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Awareness of Cognitive Impairment in Individuals with Essential Tremor

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Abstract

Objective—The extent to which individuals with ET who have clinically significant cognitive impairment are aware of their cognitive changes is unclear. Reduced awareness has important implications for everyday function and decision-making.

Methods—150 individuals with ET (109 Normal Cognition (ET-NC group), and 30 with MCI and 11 dementia (ET-CI group)) completed self-ratings and objective assessments of memory, language, and executive functioning. Discrepancy scores were calculated to assess awareness of cognitive functioning. One sample t-tests evaluated whether mean discrepancy scores in each group were comparable to zero (i.e., accurate). Analyses of Covariance(ANCOVA) compared discrepancy scores across two groups controlling for age and education.

Results—In the ET-NC group, discrepancy scores for language ($M=-0.08$, $SD=1.10$) and executive functioning ($M=-0.01$, $SD=0.99$) were comparable to zero. Memory discrepancy scores ($M=0.32$, $SD=1.22$) were greater than zero. In the ET-CI group, memory, ($M=0.78$, $SD=1.01$), language, ($M=0.46$, $SD=0.95$), and executive ($M=0.39$, $SD=1.14$) discrepancy scores were all

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greater than zero. Discrepancy scores were larger in ET-CI group than in ET-NC group for memory: $F(1,148)=4.02$, $p=0.047$, language: $F(1,148)=6.16$, $p=0.014$, and executive: $F(1,148)=4.51$, $p=0.035$.

Conclusions—Individuals with ET and normal cognition accurately assessed their language and executive abilities, demonstrating mild overconfidence in memory function. Individuals with ET and cognitive impairment overestimated their performance in all domains of functioning. Since ET is linked to increased risk for cognitive impairment, and such impairment may not be accurately perceived, cognitive functioning should be proactively and regularly screened in ET.

Keywords

Essential Tremor; cognitive impairment; awareness

1. Introduction

Essential tremor, one of the most common neurological disorders, affects 4% of adults over 40 years old¹ and is marked primarily by action tremor of the upper limbs¹. On average, compared to age-matched controls, individuals with ET exhibit a range of cognitive deficits and are at increased risk for mild cognitive impairment (MCI)² and dementia^{3, 4}. The extent to which patients with ET who develop clinically significant cognitive impairment accurately perceive their cognitive changes is not known. Limited awareness of cognitive dysfunction may have implications on early diagnosis, patient safety⁵, quality of life⁶ and caregiver burden⁷. Investigating awareness of cognitive impairment in ET is particularly important as physicians may not refer patients with ET for neuropsychological assessment without cognitive complaints by the patients themselves. Physicians may not be aware of cognitive difficulties, may not query patients about such deficits or may consider cognitive deficits to be age rather than disease-associated.

To our knowledge, this is the first study to examine awareness of clinically significant cognitive impairment in individuals with ET. Our a priori hypothesis was that on average individuals with ET with clinically significant cognitive impairment (i.e., MCI or dementia) would demonstrate impaired awareness of cognitive functioning as compared with cognitively healthy individuals with ET. Determining the integrity of awareness in cognitively impaired individuals with ET will have important implications for how and when to screen cognition in patients with ET, and for identifying individuals who are at risk for unsafe behaviors.

2. Methods and Materials

2.1 Participants and Study design

The current study included baseline data from a total of 150 ET participants enrolled in a longitudinal study of cognitive function in Essential Tremor (ET) (Clinical Pathological Study of Cognitive Impairment in Essential Tremor, NINDS R01NS086736). 27% of the sample ($n=41$) was diagnosed with clinically significant cognitive impairment at baseline, including 30 individuals with MCI and 11 with dementia. The current study has been approved by the IRB.

