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Factors Associated with Receptivity to Deep Brain Stimulation Surgery Among Essential Tremor Cases

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Abstract

Background—A sizable proportion of essential tremor (ET) patients suffer from medically-refractory ET. Although deep brain stimulation (DBS) surgery is a safe and highly effective treatment, it may be under-utilized. We are unaware of studies that assess ET patients' attitudes towards DBS surgery and the factors that motivate them towards or away from such surgery.

Methods—ET cases, enrolled in an ongoing clinical-pathological study, underwent an in-person evaluation. They were asked "What is the likelihood that you would allow yourself to have DBS surgery?", thus rating their 'surgical receptivity' from 0–100.

Results—One-third (47/146, 32.2%) of ET cases reported that they would consider DBS surgery. In univariate analyses, younger age ($p=0.017$), self-reported embarrassment ($p=0.001$), more depressive symptoms ($p=0.008$), more dysthymia ($p=0.029$), higher total tremor score (marginal $p=0.13$) and lower burden of medical comorbidity (marginal $p=0.16$) were associated with greater surgical receptivity. In multivariate logistic regression models, only self-reported embarrassment ($p=0.006$) and, marginally, younger age ($p=0.059$) were independently associated with surgical receptivity.

Conclusions—We identified a number of factors that were associated with increased receptivity to DBS surgery. Interestingly, psychosocial variables (dysthymia, depressive symptoms, self-reported embarrassment) featured prominently among these factors; indeed, self-reported embarrassment was the most robust factor. Tremor severity, though associated in univariate analyses with increased surgical receptivity, was not as robust of a predictor as was self-reported

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embarrassment. Future studies, which are community-based as well as those which also assess the patient's level of understanding about DBS will further add to the literature on this topic.

Keywords

essential tremor; deep brain stimulation surgery; clinical; embarrassment

INTRODUCTION

Essential tremor (ET) is among the most prevalent movement disorders. Unfortunately, the current pharmacopeia is of limited efficacy; for instance, research has shown that one-half of ET patients treated with the two front-line agents had discontinued both [1]. Consequently, there is a sizable proportion of patients suffering from medically-refractory ET. Deep brain stimulation (DBS) surgery is a safe and highly effective treatment, which may improve disability and health-related quality of life in ET [2].

Tremor in ET may range from mild to marked. Even in community settings, where mild tremor is often observed, approximately one-in-four cases exhibit a severe tremor in their dominant arm during at least one maneuver of the tremor examination [3]. When compared to similarly-aged controls, ET cases in community-based settings have been shown to have poorer quality of life [4], a higher preponderance of depressive symptoms [5], and lower morale [6]. Despite this, there is an anecdotal sense that patients with ET, and even those with severe tremor, seem reluctant to undergo DBS, and limited data show that the number of ET cases referred for DBS surgery is proportionally low [2].

We are unaware of any studies on ET patients' attitudes towards DBS surgery and the factors that motivate them towards or away from such surgery. The aim of this study was to gauge in a group of ET cases their receptivity to DBS surgery and, more importantly, to assess a range of demographic, clinical and psychosocial factors that might correlate with this receptivity. Our only *a priori* hypothesis was that greater tremor severity would be a major predictor of increased surgical receptivity.

METHODS

Study Subjects

ET cases were enrolled in an ongoing clinical-pathological study at Columbia University Medical Center (CUMC), New York. The study enrolled ET cases as future brain donors. ET cases were ascertained through a variety of mechanisms including advertisements in the International Essential Tremor Foundation website and newsletters, advertisements on the Tremor Action Network website, and our research study's website (www.essentialtremor.us). ET cases were recruited throughout the United States and were not restricted to the local New York area. To date, 387 ET cases have expressed an interest in enrollment. Beginning in March 2009, we began enrolling these cases at a rate of approximately 7 per month, with selection based on age, starting with the oldest first. To date, 150 of a targeted 175 ET cases have been enrolled; these 150 are distributed broadly across the country, residing in 34 of 50 US states.

