HHS Public Access

Author manuscript

Parkinsonism Relat Disord. Author manuscript; available in PMC 2021 May 01.

Published in final edited form as:

Parkinsonism Relat Disord. 2020 May ; 74: 38–42. doi:10.1016/j.parkreldis.2020.04.008.

Rate of Progression from Mild Cognitive Impairment to Dementia in an Essential Tremor Cohort: A Prospective, Longitudinal Study

Keith H. Radler, BA[1], **Maria Anna Zdrodowska, BS**[1], **Hollie Dowd, BA**[1], **Tess E.K. Cersonsky, BS**[1], **Edward D. Huey, MD**[2,3,4], **Stephanie Cosentino, PhD**[2,3], **Elan D. Louis, MD, MSc**[1,5,6]

[1]Division of Movement Disorders, Department of Neurology, Yale School of Medicine, Yale University, New Haven, CT, USA

[2]Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[3]Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[4]Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[5]Department of Chronic Disease Epidemiology, Yale School of Public Health, Yale University, New Haven, CT, USA.

[6]Center for Neuroepidemiology and Clinical Neurological Research, Yale School of Medicine, Yale University, New Haven, CT, USA.

Abstract

Background: Essential tremor (ET), among the most common neurological diseases, is associated with cognitive dysfunction. Yet, nearly all knowledge of ET-related cognitive impairment is static and cross-sectional (e.g., prevalence), with virtually no dynamic information (i.e., course and progression, conversion rates, and clinical outcomes).

Objectives: To quantify the rate of progression from mild cognitive impairment (MCI) to dementia in a cohort of elderly ET cases.

Correspondence: Elan D. Louis, MD, MS, Yale School of Medicine, Department of Neurology, 15 York Street, PO Box 208018, New Haven, CT 06520-8018, USA. Tel: (203) 785-6599. FAX: (203) 785-7826. elan.louis@yale.edu.

Author Contributions

Acquisition of data; analysis and interpretation of data; drafting/editing manuscript; final approval of work (KHR).

Acquisition of data; drafting/editing manuscript; final approval of work (MAZ, HD). Conception and design of study; drafting/editing manuscript; final approval of work (EDH, SC).

Conception and design of study; analysis and interpretation of data; drafting/editing manuscript; final approval of work (EDL).

Conflicts of Interest:

There are no conflicts of interest or competing financial interests.

Methods: 167 ET cases, enrolled in a prospective, longitudinal, clinical-pathological study, underwent an extensive neuropsychological testing battery at baseline (T1), 1.5 years (T2), and 3 years (T3). Results of these assessments informed clinical diagnoses of normal cognition (ET-NC), MCI (ET-MCI), and dementia (ET-D).

Results: At baseline, 26 cases (82.7 ± 7.7 years) were diagnosed with ET-MCI and were available for follow-up at T2. At T2, three of 26 (11.5%) had converted to ET-D. At the start of T2, 23 cases (83.6 ± 7.7 years) were diagnosed with ET-MCI and were available for follow-up at T3. At T3, six of 23 (26.1%) converted to ET-D. The average annual conversion rate from ET-MCI to ET-D was 12.5%.

Conclusions: The study of cognitive impairment in ET is a nascent field, with limited data. We show that the conversion rate from ET-MCI to ET-dementia was 12.5%. Available studies on historical controls have reported conversion rates of 2.6 – 6.3%. Data such as these systematically fill gaps in knowledge, creating a scientifically-derived knowledge base to guide physicians and patients in clinical settings.

Keywords

Essential tremor; Cognitive aging; Movement disorders; Dementia; Cerebellar diseases

Introduction

Essential tremor (ET) is one of the most common neurological diseases, with approximately seven million patients in the US [1]. Previously, ET was characterized as a largely benign, monosymptomatic movement disorder whose sole manifestation was tremor. The dialogue surrounding ET has shifted recently, with increasing recognition of non-motor symptoms. A number of studies have shown that ET cases display poorer cognitive performance and an increased prevalence of Mild Cognitive Impairment (MCI) compared to age-matched controls [2–4]. ET cases are also at increased risk of developing incident dementia [5]. Thus, a growing body of research supports an association between ET and significant cognitive dysfunction. Despite these findings, many features of cognitive impairment in ET remain undefined [6].