2.2 Procedures

Diagnosis of ET—Each case underwent a videotaped neurological examination, which included a detailed assessment of postural tremor, five tests for kinetic tremor, and the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS)⁸. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations. Rest tremor, dystonia, and other movements were noted as present vs. absent on that examination, and 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 confirmed ET diagnoses using reliable⁹ and valid¹⁰ diagnostic criteria (moderate or greater amplitude kinetic tremor on 3 tests or head tremor, in the absence of Parkinson's Disease (PD), dystonia or another known cause). Individuals also completed the long form of the Geriatric Depression Scale (GDS).

Cognitive Diagnoses / MCI and Dementia Classification—Together the test scores, informant interview, and examiner impressions informed a diagnostic case conference attended by the examiner and trained experts (S.C., E.H.). who reviewed the Clinical Dementia Rating¹¹ assigned by the examiner, the profile of neuropsychological test results, and mood based inventories to come to a consensus cognitive diagnosis (e.g., normal cognition, MCI, or dementia). Cases with a CDR score of 0 and no test impairment, or impairment on only one test, were considered normal cognition (ET-NC). Cases with impairment in multiple cognitive domains and a CDR = 1 were considered demented (ET-D). Cases were considered MCI (ET-MCI) if they had a CDR score of 0.5, and impairment ($z \leq -1.5$) on at least half of the tests in one domain (single domain MCI) OR impairment on at least half of the tests in 2 domains (multi-domain MCI).

Specific “criterion” tests within each domain were selected to operationally define impairment for the diagnosis of MCI. Criterion measures were selected based on a number of criteria including: 1) the relative purity of measurement for the construct under evaluation (e.g., Judgment of Line Orientation for the spatial domain given its relatively lesser demand on executive functioning than a measure such as Visual Puzzles); 2) the demonstrated utility of measures in previous studies; and 3) the general availability of the measure to researchers who may wish to replicate the current findings or apply these criteria in the future. Two tests per domain were used based on the recommendation of the Movement Disorder Society Task Force on PD-MCI¹². The domain of executive functioning was an exception, wherein we evaluated four different scores of executive functioning given the heterogeneous nature of this domain and its known role in ET. In order to meet criteria for impairment in a domain, impairment was required on at least 50% of the tests in that domain (i.e., 1 of 2 the two memory criterion tests, and 2 of the 4 executive functioning criterion tests).

The selected tests were as follows: California Verbal Learning Test (CVLT) long-delay, and the Logical Memory delay (memory), Digit Span Forward total score and Symbol Digit Modalities Test total oral score (attention), Verbal Fluency letter fluency score, Color-Word Interference inhibition score, Sorting Test free sorting description score, and Twenty Questions total weighted achievement score (executive function), Judgment of Line

Orientation total score and Benton Facial Recognition total score (visuospatial ability), Boston Naming Test total score and Token Test total score (language).

Cases deemed to have ET-MCI, as opposed to ET-NC or ET-D, were further stratified into subtypes of MCI. MCI subtypes were assigned based on the guidelines set forth by Petersen¹³ in which MCI is considered either primarily amnesic or primarily non-amnesic.

2.3 Measures

Subjective Cognition (Self-ratings)—In order to assess participants' subjective perception of specific cognitive abilities, participants completed a modified version of the Brief Anosognosia Scale¹⁴ in which they are asked to rate their ability to perform 14 different cognitive, motor, emotional, and functional abilities. For each item, participants rated their ability on a 5-point scale including values of: (1) very impaired, (2) below average, (3) average, (4) above average, or (5) excellent. This self-rating scale¹⁵, originally developed by Reid et al., (2006) has been used in previous studies from our lab and is correlated with other forms of self-assessment¹⁴. Of the 14 items, we focused on three abilities including the ability to *remember, find the right word when speaking, and multitask*, which mapped onto cognitive abilities measured objectively in our study in the domains of memory, language, and executive functioning, respectively.

