Supplementary Data

Supplementary Section 1. Database search strategies

1. ET & Genetic*

1.1. PubMed search strategy

(Genetic*[Title/Abstract] OR Genomic[Title/Abstract] OR GWAS[Title/Abstract] OR variant[Title/Abstract]) AND (Essential tremor[Title/Abstract] OR ET[Title/Abstract] OR tremor[Title/Abstract]) AND (Phenotype*OR clinical feature*OR Age at onset OR Tremor severity OR Tremor distribution OR Disease progression OR neurological features*)

1.2 *Scopus search strategy*

TITLE-ABS-KEY ({genetics} OR genetics OR genomic OR GWAS OR variant) AND TITLE-ABS-KEY (ET OR essential AND tremor) AND ({Phenotype} OR Tremor distribution OR Disease progression OR age at onset OR tremor severity OR {clinical feature} OR clinical features OR neurological features)

1.3 *Web of Science search strategy*

AB=(Genetics OR genetic OR genomic OR GWAS) AND AB=("essential tremor" OR ET) AND
AB=(Phenotype OR "clinical feature*" OR "disease progression" OR "tremor distribution" OR "age at onset" OR "tremor severity" OR "neurological feature*")
*Restricted to full text, English, humans, adults and a date of publication between 1 January 2015 and 31 December 2025.

2. Inclusion and exclusion criteria outlined.

Inclusion Criteria	
1	The clinical population must include adult patients diagnosed with essential tremor
2	The article must be clearly investigating genetic variants, loci, or heritable factors
3	Used observational, case-control, cohort genetic association designs.
4	Were published in peer-reviewed journals in English

Table 1 Inclusion criteria for the narrative review

Exclusion Criteria	
1	The article must not present a systematic or literature review or meta-analysis.
2	The article must not present a case study or case series.
3	Sole focus on tremor due to other causes (e.g. Parkinson's disease, dystonia, drug-induced tremor)
4	Were animal or in vitro studies

Table 2 Exclusion criteria for the narrative review

2. Supplementary Table 3. Phenotypic ascertainment and diagnostic heterogeneity across included genetic studies of ET

Study	Diagnostic criteria / assessment	ET vs ET-plus	Specialist assessment / exclusion of mimics	Longitudinal reassessment	Relevance to replication
1 Orsucci 2024	TRIG-based ET criteria; >5-year duration criterion omitted; detailed clinical examination	ET; contemporary study but families selected as dominant ET	In-person examination by investigator experienced in inherited movement disorders; dystonia, PD, drug-induced tremor, thyroid disease and other causes excluded	Limited; clinical histories available but not a formal longitudinal diagnostic study	Relatively strong phenotype ascertainment, although modification of standard duration criteria and familial selection may reduce comparability with population cohorts.

2 Ortega-Cubero 2015	Definite/probable ET using pre-2018 consensus criteria	ET-plus not assessed	Movement-disorder specialist diagnosis	No formal longitudinal reassessment reported	Conventional pre-2018 ET definition; differences from later ET/ET-plus cohorts could contribute to replication differences.

3 Clark 2015	Research ET criteria with detailed videotaped neurological examination	ET-plus not assessed	Detailed neurological/video evaluation; other diagnoses screened clinically	No systematic longitudinal reassessment reported	Stronger phenotyping than questionnaire-only studies, but pre-2018 definition means mild additional signs were not classified using current ET-plus terminology.

4 Yuan 2016	Definite ET according to Deuschl/Louis criteria	ET-plus not assessed	Two independent neurologists; PD, dystonia, myoclonus, neuropathy and other tremor causes excluded	No	Fairly well-defined classical ET phenotype; negative result less likely to be explained solely by gross misclassification.

5 Ayuso 2015	Definite ET, 1998 MDS criteria	ET-plus not assessed	Movement-disorder units; other neurological disease and thyroid abnormalities excluded	No formal reassessment reported	Familial definite-ET selection differs from sporadic/community cohorts and could contribute to inconsistent candidate-gene findings.

6 Clark 2015	Research ET criteria with videotaped examination and senior neurological review	ET-plus not assessed	Parkinsonism generally excluded, although isolated rest tremor could be retained	No systematic follow-up	Inclusion of isolated rest tremor is important: under contemporary classification some individuals might be ET-plus or diagnostically uncertain, affecting comparison with stricter cohorts.

7 Jiménez-Jiménez	Probable/definite ET using standardized pre-2018 criteria	ET-plus not assessed	Two movement-disorder neurologists	No systematic longitudinal reassessment	Some affected relatives had parkinsonian features, increasing phenotype heterogeneity and potentially contributing to inconsistent MAPT/SLC1A2/DRD3 findings.

8 Sun 2020	1998 MDS ET criteria	Originally classified as ET; molecular findings raise possibility of NOTCH2NLC-related/NIID tremor phenotype rather than conventional ET	≥2 experienced neurologists; MRI/CT; known SCA, FMR1 and other repeat disorders excluded	Follow-up performed, but duration insufficient to completely exclude later NIID manifestations	Particularly important example of apparent “ET” being a molecularly distinct tremor syndrome; inclusion/exclusion of such cases can markedly alter genetic results.

9 Diez-Fairen 2021	TRIG criteria, with >5-year-duration requirement omitted	Pre-2018-style familial ET ascertainment	Specialist assessment; dystonia, PD, enhanced physiological and drug-induced tremor excluded	No major longitudinal reclassification reported	Strong exclusion of mimics, but modified diagnostic criteria and highly selected familial cohort limit direct comparability with sporadic studies.

10 Müller 2016	ET diagnosed across multiple contributing cohorts using pre-2018 clinical criteria; 1998 MDS criteria (suplementary data)	ET-plus not assessed	Specialist ascertainment varied between contributing cohorts	No uniform longitudinal reassessment	Phenotypic harmonisation was incomplete across centres. This is important when interpreting failure to replicate earlier loci and modest GWAS effects.

11 Chao 2015	Classical ET using 1998 MDS criteria	ET-plus not assessed	Movement-disorder specialists	No reported longitudinal reassessment	Standard pre-2018 phenotype but relatively broad clinical ET definition; population-specific ascertainment may contribute to non-replication.

12 Odgerel 2019	WHIGET; possible/probable/definite ET included	ET-plus not formally assessed	Detailed family phenotyping; alternative tremor diagnoses considered	No uniform longitudinal reassessment	Inclusion of possible as well as probable/definite ETbroadens the phenotype and can weaken segregation and reproducibility of rare variants.

13 Clark 2022	WHIGET-based detailed in-person/video phenotyping	ET classification broad enough that the linkage dataset included some subjects with PD, dystonia or mild tremor statuses	Strong specialist phenotyping; analyses also examined stricter affected definitions	Some repeat/reassessment information available, but not a prospective longitudinal diagnostic study	Demonstrates how affection-status definition changes genetic analysis; phenotype refinement is particularly important in family linkage/WGS studies.

14 Hicks 2016	Definite classical ET, MDS consensus criteria; persistent bilateral postural/kinetic hand/forearm tremor	ET-plus not assessed	Standard neurological examination; tremor caused by another disorder/cause excluded; non-definite relatives coded unknown	No formal longitudinal reassessment reported	Relatively strict phenotype definition reduces heterogeneity, but single-family linkage remains vulnerable to later diagnostic reclassification.

15 Yuan 2018	Definite ET according to established pre-2018 criteria	ET-plus not assessed	Two senior neurologists; alternative movement disorders excluded	No	Classical candidate-gene cohort; negative/nominal findings should still be interpreted in context of pre-2018 phenotype definitions.

16 Agúndez 2022	Definite ET, Deuschl 1998 criteria; all cases familial	ET-plus not assessed	Specialist clinical diagnosis	No systematic longitudinal reassessment	Familial definite ET is a genetically enriched phenotype and may not replicate findings from sporadic/mixed cohorts.

17 Agúndez 2024	Definite ET using established clinical criteria	Contemporary publication, but ET-plus stratification not central/reported	Specialist clinical ascertainment	No formal longitudinal analysis reported	Negative overall association is less susceptible to obvious diagnostic contamination, but comparison with older cohorts remains limited by changing definitions.
Agúndez 2017	Definite familial ET using pre-2018 criteria	ET-plus not assessed	Specialist clinical diagnosis	No	Selected familial phenotype and candidate-gene design limit generalisability.

Emamalizadeh 2017	ET cases clinically diagnosed, but detailed formal criteria/specialist phenotyping were less clearly reported	ET-plus not assessed	Less detailed phenotype documentation than several other studies	No	Phenotypic uncertainty is a significant limitation, alongside lack of ancestry/PCA control, when interpreting the nominal association.

