

Brief Report

# Early Head Tremor in Essential Tremor: A Case Series and Commentary

Elan D. Louis<sup>1,2,3\*</sup>, Funmi M. Badejo<sup>1</sup>, Ashley D. Cristal<sup>1</sup>, James Meyers<sup>1</sup>, Nora Hernandez<sup>1</sup>, Karen P. Chen<sup>1</sup>, Kelly V. Naranjo<sup>1</sup>, Jemin Park<sup>1</sup> & Lorraine N. Clark<sup>4,5</sup>

<sup>1</sup> Division of Movement Disorders, Department of Neurology, Yale School of Medicine, New Haven, CT, USA, <sup>2</sup> Department of Chronic Disease Epidemiology, Yale School of Public Health, New Haven, CT, USA, <sup>3</sup> Center for Neuroepidemiology and Clinical Neurological Research, Yale School of Medicine, New Haven, CT, USA, <sup>4</sup> Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Columbia University, New York, NY, USA, <sup>5</sup> Department of Pathology and Cell Biology, Columbia University Medical Center, New York, NY, USA

## Abstract

**Background:** Classically, the onset of head tremor in essential tremor (ET) patients follows that of hand tremor, such that there is a somatotopic spread of involved areas. Here we present a series of seven self-reportedly “unaffected” relatives of ET cases. These seven were clinically asymptomatic and had normal levels of arm tremor on examination, yet each evidenced a transient head wobble on examination. We estimate the prevalence of this phenotype within the two studies from which cases were ascertained.

**Methods:** ET cases and their self-reportedly affected and unaffected relatives, enrolled in two family studies, underwent a medical history and videotaped neurological examination.

**Results:** In seven self-reportedly “unaffected” relatives, a transient and subtle head wobble was seen, always during sustained phonation, speech, or reading aloud. Total tremor score (a measure of arm tremor) ranged from 5 to 12 (i.e., mild tremor within the range of normal). The prevalence of this phenotype of early head tremor was 3.7% in one study and 23.1% in the other.

**Discussion:** We present a series of seven individuals who had early head tremor in an evolving transition state from normal to ET. These cases raise a number of broad clinical, phenotypic, and pathophysiological issues about ET.

**Keywords:** Essential tremor, clinical, head tremor, phenotype

**Citation:** Louis ED, Badejo FM, Cristal AD, et al. Early head tremor in essential tremor: a case series and commentary. Tremor Other Hyperkinet Mov. 2017; 7. doi: 10.7916/D8KW5MRG

\*To whom correspondence should be addressed. E-mail: elan.louis@yale.edu

Editor: Julian Benito-Leon, Hospital “12 de Octubre”, Spain

Received: January 26, 2017 Accepted: March 7, 2017 Published: xxxx

Copyright: © 2017 Louis et al. This is an open-access article distributed under the terms of the Creative Commons Attribution–Noncommercial–No Derivatives License, which permits the user to copy, distribute, and transmit the work provided that the original authors and source are credited; that no commercial use is made of the work; and that the work is not altered or transformed.

Funding: This work was supported by the National Institutes of Health (NINDS #R01 NS094607 and NINDS #R01 NS073872). This funding body played no role in the design of the study, the collection, analysis, and interpretation of data, or the writing of the manuscript.

Financial Disclosures: None.

Conflict of Interest: The authors declare no conflict of interest.

Ethics Statements: All patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

## Introduction

Head (i.e., neck) tremor is a common feature in patients with essential tremor (ET), occurring in 10.9–18.0% of ET cases in population-based studies<sup>1–3</sup> and as many as 60.6% of cases in more selected samples such as brain repositories.<sup>4</sup> Indeed, apart from the arms, the head is the region most commonly affected by tremor in patients with ET. Additional interest in head tremor in ET is based on the observation, from neuroimaging studies, that the underlying brain changes may differ from those seen in ET patients who do not have head tremor.<sup>5,6</sup>

Classically, the onset of head tremor in patients with ET is supposed to follow that of hand tremor, such that there is a typical somatotopic spread of involved areas.<sup>7–12</sup> As a corollary, isolated head tremor (i.e., head tremor in the absence of arm tremor) is reported to be rare or non-existent.<sup>13–15</sup>

Recently, in the setting of two family studies, we came across a number of ET cases with 1) no tremor by self-report, 2) no prior diagnosis of ET, 3) tremor in the arms that on examination was mild and within the normal range, and 4) the presence of a transient but unmistakable head wobble on examination.

