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Self-report depressive symptoms are dissociated from tremor severity in essential tremor

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Abstract

Background—Depressive symptoms are associated with essential tremor (ET). However, the relationship between cognitive, functional, and motor measures with depressive symptoms in ET is not yet understood.

Methods—The following measures were cross-sectionally assessed in a group of 223 subjects with ET: the Montreal Cognitive Assessment (MoCA) Scale, the Lawton Independent Activities of Daily Living (IADL) Scale, a neurologist assessment of tremor severity, and the Geriatric Depression Scale (GDS).

Results—20% (44) of the subjects met GDS criteria for depression (GDS = 10). 43% (94) of the subjects showed at least some cognitive impairment (< 24 on the MoCA), and 15.3% (34) reported

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significant functional impairment (IADL score < 7). There was no significant association between GDS score and tremor scale score. The total GDS was negatively associated with the total MoCA score (Spearman's $r=-0.15$, $p=0.03$). The total GDS was also negatively associated with the IADL score (Spearman's $r=-0.19$, $p=0.02$), (logistic model odds ratio, $OR=4.91$, $p<0.01$). Over 60% of subjects who were depressed, per GDS cut-off score (≥ 10), were not receiving medical treatment for depression.

Conclusions—There was a high point prevalence of depressive symptoms in subjects with ET. Self-report depressive symptoms are dissociated from tremor severity. Hence, these data do not support the hypothesis that depression in ET represents a psychological reaction to the tremor. There appears to be a clustering of cognitive, functional, and depressive symptoms in ET. Screening of depression in ET can improve our understanding and treatment of this disorder. There appears to be a clustering of cognitive, functional, and depressive symptoms in ET. Screening of depression in ET can improve our understanding and treatment of this disorder.

Keywords

essential tremor; depression; cognition; function; tremor; clinical

Introduction

The interaction between motor, cognitive, and neuropsychiatric symptoms in essential tremor (ET) is complex [1] ET is associated with an increased prevalence of depressive symptoms compared to controls, on measures such as the Hamilton Depression Rating Scale [2], Beck Depression Inventory [3] and on Structured Clinical Interviews (SCID) [1, 4]. ET is also often associated with physical disability and cognitive impairment, both of which can be related with an increased prevalence of depressive symptoms in other patient populations [5]. This pattern has also been observed in older persons without ET [6].

In the current study, we examine the association of tremor severity, disability, and cognition with self-reported depressive symptoms in subjects with ET. For this purpose, we obtained independent assessments of tremor (Neurologist rated), disability (informant rated), and depressive symptoms (self-reported).

Based on previous studies, neuropsychiatric symptoms can occur independent of motor symptoms in other movement disorders such as Parkinson's disease (PD) [7] and Huntington's disease [8]. Hence, we hypothesize that the severity of tremor in ET may not necessarily predict the severity of depressive symptoms in subjects with ET. Testing this hypothesis has important practical clinical implications as ET is one of the most prevalent neurological disorders, affecting up to 4% of people age 40 and older [9] and as many as 20% of individuals in their 90s [10]. The prevalence of depressive symptoms in ET varies depending on the instrument used, but approximately 25 to 35% of subjects with ET report at least moderate depressive symptoms, significantly higher than age-matched control subjects according to previous literature [1].

Depressive symptoms are associated with decreased quality of life in ET for subjects and their informants [11]. Understanding depression in ET also has important implications for

our understanding of the illness. If ET has a direct effect on mood, it supports the conceptualization of ET as a neuropsychiatric illness rather than solely a motor disorder. The effect of ET on mood presumably has a neural substrate that can be determined in future research. Finally, if ET has a direct effect on mood, other important clinical outcomes for subjects with ET such as disability and quality of life may be in part secondary to depressive symptoms. Reducing depressive symptoms may improve functioning and quality of life in ET.