20 Sazci 2019	ET diagnosed by movement-disorder specialist; exact formal consensus criteria less clearly documented	ET-plus not assessed	Specialist assessment	No	Less detailed phenotype definition plus small sample/low power makes comparison with Agúndez and other VDR studies difficult.

21 Chen 2019	1998 MDS criteria with standardized Louis examination	ET-plus not assessed	Two movement-disorder specialists independently examined cases; senior specialist adjudicated disagreement. Parkinsonism, drug-induced tremor, cerebellar tremor, dystonia and hyperthyroid tremor were excluded.	No formal longitudinal reassessment reported	Strong cross-sectional phenotype ascertainment; differences from studies with looser definitions remain a plausible contributor to candidate-gene non-replication.

22 Hor 2015	1998 MDS consensus criteria; clinical tremor rating	ET-plus not assessed	Movement-disorder specialists; additional neurological features assessed	No systematic long-term diagnostic reassessment	Incomplete segregation and later failure to consistently reproduce TENM4 cannot be attributed to genetics alone; pre-2018 phenotype definition and possible phenocopies remain relevant.

23 Ng et al. 2020	1998 MDS ET criteria	Cases initially ET; expansion-positive cases better considered possible NOTCH2NLC-related/NIID tremor phenotypes	Neurological work-up with molecular repeat testing; some expansion carriers underwent further imaging/pathological evaluation	Some longitudinal phenotype information available	Supports the point that molecular reclassification after genetic testing can explain why repeat-expansion findings vary between apparently similar ET cohorts.

25 Liu 2016	WHIGET and 1998 MDS criteria; definite/probable familial early-onset ET	ET-plus not assessed	In-person/video assessment; PD, dystonia and alternative tremors excluded	No systematic prospective reassessment	Strong phenotype ascertainment, but early-onset multigenerational families represent a highly selected subgroup and rare variants may remain family-specific.

26 Bergareche 2015	1998 MDS + WHIGET; diagnosis made at first evaluation and confirmed after a second evaluation	ET-plus terminology unavailable, although mild ataxic/rest-tremor features occurred in some relatives	Three experienced movement-disorder specialists; assessment explicitly sought dystonia, myoclonus, ataxia and polyneuropathy.	Yes — second clinical/electrophysiological evaluation used to confirm diagnosis	One of the better phenotyped family studies, but heterogeneous features plus single-family ascertainment remain important when interpreting failure to find SCN4A variants in additional families.

27 Chao 2015	Classic ET using 1998 MDS consensus	ET-plus not assessed	Consecutive tertiary-centre cases examined by movement-disorder neurologists; other neurodegenerative diseases excluded	No	Large negative replication is useful, but differs substantially from the original HTRA2 ET/PD kindred, supporting phenotype specificity as one explanation for non-replication.

28 Zhang 2021	Contemporary 2018 IPMDS framework; Fahn–Tolosa–Marin TRS and MoCA	Authors explicitly concluded affected relatives were more appropriately ET-plusbecause of mild dystonic signs	Direct examination by two neurologists; detailed video/neurological phenotyping	Re-evaluation of proband at age 74 and reassessment of a relative previously labelled ET led to rejection of that diagnosis	Particularly strong demonstration that diagnosis changes with detailed/repeated assessment. A variant apparently segregating with “ET” actually segregated with an ET-plus family phenotype.

30 Sánchez 2015	1998 MDS + WHIGET; definite ET required bilateral postural/kinetic tremor without other neurological signs	ET-plus not applicable/pre-2018	Movement-disorder neurologists; detailed exam for PD, dystonia, myoclonus, ataxia, neuropathy; TRS, MoCA, EMG	Diagnosis confirmed by team consensus after a second evaluation.	Strong cross-sectional/repeat phenotyping, but an unaffected carrier and lack of replication remain more important than phenotype quality in limiting SORT1 evidence.

31 Leng 2017	Published ET criteria; questionnaire, in-person assessment, video and EMG	Not conventional isolated ET: familial episodic-pain syndrome followed by adult-onset tremor, with later rest tremor	ET diagnosis reconfirmed by senior movement-disorder neurologist; dystonia, parkinsonism, myoclonus and ataxia specifically sought and not found.	Age-dependent phenotype documented, but not a formal serial diagnostic programme	Major phenotype-specificity issue: same variant causes familial pain without ET. Better treated as SCN11A-related syndromic tremor/phenocopy, explaining lack of generalisable ET replication.

32 Chen 2018	1998 MDS consensus criteria	ET-plus not assessed	ET cases clinically evaluated; RLS specialist separately assessed concomitant RLS	No	Candidate association was identified in a small Chinese cohort; lack of detailed modern ET/ET-plus phenotyping and RLS overlap may contribute to non-replication.

33 Diez-Fairen 2019	Re-used Müller et al. GWAS phenotype rather than performing new clinical assessment	ET-plus could not be systematically determined	No new specialist reassessment; detailed phenotype information was unavailable	No	Authors explicitly acknowledge that unrecognised phenotype variability/misdiagnosis may influence heritability estimates. This supports treating diagnostic heterogeneity as a contributor to apparent genetic inconsistency.

Supplementary Table 4: Demographic and Sample Sizes of included. Genetic studies. *ET = Essential Tremore. HCs = healthy controls.*

Study	Authors	Year	Country	Ancestry	Sample size (cases/controls/families
1	Orsucci et al.	2024	Italy	European Italian	34 ET; 14 families.
2	Ortega-Cubero et al.	2015	Spain (discovery); Italy, Germany, North America and Taiwan (replication)	European and Asian	Discovery: 456 ET / 2,715 controls; replication: 897 ET / 1,449 controls

3	Clark et al.	2015	United States	Included 93.8% ET cases and 86.1% non-Hispanic White. 28.8% of total sample reported Ashkenazi Jewish ancestry	321 ET cases / 296 controls
4	Yuan et al.	2016	China	Southern Han Chinese	200 ET cases / 426 controls
5	Ayuso et al.	2015	Spain	Spanish European ancestry	202 familial ET cases / 747 controls
6	Clark et al.	2015	United States	ET cases 93.8 non-Hispanic white v 86.0% controls. Reported 2.2% non-Hispanic black and 2.5% Hispanic et cases w/ 5.7% and 4.0% in controls. ; 38.7% ET cases	323 ET cases / 299 controls

				reported Ashkenazi Jewish ancestry	
7	Jiménez-Jiménez et al.	2016	Spain	Spanish Caucasian ancestry	45 ET + 13 unaffected relatives from 11 ET families; external healthy controls: 324 for DRD3, 308 for SLC1A2, 324 for MAPT
8	Sun et al.	2020	China	Chinese	197 familial ET pedigrees / 1,305 HC; 11 families
9	Diez-Fairen M et al.	2021	Spain, with subsequent replication datasets including European/North American participants	Discovery families: Spanish origin. Gene-burden dataset: European and North American ancestry	Step 1: Initial: 29 ET, 9 unaffected, 2 unclear ET; 8 families (n=40); Step 2: 521 unrelated ET cases / 596 controls Step 3: 789 ET / 770 controls

10	Müller SH et al.	2016	United States, Canada, Germany, Austria and Spain.	North-Western European (CEU) ancestry	Step 1/Discovery: 1,778 ET / 5,376 HC; Step 2/Discovery: 1,029 ET / 1,065 HC (independent cohort) [Total: 2,807 ET cases / 6,441 HC]
11	Chao YX et al	2015	Singapore	Chinese	450 ET / 827 HC [1,277 total]; 161/450 (36%) familial ET
12	Odgerel et al.	2019	United States	Not clearly reported.	31 affected ET, 9 unaffected relatives; 40 individuals from 8 ET families.

