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Characteristics of depression in Parkinson's Disease: Evaluating with Zung's Self-Rating Depression Scale

Fumio Kanda, Kenichi Oishi, Kenji Sekiguchi, Atsushi Kuga, Hiroshi Kobessho, Toshihiko Shirafuji, Masatsugu Higuchi, Hiroyuki Ishihara

Neurology, Kobe University Hospital, Kobe, Japan

Corresponding to Dr. Fumio Kanda, Neurology, Kobe University Hospital

7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan

E-mail: kanda@med.kobe-u.ac.jp

Running title: Depression in Parkinson's disease

Abstract:

The purpose of the study was to elucidate characteristics of depression in Parkinson’s disease (PD). Fifty-eight PD patients were evaluated with Zung’s Self-Rating Depression Scale (SDS) and the Unified Parkinson’s Disease Rating Scale (UPDRS). Scores for ”suicidal ideation” on the SDS correlated with posture and gait disturbances on the UPDRS. Twenty-six patients with spinocerebellar degeneration (SCD) were also evaluated with the SDS. SDS scores for “indecisiveness” and ”constipation” were significantly higher in PD patients than SCD patients. Our results suggest that depression is common in disabled persons but PD patients might have a characteristic clinical presentation.

Key words: depression, indecisiveness, Parkinson's disease, SDS, spinocerebellar degeneration, suicidal ideation

INTRODUCTION

Depression is one of the most common psychiatric symptoms in Parkinson's disease (PD). Symptoms of depression are reported in 40-50% of PD patients [1]. However, the mechanisms underlying depression in PD are poorly understood, and there are several factors that may contribute to its development. Many parkinsonian symptoms overlap with features of depression, including flat affect, easily fatigued, inability to work, loss of energy, reduction in libido, and preoccupation with having an incurable disease. Thus, depression in PD patients may be related to the underlying neuropathology of PD. Abnormalities in dopamine and/or other neurotransmitter pathways that are involved in PD may be responsible for depression in PD patients. Depression in PD patients may also be due to limitation of daily activity. Physical disability would be expected to contribute to depression independent of the specific cause of the disability, and extensive physical rehabilitation resulted in significant improvements in motor function as well as in symptoms of depression [2].

Although depression is more frequent in PD patients than in the general population [3], symptoms of depression in PD are different from those of major depression. In fact, up to 50% of PD patients that exhibit symptoms of depression do not meet the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria for

major depression or dysthymia [4]. However, many of these patients meet the criteria for "subsyndromal symptomatic depression" [5]. The aim of the present study was to investigate characteristics of depression in PD.

PATIENTS AND METHODS

Study protocols conformed to the ethical guidelines of the 1975 Declaration of Helsinki and were approved by the Kobe University Ethical Committee. All participants gave informed, written consent.

Fifty-eight consecutive PD patients (24 men, 34 women, 67.8 $\pm$ 10.5 year-old) who attended the outpatient clinic of Kobe University Hospital from December 2004 to January 2005 participated in the study. PD diagnosis was established by the presence of parkinsonism (e.g., akinesia/bradykinesia, rigidity, resting tremor, and retropulsion) and confirmed by magnetic resonance imaging (MRI) that revealed no abnormalities, such as multiple infarctions and localized brain atrophy. Eight patients were classified as stage I, 14 as stage II, 29 as stage III, and 7 as stage IV, according to the Hoehn and Yahr scale. PD patients with dementia or severe psychiatric disease were excluded.

Patients completed and scored the Zung's Self-Rating Depression Scale (SDS) [6]. They were also evaluated with the UPDRS administered by one of the authors. Both evaluations were performed on the same day.

