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Letter to the Editor

Depression in X-linked dystonia-parkinsonism: A case–control study

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X-linked dystonia-parkinsonism (XDP), also known as *lubag*, was originally described as endemic to Panay, Philippines [1]. XDP demonstrates a primary and progressive neuronal degeneration of the striatum and is characterized by an adult-onset movement disorder that manifests as severe and progressive dystonia with a high frequency of generalization, followed by the onset of a parkinsonian state in the later years of life [1,2]. Suicide incidence has been reported to account for 9% of the mortality in patients with XDP [1]. Despite the high suicide risk, only a few case reports refer to mood disorders in patients with XDP. The purpose of this study was to determine the prevalence of depressive symptoms among patients with XDP.

In July 2010, a field study was conducted in the islands of Luzon and Panay, Philippines. Psychiatric symptoms were investigated in 14 patients with a positive family history of dystonia consistent with X-linked recessive inheritance. No patients were taking antidepressants or dopaminergic medications. Before inclusion in this study, informed consent was obtained from all participants. Two trained psychiatrists (M.N. and J.I.) simultaneously made psychiatric diagnoses according to the DSM-IV criteria using the Mini-International Neuropsychiatric Interview. The Zung Self-Rating Depression Scale (SDS) was administered to assess depressive symptoms. Depression severity was defined as follows: no significant psychopathology (SDS $<$ 40 points), presence of minimal to mild depression (40–47 points), moderate to marked depression (48–55 points), and severe to extreme depression ($\geq$56 points). To assess depressive symptoms in residents of the islands of Panay, Philippines, 14 age-matched male controls were also enrolled. All data were analyzed using SPSS for Windows, version 19 (IBM, Armonk, NY, USA). Data are shown as mean $\pm$ standard deviation (SD). For group differences, the Mann–Whitney *U*-test were used. Spearman's rank correlations were used to evaluate the relationships between different variables. The threshold for significance was defined as $P < 0.05$, corrected using the Bonferroni method. This study was approved by the ethical committee of the University of Tokushima.

Genetic assessment proved that all 14 patients had the disease-specific SVA (short interspersed nuclear element, variable number of tandem repeats, and Alu composite) retrotransposon insertion in intron 32 of *TAF1* (TATA box-binding protein associated factor 1) [3]. The mean (SD) age of the patients at disease onset was 42.3 (9.8) y and at the time of examination was 48.2 (8.7) y. The mean duration of illness was 5.9 (4.8) y. The mean age of the 14 age-matched male control subjects was 48.0 (8.2) y. For the SDS in patients with XDP, Cronbach's α was 0.656, but increased substantially to 0.702 when SDS Item 11 was omitted.

Six (42.9%) of 14 patients had at least one current Axis I diagnosis (Table 1). Two patients (14.3%) had >2 diagnoses. Two patients (14.3%) were diagnosed with current major depression, according to the DSM-IV criteria. These two patients scored significantly higher on the SDS scale than the remaining 12 patients (mean SDS score: 60.5 vs. 45.5, respectively; $P = 0.009$). Based on the SDS score, 13 patients with XDP (92.9%) had depressive symptoms (SDS $\geq$ 40). Depressive symptoms were minimal-to-mild in 50.0%, moderate-to-marked in 21.4%, and severe-to-extreme in 21.4% of patients. In contrast, 28.6% and 14.3% of the age-matched control subjects manifested minimal-to-mild and moderate-to-marked depression, respectively. The mean SDS score of the XDP group was higher than that of the control group (47.6 ± 8.1 vs. 38.4 ± 7.6; $P = 0.004$). The odds ratio for overall depression was increased (log-OR = 2.85, 95% CI = 0.56–5.14) in patients with XDP compared to the control group. The odds ratio for moderate-to-extreme depression was increased but not significant (log-OR = 1.50, 95% CI = −0.33–3.33). The analysis of SDS sub-items revealed that 5 sub-items were significantly higher in patients with XDP compared to the control group (Table 2). The total SDS score correlated significantly with Item 1 (depressed affect) and Item 20 (dissatisfaction) in patients with XDP and with Item 14 (hopelessness) and Item 20 in Control subjects, after the Bonferroni correction (Table 2). Thus, Item 1 was considered an intrinsic item related to depression severity for patients with XDP.

Table 1
Current psychopathology in patients with XDP.

	No. of patients (%)
n	14
Panic disorder	1 (7.1%)
Agoraphobia	3 (21.4%)
Social Phobia	4 (28.6%)
Any anxiety disorder	5 (35.7%)
Bipolar disorder	1 (7.1%)
Major depression	2 (14.3%)
Any affective disorder	3 (21.4%)

Two patients have >2 diagnoses. XDP: X-linked dystonia-parkinsonism.

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Table 2
Analyses of overall SDS score (XDP vs. Control).