Previous studies have largely been restricted to static, cross-sectional descriptions of the cognitive domains involved in such deficits. Individuals with ET have been shown to perform more poorly in tasks related to executive function including those assessing theory of mind [7], verbal fluency [8], mental set shifting, inhibition, and problem solving [2]. Given the role of the cerebellum in supporting executive function [9] and the known dysfunction of the cerebellum in ET cases, neuroanatomical hypotheses have often ascribed executive deficits in ET to inefficient cerebellar-cortical networks, particularly those projecting to and from the prefrontal cortex [10]. Other neuropathological models that describe cognitive dysfunction in ET continue to be explored as well, including those that implicate compromised white matter structure [11], altered functional connectivity throughout the cerebral cortex [12], and reduced cerebral cortical gray matter volume [13]. There is growing evidence that cognitive deficits in ET may reflect the co-occurrence of a more widespread, degenerative neuropathology [11].

Despite growing knowledge of the prevalence and nature of cognitive dysfunction in ET, few studies have characterized the dynamics of this dysfunction; as such, the clinical course and outcomes of ET-related cognitive impairment have not been well-described. This study better defines ET-related cognitive impairment by presenting data on conversion rates from MCI to dementia. In doing so, we hope to expand our understanding of how cognitive impairment evolves in ET.

Methods

Study Design:

A cohort of 234 ET cases underwent an extensive motor-free neuropsychological battery as a part of the COGNET study, an ongoing, prospective, longitudinal study of cognitive function in ET (Clinical-Pathological Study of Cognitive Impairment in Essential Tremor, NINDS R01NS086736). The study, which began in July 2014, aimed to identify the profiles, neuroanatomic bases, prevalence and course of cognitive impairment in ET cases. As described previously [15], cases who met the following eligibility criteria were recruited: (1) diagnosis of ET, (2) minimum age of 55 years old, (3) no brain surgery for the treatment of ET, (4) willingness to participate in testing and enroll as a brain donor. Cases were recruited through a series of advertisements on a study website as well as other websites (International Essential Tremor Foundation). Demographic and clinical data including age, gender, ethnicity, and education were collected at baseline.

Cases were evaluated over three intervals: at baseline (T1), 18 months after baseline (T2), and 36 months after baseline (T3). The cognitive test battery was designed by a neuropsychologist (S.C.) specifically for the COGNET study. It targeted several cognitive domains including attention, executive function, visuospatial abilities, language, and memory. The test battery excluded tests whose scores rely on motor ability so as not to disadvantage subjects with more moderate or severe tremor - see [15] for a description of the battery. Trained research staff conducted in-person assessments in the homes of cases at each interval. The assessment included administration of the comprehensive cognitive battery; a clinical interview; questionnaires concerning mood, sleep, tremor experience, and physical activity; and a videotaped neurological examination [15]. Diagnosis of ET was confirmed by a senior movement disorders neurologist (E.D.L) based on evaluation of the videotaped neurological examination using the Washington Heights-Inwood Genetic Study of ET diagnostic criteria [16], which requires moderate or greater amplitude kinetic tremor during three or more tests or head tremor in the absence of Parkinson’s disease, dystonia, or other causes. These criteria have been shown to be reliable [17] and valid [18]. Total tremor score was assigned by a movement disorders neurologist (E.D.L.) following examination of the videotaped neurological examination [15]. The total tremor score (range 0–36, higher scores indicate more severe tremor) was calculated based on ratings for kinetic or postural tremor on 12 movement tasks and assigned at each interval. When available, research staff conducted a telephone interview with a designated informant (i.e., someone close to the case who knew them well). The informant answered questions relevant to the case’s everyday functioning [15].

A comprehensive summary of each case's cognitive profile was then presented at diagnostic case conferences [15]. During these conferences, a neuropsychologist (S.C.) and a psychiatrist (E.D.H.) assigned all a Clinical Dementia Rating score (0 = no dementia, 0.5 = questionable dementia, 1 = mild dementia, 2 = moderate dementia, and 3 = severe dementia) [19].

