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Involuntary emotional expression disorder (IEED) in Parkinson's disease

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Abstract

Objective—To estimate the frequency and correlates of involuntary emotional expression disorder (IEED) in Parkinson's disease (PD) using the Center for Neurologic Study-Lability Scale (CNS-LS) and recently-proposed diagnostic criteria for IEED.

Background—IEED is characterized by uncontrollable emotional episodes, typically unrelated to or in excess of the underlying mood, and occurring with minimal or no stimulus. IEED has been reported to occur in many neurological disorders and neurodegenerative diseases, but its prevalence and correlates in PD have not been well studied. Additionally, there is no published research using recently-proposed IEED diagnostic criteria in any population.

Methods—193 patients with idiopathic PD were assessed with a neuropsychiatric battery, including the CNS-LS and the 15-item Geriatric Depression Scale (GDS-15). A subset (N=100) was also administered a diagnostic interview by a blinded rater that applied criteria for both IEED and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) depressive disorders.

Results—Applying formal diagnostic criteria, 7.0% of patients were diagnosed with IEED, and an additional 7.0% had subsyndromal IEED symptoms. Applying recommended CNS-LS cutoff scores from other populations, either 42.5% (cutoff ≥13) or 16.6% (cutoff ≥17) screened positive for IEED. Depressive symptoms were associated with higher CNS-LS scores (B[SE] =0.27[.08], P =.001) but not with a diagnosis of IEED (odds ratio =1.1, [95% CI =1.0–1.3], P =.16). The CNS-LS had poor discriminant validity for an IEED diagnosis (AUC =.79, no cutoff value with sensitivity and specificity both >60%).

Conclusions—IEED and depression are overlapping but distinct disorders in PD. IEED symptoms may occur in up to 15% of PD patients, but a disorder occurs in only half of those, suggesting that often IEED symptoms are not clinically significant in this population. The CNS-LS does not appear to be a good screening instrument for IEED in PD, in part due to its high correlation with depressive symptoms.

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Keywords

Involuntary emotional expression disorder; Pseudobulbar affect; Emotional lability; Depression; Parkinson's disease

1. Introduction

Involuntary emotional expression disorder (IEED), also called pseudobulbar affect (PBA), pathological laughter and crying (PLC) and affective lability, is characterized by brief, spontaneous and uncontrollable episodes of crying or laughing that are typically unrelated to underlying mood [1,2]. This disorder may cause distress in individuals who are unable to predict when the next outburst of crying or laughing will occur, especially in social situations, and can lead to embarrassment and social withdrawal [1].

IEED has been reported to occur in a variety of neurological disorders and neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Alzheimer's disease (AD), stroke, and traumatic brain injury (TBI) [2]. It has also been reported to occur in Parkinson's disease (PD), although there has been almost no research conducted in this population.

Depression is common in PD, and episodes of tearfulness can be a sign of either a depressive disorder or IEED, so it is important that screening and diagnostic instruments distinguish between the two. A useful clinical distinction between IEED and depression is episode duration; signs and symptoms of depression are consistently present over an extended period of time, whereas the actual episodes of affective display in IEED, while often recurrent, are brief in duration. In addition, sad mood or anhedonia characterize depression, while an underlying mood change is not characteristic of IEED [2].

Varying definitions of IEED have been used over the years, with no consensus on terminology or specific diagnostic criteria. Recently, consensus diagnostic criteria for the newly-proposed term of IEED based on the Diagnostic and Statistic Manual of Mental Disorders (DSM-IV-TR) [3] format were published [2]. The new term and the proposed diagnostic criteria were meant to increase awareness of this syndrome, provide greater reliability and validity in its diagnosis, and promote treatment and further research. Consistent with the DSM-IV approach to diagnosing mental disorders, the criteria outline the specific symptoms required for a diagnosis of IEED, list exclusion criteria, and require that the symptoms cause clinically significant distress or functional impairment.

In addition to having consistency in terminology and formal diagnostic criteria for a disorder, it is important to have screening instruments with good discriminant validity that can be used in clinical care and research. One of the most commonly used instruments to screen for, assess the severity of, and monitor changes over time in IEED symptoms is the Center for Neurologic Study-Lability Scale (CNS-LS) [4]. This instrument was initially developed for and validated in ALS patients, subsequently validated in MS patients [5], and was also used to support a diagnosis of IEED and measure changes in IEED severity over time in two recent treatment trials in ALS and MS patients [6,7].