Methods

Subjects

The subjects participated in a study of the clinical-pathological features of ET (NIH / NINDS R01NS086736). This is a prospective, longitudinal study to clinically and pathologically characterize a cohort of 232 ET subjects using motor, neuropsychiatric, and neuropsychological measures. Subjects were recruited via an advertisement that listed the following eligibility criteria: 1. Diagnosis of ET (not dystonia or PD), 2. 55 years old. 3. Did not have DBS surgery for ET, 4. Willingness to perform study measures and be a brain donor. The advertisement was sent by the International Essential Tremor Foundation to all recipients of their email newsletters. Interested subjects contacted researchers who confirmed the enrollment criteria and explained the study during a telephone interview. During this phone call subject's global cognition was also assessed via the Telephone Interview for Cognitive Status (TICS) [12] to ensure sufficient levels of cognitive ability for consenting. No subjects showed evidence of severe cognitive impairment (i.e., could not consent for themselves), precluding them from participating in the study. Recruited subjects were then scheduled for an in-home evaluation, conducted by a trained research assistants, and consisting of a videotaped neurological examination and a neuropsychological assessment. Additional demographic and clinical data were collected using structured questionnaires. Subjects were enrolled from across the United States.

The study was approved by the Institute Review Boards (IRBs) at Columbia and Yale University Medical Centers and all subjects gave written informed consent to participate. All clinical ET diagnoses were reconfirmed, based on review of collected data and videotaped neurological examination, by a senior movement disorder neurologist (E.D.L.) who used published diagnostic criteria (moderate or greater amplitude kinetic tremor during three activities or a head tremor in the absence of PD, dystonia or another known cause) [13, 14].

Measures

Self-reported Depression—Subjects completed the Geriatric Depression Scale (GDS), a 30-item self-report measure of depressive symptoms [15] This is a self-administered measure of depressive symptoms designed for use in older persons in which the subject answers yes / no questions regarding symptoms of depression. Higher scores indicate more symptoms of depression. Scores of 10 and above reflect significant depression and scores of 20 or above reflect severe depression [15]. The GDS has been shown to be a reliable and valid assessment of depressive symptoms in PD [16] The GDS has not been used previously to study depression in ET [1] but it is well-suited for this task as it focuses on assessment of

affective somatic symptoms of depression (e.g., hopelessness) rather than somatic symptoms (e.g., low energy), which can often be difficult to distinguish from symptoms of medical and neurological illness in older subjects [15].

Activities of the Daily Living—The Lawton Independent Activities of Daily Living (IADL) Scale measures ability to perform tasks that support independence [17] including cooking, housekeeping, shopping transportation, finances, laundry, managing medication, and using the telephone, in contrast to basic activities of daily living (e.g., dressing, eating, toileting, etc.). The Research Assistant completed the IADL scale based on information after an interview with a knowledgeable informant (usually a spouse, but sometimes a child or friend). A lower score indicates a higher level of dependence. The Lawton IADL Scale has been shown to be reliable and valid and has a moderate to large sensitivity to change [18] and has been used previously with subjects with ET [19].

Cognition—The Montreal Cognitive Assessment (MoCA) is a brief global cognitive assessment [20] administered to the subject by the RA. It measures a range of cognitive functions including executive function, naming, memory, attention, verbal fluency, abstraction, and calculations. The MoCA score ranges from 0-30, with higher scores indicating higher preserved cognition [20]. Different cut-offs may be used as indicative of cognitive difficulties. As there is no agreed upon MoCA cut-off for ET, for this study a cutoff of 24 was selected, based on its optimum maximum of specificity and sensitivity in detecting any cognitive disorder in PD, which is another tremor disorder [21].

Videotaped Neurological Examination and Confirmation of ET—Each ET case underwent a videotaped neurological examination, which included a detailed assessment of postural tremor and five tests of kinetic tremor as well as voice tremor during sustained phonation and conversation and head tremor. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations, and the severity of postural and kinetic arm tremors were rated (0-3), resulting in a total tremor scale score (range = 0-36 [maximum]). Voice and head tremor were noted to be present (1) or absent (0). Tremor ratings using this method are highly reliable [13] and have been validated against subject measures of tremor-related disability in ET [22], performance-based measures of functional impairment in ET [23] and objective measurements of tremor in ET [24].