Next, we evaluated the SDS in patients with spinocerebellar degeneration (SCD), a chronic, progressive, and disabling neurodegenerative disease. Twenty-six SCD patients (8 men, 18 women, 65.7 $\pm$ 8.5 year-old) also participated in the study. Clinical diagnoses of SCD patients were as follows: 8 cases of olivo-ponto-cerebellar atrophy, 6 cases of cortical cerebellar atrophy, 5 cases of familial spastic paraparesis, 1 case of corticobasal degeneration, 1 case of spinocerebellar ataxia (SCA) 6, 1 case of SCA3, and 4 cases of an unknown type of cerebellar ataxia. Disability in daily activity in SCD patients was 2.8 $\pm$ 0.9 on the modified Rankin Scale. SCD patients with predominant parkinsonism, dementia, or evidence of stroke were excluded.

The average scores for each item of SDS in Japanese general population were obtained from a recent literature [7].

Statistical analysis

Comparing between total SDS score and total UPDRS scores, Pearson's correlation coefficients were calculated. In order to evaluate the relationship for individual low level items of SDS and UPDRS, correlations between SDS and UPDRS items were assessed

with a 3-factor maximum-likelihood factor analysis. Factor loading was calculated with varimax rotation. The contribution of each SDS item to depression in PD and SCD patients was assessed by logistic analysis and odds ratios, and 95% confidence intervals were calculated. *P* values < 0.05 were considered statistically significant. Statistic analyses were performed with StatView version 5.0 and SAS version 8.02 (SAS Institute, Cary, NC).

RESULTS

Clinical characteristics of the 58 PD patients are summarized in Table 1. The mean ± SD total SDS score of PD patients was 43.7 ± 9.8. PD patients scored higher on all items except for item 18 (emptiness, 2.14 ± 0.96) and item 20 (dissatisfaction, 2.43 ± 1.01), compared to the general Japanese population (2.52 and 2.66) [7].

The correlation between total SDS score and severity of PD is summarized in Table 2. The total SDS score was significantly correlated with Hoehn-Yahr stage, total UPDRS score, the UPDRS part I score, the UPDRS part II score, and the UPDRS part IV score. However, the total SDS score was not significantly correlated with the UPDRS part III score.

Item 1 of the SDS (depressive affect) was correlated with UPDRS items 3 (depression, r = 0.404) and 12 (turning in bed, r = 0.551). The average score of SDS item 19 (suicidal ideation) for PD patients was 1.60 ± 0.90, and was higher than the general Japanese population (1.32) [7]. As further exploration of correlation with low level items of SDS and UPDRS, factor loading with varimax rotation of the factor analysis are shown in Table 3. As the eigenvalue of first 3 factors accounted for 47.5% of the total variance and the scree plot showed a clear break at fourth factor, there emerged three separate factors. Factor 1 indicated that suicidal ideation was categorized with UPDRS items 11-15 and 27-29 (posture and gait disturbances) rather than with other SDS items. Factor 2 included only UPDRS items, and factor 3 included many SDS items and UPDRS items 3 (depression) and 4 (motivation/initiative).

The mean age of SCD patients and the average duration of their disease were not statistically different from PD patients (Table 1).

The mean total SDS score of SCD patients (44.9 ± 8.0) was not statistically different from that of PD patients (43.7 ± 9.8). Mean scores of individual SDS items for PD and SCD patients were shown in Table 4. As shown in Table 4, logistic analysis revealed that SDS items 8 (constipation) and 16 (indecisiveness) were significantly higher for PD patients than for SCD patients (p=0.002, p=0.007, respectively). The percentage of

correct answers was 78% using an estimated regression model by logistic analysis. It was possible, therefore, to distinguish PD and SCD patients based on the scores of particular SDS items.

DISCUSSION

Previous studies have used various depression scales to evaluate depression in PD [8]. In terms of screening accuracy, the American Academy of Neurology has recommended the Beck Depression Inventory and the Hamilton Depressive Rating Scale to screen for depression associated with PD [8]. However, PD patients do not usually report feelings of guilt or suicidal ideation, as patients with major depression do. Many PD patients with symptoms of depression do not meet DSM-IV criteria for major depression [3]. Thus, depression in PD patients should be assessed as a different clinical entity than that in general psychiatric clinical practices. However, specific scales to screen for depression in PD have not yet been established.

