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Apathy in Essential Tremor, Dystonia, and Parkinson's Disease: A Comparison with Normal Controls

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Abstract

Background—Apathy, defined as decreased goal-directed activity, has been observed in Parkinson's disease. A number of cognitive/psychiatric features have been documented in essential tremor, yet we are unaware of studies of apathy.

Methods—Using the Apathy Evaluation Scale (range = 18–72 [more apathy]), we compared 79 essential tremor cases, 20 dystonia cases, and 39 Parkinson's disease cases with 80 normal controls.

Results—The score of the Apathy Evaluation Scale was higher in essential tremor, dystonia, and Parkinson's disease cases than controls (all $P < .04$). Parkinson's disease cases had the highest scores. Analyses stratified by presence/absence of depressive symptoms indicated the presence of a group of apathetic but nondepressed cases.

Conclusions—Patients with Parkinson's disease, essential tremor, and dystonia had elevated apathy scores. Features of apathy seemed to occur in these conditions independent of depressive symptoms. The mechanistic basis for the apparent increased features of apathy in essential tremor and dystonia deserves further study.

Keywords

apathy; depression; dystonia; essential tremor; non-motor; Parkinson's disease

Apathy, a disorder of motivation with several dimensions (reduced goal-directed behavior, goal-directed cognitive activity, and emotions)^{1,2} has been observed in several neurological disorders, including Parkinson's disease (PD).^{3,4} A number of cognitive/psychiatric features have been documented in essential tremor (ET).⁵⁻⁷ Many of these features are similar to those seen in PD, although to a lesser degree.⁵⁻⁷ Yet we are unaware of studies of apathy in ET. Similarly, there are no case-control data on apathy in dystonia.⁴ Apathy and depression can be conceptualized as distinct constructs, although with some overlap.²

We assessed apathy in ET, dystonia, and PD cases, comparing them to normal controls. We hypothesized that ET cases and possibly dystonia cases would have more apathy than normal controls but less than PD cases, and that this apathy would be greater than expected from the degree of depression observed in both patient groups. Apathy was assessed in a dimensional rather than syndromic manner.

Patients and Methods

Participants were enrolled in a research study at Columbia University Medical Center (CUMC).^{8,9} ET, PD, and dystonia cases were selected randomly from a computerized billing database at the Center for Parkinson's Disease and Other Movement Disorders (CPD). Normal controls, selected from the same source population as ET cases, were recruited using random-digit telephone dialing and were frequency-matched by age, gender, and race to ET cases.

Enrollees had been diagnosed with ET, PD, or dystonia by a CPD neurologist. PD was diagnosed when 2 cardinal features of parkinsonism were present in the absence of other possible causes. Dystonia was diagnosed when sustained muscle contractions or postures were present. All PD and dystonia diagnoses were also reconfirmed based on chart review by a senior movement disorder neurologist (E.D.L.). ET was diagnosed when moderate or greater amplitude action tremor was present in the arms or head tremor was present in the absence of another known cause, and these diagnoses were reconfirmed using published diagnostic criteria.^{10,11}

Participants signed informed written consent approved by the CUMC Institutional Review Board, and were evaluated in person by a trained tester. Built into the study protocol were several clinical assessments, including the Apathy Evaluation Scale (AES),¹² a self-report 18-item scale that assesses apathy over the past 4 weeks (AES total score range = 18–72 [higher score indicating more severe apathy]).^{2,12} The AES may be divided into 4 subscores: cognitive, behavior, emotional, and other.¹²

The Frontal Assessment Battery (FAB) (range = 0 [greater frontal lobe dysfunction]–18)¹³ and Folstein Mini-Mental State Examination (MMSE)¹⁴ were administered, as was the Center for Epidemiological Studies Depression Scale (CESD-10), a self-report 10-item screening questionnaire for depressive symptoms (range = 0–30 [greater depressive symptoms]).¹⁵

Statistical analyses were carried out using SPSS (version 18.0.2; Chicago, IL, USA). The AES, CESD-10, MMSE, and FAB were not normally distributed; therefore, nonparametric tests (Kruskal-Wallis test, Mann-Whitney test, Spearman's rho) were used when assessing these variables. For our main analysis, clinical scores (AES, CESD-10, MMSE, and FAB) were compared across the multiple groups (ET, PD, dystonia, and controls) using a Kruskal-Wallis test; when a group difference was detected, Mann-Whitney tests were further employed to identify specific differences. We also assessed the relationship between apathy and depressive symptoms. For these analyses, an AES total score of ≥ 38 , designated as

“high apathy” in previous studies,¹⁶ was used. Participants were designated as depressed based on a cutoff of ≥ 20 , as recommended.⁴

Results

There were 80 ET cases, 80 controls, 40 PD cases, and 20 dystonia cases. Complete AES data were available on 79 ET cases, 80 controls, 39 PD cases, and 20 dystonia cases (12 torticollis, 3 blepharospasm, and 5 mixed or other) (Table 1).