13	Clark LN et al.	2022	United States	European ancestry; 11 families (11.1%) reported Ashkenazi Jewish ancestry	350 affected/ET, 101 unaffected + 316 pedigree members without WGS/inferred genotypes; 767 individuals total; 104 multigenerational ET families.
14	Hicks JE et al.	2016	United States	Not clearly reported.	48 ET patients from 49 families; 128 individuals were initially genotyped, with 6 removed due to low quality.
15	Yuan L et al.	2018	China	Han Chinese	200 unrelated ET cases / 432 unrelated controls
16	Agúndez JAG et al.	2022	Spain	Spanish European ancestry	272 familial ET cases / 272 controls
17	Agúndez JAG et al.	2024	Spain	Spanish European ancestry	267 familial ET cases / 270 controls

18	Agúndez JAG et al.	2017	Spain	Spanish European ancestry	202 familial ET cases / 218 healthy controls
19	Emamalizadeh B et al.	2017	Iran	Iranian	350 ET / 350 matched controls
20	Sazci A et al.	2019	Turkey	Caucasian/Turkish	239 sporadic ET / 239 controls
21	Chen J et al.	2019	China	Chinese	200 ET / 229 controls
22	Hor H et al.	2015	Spain	Spanish European ancestry	Step 1/Discovery: 4 affected members of one family (TEF-6). Step 2/WES. TENM4 was then targeted in 299 additional familial ET index cases;
23	Ng et al.	2020	Singapore	Singapore clinical cohort; specific genetic ancestry/ethnicity not reported	462 ET / 200 HC

24	Rajput et al.	2015	North America (Canada/USA)	European descent	571 ET cases; no contemporaneous study controls. Authors note >2,600 unrelated healthy individuals had previously been genotyped
25	Liu et al.	2016	United States	10% of affected WES participants reported Ashkenazi Jewish ancestry; overall ancestry was not otherwise specified	1. Initial family cohort: 52 families (52 probands + 155 relatives). 37 families had completed phenotyping/DNA collection and underwent WES. 2. 100 affected ET and 4 unaffected individuals (104 total) 3. +95 unrelated ET cases were screened for KCNS2

26	Bergareche et al.	2015	Spain	Does not explicitly define genetic ancestry. Ethnicity-matched controls were used.	Step 1: 7 individuals reported affected from 4 multi-generational family; 5 affected individuals were fully clinically evaluated, together with 3 unaffected relatives. Step2: WES was performed in 4 family members: 2 ET, 1 juvenile myoclonic epilepsy (JME), and 1 unaffected. Step 3: Follow-up screening included 76 sporadic + 25 familial Spanish ET cases +22 ET families
27	Chao et al.	2015	Singapore	Asian population; controls were matched for race, age and sex	468 ET, 778 PD, 14 coexistent ET/PD, and 517 HCs; 1,777 individuals total

28	Zhang et al.	2021	Canada	Caucasian Canadian family.	WGS performed in 4 informative family members (3 affected + 1 unaffected), followed by Sanger sequencing across all 8. 1 multigenerational family
29	Sánchez et al.	2015	Spain	Spanish European ancestry	1. Discovery: 1 family with 2 definite ET cases and 4 unaffected relatives. 2. WES: 2 affected + 2 unaffected. 3. Follow-up: SORT1 coding region in 61 ET cases (13 familial, 48 sporadic) and the exon containing p.Gly171Ala in 90 additional ET cases (28 familial, 62 sporadic). Variant also assessed against 188 Spanish control chromosomes.
30	Chen et al.	2017	China	Chinese Han	200 ET cases / 426 unrelated HCs

31	Leng et al.	2017	China (Beijing)	Chinese Han	8 adults w/ ET/2 children; 5 unaffected family members; 1 four-generation family.
32	Chen et al.,	2018	China (Shanghai)	Chinese population	200 ET cases / 201 controls.
33	Diez-Fairen et al.	2019	Multicentre — Europe and North America	Primarily North-Western European descent; analysis restricted after QC/PCA to individuals of confirmed European ancestry.	controls / families) 1. Original GWAS discovery dataset: 1,778 ET / 5,376 controls. 2. After QC: 1,751 ET / 5,311 controls.

Supplementary Table 5: Study design, Genes Findings and functional evidence of included studies.

Study	**Authors**	**Study design**	**Gene / locus (*Variant signal)* [Variant class]**	**Allele frequency (MAF, minor allele frequency)**	**Segregation pattern**	**Replication status**
1	Orsucci et al.	Family-based clinical exome sequencing study with repeat-expansion screening and segregation analysis exome sequencing studies	**CAMTA1** (*c.2207T>A, p.Leu736His*) [Missense variant (SNV)]	<1% (gnomAD v2.1; study inclusion criterion)	Variant shared by all 3 affected family members tested; unaffected relatives not reported.	Previously reported in an independent ET/tremor family, but with a different CAMTA1 variant; limited gene-level replication
			FUS (*c.1292C>T, p.Pro431Leu)* [Missense variant (SNV)]		Variant shared by both affected family members tested; unaffected relatives not reported.	Previously reported in independent ET families including (p.Gln290Ter); p.Pro431Leu itself previously identified in an ET proband from this and subsquently replicated in this family

	MYH14 (*c.4088G>A, p.Arg1363His*) [Missense variant (SNV)]		Variant shared by both affected brothers tested; unaffected relatives not reported.	No independent replication reported; single-family finding
	SGCE (*c.1007>G, p.Ala336Gly*) [Missense variant (SNV)]		Variant shared by both affected family members tested; unaffected relatives not reported.	No independent replication reported; single-family finding
	PCDH (*9c.1897T>C, p.Phe633Leu*) [Missense variant (SNV)]		Variant present in both affected family members tested; Digenic inheritance variants proposed to act together to produce the phenotype but	No independent rare-variant replication; PCDH9 region previously implicated by linkage only

			unconfirmed	
	SQSTM1 (*c.643dupG, p.Glu215fs)* [Frameshift (1-bp duplication)]		Variant present in both affected family members tested; co-occurring with PCDH9 variant	No independent replication reported; single-family finding
	ATXN1 (*Interrupted 40-CAG repeat expansion*) [Trinucleotide repeat expansion]	Not reported	Variant in 2 family menbers; mother and son	No independent replication reported; single-family finding

2	Ortega-Cubero et al.	Candidate-gene case-control association study with multicentre replication	**TREM2** (*rs75932628, p.Arg47His (R47H)*) [Missense SNP]	1. Spain: MAF 0.33% ET vs 0.05% controls, 2. Germany: MAF 0.18% ET vs 0.00% controls, 3. Italy: MAF 0.00% ET vs 0.42% controls, 4. North America: MAF 0.39% ET vs 0.29% controls, Taiwan MAF 0.00% ET vs 0.00% controls; varied substantially between populations	N/A (case-control design not family seq.); variant absent in one affected sister of a carrier.	Failed external replication — significant in Spanish discovery cohort but not replicated in Germany, Italy, North America or Taiwan
3	Clark et al.	Candidate-gene case-control repeat-expansion association study	**FMR1** (*CGG repeat length*) [Trinucleotide repeat expansion] repeat length: (1) premutation (55–200 CGG) (2) grey-zone (41–54 CGG) alleles	(1) Premutation: 0 detected in ET or controls. (2) Grey-zone: 7/321 ET (2.2%) vs 16/296 controls (5.4%)	N/A (case-control design not family seq.)	No association with ET consistent with previous studies, which had also found no FMR1 premutation alleles among ET cases

4	Yuan et al.	Candidate-gene case-control association study	**FGF20** (*rs1721100, rs1989754, rs10089600, rs12720208, rs17550360*) [SNPs]	*rs1721100: minor C allele 45.7% ET vs 49.1% controls; *rs1989754: C allele 46.8% ET vs 50.6% controls. *The other three variants were monomorphic in this cohort	N/A (case-control design not family seq.)	No positive ET association to replicate; no independent ET replication reported
5	Ayuso et al.	Candidate-gene case-control association study	**HMOX1** *(rs2071746, rs2071747*) [Common SNPs + CNVs]	1. HMOX1 rs2071746A: 58.9% ET vs 52.1% controls; rs2071746T: 41.1% ET vs 47.9% controls; 2. HMOX1 rs2071747G: 96.8% ET vs 95.5% controls; rs2071747C: 3.2% ET vs 4.5% controls	N/A (case-control design not family seq.)	No independent ET replication within this study;

			HMOX2 (*rs2270363, rs1051308)* [Common SNPs + CNVs]	1. HMOX2 rs2270363G: 67.1% ET vs 69.6% controls; HMOX2 rs2270363A: 32.9% ET vs 30.4% controls 2. HMOX2 rs1051308G: 28.5% ET vs 36.1% controls; rs1051308A: 71.5% ET vs 63.9% controls		
6	Clark et al.	Case-control repeat-expansion association study	**ATXN1** (*CAG repeat length; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat] **ATXN2** (*21-CAG repeat enriched in ET; 23-CAG repeat enriched in controls; both normal range*) [Trinucleotide repeat] **ATXN3** (*CAG repeat length; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat]	No intermediate/pathogenic expansions detected; differences observed in normal-range repeat distributions for SCA2 and SCA8. SCA2 increased frequency of 21-CAG allele in ET; increased frequency of 23-CAG allele in controls. SCA8 significant difference in the distribution of normal-range CTG repeat lengths between ET	N/A (case-control design not family seq.)	Overall negative result broadly consistent with previous ATXN repeat-expansion studies; authors note one previous Asian study found a single ET patient with an intermediate ATXN3 repeat

			CACNA1A (*CAG repeat length; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat]	and controls but no intermediate or pathogenic repeat expansions were identified.		
			ATXN7 (*CAG repeat length; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat]			
			ATXN8OS (*normal-range CTG repeat distribution associated with ET; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat]			
			ATXN10 (*ATTCT repeat length; no intermediate/pathogenic expansion detected*) [Pentanucleotide repeat]			
			PPP2R2B (*CAG repeat length; no intermediate/pathogenic expansion*			

			detected) [Trinucleotide repeat]			
			TBP (*CAG repeat length; no intermediate/pathogenic expansion detected*) [Trinucleotide repeat]			
			ATN1 (CAG repeat length; no intermediate/pathogenic expansion detected) [Trinucleotide repeat]			
7	Jiménez-Jiménez et al.	Family-based candidate-gene association study with case-control comparison	**DRD3** (*rs6280*) [missense SNP]	T allele: 69.6% ET vs 65.9% controls	Family-based analysis: no association	1. DRD3: previous results inconsistent; pooled evidence negative.
			SLC1A2 (*rs3794087*) [SNP]	T allele: 31.5% ET vs 25.0% controls	Family-based analysis: no association	2. SLC1A2: previous GWAS association with mixed replication/meta-analyses negative.