Demographic psychosocial and clinical information—Demographic and psychosocial information was collected by trained RAs via subjects' self and informant report. Demographic information included age, sex and education. Psychosocial factors included ethanol use or consumption (i.e., self-reported number of drinks consumed per week), and living arrangement coded as an ordinal variable with increasing levels of assistance (e.g., independent living, assisted living, and nursing home living). Clinical information included clinical diagnoses determined in clinical case conferences, medications and informant based neuropsychiatric symptoms. Clinical diagnoses were determined after careful review of each subject's performance in various neuropsychological, mood and neurological measures in clinical case conference meetings. These meetings were formed by a neurologist (E.D.L.), a neuropsychologist (S.C.), and a geriatric psychiatrist (E.H.) who

discussed and agreed on diagnosis of normal cognition, Mild Cognitive Impairment (MCI), dementia or cognitive impairment secondary to a non-degenerative condition such as substance abuse, stroke or trauma. Psychiatric presentation was measured through the Neuropsychiatric Inventory (NPI) [25]. The NPI is an informant-based measure of 12 neuropsychiatric symptoms including hallucinations, delusions, agitation/aggression, dysphoria/depression, irritability, euphoria, apathy, anxiety, disinhibition, aberrant motor behavior, sleep and night-time behavior changes and appetite and eating change. The NPI total score ranges from 1-144, with higher scores indicating endorsement of symptoms. Other clinical information was also included as descriptive of the sample and in our main analyses. For example, total number of current medications that could affect cognition or depression (e.g., primidone, diazepam and topiramate) was noted for each subject. This was derived from previous published literature, which coded medications based on effect on cognition[26]. Medications that treat depression were coded separately, as a dichotomous variable. This variable indicated self-report use of medications considered as antidepressants (e.g., amitriptyline, brintellix, bupropion, buspirone Hcl, citalopram, desipramine, lexapro, mirtazapine, paroxetine, prozac, sertraline, trazadone, and venlafaxine).

Statistical analyses

Summary statistics were calculated to describe the sample characteristics. Spearman correlation coefficients were used to examine bivariate associations between quantitative variables. Analysis of variance was used to detect group mean differences in measures of interest.

The main goal of the analyses was to assess the association between tremor (total tremor score) and self-report depressive symptoms (GDS score). To better understand this association we also assessed the association between self-report depressive symptoms (GDS) and disability (IADL score), and GDS and cognition (MoCA). We first estimated correlations between these measures (GDS score, total tremor score, IADL score, and MoCA). Then, to assess the independent associations of total tremor score, IADL score, and MoCA with the GDS, we used a linear model in which the GDS score was the dependent variable and total tremor score, IADL score, and MoCA the independent variables. In this model, the total GDS score was square root transformed to reduce skewness of the distribution for model assumptions, to improve model fitting, and to minimize impact of extreme values. We also applied a logistic regression model to the dichotomized GDS scores at a clinically meaningful cut-off point of 10 (cutoff for significant depressive symptoms). Occurrence of missing values reduced the sample size for total IADL scores (153 subjects total). To maximize the use of data, we categorized these two variables using cut points (with a category for missing scores when including them in the models as predictors. We considered the subjects with IADL score < 7 as impaired compared to those with IADL score ≥ 7. In order to explore if missing IADL values were affecting our main results we also ran the analyses without missing cases. Since no clinical cut-off point was available on the total tremor score, we dichotomized the scores at the observed median (total tremor score 24). To aid interpretation, odds ratios and 95% confidence intervals (CI) were also derived from parameters in the logistic models. Age was controlled on all models and other covariates that could affect the relation between our main variables of interest in the linear

and logistic models described above. These included total amount medications taken, known to affect cognition or depression [26] and ethanol (i.e., liquor) consumption per week. The categorization used for medication intake per week (i.e., 1-2 and 3-4 medications per week) allowed for an even distribution within our sample, to better capture any existing effect between low or high medication intake. Further, we re ran our models excluding subjects that had a diagnosis of dementia or cognitive impairment based on clinical case conference to adjust for the possible effect of cognition on our main measure of interest, self-reported depression.

