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Physiological and brain mechanisms contributing to postural tremor in aging with and without alcohol use disorder

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Postural instability, a concomitant of falls, can persist in people with alcohol use disorder (AUD) even with sustained sobriety. Balance testing using a force plate, which detects micromovements while standing still, can be quantified with spectral analysis and expressed as temporal frequency, an index of truncal (i.e., postural) tremor. Here, we investigated physiological and brain structural factors that may contribute to a mechanistic understanding of postural instability during quiet standing in AUD. This mixed cross-sectional/longitudinal design included 462 observations in 292 participants (age 25–75 years): 120 men and 44 women with DSM-5-determined AUD and 75 control men and 53 control women. All participants completed balance testing on a force plate under two conditions: eyes open and eyes closed, both with feet together. Most participants also underwent two-point discrimination testing on the soles of the feet and structural MRI, typically within the week of balance testing. Linear mixed-effects models revealed greater tremor in all conditions in the AUD than control group with the diagnostic differences attributed to AUD men. Age effects did not differ significantly between AUD and control groups. By contrast, stronger correlations were detected between greater tremor, measured as a 2–5 Hz/0–2 Hz frequency quotient, and smaller regional brain volumes selective to motor centers (frontal supplemental motor cortex, thalamus, pallidum, cerebellar white matter) of the AUD men. The salient signs of postural instability were attributable to AUD men who consumed alcohol exceeding NIAAA guideline limits in the year prior to testing.

Translational Psychiatry (2025)15:338 ; https://doi.org/10.1038/s41398-025-03552-8

INTRODUCTION

Epidemiological studies [1] report that 1 in 4 Americans aged 65 and older fall each year. Falls resulting in morbidities, notably broken bones and subdural hematoma, are a leading cause of emergency department visits [1–3]. Among falls risk is consumption of alcohol [4]. Acutely, drinking any amount of alcohol has the potential of impairing motor coordination required for postural stability [5]. With alcohol use disorder (AUD), instability can persist even with sustained reduction or abstinence from alcohol consumption [6, 7]. Indeed, roadside sobriety-type testing revealed poorer ability of people with AUD than control participants to stand on one leg or walk a line, especially without stabilizing sensory aids such as vision [6]. Refinements of balance testing have used a force plate, which detects micromovements as a person attempts to stand still under different testing conditions and yields a sway path [6, 7]. In addition to sway, these micromovements can be subjected to spectral analysis and expressed as temporal frequency, an index of truncal (or postural) tremor [8, 9]. Frequency band and strength of truncal tremor together provide an estimate of long-loop muscle reflexes to correct excessive sway, which is notable in the anterior-posterior axis in people with anterior cerebellar lesions [10, 11].

Early studies classified postural tremor by frequency and either presumed or measured brain lesion site as the anterior superior vermis of the cerebellum [11–14]. Of relevance to AUD, truncal tremor, which is associated with anterior cerebellum integrity, a common site of volume deficit [6, 7] and Purkinje cell shrinkage [15, 16], was pronounced in the 2–5 Hz range [7]. This pattern comports with other studies of non-AUD patients who showed evidence of 3–10 Hz axial postural tremor with suspected pathology of cerebellar outflow pathways [11, 17, 18].

More recently, application of transmagnetic brain stimulation (TMS) to the left primary motor cortex reduced tremor intensity and improved postural control in all 8 patients examined with orthostatic tremor [19]. The speculation was that TMS disrupted a faulty cerebellar-thalamic-cortical network that caused the tremor, thus invoking a multi-site source of postural instability (cf., [20–22]). Consistent with this characterization of postural control, we have observed greater tremor during quiet standing while engaged in mental arithmetic in men with AUD than control men or women or women with AUD [9]. We further found a dissociation between local tissue diffusivity, measured with MR diffusion tensor imaging, and tremor frequency exhibited by AUD men but not AUD women or controls. Specifically, greater tremor velocity in the 2–5 Hz range correlated with higher diffusivity in cerebellar and superior cingulate bundle white matter tracts, whereas greater tremor velocity in the 5–7 Hz range correlated with higher diffusivity in the motor cortex and internal capsule. Remaining to be examined are potential relations between alcohol-associated truncal tremor and regional brain volumes of

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Received: 22 March 2025 Revised: 27 June 2025 Accepted: 13 August 2025
Published online: 01 September 2025

these tremorgenic networks and whether the severity of tremor advances with age or is associated with evidence of pedal somatosensory impairment (cf., [22, 23]).

Accordingly, here we investigated physiological and brain structural factors that may contribute to a mechanistic understanding of postural instability during quiet standing in AUD and tested three hypotheses: truncal tremor would be greater in an AUD than a control group and would accelerate with aging; AUD men would exhibit greater tremor than AUD women; and greater truncal tremor in the AUD men would be related to smaller brain volumes in motor network structures measured with MRI.

METHOD

Participants

This mixed cross-sectional/longitudinal analysis included 462 test sessions (Supplementary Table 1) of balance platform testing for sway and tremor detection. Balance testing was typically conducted on the same day as MRI data acquisition; this difference was nearly the same for the 4 groups as verified by a group x sex interaction conducted with a linear model that was not significant ($t = 0.231$, $p = 0.818$) (Table 1). Although the sway path results [24] and much of the MRI volumetric data [25–27] were reported previously, the current analysis newly focused on truncal (i.e., postural) tremor and its relations with regional brain volumes and peripheral sensory status of the soles of the feet that can potentially influence postural stability [28, 29]. The data include an expanded sample collected from 12 April 2006 to 31 October 2024 and report on brain and tremor data of 128 control and 164 AUD participants, age 25–75 years (Table 1). Participants were recruited from local alcohol and drug recovery centers, post card mailings, recruitment flyers, and word of mouth. This study was approved by the Institutional Review Boards of SRI International and Stanford University School of Medicine and was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

As described previously [30], after obtaining written informed consent for study participation, all volunteers underwent Structured Clinical Interviews for DSM-IV-TR [31] to determine diagnosis for alcohol dependence/abuse and DSM-5 diagnosis for AUD [32]. Interviews included structured health questionnaires and a semi-structured timeline follow-back interview to quantify lifetime and recent alcohol use [33, 34]. Starting each study day, participants underwent breathalyzer screening for recent alcohol consumption. Participants whose breathalyzer reading exceeded 0.0 were not tested on that day and were asked to return when they had refrained from drinking. Principal exclusion criteria at study entry were history of schizophrenia, bipolar disorder, and neurological disorders other than AUD. Substance use dependence/abuse (current or in remission) for illicit drugs was common. Of the control participants, only one met DSM criteria for a substance use disorder (cannabis, which is legal in California). Of the 164 participants with AUD, 108 (65.85%) also had history of at least one substance use disorder (75 cocaine, 38 amphetamines, 24 opioids, 12 sedatives, 10 hallucinogens, 63 cannabis). Mean ± SD remission time from the most recent substance use disorder was 474.4 ± 537.16 weeks (median = 277.4 weeks). All participants also completed metal screening to ensure MRI safety.

Balance and sensory testing

Force platform data acquisition and analysis. Participants wore rubber-soled socks and stood still on a force plate with feet together and arms relaxed at their side. The test comprised three, 30 sec. trials in each of two conditions: eyes open and eyes closed. The microcomputer-controlled force plate (model 9284; Kistler, Amherst, NY) has multiple transducers and analog-digital converters and sampled data at 1000 Hz to produce sway paths for each trial of each condition. Raw data were center-of-pressure displacements (x-y pairs) and subjected to a 10 Hz low-pass filter (99 terms, −50 db Gibbs). Sway path length was expressed as the line integral [7].

Relevant to the current study, the sway data were subject to spectral analysis described previously [9], using fast Fourier transform on the anterior/posterior (A/P) and lateral/medial (M/L) sway path velocity (2-point differential of the filtered sway path). To characterize the frequency (Hz) of maximal sway velocity, data were divided into three frequency components: 0–2 Hz, 2–5 Hz, and 5–7 Hz. To account for mild, non-pathological tremor in the 0–2 Hz band detected in young, healthy adults, Baloh and colleagues [35] devised a frequency quotient (FQ), which they defined as the power of frequencies between 2 and 5 Hz over the power of frequencies between 0 and 2 Hz. This single value of the FQ reduced unwanted variance from the low frequency band, thereby increasing its ability to detect tremor in older healthy participants free of disorders and in individuals with pathologies that influence stability. We expected that the AUD participants would have a higher ratio than controls [8]. The 5–7 Hz data provided a contrast to establish selectivity of brain-tremor relations observed with the FQ.

