

**Supplementary Table 1** Clinical and pathological features of controls and ET grouped by age of tremor onset 40 years

Variables	Controls	ET Cases		<i>p</i> value (all three groups)	<i>p</i> value		
		Age of tremor onset <40 years	Age of tremor onset ≥40 years		Control vs. ET <40 years	Control vs. ET ≥40 years	ET <40 years vs. ET ≥40 years
n	30	24	36				
Age at death (years)	84.2 ± 8.6	86.2 ± 6.3	86.8 ± 4.8	0.283 <sup>a</sup>	0.540 <sup>b</sup>	0.266 <sup>b</sup>	0.929 <sup>b</sup>
Age of tremor onset (years)	NA	18.9 ± 8.6	58.4 ± 9.8				<b>&lt;0.001<sup>c</sup></b>
Duration of tremor (years)	NA	67.5 ± 9.6	28.4 ± 11.0				<b>&lt;0.001<sup>c</sup></b>
Gender				0.569 <sup>d</sup>	0.358 <sup>d</sup>	0.365 <sup>d</sup>	0.914 <sup>d</sup>
Male	15 (50.0%)	9 (37.5%)	14 (38.9%)				
Female	15 (50.0%)	15 (62.5%)	22 (61.1%)				
PC counts	10.6 ± 1.9	9.2 ± 1.3	8.7 ± 1.4	<b>0.008<sup>a</sup></b>	0.060 <sup>b</sup>	<b>0.005<sup>b</sup></b>	0.566 <sup>b</sup>
Torpedo counts	5.4 ± 4.0 Median = 4.0	25.8 ± 26.4 Median = 15.0	28.7 ± 29.6 Median = 17.0	<b>0.006<sup>e</sup></b>	<b>0.004<sup>f</sup></b>	<b>0.002<sup>f</sup></b>	0.783 <sup>f</sup>
CF synaptic density (puncta/100μm)	21.9 ± 3.6 Median = 22.5	18.46 ± 2.83 Median = 18.0	17.6 ± 1.8 Median = 17.5	<b>&lt;0.001<sup>e</sup></b>	<b>&lt;0.001<sup>f</sup></b>	<b>&lt;0.001<sup>f</sup></b>	0.344 <sup>f</sup>
Percentage of CFs extending into the PF territory	20.2 ± 9.2	27.3 ± 6.9	30.0 ± 6.6	<b>&lt;0.001<sup>a</sup></b>	<b>0.003<sup>b</sup></b>	<b>&lt;0.001<sup>b</sup></b>	0.355 <sup>b</sup>

Values represent mean ± standard deviation or number (percentage), and for variables with a non-normal distribution, the median is reported as well. Mean number of PC counts per 100x microscopic field, among 15 sampled fields. Bolded values are significant (with Bonferroni correction).

NA not applicable

<sup>a</sup>One-way analysis of variance (ANOVA)

<sup>b</sup>Post hoc multiple comparisons (Tukey HSD) in one-way analysis of variance (ANOVA)

<sup>c</sup>Independent samples *t* test

<sup>d</sup>Chi-square test

<sup>e</sup>Independent samples Kruskal-Wallis H test

<sup>f</sup>Independent samples Mann-Whitney U test

Abbreviations: PC: Purkinje cells, CF: climbing fiber, PF: parallel fiber.

**Supplementary Table 2** Clinical and pathological features of controls and ET grouped by age of tremor onset 60 years

Variables	Controls	ET Cases		<i>p</i> value (all three groups)	<i>p</i> value		
		Age of tremor onset <60 years	Age of tremor onset ≥60 years		Control vs. ET <40 years	Control vs. ET ≥40 years	ET <40 years vs. ET ≥40 years
<i>n</i>	30	41	19				
Age at death (years)	84.2 ± 8.6	86.2 ± 5.8	87.4 ± 4.4	0.238 <sup>a</sup>	0.456 <sup>b</sup>	0.235 <sup>b</sup>	0.768 <sup>b</sup>
Age of tremor onset (years)	NA	31.9 ± 17.4 Median = 28.0	65.7 ± 6.0 Median = 64.5				<b>&lt;0.001<sup>c</sup></b>
Duration of tremor (years)	NA	54.4 ± 18.4	21.7 ± 7.2				<b>&lt;0.001<sup>d</sup></b>
Gender				0.441 <sup>e</sup>	0.475 <sup>e</sup>	0.204 <sup>e</sup>	0.464 <sup>e</sup>
Male	15 (50.0%)	17 (41.5%)	6 (46.2%)				
Female	15 (50.0%)	24 (58.5%)	13 (53.8%)				
PC counts	10.6 ± 1.9	9.3 ± 1.3	8.3 ± 1.3	<b>0.001<sup>a</sup></b>	<b>0.039<sup>b</sup></b>	<b>0.001<sup>b</sup></b>	0.091 <sup>b</sup>
Torpedo counts	5.4 ± 4.0 Median = 4.0	28.4 ± 30.2 Median = 17.0	24.9 ± 22.6 Median = 16.5	<b>0.006<sup>f</sup></b>	<b>0.001<sup>c</sup></b>	<b>0.012<sup>c</sup></b>	0.810 <sup>c</sup>
CF synaptic density (puncta/100μm)	21.9 ± 3.6 Median = 22.5	18.5 ± 2.4 Median = 18.0	16.7 ± 1.5 Median = 17.0	<b>&lt;0.001<sup>f</sup></b>	<b>&lt;0.001<sup>c</sup></b>	<b>&lt;0.001<sup>c</sup></b>	<b>0.005<sup>c</sup></b>
Percentage of CFs extending into the PF territory	20.2 ± 9.2	28.3 ± 6.8	30.2 ± 6.8	<b>&lt;0.001<sup>a</sup></b>	<b>&lt;0.001<sup>b</sup></b>	<b>&lt;0.001<sup>b</sup></b>	0.649 <sup>b</sup>