Items on the Zung self-rating depression scale (SDS)	XDP ($n = 14$)	Control ($n = 14$)	*P*-value	Univariate analysis (XDP/Control)	
				Spearman's *r*	*P*-value
1. Depressed affect	2.4 ± 1.3	2.1 ± 0.9	0.406	0.803/0.199	0.001‖/0.495
2. Diurnal variation*	2.7 ± 1.0	1.9 ± 0.7	0.013†	0.268/0.532	0.355/0.050
3. Crying spells	1.6 ± 0.8	1.6 ± 0.9	1.000	0.149/0.415	0.612/0.140
4. Sleep disturbance	2.6 ± 1.2	1.9 ± 1.0	0.096	−0.008/0.575	0.978/0.031
5. Decreased appetite*	2.6 ± 1.2	2.9 ± 1.0	0.509	0.073/0.219	0.804/0.453
6. Decreased libido*	3.5 ± 0.9	2.4 ± 1.2	0.012†	0.135/0.231	0.644/0.427
7. Weight loss	3.2 ± 1.1	2.2 ± 1.1	0.018†	0.254/0.658	0.381/0.011
8. Constipation	1.9 ± 0.8	1.7 ± 0.9	0.658	0.263/0.109	0.363/0.712
9. Tachycardia	2.0 ± 1.1	1.9 ± 0.5	0.669	0.230/0.096	0.428/0.744
10. Fatigue	2.7 ± 1.3	1.9 ± 0.8	0.042†	−0.36/0.600	0.902/0.023
11. Confusion*	1.9 ± 1.1	2.1 ± 0.7	0.684	0.36/0.595	0.903/0.025
12. Psychomotor retardation*	3.0 ± 1.0	1.9 ± 0.9	0.004‡	0.437/0.613	0.118/0.020
13. Agitation	2.4 ± 1.2	2.0 ± 0.8	0.262	0.350/0.540	0.220/0.046
14. Hopelessness*	1.8 ± 1.1	1.5 ± 0.5	0.421	0.687/0.852	0.007/<0.001‖
15. Irritability	2.7 ± 1.3	2.1 ± 0.8	0.126	0.359/0.276	0.207/0.339
16. Indecisiveness*	2.0 ± 1.2	1.9 ± 0.8	0.859	0.579/0.302	0.030/0.293
17. Personal devaluation*	2.2 ± 1.4	1.4 ± 0.6	0.067	0.202/0.525	0.490/0.054
18. Emptiness*	2.7 ± 1.1	2.0 ± 1.0	0.084	0.411/0.421	0.145/0.134
19. Suicidal ideation	1.7 ± 0.6	1.7 ± 0.6	1.000	0.636/0.664	0.015/0.010
20. Dissatisfaction*	2.1 ± 1.3	1.5 ± 0.8	0.163	0.846/0.799	<0.001‖/0.001‖
SDS total score	47.6 ± 8.1	38.4 ± 7.6	0.004‡	1.000/1.000	–

Data are mean ± SD. The Mann Whitney *U*-test was used for comparison of XDP vs. Control. Correlations were assessed between each SDS sub-item as the dependent variable and the total SDS score (Spearman's rank correlation analysis). *indicates reversed items. †$P < 0.05$, ‡$P < 0.01$. ‖$P < 0.05$, after Bonferroni correction.

This is the first study to investigate psychiatric symptoms among patients with genetically verified XDP. The results of this study showed that a comparatively higher percentage of patients with XDP suffered from depressive symptoms (92.9%: SDS $\geq$ 40) and the magnitude of depressive symptoms in patients with XDP were more severe than control subjects. Based on the SDS and same cut-off criteria used in the current study, the prevalence of depressive symptoms has been reported to 63.8% in Parkinson's disease and 73.1% in patients with spino-cerebellar degeneration [4]. Mean SDS scores (47.6 ± 8.1 points) in patients with XDP were similar to those in other neurodegenerative diseases; 43.7 points in Parkinson's disease, 44.9 points in spino-cerebellar degeneration, and 44.0 points in Alzheimer's disease [4,5]. There is no data available for dystonia using the SDS. Our results provide an estimate suggesting that depressive symptoms are highly prevalent and that the magnitude of depressive symptoms in patients with XDP is equally severe in patients with other neurodegenerative diseases. Item 1 (depressed affect) could be a useful question to assess depressive symptoms in patients with XDP.

Competing interests

The authors report no competing interests concerning the materials or methods used in this study or the findings specified in this paper.

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Ryoma Morigaki
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Motor Neuroscience and Neurotherapeutics, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Masahito Nakataki
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Psychiatry, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Toshitaka Kawarai
Department of Clinical Neuroscience, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Lillian V. Lee, Rosalia A. Teleg
Department of Child Neuroscience, Philippine Children's Medical Center, Quezon Avenue, Quezon City, Philippines

Ma. Daisy P. Tabuena
Department of Internal Medicine, Section of Neurology, West Visayas State University Medical Center, Iloilo City, Philippines

Hideo Mure
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Neurosurgery, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Wataru Sako
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Clinical Neuroscience, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Paul Matthew D. Pasco
Department of Child Neuroscience, Philippine Children's Medical Center, Quezon Avenue, Quezon City, Philippines

Shinji Nagahiro
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Neurosurgery, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Junichi Iga, Tetsuro Ohmori
Department of Psychiatry, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Satoshi Goto
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Motor Neuroscience and Neurotherapeutics, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

Ryuji Kaji*
Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, University of Tokushima, Tokushima 770-8503, Japan

Department of Clinical Neuroscience, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, Tokushima 770-8503, Japan

* Corresponding author. Department of Clinical Neuroscience, Institute of Health Biosciences, Graduate School of Medical Sciences, University of Tokushima, 3-18-15, Kuramoto-Cho, Tokushima 770-8503, Japan.
Tel.: +81 88 633 7206; fax: +81 88 633 7208.
E-mail addresses: kajkyoto@mbox.kyoto-inet.or.jp, rkaji@clin.med.tokushima-u.ac.jp

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