Frequency and Correlates of Involuntary Emotional Expression Disorder in Parkinson's Disease

Gustavo M. Petracca, M.D.
Ricardo E. Jorge, M.D.
Laura Ación, M.S.
Daniel Weintraub, M.D.
Robert G. Robinson, M.D.

Involuntary emotional expression disorder (IEED) is a syndrome characterized by involuntary episodes of emotional expression, particularly crying or laughing, that occur in patients with a neurological illness, including neurodegenerative diseases. The authors assessed the frequency and clinical correlates of IEED among 131 patients with Parkinson's disease. IEED was present in 16.8% of patients overall and in 15.3% of depressed patients. The only clinical correlate of IEED diagnosis was greater severity of Parkinson's disease. The lack of an association between IEED and depression suggests that, in spite of some symptom overlap, the two disorders are distinct neuropsychiatric syndromes in Parkinson's disease.

(The Journal of Neuropsychiatry and Clinical Neurosciences 2009; 21:406–412)

Involuntary emotional expression disorder (IEED) is characterized by sudden episodes of laughing or crying that either occur spontaneously or are out of proportion to the stimuli that provoke them. A variety of terms have been used to refer to this disorder, including pseudobulbar affect, pathological crying and laughing, emotional incontinence or lability, and pathologic affect.[1,2] Recently, Cummings et al.[3] proposed the term involuntary emotional expression disorder (IEED) as an inclusive nosological concept to characterize patients with neurological disease or injury who experience episodic and involuntary bouts of uncontrollable emotional expression.

IEED has been observed in patients with stroke (10–20%),[4–9] traumatic brain injury (5–11%),[4,5] Alzheimer's disease (39%),[10] multiple sclerosis (10%),[11] amyotrophic lateral sclerosis (19–49%),[12,13] seizure disorders,[14] multiple system atrophy-cerebellar type,[15] and corticobasal degeneration.[16] However, to our knowledge there are no previous reports on the frequency and clinical correlates of IEED in Parkinson's disease.

Classic pathophysiological theories of IEED are based

Received August 9, 2007; revised December 16, 2007, and November 9, 2008; accepted November 13, 2008. Dr. Petracca is affiliated with the Institute of Neuroscience Buenos Aires (INEBA); Drs. Jorge, Ms. Ación, and Dr. Robinson are affiliated with the Department of Psychiatry, Roy C. and Lucille A. College of Medicine, at the University of Iowa; Dr. Weintraub is affiliated with the Department of Psychiatry at the University of Pennsylvania. Address correspondence to Ricardo E. Jorge, M.D., 200 Hawkins Dr., W278 GH, Iowa City, IA 52242-1009; ricardo-jorge@uiowa.edu (e-mail).

on the assumptions of serial processing and hierarchical control. According to these assumptions, IEED results from the release of cortical inhibition of brainstem centers that integrate the motor activation patterns involved in laughing and crying. Thus, IEED is an essential part of the pseudobulbar palsy syndrome associated with bilateral lesions in corticobulbar pathways. However, IEED may also be seen in patients with unilateral lesions that do not involve motor or premotor areas. For instance, Ross and Rush[17] reported that IEED may result from lesions of the right inferior frontal lobe in association with a major depressive disorder. More recently, Parvizi et al.[15] suggested that the critical lesion or dysfunction eliciting IEED is located along fronto-ponto-cerebellar pathways.[18] IEED can be seen in neurological disorders without any demonstrable lesions but with disruptions in fronto-subcortical circuits. For instance, McCullagh et al.[13] studied amyotrophic lateral sclerosis patients and implicated the prefrontal cortex in the pathophysiology of IEED.

There is also evidence that IEED is related to disruption of monoaminergic modulation of both limbic structures and bulbar motor networks.[19] If this hypothesis is correct, IEED should be a relatively frequent finding among patients with Parkinson's disease, who undergo a selective degeneration of aminergic pathways and brainstem nuclei.[6,7,18,20]

In spite of Parkinson's disease being the second most common neurodegenerative disease, little is known about IEED in Parkinson's disease. Thus, the aim of the present study was to examine the frequency and clinical correlates of IEED in Parkinson's disease. We hypothesized that IEED would be relatively common among Parkinson's disease patients, IEED would occur without comorbid depression, and IEED would be associated with excess disability.

