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Macrographia in Essential Tremor: A Study of Patients With and Without Rest Tremor

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Studies have reported the presence of mild bradykinesia in patients with essential tremor (ET).¹ Based on these studies, we hypothesized that ET patients, and especially those with rest tremor, might exhibit micrographia in comparison with age-matched controls.

100 ET cases and 100 controls were enrolled in a clinical-epidemiological study at Columbia University Medical Center. Each signed informed consent approved by Medical Center Ethics Board, and had a detailed assessment (questionnaires, videotaped examination). Tremor severity measurements included the Tremor Disability Questionnaire (TDQ)² and total tremor score (TTS).²

Each subject copied 3 standardized phrases (21 words) in a set of 3 boxes (12.8 × 166.6, 25.5 × 166.6, and 12.8 × 166.6 mm) on a sheet of paper. Writing samples were scanned (600 dpi) and filed in JPEG format. A movement disorder neurologist (H.R.M-H.) measured the

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Conflict of Interest Statement:

The authors declare that there are no conflicts of interest and no competing financial interests.

Contributions of Each Author:

Hector R. Martinez-Hernandez: study design, analysis and interpretation of data, initial draft and critical revision of manuscript for important intellectual content.

Elan D. Louis: study conception and design, analysis and interpretation of data, study supervision, initial draft and critical revision of manuscript for important intellectual content.

Statistical Analyses: Hector R. Martinez-Hernandez, MD and Elan D. Louis, MD, MSc, Columbia University, performed the statistical analyses.

Ethics approval: This study was approved by Columbia University Medical Center Internal Review Board.

height and width (mm) of the most commonly repeated letters (“t” [used 9×], “e” [used 8×], “a” [used 7×], “r” [used 7×]) using the software program GIMP version 2.8 (GNU Image Manipulating Program). For “i” (used 7×), only height was measured.

Cases and controls were similar in demographic characteristics (Table). For each of the most commonly repeated letters, height and width measurements were higher in cases than controls (68 of 69 p values < 0.05). Mean width and mean height measurements for each letter (nine comparisons), were greater in cases than controls (Table). For each letter, we also compared the dimensions (height and width) of the first vs. last letter; only “e” showed a decrement (Supplementary table). An increment of letter height was observed (in cases and controls) for “ás” and “ts” and in width for “ás” and “s”.

The 15 cases with rest tremor were compared to 85 without rest tremor, in terms of height and width measurements. In 66 of 69 comparisons, the two groups were similar; in 3 of 69 comparisons (heights of “i1”, “i5”, and “a2”), the dimensions were smaller in ET cases with rest tremor.

Mean dimensions were correlated with tremor duration in 5 of 9 comparisons (Pearson’s $r = 0.22 - 0.33$, $p < 0.05$), with TTS in 8 of 9 comparisons (Pearson’s $r = 0.29 - 0.42$, $p < 0.001$), and with TDQ in 4 of 9 comparisons (Pearson’s $r = 0.27 - 0.35$, $p < 0.05$).

This is the first objective description of handwriting size in ET, and the first to report macrographia. Macrographia has been described in other conditions, including Huntington’s disease,³ autism spectrum disorder,⁴ and children with cerebellar lesions or attention-deficit/hyperactivity disorder.⁵ It has been associated with a cerebellar dysfunction in these reports.

ET has been recast as a cerebellar disorder, with intention tremor, gait ataxia and saccadic eye movement abnormalities, and neuroimaging and histopathological evidence point to a central role of the cerebellum in disease pathogenesis. Macrographia could be the result of cerebellar dysfunction in ET or a compensatory mechanism attempting to clarify writing with larger letters.

The utility of handwriting analysis, in helping differentiate ET from PD in cases where the phenotype presents a challenge, remains to be determined.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table

Demographic and clinical characteristics of 100 ET cases and 100 controls

Characteristics	Cases	Controls	Significance
Age (years)	67.0 ± 15.6	63.6 ± 12.1	p = 0.09 ^a
Male gender	57 (57)	56 (56)	p = 0.88 ^b
Right-handed (%)	93 (93)	90 (90)	p = 0.65 ^b
Script (vs Print)	65 (65)	62 (62)	p = 0.66 ^b
Age at onset (years)	47.5 ± 21.6	Not applicable	Not applicable
Tremor duration (years)	19.5 ± 18.1	Not applicable	Not applicable
Proportion with rest tremor in the dominant arm	15 (0)	0 (0)	p < 0.001 ^b
TDQ mean score	51.19 ± 29.57	Not applicable	Not applicable
TTS mean score	19.53 ± 7.67	Not applicable	Not applicable
i height (mm)	3.48 ± 1.50	2.65 ± 0.76	p < 0.001 ^a
a height (mm)	3.74 ± 1.45	3.03 ± 0.86	p < 0.001 ^a
a width (mm)	4.18 ± 1.39	3.20 ± 0.74	p < 0.001 ^a
r height (mm)	3.69 ± 1.45	2.98 ± 0.87	p < 0.001 ^a
r width (mm)	4.34 ± 1.44	3.34 ± 0.86	p < 0.001 ^a
t height (mm)	6.74 ± 2.89	5.42 ± 1.62	p < 0.001 ^a
t width (mm)	5.85 ± 2.51	4.49 ± 1.36	p < 0.001 ^a
e height (mm)	3.56 ± 1.29	2.84 ± 0.70	p < 0.001 ^a
e width (mm)	4.15 ± 1.46	3.05 ± 0.75	p < 0.001 ^a

Values represent mean ± standard deviation or numbers (percentage).

TDQ = tremor disability questionnaire. TTS = total tremor score

^aStudent's t test.^b χ^2 test.