Evaluation

Upon enrollment, each case signed a written informed consent form, approved by the CUMC institutional ethics committee, and then underwent a standardized in-person evaluation in their home by the same trained tester. The in-person evaluation included the collection of demographic and clinical data using structured questionnaires. The Cumulative

Illness Rating Scale (CIRS) was used to assess the participant's burden of medical illness. The CIRS rates (0–3) medical comorbidity in 14 bodily systems; CIRS scores range from 0–42 (greatest disease burden) [7]. The Folstein Mini-Mental State Exam [8] was also administered to assess cognition. Depressive symptoms were assessed using the Beck Depression Inventory, for which 21 items were rated from 0–3 (total score = 0–63 [maximal symptoms]) [9]. The Cornell Dysthymia Rating Scale [10] was also administered. This scale (22 items, 0–4 range per item) has items for poor concentration, indecisiveness, low productivity, social withdrawal, and related symptoms typical of dysthymia. We also included a set of questions that assessed tremor-related functional difficulties during a broad range of daily tasks (e.g., signing name, drinking from a glass, using a spoon, dialing a telephone, unlocking a door with a key); these items (each rated as 0 [no difficulty], 1 [mild difficulty] and 2 [clear difficulty]) were obtained from a valid and reliable tremor disability questionnaire [11]. Other clinical questions, used in our ongoing epidemiological studies, were “Do other people often tell you that you have tremor?” (a general measure of awareness of tremor) and “Does your tremor currently embarrass you?” (a measure of psychic discomfort resulting from tremor).

Each case was asked “What is the likelihood that you would allow yourself to have DBS surgery?” Anchor points were provided, 0 (not likely), 10–20 (a little likely), 30–50 (somewhat likely), 60–70 (quite likely), and 90–100 (extremely likely), but possible responses could range between 0 and 100. The 0–100 value was labeled ‘surgical receptivity’.

Each case underwent a standardized videotaped neurological examination, which included a detailed assessment of postural tremor and five tests of kinetic tremor, as well as assessments of head (neck), jaw and voice tremors. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations and the severity of postural and kinetic tremors were rated (0–4), resulting in a total tremor score (range = 0–48 [maximum]) and a tremor score in the dominant arm (0–24).

The diagnosis of ET was re-confirmed in each ET case using research diagnostic criteria (moderate or greater amplitude kinetic tremor observed during three or more activities or a head tremor, in the absence of Parkinson's disease).

Statistical Analyses

Analyses were carried out using SPSS (version 18.0.2; Chicago, Illinois). The surgical receptivity variable was not normally distributed (Kolmogorov Smirnov $z = 4.57$, $p < 0.001$); hence non-parametric tests were used when assessing this variable (Spearman's r , Mann-Whitney test, Kruskal-Wallis test). We identified six factors that correlated with surgical receptivity; to assess the independent effects of these six factors on surgical receptivity, we used multivariate logistic regression models in which the outcome variable, surgical receptivity, was recoded as a simple ‘yes’ (i.e., values >0) vs. ‘no (values of 0)’, yielding odds ratios (OR) and 95% confidence intervals (CI). Logistic regression models were used because linear regression models were not possible given the non-normal distribution of the surgical receptivity variable when it was coded from 0–100. Colinearity between independent variables was assessed and considered in the formulation of these models. In one analysis, ET cases were stratified into those with severe tremor vs. those with mild to moderate tremor, using a cut-off point utilized in prior analyses [12].

RESULTS

Of 150 enrolled ET cases, 4 had missing data, leaving 146 ET cases for analysis (Tables 1 and 2). One-third of cases ($47/146 = 32.2\%$) reported that they would allow themselves to

consider DBS surgery (i.e., surgical receptivity >0); the remaining 99 (67.8%) said that they would not (i.e., surgical receptivity = 0). Twenty-three (48.9%) of the 47 who reported that they would consider DBS surgery had a score ≥ 50 (Table 1). The mean $\pm$ standard deviation surgical receptivity score was 13.6 ± 26.0 .