During case conferences at each interval, based on CDR, cognitive test performance, and informant interview, each case was assigned one of three primary cognitive diagnoses: normal cognition (ET-NC), mild cognitive impairment (ET-MCI), and dementia (ET-D) [15]. Impairment on a single test was defined as a z-score ≤ −1.5. Normal cognition included: no impairment (CDR 0, no impairment on any test); impairment of unlikely clinical significance (CDR 0, impairment on 1 test); impairment of possible clinical significance (CDR 0 or 0.5, impairment in ≥ 1 test but not meeting operational criteria for MCI); questionable or isolated functional impairment (CDR 0.5, no impairment on any test). MCI was defined as a CDR of 0.5 and impairment (z-score ≤ −1.5) on 2 MCI-designated tests. Dementia was defined as a CDR ≥ 1 and impairment in multiple domains. As described previously [15], specific tests in each domain were *a priori* selected for diagnosis of MCI based on: (1) relative purity of measurement for the construct under evaluation; (2) demonstrated utility of measures for defining MCI in previous studies; and (3) general availability of the measure to researchers who wish to replicate findings. Selecting specific tests in each domain also prevented over-sampling of domains with more sub-scores generated from a single test (e.g., immediate and delayed memory from a memory test as compared to a single score from a naming test). MCI was further stratified into amnestic (single domain and multi-domain) and non-amnestic (single domain and multi-domain).

All portions of the study were approved by the Yale University and Columbia University Internal Review Boards, and all cases granted signed, informed consent upon enrollment.

Final Sample:

Excluded from this analysis were 33 cases who only underwent one evaluation. Of these 33 cases, 18 died before their second evaluation, 7 refused further evaluation, and 8 were excluded from future evaluation due to the assignment of an alternative diagnosis upon video examination review (7 dystonia and 1 psychogenic tremor). This first level of exclusion left 201 of 234 ET cases who had undergone more than one evaluation. Of these, we further excluded 21 cases who had additional or alternative diagnoses during one or more interval (4 Parkinson's disease and 17 dystonia) as well as nine cases that had baseline (T1) dementia. We also excluded 4 cases whose cognitive diagnoses were complicated by substance abuse, stroke, or head trauma. As a result of these exclusions (total = 67), 167 of 234 COGNET cases were eligible for this analysis.

Statistical Analyses:

We used the Statistical Package for Social Sciences (SPSS) software version 26 for analysis. Analysis utilized diagnostic data from two distinct timeframes: the eighteen-month period between T1 and T2 and the eighteen-month period between T2 and T3. In order to calculate a conversion rate, we assessed the number of converters and non-converters for each interval

period. We divided the number of cases of ET-MCI that converted to ET-D by the total number of ET-MCI cases that had a follow-up evaluation. We then divided this result by the average length of the interval in years to arrive at an annual conversion rate for that interval period. We used the mean of the two resulting annual conversion rates, to arrive at an overall annual conversion rate from MCI to dementia.

Our sample size was not adequately powered to compare converters to non-converters. For example, using data from our 23 non-converters at T1, and assuming alpha = 0.05, two-sided tests, and a mere 5 year higher age in converters than non-converters (i.e., 87.4 vs. 82.4 years), our study would have required 41 subjects in each group rather than the 23 converters and 3 converters we had. Hence, our comparisons of converters to non-converters were deemed exploratory analyses to be used for future hypothesis testing. In these exploratory analyses, we compared several clinical and demographic variables that were collected as part of the COGNET study (age, gender, race, education, prescription medications, cigarette smoking, tremor onset, tremor duration). These analyses used either chi-square tests (for categorical variables such as gender or race) or independent sample (Student's) t tests (for continuous variables such as age and years of education). As these were exploratory analyses, we recognize that a p value > 0.05 does not constitute a null result.

Results

At baseline, there were 26 ET cases (age 82.7 ± 7.7 years) diagnosed as ET-MCI who had a follow-up evaluation at T2. For these 26 cases, the average length of the interval between T1 and T2 evaluations was 1.5 ± 0.2 years (range 1.1 – 2.0, median: 1.5). At T2, three of these 26 cases had converted to ET-D (11.5%, 95% confidence interval = 0.0% – 23.8%). The annual conversion rate for the period between T1 and T2 was 7.7%. At the start of T2 there were 23 ET-MCI cases (age 83.8 ± 7.6 years) that were available for follow up at T3. Eight of these 23 cases were incident MCI cases. For these 23 cases, the average length of the interval between T2 and T3 evaluations was 1.5 ± 0.2 years (range 1.1–1.8, median: 1.5). At T3, six of the 23 cases (26.1%, 95% confidence interval = 8.1% – 44.0%) had converted to ET-D. The annual conversion rate for the period between T2 and T3 was 17.4%. The overall annual conversion rate from MCI to dementia for both interval periods was 12.5%.