Values represent mean ± standard deviation or number (percentage), and for variables with a non-normal distribution, the median is reported as well. Mean number of PC counts per 100x microscopic field, among 15 sampled fields. Bolded values are significant (with Bonferroni correction).

NA not applicable

<sup>a</sup>One-way analysis of variance (ANOVA)

<sup>b</sup>Post hoc multiple comparisons (Tukey HSD) in one-way analysis of variance (ANOVA)

<sup>c</sup>Independent samples Mann-Whitney U test

<sup>d</sup>Independent samples *t* test

<sup>e</sup>Chi-square test

<sup>f</sup>Independent samples Kruskal-Wallis H test

Abbreviations: PC: Purkinje cells, CF: climbing fiber, PF: parallel fiber.

**Supplementary Table 3** Clinical and pathological features of controls and essential tremor grouped by childhood ( $\leq 18$  years) vs. adult ( $> 18$  years) onset

Variables	Controls	ET Cases		<i>p</i> value (all three groups)	<i>p</i> value		
		Age of tremor onset <20 years	Age of tremor onset $\geq 20$ years		Control vs. ET <20 years	Control vs. ET $\geq 20$ years	ET <20 years vs. ET $\geq 20$ years
n	30	13	47				
Age at death (years)	84.2 $\pm$ 8.6	86.0 $\pm$ 7.0	86.7 $\pm$ 5.0	0.285 <sup>a</sup>	0.704 <sup>b</sup>	0.256 <sup>b</sup>	0.939 <sup>b</sup>
Age of tremor onset (years)	NA	12.5 $\pm$ 3.7 Median = 13.0	50.9 $\pm$ 16.4 Median = 55.0				<b>&lt;0.001<sup>c</sup></b>
Duration of tremor (years)	NA	73.0 $\pm$ 8.5 Median = 74.0	36.0 $\pm$ 17.2 Median = 32.0				<b>&lt;0.001<sup>c</sup></b>
Gender				0.471 <sup>d</sup>	0.244 <sup>d</sup>	0.409 <sup>d</sup>	0.526 <sup>d</sup>
Male	15 (50.0%)	4 (30.8%)	19 (40.4%)				
Female	15 (50.0%)	9 (69.2%)	28 (59.6%)				
PC counts	10.6 $\pm$ 1.9	9.1 $\pm$ 1.2	8.9 $\pm$ 1.4	<b>0.011<sup>a</sup></b>	0.094 <sup>b</sup>	<b>0.008<sup>b</sup></b>	0.888 <sup>b</sup>
Torpedo counts	5.4 $\pm$ 4.0 Median = 4.0	26.7 $\pm$ 27.9 Median = 21.0	27.6 $\pm$ 28.4 Median = 16.5	<b>0.006<sup>e</sup></b>	<b>0.004<sup>c</sup></b>	<b>0.002<sup>c</sup></b>	0.816 <sup>c</sup>
CF synaptic density (puncta/100 $\mu$ m)	21.9 $\pm$ 3.6 Median = 22.5	18.6 $\pm$ 3.0 Median = 18.0	17.8 $\pm$ 2.1 Median = 18.0	<b>&lt;0.001<sup>e</sup></b>	<b>0.005<sup>c</sup></b>	<b>&lt;0.001<sup>c</sup></b>	0.399 <sup>c</sup>
Percentage of CF extending into PF territory	20.2 $\pm$ 9.2	27.4 $\pm$ 4.4	29.3 $\pm$ 7.3	<b>&lt;0.001<sup>a</sup></b>	0.016 <sup>b</sup>	<b>&lt;0.001<sup>b</sup></b>	0.696 <sup>b</sup>

Values represent mean  $\pm$  standard deviation or number (percentage), and for variables with a non-normal distribution, the median is reported as well. Mean number of PC counts per 100 $\times$  microscopic field, among 15 sampled fields. Bolded values are significant (with Bonferroni Correction).