Results

Subject characteristics

A total of 330 people responded to the study advertisement and contacted us. Of these, 69 did not express further interest in participating in the study after initial contact and discussion with study staff, 15 did not meet eligibility criteria, and 7 were enrolled but and withdrew after initial visits. An additional 14 were excluded after the initial visit due to PD, dystonia or psychogenic tremor and 2 subjects were excluded due to missing data on our primary variable of interest (e.g., self-reported depression as measured by the GDS). Subjects were not excluded from the study if they had cognitive impairment.

The final sample of 223 subjects included in this study based on available data points of our primary measure of interest (i.e., GDS, self-reported depression). See Table 1 for subject characteristics. Overall, there were no significant differences in years of education between subjects included ($M=14.79$, $SD=2.99$) and those excluded from this study ($M=15.59$, $SD=2.69$), ($t(240)=-1.39$, $p=.16$). Similarly, no differences were observed regarding sex ($\chi^2(1) = 1.26$, $p=.26$). Regarding global cognition, MoCA scores also did not differ between those included in the study ($M=25.41$, $SD=4.62$) and those excluded from it ($M=24.33$, $SD=3.78$), ($t(236)=1.12$, $p=.26$). However, participants included in this study were on average 2 - 3 years younger ($M=79.03$, $SD=9.48$) than those excluded ($M=81.84$, $SD=8.41$), ($t(277)=2.07$, $p=.04$).

A total of 44 (19.7%) subjects met GDS score criteria for depression (GDS ≥ 10). Out of these, 16 (36.4%) reported antidepressant use. Based on clinical case conference consensus a total of 168 (75.3%) were deemed normal, 37 (16.6%) were diagnosed as MCI, 16 (7.2 %) as demented, and 2 (0.9%) cognitively impaired related to substance abuse, trauma or stroke. Self-reported depression was not significantly different between subjects with diagnosis of MCI ($M=7.59$, $SD=6.05$), dementia or cognitive impairment ($M=7.6$, $SD=6.55$), and cognitively normal subjects ($M=6.08$, $SD=4.77$) ($F(2,220)=1.78$, $p=.17$). Based on informant report, 34 (15.3%) of our subjects were considered as having significant functional impairment (IADL score < 7). Of note over 80% of our informants were spouses and children of the subjects. We ran analyses to explore if there were any significant differences in disability reported by each informant group but found none ($F(2,1)=2.02$, $p=.14$).

Association between tremor severity and self-report depressive symptoms

There was not a significant relation between total tremor and GDS scores (Spearman's $r=0.09$, $p=0.18$), nor were the linear ($b=0.005$, $p=0.97$) or logistic ($b=-0.08$, $p=0.83$) models of an association between total tremor and GDS scores significant after controlling for age, education, medications that could affect cognition, depression, and ethanol use (Table 3). Similar results were found after excluding participants with a diagnosis of dementia or cognitive impairment in the linear ($b=0.15$, $p=0.84$) and logistic ($b=0.80$, $p=0.58$) models (Table 4) and when excluding cases with missing values in IADL ($n=70$) and ethanol use ($N=3$) (Table 5).

Association between cognition and self-report depressive symptoms

The total GDS was negatively correlated with the total MoCA score. Greater cognitive impairment was associated with more depressive symptoms (Spearman's $r=-0.15$, $p=0.03$) (Table 2). In the linear model, lower MoCA scores were qualitatively related to higher GDS but this relationship was not significant ($b=0.32$, $p=0.052$).