We examined the demographic and clinical correlates of surgical receptivity (Table 2). Older cases were less receptive to surgery ($r = -20$, $p = 0.017$); gender was not a significant factor. More dysthymia (Cornell Dysthymia Rating Scale score, $r = 20$, $p = 0.029$), more depressive symptoms (Beck Depression Inventory score, $r = 0.23$, $p = 0.008$) and self-reported embarrassment ($p = 0.001$) were associated with greater surgical receptivity (Table 2). The most robust correlation was with self-reported embarrassment (Table 2). Two factors that were only marginally associated with greater surgical receptivity were higher total tremor score ($r = 0.13$, $p = 0.13$) and lower CIRS score (i.e., lower burden of medical comorbidity, $r = -0.12$, $p = 0.16$). Surgical receptivity was not associated to a significant degree with any of the five functional disability items (Table 2).

We further assessed the six factors identified above. First, in six univariate logistic regression models, we examined the association between each of the six variables and surgical receptivity coded as 'yes' vs. 'no'. In these six models, younger age (OR = 0.92, 95% CI = 0.86–0.99, $p = 0.02$), higher Cornell Dysthymia Rating Scale score (OR = 1.05, 95% CI = 1.003–1.092, $p = 0.037$), higher Beck Depression Inventory score (OR = 1.06, 95% CI = 0.999–1.11, $p = 0.056$), presence of self-reported embarrassment (OR = 3.09, 95% CI = 1.50–6.33, $p = 0.002$) and higher total tremor score (OR = 1.05, 95% CI = 1.002–1.10, $p = 0.04$) were each associated with surgical receptivity. In a multivariate logistic regression model, however, only self-reported embarrassment (OR = 2.82, 95% CI = 1.36–5.86, $p = 0.006$) and, marginally, younger age (OR = 0.93, 95% CI = 0.87–1.003, $p = 0.059$) were independently associated with surgical receptivity whereas the other variables were not. Thus, the total tremor score was not independently associated with surgical receptivity in the final logistic regression model. When we separately examined each of the 22 items in the Cornell Dysthymia Rating Scale score and the 21 items in the Beck Depression Inventory; we found that only the Cornell Dysthymia Rating Scale item that assessed guilt (feelings of self-reproach) was independently associated with surgical receptivity (OR = 1.59, 95% CI = 1.03–2.46, $p = 0.037$) in a multivariate logistic regression model that also included self-reported embarrassment (OR = 2.76, 95% CI = 1.30–5.87, $p = 0.009$) and age (OR = 0.94, 95% CI = 0.87–1.008, $p = 0.078$).

ET cases were stratified into those with severe tremor (total tremor score >27, $n = 46$) vs. those with mild to moderate tremor (total tremor score ≤ 27 , $n = 100$). The results of those analyses were similar in that self-reported embarrassment was the predictor of surgical receptivity in the final multivariate logistic regression model in each stratum (for cases with mild to moderate tremor, OR = 2.54, 95% CI = 1.01–6.38, $p = 0.047$; for cases with severe tremor, OR = 4.69, 95% CI = 1.23–17.88, $p = 0.02$). Total tremor score was not a predictor in these models (data not shown).

DISCUSSION

We identified a number of factors among ET patients that were associated with increased receptivity to DBS surgery. Interestingly, psychosocial variables (dysthymia, depressive symptoms, self-reported embarrassment) featured prominently among these factors; indeed, self-reported embarrassment was the most robust factor. Our only *a priori* hypothesis was that greater tremor severity would be a major predictor of increased surgical receptivity. Although tremor severity was associated with increased surgical receptivity in initial

analyses, it was not as robust of a predictor as was self-reported embarrassment and, in the final multivariate model, was not a significant factor.