METHODS

Patients

We assessed a series of 131 patients meeting the United Kingdom Parkinson's Disease Society Brain Bank[21] clinical criteria for idiopathic Parkinson's disease who were followed at a general neurology clinic of a tertiary care hospital in Buenos Aires, Argentina. After the methodology of the study was fully explained, an informed written consent was obtained from all the participants. Patients were assessed by a neurologist who was blind to the psychiatric data and a psychiatrist blind to neurological findings.

In order to examine as homogeneous a group of Parkinson's disease patients as possible, patients with radiological evidence of cerebrovascular lesions (i.e., MRI scans revealing focal lesions that were hypointense in T1 and hyperintense in FLAIR sequences and were greater than 3 mm along their major axis in transversal views) were excluded from the study. Other exclusion criteria were a history of cognitive decline starting 1 year or less from the onset of parkinsonian signs, a history of neuroleptic medication exposure, and lack of therapeutic response to antiparkinsonian drugs.

Neurological Examination

The neurological examination was conducted by a neurologist blinded to the neuropsychiatric results. Parkinson's disease symptoms were rated with parts I-IV of the Unified Parkinson's Disease Rating Scale (UPDRS),[22] and overall severity of Parkinson's disease was rated with the Hoehn and Yahr Staging Scale.[23] Higher scores indicate greater severity of impairment on both instruments.

Psychiatric Examination

The Pathological Laughing and Crying Scale[19] is a reliable and valid interviewer-rated scale that rates severity of IEED symptoms (higher scores indicating greater severity), including the frequency of crying or laughing episodes, duration and degree of voluntary control of episodes, their relationship to triggering events, inappropriateness in relation to prevailing mood, and degree of resultant distress. The scale is administered to the patient with at least one first-degree relative or caregiver serving as an informant. The time frame for including symptoms was established *a priori* as the 4-week period preceding the assessment.

Diagnosis of Involuntary Emotional Expression Disorder

Patients were considered to have IEED if they met all of the three following criteria: they scored 2 or 3 (i.e., more impaired) on item 2 of the Pathological Laughing and Crying Scale assessing the frequency of crying episodes; they scored 2 or 3 on item 13 of the Pathological Laughing and Crying Scale assessing loss of voluntary control of emotions during episodes; and they scored 2 or 3 on item 18 of the Pathological Laughing and Crying Scale assessing distress and embarrassment associated with

the episodes. In addition, a total score ≥10 was required for a patient to be diagnosed as having IEED.

The Structured Clinical Interview for DSM-IV (SCID),[8] a semistructured interview, was used to assess the presence of axis I DSM-IV disorders. The SCID was conducted with the patient and an informed other in frequent contact with the patient (i.e., at least 3 times per week during the past 6 months). The Hamilton Depression and Anxiety Rating Scales (HAM-D, HAM-A)[8,9,24] were used to assess the severity of depression and anxiety symptoms, respectively. Higher scores on both scales indicate greater severity of symptoms.

The Apathy and Irritability Scales[25,26] are interviewer-rated scales that assess severity of apathy and anxiety, respectively. Scores were based on information obtained from the patient and a relative or caregiver. For both instruments, higher scores indicate greater severity of symptoms. The Overt Aggression Scale[27] measures the severity of four specific aspects of aggressive behavior (i.e., verbal aggression, and physical aggression against self, objects and other people). It is an interviewer-rated scale based on observable criteria and information obtained from the patient and an informed other. The Hachinski Ischemic Scale[28] assesses the contribution of cerebrovascular disease to the etiology of dementia. Higher scores indicate increased severity of cardiovascular risk factors.

Mini-Mental State Examination (MMSE)[29] was used as a measure of global cognitive abilities. The Functional Independence Measure[30] assesses patients' level of functioning in basic and instrumental activities of daily living (e.g., self-care, sphincter control, mobility, locomotion, communication, and social cognition). Higher scores indicate greater independence in performing activities of daily livings.

Statistical Analysis

The Wilcoxon-Mann-Whitney U test was use to compare group means, as much of the data did not meet the homogeneity of variance and normality assumption required by the standard t test. Frequencies between groups were compared using Fisher's exact test. We used simple linear regression to control for covariates. Since the residual analysis in each case was satisfactory, no further transformations of the data were necessary. All p values reported are two-tailed, and significance level was set at 0.05.