2-point pedal discrimination. As described [30], starting with the dominant side determined from handedness, the examiner touched the sole of one foot with 1 or 2 points of a 3-point aesthesiometer, to which the participant (with eyes closed) responded "one" or "two." Testing avoided calloused skin and proceeded with descending limits (starting at 50 mm distance between points); the threshold was the shortest distance on which fewer than 3 errors were made [36]; thus, high scores were in the impaired direction. The procedure was repeated with the other foot. The score was the mean of the left and right thresholds.

Falls questionnaire. At initial test, about one-third of AUD participants (56 of 159 AUD) and half of control participants (60 of 122 control) completed a falls questionnaire [37], which was begun several years after study initiation. Participants were asked how many times they remembered having fallen to the ground in the past year. The range recorded was 0–6 occasions.

Neuroimaging acquisition and analysis

MRI data were acquired at SRI International on a GE 3 Tesla Discovery MR750 system (Waukesha, WI, U.S.A.) with ASSET for parallel and accelerated imaging on an 8-channel head coil. Volumetric analysis was based on data collected with two MRI protocols: T1-weighted (T1-w) MRI for anatomical localization [3D axial IR-Prep (inversion prepared) SPGR (SPoiled Gradient Recalled); Repetition Time (TR) = 6.5 ms, Echo Time (TE) = 1.54 ms, thickness (thick) = 1.25 mm, locations (loc) = 124, skip = 0]; and T2-weighted (T2-w) MRI merged with T1 data for skull stripping [3D isotropic FSE [Fast Spin Echo; GE name = CUBE; TR = 2500 ms, effective TE = 99 ms, echo train length (ETL) = 100 ms, thick = 1 mm, loc = 150, FOV = 256 mm, xy_matrix = 256 × 256, resolution = 1 × 1 × 1 mm].

Brain structural analysis proceeded using the SIBIS pipeline [38]. T1-w and T2-w MRI data were corrected for noise [39] and field inhomogeneity via N4ITK [40]. T2-w images were then aligned to T1-w images via CMTK [41]. The SRI24 atlas [42] was non-rigidly aligned to T1-w images via ANTS [43], and the SRI24 mask was used to refine inhomogeneity correction of both modalities. Next, an improved brain mask was created by majority voting [44] across maps extracted by FSL BET [45], AFNI 3dSkullStrip [46], FreeSurfer mri_gcut [47], and the Robust Brain Extraction method [48]. Atropos generated brain tissue segmentations (gray matter, white matter, and CSF) [49]. Regarding majority voting, a voxel was labelled inside the brain if a majority of masks agreed; otherwise, the voxel was labelled outside the brain. The resulting probabilistic label maps of each time point were overlaid with the SRI24 atlas to define cortical and subcortical regions in each brain lobe.

Parcellation of the thalamus, described previously [27, 50, 51], used the THalamus Optimized Multi-Atlas Segmentation (THOMAS). This histogram-based polynomial synthesis (HIPS) algorithm first synthesized white matter nulled-like images from standard T1-w images prior to THOMAS segmentation [52]. Then the multi-atlas segmentation method [52] produced separate unilateral estimates of 10 bilateral nuclei (10 left and 10 right, unilateral volumes): Anterior Ventral (AV), Ventral Lateral anterior (VLa), Ventral Lateral posterior (VLp), Ventral anterior (VA), Ventral Posterior lateral (VPl), Pulvinar (Pul), Lateral Geniculate Nucleus (LGN), Medial Geniculate Nucleus (MGN), Centromedian (CM), and Mediodorsal (MD). Parcellation included about 70% of the total thalamic volume. Because thalamic volume is highly correlated with brain size [51], all thalamic measures were adjusted for intracranial volume (ICV) with regression analysis.

As described [53], the cerebellum was extracted from the processed MR images based on the aligned cerebellum mask of the SRI24 atlas [42]. The Spatially Unblased aTlas for the cerebellum (SUIT) [54, 55] was then non-rigidly aligned to the cerebellum of the baseline scan and propagated to the other time points via the intra-visit alignments. The aligned atlas was used by longitudinal consistent Atropos [56] to generate probability maps of the gray matter, white matter, and CSF within the cerebellum on the T1-w images. Those probability maps were overlaid with the parcellations of

Table 1. Study entry demographics of the study groups at first test session: mean (SD) or frequency count of participants with tremor scores.

	Control ($N = 128$)		AUD ($N = 164$)			*lm (ANOVA)*		
	Men	**Women**	**Men**	**Women**		**Group**	**Sex**	**Age**
Age (yrs)	53.5	52.3	51.0	50.7	t=	−1.431	0.477	—
	(13.89)	(14.77)	(11.07)	(9.10)	p=	0.1540	0.6340	—
n =	75	53	120	44				
Education (yrs)	16.1	16.5	13.2	14.1	t=	−9.328	−2.11	4.093
	(2.39)	(2.31)	(2.40)	(2.18)	p=	0.0000	0.0358	0.0007
n =	65	50	112	41				
Socioeconomic status	24.5	23.6	42.8	37.1	t=	9.806	2.039	−3.155
(lower Score=higher status)	(11.75)	(10.99)	(15.51)	(14.16)	p=	0.0000	0.0424	0.0018
n =	71	51	116	43				
Body Mass Index (BMI)	26.0	25.4	27.0	27.2	t=	2.271	0.379	0.770
	(3.72)	(5.24)	(4.09)	(5.13)	p=	0.0240	0.7050	0.4420
n =	67	48	110	41				
Diastolic blood pressure (dBP)	76.5	73.4	79.2	78.8	t=	2.516	0.990	2.165
	(13.19)	(8.29)	(10.90)	(11.85)	p=	0.0125	0.3232	0.0314
n =	60	37	105	38				
Systolic blood pressure (sBP)	127.6	120.1	131.8	122.2	t=	1.616	3.449	2.347
	(19.50)	(17.93)	(16.88)	(17.87)	p=	0.1075	0.0007	0.0198
n =	60	37	105	38				
Global Assessment of Functioning (GAF)	84.6	86.0	68.1	68.7	t=	−15.404	−0.903	0.851
	(6.56)	(4.90)	(10.17)	(10.45)	p=	0.0000	0.3670	0.3950
n =	64	49	112	41				
2-point pedal discrimination	36.5	34.8	40.5	39.7	t=	2.741	0.431	8.318
	(14.12)	(19.06)	(19.02)	(22.34)	p=	0.0066	0.6671	0.0000
n =	58	43	107	39				
Number of falls in past year (all visits)[a]								
0/1/2/3/4/5/6 =	37/10/3/3/0/0/1	21/6/4/0/1/1/0	23/6/7/4/3/2/3	13/3/0/0/0/0/2	$\chi2 = 10.724$, $p = 0.0973$			
Beck Depression Inventory II (BDI)	2.1	2.4	8.5	11.2	t=	8.806	−1.810	−0.530
	(3.41)	(3.70)	(7.39)	(9.59)	p=	0.0000	0.0714	0.5965
n =	64	49	111	41				
Lifetime alcohol consumption (kg)	44.3	23.1	1353.6	865.6	t=	13.067	2.678	3.417
	(69.79)	(31.74)	(1071.69)	(581.74)	p=	0.0000	0.0079	0.0007
n =	70	49	115	41				
Total alcohol in past year (kg)	1.0	1.0	34.0	21.0	t=	9.741	2.185	−0.732
	(1.70)	(1.42)	(32.53)	(26.00)	p=	0.0000	0.0297	0.4647
n =	68	49	115	41				
Age at AUD diagnosis	—	—	24.9	26.5	t=	—	−0.921	4.071
	—	—	(9.52)	(9.99)	p=	—	0.3588	0.0001
n =	—	—	111	41				
Absolute days between MRI and balance	6.3	8.4	4.1	5.6				Group x Sex
	(13.21)	(14.49)	(8.17)	(12.24)	t=	−1.505	−1.262	0.231
n for all visits =	124	93	154	73	p=	0.133	0.208	0.818
Race: Black/White/Asian/other[b] *n* =	13/32/21/9	5/32/9/7	42/52/4/22	16/20/1/7	$\chi2 = 45.513$, $p < 0.00001$			

[a]$\chi2$ collapsed falls into 3 categories: 0, 1–3, 4–6; Control men vs. AUD men for falls: $\chi2 = 8.418$, $p = 0.0149$.
[b]Other includes mixed + other + unknown.

SUIT to compute for each region its gray matter, white matter, or CSF volume. Tissue probability maps were used to compensate for partial voluming within the cerebellum.

Statistical analysis

Statistical analysis was performed using R 3.5.1 (R Core Team, 2019). Taking advantage of the fact that several participants had multiple data sets across time, the primary statistic was a linear mixed effects model (*lmer*) to test the relations among frequency bands, test conditions (eyes open or closed), and each regional brain volume as a function of diagnostic group (control vs. AUD) + age^2. Native tremor values were extremely skewed, ranging from 1.3–11.9 Hz. After logging, the skew values range was reduced to 0.5–2.2 Hz. Thus, logged frequencies were used in all analyses.