Given the lack of published data in the aforementioned areas, the aims of this study were to report on the frequency and correlates of IEED in PD using both the CNS-LS and the new IEED diagnostic criteria, examine the overlap between IEED and depression, and determine the discriminant validity of the CNS-LS in PD against a diagnostic interview applying the new IEED diagnostic criteria.

2. Methods

2.1. Participants

A convenience sample of 193 patients (79.3% male) diagnosed with idiopathic PD [8] were recruited during routine clinical care at the Parkinson's Disease Research, Education and Clinical Center (PADRECC) at the Philadelphia VA Medical Center ($N = 162$) and at the Parkinson's Disease and Movement Disorders Center (PDMDC) at the University of Pennsylvania ($N = 31$). The Institutional Review Boards at both institutions approved the study, and written informed consent was obtained from all patients prior to study participation.

2.2. Procedure

Trained research assistants administered the psychiatric and neuropsychological assessments. The diagnostic criteria for both IEED and a DSM-IV diagnosis of depression (either major or minor depressive episode) using the Structured Clinical Interview for DSM-IV [9] were applied by a geriatric psychiatrist (DW) or trained research coordinator who was blinded to the subject's CNS-LS and 15-item Geriatric Depression Scale (GDS-15) scores. When available, an informed other was used to corroborate a subject's answers, although preference was given to subjects' responses. As the proposed diagnostic criteria for IEED were not published until after the study commenced, a subset ($N = 100$) of the entire study population was assessed with these criteria.

2.3. Measures

2.3.1. Demographics and clinical characteristics—Patients provided basic demographic and clinical information, which was verified by chart review when indicated. Movement disorder specialists administered the Unified Parkinson's Disease Rating Scale (UPDRS) [10] as part of routine clinical care, and motor scores were obtained from subjects' clinical charts.

2.3.2. Mini-Mental State Examination (MMSE)—Global cognitive ability was assessed with the MMSE [11].

2.3.3. 15-Item Geriatric Depression Scale (GDS-15)—The GDS-15 [12] is a 15-item screening instrument for depression. Total scores range from 0 to 15, with higher scores indicating more severe depression, and a cutoff score ≥5 has been shown to have good sensitivity and specificity for a diagnosis of depression (major or minor) in PD [13,14].

2.3.4. Center for Neurologic Study-Lability Scale (CNS-LS)—The CNS-LS is a 7-item, self-rated instrument used to measure severity of IEED symptoms. This instrument assesses the frequency and intensity of crying (3 questions) and laughing (4 questions). Each question is rated on a Likert scale of 1 (applies never) to 5 (applies most of the time), with a possible overall score ranging from 7 to 35. A total score of ≥13 or higher has been recommended as a cutoff for clinically significant IEED symptoms in ALS patients [6], and a cutoff of ≥17 has been recommended in MS patients [5].

2.3.5. Diagnostic criteria for involuntary emotional expression disorder (IEED)—For a diagnosis of IEED, patients must exhibit episodes of involuntary crying, laughing, or related emotional displays resulting from a brain disorder, and symptoms cannot be accounted for by another neurologic or psychiatric disorder or be a result of the direct physiological effect of a substance. Furthermore, these episodes must cause clinically significant distress or functional impairment (Table 1). A patient was considered to have

subsyndromal IEED symptoms if he/she endorsed the gateway question (i.e., reported episodes of involuntary emotional displays) but did not meet all of the other IEED diagnostic criteria.

2.3.6. Structured clinical interview for DSM-IV (SCID) – depression module—A DSM-IV-TR diagnosis of a depressive disorder was made using the SCID format [9]. Subjects were given a DSM-IV-TR diagnosis of no depressive disorder, minor depression, or major depression, the latter two combined for "any depressive disorder".

2.4. Data analysis

All statistical procedures were performed with SPSS 15.0 [15]. *T*-tests and chi-square tests were performed to analyze the association between depression and IEED variables. Linear and logistic regression univariate analyses were used to examine predictors of CNS-LS score and an IEED diagnosis, respectively. Variables that suggested an association ($P \leq .10$) with CNS-LS score or IEED diagnosis on univariate analysis were entered into multivariate linear or logistic regression analyses, respectively. For the multivariate analyses, a Bonferroni correction for multiple comparisons was made.

3. Results

3.1. Frequency of IEED and depression symptoms

The demographic and clinical characteristics for the subjects are listed in Table 2. Applying the IEED diagnostic criteria, 7.0% of patients had a diagnosis of IEED, while an additional 7.0% reported subsyndromal IEED symptoms. Applying the same CNS-LS cutoff scores previously used in studies of ALS and MS patients, either 42.5% (CNS-LS cutoff ≥13) or 16.6% (CNS-LS cutoff ≥17) of patients demonstrated clinically significant IEED symptoms. A depressive disorder was diagnosed in 33.2% of patients, with 23.3% and 9.8% of the sample meeting criteria for major and minor depression, respectively.