RESULTS

Frequency of IEED and Demographic Variables Twenty-two (16.8%) patients had active IEED, all of them with crying episodes only (we did not observe cases of pathological laughter). These 22 patients constituted the IEED group, whereas the rest (n=109) of the Parkinson's disease patients were categorized as the non-IEED group. There were no between-group differences in demographic variables (Table 1).

TABLE 1. Demographic and Psychiatric Findings

Variable	Parkinson's Disease Without IEED (n=109)		Parkinson's Disease With IEED (n=22)		Analysis	
					Test[a]	p
Gender (% females)	49.5		36.3			0.35[b]
	Mean	SD	Mean	SD		
Age	65.0	10.0	63.8	9.6	1,329.0	0.45
Education (years)	10.2	4.6	9.4	5.3	1,305.5	0.37
Duration of illness (years)	5.1	4.0	7.2	5.5	1,648.5	0.09
Pathological Laughing and Crying Scale - Crying	3.6	4.0	11.0	1.1	2,583.5	<0.0001
Pathological Laughing and Crying Scale - Laughing	0.0	0.0	0.0	0.0		
Hamilton Depression Rating Scale	9.8	7.3	12.5	7.0	1,741.0	0.08
Hamilton Anxiety Rating Scale	8.4	6.7	10.9	7.9	1,685.0	0.13
Apathy Scale	14.9	9.12	16.0	8.5	1,525.5	0.50
Irritability Scales	11.5	8.0	13.7	7.2	1,636.0	0.15
Overt Aggression Scale	1.1	3.9	0.3	0.8	910.5	0.54
Hachinski Ischemic Scale	1.9	2.1	2.5	1.8	1,544.0	0.08
Mini-Mental State Examination	24.5	5.0	22.9	4.9	1,164.0	0.08
Functional Independence Measure	64.7	10.9	63.3	11.9	1,115.0	0.57

[a] Wilcoxon-Mann-Whitney U except when otherwise indicated
[b] Fisher's exact test
IEED=involuntary emotional expression disorder

Psychiatric Variables Eleven (50.0%) of the IEED patients met DSM-IV criteria for a depressive disorder (major depression [n=7] or dysthymia [n=4]). In the non-IEED group, 48 (44.0%) met DSM-IV criteria for depression (major depression [n=25] or dysthymia [n=23]). There were no differences between the IEED and the non-IEED groups in the frequency of major depression or dysthymia. In addition, there were no between-group differences in the severity of anxiety symptoms, apathy, irritability, or aggressiveness (Table 1).

Patients received antidepressants to reduce depressive symptoms. Benzodiazepines and/or atypical neuroleptics were indicated to treat anxiety, agitation, or psychotic symptoms. However, there were no significant differences between the IEED and the non-IEED groups in the percentage of patients taking this type of medications (Table 2).

Parkinson's Disease-Related Variables Of the 22 patients with IEED, seven patients (33.3%) were classified as having severe Parkinson's disease (Hoehn and Yahr stages 4 or 5), compared with 12 of 109 patients (11.0%) without IEED (p=0.02).

Patients with IEED had greater UPDRS salivation (p=0.02), axial rigidity (p=0.04), bradykinesia (p=0.07), and gait disturbance (p=0.19) scores than patients without IEED (Table 2). In addition, the IEED group showed significant functional impairment in the UPDRS activities of daily living section (Table 2). In a linear regression model that included IEED status, duration of illness, and severity of depression, IEED status no longer predicted UPDRS-activities of daily living score. Moreover, there were no significant differences between the IEED and the non-IEED groups in any other clinical variable (Tables 1 and 2).

IEED and Comorbid Depression

When comparing IEED patients with (n=11) and without depression (n=11), depressed IEED patients had significantly higher HAM-D, HAM-A, and Apathy Scale scores (Table 3). There were no significant between-group differences in Overt Aggression Scale or Irritability Scale scores.

Patients with IEED and depression had significantly higher Hachinski Ischemic Scale scores (Table 3) than nondepressed IEED patients. There were no significant differences between the two groups in any non-mood UPDRS item, Functional Independence Measure, or MMSE scores (Table 3).