To account for differences in demographic characteristics and variables potentially correlating with the primary metrics, linear mixed-models multiple regression analysis included diagnosis, age, age^2, sex, years of education, 2-point pedal discrimination, amount of alcohol consumed over a lifetime, and age at AUD onset. Analyses were repeated after eliminating variables that did not contribute significantly to the main effect determined with Akaike Information Criterion. The model outputs for group differences produced t and *p* values. Within-group analysis examined relations between tremor frequency and regional brain volumes accounting for the demographic variables noted above that were significant contributors in the multiple regressions. Family-wise Bonferroni correction was applied to account for multiple comparisons in each primary analysis as noted in the tables.

Brain volumes of individuals were adjusted for age and ICV based on the control values at initial exam using regression analysis. The standardized residuals for each regional brain volume were then applied to the raw values of each participant in each group. Adjustment for ICV accounts for much of the variance attributed to sex differences [26, 57].

RESULTS

The statistical test results are presented in the tables and figures. For all analyses, tremor expressed in Hz was log transformed.

Comparison of diagnostic groups on demographic variables

The AUD and control groups were not statistically different in age or number of falls reported over the past year, although the AUD men reported more falls than control men ($\chi^2 = 8.418$, $p = 0.0149$). Compared with the control group, the AUD group had fewer years of education, lower SES and GAF, higher BMI and diastolic blood pressure, more depressive symptoms, and poorer 2-point pedal discrimination. The AUD group had more men than women and a larger Black representation than the control group. As expected, the AUD group had consumed significantly more alcohol over their lifetime and over the year prior to testing than the control group. Although the men with AUD had consumed more alcohol than the women with AUD, the groups did not differ significantly in age at AUD onset (Table 1).

Group and sex differences in tremor frequency and velocity

Grand average velocity spectra by group and sex are presented in Fig. 1. A series of linear models tested group and sex effects for each test condition and frequency band. These analyses were based on all available data for all participants, such that data of participants with multiple visits were averaged, thus counting the data of each person only once. The results indicated that tremor was significantly greater in the AUD group than the control group in all but one condition, which did not meet statistical criterion for multiple comparisons (Supplementary Table 2; Fig. 2). On average, men exhibited greater tremor than women; inspection of the plots and means reveal that the sex effects were attributable to the AUD men. For men and women in each group, the tremor was less with eyes open than eyes closed (Supplementary Fig. 1)

Effects of age and sex on tremor

A series of omnibus linear mixed models (*lmer)* with multiple regression was conducted for each balance condition as a function of group with age, age + age^2, and sex as covariates. The *lmer* analyses revealed significant contributions from group (AUD > control) and age^2 (greater tremor with older age) in all conditions. Sex contributed significantly to three frequency quotient conditions and marginally to the fourth (men had greater tremor than women) (Supplementary Table 3). By contrast, sex differences in the 5–7 Hz frequency band were not forthcoming in any of the four conditions.

Follow-up analyses conducted separately by sex indicated that the mainstay of the group effects was attributed to AUD men. Whereas all group differences were significant for the AUD men compared with control men, only two conditions—eyes open and eyes closed in the medial/lateral axis for 5–7 Hz—were marginally different for AUD women compared with control women. For all group differences, tremor was greater in AUD than control participants. The age fits also differed by sex, where all but two conditions (FQ of eyes open and eyes closed in the medial/lateral axis) were best described by quadratic (age + age^2) fits for the AUD men, whereas linear fits best described the relation between 5–7 Hz tremor with eyes open for the AUD women. In these cases, tremor was greater with older age (Supplementary Table 3; Supplementary Fig. 2). Despite differences in group, vison condition, and age in tremor intensity, neither AUD men nor AUD women showed disproportionately greater tremor with older age relative to their control counterparts.

Relation between 2-point pedal discrimination and tremor

For all test conditions, greater tremor was related to poorer discrimination of 2-points on the soles of the feet for control men and women and AUD men. These correlations were consistent across these three groups and significant in all but one instance with multiple comparison correction: the 5–7 Hz while balancing with eyes open (Supplementary Table 4). Additional correlations between 2-point discrimination and tremor (especially in the anterior/posterior axis with eyes closed) occurred in control men and women and AUD men. The AUD women did not exhibit these relations in any condition.

Relations between regional brain volumes and tremor

A total of 55 regional brain volumes were tested as potential correlates of tremor frequency and strength in control and AUD men and women. To correct for multiple comparisons, only directional *p*-values ≤ 0.001 (greater tremor with smaller volumes) were considered significant. None of the correlations between tremor and cortical volume met criterion for significance in the control or AUD women or the control men (Supplementary Fig. 3–8). By contrast, six correlations met significance criterion for the AUD men, and all involved thalamic nuclei and subcortical motor system structures (Figs. 3, 4, turquoise outlined heatmap squares). Specifically, greater tremor, expressed as frequency quotients in the anterior/posterior sway axis in the eyes closed and open conditions, correlated with smaller pallidal volumes. Significant correlations emerged between two thalamic nuclei (anterior ventral and ventral lateral posterior) and 5–7 Hz tremor in both sway axes with eyes open. In general, the brain-tremor heatmaps revealed many more negative correlations (deeper blue) in the AUD men than control men for the thalamic, subcortical, and cerebellar (Figs. 3, 4; Supplementary Fig. 7) volumes although most did not meet criteria after correcting for multiple comparisons.

With a less stringent criterion ($p \leq 0.01$, orange outlined heatmap squares), seven relations emerged with thalamic nuclei for the control men. For the AUD men, seven additional correlations emerged with volumes of thalamic nuclei (Fig. 3), three with pallidal volumes (Fig. 4), and six trends with cerebellar white matter volumes (Supplementary Fig. 7). In addition, five correlations met the weaker significance criterion in the AUD women (but none for the control women) and involved the

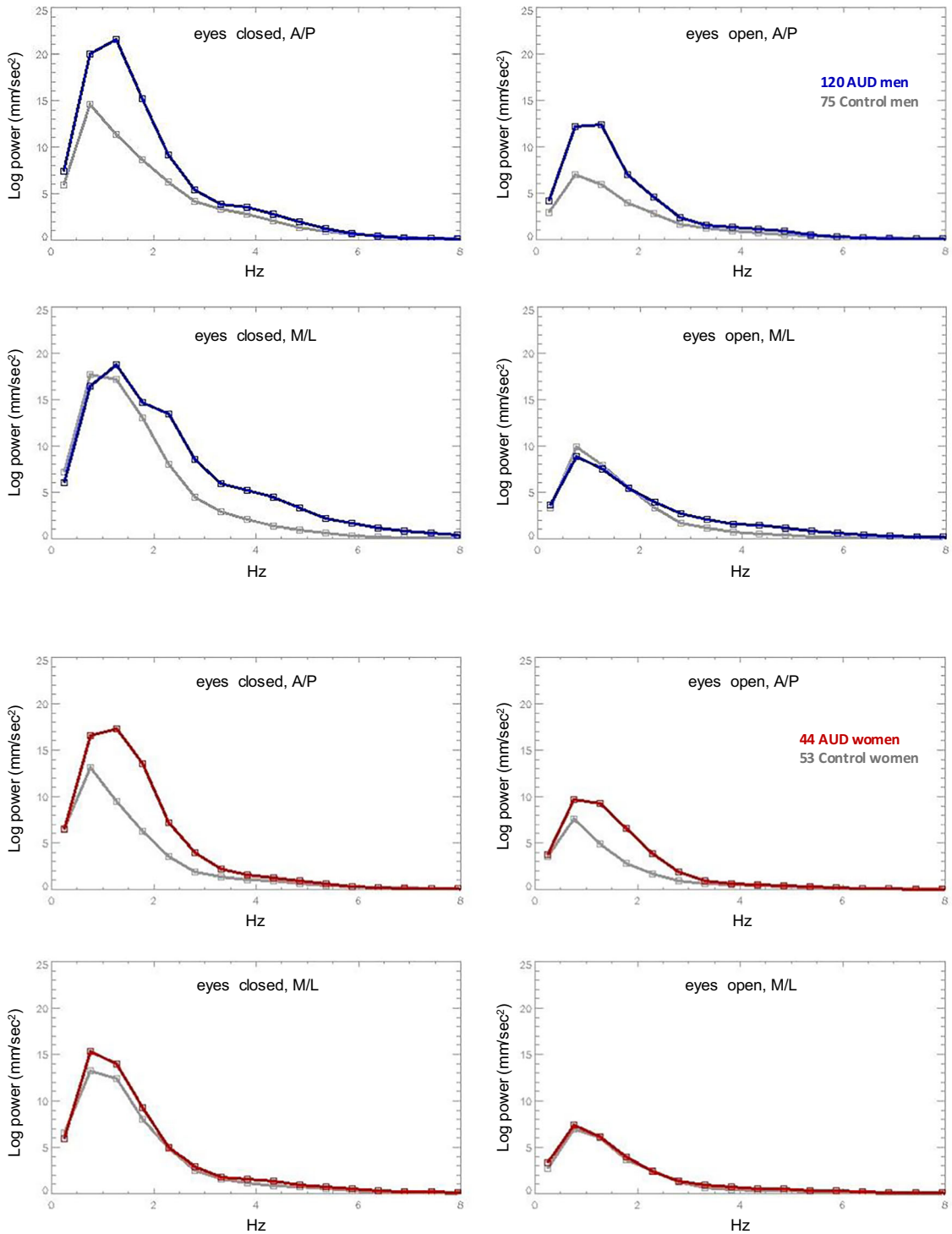

Fig. 1 Control and AUD tremor grand averages at initial test. Grand averages of postural tremor frequency on the A/P (anterior/posterior) and M/L (medial/lateral) axis in each test condition (eyes closed on the left, eyes open on the right) for each group: control men and women (gray) and AUD men (blue) and women (red).