			MAPT (*rs1052553*) [SNP/haplotype-tagging variant]	A allele: 87.0% ET vs 72.8% controls	TDT/DFAM family-based testing did not support association.	3. MAPT: previous association not consistently replicated; present family-based analysis negative.
8	Sun et al.	Familial genetic study combining linkage analysis, WES, long-read WGS, RP-PCR and GC-PCR with segregation analysis	**NOTCH2NLC** (*5′-region GGC repeat expansion, 60–250 repeats*) [Trinucleotide repeat expansion]	Expansion identified in 11/197 pedigrees/familes (5.58%)	Co-segregated with tremor across 11 families; all tested unaffected family members carried normal-range repeats (<50 repeats).	Strong within-cohort familial replication across 11 pedigrees, but relationship specifically to ET remains uncertain because the same expansion is associated with NIID
9	Diez-Fairen M et al.	Step 1: Family-based WES with segregation analysis Step 2: independent case-control variant association Step 3:gene-based rare-variant	**CCDC183** (*rs749875462; c.1025G>A, p.Trp342*) [nonsense SNV]	Step 2: case-control 0.013 ET vs 0.003 controls	Family A; present only in affected tested members; additional unaffected relative confirmed negative	Step 3: independent 789 ET / 770 control dataset > no significant rare-variant burden detecetd

		burden analysis	**MMP10** (*rs535864157; c.32_33delGT*) [frameshift deletion]	Step 2: case-control 0.005 ET vs 0 controls	Family F; 3 affected carriers, absent in one unaffected relative	
			GPR151 (*rs114285050; c.283C>T, p.Arg95*) [nonsense SNV]	Step 2: case-control 0.013 ET vs 0.005 controls	Family H; 4 affected carriers	
10	Müller SH et al.	Common-variant GWAS incoprorating two-stage GWAS with independent replication + cerebellar expression/eQTL analysis	**STK32B** (*rs10937625*) [intronic SNP]	ET 0.2182 vs HC 0.2615	N/A (population-based GWAS)	STK32B rs10937625 replicated in the independent second-stage cohort [Bonferroni threshold of $p<8.47\times10^{-4}$]
			PPARGC1A (*rs17590046*) [intronic SNP]	ET 0.1668 vs HC 0.2054		PPARGC1A rs17590046 replicated in the independent second-stage cohort [Bonferroni threshold of $p<8.47\times10^{-4}$]

			CTNNA3 (*rs12764057, rs10822974, rs7903491*) [intronic SNP]	*1. rs12764057*: ET 0.4175 vs HC 0.3721; 2. *rs10822974*: ET 0.4976 vs HC 0.5412; 3. *rs7903491*: ET 0.4191 vs HC 0.4609		Replication significant only in the combined discovery + replication analysis; failed indepnedent replication.
11	Chao YX et al	Candidate-gene case-control association study	**LRRK2** (*rs33949390; c.4883G>C; p.Arg1628Pro/R1628P*) [missense SNP]	ET: 40/450 R1628P carriers (8.9%) vs Controls: 37/827 carriers (4.5%)	N/A (case-control design not family seq.)	No independent ET replication within this study;
12	Odgerel et al.	Family-based whole-genome sequencing (WGS) with rare-variant burden analysis, segregation analysis, SV/CNV analysis .	**CACNA1G** (*c.1367G>A; p.Arg456Gln*) [missense SNV]	MAF <1% after filtering against 1000 Genomes Phase 3/dbSNP common database. Only AF reported is for SLIT3 0.0006407 in ExAC (72/112,370 alleles; 2 homozygotes).	Rare family-specific candidate variants were nominated in 5/8 (62.5%) families; however, none represented independently replicated molecular diagnoses of ET.	Replicated only within families with no independent ET cohort replication.
			SLIT3 (rs144799628; *c.3505G>C; p.Val1169Leu)* [missense SNV]			
			KARS (*c.1517G>A; p.Arg506His*) [missense SNV]			
			KIF5A (*c.2769G>A; p.Arg923*) [synonymous SNV]			

			NTRK1 (*c.122+2627T>C*) [intronic SNV]			
13	Clark LN et al.	Family-based WGS with parametric linkage/joint linkage-association analysis and rare-variant non-parametric linkage (CHP-NPL); additional SNV/indel, CNV/SV and repeat-expansion analysis	**RBFOX1** (*rs8051198*) [intronic linkage-marker SNP]	RBFOX1 c.4-2A>G: 7.4×10^{-6} (gnomAD v2.1.1; 1/135,582 alleles, 0 homozygotes); Pseudomarker linkage variants: MAF ≥1% inclusion criterion, individual AFs not reported; CHP-NPL gene-level signals: N/A; STH p.Q7R: not reported.	RBFOX1 c.4-2A>G was present in affected and absent from unaffected family members with available DNA in one family (Family F)	Discovery cohort only with no independent stage-2 replication cohort.

	STH (*c.20A>G; p.Gln7Arg/Q7R*) [missense SNV]		Partial/family-specific segregation — present in affected and absent from unaffected members with available DNA in Family F; present in 2/3 affected members with DNA in Family E.	
	BTC (*rs10012100*) [linkage-marker SNP]		Not assessed	
	N6AMT1 (*rs2831975*) [linkage-marker SNP]		Not assessed	
	PCDH9 (*rs56402633, rs288791*) [linkage-marker SNPs]		Not assessed	
	EYA1 (*rs4439163*) [intronic linkage-marker SNP]		Not assessed	
	MAPT (*rs8076152*) [intronic linkage-marker SNP]		Not assessed	

			COL9A2, SOX8, DIAPH3, STAU2, SCARB2, NRXN3 [Other significant linkage loci]		Not identified.	
			TUBB2A, VPS33B, STEAP1B, SPINK5, ZRANB1, TBC1D3C, PDPR, NPY4R, ETS2, ZNF736, SPATA21, ARL17A, PZP, BLK, CCDC94 [CHP-NPL nominated 15 additional gene-level rare-variant linkage signals.]		Not identified.	
14	Hicks JE et al.	Family-based genome-wide parametric linkage + IBD segment mapping, followed by WES of linked pedigrees.	**Chromosome 5q35** (*LOD=3.563; IBD-shared region*) [linkage locus]; 41 possible genes Note: WES did not identify a candidate causal gene/variant within the 5q35 linked region.	AF— none identified. SNPs with MAF <5% were excluded. Linkage-marker analysis; assumed disease-allele frequency in linkage model = 0.1%.	5q35 linked region: shared IBD by all affected pairs in Family 4; no specific causal variant identified for variant-level segregation analysis.	NA

15	Yuan L et al.	Candidate-gene case–control association study	**MC1R** (*rs34090186; c.200G>A; p.Arg67Gln/R67Q*) [missense SNP]; 14 other tested candidate genes & 22 variants: no significant association found.	A allele: 2.5% ET vs 0.9% controls	N/A (case-control design not family seq.)	No independent ET replication within this study;
16	Agúndez JAG et al.	Candidate-gene case–control association study	**VDR** (*rs2228570/FokI; p.Met1 start-loss*) [start-loss SNV]	rs2228570: A 33.5% ET vs 36.8% controls	N/A (case-control design not family seq.)	VDR rs2228570: previous positive association (Sazci et al., 2019); directionally consistent but not independently replicated in the present cohort (OR 0.68, p=.146). Pooled analysis with the previous study (511 ET/511 controls) was significant (OR 0.59, p=.015).
			VDR (*rs731236/TaqI; p.Ile352Ile*) [synonymous SNV]	rs731236: G 36.6% vs 42.8%;		Negative replication / consistent null finding with other studies.