TABLE 2. Neurological Findings

	Parkinson's Disease Without IEED (n=109)		Parkinson's Disease With IEED (n=22)		Analysis	
					Test[a]	p
	Mean	SD	Mean	SD		
Age	65.0	10.0	63.8	9.6	1,329.0	0.45
UPDRS-Mentation/Mood	4.3	3.2	3.6	2.5	866.5	0.53
UPDRS-ADLs	11.1	7.6	15.2	8.0	1,327.0	0.03
UPDRS-Salivation	0.6	0.9	1.2	1.1	1,405.0	0.02
UPDRS-Motor	18.1	10.1	21.6	12.1	1,267.5	0.32
UPDRS-Axial Rigidity	0.9	1.1	1.5	1.4	1,401.0	0.04
UPDRS-Bradykinesia	1.3	1.0	1.8	1.2	1,368.0	0.07
UPDRS-Gait	0.9	0.8	1.3	1.1	1,298.5	0.19
UPDRS-Complications of Therapy	2.0	3.1	1.7	2.6	955.5	0.66
UPDRS-Clinical fluctuations, average of "off periods" in walking day	0.3	0.7	0.3	0.6	1,059.5	0.65
Levodopa (mg/day)	557.7	385.8	598.6	419.1	917.5	0.61
Bromocriptine (mg/day)	1.2	4.0	2.5	6.0	929.5	0.56
	n	%	n	%		
Hohen and Yahr						0.02
Stages 1-2	52	57.1	9	50.0		
Stage 3	29	31.9	3	16.7		
Stages 4-5	10	11.0	6	33.3		
Anxiolytics	26	31.0	2	12.5		0.23[b]
Antidepressants	17	20.7	1	5.9		0.19[b]

[a] Wilcoxon-Mann-Whitney U unless otherwise indicated
[b] Fisher's exact test
UPDRS=Unified Parkinson's Disease Rating Scale

DISCUSSION

Involuntary emotional expression disorder (IEED) was present in 16.8% of Parkinson's disease patients followed in a general neurology clinic at a tertiary metropolitan hospital. Excluding Parkinson's disease patients with a comorbid depressive disorder, the frequency of IEED was 15.3%. The proportion of patients in advanced stages of the disease was significantly greater among patients with IEED. A greater impairment in activities of daily living was found in the IEED group measured by the UPDRS activities of daily living. However this was not detected by the Functional Independence Measure. The UPDRS activities of daily living is a more sensible and specific measure of activities of daily living impairment than the Functional Independence Measure among patients with Parkinson's disease. In addition, its high longitudinal reproducibility values make the former a precise measure of change. A 2-point increase in this scale is considered clinically meaningful. Thus, the 4-point difference between the means of the IEED and the non-IEED groups is suggestive of greater disability among patients with IEED.[31] However, there were no other between-group differences in demographic or clinical variables.

Before further discussion of these findings, we need to point out the limitations of our study. Patients included in this study were enrolled in a tertiary care center and might not be representative of other Parkinson's disease groups. However, all our patients met stringent clinical criteria for Parkinson's disease, including a positive response to L-dopa therapy. The neuropsychological evaluation of these patients was limited to a single global cognitive measure (i.e., the MMSE). A more extensive neuropsychological battery would be necessary to examine more subtle cognitive correlates of IEED. Although the difference is not statistically significant, the proportion of patients taking antidepressants was higher among patients without IEED. As antidepressants have been used to treat emotional dysregulation (usually in a lower dose than that used to treat clinical depression), our results might be biased, leading to an underestimation of the frequency of IEED. Another limitation is the exploratory nature of this study and the consequent lack of power to detect significant differences. Finally, the recent definition and diagnosis criteria for IEED were not available at the time of data collection.[3]

Given these limitations, IEED appears to be relatively common in Parkinson's disease, particularly in latter stages of the illness. Although IEED can co-occur with depression, it occurred just as frequently in Parkinson's disease patients without depression, suggesting that this form of emotional dysregulation is distinct from depression and should be included in the differential