inferior parietal cortex, thalamic lateral geniculate nucleus, and the pallidum (Supplementary Fig. 5, 6).

We then tested differences between brain-tremor correlations observed in AUD men relative to control men and found four differences ($p \leq 0.01$), where the negative correlations involving the frequency quotient were significantly greater in the AUD than control men. Three differences involved the eyes open condition in the anterior/posterior axis: frontal supplementary motor cortex, $r = -3.129$, $p < 0.001$; putamen, $r = -3.332$, $p \leq 0.001$; and pallidum, $r = -3.784$, $p \leq 0.0001$. The fourth difference occurred for the correlation between the eyes closed condition in the anterior/posterior axis and the pallidum, $r = -2.738$, $p \leq 0.01$.

Influence of alcohol consumption history on tremor

Correlations based on age of AUD onset indicated that the older the onset age, the greater the tremor in both AUD men and

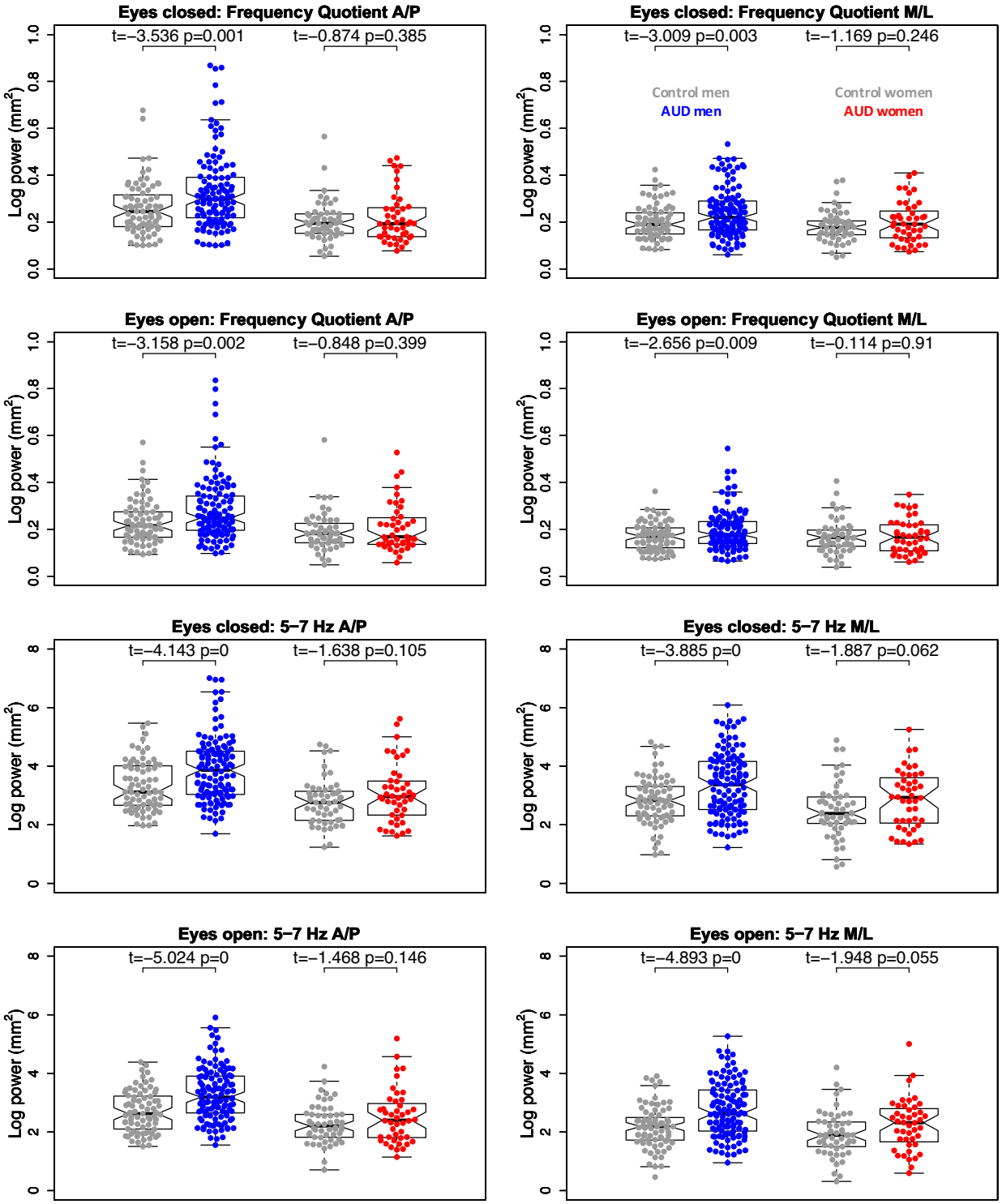

Fig. 2 Control vs. AUD tremor differences across all visits. Bee swarm log power plots overlaid with box plots of the distributions of tremor from all test sessions for the frequency quotient (FQ = 2–5/0–2 Hz) and 5–7 Hz on the A/P (anterior/posterior) and M/L (medial/lateral) axis in each test condition (eyes closed on the left, eyes open on the right) for each group: control men and women and AUD men and women.

women. The only correlations meeting criteria for multiple comparisons ($p \leq 0.0125$, 1-tailed) were for the eyes closed condition and involved anterior/posterior tremor in both frequency bands for the AUD women and the frequency quotient tremor in both directions for the AUD men (Supplementary Fig. 9).

Although none of the correlations between greater tremor intensity and more alcohol consumed over a lifetime was significant for either men or women with AUD, several relations emerged when considering drinking more proximal to testing. Here, we used the timeline consumption reports provided by each