Of the 26 ET-MCI cases at baseline, 17 (76.3%) were amnestic MCI (7 single domain and 10 multi-domain) and 9 (34.6%) were non-amnestic MCI (5 single domain and 4 multi-domain). The three converters at T2 included 1 amnestic single domain MCI and 2 amnestic multi-domain MCI. Of the 23 ET-MCI cases at T2, 16 (69.6%) were amnestic MCI (4 single domain and 12 multi-domain) and 7 (30.4%) were non-amnestic MCI (1 single domain and 6 multi-domain). The six converters at T3 included 2 amnestic single domain MCI, 3 amnestic multi-domain MCI, and 1 non-amnestic single domain MCI.

In exploratory analyses, we also compared converters and non-converters for the period between T1 and T2 and the period between T2 and T3 as shown in Tables 1 and 2, respectively and compare these data. As noted above, these analyses were of limited power and deemed solely exploratory, and we recognize that a p value > 0.05 does not constitute a null result.

Discussion

Only one previous study, with a small sample size (n = 52), a clinic-based ascertainment scheme, a relatively young population, and a relatively short follow-up interval (2 years), reported a conversion rate from MCI to dementia in a sample of ET cases. That study recruited 52 cases age 50 years and older from a movement disorder clinic. Hence, the novelty of the current study, aside from the fact that it is only the second study to assess conversion rates, is the tripling of sample size (i.e., 167 vs. 52), the use of a non-clinic based ascertainment scheme that was therefore less likely to enroll ET cases with more co-morbidity, the older population (i.e., enrollment of individuals more in the age range of those who typically develop MCI and dementia) and the longer follow-up interval (three study visits each 18 months apart vs. a 2 year follow-up). In the prior study, four of sixteen subjects who were diagnosed with MCI at baseline converted to dementia over a two-year interval, resulting in an annual conversion rate of 12.5% [20]. The results are similar to those we present here with a larger sample and longer follow-up interval.

The annual conversion rate from MCI to dementia is an important finding, especially when compared to rates that occur in the general population as well as in Parkinson's disease. In the general population, previous studies have shown annual conversion rates from MCI to dementia that range from 2.6 – 6.3% [21–23]. The conversion rate in ET is in line with recent findings of greater burden of cognitive dysfunction in ET as compared to the general population [2–4] The conversion rate from MCI to dementia in Parkinson's disease has also been investigated. As in our ET cohort, the rate of conversion in Parkinson's disease is elevated when compared to the general population. The annual rates of conversion from MCI to dementia in Parkinson's disease reported by these studies range from 7.6 – 15.5% [24–27]. While the annual conversion rates in our study differed during the two interval periods, the confidence intervals of the proportions overlapped suggesting that the actual conversion rate is reflected by their average. Describing data relevant to ET-related cognitive impairment is essential for improved patient care. Identifying conversion rates is a critical first step in developing improved systems of patient management that address clinically relevant concerns of ET-related cognitive impairment. Cognitive impairment in ET is associated with enfeeblement [28] and greater caregiver burden [29]. With greater knowledge that expands upon the data presented here, providers can make recommendations that directly address these ET-related issues.

While impaired cognition is becoming increasingly relevant in the clinical dialogue surrounding ET, clinicians have limited ability to provide prognostic guidance due to insufficient knowledge. By addressing areas of uncertainty, research of this kind will allow clinicians to offer specific guidance regarding course and outcomes for ET-related cognitive impairment. Additionally, cognitive dysfunction can be devastating to ET patients and caregivers; increased preparedness and knowledge of the expected course can alleviate some of the burden. As such, it is important to quantify previously undescribed conversion rates in ET. Data presented here will inform clinical dialogue and aid clinicians in counseling patients and families.