3.2. Association between IEED and depression symptoms

Examining depression as a categorical variable using either the recommended GDS-15 cutoff score or a DSM-IV-TR diagnosis of major or minor depression, there was a consistent and strong association between CNS-LS score and depression (Table 3). In contrast, there was a weaker association between IEED diagnostic criteria and a DSM-IV-TR diagnosis of depression, and no association with clinically significant depression as assessed by GDS-15 score.

3.3. Correlates of IEED diagnosis or symptoms

Female sex and increasing severity of depression determined by GDS-15 score were associated with increasing CNS-LS score on univariate analysis (Table 4); only higher GDS score remained associated on multivariate analysis. Correcting for multiple comparisons, no clinical or demographic variables were associated with a diagnosis of IEED on univariate or multivariate analyses. Similar analyses were run substituting presence of IEED symptoms *or* diagnosis for IEED diagnosis, and no demographic or clinical variables were associated with the presence of IEED symptoms on multivariate analysis (data not shown).

3.4. Discriminant validity of CNS-LS for IEED

Using the results of the diagnostic interview, which applied the proposed IEED criteria, the area under the curve (AUC) for the CNS-LS was 0.788, and the cutoff point that provided maximum sensitivity and specificity was a score of ≥11 (sensitivity =100%, specificity =48%, positive predictive value [PPV] =13%, and negative predictive value [NPV] =100%).

Substituting presence of either IEED symptoms *or* disorder for presence of a disorder, the AUC was 0.782, and the cutoff point that provided maximum sensitivity and specificity remained a score of ≥11 (sensitivity =93%, specificity =51%, PPV =24%, and NPV =98%).

4. Discussion

We found that IEED symptoms are relatively common in PD, but a diagnosis of IEED occurs in only about half of those with symptoms. In addition, our results suggest that although there is overlap between depression and IEED, they also appear to be distinct clinical phenomena or disorders. Finally, we found that the CNS-LS, commonly used in different populations to assess severity of IEED symptoms, has poor discriminant validity for a diagnosis of IEED in PD.

Widely varying rates of IEED have been reported for different patient populations. The highest rates have been reported in ALS, with estimates ranging from 20 to 50% [4]. Prevalence estimates also exist for stroke (10–20%), TBI (5–11%), AD (39% in a single study), and MS patients (10% in a single study). Our results suggest that the prevalence of IEED in PD, at least when applying formal diagnostic criteria, is at the low end of the range of rates reported for other neurological disorders and neurodegenerative diseases.

We found a significantly lower IEED frequency when applying formal diagnostic criteria as opposed to the CNS-LS cutoff points recommended for use in ALS and MS. There are several possible explanations for this. First, a diagnosis of IEED requires that the symptoms produce “clinically significant distress or impairment in social or occupational functioning” [2]. Thus, although 14% of patients had IEED symptoms, only half of those met the criterion for distress or impairment. Second, IEED criteria specify that the symptoms may be “in excess of the corresponding mood state” and “are not better accounted for by another psychiatric disorder”, including depression, which is meant to distinguish IEED symptoms from overlapping symptoms present as part of a depressive disorder [2]. A similar distinction does not exist for the CNS-LS. In support of this explanation, we found that depression measures were strongly associated with the CNS-LS score than with either an IEED diagnosis or symptoms. Finally, the CNS-LS cutoff points that we applied here were not validated against formal diagnostic criteria, so the discriminant validity of the cutoff points used in ALS and MS are unknown.

Assessing the discriminant validity of the CNS-LS, we found that no cutoff point provided both adequate sensitivity and specificity (i.e., both values >60%) for a diagnosis of IEED. In contrast, in ALS a cutoff score of ≥13 had 84% sensitivity and 81% specificity for a diagnosis of “affective lability” [4], and in MS a cutoff score of ≥17 had 94% sensitivity and 83% specificity for a diagnosis of PBA or PLC [5]. However, in these studies a diagnosis was based either on “clinical judgment” [5] or on the general criteria of “sudden outbursts of laughter, crying, or other strong affect that occurred spontaneously, or were inappropriate given the context” [4]. It is not clear if the low sensitivity and specificity of the CNS-LS in PD compared with other populations reflects qualitative differences in the symptom profile of IEED in PD (e.g., less common spontaneous laughter compared with ALS or MS), non-specificity of the CNS-LS in PD due to its high correlation with depressive symptoms, or limited overlap between the items on the CNS-LS and the IEED diagnostic criteria.

