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## What is the Functional Significance of Non-dominant Arm Tremor in Essential Tremor?

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### Abstract

**Background**—Tremor in the dominant arm is often the focus of clinical attention in essential tremor (ET) yet many daily activities require both arms. The functional relevance of non-dominant arm tremor has rarely been studied.

**Methods**—In 181 right-handed ET patients, action tremor in each arm was rated using a clinical ratings scale. Tremor disability was self-reported and a performance-based test of function was administered.

**Results**—Independently of tremor on the right, greater tremor severity on the left was associated with greater self-reported disability ( $p=0.02$ ) and greater performance-based dysfunction ( $p<0.001$ ). In 5.0% of patients, tremor was largely restricted to the non-dominant arm.

**Conclusions**—Non-dominant arm tremor, independent of dominant arm tremor, had a significant functional correlate, contributing to both greater perceived and greater observable functional difficulty. In 5% of patients, tremor in the non-dominant arm was the likely motivator for seeking care, which is another indication of its functional significance.

### Keywords

essential tremor; clinical; function; disability

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#### Author Contributions

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## Introduction

Although arm tremor in essential tremor (ET) it is typically asymmetric,<sup>1-3</sup> it is rarely unilateral.<sup>4-6</sup> Therefore, in the large majority of patients, both arms are typically involved. Dominant arm tremor is often the focus of therapeutic interventions. Yet there are ET patients who present mainly with non-dominant arm tremor.<sup>7, 8</sup> Also, while a great many daily activities require only the dominant arm (e.g., holding a pen, putting a key in a lock), other daily tasks require both arms (e.g., holding a knife and a fork, typing, washing dishes, tying shoe laces),<sup>9, 10</sup> suggesting that tremor in the non-dominant arm might be of quantifiable functional relevance in most ET patients.

How functionally relevant is non-dominant arm tremor in ET? To our knowledge, there has been only one prior attempt to systematically study this issue in a sample of 30 ET patients.<sup>11</sup>

We explored this issue across a group of 181 ET patients. We hypothesized that (1) non-dominant arm tremor would correlate significantly with several measures of functional difficulty, (2) its association with functional difficulty would be independent of dominant arm tremor, and (3) in some patients, whose proportion we will estimate using this sample, tremor in the non-dominant arm is the sole motivator for seeking neurological care.

We hope that these data will provide a more complete understanding of all sources of disability in ET. The clinical relevance of these results is that disability may be an important motivator of health seeking behavior.

## Methods

### Subjects

As described previously,<sup>12</sup> ET patients (>age 18) seen at the Neurological Institute of New York, Columbia University Medical Center (CUMC) were enrolled in an ongoing clinical-epidemiological study. Each signed informed written consent approved by the CUMC Institutional Review Board. Two-hundred-eleven ET patients qualified for a diagnosis of ET using published diagnostic criteria;<sup>12</sup> none had Parkinson's disease or dystonia. Of these, 192 who were right-handed. We excluded 11 (5.7%) who had surgery (all DBS, including 3 right brain, 6 left brain, 2 bilateral). Hence, 181 patients remained.

### Evaluation

Demographic and medical histories were obtained, including all medications used to treat tremor. The Cumulative Illness Rating Scale was used to quantify medical co-morbidity in 14 body systems (0 – 3 ratings in each system, range = 0 – 42 [maximum morbidity]).<sup>13</sup> A brief 10-item version of a validated tremor disability questionnaire was administered.<sup>14</sup> Using this questionnaire, difficulty was self-reported (0 = none, 1 = need to modify or loss of efficiency, 2 = disability) on a range of daily activities (e.g., signing name, dialing a telephone, tying shoe laces, cutting nails, carrying a cup); the score ranged from 0 – 20 (most impaired).<sup>14</sup> In a sub-sample of 122 patients enrolled before 2006, a valid performance-based test of function in ET was also performed; the test included 15 items (e.g., signing name, dialing a telephone, carrying a cup and saucer, threading needle, placing bills in a wallet) that were rated from 0 (no difficulty) to 4 (unable to perform the task), and the score ranged from 0 – 60 (most impaired).<sup>15</sup> A videotaped neurological examination was performed on all patients (arm extension, pouring, using spoon, drinking, finger-nose-finger, drawing spirals with each arm, 12 tests total). A neurologist specializing in movement disorders (E.D.L.) used a reliable<sup>16</sup> and validated<sup>15</sup> clinical rating scale to rate tremor during each test: 0 (none), 1 (mild or intermittent), 2 (moderate and usually present), 3

(severe). These ratings resulted in a tremor score for each arm (range = 0 – 18) and a total tremor score (range = 0 – 36).<sup>12</sup> Head (neck), voice and jaw tremors were noted to be present or absent on videotaped examination.