			VDR (*rs7975232/ApaI*) [intronic SNV]	rs7975232: A 52.2% vs 57.0%		No independent ET replication
			VDR (*rs739837*) [3′UTR SNV]	rs739837: T 52.4% vs 56.1%;		No independent ET replication
			VDR (*rs78783628*) [3′UTR SNV]	s78783628: deletion 47.7% vs 46%		No independent ET replication
			GC (*rs7041; p.Asp451Glu*) [missense SNV]	rs7041: C 63.0% vs 53.5%		No independent ET replication
			GC (r*s4588; p.Thr455Lys*) [missense SNV]	rs4588: T 30.6% vs 32.5%.		No independent ET replication
17	Agúndez JAG et al.	Candidate-gene case–control association study	**CD4** (rs1922452; A>G) [intronic SNV]	rs1922452 G allele 62.0% in ET vs 60.0% in controls	N/A (case-control design not family seq.)	No independent ET replication.
			CD4 (rs951818; C>A) [non-coding transcript exonic SNV]	rs951818 C allele 40.6% vs 40.6%		No independent ET replication.
			LAG3 (rs870849) [missense SNV]	rs870849 C allele 59.4% vs 62.2%		No independent ET replication.

18	Agúndez JAG et al.	Candidate-gene case–control association study with gene–gene interaction analysis	**ALAD** (*rs1800435; c.177G>C; p.Lys59Asn*) [missense SNP]; secondary interaction analysis with previously genotyped HMOX1/HMOX2 variants (See study 5)	C allele: 91.3% ET vs 90.8% controls; > ALAD rs1800435 CC genotype 26.8% ET vs 35.8% controls; G allele: 8.7% vs 9.2%;	N/A (case-control design not family seq.)	ALAD rs1800435: no direct association in this cohort; previous small study (Louis et al.) showed only a non-significant association but reported a lead–genotype interaction. ALAD–HMOX2 interaction identified here has not been independently replicated.
19	Emamalizadeh B et al.	Candidate-gene case–control association study	**RIT2** *rs12456492* [intronic SNP];	RIT2 rs12456492: G allele frequency 45% in ET cases vs 38% in controls	N/A (case-control design not family seq.)	No independent ET replication; rs12456492 is an established/repeatedly studied PD susceptibility signal, but its association with ET was newly reported here.

			RIT2 *rs16976358* [downstream SNP]	RIT2 rs16976358: C allele frequency 14% in ET cases vs 12% in controls		
20	Sazci A et al.	Candidate-gene case–control association study	**VDR** (*rs2228570/FokI*) [start-codon SNP]	VDR rs2228570 C allele 75% in ET cases vs 69% in controls;T allele 25% in ET cases vs 31% in controls.	N/A (case-control design not family seq.)	No independent replication within the study; subsequent independent study (Study 16) did not replicate.
21	Chen J et al.	Candidate-gene case–control association study	**HMOX1** (*rs2071746*) [upstream/promoter SNP]	rs2071746 minor A allele 44% ET vs 46% controls	N/A (case-control design not family seq.)	No independent replication within the study; HMOX1 rs2071746 and HMOX2 rs1051308 failed to repilcate.
			HMOX2 (*rs4786504*) [SNP] **HMOX2** (*rs1051308*) [3′UTR SNP]	rs4786504: AF not reported; rs1051308 G: 37% ET vs 37% controls		
			VDR (*rs731236*) [synonymous SNP]	rs731236 C: 7% ET vs 5% controls		
			IL17A (*rs8193036*) [SNP]	rs8193036 T: 30% ET vs 30% controls		

	IL1B (*rs1143643*) [intronic SNP] **IL1B** (*rs1143634*) [synonymous SNP] **IL1B** (*rs1143633*) [intronic SNP]	rs1143643 G: 46% ET vs 43% controls; rs1143634 T: 4% ET vs 2% controls; rs1143633 G: 38% ET vs 34% controls		
	NOS1 (*rs693534*) [SNP] **NOS1** (r*s7977109*) [SNP]	rs693534 A: 27% ET vs 27% controls; rs7977109 G: 22% ET vs 23% controls		
	ADH1B (*rs6413413*) [SNP] **ADH1B** (*rs1229984*) [missense SNP]	rs6413413: AF not reported; rs1229984 G: 33% ET vs 32% controls;		

22	Hor H et al.	Family-based WES followed by targeted TENM4 resequencing, segregation analysis and experimental functional studies	**TENM4** (*c.4100C>A; p.Thr1367Asn/T1367N*) [missense SNV] **TENM4** (*c.4324G>A; p.Ala1442Thr/A1442T*) [missense SNV] **TENM4** (*c.3412G>A; p.Val1138Met/V1138M*) [missense SNV]	TENM4 c.4100C>A (p.T1367N) was absent from both 1000 Genomes and EVS; c.4324G>A (p.A1442T) had an EVS MAF of 0; and c.3412G>A (p.V1138M) had no available EVS MAF (NA). All three variants met the study's rare-variant criterion of MAF <0.1%.	Incomplete segregation: variants tracked with ET in three families but affected non-carriers and unaffected carriers occurred; mutant alleles were over-transmitted to affected offspring (12/15 transmissions; p<.02).	Within-study recurrence across three families, but no independent external replication in this study.

23	Ng et al.	Targeted repeat-expansion screening study with longitudinal phenotyping.	**NOTCH2NLC** (5′-region GGC repeat expansion; four carriers had 80, 83, 90 and 107 repeats & 4 ET patients carried intermediate expansions of 47–53 repeats.)	Expanded repeats >80 units occurred in 4/462 ET cases (0.86%), all of whom had sporadic ET; this corresponds to 4/285 sporadic cases (1.4%). 0/200 controls and no familial ET cases had repeats ≥60. Four further ET cases had 47–53 intermediate repeats.	N/A for the expansion-positive cases of non-familial ET	Provides independent support for the earlier Sun et al. 2020 NOTCH2NLC finding, but in sporadic rather than familial ET.
24	Rajput et al.	Targeted candidate-variant screening study.	**DNAJC13** (*rs387907571; c.2564A>G; p.Asn855Ser*) [missense variant]	2/571 ET patients were heterozygous carriers, giving a reported carrier frequency of 0.3% & 0/>2,600	No additional affected relatives were not analysed for segregation analysis.	No independent ET replication within this study.
			VPS35 (*rs188286943; c.1858G>A; p.Asp620Asn*) [missense variant]	0/571 & 0/>2,600		

25	Liu et al.	Family-based whole-exome sequencing (WES) with segregation analysis	**NOS3** (*c.46G>A; p.Gly16Ser*) [missense variant] **NOS3** (*c.164C>T; p.Pro55Leu*) [missense variant]	1.969×10^{-5} (ExAC)	NOS3 p.Gly16Ser: present in all 3 affected tested and absent in an unaffected relative. NOS3 p.Pro55Leu: present in 3 affected relatives (mother + dizygotic twins), but the affected father was a non-carrier, considered a possible phenocopy.	No independent ET replication within this study.
			KCNS2 (*c.1137T>A; p.Asp379Glu*) [missense variant]	Not detected (ExAC/1000 Genomes)	KCNS2 p.Asp379Glu : present in all affected tested and absent in an unaffected relative.	

			HAPLN4 (*c.1048G>C; p.Gly350Arg*) [missense variant]	0.00002917 (ExAC)	HAPLN4 p.Gly350Arg: present in 3 affected cases; other relatives unavailable.	
			USP46 (*c.398C>T; p.Ala133Val)* [missense variant]	Not detected (ExAC/1000 Genomes)	USP46 p.Ala133Val: present in 5 affected cases; additional relatives unavailable.	
26	Bergareche et al.	Family-based WES with segregation analysis, targeted replication screening, brain-expression studies and experimental electrophysiological functional validation.	**SCN4A** (*c.4609G>A; p.Gly1537Ser; rs571210585*) [missense SNV]	ExAC AF 6.63×10^{-5} (8/120,668 alleles); absent from 94 ethnicity-matched controls (188 chromosomes) and initially absent from >10,000 individuals in public databases.	SCN4A p.Gly1537Ser variant was found in the genotyped relatives with ET and was absent from the three genotyped unaffected relatives.	No independent variant-level replication. p.Gly1537Ser was subsequently screened in 101 additional ET cases. Sequencing the complete SCN4A coding region in another 22 familial ET cases identified no additional candidate mutation.

27	Chao et al.	Targeted candidate-variant case-control study	**HTRA2** *(p.G399S)* [missense variant]	1 heterozygous control only; 0.02% in their Asian population.	N/A (case-control design not family seq.)	Failed to replicate the previously reported HTRA2 p.G399S.
28	Zhang et al.	Family-based WGS with segregation analysis.	**TCP10L** (*rs151233771; c.269G>A; p.Arg90Gln*) [missense variant]	0.000015 (gnomAD_NFE)	Co-segregated with confirmed ET in the available family - present in all 3 confirmed affected individuals and absent in 5 unaffected relatives,	No independent replication.