There are several limitations to this study. First, the sample consisted primarily of elderly white males receiving specialty care, so the findings cannot be generalized to all PD patients. Second, although the CNS-LS was developed as a self-administered instrument, research staff administered the instrument to some of the patients in this study; however, it was still self-rated (the interviewer simply recorded the subject’s responses). Finally, the patients in this study generally had mild to moderate PD, so it is not clear if any of the

results, including IEED frequency, would have differed if more patients with advanced disease had been included.

While it appears that IEED symptoms are not uncommon in PD, clinically significant symptoms appear to be. IEED symptoms may contribute to depression, or vice versa, but the two disorders can be distinct, so a thorough clinical assessment is indicated when a patient presents with episodes of involuntary emotional expression. As up to 10% of PD patients may have IEED symptoms that lead to significant distress or functional impairment, it is important to have good screening and rating instruments. The development of a brief screening instrument that at a minimum incorporates the first four items of the proposed IEED diagnostic criteria is an appropriate starting point. Future research should apply the new IEED diagnostic criteria, along with existing and new rating and screening instruments, in larger samples of PD patients and other relevant patient populations to determine the true prevalence of IEED and the validity of screening measures.

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References

1. Shaibani AT, Sabbagh MN. Laughter and crying in neurologic disorders. Neuropsychiatry. 1994; 7:243–50.
2. Cummings JL, Arciniegas DB, Brooks BR, Herndon RM, Lauterbach EC, Pioro EP, et al. Defining and diagnosing involuntary emotional expression disorder. CNS Spectrums. 2006; 11:1–7. [PubMed: 16816786]
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: American Psychiatric Association; 2000. Text Revision
4. Moore SR, Gresham LS, Bromberg MB, Kasarkis EJ, Smith RA. A self report measure of affective lability. J Neurol Neurosurg Psychiatry. 1997; 63:89–93. [PubMed: 9221973]
5. Smith RA, Berg JE, Pope LE, Callahan JD, Wynn D, Thisted RA. Validation of the CNS emotional lability scale for pseudobulbar affect (pathological laughing and crying) in multiple sclerosis patients. Mult Scler. 2004; 10:679–85. [PubMed: 15584494]
6. Brooks BR, Thisted RA, Appel SH, Bradley WG, Olney RK, Berg JE, et al. Treatment of pseudobulbar affect in ALS with dextromethorphan/quinidine: a randomized trial. Neurology. 2004; 63:1364–70. [PubMed: 15505150]
7. Panitch HS, Thisted RA, Smith RA, Wynn DR, Wymer JP, Achiron A, et al. Randomized, controlled trial of dextromethorphan/quinidine for pseudo-bulbar affect in multiple sclerosis. Ann Neurol. 2006; 59:780–7. [PubMed: 16634036]
8. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson's disease. Arch Neurol. 1999; 56:33–9. [PubMed: 9923759]
9. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Clinician Version. Washington, DC: American Psychiatric Press; 1996. Structured clinical interview for DSM-IV axis i disorders (SCID).
10. Fahn, S.; Elton, RL. the UPDRS Development Committee. Unified Parkinson's disease rating scale. In: Fahn, S.; Marsden, CD.; Calne, D.; Goldstein, M., editors. Recent developments in Parkinson's disease. Florham Park, NJ: Macmillan Health Care Information; 1987. p. 153-63.
11. 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; 12:196–8.
12. Sheikh, JI.; Yesavage, JA. Geriatric depression scale (GDS): recent evidence and development of a shorter version. In: Brink, TL., editor. Clinical gerontology: a guide to assessment and intervention. New York: The Haworth Press; 1986. p. 165-73.
13. Weintraub D, Oehlberg KA, Katz IR, Stern MB. Test characteristics of the 15-item geriatric depression scale and Hamilton depression rating scale in Parkinson's disease. Am J Geriatr Psychiatry. 2006; 14:169–75. [PubMed: 16473982]

14. Weintraub D, Saboe K, Stern MB. Effect of age on geriatric depression scale performance in Parkinson's disease. Mov Disord. 2007; 28:1331–5. [PubMed: 17546674]

15. SPSS for Windows. Version 15.0. Chicago: SPSS Inc; 2007.

Table 1

Necessary elements from proposed diagnostic criteria for IEED.