Objective Cognitive Testing—In addition to subjective ratings, participants completed a comprehensive battery of tests that included measures of global cognition (Montreal Cognitive Assessment¹⁶, Mini-Mental State Exam¹⁷, pre-morbid intelligence (Wechsler Test of Adult Reading¹⁸ and specific cognitive domains, including **attention** (Digit Span Forward¹⁹, Symbol Digit Modalities Test, **memory** (California Verbal Learning Test, Wechsler Memory Scale Revised (WMS-R) Logical Memory, Verbal Paired Associates subtests, **executive function** (Digit Span Backward¹⁹, Delis-Kaplan Executive Function System²⁰, Verbal Fluency, Color-Word Interference, Sorting, and Twenty Questions subtests), **visuospatial ability** (Benton Judgment of Line Orientation²¹, Benton Facial Recognition Test, Wechsler Adult Intelligence Scale IV (WAIS-IV): Visual Puzzles subtest¹⁹ and **language** (Multilingual Aphasia Examination: Token Test²², Boston Naming Test²³. Test scores were converted to demographically adjusted standardized scores (z-scores or scaled scores depending on the normative scores provided) using published normative data. From this battery, three tests assessing abilities covered in the subjective ratings were selected for analysis (described below). In order to compare performance on selected objective tests directly with the subjective ratings provided on a 5-point ordinal scale described above, standardized scores from neuropsychological tests were considered in terms of corresponding and commonly used ordinal descriptors (See Table 1)^{24, 25}.

Domains of Awareness—In order to derive measures of awareness in the domains of memory, language, and executive functioning, the three self-ratings were paired in an a priori manner to objective neuropsychological tests commonly used to assess these cognitive domains. In addition to the theoretical bases for pairing the individual ratings and tests, we considered a significant bivariate association between the paired ratings and tests (i.e., memory rating and memory test) in the ET-NC group to be empirical support for the pairing.

Memory: Participants' subjective rating of *remembering* was examined in relation to performance on the 16-word CVLT-II, a commonly used word list learning test assessing short and long term free recall and recognition²⁶. In the current study, long delay free recall was used as the dependent variable.

Language: Participants' subjective rating of *finding the right word when speaking* was examined in relation to performance on the D-KEFS Phonemic Fluency test²⁰. This test assesses participants' ability to rapidly generate words beginning with specified letters. The dependent variable for this test is the total number of words generated across three 60-second trials.

Executive Function: Participants' subjective rating of *multitasking* (the ability to do more than one task at the same time) was examined in relation to performance on the D-KEFS Verbal Fluency Switching Task²⁰. Multitasking in everyday life requires the ability to rapidly and efficiently shift attention between different tasks. The D-KEFS fluency switching task was designed to assess one's ability to shift attentions between two competing tasks, requiring the participant to generate as many words as possible in 60 seconds, alternating between words from two specified semantic categories. Performance on this task has been shown to correlate with other forms of task switching²⁷. The dependent variable for this test is the total number of words accurately generated²⁸.

Awareness Scores—Discrepancy scores (i.e., awareness scores) were calculated by subtracting ordinal objective scores from self-ratings in each domain. Previous studies have used similar methodologies to assess awareness of cognitive functioning (i.e., metacognition)^{24, 25, 29, 30}. A discrepancy score of zero reflects accurate self-assessment whereas negative discrepancy scores reflect under-confidence and positive scores reflect over-confidence.

2.4 Statistical Analyses

All analyses were computed using SPSS version 21. Demographic and mood variables (age, ethnicity, gender, years of education, depression) were compared across the ET-NC and ET-CI groups using chi square tests and one-way ANOVAs. One sample t-tests were used to determine if the average awareness score in each group was statistically different from zero, thus reflecting significant under or over-confidence. ANCOVAs were then used to compare differences in mean self-awareness between ET patients with normal cognition versus those with cognitive impairment (MCI/dementia) controlling for demographic variables that differed across the groups, including age and education. Depression was one of these variables, and was measured by the Geriatric Depression Scale (GDS) ranging from a score of 0 to 30³¹.

