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Tremor and Other Hyperkinetic Movements

Brief Report

Mirror Movements in Essential Tremor: Prevalence and Relationship to Mini-Mental Status Test Scores

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Abstract

Background: Mirror movements (MM) are mirror reversals of contralateral, voluntary alternating or repetitive limb movements. MM have been described in age-related neurological diseases, including essential tremor (ET). MM could represent a motor release sign. Cognitive dysfunction (especially executive dysfunction) and dementia have also been reported among ET patients. It is conceivable that MM and cognitive dysfunction in ET arise from the same underlying anatomical or physiological substrate. Hence, the underlying clinical question is whether MM are a simple and easily elicited motor marker for incipient cognitive change or dementia in ET? Identifying such a marker would have value to clinicians, and we are unaware of prior studies that have assessed this issue.

Methods: The Folstein Mini-Mental State Exam (FMMSE) and the Modified Mini-Mental Status Examination (mMMSE) were administered to 148 ET cases enrolled in a cross-sectional clinical study.

Results: MM were present in 115 out of 148 (77.7%) ET cases. In analyses that considered age, there were no differences in FMMSE or mMMSE scores between participants with vs. without MMs (all p values >0.05).

Discussion: These data suggest that MM, while present in a considerable number of ET cases, would not be a useful motor marker for incipient cognitive change in ET cases.

Keywords: Essential tremor, mirror movements, clinical, cognition, dementia

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Introduction

Mirror movements (MM) are mirror reversals of contralateral, voluntary alternating, or repetitive limb movements.[1] MM have been described in age-related neurological diseases that manifest both motor and cognitive features, including Parkinson's disease (PD), corticobasal degeneration, Huntington's disease, and, most recently, essential tremor (ET).[1] A curious motor overflow phenomenon, they are of unclear significance, although they could represent a motor release sign.[1]

Aside from motor features, cognitive dysfunction (especially executive dysfunction) has also been reported among ET patients.[2–5] The basis for the cognitive difficulty in ET is unclear, but it could arise from dysfunction of circuits that involve the pre-frontal or frontal cortices, among other structures.[5]

Given these observations, it is conceivable that MM and cognitive dysfunction in ET arise from the same underlying anatomical or physiological substrate. In order to test this hypothesis, one would assess whether MM and cognitive dysfunction were correlated in a group of ET patients, and this was our aim. The underlying clinical question is: are MM a simple and easily elicited motor marker for incipient cognitive change or dementia in ET? Identifying such a marker would have clinical value. We are unaware of prior studies that have attempted to address this issue.

Methods

ET cases were enrolled in an ongoing clinical-pathological study at Columbia University Medical Center (CUMC), New York.[6,7] The study enrolled ET cases as future brain donors. ET cases were ascertained through a variety of mechanisms, including advertisements on the International Essential Tremor Foundation website, and newsletters and 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 New York. To date, 387 ET cases have expressed interest in enrollment. Beginning in March 2009, we began enrolling these cases at a rate of approximately seven per month, with selection based on age, starting with the oldest. 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.

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. To assess cognition, we administered the Folstein Mini-Mental State Exam (FMMSE, range 0–30 (no impairment))[8] and the Modified Mini-Mental Status Examination (mMMSE, range 0–57 (no impairment)).[9] The mMMSE included several tests of executive dysfunction (backwards digit span, serial sevens, spelling "world" backwards, adding change, range 0–11 (no impairment)).

During a videotaped motor examination, participants were seated facing the trained tester. As described previously,[1] participants were instructed to perform four unilateral voluntary motor tasks with either the right or left hand or foot: finger taps, opening and closing the hand, hand pronation–supination, and ankle flexion–extension foot taps (i.e. eight tasks total). For each task, they were asked to perform at least 10 repetitions. During these activities, their inactive arm was resting in their lap and their inactive foot planted lightly on the ground. As described,[1,10] MM were scored (E.D.L.) on the videotape using a three-item scale that included a measure of MM amplitude (range of excursion), distribution (extent to which the movements matched those of the task performing limb), and proportion (fraction of time during which movements were noted). These three items yielded a score from 0 to 10 for each of the eight tasks and a MM total score (range 0–80 (maximum)) for each participant. Although MM are often repetitive, the scorer was careful to consider the speed and quality of the movements and to distinguish these overflow movements from the kinetic tremor of ET.

During the videotaped examination, postural and kinetic tremor in each arm was tested, and then rated (range 0–4 for each item, E.D.L.), and a total tremor score (range 0–46) was assigned to each case.[1] The diagnosis of ET was reconfirmed 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 PD).[1,11] Analyses were carried out using SPSS (version 18.0.2; Chicago, Illinois).

Results

Of 150 enrolled ET cases, two had missing data items, leaving 148 ET cases available for analysis (Table 1). MM were present in 115 out of 148 (77.7%) cases. They were present in the arms in 60 out of 148 (40.5%) cases, in the legs in 102 out of 148 (68.9%) cases, and in both in 47 out of 148 (31.8%) cases. Cases with MM were younger than those without MM, but were similar in terms of gender, educational level, total tremor score, age of onset of tremor, tremor duration, and proportion with tremor at rest (Table 1). The FMMSE, mMMSE, and mMMSE executive function scores were either marginally higher or higher in participants with MM than in participants without MM (Table 1). The FMMSE score was associated with marginally higher MM total scores (Spearman's $r = 0.14$, $p = 0.09$) and the mMMSE score was associated with marginally higher MM total scores (Spearman's $r = 0.15$, $p = 0.08$). However, in analyses that stratified the sample based on age, which was an important confounder to consider, there were no differences in FMMSE or mMMSE scores between participants with vs. without MMs (all p values >0.05).