TABLE 3. Psychiatric and Neurological Findings in IEED Patients

	Parkinson's Disease With IEED Without Depression (n=11)		Parkinson's Disease With IEED and Depression (n=11)		Analysis	
					Test[a]	p
Gender (% females)	27.3		45.5			0.66[b]
	Mean	SD	Mean	SD		
Age	63.6	13.3	63.9	3.9	126.5	1.00
Education (years)	11.2	5.9	7.6	4.2	149.5	0.15
Duration of illness (years)	7.3	5.8	7.0	5.4	129.0	0.90
Hamilton Depression Rating Scale	7.0	2.9	18.0	5.3	69.5	0.001
Hamilton Anxiety Rating Scale	5.5	3.8	16.2	7.3	72.5	0.002
Apathy Scale	10.8	5.5	21.3	7.8	80.5	0.007
Hachinski Ischemic Scale	1.5	1.3	3.4	1.8	77.5	0.03
Pathological Laughing and Crying Scale - Crying	10.3	3.5	10.6	1.0	148.5	0.15
Mini-Mental State Examination	23.3	5.8	22.5	4.0	140.0	0.40
Functional Independence Measure	67.7	4.2	59.3	15.2	104.5	0.26
UPDRS-mentation/mood	1.9	1.6	5.6	1.7	104.5	0.007
UPDRS-motor	20.9	12.1	22.3	12.8	92.5	0.87
UPDRS-postural stability	0.6	0.8	1.7	1.3	112.0	0.08
UPDRS-activities of daily living	13.9	6.0	16.6	9.9	84.0	0.93
UPDRS-complications of therapy	1.9	3.3	1.4	1.5	77.5	0.92

[a] Wilcoxon-Mann-Whitney U unless otherwise indicated
[b] Fisher's exact test
UPDRS=Unified Parkinson's Disease Rating Scale; IEED=involuntary emotional expression disorder

diagnosis of emotional disturbances associated with Parkinson's disease.[6]

Patients with Parkinson's disease might have coexistent ischemic lesions in the deep hemispheric white matter that might contribute to a rapidly progressive course and cognitive decline.[32–34] It is plausible that these ischemic lesions could also contribute to the onset of IEED. However, we took special care to exclude Parkinson's disease patients with MRI evidence of focal ischemic lesions and/or extensive white matter disease, suggesting that IEED may occur in the absence of coexistent ischemic lesions.

IEED may also occur associated with impairment in the functional integrity of the prefrontal cortex among patients with amyotrophic lateral sclerosis[13] and multiple sclerosis.[11] Recently, Woolley et al.[35] reported the case of a patient with gradually progressive frontal atrophy who was selectively impaired in emotional expression and autonomic reactivity. The left inferior frontal gyrus was the area that showed the most important atrophic changes. Interestingly, this prefrontal area has been shown to have reduced glucose metabolic rates among patients with depression and Parkinson's disease.[36] Further studies will need to examine the role of neural circuits involving the ventral aspects of the prefrontal cortex in emotional expression of Parkinson's disease patients, including whether or not the left prefrontal cortex has an inhibitory effect.

We thank Drs. Marcelo Merello, Eran Chemerinski, and Janus Kremer for data collection. We especially thank Dr. Sergio E. Starkstein for his valuable advice and comments on the manuscript.

