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Reported Hearing Impairment in Essential Tremor: A Population-Based Case-Control Study

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on behalf of the Neurological Disorders in Central Spain (NEDICES) Study Group

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Key Words
Essential tremor · Hearing impairment · Population-based case-control study

Abstract
In a population-based sample, we determined whether a larger proportion of essential tremor (ET) cases reported hearing impairment compared with controls. Ninety-six (38.7%) of 248 ET cases versus 1,371 (29.4%) of 4,669 controls (p = 0.002) reported hearing impairment. In a logistic regression analysis adjusted for age, gender, educational level, depressive symptoms, and dementia, participants who reported hearing impairment were 30% more likely to suffer from ET than were controls (odds ratio 1.3; 95% confidence interval 1.01–1.7; p = 0.04). ET seemed to be associated with reported hearing impairment. The basis for this finding, which has been noted in several studies, deserves further exploration.

Introduction

Recent studies suggest that nonmotor features (mild cognitive deficits and personality changes) can occur in patients with essential tremor (ET) [1, 2]. A recent case-control study demonstrated an association between ET and hearing impairment [3]. In another study, a large proportion of ET cases wore hearing aids, although that study did not have a case-control design [4]. In both studies [3, 4], patients were ascertained through clinics/treatment settings and selection factors (e.g. selection of ET patients with severer, disabling, or unusual forms of the disease), which could have influenced the findings. Our aim in this population-based study was to determine whether a larger proportion of mild, early, untreated (i.e., nascent) ET cases reported hearing impairment when compared with controls.

Methods

The data for the analyses were derived from the Neurological Disorders in Central Spain (NEDICES) study, a longitudinal, population-based survey of age-associated conditions of the elderly [5, 6]. The study population comprised elderly subjects, >65 years of age, from three communities in central Spain, as detailed previously [5, 6]. Signed informed consent was obtained upon enrolment.

The other members of the Neurological Disorders in Central Spain (NEDICES) Study Group are listed in the Appendix.

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Briefly, at the time of their baseline assessment (1994–1995), 5,278 elderly subjects were interviewed using a 800-item screening questionnaire that assessed demographic factors, medical conditions [e.g. diabetes, hypertension, stroke, and visual deficits ('do you suffer from or has a physician told you that you suffer from visual impairment?')], and questions that assessed hearing impairment ('do you suffer from or has a physician told you that you suffer from hearing impairment?'), speech disturbance, and depressive symptoms ('do you suffer from depression?'). The diagnosis of dementia was based on DSM-IV criteria [7], and required evidence of cognitive impairment (based on a neuropsychological test battery and a clinical mental status examination) as well as impairment in social or occupational function.

The diagnosis of ET has been detailed previously [8, 9] and involved a screening question and a detailed neurological examination during which participants were asked to perform three manual tasks to assess postural and kinetic tremors. Subjects were diagnosed as having ET if they had an action tremor of the arms or head tremor without any other recognizable cause. The tremor had to be of gradual onset and (1) present for at least 1 year or (2) accompanied by a family history of the same disorder (at least one reportedly affected first-degree relative). Finally, as in previous studies [8, 9], on an Archimedes spiral, tremor severity had to be moderate or greater (rating ≥ 2 according to the Washington Heights-Inwood Genetic Study of ET rating scale) [10]. Subjects with tremor related to alcohol withdrawal, hyperthyroidism, anxiety, Parkinson's disease, antidopaminergic drug intake, lithium therapy, or other known causes of tremor were not considered to have ET.

Of the 5,278 subjects evaluated at baseline, there were 256 (4.8%) prevalent ET cases [8]. The screening question for hearing impairment was available in 248 (96.9%) of the 256 prevalent cases and in 4,669 (93.0%) of the 5,022 controls.

Statistical analyses were performed with a microcomputer version of the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, Ill., USA). All tests were two sided, and with $\alpha = 0.05$. To assess the association between hearing impairment and ET, we compared ET cases (n = 248) to all non-ET participants from the cohort (n = 4,669). To test the hypothesis that diagnosis (ET case vs. control) was associated with reported hearing impairment, data were assessed using logistic regression analyses, yielding odds ratios (ORs) and 95% confidence intervals (CIs). In multivariate logistic regression models, we adjusted for age in years, gender, educational level, depressive symptoms (yes vs. no to the question, 'do you suffer from depression?'), use of an antidepressant medication (yes vs. no), and dementia. A variety of subjective physical complaints (e.g. pain and possibly hearing impairment) may occur in patients with depression; hence, reported hearing impairment could be a proxy for depression. Therefore, depression was a particularly important factor to consider in our analyses, and in one analysis, we excluded all participants who had depressive symptoms or were taking an antidepressant medication.