Association between disability and self-report depressive symptoms

The total IADL score was negatively correlated with the total GDS (Spearman's $r=-0.19$, $p=0.02$), and total tremor score (Spearman's $r=-0.37$, $p<0.01$). Hence, increased depressive symptoms and tremor were associated with increased disability. The total IADL score was positively correlated with the MoCA (Spearman's $r=0.49$, $p<0.01$). These results indicate that better cognition was associated with less disability (Table 2). The logistic model indicated that the odds of high GDS were significantly higher in the group with low total IADL score (<7) than the group with higher total IADL score ($OR=4.97$, $p<0.01$) (Table 3).

Discussion

Tremor severity was not associated to depressive symptoms in this group of subjects with ET. Tremor severity was correlated with disability, suggesting that the lack of a statistically significant association, was not due to using a poor measure of tremor severity. This was a cross-sectional study; hence, causation cannot be inferred. However, a necessary step in establishing causation is demonstrating an association. These findings do not support the causal link between the depression and tremor severity, namely, that depression in ET is simply a psychological reaction to the tremor. Although it is possible that individuals may experience high negative affect towards a mild tremor, or that individuals with severe tremor may not necessarily react negatively to it, the current study suggests that overall, there is no association between self-reported depression and clinician-rated tremor in this sample of individuals with ET. The current study's finding differs from one previous study in which a score of tremor severity was significantly correlated with the total Hamilton Depression Rating Scale score in subjects with ET [2]

The ET subjects in this study report greater depressive symptoms than what has been shown in control populations (older adults) in previous literature, although on the lower end of the range reported in previous studies of ET subjects [27]. A meta-analysis of seven studies that used the 30-item GDS in a primary care setting in older persons without ET found a 15%

prevalence of depression, which is lower than the prevalence of 20% we observed in subjects with ET in this study [27]. Previous studies have reported a prevalence of 36% of moderate to severe depressive symptoms on the Beck Depression Inventory [3] and a prevalence of depressive disorders of 27% on the Structured Clinical Interview (SCID-I) [4] in subjects with ET. We observed a clustering of cognitive, functional, and depressive symptoms in subjects with ET (Table 2). A similar clustering has been observed in subjects with other neurological disorders including Alzheimer's disease (AD) [6] and PD [7]. Some of this may reflect symptom overlap between the syndromes of dementia, depression, and functional impairment (e.g., withdrawal from social activities). However, it appears that AD and PD can have a direct effect on depressive symptoms independent of disability through neurodegeneration of brain structures involved in the regulation of mood. Evidence in support of this assertion include the increased prevalence of depressive symptoms in subjects with neurological illnesses that affect the brain and that, for both PD and AD, a depressive prodrome can precede cognitive and motor symptoms by several years [28, 29]. There is early evidence that depressive symptoms can be a risk factor for the later development of ET [30]. Many neurological disorders with prominent movement symptoms, including PD, have been re-framed recently as multi-system disorders with motor, cognitive, neuropsychiatric, and other (e.g., autonomic) symptoms. ET may prove to have a similar, multi-system presentation. The effect sizes of the relations between self-reported depression, cognition and functional activity were relatively low (e.g., 15% and 19% of variance of self-reported depression was explained by cognition and daily functioning respectively). These findings suggest that other factors not considered in this study may contribute to self-reported depression. Future research could include other factors (i.e., perceived stress, quality of interpersonal relationships) to explore their contribution to the variance in self-reported depression in ET."