Data presented here should be understood in the context of a number of limitations. There is no control group associated with this study; instead we compared our conversion rate to rates obtained from similar prospective, longitudinal studies of similarly aged individuals in the general and Parkinson's disease populations. These conversion rates for the general and Parkinson's disease populations were obtained from studies which largely involved elderly cohorts [21–27]. Because of this use of historical comparison and control groups, differences across studies could confound attempts at strict comparisons, and assertions that the conversion rate is elevated in ET should be approached with appropriate caution. The majority of COGNET cases were cognitively normal, meaning that only a fraction of the cohort was relevant to this study of abnormal cognition. The groups on which we based our statistical analyses (converters and non-converters), were, as a result, small. The duration of follow-up was limited to two eighteen-month periods. Longer follow-up would likely result in a more precise estimate of conversion rate and we are hopeful that the continuation of COGNET will allow for refinement of the data. All cases in COGNET self-referred and so may not represent the broader ET population. This study was focused on conversion rates, although other data were collected. However, these data did not include genetic or imaging data, which would have been of interest.

The study also had considerable strengths. The COGNET study provided an ideal context for obtaining a robust estimate of conversion rate from MCI to dementia in ET. COGNET is the first study of its kind to track a population-based cohort of ET cases during regularly interspersed intervals. Another positive aspect of the study includes the careful assignment of ET diagnoses and exclusion of other diagnoses by a movement disorders specialist as well as the assignment of cognitive diagnoses by neuropsychologists.

In conclusion, we present an annual conversion rate from MCI to dementia of 12.5% in a cohort of elderly ET cases. Available studies on historical controls have reported conversion rates of 2.6 – 6.3%. This finding supports growing evidence of the association between ET and significant cognitive dysfunction. Data such as these systematically fill gaps in knowledge and create a scientifically-derived knowledge base to guide physicians, patients, and families in clinical settings.

Acknowledgements

Funding by the National Institutes of Health R01NS086736

References

1. Louis ED, Ottman R. How many people in the USA have essential tremor? Deriving a population estimate based on epidemiological data. Tremor Other Hyperkinet Mov (N Y) 2014;4:259. [PubMed: 25157323]
2. Gasparini M, Bonifati V, Fabrizio E, Fabbrini G, Brusa L, Lenzi GL, Meco G, Frontal lobe dysfunction in essential tremor: a preliminary study, J. Neurol 248 (5) (2001) 399–402. [PubMed: 11437162]
3. Benito-Leon J, Louis ED, Bermejo-Pareja F, Population-based case-control study of cognitive function in essential tremor, Neurology 66 (1) (2006) 69–74. [PubMed: 16401849]