3. Results

The mean age and education of the overall sample was 79.39 ($SD=9.48$ years) and 15.92 ($SD= 3.07$), respectively. The sample included 59 (39%) males and 91 (61%) females. See Table 2 for descriptive characteristics by cognitive group. When comparing the ET-NC and ET-CI group, Participants in the ET-CI group tended to be, on average, older, ($p<0.001$), less

educated ($p=0.02$), and marginally more depressed ($p=0.05$). Hence, these variables were included as covariates in the primary analyses examining awareness across groups.

Pairing of Objective Tests and Subjective Ratings: To ensure that the a priori pairings of subjective ratings with specific objective tests were reasonable we conducted bivariate correlations between the test scores and ratings within the ET-NC group. The CVLT long-delay free recall scores were significantly associated with ratings of one's ability to remember ($r=0.18$, $p<0.05$), the VFT Letter task scores were associated with ratings of one's ability to find the right word when speaking ($r=0.18$, $p<0.05$) and VFT switching scores were associated with the ratings of one's ability to multitask ($r=0.29$, $p<0.001$).

Objective Performance: Mean objective performance in each domain by group is presented in Table 3. As expected, when analyzing the ordinal ratings, the ET-CI group performed more poorly on measures of memory, $F(1,148)=55.05$, $p<.001$, language, $F(1,148)=20.05$, $p<.001$, and executive functioning, $F(1,148)=46.82$, $p<.001$ than the ET-NC group.

Self-Ratings: Mean self-ratings for each domain are also presented in Table 3. On average, ET-NC individuals made higher self-ratings than the ET-CI group for the domains of memory, ($F(1,148)=15.11$, $p<0.001$ and executive function, $F(1,148)=11.17$, $p<0.001$. There was no difference in language ratings across the two groups, $F(1,148)=0.45$, $p=0.50$.

Awareness: Average discrepancy (i.e., awareness) scores and the results of one-sample t-tests and between group analyses comparing discrepancy scores across the ET-NC and ET-CI groups are presented in Table 4. In the ET-NC group, only the memory discrepancy score was significantly greater than zero. In contrast, the ET-CI group's average discrepancy score was significantly greater than zero for all three domains as noted by the asterisks in Table 4. Between group analyses adjusted for age, years of education, and depression were used to compare discrepancy scores across the ET-NC and ET-CI groups. Discrepancy scores for all three domains were significantly higher in the ET-CI group than in the ET-NC group and neither age, years of education, nor depression accounted for these differences. For descriptive purposes and qualitative examination, Table 5 breaks down mean awareness scores within the CI group as a function of ET-MCI (amnesic versus non-amnesic) and ET-D groups.

4. Discussion

This study investigated the degree to which individuals with ET with cognitive impairment, who meet criteria for MCI or dementia, are aware of their cognitive deficits. Investigating awareness of cognitive impairment in ET is particularly important as physicians may not refer movement disorder patients for neuropsychological assessment without cognitive complaints by the patients themselves. We asked ET patients with both normal cognition and cognitive impairment to rate their cognitive functioning in three specific abilities spanning the domains of memory, language, and executive functioning, and these ratings were directly compared to objective assessments of such abilities to determine level of awareness in each cognitive domain. ET patients with normal cognition made largely accurate assessments, as

defined by discrepancy scores not statistically different from zero in the domains of language and executive functioning. While estimations for memory performance reflected some degree of overconfidence, we may consider this a “normal” estimation style as it is what is observed in this group of cognitive healthy older adults with ET. Moreover, overconfidence in physical (i.e., driving) and cognitive abilities (i.e., memory) has been a well-established phenomenon in healthy older adults, as their predicted performance often is greater than actual performance^{32–34}. In contrast, in the current paper older adults with ET with cognitive impairment (mild cognitive impairment and those with dementia) demonstrated limited awareness of their deficits, significantly over-estimating their performance in all three domains as indicated both by discrepancy scores significantly greater than zero, as well as by discrepancy scores that were significantly greater (i.e., more positive) than the cognitively healthy group.