Our main findings have several clinical implications, most importantly, that based on self-report, 20% of ET subjects endorse depression. These results, also supported by previous studies [3, 4], highlight the need to consider depression when examining subjects with ET. Regarding depressive symptoms solely as an understandable reaction to aging, physical symptoms, or disability often results in therapeutic nihilism and under-treatment of depression, especially in older persons [31]. Depressive symptoms and depression may be under-recognized and under-treated in ET. In this study we found that over 60% of subjects that were depressed were not being treated (e.g., they were not taking antidepressants). Although these individuals might have sought other treatments such as psychotherapy, a previous study found that subjects with ET report difficulties meeting their mental health needs in their care [1]. Changing perception of depressive symptoms as a symptom of ET can improve detection and treatment of depressive symptoms, as has occurred for PD. Depressive symptoms are now seen as a common aspect of PD [7] and the American Academy of Neurology has identified assessment and recognition of depression in PD as one of the highest ranked indicators for improving care of subjects with PD [32]. Changing perception of depression can also help reduce the stigma of a diagnosis of depression in subjects with ET. ET is generally evaluated and treated by neurologists, some of whom may not feel comfortable treating depression in ET. Improvement of depressive symptoms in the elderly can improve life satisfaction, and reduce disability [33]. We do not currently know

how having ET affects response to antidepressant treatment, but this is an important topic for further research. Reduction of symptoms of depression is associated with an improvement in ability to perform IADLs in subjects with AD [34] and may be in ET as well, although we do not currently have data on this topic.

A limitation of the current analyses is that they are cross-sectional, which limits our ability to truly assign directionality to the symptoms, in addition to not having a control group which would allow for a clear comparison group. Another limitation is that the current paper only focused on depressive symptoms, instead of a range of neuropsychiatric symptoms. Studies have shown a high prevalence of anxiety disorders, including social phobia, in subjects with ET. Since some subjects did not have an informant, there were missing IADL data. As the NPI was also informant based, these data were also missing for the NPI scale, but all subjects had the majority of the other measures of interest. Also, it is unclear how representative the subjects who participated in the current study are to the general population of persons with ET. The study subjects may have been more likely to volunteer for the study because they were more bothered by their ET diagnosis and hence, more likely to suffer from depression. Finally, although there are tremor specific ADL scales (e.g., Fahn-Tolosa-Marín scale (FTM) [35], we did not include these tremor specific ADL measures in our study. A goal of this study was to assess the impact of non-motor symptoms, including cognitive and psychiatric symptoms, on functioning in patients with ET. The Lawton IADL scale [17] assesses the ability to perform tasks that support independence broadly, and thus was better suited to meet this goal than a tremor specific ADL scale. Strengths of the current study include that we used objective independent measures of tremor, function, and cognition and that the results have clear clinical implications. Finally, although this study included various key factors that could affect the relation between depression, cognition and tremor, other factors that were not included in this study, might have impacted this relationship. Future research should examine how these other factors, such as comorbidities and psychosocial factors, can impact the relationship between depression and ET.

In summary, the current study suggests that depressive symptoms in ET are not directly related to the tremor. ET subjects may benefit from screening of depression and treated if indicated, as cognitive impairment and disability may be associated factors also present. Future projects should collect longitudinal data on the cognitive, neuropsychiatric, and motor symptoms of ET to better define the motor and non-motor syndromes that characterize this disorder and to determine the temporal relationship between the symptoms.

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Highlights

- Self-report depressive symptoms are common in ET patients
- Depressive symptoms were associated with poorer cognition and functional impairment, but not tremor severity
- This finding suggests that depressive symptoms in ET are not primarily a reaction to tremor

Table 1

Sample characteristics (n = 223)