Discussion

In this study, MM were present in a large proportion (77.7%) of ET cases. This is a higher proportion than in our prior study (32.7%),[1] although the two samples differed substantially in terms of age as well as disease duration and severity. Also, in the prior study, ET patients were ascertained in the setting of a clinical-epidemiological study whereas in the current study, the participants were ET cases enrolled as future brain donors. Prior work has shown that the latter are a selected group with a larger proportion exhibiting rest tremor, cranial tremors, and other motor phenomenology.[7]

Several prospective, population-based studies have revealed a higher risk of incident dementia among ET cases,[3,4] with prevalence data revealing as many as one in four ET cases (mean age 80.9 $\pm$ 7.5) having dementia.[3] It would be helpful to identify markers for emerging dementia in ET, and perhaps other than age none has been identified to date. It is conceivable that MM and cognitive dysfunction in ET arise from the same underlying anatomical or physiological substrate and that MM could serve as an easily elicited motor marker for incipient cognitive change or dementia in ET. This was the rationale in this study to examine whether there was an association between cognition and MM in ET. In the present analyses, in contrast to the hypothesized relationship (MM might be associated with poorer cognition), initial univariate analyses suggested that MM in ET were marginally associated with higher cognitive test scores. However, adjustments for age revealed no significant case–control difference.

This study had several limitations. First, we recognize that the study enrolled ET cases and no control group; hence, we were not able to compare the prevalence in ET to a group of controls as we had done previously.[1] Our prior data indicated that 23.7% of controls had MM.[1] However, this was not the aim of the present study. Second, our cases were a group of highly motivated brain donors and they may not be representative of all ET cases. Hence, studies that sample other groups of cases would be useful. Finally, the measures of cognitive

Table 1. Demographic and Clinical Characteristics of 148 ET Cases

	All ET Cases (N = 148)	ET Cases with MM (N = 115)	ET Cases without MM (N = 33)
Age (years)	84.3 ± 5.5	83.7 ± 5.4[a]	86.5 ± 5.2
	range 74–102		
Gender (female)	88 (59.5)	69 (60.0)	19 (57.6)
Educational level			
<High school	7 (4.7)	5 (4.3)	2 (6.1)
High school diploma	46 (31.1)	38 (33.0)	8 (24.2)
Some college	14 (9.5)	12 (10.4)	2 (6.1)
Bachelors degree or higher	81 (54.7)	60 (52.2)	21 (63.6)
Total tremor score[1]	24.9 ± 7.3	24.6 ± 7.1	26.1 ± 7.7
Age of tremor onset (years)	42.4 ± 22.9	42.1 ± 22.2	43.2 ± 25.4
Tremor duration (years)	41.8 ± 22.2	41.4 ± 21.9	43.2 ± 23.8
Arm tremor at rest	52 (35.1)	37 (32.2)	15 (45.5)
FMMSE[2]	26.9 ± 2.7	27.1 ± 2.7[b]	26.2 ± 2.6
	Median 27.0	Median 28.0	Median 26.0
	Range 11–30	Range 11–30	Range 20–30
	(<24 in 11 (7.4%))	(<24 in 7 (6.1%))	(<24 in 4 (12.1%))
mMMSE[3]	49.1 ± 5.9	49.5 ± 5.8[c]	47.7 ± 6.0
	Median 50.0	Median 50.0	Median 49.0
	Range 18–57	Range 18 – 57	Range 35–56
mMMSE executive function score[4]	9.1 ± 1.9	9.2 ± 1.9[d]	8.6 ± 2.0
	Median 10.0	Median 10.0	Median 9.0
	Range 3–11	Range 4–11	Range 3–11
MM total score[5]	9.7 ± 9.6	12.5 ± 9.1	0 ± 0.0
	Median 8.0	Median 10.0	Median 0.0
	Range 0–50	Range 3–50	Range 0–0

Abbreviations: ET, essential tremor; FMMSE, Folstein Mini-Mental State Exam; MM, mirror movements; mMMSE, Modified Mini-Mental Status Examination
Values are either means ± standard deviation or number (percentage).
[a]p = 0.01 (Student t test) compared to ET cases without MM.
[b]p = 0.03 (Mann–Whitney test) compared to ET cases without MM.
[c]p = 0.09 (Mann–Whitney test) compared to ET cases without MM.
[d]p = 0.10 (Mann–Whitney test) compared to ET cases without MM.
[1]Potential range 0–46.
[2]Folstein Mini-Mental State Exam (potential range 0–30 (no impairment)).
[3]Modified Mini-Mental Status Examination (potential range 0–57 (no impairment)).
[4]Potential range 0–11 (no impairment).
[5]Potential range 0–80 (maximum).

function that we used were mental status test scores rather than detailed neuropsychological test batteries. The study had strengths as well. First, we are not aware of any studies that have attempted to address this particular issue in ET. Furthermore, MM were carefully evaluated in a uniform manner using a detailed clinical assessment.

These data suggest that MM, although present in a considerable number of ET cases, would not be a useful motor marker for incipient cognitive change in ET cases.

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