29	Sánchez et al.	Family-based WES with segregation analysis, follow-up candidate-gene screening and experimental functional studies.	**SORT1** (*c.512G>C; p.Gly171Ala*) [Heterozygous missense SNV]	ExAC overall frequency 5.769 × 10^{-5} (~0.0058%)	Co-segregated with 2 ET in the discovery family; unaffected 43-year-old son also carried the variant and was considered potentially at risk because of possible variable age at onset this representing the incomplete nature of disease.	No independent replication was achieved - not seen in 90 additional ET cases including in the while sequencing of SORT1 in 61 ET cases
30	Chen et al.	Candidate-gene case-control association study	**PITX3** (*rs3758549; rs4919621*) [promoter-region SNP; intronic SNP (intron 3)]	1. rs3758549: C = 86.0% ET vs 81.7% HCs; T = 14.0% vs 18.3%, 2. rs4919621: T = 76.3% ET vs 77.8% controls; A = 23.7% vs 22.2%	N/A (case-control design not family seq.)	No ET association identified.

31	Leng et al.	Single-family WES followed by Sanger segregation analysis.	**SCN11A** (*c.673C>T; p.Arg225Cys (R225C)*) [Heterozygous missense SNV]	Study did not provide a population allele frequency	SCN11A variant was present in all 8 affected family members tested and absent from all 5 unaffected relatives tested.	No independent replication for ET.
32	Chen et al.,	Candidate-locus case-control association study	**MAP2K5/SKOR1** (*GCGGG haplotype: rs4489954–rs3784709–rs2241420–rs1026732–rs6494696*) [five-SNP haplotype]	Haplotype frequency: 31.9% ET vs 15.5% controls	N/A (case-control design not family seq.)	No independent ET replication cohort.

33	Diez-Fairen et al.	Genome-wide SNP-based heritability analysis of existing GWAS data using GREML-LDMS; dominance variance assessed using GCTA-GREMLd. Also performed 10-Mb regional heritability analysis, PD/RLS genetic risk scores and LD-score regression across 832 traits.	**Genome-wide common variants** (*chr6 and chr21 regions showed highest heritability estimate*s) [common SNPs]	N/A — genome-wide analysis	N/A — population-level genome-wide analysis,	Not applicable as variant replication; regional heritability signals require validation in larger/diverse cohorts

Supplementary Table 6. Summary of Key Findings and Overall Evidence Strength of Included Studies.

Study	Authors	Functional evidence	Implicated biological pathway(s)	Summary of key findings
1	Orsucci et al.	N/A for ET — no functional experiments performed	Encodes the calmodulin binding transcription activator 1. Implicated in synaptic function	Among 34 individuals from 14 families with dominant ET, rare variants potentially contributing to ET were identified in CAMTA1 (3 affected family members), FUS (2), MYH14 (2) and SGCE (2). Two affected members of a further family carried both PCDH9 and SQSTM1 variants, raising the possibility of digenic inheritance. An interrupted 40-CAG ATXN1 repeat was identified in two affected members of another family. Overall, 8/14 families (57%) remained negative following exome and repeat-expansion analyses. Identified exome variants met the study's <1% allele-frequency threshold and
			Encodes an RNA binding protein. Implicated in ranscription regulation, RNA splicing, RNA transport, DNA repair and damage response.	
			Encodes a member of the myosin superfamily (heavy chain 14). Myosins are actindependent motor proteins with diverse functions including regulation of cytokinesis, cell motility, and cell polarity.	

		Encodes the sarcoglycan epsilon. Components of the dystrophin-glycoprotein complex, linking the actin cytoskeleton to the extracellular matrix; expressed in the brain in particular white matter	had CADD scores >20, but most lacked independent variant-level replication or experimental functional validation.
		Encoding protocadherin-9. Calcium-dependent cell adhesion and recognition proteins.	
		Encodes a scaffolding protein/Sequestosome 1. Regulates processes like signaling, apoptosis, transcription regulation, and ubiquitin-mediated autophagy.	

			Encodes a polyglutamine (polyQ) tract in the ataxin-1 protein. SCA1-related mechanism; unclear exact	
2	Ortega-Cubero et al.	N/A for ET — no functional experiments performed	Encodes the TREM2 protein. Cell-surface receptor expressed predominantly on microglia in the central nervous system. Linked to microglial immune signalling / phagocytosis and neuroinflammation.	Spanish association: OR 5.97 (95% CI 1.203–29.626), p=0.042; association absent in replication populations and in pooled analysis. Calculated from only six carriers (3ET and 3 HC).
3	Clark et al.	N/A for ET — no functional experiments performed	Encodes for Fragile X Messenger Ribonucleoprotein Protein. Implicated in RNA processing and translational regulation / synaptic function.	No FMR1 premutation (55–200 CGG) alleles were identified. Grey-zone (55–200 CGG) alleles were less frequent in ET than controls (2.2% vs 5.4%; χ^2 = 4.69, p = 0.03), opposite to the hypothesised risk association; overall, no evidence supported FMR1 CGG expansions as an ET risk factor.

4	Yuan et al.	No ET-specific functional studies; variants were selected partly based on prior PD evidence/predicted functional relevance	FGF20 encodes fibroblast growth factor 20 (FGF20). FGF signalling / neurotrophic signalling and dopaminergic neuronal survival.	No significant association between the tested FGF20 variants or haplotypes and ET. For rs1721100 and rs1989754, allelic associations were non-significant (p = 0.274, OR 0.876 [95% CI 0.690–1.111] and p = 0.205, OR 0.858 [95% CI 0.676–1.088], respectively), despite >80% reported statistical power. The remaining three variants were monomorphic and had low statistical power, limiting conclusions regarding their association with ET.
5	Ayuso et al.	No ET-specific experimental functional evidence; proposed oxidative-stress mechanism was described by authors as speculative	HMOX1 and HMOX2 encode heme oxygenase-1 (HO-1) and heme oxygenase-2 (HO-2), respectively. These enzymes catalyse heme degradation to biliverdin, free iron and carbon monoxide.	Weak associations were identified between HMOX1 rs2071746T (41.1% ET vs 47.9% controls; OR 0.76, 95% CI 0.60–0.95; corrected p = 0.015) and HMOX2 rs1051308G (28.5% vs 36.1%; OR 0.71, 95% CI 0.55–0.90; corrected p = 0.020) and reduced odds of familial ET. No significant associations were found for rs2071747 or rs2270363, and CNVs were absent in ET cases. Findings lacked independent ET replication and require validation in other populations.

6	Clark et al.	None specific to ET	Cerebellar neurodegeneration; polyglutamine/repeat-mediated toxicity, RNA processing and transcriptional regulation, protein homeostasis, and calcium-channel signalling.	No intermediate or pathogenic repeat expansions were identified across the 10 hereditary ataxia loci in 323 ET cases. Significant differences in normal-range repeat distributions were observed for ATXN2 (p = 0.004; 21-CAG repeat more frequent in ET and 23-CAG repeat more frequent in controls) and ATXN8OS (p = 0.02).
7	Jiménez-Jiménez et al.	No ET-specific functional experiments performed	DRD3 encodes dopamine D3 receptor. Impicated in the Dopaminergic signalling. SLC1A2 encodes the major glial glutamate transporter EAAT2/GLT-1.	No association was identified between familial ET and DRD3 rs6280 (T allele: 69.6% ET vs 65.9% controls; OR 1.18, 95% CI 0.72–1.95; p=0.486) or SLC1A2 rs3794087 (T allele: 31.5% vs

			MAPT encodes tau. Impicated in microtubule stability.	25.0%; OR 1.38, 95% CI 0.83–2.28; p=0.183). MAPT rs1052553A was more frequent in ET (87.0% vs 72.8%; OR 2.49, 95% CI 1.28–4.93; p=0.004), but the association was non-significant when one affected individual per family was analysed (p=0.059) and was not supported by family-based TDT/DFAM analyses.
8	Sun et al.	p62- and ubiquitin-positive intranuclear inclusions detected in skin biopsies of all 3 expansion-positive probands biopsied	Repeat-expansion-associated neurodegeneration / neuronal intranuclear inclusion formation (NIID-related pathway)	197 familial ET pedigrees/families screened; NOTCH2NLC GGC expansions >60 repeats identified in 11 families (5.58%), with affected carriers having 60–250 repeats. The 27 expansion-positive patients from those 11 families had predominantly kinetic/postural tremor without cognitive impairment, peripheral neuropathy, cerebellar ataxia or pyramidal signs. MRI did not demonstrate severe leukodystrophy or cerebellar atrophy. Across those 27 affected carriers of 60–250 GGC repeats, mean 117.75 ± 44.96. All tested unaffected members of those 11 families had normal repeats (6–23). Compared with

				expansion-negative ET probands, expansion-positive probands had greater tremor severity (TETRAS-I 34.69 vs 15.16; p=0.013) and poorer ADL scores (TETRAS-II 32.50 vs 11.13; p=0.011). Within expansion-positive families, younger generations had an earlier age at onset than parental generations (38.45 vs 54.89 years; p=0.007), consistent with genetic anticipation.
9	Diez-Fairen M et al.	No ET-specific functional experiments performed	CCDC183 coiled-coil domain-containing protein 183. Involved in function/pathway poorly characterised.	WES of 40 individuals from eight multigenerational Spanish ET families identified 15 rare protein-altering variants that perfectly segregated with disease in seven families. CCDC183 rs749875462 (OR 4.04, p=0.0087), MMP10 rs535864157 (p=0.0220) and

			Encodes matrix metalloproteinase-10 (stromelysin-2). Extracellular-matrix remodelling and neuroinflammatory responses.	GPR151 rs114285050 (OR 2.69, p=0.0425) showed nominal associations in 521 ET cases and 596 controls, but none survived Bonferroni correction. Subsequent rare-variant burden analysis in 789 ET cases and 770 controls showed no significant enrichment in these genes, leaving them as unreplicated family-specific candidates requiring further validation.
			GPR151 encodes G-protein-coupled receptor 151. Involbed in G-protein-coupled receptor signalling.	