We have previously demonstrated on a personality inventory, higher harm avoidance scores in ET cases compared with controls [13]. The explanation for this finding is unclear, but among the possible explanations are a post-morbid personality profile (i.e., a psychic response to having disabling tremor), a pre-morbid and innate personality type, or most interestingly, a personality profile that is a primary biological feature of the underlying disease, as has been observed to occur in the setting of other movement disorders (e.g., Parkinson's disease, Huntington's disease). It is conceivable that harm avoidance and greater propensity for embarrassment could be related to the same underlying biopsychosocial factor, although this is not known. If, however, it were the case, it would raise the possibility that surgical receptivity might also have an underlying biological basis. The links between harm avoidance, embarrassment and surgical receptivity deserve additional exploration.

One issue is that the cases we sampled had volunteered to serve as brain donors; it is therefore possible that they had ET that was on the more severe end of the disease spectrum. This would not invalidate our results but could potentially lessen their applicability to ET cases with milder tremor. This being said, our sample was not restricted to severe ET cases only and was comprised of a mix of patients with a range of tremor severities. Our analyses, which stratified cases based on tremor severity, also indicated that our primary finding was applicable to both severe ET cases as well as mild to moderate ET cases. Nonetheless, it is still important to recognize that these cases, as research volunteers and prospective brain donors, may have had higher levels of surgical receptivity than an unselected group of cases dwelling in the population.

Although the mean age of tremor onset in our cases was 42.6 years, the mean current age was 84.5 years. This would not invalidate our results but could potentially lessen their applicability to younger ET cases. We think, however, that embarrassment might be an even greater motivating feature among younger individuals, as these are still integrated into workplace settings.

A limitation of the study is that we assessed receptivity to surgery. We did not compare a group of ET cases who had had surgery to a group who had not had surgery, as that would have required a different study design and it would have addressed a different research question. All of our cases had heard of DBS surgery, yet a second limitation is that we did not assess the patient's level of knowledge about DBS; lack of knowledge about the mechanisms and/or efficacy of the surgery could have influenced level of receptivity to surgery. A third limitation is that the study was not community-based; sampling a community-dwelling group of cases might yield different results both with respect to the prevalence of surgical receptivity as well as some of the factors that motivate patients to consider the surgery. Finally, it would be useful in future studies to ask patients other questions. For example, whether, if their tremor were to worsen, they would become more receptive to DBS surgery. This study had a number of strengths. First, a wide range of demographic, clinical and psychosocial variables were explored. Second, ET cases were not drawn from a single clinic or a single region but distributed broadly across the United States. Third, using multivariate modeling, we were able to examine the independent effects of these various factors on receptivity towards surgery. Finally, this is the only study to our knowledge to have assessed ET patients' attitudes towards DBS surgery and their motivations towards or away from such surgery.

In summary, we identified a number of factors that were associated with increased receptivity to DBS surgery. Of particular interest is that psychosocial variables (dysthymia, depressive symptoms, self-reported embarrassment) featured prominently among these factors; indeed, self-reported embarrassment was the most robust factor, and was even more robust than tremor severity or tremor-related disability.

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Table 1

Surgical receptivity scores in 146 ET cases

Surgical receptivity score	Number (%) ET cases
0	99 (67.8)
10	13 (8.9)
20	7 (4.8)
30	2 (1.4)
40	2 (1.4)
50	9 (6.2)
60	2 (1.4)
70	2 (1.4)
75	1 (0.7)
80	4 (2.7)
90	2 (1.4)
95	1 (0.7)
100	2 (1.4)