Table 1. Demographic and clinical characteristics of ET cases and control subjects

Characteristics	ET cases (n = 248)	Controls (n = 4,669)	p value
Median age, years	75 (69–80)	73 (68–79)	0.001[a]
Gender			
Men	104 (41.9)	1,985 (42.5)	NS[b]
Women	144 (58.1)	2,684 (57.5)	
Educational level			
Illiterate	50 (20.2)	594 (12.8)	0.006[b]
Can read and write	99 (39.9)	1,902 (40.9)	
Primary studies	66 (26.6)	1,506 (32.4)	
Secondary studies	33 (13.3)	644 (13.9)	
Reported hearing impairment			
Yes	96 (38.7)	1,371 (29.4)	0.002[b]
No	152 (61.3)	3,298 (70.6)	
Reported depressive symptoms			
Yes	101 (40.7)	1,123 (25.8)	<0.001[b]
No	147 (59.3)	3,234 (74.2)	
Diabetes			
Yes	42 (16.9)	769 (16.6)	NS[b]
No	206 (83.1)	3,853 (83.4)	
Hypertension			
Yes	114 (46.0)	1,993 (43.0)	NS[b]
No	134 (54.0)	2,646 (57.0)	
Heart disease			
Yes	24 (9.7)	461 (9.9)	NS[b]
No	224 (90.3)	4,176 (90.1)	
Reported visual deficits			
Yes	130 (52.4)	2,404 (53.3)	NS[b]
No	118 (47.6)	2,106 (46.7)	
Reported speech disturbance			
Yes	22 (9.9)	255 (6.7)	NS[b]
No	200 (90.1)	3,575 (93.3)	
Stroke			
Yes	14 (5.6)	233 (5.0)	NS[b]
No	234 (94.4)	4,429 (95.0)	

NS = Not significant. Figures in parentheses are percentages or interquartile ranges.

[a] Mann-Whitney U test. [b] χ^2 test. Due to missing data, in several control cells, the total number was <4,669.

Results

The 248 ET cases were older and less educated than the 4,669 controls, but their gender distribution was similar (table 1). Two hundred (80.6%) of the 248 cases had not been diagnosed with ET prior to our study; only 13 (5.2%) cases were taking medications to treat ET. The median tremor duration in ET cases was 5 years (interquartile range, 3–10). Ninety-six (38.7%) of the 248 ET cases versus 1,371 (29.4%) of the 4,669 controls (p = 0.002) reported hearing impairment. In an unadjusted logistic regression analysis, hearing impairment was associated with ET (OR = 1.5; 95% CI = 1.2–2.0; p = 0.002). In a logistic regression analysis adjusted for age, gender, educational level, depressive symptoms (yes vs. no to the question, 'do

Table 2. Correlates of hearing impairment among ET cases and control subjects

Characteristics	ET cases who reported hearing impairment (n = 96)	ET cases who did not report hearing impairment (n = 152)	p value	Controls who reported hearing impairment (n = 1,371)	Controls who did not report hearing impairment (n = 3,298)	p value
Median age, years	77 (70–81.7)	74 (69–80)	NS[a]	75 (70–82)	72 (68–77)	<0.001[a]
Gender						
Men	37 (38.5)	67 (44.1)	NS[b]	581 (42.4)	1,404 (42.6)	NS[b]
Women	59 (61.5)	85 (55.9)		790 (57.6)	1,894 (57.4)	
Reported depressive symptoms						
Yes	38 (39.6)	63 (41.4)	NS[b]	370 (28.7)	753 (24.6)	0.005[b]
No	58 (60.4)	89 (58.6)		921 (71.3)	2,313 (75.4)	
Dementia						
Yes	4 (4.2)	8 (5.3)	NS[b]	112 (8.2)	136 (4.1)	<0.001[b]
No	92 (95.8)	144 (94.7)		1,259 (91.8)	3,162 (95.9)	

NS = Not significant. Figures in parentheses are percentages or interquartile ranges. [a] Mann-Whitney U test. [b] χ^2 test.

you suffer from depression?') and dementia, participants who reported hearing impairment were 30% more likely to suffer from ET than controls (OR = 1.3; 95% CI = 1.01–1.7; p = 0.04).