Qualitative examination of performance across the normal controls, MCI, and dementia groups reveals increasing over-confidence in performance across the three groups in line with the severity of the cognitive diagnosis, such that participants with dementia had higher discrepancy scores than the MCI group, who then had higher discrepancy scores than the control group. There also appears to be some difference in discrepancy scores as a function of MCI phenotype, although it does not appear that either the amnesic or non-amnesic groups are driving all of the observed differences in awareness across domains. The relatively small effect size observed in the combined analyses of ET-NC versus ET-CI, such that 2.9–4.1% of the variance in awareness score was accounted by presence of cognitive impairment, may have been driven by the large number of individuals with MCI in the CI group. Future work may demonstrate a larger effect in analyses examining cognitively healthy ET patients versus those with dementia only.

Accumulating evidence has shown that cognitive abilities are compromised in some individuals with ET. Examples of cognitive deficits found in ET include problems in memory, executive functioning, visuospatial skills, verbal fluency, and attention^{2, 3, 35}. The etiology of these deficits has yet to be clearly determined. Cognitive changes may reflect ET-related pathology including dysfunction or death of Purkinje cells³⁶, reorganization of neighboring neuronal populations in the cerebellar cortex,³⁷ structural changes in the white matter, and gray matter areas of the brain³⁶. It is also possible that cognitive changes in ET reflect a co-morbid degenerative condition. Indeed, there is evidence that individuals with ET are at increased risk of co-morbid neurodegenerative disorders, such as Parkinson’s disease³ Alzheimer’s disease and progressive supranuclear palsy (PSP)^{35, 38}. Awareness may deteriorate in ET patients with cognitive impairment as a result of compromise to brain regions that are critical for supporting self-evaluation, and which may be directly or indirectly affected by ET pathology or co-occurring pathologies. It is unclear whether disordered awareness of deficit (also referred to as anosognosia) could arise in individuals with ET pathology alone, and this is perhaps less likely than the possibility that comorbid pathology is required to produce this symptom.

Indeed, disordered awareness is a well-established symptom of MCI and dementia across a range of neurologic diseases and conditions including AD, FTD, stroke, and brain injury^{6, 39–42}. Disordered awareness has significant clinical and practical implications, such

as reduced decision making capacity⁴³ poor quality of life⁶ and increased caregiver burden⁷ even in MCI⁴⁴. Additionally, disordered awareness has been previously associated with poorer functional outcomes in Parkinson's and AD^{45, 46} and was also the primary clinical correlate associated with dangerous behaviors in AD⁴⁰.

This study has several strengths that should be considered. These include obtaining a large sample of individuals diagnosed with ET who received consensus diagnoses of normal cognition, MCI, and dementia based on clinical consideration of performance on a comprehensive objective neuropsychological testing battery as well as detailed interviews of the patients' everyday functioning. Additionally, all participants were well characterized both neurologically and neuropsychologically and the neuropsychological tests were chosen to minimize motor demands. This study was to some extent limited by the combination of participants with dementia and MCI into one "cognitively impaired" group and future work with larger samples may benefit from separating these groups to determine the integrity of awareness in ET-MCI versus ET-dementia. Given the majority of the sample was quite old, it is possible this sample is not generalizable to younger samples of individuals with ET. Additionally, including non-ET groups with and without cognitive impairment as a point of comparison will allow a clearer depiction of the way in which disordered awareness may manifest specifically in ET. Finally, self-ratings of cognitive function were based on one single item for each of the three cognitive domains. As a result, the ratings may be less reliable and robust than ratings based on multiple items for each domain. These limitations offer possible lines of future research to gain further insight into awareness deficits associated with ET, and the clinical/therapeutic implications of each for patients, caregivers, and physicians.