References

1. Arciniegas DB: A clinical overview of pseudobulbar affect. Am J Geriatr Pharmacother 2005; 3:4–8; quiz 16–17
2. Schiffer R, Pope LE: Review of pseudobulbar affect including a novel and potential therapy. J Neuropsychiatry Clin Neurosci 2005; 17:447–454
3. Cummings JL, Arciniegas DB, Brooks BR, et al: Defining and diagnosing involuntary emotional expression disorder. CNS Spectr 2006; 11:1–7
4. Tateno A, Jorge RE, Robinson RG: Pathological laughing and crying following traumatic brain injury. J Neuropsychiatry Clin Neurosci 2004; 16:426–434
5. Zeilig G, Drubach DA, Katz-Zeilig M, et al: Pathological laughter and crying in patients with closed traumatic brain injury. Brain Inj 1996; 10:591–597
6. Weintraub D, Stern MB: Psychiatric complications in Parkinson disease. Am J Geriatr Psychiatry 2005; 13:844–851
7. Schapira AH, Bezard E, Brotchie J, et al: Novel pharmacological targets for the treatment of Parkinson's disease. Nat Rev Drug Discov 2006; 5:845–854
8. Spitzer RL, Williams JBW, Gibbon M: Structured Clinical Interview for DSM-IV (SCID). New York, Biometric Research, New York State Psychiatric Institute, 1995
9. Hamilton M: The assessment of anxiety state of rating. Br J Med Psychol 1959; 32:50–55
10. Starkstein SE, Migliorelli R, Teson A, et al: Prevalence and clinical correlates of pathological affective display in Alzheimer's disease. J Neurol Neurosurg Psychiatry 1995; 59:55–60
11. Feinstein A, O'Connor P, Gray T, et al: Pathological laughing and crying in multiple sclerosis: a preliminary report suggesting a role for the prefrontal cortex. Mult Scler 1999; 5:69–73
12. Gallagher JP: Pathologic laughter and crying in ALS: a search for their origin. Acta Neurol Scand 1989; 80:114–117
13. McCullagh S, Moore M, Gawel M, et al: Pathological laughing and crying in amyotrophic lateral sclerosis: an association with prefrontal cognitive dysfunction. J Neurol Sci 1999; 169: 43–48
14. Arroyo S, Lesser RP, Gordon B, et al: Mirth, laughter, and gelastic seizures. Brain 1993; 116:757–780
15. Parvizi J, Joseph J, Press DZ, et al: Pathological laughter and crying in patients with multiple system atrophy-cerebellar type. Mov Disord 2007
16. Thumler BH, Urban PP, Davids E, et al: Dysarthria and pathological laughter/crying as presenting symptoms of corticobasal-ganglionic degeneration syndrome. J Neurol 2003; 250: 1107–1108
17. Ross ED, Rush AJ: Diagnosis and neuroanatomical correlates of depression in brain-damaged patients: implications for a neurology of depression. Arch Gen Psychiatry 1981; 38:1344–1354
18. Parvizi J, Anderson SW, Martin CO, et al: Pathological laughter and crying: a link to the cerebellum. Brain 2001; 124:1708–1719
19. Robinson RG, Parikh RM, Lipsey JR, et al: Pathological laughing and crying following stroke: validation of a measurement scale and a double-blind treatment study. Am J Psychiatry 1993; 150:286–293
20. McDonald WM, Richard IH, DeLong MR: Prevalence, etiology, and treatment of depression in Parkinson's disease. Biol Psychiatry 2003; 54:363–375
21. Gibb WR, Lees AJ: The significance of the Lewy body in the diagnosis of idiopathic Parkinson's disease. Neuropathol Appl Neurobiol 1989; 15:27–44
22. Martinez-Martin P, Gil-Nagel A, Gracia LM, et al: Unified Parkinson's Disease Rating Scale characteristics and structure. The Cooperative Multicentric Group. Mov Disord 1994; 9:76–83
23. Goetz CG, Poewe W, Rascol O, et al: Movement Disorder Society Task Force report on the Hoehn and Yahr Staging Scale: status and recommendations. Mov Disord 2004; 19:1020–1028
24. Hamilton MA: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62

25. Starkstein SE, Mayberg HS, Preziosi TJ, et al: Reliability, validity, and clinical correlates of apathy in Parkinson's disease. J Neuropsychiatry Clin Neurosci 1992; 4:134–139
26. Chemerinski E, Petracca G, Teson A, et al: Prevalence and correlates of aggressive behavior in Alzheimer's disease. J Neuropsychiatry Clin Neurosci 1998; 10:421–425
27. Yudofsky SC, Silver JM, Jackson W, et al: The overt aggression scale for the objective rating of verbal and physical aggression. Am J Psychiatry 1986; 143:35–39
28. Hachinski V, Norris JW: The Acute Stroke. Philadelphia, FA Davis, 1985
29. Folstein MF, Folstein SE, McHugh PR: "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189–198
30. Forer S, Granger CV: Functional Independence Measure. Buffalo, The Buffalo General Hospital State University of New York at Buffalo, 1987
31. Martinez-Martin P, Prieto L, Forjaz MJ: Longitudinal metric properties of disability rating scales for Parkinson's disease. Value Health 2006; 9:386–393
32. Beyer MK, Aarsland D, Greve OJ, et al: Visual rating of white matter hyperintensities in Parkinson's disease. Mov Disord 2006; 21:223–229
33. Burton EJ, McKeith IG, Burn DJ, et al: Progression of white matter hyperintensities in Alzheimer disease, dementia with Lewy bodies, and Parkinson disease dementia: a comparison with normal aging. Am J Geriatr Psychiatry 2006; 14:842–849
34. Piccini P, Pavese N, Canapicchi R, et al: White matter hyperintensities in Parkinson's disease: clinical correlations. Arch Neurol 1995; 52:191–194
35. Woolley JD, Gorno-Tempini ML, Werner K, et al: The autonomic and behavioral profile of emotional dysregulation. Neurology 2004; 63:1740–1743
36. Mayberg HS, Starkstein SE, Sadzot B, et al: Selective hypometabolism in the inferior frontal lobe in depressed patients with Parkinson's disease. Ann Neurol 1990; 28:57–64