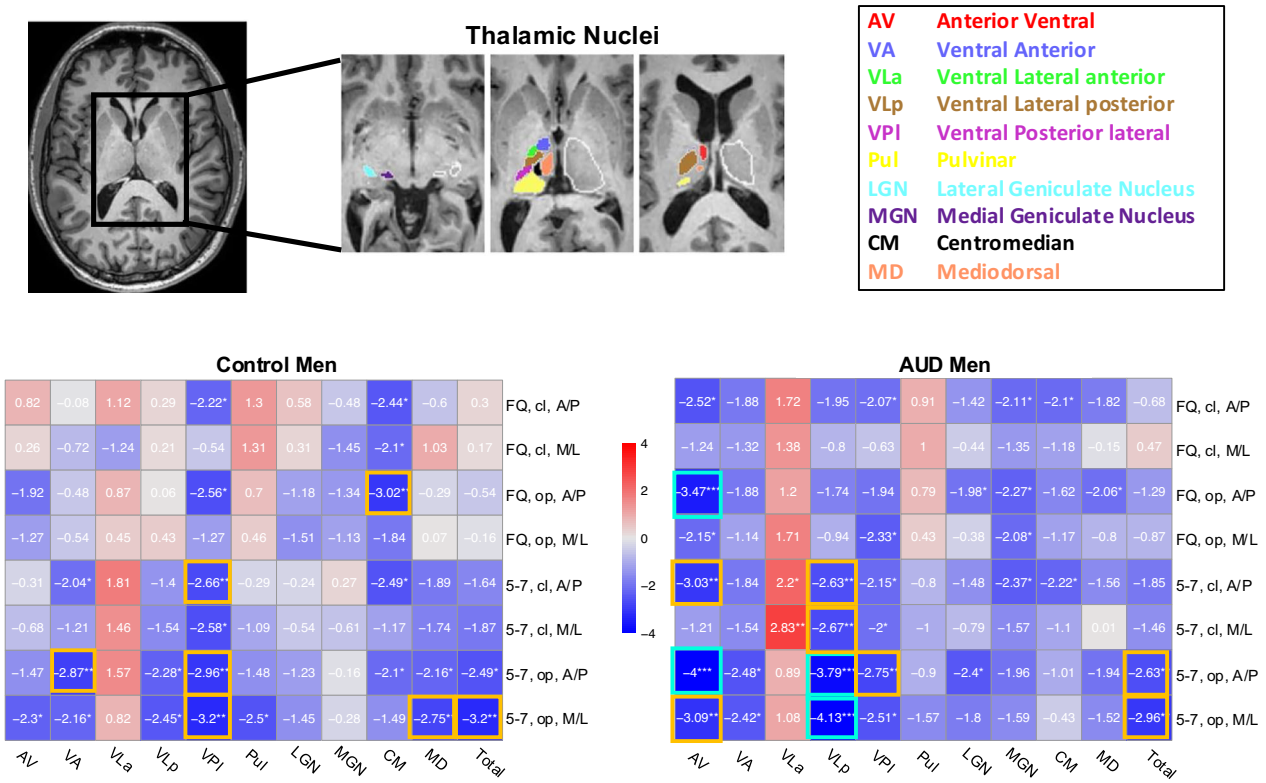

Fig. 3 Thalamic-tremor correlations for control and AUD men. Top: Axial MR images from T1-weighted data (top) of a control man. The cut-outs are from three different axial levels of volumes employed in the analysis process. From radiological orientation, the white outline in the left hemispheres (right side of the cut-out images) encompasses the total thalamus on that slice; the color-coding on the right hemispheres (left side of the cut-out images) indicates the 10 thalamic nuclei taken from [27]. Bottom: Heat maps of correlations between each thalamic nuclear volume and tremor metric. Control men are on the left, and AUD men are on the right. The turquois boxes indicate correlations meeting Bonferroni correction ($p \leq 0.001$); the orange boxes indicate correlations meeting less stringent criteria ($p \leq 0.01$).

participant at each balance test session to estimate how many drinks were consumed each day in the prior year. We then divided the AUD groups into those who drank within the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines versus those who exceeded the guidelines by sex, where the guideline limits were 0–2 drinks per day for men and 0–1 drink per day for women. Comparisons for each balance measure included AUD participants in the exceed criteria group, the non-exceeds criteria group, and control participants controlling for sex. Follow-up analyses compared the exceeds and non-exceeds AUD groups for each sex separately. Sex was a significant factor in the combined groups. The follow-up analyses of each sex separately revealed that the AUD effect was attributable to the AUD men only and only to those AUD men who exceeded the NIAAA limits in the preceding year (Fig. 5 and Supplementary Table 5).

Having found that AUD men reported more falls in the year before testing than control men (Table 1), we questioned whether the frequency of falls was greater in the exceeds than the non-exceeds AUD men. The number of falls reported by the AUD exceeds men was significantly greater than the number reported by the control men ($\chi^2 = 11.731$, $p = 0.0028$) but not significantly greater by the AUD non-exceeds men ($\chi^2 = 2.745$, $p = 0.2534$).

DISCUSSION

Our search for physiological and brain structural factors contributing to postural tremor during quiet standing in aging and AUD largely supported the three main hypotheses tested: truncal tremor was greater in the AUD than control group and advanced with aging in AUD and control participants but did so at similar rates; AUD men exhibited greater tremor than AUD women; and greater truncal tremor in the AUD men correlated with smaller brain volumes of motor network structures. In addition, greater tremor was related to poorer 2-point pedal discrimination in control men and women and AUD men and to alcohol consumption levels that exceeded NIAAA guideline limits in AUD men estimated from their reported drinking patterns over the year prior to testing. Together, these findings point to both peripheral and central nervous system contributions and recent heavy drinking to postural instability notable in AUD men.

Characterizing tremor in AUD men and women

The tremor was prominent in the AUD men and greatest in the 2–5 Hz range, expressed as the frequency quotient (FQ = 2–5 Hz/0–2 Hz). Because of its prominence and occurrence while attempting to stand still, it could be described as either a mild Holmes tremor or a cerebellar tremor, the latter supported by the modest correlations between tremor and cerebellar white matter volumes. An early study [58] found higher 2–6 Hz frequency peaks during dynamic posturography in 23 AUD men and women compared with 12 controls with little differentiation when the frequency band was divided (i.e., 2–4 and 4–6 Hz); also observed was a correlation between greater 2–6 Hz sway power and (log) number of drinks consumed over a lifetime. Although parkinsonian tremor is also marked a 3 Hz velocity, Parkinson's disease was a study exclusion criterion.

In seeking factors that rendered AUD men more vulnerable than AUD women to measurable truncal tremor, we considered lifetime alcohol consumption, which was greater in AUD men than women, and age of AUD onset, which was younger by an average of 2 years in the men. Although amount of alcohol drunk over a

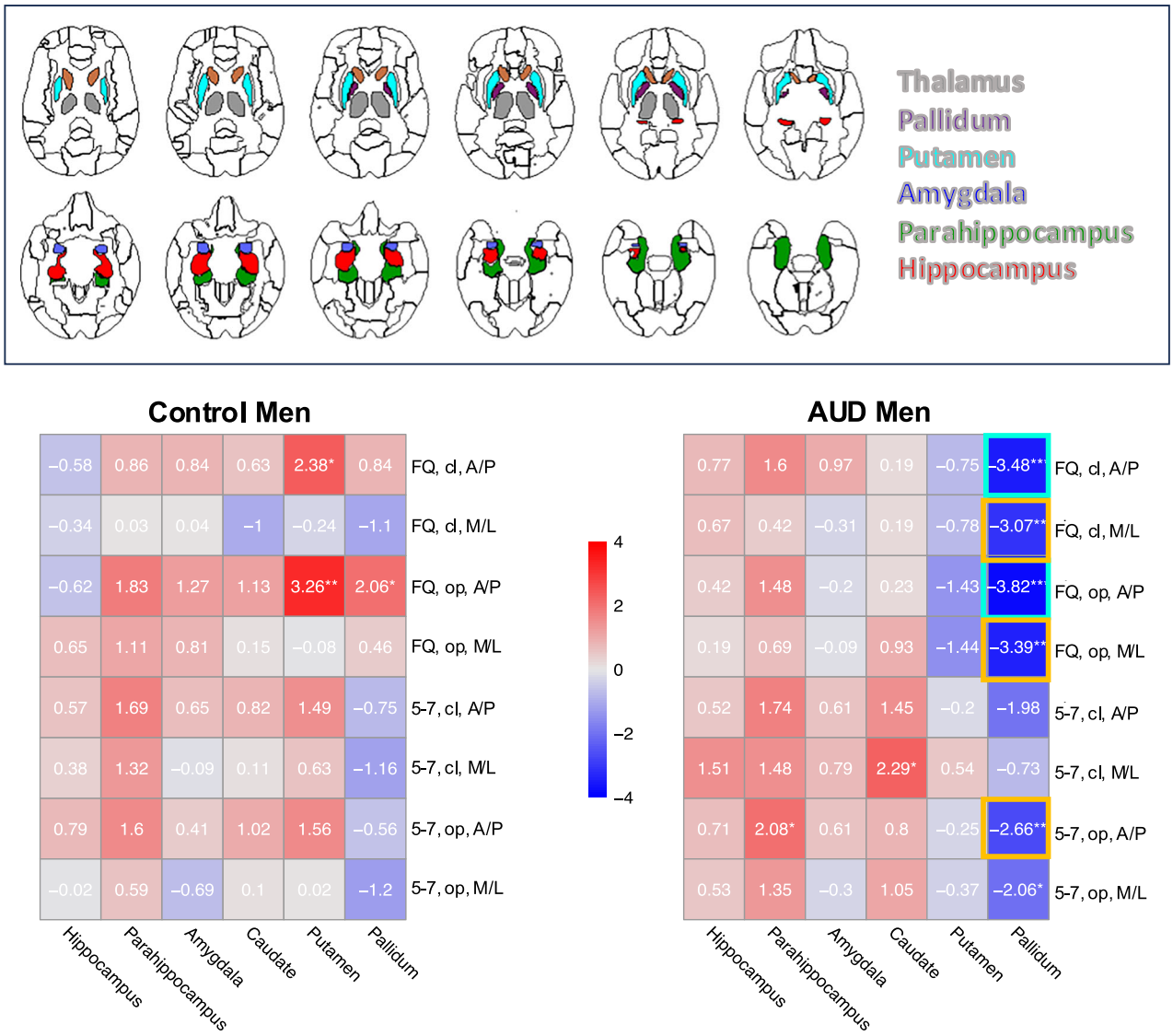

Fig. 4 Subcortical-tremor correlations for control and AUD men. Top: Outlines of axial images from the SRI24 parcellation atlas displaying the subcortical regions used in the analysis. Bottom: Heat maps of correlations between each subcortical volume and tremor metric. Control men are on the left, and AUD men are on the right. The turquois boxes indicate correlations meeting Bonferroni correction ($p \leq 0.001$); the orange boxes indicate correlations meeting less stringent criteria ($p \leq 0.01$).

lifetime did not correlate with tremor in either AUD men or women, stronger tremor in the A/P axis with eyes open was related to older age of AUD onset in both men and women (Supplementary Fig. 9) and is consistent with reports of people with AUD and with cerebellar damage to exhibit sway and tremor in this axis (e.g., [10, 11, 17]). This characterization of AUD-related truncal tremor differs, however, from that of an earlier study, which reported that although far more people with AUD exhibited postural tremor than controls, tremor severity was not related to age or duration of drinking [59].