Reported hearing impairment was more prevalent in ET cases than controls, as were depressive symptoms (table 1). By contrast, other reported medical conditions (diabetes, hypertension, heart disease), as well as other subjective special sensory complaints [e.g. reported visual deficits ('do you suffer from or has a physician told you that you suffer from visual impairment?')] and other subjective complaints (speech disturbance) were no more common in ET cases than controls (table 1), suggesting that the association between ET and reported hearing impairment was specific.

Sixteen (6.5%) ET cases versus 110 (2.4%) controls were taking an antidepressant medication (p = 0.001), yet when we adjusted for age, gender, educational level, dementia, and use of an antidepressant medication in a logistic regression model, the association between hearing impairment and ET remained (OR = 1.4; 95% CI = 1.1–1.8; p = 0.018). In an analysis in which we excluded all participants who had depressive symptoms or were taking an antidepressant medication, and adjusted for age, gender, educational level, and dementia, there was an association between hearing impairment and ET (OR = 1.5; 95% CI = 1.05–2.1; p = 0.024).

One hundred and sixteen (7.9%) participants who had reported hearing impairment had dementia versus 144 (4.2%) who had not reported hearing impairment (p < 0.001). In an analysis in which we excluded all participants who had dementia, and adjusted for age, gender, educational level, and depressive symptoms, there was an association between hearing impairment and ET (OR = 1.4; 95% CI = 1.05–1.8; p = 0.021).

Table 2 shows the correlates of hearing impairment among ET cases and control subjects. ET cases who reported hearing impairment did not differ in terms of age, gender, depression symptoms or dementia from ET cases who did not report hearing impairment (table 2). With respect to controls, those who reported hearing impairment were older and a larger proportion had depressive symptoms and dementia compared with those who did not report hearing impairment (table 2).

While information on tremor severity was not routinely collected, data showed that 4 (30.8%) of the 13 ET cases whose tremor was severe enough to take medication had hearing impairment versus 92 (39.1%) of 235 untreated (i.e., presumably milder) ET cases (χ^2 = 0.37, p = 0.55). Age of onset of tremor was significantly higher [median 71 years (interquartile range 65–77) vs. median 66 years (interquartile range 59–74); Mann-Whitney U test, p = 0.004] and tremor duration was significantly lower [median 4 years (interquartile range 2–9.7) vs. median 5 years (interquartile range 3–11); Mann-Whitney U test, p = 0.017] in ET cases who reported hearing impairment than in ET cases who did not report hearing impairment. In logistic regression analyses adjusted for current age, the associations with hearing impairment remained unchanged (for age of onset of tremor, OR = 1.03, 95% CI = 1.001–1.06, p = 0.04, and for tremor duration, OR = 0.97, 95% CI = 0.95–0.999, p = 0.04).

Discussion

Using a population-based sample of prevalent ET cases living in three communities in central Spain, we examined the association between ET and reported hearing impairment. Most of our cases were previously undiagnosed with ET and few were taking medication for their tremor, as has been reported in other population-based samples [11, 12]. The use of such mild cases may have made it more difficult to detect medical comorbidities such as hearing impairment, thereby biasing our estimate of the association between hearing impairment and ET towards the null hypothesis. A larger proportion of cases reported hearing impairment compared with their counterparts without tremor (i.e., controls). In contrast, other reported medical conditions (diabetes, hypertension, heart disease, visual deficits and stroke) were no more common in ET cases than controls. Adjustments for depressive symptoms, dementia, use of antidepressant medications, demographic factors, and educational level did not modify the results, indicating that the association between ET and hearing impairment was not likely to have been the result of depression or other measured confounding variables.

In sum, previous studies [3, 4], as well as our own, suggest that ET may be associated with hearing impairment. If indeed there is hearing impairment in ET, the anatomical basis is not clear. Several possibilities have been proposed [3]. Abnormalities within the cerebello-thalamocortical pathways are thought to be involved in ET [1, 2]. Auditory input also proceeds to the ventral thalamus (medial geniculate body) before relaying to the transverse temporal gyrus (auditory cortex) [3]. It is conceivable that abnormalities in the ventral thalamus could result in both tremor and hearing loss [3]. Postmortem studies [4] may wish to focus future attention on the investigation of pathological changes in these brain structures (e.g. thalamus, transverse temporal gyrus) in ET patients with hearing impairment. In addition, future studies may wish to determine whether therapeutic thalamic deep brain stimulation procedures for ET have effects on hearing impairment.