Variable	Mean $\pm$ SD (range) or % (n/N)
Age in years	79.0 $\pm$ 9.5 (55, 96)
Years of education	15.7 $\pm$ 2.7 (2, 20)
Sex (% Female)	61.0% (136/223)
GDS Total Score	6.5 $\pm$ 5.2 (0, 26)
Significant depressive symptoms (GDS $\geq$ 10)	19.7% (44/223)
MoCA score	24.3 $\pm$ 3.8 (10, 30)
Cognitive ability impaired (MoCA $\leq$ 24)	42.5% (94/221)
Total tremor score	23.9 $\pm$ 5.6 (10.50,36)
Total tremor score $>$ 24	48.7% (108/222)
IADL total score	7.1 $\pm$ 1.8 (0, 8)
Functional impairment (IADL $<$ 7)	15.26% (34/153)
Ethanol consumed per week (unit/week)	22.8% (49/215)
Level of assistance in living arrangement *	
Independent living	79.6 % (121/152)
Assisted living	9.2 % (14/152)
Nursing home	11.2 % (17/152)
Cognitive diagnosis	
MCI	16.6% (37/223)
Dementia	7.2% (16/223)
Cognitively impaired	0.9% (2/223)
Neuropsychiatric Inventory (NPI) Score *	1.6 $\pm$ 2.6 (0,12)
Medication Use	
Number of medications taken that could affect cognition or depression	
1-2	45.7% (102/223)
3-4	6.3% (14/223)
Antidepressant medication use	19.7% (44/223)

* NPI score sample N=155; Living arrangement sample N=152.

SD = Standard Deviation, (n/N) = (frequency/total N) GDS = Geriatric Depression Scale, MoCA = Montreal Cognitive Assessment, IADL scale = Lawton Independent Activities of Daily Living (IADL) Scale; MCI= Mild cognitive impairment

Table 2

Spearman Correlation Coefficient for bivariate associations (n=223).

	GDS score	IADL scale score (n=153)	MoCA score	Total tremor score	Age	Education	Living arrangement
IADL scale score	-.19 <i>p</i> = .02	1					
MoCA score	-.15 <i>p</i> = .03	.49 <i>p</i> < .0001	1				
Total tremor score	.09 <i>p</i> = .18	-.37 <i>p</i> < .0001	-.20 <i>p</i> = .0002	1			
Age (years)	.11 <i>p</i> = .10	-.48 <i>p</i> < .0001	-.47 <i>p</i> < .0001	.30 <i>p</i> < .0001	1		
Education (years)	-.11 <i>p</i> = .10	.02 <i>p</i> = .86	.15 <i>p</i> < .0001	-.14 <i>p</i> = .04	-.06 <i>p</i> = .35	1	
Living arrangement	.03 <i>p</i> = .63	-.42 <i>p</i> < .0001	-.14 <i>p</i> = .04	.08 <i>p</i> = .25	.31 <i>p</i> < .0001	.03 <i>p</i> = .71	1
Ethanol consumed per week (unit/week)	.06 <i>p</i> = .46	-.10 <i>p</i> = .31	.01 <i>p</i> = .87	.12 <i>p</i> = .13	.02 <i>p</i> = .78	.04 <i>p</i> = .65	.10 <i>p</i> = .20

GDS = Geriatric Depression Scale, MoCA = Montreal Cognitive Assessment, IADL scale = Lawton Independent Activities of Daily Living (IADL) Scale

Table 3

Regression models for the association between clinical variables and GDS score.

N=223	Linear model for GDS score		Logistic model for GDS score 10 vs. <10	
Clinical variable	b (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	−0.002 (−0.02, 0.02)	0.97	0.96 (0.92, 1.01)	0.11
Education (years)	−0.03 (−0.08, 0.02)	0.30	1.04 (0.92, 1.18)	0.57
MoCA score (< 24 vs. ≥ 24)	0.32 (0.02, 0.65)	0.052	1.79 (0.79, 4.02)	0.16
IADL score (< 7 vs. ≥ 7)	0.37 (−0.08, 0.83)	0.11	4.97 (1.72, 14.35)	<0.01
Total tremor score (< 24 vs. ≥ 24)	0.004 (−0.29, 0.30)	0.97	0.97 (0.45, 1.91)	0.83
Medications that can affect cognition and depression				
1-2	−0.08 (−0.41, 0.25)	0.62	1.10 (0.48, 2.53)	0.81
2-3	0.19 (−0.18, 0.57)	0.32	1.03 (0.42, 2.56)	0.94
Ethanol consumed per week (unit/week)	0.33 (−0.01, 0.67)	0.06	2.52 (1.15, 5.52)	0.02
	R ² = 0.083		R ² = 0.077	

The first column of results reports the estimated coefficient (b) and 95% confidence interval (CI) in a linear regression model using the square root transformed total GDS score as the dependent variable. The second column of results reports the odds ratio (OR) and 95% CI derived from a logistic model using a dichotomous measure of depressive symptoms (total GDS ≥ 10 vs. <10) as the dependent variable. Controlled for age and education. Significant associations are bolded.