A metric we created to differentiate alcohol consumption levels more proximal to balance testing than total lifetime consumption was based on whether estimated drinking levels over the year prior to testing fell within or exceeded NIAAA sex-linked guidelines. Although this subgrouping did not distinguish postural tremor levels in AUD women, it did in AUD men. Specifically, AUD men who consumed alcohol exceeding the NIAAA guideline limits over the previous year were solely responsible for abnormally greater postural tremor compared with control men. Although the AUD men in the non-exceeds group exhibited greater tremor than the controls, none of the differences was significant. These results suggest that recency and amount of drinking remain relevant factors to postural stability in AUD.

Tremor axis, frequency band, and brain correlates

The relations between tremor intensity and regional brain volumes mapped onto nodes of the brain's motor system, involving the cerebellum, thalamus, pallidum, and supplemental motor cortex. These modest to strong tremor-brain correlations included thalamic nuclei (AV, Vlp, and VPl), globus pallidus, and four lobules of cerebellar white matter (VIIb, VIIIa, VIIIb, IX), which are nodes of the dorsal attentional network and the oculomotor control network [60]. The cerebellar white matter loci may indirectly reflect the integrity of deep nuclei of the cerebellum that project to thalamic targets but are below MRI detection [21, 22, 61]. One relation between tremor and cortical sites involved the supplemental motor cortex. This relation along with others involving the putamen and pallidum was identified when

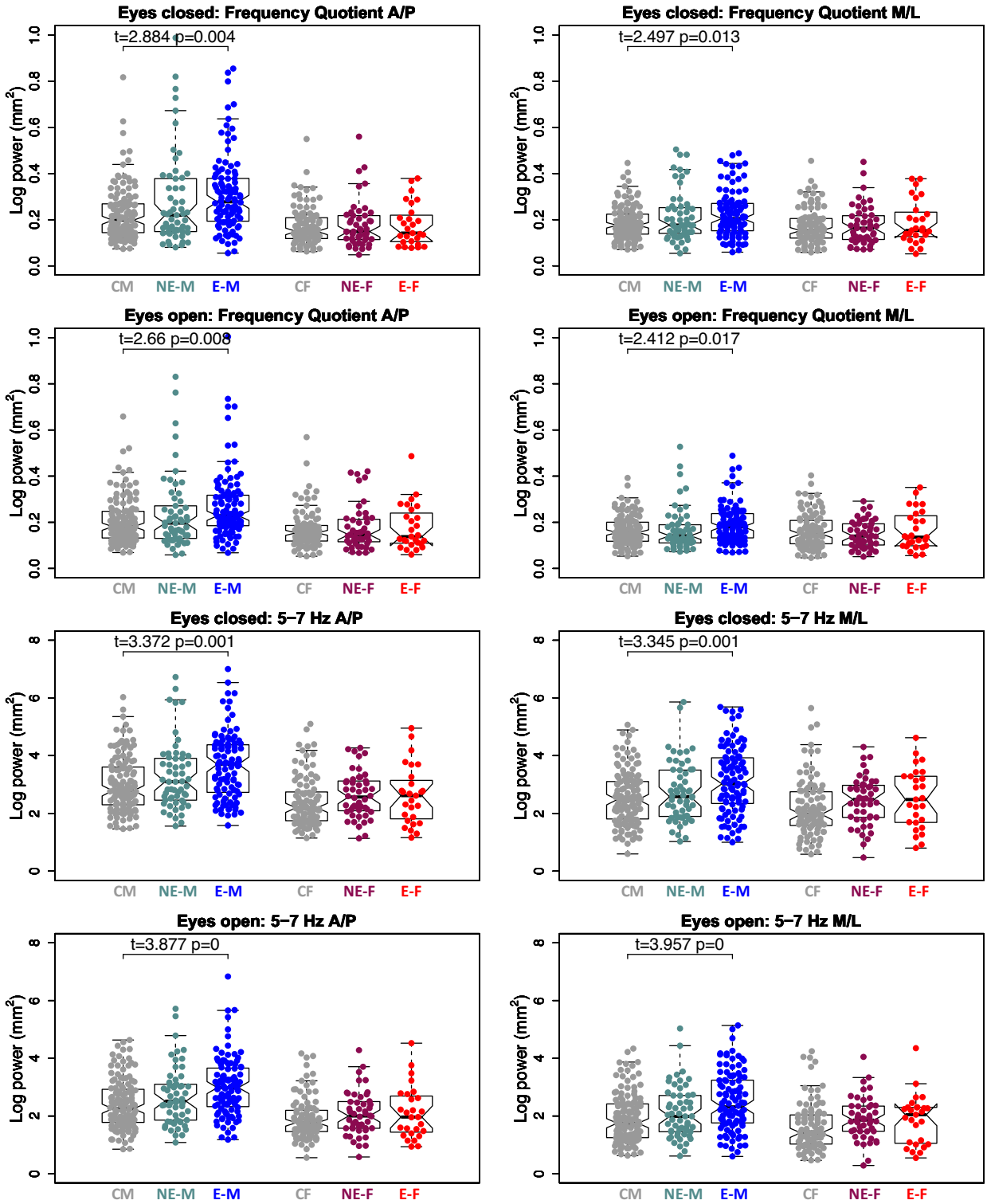

Fig. 5 Exceeds vs. Non-exceeds NIAAA drinking limits. Bee swarm and box plots for all visits of each visit for each group: male controls (CM), non-exceeds AUD men (NE-M), exceeds AUD men (E-M), female controls (CF), non-exceeds AUD -female (NE-F), and exceeds AUD - female (E-F). The exceeds groups were estimated to have consumed alcohol over the year prior to testing exceeding the NIAAA guidelines of no more than 1 drink per day for women and 2 drinks per day for men. The non-exceeds groups were estimated to have consumed alcohol within the guidelines, with some reporting complete abstinence.

testing differences between correlations in the control and AUD groups. A commonality across those associations was that 3 Hz truncal tremor was in the A/P axis, which has been documented to be salient in people with anterior cerebellar pathology, including AUD (e.g., [11, 17, 62]).

Selective thalamic nuclei, notably the ventral lateral nucleus, contribute to motor function through reception of motor input from the cerebellum and the globus pallidus; the latter two structures serve to regulate and smooth movements. Melo [63] described hemiataxia-hypesthesia, a "thalamic ataxia syndrome,"

with some sensory loss of touch on the affected side arising from a stroke involving the contralateral ventral lateral and ventral posterior thalamus identified on CT or MRI. The ataxia reported was not tested with upright standing, but rather noted solely as upper limb dysmetria and dysdiadochokinesia. Perhaps closer to the AUD tremor frequency and related brain nodes is Holmes tremor. Signs of tremor in our AUD men overlapped with two (postural and action) of three (not resting) signs of Holmes tremor, [64–66] albeit far milder than often observed in Holmes tremor. Brain regional commonalities of these tremors are integrity of the globus pallidus and ventral posterior thalamic nuclei. Despite the involvement of the cerebellum in both tremor types, the loci were different, being focal to the cerebellar cortex and lobules VI and X in Holmes tremor [18] but involving cerebellar white matter lobules VIIb, VIIIa, VIIIb, and IX in AUD tremor herein. Taken together, the correlations observed tracked an AUD-related tremoragenic brain network with the possibility that disruption of any of its nodes could initiate or exacerbate tremor (cf., [21, 22, 64]).

An early study of progressive cerebellar anterior lobe atrophy conducted over 3.5 years reported a tremor frequency shift from 3.5–2.3 Hz in anteroposterior sway with eyes closed; this decreasing shift in the dominant postural tremor frequency occurred with an increase in long-loop muscle reflex latencies used to stabilize sway [11]. Mauritz and colleagues also referred to a series of relevant studies that identified neural system of these responses that involved the cerebellar interpositus nucleus connecting to motor regions of the precentral cortex via the ventrolateral thalamus [21].