### Statistical Analyses

Analyses were performed in SPSS (version 17). Tremor severity on the left, tremor severity on the right, tremor disability score, and performance-based test score were all normally distributed. Pearson's correlation coefficients ( $r$ ) were used to assess correlations. We also stratified right tremor score into quartiles and, in a linear regression analysis, examined the association between increasing quartile (independent variable) and tremor disability score. We repeated the analyses, using quartiles of left tremor score. These two analyses were repeated, using performance based test score rather than tremor disability score as the outcome variable. In a multivariate linear regression analysis, we examined the independent effects of tremor severity on the left, tremor severity on the right, age, gender, presence of any cranial tremor (neck, voice, jaw), Cumulative Illness Rating Scale Score, and use of tremor medication (currently takes an ET medication; yes vs. no) on tremor disability score (dependent variable) or on performance-based test score (dependent variable in another model).

## Results

### General

There were 181 ET patients (Table 1). The majority (106 or 58.6%) was currently taking ET medication. Tremor severity on the right was associated with that on the left ( $r = 0.52$ ,  $p < 0.001$ ).

### Self-reported Tremor Disability

Greater tremor severity on the right ( $r = 0.61$ ,  $p < 0.001$ ) and left ( $r = 0.44$ ,  $p < 0.001$ ) were each associated with increased tremor disability scores. We stratified the right and left tremor scores into quartiles (Table 2) and, in tests for trend (linear regression models), increasingly higher quartile was associated with increasingly greater disability in both the right arm ( $p < 0.001$ ) and the left arm ( $p < 0.001$ ). Twenty-eight patients had no or only mild right arm tremor (i.e., all postural and kinetic tremor ratings on right = 0 or 1); in these 28, greater tremor severity on the left was marginally associated with increased tremor disability scores ( $r = 0.26$ ,  $p = 0.19$ ) but greater tremor severity on the right was not associated with increased tremor disability scores ( $r = 0.11$ ,  $p = 0.59$ ).

In a multivariate linear regression analysis, tremor severity on the left ( $\beta = 0.23$ ,  $p = 0.02$ ) and tremor severity on the right ( $\beta = 0.73$ ,  $p < 0.001$ ) were *independent* predictors of tremor disability score but, age, gender, presence of any cranial tremor, Cumulative Illness Rating Scale Score and use of tremor medication were not predictors of tremor disability score. The  $\beta$  of 0.23 (left arm tremor) indicated that for every ten point increase in the left arm tremor score, self-reported functional disability increased 2.3 points.

### Performance-based Test of Function

Greater tremor severity on the right ( $r = 0.75$ ,  $p < 0.001$ ) and left ( $r = 0.60$ ,  $p < 0.001$ ) were associated with greater performance-based test scores (more dysfunction). In tests for trend, increasingly higher tremor score quartile was associated with increasingly higher performance-based test score in both the right ( $p < 0.001$ ) and left arms ( $p < 0.001$ ). In the 28 patients with no or only mild right arm tremor, greater tremor severity on the left ( $r = 0.56$ ,  $p = 0.01$ ) but not the right ( $r = 0.13$ ,  $p = 0.60$ ) was associated with increased performance-based test scores.

In a multivariate linear regression analysis, tremor severity on the left ( $\beta = 0.73$ ,  $p < 0.001$ ), tremor severity on the right ( $\beta = 1.48$ ,  $p < 0.001$ ) and age ( $\beta = 0.22$ ,  $p < 0.001$ ) were *independent* predictors of tremor disability score but gender, cranial tremor, Cumulative Illness Rating Scale Score, and use of tremor medication were not. The beta of 0.73 (left arm tremor) indicated that for every ten point increase in left arm tremor score, self-reported functional disability increased 7.3 points.

### Patients With Tremor Largely Restricted to the Non-dominant Arm

There were nine (5.0%) patients whose likely motivation for seeking treatment at CUMC was non-dominant arm tremor. On examination, they had moderate or greater kinetic tremor in the left arm (i.e., at least one kinetic tremor rating  $>2$ ) yet none or only mild right arm tremor (i.e., all postural and kinetic tremor ratings = 0 or 1) and no cranial (neck, voice, jaw) tremor.

### Discussion

Non-dominant arm tremor contributed to both greater self-reported disability and poorer performance-based function in this sample of 181 ET patients. Moreover, in statistical models, its contribution to functional difficulty was independent from that of the tremor in the dominant arm. For one-in-twenty ET patients, non-dominant arm tremor seemed to be the main motivation behind seeking neurological care.