To elucidate depression in PD, we chose to use the SDS [6,9]. The SDS is one of the most frequently used scales for evaluating depression in Japan [10]. SDS scores were significantly associated with experienced quality of life on the SF-36 [11]. SDS items cover all symptoms of depression and are divided into pervasive affect, physiological equivalents or concomitants, and psychological concomitants [6]. Several studies have used the SDS to evaluate depression in PD [11,12,13].

In our study, the mean total SDS score was higher in PD patients and SCD patients than in a healthy Japanese population [7]. Prevalence of depression ($\geq$ 40 total SDS

score) in PD patients and SCD patients was as high as 63.8% and 73.1% in the patient populations compared to 37% in a healthy Japanese population [14]. The higher SDS scores in PD and SCD patients appear to depend on disability in daily activity. PD and SCD are neurodegenerative diseases that progressively worsen until patients become bedridden. Regardless of their specific type, chronic and debilitating diseases are associated with high rates of depression, and diseases that affect the central nervous system are associated with the highest rates of depression [15].

In PD patients, cognitive impairment, high UPDRS scores, high L-DOPA requirements, and the presence of motor fluctuations are risk factors for depression [16]. Although any disabling condition is a risk factor for depression, a consistent relationship between the severity of depression and the degree of physical impairment or functional disability from parkinsonism has not been identified. Two clinical studies found depression to be most common in Hoehn-Yahr stages I, III, and IV [17,18]. Our study revealed a statistically significant correlation between total SDS score and Hoehn-Yahr stage or total UPDRS score. UPDRS part III (motor functions) scores, however, did not correlate with total SDS scores. This indicates that a link between overall motor disability and depression is based on patient self-ratings rather than standardized clinical evaluations.

Depression in PD is qualitatively different from primary major depression. Self-blame, guilt, delusions, a sense of failure, self-destructive thoughts, and suicide are less frequent in PD patients [19]. However, the average score of SDS item 19 (suicidal ideation) was higher in our PD patients than in the general Japanese population [7]. It was similar to those in patients with anxiety reaction, personality disorders, or transient situational adjustment reactions, while it was lower than those in patients with major depression [9]. To ascertain specific clinical signs and symptoms related to suicidal ideation, we examined the factor analysis for a relationship between SDS and UPDRS items. We found that suicidal ideation in SDS was categorized with UPDRS items 11-15 and 27-29 (posture and gait disturbances) rather than with other SDS items. UPDRS items pertaining to hand tremor and rigidity did not correlate with suicidal ideation. Suicide is an irreparable event in depressed patients. Our results indicate that close attention must be paid to patients with posture and gait disturbances to thwart suicide attempts.

It is possible that there is a specific association between symptoms of depression and neuropathological processes. The pathological hallmark of PD is a reduction of dopamine neurons in the substantia nigra. Neuron loss has also been reported in the medulla oblongata and neocortex [20]. Psychopathology and cognitive impairment are reported to be more frequent in patients with cerebellar degeneration with concomitant

basal ganglia involvement [21]. In the present study, the total SDS scores in PD patients were similar to those in SCD patients, and logistic analysis of each SDS item revealed some characteristic differences between PD and SCD. The scores for SDS items concerning constipation and indecisiveness were significantly higher in PD than SCD. It appears that constipation might not be a symptom of depression in PD patients but rather a complication of PD or antiparkinsonian treatment. On the other hand, indecisiveness might be a characteristic symptom of PD. In other words, PD patients have difficulties in decision-making, and difficulty making decisions might be attributable to the neuropathology of PD. It is possible to distinguish PD and SCD patients based on the scores for particular SDS items. The percentage of correct answers was as high as 78% using an estimated regression model by logistic analysis.