GDS = Geriatric Depression Scale, MoCA = Montreal Cognitive Assessment, IADL scale = Lawton Independent Activities of Daily Living (IADL) Scale

Table 4

Regression models excluding subjects with dementia or cognitive impairment.

N=204	Linear model for GDS score		Logistic model for GDS score 10 vs. <10	
Clinical variable	b (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	0.0002 (−0.2, 0.2)	0.98	0.96 (0.92, 1.01)	0.80
Education (years)	−0.02 (−0.07, 0.03)	0.44	1.06 (0.93, 1.22)	0.36
MoCA score (< 24 vs. ≥ 24)	0.36 (0.01, 0.72)	0.04	2.02 (0.87, 4.70)	0.10
IADL score (< 7 vs. ≥ 7)	0.60 (0.03, 0.69)	0.02	7.28 (2.30, 23.16)	<0.01
Total tremor score (< 24 vs. ≥ 24)	0.15 (−0.3, 0.27)	0.84	0.80 (0.37, 1.74)	0.58
Ethanol consumed per week (unit /week)	0.36 (0.01, 0.72)	0.04	2.90 (1.24, 6.77)	0.01
	R ² = 0.08		R ² = 0.09	

The first column of results reports the estimated coefficient (b) and 95% confidence interval (CI) in a linear regression model using the square root transformed total GDS score as the dependent variable. The second column of results reports the odds ratio (OR) and 95% CI derived from a logistic model using a dichotomous measure of depressive symptoms (total GDS ≥ 10 vs. <10) as the dependent variable. Controlled for age and education. Significant associations are bolded.

GDS = Geriatric Depression Scale, MoCA = Montreal Cognitive Assessment, IADL scale = Lawton Independent Activities of Daily Living (IADL) Scale

Table 5

Regression models excluding those participants with missing values.

N=150	Linear model for GDS score		Logistic model for GDS score 10 vs. <10	
Clinical variable	b (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	−0.002 (−.02, .02)	0.85	0.94 (0.88, 0.99)	0.03
Education (years)	−0.03 (−0.09, 0.04)	0.46	1.11 (0.94, 1.32)	0.23
MoCA score (< 24 vs. ≥ 24)	0.29 (−0.12, 0.70)	0.16	1.82 (0.64, 5.16)	0.25
IADL score (< 7 vs. ≥ 7)	0.39 (−0.10, 0.88)	0.12	6.38 (1.89, 21.50)	0.003
Total tremor score (< 24 vs. ≥ 24)	0.05 (−0.94, 0.44)	0.80	1.46 (0.43, 3.07)	0.78
Medications that can affect cognition and depression				
1-2	−0.13 (−0.54, 0.27)	0.52	1.12 (0.41, 3.27)	0.77
2-3	0.19 (−0.27, 0.66)	0.42	0.74 (0.23, 2.37)	0.61
Ethanol consumed per week (unit/week)	0.26 (−0.19, 0.71)	0.26	1.80 (0.61, 5.32)	0.29
	R ² = 0.08		R ² = 0.10	

The first column of results reports the estimated coefficient (b) and 95% confidence interval (CI) in a linear regression model using the square root transformed total GDS score as the dependent variable. The second column of results reports the odds ratio (OR) and 95% CI derived from a logistic model using a dichotomous measure of depressive symptoms (total GDS 10 vs. <10) as the dependent variable. Controlled for age and education. Significant associations are bolded