We observed that every ten point increase in left arm tremor score was associated with an approximate 2.3 point increase in self-reported disability. Given the observation that our average patient had a tremor score on the left that was 10.1, in functional terms, this tremor would likely contribute to a loss of efficiency in 2 - 3 additional daily activities. We also showed that every ten point increase in left arm tremor score was associated with a 7.3 point increase in performance-based test score (i.e., either additional mild difficulty on approximately 7 daily tasks or moderate difficulty on 3 - 4 or severe difficulty on approximately 2).

In an interesting study of 30 ET patients whose upper limb function was assessed with three timed functional tests, greater severity of tremor in the non-dominant arm was associated with greater time to complete these tasks using that arm.<sup>11</sup> The impact of this non-dominant arm tremor was not assessed relative to daily tasks (e.g., tying shoe laces, typing etc). No other studies have addressed this issue.

Tremor was not measured using accelerometry. Nevertheless, the use of clinician-based ratings ensured that the observed increases in tremor severity were ones that were clinically detectable and relevant. In our analyses, we included medication use as a covariate, in an attempt to assess the association between tremor severity and disability independent of such use. Nevertheless, nearly 60% of our cases were using tremor medications and they were not asked to withhold these medications prior to evaluation. The use of these medications could have reduced tremor, causing us to underestimate the impact of tremor severity on disability. It is also possible that a patient with very severe right arm tremor might be using the left (non-dominant) arm in order to facilitate daily activities. For this reason, our multivariate statistical models included a term for both right and left arm tremors so that we could examine the independent effects of each on disability. The study had a number of strengths, including the large sample size, the use of both self-reported and performance-based measures of function and the use of functional measures that were specifically designed to assess the effects of tremor in ET.

In summary, non-dominant arm tremor, independent of dominant arm tremor, seemed to have a significant functional correlate in ET, contributing to greater perceived as well as observable functional difficulty with daily tasks. In 5% of patients, tremor in the non-dominant arm seemed to be the motivator for seeking treatment, which is another indication of its importance.

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**Table 1**

## Clinical characteristics of 181 ET patients

Age (years)(range)	67.5 ± 16.1 (18 – 95)
Female	96 (53.0)
Duration of tremor (years)	19.6 ± 17.5
Age of tremor onset (years)	47.9 ± 21.7
Cumulative Illness Rating Scale Score (range = 0 – 42)	5.2 ± 3.7
Head (neck) tremor on examination	67 (37.0)
Voice tremor on examination	59 (32.6)
Jaw tremor on examination	25 (13.8)
Head, voice or jaw tremor on examination	99 (54.7)
Family history of ET (≥1 reportedly affected relative)	104 (57.5)
Currently takes ET medication	106 (58.6)
ET surgery	0 (0.0)
Tremor score (right arm) (range = 0 – 18)	9.7 ± 4.2
Tremor score (left arm) (range = 0 – 18)	9.9 ± 4.2
Total tremor score (right and left arms) (range = 0 – 36)	19.6 ± 7.3
Tremor disability score (range = 0 – 20)	10.1 ± 5.7
Performance-based test score (range = 0 – 60)	18.7 ± 12.6

Values are mean ± standard deviation or proportions (percentage).

**Table 2**

## Function by tremor severity quartiles

	Tremor disability score	Performance-based test score
Right tremor score quartile		
Lowest quartile ( $\leq 6$ )[N = 43]	5.3 $\pm$ 5.0	8.5 $\pm$ 8.1
2 <sup>nd</sup> quartile (7 – 10)[N = 58]	8.9 $\pm$ 4.6	14.8 $\pm$ 8.5
3 <sup>rd</sup> quartile (11 – 12)[N = 33]	11.7 $\pm$ 4.4	19.4 $\pm$ 6.8
Highest quartile ( $\geq 13$ )[N = 47]	14.9 $\pm$ 4.2	32.3 $\pm$ 11.1
Left tremor score quartile		
Lowest quartile ( $\leq 6$ )[N = 45]	7.4 $\pm$ 5.8	12.3 $\pm$ 10.6
2 <sup>nd</sup> quartile (7 – 10)[N = 57]	8.5 $\pm$ 5.5	13.1 $\pm$ 9.1
3 <sup>rd</sup> quartile (11 – 13)[N = 37]	12.0 $\pm$ 4.4	18.5 $\pm$ 8.6
Highest quartile ( $\geq 14$ )[N = 42]	13.5 $\pm$ 4.8	30.5 $\pm$ 11.9

Values are mean  $\pm$  standard deviation.

In tests for trend, higher quartile was associated with higher tremor disability score on both the right (beta = 3.1,  $p < 0.001$ ) as well as the left (beta = 2.2,  $p < 0.001$ ).

In tests for trend, higher quartile was associated with higher performance-based test score on both the right (beta = 7.8,  $p < 0.001$ ) as well as the left (beta = 6.4,  $p < 0.001$ ).