Treatment for depression in PD is controversial. Controlled clinical trials to sufficiently assess the efficacy of antidepressants in PD are lacking [1]. Some dopamine agonist treatments were reported to improve symptoms of depression in PD patients [13], but L-DOPA has not consistently been found to alleviate them [22]. It was recommended that depression associated with PD be treated with selective serotonin reuptake inhibitors [23]. Prior to treatment, however, characteristics of depression must be fully evaluated in each patient.

It appears that there are three types of depression in PD. The first is major depression that is unrelated with PD. These patients must be appropriately treated for depression regardless of PD symptoms. The second is reactive depression that is proportional to disabilities due to PD. In those cases, antiparkinsonian treatments might alleviate some of the symptoms of depression. The third is related to neuropathological changes in PD. Presumably, there will be no effective treatment for this type of depression until treatment for the specific neuropathological changes is available. Further studies are needed to determine optimal antidepressant therapy in PD.

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TABLE 1. ***Clinical characteristics of patients***

	Parkinson's Disease (n=58)	Spinocerebellar Degeneration (n=26)
Age	67.8 ± 10.5	65.7 ± 8.5
Sex (Male:Female)	24: 34	8:18
Duration of disease	8.0 ± 5.4	6.8 ± 5.3
Hoehn-Yahr stage	2.5 ± 0.9	
mRankin score		2.8 ± 0.9
UPDRS score	36.4 ± 16.5	

TABLE 2. ***Total SDS scores in PD patients compared to disease severity.***

	Correlation coefficient	p-value
Hohen-Yahr stage	0.320	<0.0001
UPDRS total	0.363	0.0056
UPDRS I	0.686	<0.0001
UPDRS II	0.263	0.0500
UPDRS III	0.189	0.1635
UPDRS IV	0.274	0.0409

TABLE 3. ***Factor loading by varimax rotation of factor analysis***

				Factor1	Factor2	Factor3
SDS		1	Depressed affect	0.365	-0.075	**0.492**
		2	Diurnal variation	0.072	0.021	0.258
		3	Crying spells	0.186	-0.105	0.307
		4	Sleep disturbance	0.064	-0.122	**0.400**
		5	Decreased appetite	0.024	0.053	0.099
		6	Decreased libido	0.000	0.063	0.177
		7	Weight loss	0.130	0.287	0.233
		8	Constipation	0.124	0.180	0.247
		9	Tachycardia	-0.144	-0.089	0.372
		10	Fatigue	0.033	0.190	0.334
		11	Confusion	0.130	-0.031	**0.550**
		12	Psychomotor retardation	0.157	0.113	**0.615**
		13	Agitation	0.243	0.091	**0.403**
		14	Hopelessness	0.061	0.007	**0.408**
		15	Irritability	0.227	0.007	**0.599**
		16	Indecisiveness	-0.099	0.244	**0.447**
		17	Personal devaluation	-0.003	-0.032	**0.599**
		18	Emptiness	-0.141	0.181	**0.596**
		19	Suicidal ideation	**0.552**	-0.145	**0.493**
		20	Dissatisfaction	0.192	-0.017	**0.759**
UPDRS	I	1	Intellectual Impairment	0.212	0.351	0.125
		2	Thought Disorder	0.293	0.085	0.275
		3	Depression	0.162	-0.085	**0.713**
		4	Motivation/Initiative	-0.005	-0.051	**0.526**
	II	5	Speech	0.341	**0.508**	0.022
		6	Salivation	0.382	**0.501**	-0.076
		7	Swallowing	0.337	0.061	-0.005
		8	Handwriting	0.318	**0.605**	-0.137
		9	Cutting food and handling utensils	0.205	**0.464**	0.070
		10	Dressing	**0.466**	**0.517**	0.206
		11	Hygiene	**0.685**	**0.464**	0.173
		12	Turning in bed and adjusting bed clothes	**0.792**	0.122	0.269
		13	Falling (unrelated to freezing)	**0.638**	0.298	0.148
		14	Freezing when walking	**0.803**	-0.007	-0.067
		15	Walking	**0.782**	0.200	0.085
		16	Tremor	-0.248	0.277	-0.135
		17	Sensory complaints related to parkinsonism	0.145	0.364	0.057
	III	18	Speech	0.153	**0.546**	0.118
		19	Facial Expression	0.148	**0.599**	0.212
		20	Tremor at rest	-0.385	0.297	-0.078
		21	Action or Postural Tremor of hands	-0.028	0.300	0.007
		22	Rigidity	-0.036	**0.692**	-0.097
		23	Finger Taps	0.112	**0.665**	0.042
		24	Hand Movements	-0.016	0.258	-0.038
		25	Rapid Alternating Movements of Hands	-0.089	**0.658**	0.087
		26	Leg Agility	0.243	**0.407**	-0.243
		27	Arising from Chair	**0.686**	0.383	0.139
		28	Posture	**0.651**	0.377	0.236
		29	Gait	**0.666**	**0.448**	0.163
		30	Postural Stability	**0.483**	0.267	0.196
		31	Body Bradykinesia and Hypokinesia	**0.448**	**0.690**	0.019