A complaint of depressive symptoms was more common in ET cases than in control subjects. Depressive symptoms have been studied in detail in ET. In a previous population-based door-to-door survey in Mersin, Turkey, depressive symptom scores were higher in ET cases compared with matched controls [11]. Whether this possible preponderance of depressive symptoms in ET represents a reaction to disabling effects of tremor or whether the tremor and the mood disturbance are both due to a common underlying biological factor is not known. Regardless, the association between ET and hearing impairment in the current study was not a function of depressive symptoms or use of an antidepressant medication.

Of interest is the fact that the age of onset of ET was significantly higher in those who reported hearing impairment. This is in line with other recent studies in ET, which suggest that elderly-onset ET is associated with an increased risk of other comorbidities such as incident dementia [13, 14].

Our study has limitations. Clearly, we did not assess prior exposure to noise, which can be a strong predictor of hearing loss. Furthermore, complaints of hearing impairment can also result from impaired attention and problems with receptive language, which we did not assess in detail. Second, as this study was part of a large epidemiological survey, we assessed reported hearing impairment with a single question and did not collect data on objective measures of hearing impairment, which have been assessed in a previous study [4]. Hence, although we demonstrated a difference between cases and controls in a subjective measure of hearing, we were not able to go beyond this to comment on objective measures of hearing loss or use of hearing aids. Despite this, other subjective medical conditions [e.g. reported visual deficits ('do you suffer from or has a physician told you that you suffer from visual impairment?'), speech disturbances] were no more common in ET cases than controls, indicating that the association between ET and reported hearing impairment was specific. Although our method of diagnosing ET has resulted in estimates of disease prevalence that are similar to those of other European studies [8], it is possible that we misclassified some persons with ET as normal or vice versa. However, this would have biased our estimate of the association between hearing impairment and ET towards the null hypothesis; in other words, misclassification would have resulted in a conservative estimate of the true association. The main strengths of the study were the large sample size, the adjustment for other potential confounders (e.g. education, depression), and most importantly, the population-based design, thereby allowing us to assess a group of relatively mild ET cases unselected for medical treatment or surgery.

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Appendix

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References

1 Louis ED: Essential tremor. Lancet Neurol 2005;4:100–110.
2 Benito-León J, Louis ED: Essential tremor: emerging views of a common disorder. Nat Clin Pract Neurol 2006;2:666–678.
3 Ondo WG, Sutton L, Vuong KD, Lai D, Jankovic J: Hearing impairment in essential tremor. Neurology 2003;61:1093–1097.
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.
5 Bermejo F, Gabriel R, Vega S, Morales JM, Rocca WA, Anderson DW: Problems and issues with door-to-door, two-phase surveys: an illustration from central Spain. Neuroepidemiology 2001;20:225–231.
6 Morales JM, Bermejo FP, Benito-León J, Rivera-Navarro J, Trincado R, Gabriel SR, Vega S, NEDICES Study Group: Methods and demographic findings of the baseline survey of the NEDICES cohort. Public Health 2004; 118:426–433.
7 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. Washington, American Psychiatric Association, 1994.
8 Benito-León 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.
9 Benito-León J, Bermejo-Pareja F, Louis ED: Incidence of essential tremor in three elderly populations of central Spain. Neurology 2005;64:1721–1725.
10 Louis ED, Barnes L, Wendt KJ, Ford B, Sangiorgio M, Tabbal S, Lewis L, Kaufmann P, Moskowitz C, Comella CL, Goetz CC, Lang AE: A teaching videotape for the assessment of essential tremor. Mov Disord 2001;16:89–93.
11 Dogu O, Louis ED, Sevim S, Kaleagasi H, Aral M: Clinical characteristics of essential tremor in Mersin, Turkey: a population-based door-to-door study. J Neurol 2005; 252:570–574.
12 Louis ED, Ford B, Wendt KJ, Cameron G: Clinical characteristics of essential tremor: data from a population-based cohort. Mov Disord 1998;13:803–808.
13 Bermejo-Pareja F, Louis ED, Benito-León J; Neurological Disorders in Central Spain (NEDICES) Study Group: Risk of incident dementia in essential tremor: a population-based study. Mov Disord 2007;22:1573–1580.
14 Benito-León J, Louis ED, Bermejo-Pareja F; Neurological Disorders in Central Spain Study Group: Elderly-onset essential tremor is associated with dementia. Neurology 2006;66:1500–1505.