1	Episodes of involuntary or exaggerated emotional expression that result from a brain disorder, including episodes of laughing, crying, or related emotional displays.
2	Episodes represent a change from the person's usual emotional reactivity.
3	Episodes may be incongruent with the person's mood or in excess of the corresponding mood state.
4	Episodes are independent or in excess of any provoking stimulus.
5	The disturbance causes clinically significant distress or impairment in social or occupational functioning.
6	The symptoms are not better accounted for by another neurologic or psychiatric disorder (e.g., gelastic or dacrystic epilepsy, facial dystonia, facial or vocal tics, facial dyskinesias, mania, depression, panic disorder, psychosis).
7	The symptoms are not the direct physiological effect of a substance (e.g., drug of abuse or medication).

From Cummings JL, Arciniegas DB, Brooks BR, et al. CNS Spectrums Vol 11 (Suppl 6):1–7, 2006.

Table 2

Demographic and clinical characteristics.

Variable	*N*	Mean (SD) or Percentage
Demographic characteristics	193	
Age		65.8 (10.7)
Sex (% males)		79.3%
Marital status (% married)		77.2%
Education (# years)		15.4 (3.3)
Parkinson's disease variables	193	
Disease duration (# years)		7.3 (5.5)
Levodopa dosage (mg/day)		538.9 (381.1)
Dopamine agonist use (% yes)		50.8%
Sidedness of PD symptoms		
Right sided predominant		39.4%
Left sided predominant		37.8%
Mixed		22.8%
UPDRS motor subscore		21.9 (10.8)
Hoehn and Yahr stage		2.3 (0.7)
Schwab and England score		88.5 (12.7)
Psychiatric and cognitive variables	193	
GDS-15 score		4.4 (4.0)
Any depression (% yes)		33.2%
Major depression (% yes)		23.3%
Minor depression (% yes)		9.8%
Antidepressant use (% yes)		28.0%
MMSE score		28.0 (2.6)
IEED variables		
CNS-LS score	193	12.4 (4.5)
CNS-LS positive-13 cutoff (% yes)		42.5%
CNS-LS positive-17 cutoff (% yes)		16.6%
IEED diagnosis (% yes)	100	7.0%
IEED symptoms or diagnosis (% yes)		14.0%

Table 3

Association between depression status and IEED variables.

Depression variable	IEED variable		
	CNS-LS score[a]	IEED diagnosis positive[b]	IEED symptoms or diagnosis[b]
GDS-positive score	$t = -3.9$, df = 191, $P < .001$	$\chi^2 = 2.9$, df =1, $P = .09$	$\chi^2 < 0.1$, df =1, $P = .97$
Any depression diagnosis	$t = -3.8$, df =191, $P < .001$	$\chi^2 = 4.9$, df =1, $P = .03$	$\chi^2 = 0.3$, df =1, $P = .59$
Major depression	$t = -2.8$, df =191, $P = .005$	$\chi^2 = 0.3$, df =1, $P = .59$	$\chi^2 = 0.1$, df =1, $P = .77$
Minor depression	$t = -1.9$, df =191, $P = .06$	$\chi^2 = 6.8$, df =1, $P = .009$	$\chi^2 = 2.0$, df =1, $P = .16$

[a] *T*-test.

[b] Chi-square.

Table 4

Correlates of CNS-LS score and IEED diagnosis.

Variable	CNS-LS score (B [SE], *P* value)		IEED diagnosis (Odds ratio [95% CI], *P* value)	
	Univariate	Multivariate	Univariate	Multivariate
Age	−.05 [.03], .07	−.04 [.03], .15	1.0 [1.0–1.1], .33	–
Sex	2.41 [.77], .002[a]	1.61 [.78], .04	1.1 [0.1–10.2], .92	–
Education	−.05 [.10], .60	–	1.0 [0.8–1.3], .41	–
Disease duration	.06 [.06], .34	–	1.1 [1.0–1.2], .26	–
MMSE score	.03 [.12], .83	–	0.8 [0.7–1.0], .04	0.9 [0.7–1.1], .29
Levodopa dosage	<.01 [<.01], .62	–	1.0 [1.0–1.0], .20	–
Dopamine agonist use	−.24 [.64], .71	–	1.2 [0.3–5.6], .82	–
Antidepressant use	.91 [.71], .20	–	1.7 [0.3–9.3], .56	–
UPDRS motor subscore	<.01 [.03], .88	–	1.1 [1.0–1.1], .03	1.1 [1.0–1.1], .15
Hoehn & Yahr stage	.03 [.47], .94	–	2.2 [0.7–6.4], .16	–
GDS-15 score	.32 [.08], <.001[a]	.27 [.08], .001[a]	1.1 [1.0–1.3], .16	–

[a]Significant after correction for multiple comparisons.