TABLE 4. ***Mean scores and adjusted odds ratio of each SDS item for PD patients compared to SCD patients by logistic analysis.***

	PD	SCD	Odds Ratio			
SDS Parameter	Mean ± SD	Mean ± SD	Point Estimate	95% Confidence Limits		p-value
1. Depressed affect	1.74 ± 0.74	1.54 ± 0.71	2.542	0.784	8.245	0.120
2. Diurnal variation	2.50 ± 1.34	2.92 ± 1.38	0.591	0.343	1.016	0.057
3. Crying spells	1.47 ± 0.83	1.54 ± 0.71	0.595	0.206	1.724	0.339
4. Sleep disturbance	1.71 ± 1.01	1.73 ± 0.78	0.893	0.400	1.993	0.782
5. Decreased appetite	1.64 ± 1.04	1.69 ± 1.23	1.777	0.865	3.648	0.117
6. Decreased libido	3.28 ± 1.13	3.69 ± 0.74	0.637	0.290	1.400	0.262
7. Weight loss	1.88 ± 1.14	1.77 ± 1.18	0.873	0.439	1.736	0.699
8. Constipation	**2.48 ± 1.19**	**1.88 ± 1.14**	**3.470**	**1.606**	**7.497**	**0.002**
9. Tachycardia	1.74 ± 0.87	1.73 ± 1.04	1.097	0.523	2.299	0.807
10. Fatigue	2.52 ± 1.00	2.50 ± 1.24	0.936	0.455	1.924	0.857
11. Confusion	2.43 ± 1.13	2.42 ± 1.30	1.351	0.608	3.001	0.460
12. Psychomotor retardation	2.31 ± 1.25	2.62 ± 1.33	0.638	0.335	1.215	0.171
13. Agitation	1.81 ± 1.10	1.73 ± 1.25	1.274	0.599	2.706	0.529
14. Hopelessness	2.88 ± 1.06	3.27 ± 1.12	0.695	0.337	1.434	0.325
15. Irritability	1.79 ± 0.97	1.88 ± 1.24	0.693	0.282	1.706	0.425
16. Indecisiveness	**2.64 ± 1.07**	**2.31 ± 1.26**	**3.006**	**1.354**	**6.674**	**0.007**
17. Personal devaluation	2.76 ± 1.16	2.88 ± 1.11	0.816	0.368	1.812	0.618
18. Emptiness	2.14 ± 0.96	2.38 ± 1.17	0.483	0.201	1.160	0.104
19. Suicidal ideation	1.60 ± 0.90	1.62 ± 1.02	0.861	0.405	1.831	0.698
20. Dissatisfaction	2.43 ± 1.01	2.81 ± 1.17	0.881	0.378	2.056	0.770