0.4±0.5**	0.4±0.5**	0.4±0.5	0.3±0.5	0.4±0.5§§	0.5±0.5§§	0.4±0.5
problems with memory	0.2±0.4	0.4±0.5	0.5±0.5**,†	0.4±0.5	0.3±0.5	0.4±0.5	0.4±0.5	0.2±0.4
worthlessness	0.0±0.2	0.3±0.5**	0.3±0.5**	0.0±0.0	0.2±0.4	0.3±0.5§§	0.3±0.5§§	0.2±0.4
situation cannot be done	0.2±0.4	0.5±0.5**	0.6±0.5**	0.3±0.5	0.3±0.5¶	0.5±0.5§§	0.5±0.5§§	0.8±0.4§§
feeling of poverty	0.0±0.2	0.2±0.4**	0.2±0.4**	0.0±0.0	0.1±0.3	0.3±0.4§§	0.2±0.4	0.3±0.5
AS subscale								
learning new things	1.4±0.8	1.2±0.9	1.7±1.0††	1.7±0.7	1.1±0.9¶	1.1±1.0¶¶	1.4±0.8	1.8±0.7
have some interest	1.0±0.8	1.3±0.9**	1.6±1.0**	1.3±0.9	1.2±0.9	1.4±1.0	1.4±0.9	1.4±0.8
concern about condition	0.7±0.7	0.9±0.8	0.9±1.0	0.8±0.8	0.6±0.7	0.8±0.8	1.1±0.8	1.0±0.9
engrossed in some things	1.2±0.8	1.2±0.9	1.7±0.9**,††	1.7±0.9	1.1±0.9¶¶	1.1±0.9¶¶	1.4±0.8	1.7±0.9
looking for something to do	1.0±0.7	1.2±0.9	1.4±1.0**	1.2±0.7	1.0±0.9	1.2±1.0	1.3±0.9	1.2±0.7
plans for the future	1.4±0.8	1.6±0.9*	1.9±0.9**	2.0±0.5	1.4±0.9	1.5±1.0	1.8±0.9§	1.9±0.9
motivations	1.2±0.8	1.3±0.9**	1.6±0.9**,†	1.6±0.5	1.2±0.9	1.3±1.0	1.4±0.9	1.4±1.0
energy for daily activities	1.1±0.7	1.3±0.9	1.5±0.9**	1.3±0.7	1.1±0.8	1.3±0.8	1.5±0.9§	1.5±0.8
no idea about what to do	0.1±0.3	0.7±0.9**	1.0±1.0**	0.1±0.3	0.3±0.6¶¶	0.7±0.8§§	0.9±1.0§§	0.8±0.7§§
indifference	0.1±0.3	0.5±0.8**	1.0±1.1**,††	0.1±0.3¶	0.4±0.7¶¶	0.5±0.9§§,¶¶	0.7±0.9§§	0.9±0.9§§
lack of concern	0.0±0.2	0.5±0.9**	1.0±1.0**,††	0.0±0.0¶¶	0.3±0.8¶¶	0.4±0.8§§,¶¶	0.7±0.9§§	0.8±1.0§
need a push to get started	0.1±0.4	0.5±0.8**	0.9±1.1**,††	0.0±0.0¶	0.3±0.6¶¶	0.4±0.9¶¶	0.7±0.9§§	0.8±0.7§§
apathy	0.3±0.7	0.6±0.8**	1.2±1.0**,††	0.2±0.4	0.5±0.7¶¶	0.6±0.8¶¶	0.8±0.9§§	1.1±0.8§§
spiritless	0.2±0.4	0.7±0.8**	1.2±1.1**,††	0.3±0.7	0.4±0.7¶¶	0.6±0.7§§,¶¶	0.9±0.9§§	1.4±0.9§§
ABS subscale								
wandering in/outside home	0.0±0.0	0.3±1.0	0.4±1.4	0.0±0.0	0.2±1.0	0.1±0.6	0.5±1.3§§	0.0±0.0
eating or toilet problem	0.0±0.0	0.4±1.3**	0.2±0.8	0.0±0.0	0.2±1.1	0.2±0.7	0.6±1.5§§	1.9±2.7§§
delusion or hallucination	0.0±0.2	0.6±1.5**	0.3±0.9	0.0±0.0	0.6±1.5	0.4±1.0	0.9±1.8	0.3±0.7
offensive and abusive words	0.1±0.5	0.4±0.9*	0.5±1.0*	0.0±0.0	0.6±1.2	0.3±0.7	0.5±0.8§§	1.0±1.1
day-night reversal	0.0±0.2	0.4±1.0**	0.6±1.4**	0.0±0.0	0.4±1.1	0.1±0.6	0.7±1.2§§	0.0±0.0
excitation and agitation	0.0±0.2	0.2±0.5	0.2±0.6	0.0±0.0	0.2±0.6	0.1±0.3	0.3±0.7§	0.0±0.0
apathy and indifference	0.0±0.2	0.2±0.6*	0.2±0.6	0.2±0.4	0.2±0.4	0.1±0.4	0.3±0.6	0.8±0.9§§
depressive and gloomy mood	0.0±0.1	0.1±0.3	0.1±0.3	0.0±0.0	0.0±0.2	0.1±0.3	0.1±0.3	0.1±0.4
violent force	0.0±0.0	0.0±0.1	0.0±0.2	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.2	0.0±0.4
high irritability	0.0±0.2	0.0±0.2	0.0±0.2	0.0±0.0	0.1±0.3	0.0±0.0	0.0±0.2	0.0±0.0