Aging

Overall, tremor was stronger with older age in all four groups, but the statistical age functions differed by tremor band, test condition, and sex. Age was best fit with a quadratic (age + age^2) function with more rapid change with advancing age for the control men and women and the AUD men. Despite the overall greater tremor exhibited by the AUD men, their tremor did not show faster aging than the controls. The AUD women showed a linear aging effect on tremor in the M/L axis and only for the eyes open condition at 5–7 Hz. The absence of an age-AUD interaction in tremor intensity comports with the same pattern of effects observed in these data when analyzed in terms of path length [24] but differs from the pattern observed previously of greater frontal cortical volume deficits associated with older than younger onset age of AUD and accelerated volume deficits in AUD than control participants [25].

Limitations

Several study limitations should be acknowledged. Firstly, the men and women with AUD were not matched on alcohol consumption variables, including lifetime alcohol consumption and recency of consumption. Further, the sex distributions were biased with AUD men outnumbering the AUD women by nearly 3-fold. Within this limitation, we had no evidence of "telescoping" where AUD women would exhibit significantly greater dysfunction than AUD men with similar drinking history factors (for reviews, [67–70]). AUD men commonly drink more than AUD women, as observed here, yet postural tremor magnitude did not correlate significantly amount of alcohol consumed in a lifetime although greater tremor was present in AUD men who had resumed drinking at levels exceeding the NIAAA guidelines. Another limitation is the lack of objective measurement of muscle response while balancing. Such data could inform static posture data regarding long-loop muscle responsivity that occurs with long excursions in sway requiring correction to avoid falls.

CONCLUSIONS

The salient signs of postural tremor were attributable to AUD men who consumed alcohol exceeding NIAAA guideline limits in the year prior to testing and may have also contributed to their reports of having experienced more falls in the past year than control men. Age-related postural tremor especially when combined with continued drinking in individuals with AUD are vulnerability factors for falls possibly related to compromised ability to engage long loop reflexes to correct for instability. On a positive note, AUD men and women were able quell their excessive tremor with information from vision as did their control counterparts. This visually-based improvement occurred despite relations between greater tremor and smaller volumes of motor structures in tremoragenic brain networks, indicating the critical role of adequate lighting to mitigate postural tremor and possibly falling, for example, while walking or rising from bed at night.

DATA AVAILABILITY

De-identified data will be made available if requested.

REFERENCES

1. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web–based Injury Statistics Query and Reporting System (WISQARS) Reviewed: May 16, 2024. Available at: https://www.cdc.gov/falls/about/index.html#:~:text=Falls%20can%20be%20prevented.,injury%20death%20for%20that%20group.
2. Cook A, Swindall R, Spencer K, Wadle C, Cage SA, Mohiuddin M, et al. Hospitalization and readmission after single-level fall: a population-based sample. Inj Epidemiol. 2023;10:49.
3. Reider L, Falvey JR, Okoye SM, Wolff JL, Levy JF. Cost of U.S emergency department and inpatient visits for fall injuries in older adults. Injury. 2024;55:111199.
4. Itzkowitz NG, Burford KG, Crowe RP, Wang HE, Lo AX, Rundle AG Prevalence of indications of alcohol and drug use among patients treated for injurious falls by emergency medical services in the USA. Inj Prev. 2025. https://doi.org/10.1136/ip-2024-045447.
5. Houa M, Tomberg C, Noel X. Alcohol and its impact on motor control. J Psychophysiol. 2010;24:259–63.
6. Sullivan EV, Deshmukh A, Desmond JE, Lim KO, Pfefferbaum A. Cerebellar volume decline in normal aging, alcoholism, and Korsakoff's syndrome: relation to ataxia. Neuropsychology. 2000;14:341–52.
7. Sullivan EV, Rose J, Pfefferbaum A. Effect of vision, touch and stance on cerebellar vermian-related sway and tremor: a quantitative physiological and MRI study. Cereb Cortex. 2006;16:1077–86.
8. Baloh RW, Jacobson KM, Beykirch K, Honrubia V. Static and dynamic posturography in patients with vestibular and cerebellar lesions. Arch Neurol. 1998;55:649–54.
9. Sullivan EV, Zahr NM, Rohlfing T, Pfefferbaum A. Cognitive demands during quiet standing elicit truncal tremor in two frequency bands: differential relations to tissue integrity of corticospinal tracts and cortical targets. Front Hum Neurosci. 2015;9:175.
10. Diener HC, Dichgans J, Bacher M, Guschlbauer B. Characteristic alterations of long-loop "reflexes" in patients with Friedreich's disease and late atrophy of the cerebellar anterior lobe. J Neurol Neurosurg Psychiatry. 1984;47:679–85.
11. Mauritz KH, Schmitt C, Dichgans J. Delayed and enhanced long latency reflexes as the possible cause of postural tremor in late cerebellar atrophy. Brain. 1981;104:97–116.
12. Deuschl G, Bergman H. Pathophysiology of nonparkinsonian tremors. Mov Disord. 2002;17:S41–8.
13. Silfverskiold BP. Cortical cerebellar degeneration associated with a specific disorder of standing and locomotion. Acta Neurol Scand. 1977;55:257–72.
14. Gilman S. A mechanism underlying cerebellar hypotonia. Trans Am Neurol Assoc. 1968;93:213–5.
15. Andersen BB. Reduction of Purkinje cell volume in cerebellum of alcoholics. Brain Res. 2004;1007:10–8.
16. Dlugos CA, Pentney RJ. Morphometric evidence that the total number of synapses on Purkinje neurons of old F344 rats is reduced after long-term ethanol treatment and restored to control levels after recovery. Alcohol Alcohol. 1997;32:161–72.
17. Brown P, Rothwell JC, Stevens JM, Lees AJ, Marsden CD. Cerebellar axial postural tremor. Mov Disord. 1997;12:977–84.
18. Manto M. Cerebellar motor syndrome from children to the elderly. Handb Clin Neurol. 2018;154:151–66.
19. Schoeberl F, Dowsett J, Pradhan C, Grabova D, Kohler A, Taylor P, et al. TMS of the left primary motor cortex improves tremor intensity and postural control in primary orthostatic tremor. J Neurol. 2024;271:2938–47.