Our goal here is to present this series of seven cases, highlighting their clinical features and presenting a visual record of the phenomenon. We also wish to determine how common this phenotype is, estimating its prevalence within the two studies from which the cases were ascertained. Finally, we raise a number of broader clinical, phenotypic, and pathophysiological issues about ET in our discussion.

### Methods

ET cases and their relatives were enrolled in two family studies, described below. Each enrollee underwent a demographic and medical history and a videotaped neurological examination, as described below. All enrollees signed written informed consent approved by the Yale University institutional ethics board.

#### **Family study of the environmental epidemiology of ET**

ET cases and their first-degree relatives were enrolled in a study of the environmental epidemiology of ET (May 2016 to present). ET cases were ascertained from several sources, including study advertisements to the membership of the International Essential Tremor Foundation, membership in current ET research studies at Yale, and the clinical practice of the Yale Movement Disorders Group. The goal of the study was to enroll unaffected first-degree relatives to complete an environmental risk factor assessment, including a measurement of blood harmaline concentration. Prior to their in-person assessment, family members were interviewed by telephone, during which a 12-item tremor screening questionnaire<sup>16</sup> was administered, and they were also asked about prior diagnosis of ET. They also submitted four hand-drawn spirals (two right and two left), which were rated by a senior movement disorder neurologist (E.D.L.) using the following scale: 0 (absolutely no oscillations anywhere), 0.5 (subtle, low-amplitude oscillations are present in a few spots; oscillations are not consistently present throughout the spiral), 1 (low-amplitude oscillations are present in multiple places; examining at least one of the spiral's quadrants reveals the presence of these low-amplitude oscillations that occur in each larger and larger line of the spiral within that quadrant), 1.5 (low-amplitude oscillations are present in multiple places and oscillations can at times reach moderate amplitude), 2 (moderate-amplitude oscillations that are present in many areas of the spiral), 3 (oscillations reach large amplitude in one or more places; lines may overlap; pen may lift off the paper) (see examples in Louis et al).<sup>17</sup> Relatives were initially categorized as unaffected if they met each of the following criteria: 1) they did not report tremor during the 12-item telephone-administered tremor screening questionnaire,<sup>16</sup> 2) they had never been assigned an ET diagnosis by a treating physician, and 3) their two right and two left-hand-drawn screening spirals were assigned tremor scores  $\leq 1.0$ . To date, 26 relatives initially categorized as unaffected have been enrolled.

#### **Family study of essential tremor**

ET cases and their affected and unaffected first- and second-degree relatives were enrolled in the Family Study of Essential Tremor (FASET), a genetics study of ET (Phase 1, 2011–2014 and Phase 2, 2015 to present).<sup>18</sup> The study was advertised on ET society websites

and e-mail outreach to their membership. Based upon a telephone interview with the proband, relatives were identified. Prior to their in-person assessment, relatives were categorized as unaffected if they met each of the following criteria: 1) they did not report tremor during a three-item telephone screening questionnaire, 2) they had never been assigned an ET diagnosis by a treating physician, and 3) their two right- and two left-hand-drawn screening spirals were assigned tremor scores  $\leq 1.0$ . To date, 27 relatives initially categorized as unaffected have been enrolled.

#### **In-person assessment**

In both studies, all enrollees were evaluated in person by a trained tester who administered structured clinical questionnaires that elicited demographic and clinical information. As in our previous studies,<sup>19</sup> each enrollee underwent a 20–30-minute standardized videotaped neurological examination, which included a detailed assessment of postural tremor, five tests for kinetic tremor, the motor portion of the Unified Parkinson's Disease Rating Scale<sup>20</sup> excluding an assessment of rigidity, and a comprehensive assessment of dystonia. The examination also included a detailed assessment of head, jaw, and voice tremors. For head tremor, enrollees first were assessed while seated quietly and facing the camera, during brief conversational speech, during sustained phonation ("ahh" and "eee" for 10–15 seconds each) and while reading a standard passage from a sheet of paper. Head tremor was also potentially detectable during much of the remainder of the 20–30-minute videotaped assessment (e.g., while drinking water from a cup, while using a spoon, while touching finger-to-nose). A senior movement disorders neurologist reviewed all videotaped examinations. The severity of postural and kinetic tremors were rated (0–3), resulting in a total tremor score (range 0–36 (maximum)), a measure of the severity of the action tremor. Based on the videotaped examination, the senior movement disorders neurologist assigned ET diagnoses to relatives using published diagnostic criteria (moderate or greater amplitude kinetic tremor on  $\geq 3$  tests, or head tremor, in the absence of Parkinson's disease or dystonia).

#### **Statistical analyses**

We calculated 95% confidence intervals (CI) on prevalence estimates.