indifference (respectively, *p<0.05), and eating or toilet problem, delusion or hallucination, and day-night reversal (respectively, **p<0.01). Those of PSP were significantly worser than control in offensive and abusive words (*p<0.05), and day-night reversal (**p<0.01). There was no significant difference between PD and PSP **(Table 3)**.

Most ADL subscales of PD and PSP were significantly declined than control, and tended to be worse with progression of H-Y stages (data not shown). Subscale scores of clothes, bathing, and cash management in PSP were significantly worser than total PD († p<0.05).

Discussion

In this clinic-based cross-sectional study, we found that the cognitive, affective and ADL functions of PD and PSP were significantly decreased comparing with age-matched control subjects, and that the cognitive functions and apathy score of PSP were significantly worser than PD. Within PD, cognitive, affective and ADL functional declines became worser in an H-Y stage-dependent manner, and these functions of PSP were similar to PD with H-Y stages Ⅳ and Ⅴ.

Although both PD and PSP caused cognitive declines such as executive functions, attention, and memory [3,5,19,20] cognitive disturbance in PSP was more frequent and severer than PD [5]. Our present study also revealed that scores of all 4 standard cognitive functional tests were significantly worser in PSP than PD, especially in "orientation", "registration", "calculation", "repeat sentence", "obey a written command", "**Figure** copy", "recall", "backward digit span", "visual retention", "word and letter fluency", "conceptualization", "programming", and "conflict". Impairments to "recent and working memory", "initiation", "search strategies", "executive functions", and "attention/concentration" were severer in PSP than PD patients, probably because neurodegeneration in PSP was exaggerated not only in the midbrain, caudate nuclei, thalamus, hypothalamus, but also the frontal cortex and parahippocampal gyrus. A previous study reported a decrease of regional Cerebral Blood Flow (rCBF) in the pre-supplementary motor cortex and prefrontal cortex compared with normal control subjects and PD patients [15,21].

Previous studies showed more frequent prevalence of depression to be 4-70% in PD than apathy (15-50%), [22-24] but contrasting findings have also been reported [25,26]. On the other hand, PSP showed more apathy (35-91%), followed by depression, agitation, irritability, and disinhibition [8-10]. The present study basically confirmed the above previous reports, but the mean depressive scores were similar between PD and PSP **(Figures 1e and Table 3)**. BPSD score measured by ABS was worser both in total PD and PSP than control, and was worser in H-Y stage-dependent manner within PD **(Figures 1g and Table 3)**. Significant deteriorations of both instrumental and basic ADL in total PD and PSP suggested daily life problems, especially in the 3 items such as clothes, bathing, and cash management in PSP († $p<0.05$), corresponding to the frontal cerebral cortical dysfunction in PSP.

Among PD patients, there was no significant difference in cognitive, affective, and ADL functions in early stage PD (H-Y stage I) from the control, but these functions became worser at the advanced stage (H-Y stages IV and V) similar to PSP **(Figures 1a-1h) (Tables 2 and 3)**. MoCA was worser in PD at stages II and more **(Figure 1d and Table 2)**, and ABS and ADCS-ADL scores were worser at stage IV and more, suggesting more dysfunctions in PD relating to not only motor symptoms but also cognitive and affective functional declines after moderate stage [27,28].

In summary, the present study demonstrated that both PD and PSP were associated with cognitive, affective, and ADL functional declines than the age- and gender-matched control **(Figures 1a-1h) (Tables 2 and 3)**. However, "recent and working memory", "initiation", "search strategies", "executive functions", and "attention, concentration" were worser in PSP than PD, and PSP was more apathetic than PD. The present study also showed that cognitive, affective, and ADL functions of PD become similar to or even worse than PSP in an H-Y stage-dependent manner.

References

1 Kataoka H, Sawa N, Sugie K, Ueno S (2014) Can dopamine agonists trigger tactile hallucinations in patients with Parkinson's disease? J Neurol Sci 347: 361-363.

2 Japan Intractable Disasesa Information Center: Parkinson's disease 2017, July; http://www.nanbyou.or.jp/entry/314

3 Chaudhuri KR, Healy DG, Schapira AH, National Institute for Clinical Excellence (2006) Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol 5: 235-245.

4 Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, et al. (2007) Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord 22: 1689-1707.