10	Müller SH et al.	STK32B expression was significantly increased in lateral cerebellar cortex from 19 ET cases vs 17 controls (p=0.026) but not associated with rs10937625 genotype. The allele itslef was asscoiated with reduced STK32B expression in cerebellar cortex and found in DNase-hypersensitive regulatory region (Public Braineac eQTL data).	Encodes for serine/threonine kinase 32B. Implcated in serine/threonine kinase signalling with link to possible cerebellar regulation.	A two-stage GWAS of 2,807 ET cases and 6,441 controls of North-Western European ancestry identified independently replicated associations at STK32B rs10937625 (combined OR 0.80, $p=5.21\times10^{-10}$) and PPARGC1A rs17590046 (OR 0.79, $p=1.39\times10^{-9}$). STK32B expression was increased in ET cerebellar cortex (p=0.026), with public eQTL data linking the protective allele to reduced cerebellar expression. CTNNA3 rs12764057 reached genome-wide significance in the combined analysis (OR 1.17, $p=1.19\times10^{-8}$) but failed independent replication. Previously reported LINGO1 and SLC1A2 signals were not replicated.
		No disease/ genotype-associated expression differences.	Encodes for PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha). Involved in energy metabolism and mitochondrial function	

		No disease/ genotype-associated expression differences.	Encodes for catenin alpha-3. Linked to cell–cell adhesion.	
11	Chao YX et al	None specific to ET or R1628P.	Encodes eucine-rich repeat kinase 2. Implicated in kinase/GTPase signalling; neurodegenerative pathways associated with PD	LRRK2 R1628P carriers were more frequent among ET cases than controls (8.9% vs 4.5%; OR 2.20, 95% CI 1.30–3.73; p=0.0035) in a predominantly ethnic Chinese Singaporean cohort. However, the candidate-gene association was not independently replicated within the study and lacked ET-specific functional validation. As R1628P is a known PD risk variant and some ET cases may subsequently develop PD, the finding may reflect shared ET–PD susceptibility or diagnostic/phenotypic overlap rather than an ET-specific genetic association.

12	Odgerel et al.	Experimental functional studies were performed only for CACNA1G. Performed electrophysiological functional analysis of the CaV3.1 T-type calcium channel and supporting an effect on T-type Ca^{2+} channel function/neuronal excitability.	Encodes for CaV3.1. Implicated in T-type calcium-channel signalling / neuronal excitability and rhythmic firing in cerebellothlalmic circuitary.	WGS of 40 individuals from eight familial ET pedigrees nominated rare candidate variants in 5/8 (62.5%) families, including CACNA1G, SLIT3, KARS, KIF5A and NTRK1. CACNA1G variants were identified in additional ET families and underwent electrophysiological testing, while a SLIT3 variant showed locomotor abnormalities in a Drosophila model. However, the variants remained family-specific and lacked independent genetic replication, supporting their classification as candidate rather than established causal ET

	Experimental functional studies performed for SLIT3. Drosophila model carrying the equivalent slit p.Val1187Leu varian. significantly slower climbing than wild-type flies across the lifespan ($p<0.05$) but no ET pathogenesis in humans demonstrated.	Encodes for slit guidance ligand 3. Impliacted in SLIT–ROBO signalling / axon guidance and neural development.	genes.
	No experimental functional studies of KARS.	Encodes for Lysyl-tRNA synthetase (KARS1). Involved in aminoacyl-tRNA synthesis / protein translation.	

		No experimental functional studies of KIF5A.	Encodes for Kinesin family member 5A. Microtubule-dependent axonal transport / neuronal intracellular trafficking.	
		No experimental functional studies of NTRK1	Encodes for TrkA, the high-affinity receptor tyrosine kinase for nerve growth factor (NGF). Linked to neurotrophin signalling / neuronal survival and differentiation.	
13	Clark LN et al.	No ET-specific functional experiments performed	Encodes RNA-binding Fox-1 homolog 1. Linked to neuronal development/function; PI3K–AKT signalling	WGS/linkage analysis of 104 multigenerational ET families identified multiple candidate linkage regions, including BTC (HLOD=4.53), N6AMT1 (4.31), PCDH9 (4.21), EYA1 (4.04), RBFOX1 (4.02) and MAPT (3.99). A rare RBFOX1 canonical

			splice-acceptor variant (c.4-2A>G; AF=7.4×10^{-6}) co-segregated with ET in one family and was predicted in silico to disrupt splicing. CHP-NPL identified 15 additional linked gene regions, including TUBB2A (LOD=7.42, $p=5.0\times10^{-9}$). However, no independent replication cohort or experimental validation of the RBFOX1 variant was undertaken, leaving these as candidate loci/family-specific variants rather than established ET genes.
		Encodes fo Betacellulin; epidermal growth factor (EGF)-family ligand. Link to signalling in PI3K–AKT and ERK/MAPK pathways; neurotrophic signalling	
		Encodes for N-6 adenine-specific DNA methyltransferase 1; oxidative stress and DNA-damage response	
		Encodes for Protocadherin-9. Linked to neuronal cell adhesion and synaptic organisation.	

		EYA transcriptional coactivator and phosphatase; transcriptional regulation and neural/cerebellar development.	
		Encodes for microtubule-associated protein tau. Implicated in microtubule stability/axonal transport.	

14	Hicks JE et al.	None		Genome-wide significant linkage to chromosome 5q35 was identified in one large ET pedigree (LOD=3.563), with IBD mapping narrowing the candidate interval to ~5.1 Mb shared by all affected pairs. The interval contained 41 genes, including the biologically plausible GABA-A receptor subunit gene GABRP; however, WES identified no potential causative coding variant. The locus was not implicated in the other four families and was not independently replicated.
15	Yuan L et al.	No ET-specific functional experiments performed	MC1R encodes the melanocortin-1 receptor. Implicated in neuroprotective/dopaminergic neuronal signalling pathways.	Candidate-gene association study of 200 Han Chinese ET cases and 432 controls, 23 variants across 15 genes were examined. MC1R rs34090186 (c.200G>A; p.Arg67Gln) was nominally associated with ET, with the A allele occurring in 2.5% of cases versus 0.9% of controls (OR 2.74, 95% CI 1.08–7.01; p=.028). No significant associations were identified for the other tested variants or haplotypes. The MC1R finding was also not independently

				replicated, lacked ET-specific functional validation.
16	Agúndez JAG et al.	No ET-specific functional experiments performed	VDR encodes the vitamin D receptor. Vitamin D transport and receptor signalling implicated potential modulation neurotransmission.	In 272 Spanish-European familial ET cases and 272 controls, GC rs7041 was associated with ET under a recessive model (CC: 39.3% vs 26.1%; OR 1.82, 95% CI 1.27–2.63; p=.001, FDR-corrected p=.007), remaining significant after adjustment for age. VDR rs2228570 was not associated with ET in this cohort (OR 0.68; p=.146), although pooled analysis with a previous study (511 ET/511 controls) suggested a protective association for the minor-allele homozygous genotype (OR 0.59;

			GC encodes vitamin D-binding protein. Responsible for binding and transporting vitamin D and its circulating metabolites to target tissues.	p=.015). Other VDR/GC variants were not associated with ET. Neither finding had ET-specific experimental functional validation; GC rs7041 lacked independent ET replication and VDR rs2228570 failed direct replication in this cohort.
17	Agúndez JAG et al.	No ET-specific functional experiments performed	CD4 encodes the CD4 membrane glycoprotein. Is an important mediator of T-cell immune and inflammatory responses; linked to possible neuroinflammatory	267 Spanish-European familial ET cases and 270 controls, no significant association was identified between overall ET risk and CD4 rs1922452, CD4 rs951818 or LAG3 rs870849. A nominal male-specific association was observed for LAG3 rs870849C (55.8% ET vs 65.8% controls; OR 0.66, 95% CI 0.46–0.94; p=.020), but did not survive False Discovery Rate correction (Pc=.060). No variant influenced age at tremor onset. With no independent ET replication or variant-specific