<sup>a</sup>One-way analysis of variance (ANOVA)

<sup>b</sup>Post hoc multiple comparisons (Tukey HSD) in one-way analysis of variance (ANOVA)

<sup>c</sup>Independent samples Mann-Whitney U test

<sup>d</sup>Chi-square test

<sup>e</sup>Independent samples Kruskal-Wallis H test

Abbreviations: PC: Purkinje cells, CF: climbing fiber, PF: parallel fiber.

**Supplementary Table 4** Clinical and pathological features of ET grouped by head tremor

Variables	Controls	ET Cases		<i>p</i> value (all three groups)	<i>p</i> value		
		Head tremor	No head tremor		Control vs. head tremor	Control vs. no head tremor	Head tremor vs. no head tremor
n	30	36	24				
Age at death (years)	84.2 ± 8.5 Median = 84.0	85.6 ± 5.8 Median = 86.5	87.9 ± 4.6 Median = 89.0	0.068 <sup>a</sup>	0.363 <sup>b</sup>	0.036 <sup>b</sup>	0.071 <sup>b</sup>
Age of tremor onset (years)		38.8 ± 23.3 Median = 41.0	48.3 ± 17.8 Median = 54.0				0.149 <sup>b</sup>
Duration of tremor (years)		46.6 ± 23.9	40.1 ± 18.3				0.260 <sup>c</sup>
Gender				0.073 <sup>d</sup>	0.064 <sup>d</sup>	0.761 <sup>d</sup>	0.039 <sup>d</sup>
Male	15 (50.0%)	10 (27.8%)	13 (54.2%)				
Female	15 (50.0%)	26 (72.2%)	11 (45.8%)				
Purkinje cell counts	10.6 ± 1.9	8.9 ± 1.2	9.1 ± 1.7	<b>0.011<sup>e</sup></b>	<b>0.008<sup>f</sup></b>	0.058 <sup>f</sup>	0.853 <sup>f</sup>
Torpedo counts	5.4 ± 4.0 Median = 4.0	26.2 ± 27.3 Median = 16.0	30.2 ± 30.4 Median = 19.0	<b>0.005<sup>a</sup></b>	<b>0.003<sup>b</sup></b>	<b>0.001<sup>b</sup></b>	0.506 <sup>b</sup>
CF synaptic density (puncta/100 um)	21.9 ± 3.6 Median = 22.5	18.5 ± 2.4 Median = 18.0	17.2 ± 1.8 Median = 17.0	<b>&lt;0.001<sup>a</sup></b>	<b>&lt;0.001<sup>b</sup></b>	<b>&lt;0.001<sup>b</sup></b>	0.031 <sup>b</sup>
Percentage of CF extending into outer 20% ML	20.2 ± 9.2	27.5 ± 6.5	31.1 ± 6.9	<b>&lt;0.001<sup>e</sup></b>	<b>0.001<sup>f</sup></b>	<b>&lt;0.001<sup>f</sup></b>	0.172 <sup>f</sup>

Values represent mean ± standard deviation or number (percentage), and for variables with a non-normal distribution, the median is reported as well. Mean number of PC counts per 100× microscopic field, among 15 sampled fields. 48 ET cases had head tremor assessed using a video examination, and the other 12 had head tremor assessed using clinical information. Bolded values are significant (with Bonferroni correction).

<sup>a</sup>Independent samples Kruskal-Wallis H test

<sup>b</sup>Independent samples Mann-Whitney U test

<sup>c</sup>Independent sample *t* test

<sup>d</sup>Chi-square test

<sup>e</sup>One-way analysis of variance (ANOVA)

<sup>f</sup>Post hoc multiple comparisons (Tukey HSD) in one-way analysis of variance (ANOVA)

Abbreviations: PC: Purkinje cells, CF: climbing fiber, PF: parallel fiber.

**Supplementary Table 5** Correlations of clinical and pathological characteristics with climbing fiber pathology

	CF synaptic density		Percentage of CFs in PF Territory	
	r <sup>a</sup>	p value	r <sup>a</sup>	p value
Duration of tremor	0.183	0.161	-0.207	0.112
Tremor Severity (TTS)	0.084	0.566	-0.037	0.802
PC count	0.389	<b>0.005</b>	-0.345	<b>0.014</b>
Torpedo counts	-0.304	<b>0.032</b>	0.374	<b>0.007</b>
CF synaptic density			-0.39	<b>&lt;0.001</b>
Percentage of CFs in the PF Territory	-0.39	<b>&lt;0.001</b>		

Bolded values are significant

<sup>a</sup>Spearman's correlation coefficient

Abbreviations: PC: Purkinje cells, CF: climbing fiber, PF: parallel fiber, TTS: total tremor score.