20. Masdeu JC. Gait and balance disorders. Handb Clin Neurol. 2016;136:939–55.
21. Murphy JT, Kwan HC, MacKay WA, Wong YC. Physiological basis of cerebellar dysmetria. Can J Neurol Sci. 1975;2:279–84.
22. Coffman KA, Dum RP, Strick PL. Cerebellar vermis is a target of projections from the motor areas in the cerebral cortex. Proc Natl Acad Sci USA. 2011;108:16068–73.
23. Sullivan EV, Zahr NM, Sassoon SA, Pohl KM, Pfefferbaum A. Postural instability in HIV infection: relation to central and peripheral nervous system markers. AIDS. 2023;37:1085–96.
24. Sullivan EV, Zahr NM, Sassoon SA, Pfefferbaum A. Disturbed sensory physiology underlies poor balance and disrupts activities of daily living in alcohol use disorder. Addict Biol. 2021;26:e12966.
25. Sullivan EV, Zahr NM, Sassoon SA, Thompson WK, Kwon D, Pohl KM, et al. The role of aging, drug dependence, and hepatitis C comorbidity in alcoholism cortical compromise. JAMA Psychiatry. 2018;75:474–83.
26. Pfefferbaum A, Zahr NM, Sassoon SA, Kwon D, Pohl KM, Sullivan EV. Accelerated and premature aging characterizing regional cortical volume loss in human immunodeficiency virus infection: contributions from alcohol, substance use, and hepatitis C coinfection. Biol Psychiatry Cogn Neurosci Neuroimaging. 2018;3:844–59.
27. Pfefferbaum A, Zahr NM, Sassoon SA, Fama R, Saranathan M, Pohl KM, et al. Aging, HIV infection, and alcohol exert synergist effects on regional thalamic volumes resulting in functional impairment. Neuroimage Clin. 2024;44:103684.
28. Bauer LO, Ceballos NA, Shanley JD, Wolfson LI. Sensorimotor dysfunction in HIV/AIDS: effects of antiretroviral treatment and comorbid psychiatric disorders. AIDS. 2005;19:495–502.
29. Ducic I, Taylor NS, Dellon AL. Relationship between peripheral nerve decompression and gain of pedal sensibility and balance in patients with peripheral neuropathy. Ann Plast Surg. 2006;56:145–50.
30. Sullivan EV, Zahr NM, Zhao Q, Pohl KM, Sassoon SA, Pfefferbaum A. Contributions of cerebral white matter hyperintensities to postural instability in aging with and without alcohol use disorder. Biol Psychiatry Cogn Neurosci Neuroimaging. 2024;9:998–1009.
31. First M. Diagnostic and statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR). Washington, DC: American Psychiatric Association; 2000.
32. American Psychiatric Association. Diagnostic and statistical manual of mental disorder (DSM-V). Washington, D.C.: American Psychiatric Association; 2013.
33. Skinner HA. Development and validation of a lifetime alcohol consumption assessment procedure. Toronto, Canada: Addiction Research Foundation; 1982.
34. Skinner HA, Sheu WJ. Reliability of alcohol use indices: the lifetime drinking history and the MAST. J Stud Alcohol. 1982;43:1157–70.
35. Baloh RW, Fife TD, Zwerling L, Socotch T, Jacobson K, Bell T, et al. Comparison of static and dynamic posturography in young and older normal people. J Am Geriatr Soc. 1994;42:405–12.
36. Corkin S, Milner B, Rasmussen T. Somatosensory thresholds–contrasting effects of postcentral-gyrus and posterior parietal-lobe excisions. Arch Neurol. 1970;23:41–58.
37. Sullivan EV, Zahr NM, Sassoon SA, Pfefferbaum A. Aging accelerates postural instability in HIV infection: contributing sensory biomarkers. J Neuroimmune Pharmacol. 2022;17:538–52.
38. Adeli E, Zahr NM, Pfefferbaum A, Sullivan EV, Pohl KM. Novel machine learning identifies brain patterns distinguishing diagnostic membership of human immunodeficiency virus, alcoholism, and their comorbidity of individuals. Biol Psychiatry Cogn Neurosci Neuroimaging. 2019;4:589–99.
39. Coupe P, Yger P, Prima S, Hellier P, Kervrann C, Barillot C. An optimized blockwise nonlocal means denoising filter for 3-D magnetic resonance images. IEEE Trans Med Imaging. 2008;27:425–41.
40. Tustison NJ, Avants BB, Cook PA, Zheng Y, Egan A, Yushkevich PA, et al. N4ITK: improved N3 bias correction. IEEE Trans Med Imaging. 2010;29:1310–20.
41. Rohlfing T, Maurer CR. Nonrigid image registration in shared-memory multiprocessor environments with application to brains, breasts, and bees. IEEE Trans Inf Technol Biomed. 2003;7:16–25.
42. Rohlfing T, Zahr NM, Sullivan EV, Pfefferbaum A. The SRI24 multichannel atlas of normal adult human brain structure. Hum Brain Mapp. 2010;31:798–819.
43. Avants BB, Epstein CL, Grossman M, Gee JC. Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain. Med Image Anal. 2008;12:26–41.
44. Rohlfing T, Russakoff DB, Maurer CR Jr. Performance-based classifier combination in atlas-based image segmentation using expectation-maximization parameter estimation. IEEE Trans Med Imaging. 2004;23:983–94.
45. Smith SM. Fast robust automated brain extraction. Hum Brain Mapp. 2002;17:143–55.
46. Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res. 1996;29:162–73.
47. Sadananthan SA, Zheng W, Chee MW, Zagorodnov V. Skull stripping using graph cuts. Neuroimage. 2010;49:225–39.
48. Iglesias JE, Liu CY, Thompson PM, Tu Z. Robust brain extraction across datasets and comparison with publicly available methods. IEEE Trans Med Imaging. 2011;30:1617–34.
49. Avants BB, Tustison NJ, Wu J, Cook PA, Gee JC. An open source multivariate framework for n-tissue segmentation with evaluation on public data. Neuroinformatics. 2011;9:381–400.
50. Fama R, Sassoon SA, Muller-Oehring EM, Saranathan M, Pohl KM, Zahr NM, et al. Anterior and posterior thalamic volumes differentially correlate with memory, attention, and motor processes in HIV infection and alcohol use disorder comorbidity. Brain Res Bull. 2024;217:111085.
51. Pfefferbaum A, Sullivan EV, Zahr NM, Pohl KM, Saranathan M. Multi-atlas thalamic nuclei segmentation on standard T1-weighed MRI with application to normal aging. Hum Brain Mapp. 2023;44:612–28.
52. Vidal JP, Danet L, Peran P, Pariente J, Bach Cuadra M, Zahr NM, et al. Robust thalamic nuclei segmentation from T1-weighted MRI using polynomial intensity transformation. Brain Struct Funct. 2024;229:1087–101.
53. Sullivan EV, Moore EM, Lane B, Pohl KM, Riley EP, Pfefferbaum A. Graded cerebellar lobular volume deficits in adolescents and young adults with fetal alcohol spectrum disorders (FASD). Cereb Cortex. 2020;30:4729–46.
54. Manjon JV, Coupe P. volBrain: an online MRI brain volumetry system. Front Neuroinform. 2016;10:30.
55. Romero JE, Coupe P, Giraud R, Ta VT, Fonov V, Park MTM, et al. CERES: a new cerebellum lobule segmentation method. Neuroimage. 2017;147:916–24.
56. Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC. A reproducible evaluation of ANTs similarity metric performance in brain image registration. Neuroimage. 2011;54:2033–44.
57. Pfefferbaum A, Kwon D, Brumback T, Thompson WK, Cummins K, Tapert SF, et al. Altered brain developmental trajectories in adolescents after initiating drinking. Am J Psychiatry. 2018;175:370–80.
58. Ahmad S, Rohrbaugh JW, Anokhin AP, Sirevaag EJ, Goebel JA. Effects of lifetime ethanol consumption on postural control: a computerized dynamic posturography study. J Vestib Res. 2002;12:53–64.
59. Koller W, O'Hara R, Dorus W, Bauer J. Tremor in chronic alcoholism. Neurology. 1985;35:1660–2.
60. Stephen R, Elizabeth Y, Christophe H. Participation of the caudal cerebellar lobule IX to the dorsal attentional network. Cerebellum Ataxias. 2018;5:9.
61. Mergner T, Schweigart G, Fennell L, Maurer C. Posture control in vestibular-loss patients. Ann N Y Acad Sci. 2009;1164:206–15.
62. Diener HC, Dichgans J, Bacher M, Guschlbauer B. Improvement of ataxia in alcoholic cerebellar atrophy through alcohol abstinence. J Neurol. 1984;231:258–62.
63. Melo TP, Bogousslavsky J. Hemiataxia-hypesthesia: a thalamic stroke syndrome. J Neurol Neurosurg Psychiatry. 1992;55:581–4.
64. Joutsa J, Shih LC, Fox MD. Mapping holmes tremor circuit using the human brain connectome. Ann Neurol. 2019;86:812–20.
65. Frucht SJ. Evaluation of patients with tremor. Pract Neurol. 2018:58–62. https://practicalneurology.com/diseases-diagnoses/movement-disorders/evaluation-of-patients-with-tremor/30247/.
66. Holmes G. On certain tremors in organic cerebral lesions. Brain. 1904;27:327–75.
67. Nixon SJ, Garcia CC, Lewis B. Women's use of alcohol: neurobiobehavioral concomitants and consequences. Front Neuroendocrinol. 2023;70:101079.
68. Kirsch DE, Belnap MA, Kady A, Ray LA. A narrative review on alcohol use in women: insight into the telescoping hypothesis from a biopsychosocial perspective. Am J Drug Alcohol Abuse. 2025;51:14–30.
69. Fama R, Le Berre AP, Sullivan EV. Alcohol's unique effects on cognition in women: a 2020 (Re)view to envision future research and treatment. Alcohol Res. 2020;40:03.
70. Ellis RL, Hallgren KA, Williams EC, Glass JE, Rhew IC, Oliver M, et al. Variations in documentation of alcohol use disorder (AUD) diagnoses across race, ethnicity, and sex in a health system that assesses AUD symptoms as part of routine primary care. J Subst Use Addict Treat. 2025;172:209654.

AUTHOR CONTRIBUTIONS

EVS and AP: Study design, data acquisition and oversight, data analysis, figure and table construction, manuscript writing (all drafts). EVS, SAS, and NMZ: Subject recruitment and data curation. SAS: SCID and alcohol interviews and clinical data curation. AP, MS, KMP: MRI data processing. AP: Statistical analysis. All authors contributed to intellectual discussions and manuscript editing.

FUNDING

The National Institutes of Health (AA005965 to AP, AA010723 to EVS, AG081144 and EB032674 to MK) provided financial support for the conduct of the research.

COMPETING INTERESTS

The authors declare no competing interests.

SUBMISSION DECLARATION AND VERIFICATION

We note in the Methods that the mainstay of the sway path force platform and neuroimaging data was published separately but not in terms of postural tremor. The current analysis repurposed and jointly analyzed published data to address questions regarding the potential contributions of regional brain volumes to truncal (postural) tremor and instability measured with force platform technology in healthy aging and AUD.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41398-025-03552-8.

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