4.1 Conclusions

The current findings thus have clinical and practical implications for patients with ET, their caregivers, and physicians. Self-report, such as subjective memory complaint, is often used by physicians as one of the first signs that the patient may need neuropsychological or medical treatment for memory deficits¹⁵. As patients with ET may be unaware of such deficits, a thorough interview should entail the collection of collateral information regarding cognitive changes from a knowledgeable informant. Physicians may also benefit from conducting neuropsychological screening whether or not the patient has cognitive complaints to improve the early detection of dementia⁴⁷. The need for cognitive screening is also underscored by the likely heterogeneous etiology of cognitive deficits in ET, as specific cognitive profiles may require have different prognoses³.

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Table 1

Ordinal groupings for standardized neuropsychological scores

Standardized Scores		Ordinal Scores
z-scores	Scaled Scores	
2.0	16	Excellent
> 1.0 and < 2.0	13 and 15	Above Average
> -1.0 to 1.0	7 and 15	Average
> -2.0 and -1.0	4 and 6	Below Average
-2.0	3	Very Impaired

Note: For each item, participants rated their ability on a 5-point scale including values of: (1) very impaired, (2) below average, (3) average, (4) above average, or (5) excellent.

Table 2

Demographic variables and mood by cognitive diagnosis

	ET-NC Group (N=109) M(SD)	ET-CI Group (N=41) (M=SD)	<i>p</i> -value	<i>F</i>
Age in years	77.7(9.6)	84.0(7.5)	0.000	14.718
% Female	68(62.4%)	23(56.1%)	0.486	X(1)=0.494
Years of Education	16.3(3.1)	14.9(2.7)	0.018	5.692
% Caucasian	104(96.3%)	41(100%)	0.762	X(3)=1.162
Depression(GDS)	6.1(4.9)	7.9(6.2)	0.054	3.769

Table 3

Objective cognitive scores and self-ratings by group

Domain	Objective standardized score M(SD)		Objective ordinal score M(SD)		Self-rating M(SD)	
	ET-NC	ET-CI	ET-NC	ET-CI	ET-NC	ET-CI
Memory	0.04 (1.06)	-1.51 (0.90)	3.05 (0.83)	1.98 (0.65)**	3.37 (0.87)	2.76 (0.83)**
Language	0.43 (1.51)	-0.67 (1.19)	3.23 (0.77)	2.59 (0.84)**	3.15 (0.81)	3.05 (0.74)
Executive	10.97(3.12) [^]	6.76 (3.35) [^]	3.27 (0.72)	2.34 (0.79)**	3.26 (0.82)	2.73 (0.95)**

Note. Objective scores for memory and language are presented as z-scores, and as scaled scores for the executive function domain.

[^] = scaled score.

** p < 0.001

Table 4
Discrepancy Scores in ET individuals with and without cognitive impairment (N=150)

Domain	ET-NC Group M(SD)	ET-CI Group M(SD)	F	p-value	η_p^2
Memory	0.32 (1.22) **	0.78 (1.01) ***	4.02	0.038	0.029
Language	-0.08 (1.10)	0.46 (0.95) **	6.16	0.014	0.041
Executive Functioning	-0.01 (0.99)	0.39 (1.14) *	4.51	0.028	0.033

Note. P-value column depicts between group differences across Normal Cognition (NC) vs. Cognitively Impaired (CI) group adjusting for age, years of education, and depression in ANCOVA.

p < 0.001,
**
p < .01,
*
p < .05 as per one-sample t-test results comparing mean value of each group to zero to determine the presence of significant under or over confidence.

Table 5

Discrepancy Scores according to Phenotype of MCI and dementia

Domain Discrepancy Score	ET-NC (n =109)	ET-CI (n=41)	ALL MCI (n=30)	aMCI (n=21)	naMCI (n=9)	Dementia (n=11)
Memory	0.32(1.22)	0.78(1.01)	0.60(0.93)	0.76(0.63)	0.22(1.39)	1.27(1.10)
Language	-0.08(1.10)	0.46(0.95)	0.40(0.89)	0.29(0.90)	0.67(0.87)	0.64(1.12)
Executive Functioning	-0.01(0.99)	0.39(1.14)	0.27(1.08)	0.33(1.11)	0.11(1.05)	0.72(1.27)