Table 2

Demographic and clinical characteristics of 146 ET cases

Demographic or clinical characteristic	Data	Correlation (r) between characteristic and surgical receptivity or Surgical receptivity within stratum of each characteristic
Age *	84.5 ± 5.4	r = -0.20, p = 0.017
Age range *	74–102	
Gender		
Female	88 (60.3)	14.7 ± 26.8
Male	58 (39.7)	12.1 ± 24.9
		p = 0.70 ^a
Age of tremor onset *	42.6 ± 22.9	r = -0.07, p = 0.42
Tremor duration *	41.9 ± 22.1	r = 0.03, p = 0.76
Currently married	67 (45.9)	r = -0.09, p = 0.31
Education **		
No degree	5 (3.4)	34.0 ± 47.8
High school diploma	47 (32.2)	16.0 ± 29.1
Associates degree	13 (8.9)	15.4 ± 29.0
Bachelor's degree	38 (26.0)	10.3 ± 21.2
Master's degree	29 (19.9)	14.5 ± 25.6
Doctorate degree	13 (8.9)	4.6 ± 7.8
		p = 0.87 ^b
Education **		
High school diploma or lower	52 (35.6)	17.7 ± 31.1
College degree or higher	80 (54.8)	10.9 ± 21.5
		p = 0.80 ^a
Number of bedrooms in home	2.5 ± 1.1	r = -0.04, p = 0.65
Mini Mental Status Test score	27.0 ± 2.4	r = 0.08, p = 0.34
Cumulative Illness Rating Scale score	10.7 ± 5.2	r = -0.12, p = 0.16
Number of years since most recent hospitalization	7.8 ± 12.8	r = 0.06, p = 0.47
Total tremor score	24.7 ± 7.6	r = 0.13, p = 0.13
Tremor score in dominant arm	12.0 ± 4.1	r = 0.07, p = 0.42
Head (neck) tremor		
Yes	77 (52.7)	12.2 ± 24.8
No	69 (47.3)	15.2 ± 27.3
		p = 0.50 ^a

Demographic or clinical characteristic	Data	Correlation (r) between characteristic and surgical receptivity or Surgical receptivity within stratum of each characteristic
Jaw tremor		
Yes	62 (42.5)	12.5 ± 23.2
No	84 (57.5)	14.5 ± 28.0
		p = 0.88 ^a
Voice tremor		
Yes	70 (47.9)	18.4 ± 31.0
No	67 (52.1)	9.2 ± 19.5
		p = 0.18 ^a
Beck Depression Inventory Score	9.5 ± 6.9	r = 0.23, p = 0.008
Cornell Dysthymia Rating Scale Score	21.9 ± 9.1	r = 0.20, p = 0.029
“Do other people often tell you that you have tremor?”		
Yes	36 (24.8)	16.7 ± 27.9
No	110 (75.2)	12.8 ± 25.5
		p = 0.14 ^a
“Does your tremor currently embarrass you?”		
Yes	60 (41.1)	21.2 ± 31.2
No	86 (58.9)	8.4 ± 20.2
		p = 0.001 ^a
Difficulty signing name		
No difficulty	13 (8.9)	19.2 ± 22.9
Mild difficulty	30 (20.5)	6.3 ± 17.1
Clear difficulty	103 (70.5)	16.3 ± 28.1
		p = 0.13 ^b
Difficulty drinking from a glass		
No difficulty	30 (20.5)	7.0 ± 14.9
Mild difficulty	22 (15.1)	6.8 ± 12.9
Clear difficulty	94 (64.4)	17.3 ± 30.1
		p = 0.33 ^b
Difficulty using a spoon		
No difficulty	21 (14.4)	9.5 ± 24.4
Mild difficulty	24 (16.4)	17.9 ± 28.1
Clear difficulty	101 (69.2)	13.5 ± 25.9
		p = 0.22 ^b
Difficulty dialing a telephone ^{**}		
No difficulty	73 (50.0)	9.6 ± 20.6
Mild difficulty	43 (29.5)	14.2 ± 27.0
Clear difficulty	29 (19.9)	21.7 ± 34.0
		p = 0.25 ^b

Demographic or clinical characteristic	Data	Correlation (r) between characteristic and surgical receptivity or Surgical receptivity within stratum of each characteristic
Difficulty unlocking a door with a key **		
No difficulty	53 (36.3)	13.4 ± 24.7
Mild difficulty	52 (35.6)	13.6 ± 26.5
Clear difficulty	40 (27.4)	14.4 ± 27.8
		p = 0.96 ^b

Values are either mean ± standard deviation or number (percentage).

* Years.

** Data were missing on one ET case. Correlation coefficients (r) are Spearman's correlation coefficients.

^a Mann-Whitney test.

^b Kruskal-Wallis test