4. Benito-Leon J, Louis ED, Mitchell AJ, Bermejo-Pareja F Elderly-onset essential tremor and mild cognitive impairment: a population-based study (NEDICES) J. Alzheimers Dis, 23 (4) (2011), pp. 727–735. [PubMed: 21304183]
5. Thawani SP, Schupf N, Louis ED, Essential tremor is associated with dementia: prospective population-based study in New York, Neurology 73 (8) (2009) 621–625. [PubMed: 19704081]
6. Louis ED, Louis JL, Cosentino S, Mind the gaps: What we don't know about cognitive impairment in essential tremor, Parkinsonism Relat Disord 16 (2019) 10–19.
7. Santangelo G, Trojano L, Barone P, Errico D, Improta I, Agosti V, Grossi D, Sorrentino G, Vitale C, Cognitive and affective theory of mind in patients with essential tremor, J. Neurol 260 (2) (2013) 513–520. [PubMed: 23014693]
8. Sanchez-Ferro A, Benito-Leon J, Louis ED, Contador I, Hernandez-Gallego J, Puertas-Martin V, Bermejo-Pareja F, Cognition in non-demented Parkinson's disease vs essential tremor: a population-based study, Acta Neurol. Scand 136 (5) (2017) 393–400. [PubMed: 28261780]
9. Koziol LF, Budding D, Andreasen N, D'Arrigo S, Bulgheroni S, Imamizu H, Ito M, Manto M, Marvel C, Parker K, Pezzulo G, Ramnani N, Riva D, Schmahmann J, Vandervert L, Yamazaki T, Consensus paper: the cerebellum's role in movement and cognition, Cerebellum 13 (1) (2014) 151–177. [PubMed: 23996631]
10. Rapoport M, van Reekum R, Mayberg H, The role of the cerebellum in cognition and behavior: a selective review, J. Neuropsychiatry Clin. Neurosci 12 (2) (2000) 193–198. [PubMed: 11001597]
11. Benito-Leon J, Mato-Abad V, Louis ED, Hernandez-Tamames JA, Alvarez-Linera J, Bermejo-Pareja F, Domingo-Santos A, Collado L, Romero JP, White matter microstructural changes are related to cognitive dysfunction in essential tremor, Sci. Rep 7 (1) (2017) 2978. [PubMed: 28592900]
12. Lenka A, Bhalsing KS, Panda R, Jhunjhunwala K, Naduthota RM, Saini J, Bharath RD, Yadav R, Pal PK, Role of altered cerebello-thalamo-cortical network in the neurobiology of essential tremor, Neuroradiology 59 (2) (2017) 157–168. [PubMed: 28062908]
13. Cameron E, Dyke JP, Hernandez N, Louis ED, Dydak U, Cerebral gray matter volume losses in essential tremor: a case-control study using high resolution tissue probability maps, Park. Relat. Disord 51 (2018) 85–90.
14. Amieva H, Letenneur L, Dartigues JF, Rouch-Leroyer I, Sourgen C, D'Alchee-Biree F, et al. (2004). Annual rate and predictors of conversion to dementia in subjects presenting mild cognitive impairment criteria defined according to a population-based study. Dement. Geriatr. Cogn. Disord 18 87–93. [PubMed: 15087583]
15. Cersonsky TEK, Kellner S, Chapman S, Huey ED, Louis ED, Cosentino S. Profiles of Normal Cognition in Essential Tremor. J Int Neuropsychol Soc. 2019 Oct 4:1–13.
16. Louis ED, Ottman R, Ford B, Pullman S, Martinez M, Fahn S, & Hauser WA (1997). The Washington heights-inwood genetic study of essential tremor: methodologic issues in essential-tremor research. Neuroepidemiology, 16(3), 124–133. [PubMed: 9159767]
17. Louis ED, Ford B, & Bismuth B (1998). Reliability between two observers using a protocol for diagnosing essential tremor. Movement Disorders, 13(2), 287–293. [PubMed: 9539343]
18. Louis ED, Wendt KJ, Albert SM, Pullman SL, Yu Q, & Andrews H (1999). Validity of a performance-based test of function in essential tremor. Archives of Neurology, 56(7), 841–846. [PubMed: 10404986]
19. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993;43(11):2412–2414.
20. Sinoff G, Badarny S, Mild cognitive impairment, dementia, and affective disorders in essential tremor: a prospective study, Tremor. Other Hyperkinet. Mov. (N Y) 4 (2014) 227. [PubMed: 25009763]
21. Mitchell AJ, Shiri-Feshki M, Temporal trends in the long term risk of progression of mild cognitive impairment: a pooled analysis, J. Neurol. Neurosurg. Psychiatr 79 (12) (2008) 1386–1391.
22. Wong CH, Leung GT, Fung AW, Chan WC, Lam LC, Cognitive predictors for five-year conversion to dementia in community-dwelling Chinese older adults, Int. Psychogeriatr 25 (7) (2013) 1125–1134. [PubMed: 23544873]

23. Limongi F, Siviero P, Noale M, Gesmundo A, Crepaldi G, Maggi S, Prevalence and conversion to dementia of Mild Cognitive Impairment in an elderly Italian population, Aging Clin. Exp. Res 29 (3) (2017) 361–370. [PubMed: 28353219]

24. Pedersen KF, Larsen JP, Tysnes OB, Alves G, Natural course of mild cognitive impairment in Parkinson disease: a 5-year population-based study, Neurology 88 (8) (2017) 767–774. [PubMed: 28108638]

25. Cholerton B, Johnson CO, Fish B, Quinn JF, Chung KA, Peterson-Hiller AL, Rosenthal LS, Dawson TM, Albert MS, Hu SC, Mata IF, Leverenz JB, Poston KL, Montine TJ, Zabetian CP, Edwards KL, Sex differences in progression to mild cognitive impairment and dementia in Parkinson's disease, Park. Relat. Disord (2018).