5 Cordato NJ, Halliday GM, Caine D, Morris JG (2006) Comparison of motor, cognitive, and behavioral features in progressive supranuclear palsy and Parkinson's disease. Mov Disord 21: 632-638.

6 Litvan I, Agid Y, Calne D, Campbell G, Dubois B, et al. (1996) Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. Neurology 47: 1-9.

7 Steele JC, Richardson JC, Okszewski J. Progressive supranuclear palsy (1964) A heterogeneous degeneraton involving the brain stem, basal ganglia and cerebellum with vertical gaze and pseudobulbar palsy, nuchal dystonia and dementia. Arch Neurol 10: 333-359.

8 Bak TH, Crawford LM, Berrios G, Hodges JR (2010) Behavioural symptoms in progressive supranuclear palsy and frontotemporal dementia. J Neurol Neurosurg Psychiatry 81: 1057-1059.

9 Gerstenecker A, Duff K, Mast B, Litvan I (2013) ENGENE-PSP Study Group. Behavioral abnormalities in progressive supranuclear palsy. Psychiatry Res 210: 1205-1210.

10 Litvan I (1994) Cognitive disturbances in progressive supranuclear palsy. J Neural Transm Suppl 42: 69-78.

11 Amano N, Takahashi T, Yagishita S, Inoue M, Matsushita M (1996) Abnormal glial cytoskeleton in progressive supranuclear palsy. Neuropathology 16: 139-144.

12 Verny M, Duyckaerts C, Agid Y, Hauw JJ (1996) The significance of cortical pathology in progressive supranuclear palsy. Clinico-pathological data in 10 cases. Brain 119: 1123-1136.

13 Brenneis C, Seppi K, Schocke M, Benke T, Wenning GK, et al. (2004) Voxel based morphometry reveals a distinct pattern of frontal atrophy in progressive supranuclear palsy. J Neurol Neurosurg Psychiatry 75: 246-249.

14 Cordato NJ, Duggins AJ, Halliday GM, Morris JG, Pantelis C (2005) Clinical deficits correlate with regional cerebral atrophy in progressive supranuclear palsy. Brain 128: 1259-1266.

15 Kurata T, Kametaka S, Ohta Y, Morimoto N, Deguchi S, et al. (2011)

PSP as distinguished from CBD, MSA-P and PD by clinical and imaging differences at an early stage. Intern Med 50: 2775-2781.

16 Fukui Y, Hishikawa N, Sato K, Yunoki T1, Kono S, et al. (2015) Differentiating progressive supranuclear palsy from Parkinson's disease by MRI-based dynamic cerebrospinal fluid flow. J Neurol Sci 357: 178-182.

17 Hughes AJ, Daniel SE, Kilford L, Lees AJ (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 55: 181-184.

18 Abe K, Yamashita T, Hishikawa N, et al. (2015) A new simple score (ABS) for assessing behavioral and psychological symptoms of dementia. J Neurol Sci 350: 14–17.

19 Grover S, Somaiya M, Kumar S, Avasthi A (2015) Psychiatric aspects of Parkinson's disease. J Neurosci Rural Pract 6: 65-76.

20 Litvan I, Mega MS, Cummings JL, Fairbanks L (1996) Neuropsychiatric aspects of progressive supranuclear palsy. Neurology 47: 1184-1189.

21 Varrone A, Pagani M, Salvatore E, Salmaso D (2007) Identification by [99mTc]ECD SPECT of anterior cingulate hypoperfusion in progressive supranuclear palsy, in comparison with Parkinson's disease. Eur J Nucl Med Mol Imaging 34: 1071-1081.

22 Cummings JL (1992) Depression and Parkinson's disease: a review. Am J Psychiatry 149: 443-454.

23 Starkstein SE, Merello M, Jorge R, Brockman S, Bruce D, et al. (2009) The syndromal validity and nosological position of apathy in Parkinson's disease. Mov Disord 24: 1211-1216.

24 Pedersen KF, Larsen JP, Alves G, Aarsland D (2009) Prevalence and clinical correlates of apathy in Parkinson's disease: a community-based study. Parkinsonism Relat Disord. 15: 295-299.

25 Borroni B, Turla M, Bertasi V, Agosti C, Gilberti N, et al. (2008) Cognitive and behavioral assessment in the early stages of neurodegenerative extrapyramidal syndromes. Arch Gerontol Geriatr 47: 53-61.

26 Ziropadja Lj, Stefanova E, Petrovic M, Stojkovic T, Kostic VS (2012) Apathy and depression in Parkinson's disease: the Belgrade PD study report. Parkinsonism Relat Disord 18: 339-342.

27 Foltynie T, Brayne CE, Robbins TW, Barker RA (2004) The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. Brain 127: 550-560.

28 Williams-Gray CH, Foltynie T, Brayne CE, Robbins TW, Barker RA (2007) Evolution of cognitive dysfunction in an incident Parkinson's disease cohort. Brain 130: 1787-1798.