### Results

There were seven cases in whom a subtle horizontal head wobble was seen fleetingly. In each case, the movement was seen in the setting of sustained phonation, speech or reading aloud during the videotaped neurological examination (Video 1). Six cases were ascertained from the Family Study of the Environmental Epidemiology of ET (cases 1–6, Table 1) and one from FASET (case 7, Table 1). All were from separate families. The age range was 41–73 years (mean 57.9 years, median 60.5 years) and all were women (Table 1).

One (case 6) had voice tremor on videotaped neurological examination, but none had jaw tremor and none had tremor ratings of 2 (moderate tremor) or higher in the arms on that examination. The total tremor scores ranged from 5 to 12 (mean 8.1, median 8).



Table 1. Demographic and Clinical Features of ET Cases

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (years)	52	54	67	41	73	67	51
Gender	F	F	F	F	F	F	F
Hand dominance	L	R	R	R	R	R	L
Proband's age of tremor onset	11	Unknown	16	15	53	7	7
Number of affected first-degree relatives	2	1	4	1	2	2	2
Voice tremor <sup>1</sup>	No	No	No	No	No	Yes	No
Jaw tremor <sup>1</sup>	No	No	No	No	No	No	No
Tremor rating on R extension <sup>1</sup>	0	0	0	0.5	0	0.5	0
Tremor rating on L Extension <sup>1</sup>	0	0	0	0.5	0	0.5	0
Tremor rating on R pouring <sup>1</sup>	0.5	0	0	1	0.5	0.5	1
Tremor rating on L pouring <sup>1</sup>	0.5	0	0	0	0.5	0	1
Tremor rating on R using spoon <sup>1</sup>	0.5	0.5	1	1	0	1	0.5
Tremor rating on L using spoon <sup>1</sup>	1	1.5	1	1.5	1.5	0.5	0.5
Tremor rating on R drinking <sup>1</sup>	0.5	1	0	1	1.5	0.5	0.5
Tremor rating on L drinking <sup>1</sup>	0.5	0	0.5	1	1.5	0.5	1
Tremor rating on R FNF <sup>1</sup>	1	1.5	0.5	1	0.5	1	1
Tremor rating on L FNF <sup>1</sup>	0.5	1.5	1	1.5	0.5	1.5	1
Tremor rating on R drawing <sup>1</sup>	0.5	1	0	1.5	1	1	1.5
Tremor rating on L drawing <sup>1</sup>	1	1	1	1.5	0.5	1	1
Total tremor score	6.5	8	5	12	8	8.5	9

Abbreviations: F, Female; FNF, Finger–Nose–Finger Maneuver; L, Left; R, Right.  
<sup>1</sup>On videotaped neurological examination.