As expected, fewer PD cases than controls were women ($\chi^2 = 7.46_{[df=1]}$, $P = .006$), but gender was otherwise similar across the remaining 3 diagnostic groups (Table 1).

The CESD-10 score differed across the 4 diagnostic groups (Kruskal-Wallis test $_{[df=3]} = 13.30$, $P = .004$; Table 1), being higher in ET and PD cases than controls (Table 1), indicating more depressive symptoms in those groups.

The AES total score differed across the 4 diagnostic groups (Kruskal-Wallis test $_{[df=3]} = 13.40$, $P = .004$; more specifically, it was higher (ie, more apathy) in ET, dystonia, and PD cases than controls, with the PD cases having the highest scores (Table 1). Results were similar after removing 16 (7.4%) participants with low MMSE scores (range = 23–26) (data not shown).

The AES subscores also differed by diagnostic group (for the cognitive subscore, Kruskal-Wallis test $_{[df=3]} = 6.36$, $P = .095$; for the behavior subscore, Kruskal-Wallis test $_{[df=3]} = 16.77$, $P = .001$; for the emotional subscore, Kruskal-Wallis test $_{[df=3]} = 9.43$, $P = .02$; for the other subscore, Kruskal-Wallis test $_{[df=3]} = 11.38$, $P = .01$). These group differences were largely due to the ET and PD groups, which differed from controls in terms of most AES subscores (Table 1), indicating a broad involvement of apathy domains in ET and PD.

The AES total score was correlated to a moderate degree with the CESD-10 score (Spearman's $r = 0.43$, $P < .001$) (ie, more apathy correlated to a moderate degree with more depressive symptoms) and marginally with the FAB score (Spearman's $r = -0.16$, $P = .02$) (ie, more apathy was correlated marginally with more frontal lobe dysfunction), but not with the MMSE scores (Spearman's $r = -0.09$, $P = .21$).

We further assessed the relationship between apathy and depressive symptoms. As detailed in the Patients and Methods section, participants were first designated as having depression based on a CESD-10 score ≥ 20 and stratified into highly apathetic versus others, based on having had an AES total score ≥ 38 . Four of 6 highly apathetic ET cases were not depressed, 7 of 8 highly apathetic PD cases were not depressed, and the 1 highly apathetic dystonia case was depressed. We also determined that the AES total score was higher among ET, dystonia, and PD cases than controls, after having removed 33 (15.1%) of 218 participants who were currently taking an antidepressant medication (Table 1; bottom row).

In the control sample, the AES total score was not correlated with age in years (Spearman's $r = -0.04$, $P = .70$), years of education (-0.03 , $P = .80$), or gender ($P = .050$), indicating that these demographic variables were not confounding factors.

In ET cases, the AES total score was not correlated with total tremor score (Spearman's $r = -0.06$, $P = .68$), age of tremor onset (Spearman's $r = -0.02$, $P = .87$), tremor duration (Spearman's $r = 0.001$, $P = .99$), FAB score (Spearman's $r = 0.03$, $P = .79$), or MMSE score (Spearman's $r = 0.01$, $P = .93$).

Discussion

Apathy scores were higher in ET, dystonia, and PD cases than controls, with the PD group having the highest scores (ie, the most apathy). While depressive symptoms were more marked in the 3 disease groups than in the controls, in analyses that removed all participants currently on antidepressant medications, apathy scores remained higher in the 3 disease groups than controls. Furthermore, analyses that stratified by presence or absence of depressive symptoms indicated the presence of a group of cases with features of apathy but not depression. In ET and PD cases, other AES subscores (behavior, other) aside from the emotional subscore, differed from those of controls. These data all suggest that while features of apathy occur in these 3 disease groups as a function of depression, they likely occur independently of depression as well.

One study¹⁷ found that decreased vigor was reported by ET cases, but we are unaware of studies of apathy in ET. We are aware of only 1 study that examined apathy in dystonia,⁴ although that study did not enroll a normal control group. The functional and therapeutic impact of apathy has yet to be explored in ET or dystonia.

The study had limitations. The AES is a self-report scale; patients with anosognosia associated with frontal dysfunction may underreport apathy on the AES. Future studies may wish to explore the use of additional apathy scales. Also, future studies may want to incorporate the Structured Clinical Interview for Diagnostic and Statistical Manual, 4th edition, Text Revision (DSM-IV-TR) (SCID).¹⁸

This study had several strengths. This the first case-control study to directly look at the issue of apathy in ET and the only study to compare dystonia cases to controls. A rich and varied study sample was assembled, not only of ET cases and a nondiseased control group, but also patients with 2 other movement disorders (PD, dystonia). Aside from apathy, depressive symptoms and anti-depressant medication use were evaluated to try to separate apathy from depressive symptoms.