26. Hobson P, Meara J, Mild cognitive impairment in Parkinson's disease and its progression onto dementia: a 16-year outcome evaluation of the Denbighshire cohort, Int. J. Geriatr. Psychiatry 30 (10) (2015) 1048–1055. [PubMed: 25676160]

27. Janvin CC, Larsen JP, Aarsland D, Hugdahl K, Subtypes of mild cognitive impairment in Parkinson's disease: progression to dementia, Mov. Disord 21 (9) (2006) 1343–1349. [PubMed: 16721732]

28. K Cersonsky TE, Diaz DT, Kellner S, Hickman R, Zdrodowska MA, Monin JK, Louis ED, Enfeeblement in Elders with Essential Tremor: Characterizing the Phenomenon and Its Role in Caregiver Burden, Tremor. Other Hyperkinet. Mov. (N Y) (2019); 9.

29. Morgan S, Kellner S, Gutierrez J, Collins K, Rohl B, Migliore F, et al. The experience of essential tremor caregivers: burden and its correlates. Front Neurol 2017;8:396 [PubMed: 28855888]

- Knowledge of essential tremor (ET)-related cognitive impairment is static.
- 167 ET cases enrolled in a prospective, longitudinal neuropsychological study.
- Annual conversion rate from mild cognitive impairment (MCI) to dementia was 12.5%.
- Data such as these systematically fill gaps in knowledge and guide physicians.

Table 1:

Clinical characteristics of converters and non-converters for the interval between T1 and T2

	All Cases N = 26	Converters N = 3	Non-Converters N = 23	Comparison[1]
Age in years	82.7 ± 7.7	85.0 ± 5.6	82.4 ± 8.0	p = 0.59[a]
Gender (Female)	12 (46.2)	1 (33.3)	11 (47.8)	p = 0.64[b]
Race (White)	26 (100)	3 (100)	23 (100)	p = 1.00[b]
Education in years	14.9 ± 2.9	14.7 ± 2.3	14.9 ± 3.0	p = 0.88[a]
Number of prescription medications	7.3 ± 4.4	5.7 ± 4.2	7.5 ± 4.4	p = 0.50[a]
Current cigarette smoker	0 (0.0)	0 (0.0)	0 (0.0)	p = 1.00[b]
Age of tremor onset in years	44.5 ± 24.0	53.0 ± 2.8	43.7 ± 24.9	p = 0.61[a]
Total tremor score	20.2 ± 4.6	22.8 ± 2.3	19.8 ± 4.7	p = 0.30[a]
Tremor duration in years	37.9 ± 22.0	29.0 ± 5.7	38.7 ± 22.7	p = 0.56[a]

All values represent mean ± standard deviation or number (percentage).

All values are those obtained at the start of the interval period

[1] Converters to non-converters.

[a] Independent samples t test

[b] Chi-square test

Table 2:

Clinical characteristics of converters and non-converters for the interval between T2 and T3

	All Cases N = 23	Converters N = 6	Non-Converters N = 17	Comparison[1]
Age in years	83.6 ± 7.7	87.0 ± 4.6	82.4 ± 8.3	p = 0.22[a]
Gender (Female)	16 (69.6)	5 (83.3)	13 (68.4)	p = 0.39[b]
Race (White)	24 (100)	6 (100)	17 (100)	p = 1.00[b]
Education in years	15.2 ± 3.2	14.8 ± 3.4	15.3 ± 3.2	p = 0.75[a]
Number of prescription medications	6.5 ± 3.9	6.2 ± 4.8	6.6 ± 3.7	p = 0.83[a]
Current cigarette smoker	0 (0.0)	0 (0.0)	0 (0.0)	p = 1.00[b]
Age of tremor onset in years	41.3 ± 22.5	54.3 ± 26.4	36.8 ± 19.8	p = 0.10[a]
Total tremor score	21.1 ± 4.9	21.3 ± 6.7	21.0 ± 4.4	p = 0.90[a]
Tremor duration in years	42.3 ± 21.9	32.7 ± 25.3	45.6 ± 20.2	p = 0.22[a]

All values represent mean ± standard deviation or number (percentage).

All values are those obtained at the start of the interval period

[1] Converters to non-converters.

[a] Independent samples t test

[b] Chi-square test