## References

1. Dogu O, Louis ED, Sevim S, Kalegasi H, Aral M. Clinical characteristics of essential tremor in Mersin, Turkey. A population-based door-to-door study. *J Neurol* 2005;252:570–574. doi: 10.1007/s00415-005-0700-8
2. Louis ED, Ford B, Wendt KJ, Cameron G. Clinical characteristics of essential tremor: data from a community-based study. *Mov Disord* 1998;13:803–808. doi: 10.1002/mds.870130508
3. Benito-Leon J, Bermejo-Pareja F, Morales JM, Vega S, Molina JA. Prevalence of essential tremor in three elderly populations of central Spain. *Mov Disord* 2003;18:389–394. doi: 10.1002/mds.10376
4. Louis ED, Borden S, Moskowitz CB. Essential tremor centralized brain repository: diagnostic validity and clinical characteristics of a highly selected group of essential tremor cases. *Mov Disord* 2005;20:1361–1365. doi: 10.1002/mds.20583
5. Quattrone A, Cerasa A, Messina D, et al. Essential head tremor is associated with cerebellar vermis atrophy: a volumetric and voxel-based morphometry MR imaging study. *Am J Neuroradiol* 2008;29:1692–1697. doi: 10.3174/ajnr.A1190
6. Cerasa A, Messina D, Nicoletti G, et al. Cerebellar atrophy in essential tremor using an automated segmentation method. *Am J Neuroradiol* 2009;30:1240–1243. doi: 10.3174/ajnr.A1544
7. Critchley M. Observations of essential (heredofamilial) tremor. *Brain* 1949;72:113–139. doi: 10.1093/brain/72.2.113
8. Louis ED. Twelve clinical pearls to help distinguish essential tremor from other tremors. *Expert Rev Neurother* 2014;14:1057–1065. doi: 10.1586/14737175.2014.936389
9. Louis ED. Diagnosis and management of tremor. *Continuum (Minneapolis)* 2016;22:1143–1158.
10. Davis CH, Jr., Kunkle EC. Benign essential (heredofamilial) tremor. *Arch Intern Med* 1951;87:808–816. doi: 10.1001/archinte.1951.03810060035004
11. Findley LJ, Gresty MA. Tremor. *Br J Hosp Med* 1981;26:16–32.
12. Koller WC, Busenbark KL. Essential tremor. In: Watts RL, Koller WC, editors. *Movement Disorders: Neurologic Principles and Practice*. New York: McGraw-Hill, 1997: p. 365–385.
13. Louis ED, Dogu O. Isolated head tremor: part of the clinical spectrum of essential tremor? Data from population-based and clinic-based case samples. *Mov Disord* 2009;24:2281–2285. doi: 10.1002/mds.22777
14. Koller WC, Glatt S, Biary N, Rubino FA. Essential tremor variants: effect of treatment. *Clin Neuropharmacol* 1987;10:342–350. doi: 10.1097/00002826-198708000-00004
15. Ashenhurst EM. The nature of essential tremor. *Can Med Assoc J* 1973;109:876–878.
16. Louis ED, Ford B, Lee H, Andrews H. Does a screening questionnaire for essential tremor agree with the physician's examination? *Neurology* 1998;50:1351–1357. doi: 10.1212/WNL.50.5.1351
17. Louis ED, Zhao Q, Meng H, Ding D. Screening for action tremor in epidemiological field surveys: Assessing the reliability of a semi-quantitative, visual, template-based scale for rating hand-drawn spirals. *Tremor Other Hyperkinet Mov* 2012;2. doi: 10.7916/D8QZ28QP
18. Louis ED, Hernandez N, Ionita-Laza I, Ottman R, Clark LN. Does rate of progression run in essential tremor families? Slower vs. faster progressors. *Parkinsonism Relat Disord* 2013;19:363–366. doi: 10.1016/j.parkreldis.2012.10.005
19. Rao AK, Gilman A, Louis ED. Balance confidence and falls in nondemented essential tremor patients: the role of cognition. *Arch Phys Med Rehabil* 2014;95:1832–1837. doi: 10.1016/j.apmr.2014.04.001
20. Goetz CG, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): process, format, and clinimetric testing plan. *Mov Disord* 2007;22:41–47. doi: 10.1002/mds.21198
21. Louis ED. Essential tremor with head tremor: Trait or state? *Can J Neurol Sci* 2016;43:443–444. doi: 10.1017/cjn.2015.352
22. Lenka A, Bhalsing KS, Jhunjhunwala KR, Chandran V, Pal PK. Are patients with limb and head tremor a clinically distinct subtype of essential tremor? *Can J Neurol Sci* 2015;42:181–186. doi: 10.1017/cjn.2015.23
23. Wright BA, Michalec M, Louis ED. Triggering essential head tremor with sustained phonation: A clinical phenomenon with potential diagnostic value. *Parkinsonism Relat Disord* 2014;20:230–232. doi: 10.1016/j.parkreldis.2013.10.019
24. Hubble JP, Busenbark KL, Pahwa R, Lyons K, Koller WC. Clinical expression of essential tremor: effects of gender and age. *Mov Disord* 1997;12:969–972. doi: 10.1002/mds.870120620
25. Hardesty DE, Maraganore DM, Matsumoto JY, Louis ED. Increased risk of head tremor in women with essential tremor: longitudinal data from the Rochester Epidemiology Project. *Mov Disord* 2004;19:529–533. doi: 10.1002/mds.20096
26. Louis ED, Pellegrino KM, Rios E. Unawareness of head tremor in essential tremor: A study of three samples of essential tremor patients. *Mov Disord* 2008;23:2423–2424. doi: 10.1002/mds.22011
27. Louis ED, Ford B, Pullman S, Baron K. How normal is 'normal'? Mild tremor in a multiethnic cohort of normal subjects. *Arch Neurol* 1998;55:222–227. doi: 10.1001/archneur.55.2.222
28. Louis ED, Ford B, Frucht S, Ottman R. Mild tremor in relatives of patients with essential tremor: what does this tell us about the penetrance of the disease? *Arch Neurol* 2001;58:1584–1589. doi: 10.1001/archneur.58.10.1584
29. Louis ED, Dogu O, Ottman R. Subclinical tremor in normal controls with versus without a family history of essential tremor: data from the United States and Turkey. *Eur J Neurol* 2010;17:607–611. doi: 10.1111/j.1468-1331.2009.02875.x