In summary, apathy scores were higher in ET, dystonia, and PD cases than controls, with the PD cases having the highest scores. The mechanistic basis for the apparent increased features of apathy in both ET and dystonia is not known and it deserves further study, as does the functional impact of apathy on quality of life.

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Table 1

Demographic and clinical characteristics of participants

	ET (n = 79)	Dystonia (n = 20)	PD (n = 39)	Controls (n = 80)	Significance (comparison across 4 diagnostic groups)
Demographic					
Age (y)	70.8 ± 13.4	68.9 ± 8.5	68.1 ± 8.0	70.8 ± 9.6	ANOVA, $F = 0.52$, $P = .54$
Education (y)	15.9 ± 2.5	15.0 ± 2.9	15.9 ± 3.0	16.3 ± 2.4	ANOVA, $F = 1.61$, $P = .19$
Women	46 (58.2%)	13 (65.0%)	13 (33.3%)	48 (60.0%)	$\chi^2_{(df=3)} = 9.35$, $P = .025$
Clinical					
CESD-10 score	8.5 ± 6.2 [7.0]	7.9 ± 5.7 [7.0]	9.2 ± 6.1 [8.0]	5.6 ± 4.3 [5.0]	Kruskal-Wallis test [$df = 3$] = 13.30, $P = .004$
MMSE score	29.0 ± 1.4 [30.0]	28.5 ± 1.7 [29.0]	28.6 ± 1.5 [29.0]	29.0 ± 1.4 [30.0]	Kruskal-Wallis test [$df = 3$] = 3.33, $P = .34$
FAB score	16.2 ± 1.9 [17.0]	16.0 ± 1.7 [16.0]	15.6 ± 2.2 [16.0]	16.6 ± 1.6 [17.0]	Kruskal-Wallis test [$df = 3$] = 6.71, $P = .08$
AES scores					
AES total score	26.9 ± 7.2 [25.0]	26.7 ± 5.8 [26.0]	29.2 ± 8.5 [27.0]	24.3 ± 6.3 [22.0]	Kruskal-Wallis test [$df = 3$] = 13.40, $P = .004$
Cognitive subscore	11.9 ± 3.3 [12.0]	12.5 ± 3.3 [12.0]	12.8 ± 4.4 [12.0]	11.1 ± 3.1 [10.0]	Kruskal-Wallis test [$df = 3$] = 6.36, $P = .095$
Behavior subscore	7.2 ± 2.3 [6.0]	6.9 ± 1.4 [7.0]	8.1 ± 2.5 [8.0]	6.4 ± 1.7 [6.0]	Kruskal-Wallis test [$df = 3$] = 16.77, $P = .001$
Emotional subscore	3.4 ± 1.1 [3.0]	3.1 ± 0.9 [3.0]	3.5 ± 1.3 [3.0]	3.0 ± 1.1 [3.0]	Kruskal-Wallis test [$df = 3$] = 9.43, $P = .02$
Other subscore	4.4 ± 1.4 [4.0]	4.2 ± 1.3 [4.0]	4.7 ± 1.7 [5.0]	3.9 ± 1.4 [3.0]	Kruskal-Wallis test [$df = 3$] = 11.38, $P = .01$
AES total score ^a	27.1 ± 7.3 [26.0]	26.2 ± 3.8 [26.0]	27.6 ± 6.7 [26.5]	24.3 ± 6.4 [22.0]	Kruskal-Wallis test [$df = 3$] = 10.15, $P = .02$

Values are means ± standard deviations [median] or numbers (percentages).

ET, essential tremor; PD, Parkinson's disease; ANOVA, analysis of variance; df, degrees of freedom; CESD-10, Center for Epidemiological Studies Depression Scale; MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery; AES, Apathy Evaluation Scale.

^a After removal of 11/79 (13.9%) ET cases, 8/80 (10.0%) controls, 3/20 (15.0%) dystonia cases, and 11/39 (28.2%) PD cases who were taking an antidepressant medication.

* $P < .10$ in a Mann-Whitney test ($df = 1$) comparing this group to controls.

** $P < .05$ in a Mann-Whitney test ($df = 1$) comparing this group to controls.

*** $P < .01$ in a Mann-Whitney test ($df = 1$) comparing this group to controls.

**** $P < .001$ in a Mann-Whitney test ($df = 1$) comparing this group to controls.