			LAG3 encodes lymphocyte activation gene-3 protein (CD223). Is an immune-checkpoint receptor involved in regulating T-cell activation linked to possible neuroinflammatory signalling.	functional validation, the study provides evidence against a major association of these variants with ET and only very limited evidence for a possible sex-specific LAG3 effect.
18	Agúndez JAG et al.	No ET-specific functional experiments performed	ALAD encodes δ-aminolevulinic acid dehydratase. Implicated in haem biosynthesis and catabolism / oxidative-stress and metal-toxicity pathways	202 Caucasian Spanish familial ET cases and 218 controls, ALAD rs1800435 was not independently associated with ET (G allele 8.7% vs 9.2%; OR 0.94, p=.795). Among ALAD rs1800435CC homozygotes, however, HMOX2 rs1051308G was less frequent in ET than controls (26.8% vs 35.8%; OR 0.66, 95% CI 0.47–0.92; p=.011, FDR-corrected p=.044), suggesting a possible protective gene–gene interaction. The interaction had limited statistical power, was not independently replicated and lacked ET-specific functional validation, providing very limited evidence for a role in

				ET susceptibility.
19	Emamalizadeh B et al.	No ET-specific functional experiments performed	RIT2 encodes Rin (Ras-like without CAAX 2). Implicated in the Ras-family small-GTPase signalling / neuronal differentiation and survival; dopaminergic signalling and dopamine-transporter trafficking.	RIT2 rs12456492G was more frequent in Iranian ET cases than controls (45% vs 38%; OR 1.37, 95% CI 1.11–1.70; p=.003), with an association under the recessive model (OR 2.21; p<.0001). RIT2 rs16976358 was not associated with ET. However, no correction for multiple testing or independent ET replication was reported, population stratification could not be formally assessed, and no ET-specific functional validation was performed, providing very limited evidence for RIT2 as an ET susceptibility gene.

20	Sazci A et al.	No ET-specific functional experiments performed	VDR encodes the vitamin D receptor. Vitamin D transport and receptor signalling implicated potential modulation neurotransmission.	VDR rs2228570 was nominally associated with sporadic ET, with the C allele more frequent in cases than controls (75% vs 69%; OR 2.21, 95% CI 1.05–4.64; p=.033) and the TT genotype less frequent in ET (4.6% vs 9.6%; OR 0.45; p=.033). The association was stronger in men but absent in women. However, the study had low statistical power (31%), no multiple-testing correction or ET-specific functional validation, and the association was not directly replicated in a subsequent independent cohort.
21	Chen J et al.	No ET-specific functional experiments performed.	HMOX1 and HMOX2 encode heme oxygenase-1 (HO-1) and heme oxygenase-2 (HO-2), respectively. These enzymes catalyse heme degradation to biliverdin, free iron and carbon monoxide.	200 Chinese ET cases without RLS and 229 controls, IL1B rs1143633 was associated with ET under a recessive model (GG: 16.9% ET vs 7.5% controls; adjusted OR 2.57, 95% CI 1.38–4.81; p=.003) and remained significant after Bonferroni correction (p=.024), although the

	VDR encodes the vitamin D receptor. Vitamin D transport and receptor signalling implicated potential modulation neurotransmission.	allele-level association was not significant. IL1B rs1143643 showed a nominal association that did not survive correction, while the remaining variants, including previously reported HMOX1 rs2071746 and HMOX2 rs1051308, were not associated with ET.
	IL17A encode for Interleukin-17A, a pro-inflammatory cytokine. Linked to immune/inflammatory signalling; neuroinflammation.	
	IL1B Interleukin-1β, a pro-inflammatory cytokine. Pro-inflammatory cytokine signalling; neuroinflammation.	
	NOS1 encode for neuronal nitric oxide synthase (nNOS). Implicated in neuronal signalling and oxidative/nitrosative stress.	

			ADH1B encodes for Alcohol dehydrogenase 1B. Linked to alcohol/ethanol metabolism; cellular redox metabolism	
22	Hor H et al.	Experimental non-human evidence only — mutant TENM4 altered membrane localisation in murine oligodendroglial cells and caused axon-guidance abnormalities in zebrafish, consistent with a dominant-negative effect; no human functional validation.	TENM4 encodes teneurin-4. Impicated in xxon guidance and neuronal pathfinding; oligodendrocyte maturation and central myelination; neuronal/synaptic organisation.	WES followed by targeted resequencing identified three rare TENM4 missense variants (p.T1367N, p.A1442T and p.V1138M) across three Spanish familial ET pedigrees. The variants showed incomplete familial segregation, although mutant alleles were significantly over-transmitted to affected offspring (12/15 transmissions; p<.02). Experimental non-human studies showed altered TENM4 membrane localisation in oligodendroglial cells and abnormal axon pathfinding in zebrafish, supporting a proposed dominant-negative effect.

23	Ng et al.	No ET-specific functional experiments performed.	Repeat-expansion-associated neurodegeneration / NOTCH2NLC-related neuronal intranuclear inclusion disease (NIID)	NOTCH2NLC GGC repeat expansions >80 units were identified in 4/462 ET cases (0.86%; 1.4% of sporadic ET), but in no controls or familial ET cases. Longitudinal follow-up demonstrated marked variable expressivity: one carrier maintained an isolated ET phenotype for >40 years, whereas another subsequently developed clinically and pathologically supported NIID. The findings independently support an association between NOTCH2NLC expansion and tremor but also strengthen the possibility that some apparently sporadic ET cases represent a tremor-predominant NOTCH2NLC-related/NIID phenotype.
24	Rajput et al.	No ET-specific functional experiments performed.	Encodes for DnaJ homolog subfamily C member 13 (RME-8), a protein involved in clathrin dynamics and endosomal trafficking/recycling.	DNAJC13 N855S was identified in 2/571 (0.3%) ET patients of European descent, both with a family history of ET, whereas VPS35 D620N was absent. The two DNAJC13 carriers appeared to share elements of the

			Encodes vacuolar protein sorting-associated protein 35. Involved in endosomal sorting and recycling of membrane proteins.	previously reported PD-associated haplotype, but affected relatives were unavailable for segregation testing. The study therefore suggested possible overlap between PD and ET through endosomal-trafficking pathways, but did not establish DNAJC13 N855S as an ET-causing variant.
25	Liu et al.	No ET-specific functional experiments performed.	NOS3 encodes endothelial nitric oxide synthase, converting L-arginine to nitric oxide (NO). NO signalling part of neuronal/synaptic and vascular function.	WES of 37 early-onset, multigenerational ET families identified rare segregating missense variants in four candidate genes across five families: two different NOS3 variants in two families and variants in KCNS2, HAPLN4 and USP46 in one family each. The variants were extremely rare or absent from population databases and showed varying degrees of within-family segregation. However, KCNS2 p.Asp379Glu was absent from an additional 95 ET cases, none of the candidates received
			KCNS2 encodes the Kv9.2 potassium-channel α-subunit, modulating Kv2.1/Kv2.2. Linked to neuronal membrane excitability and synaptic transmission.	

		HAPLN4 (BRAL2) encodes a link protein of perineuronal nets, particularly around cerebellar/GABAergic neurons	independent external replication, and no direct experimental functional validation was performed. The study therefore nominated biologically plausible rare family-specific candidates rather than establishing causal ET genes.
		USP46 encodes a deubiquitinating enzyme implicated in regulation of GABA synthesis/GABAergic signalling.	

26	Bergareche et al.	SCN4A expression was demonstrated in mouse brain and human cerebral cortex. Whole-cell patch-clamp experiments showed significantly faster mutant-channel inactivation near threshold (−40 and −35 mV) and altered ion selectivity. Mutant relative conductance for K^+ and NH_4^+ was approximately 3.2–3.9-fold greater than WT, supporting a change-of-function effect.	SCN4A encodes the Nav1.4 voltage-gated sodium-channel α-subunit. Voltage-gated sodium-channel signalling / neuronal membrane excitability and oscillatory activity.	WES in a four-generation Spanish family identified the rare SCN4A p.Gly1537Ser variant segregating with an ET phenotype. The variant was extremely rare (ExAC 6.63×10^{-5}), and experimental patch-clamp studies demonstrated altered channel kinetics and markedly increased K^+/NH_4^+ conductance, providing substantial functional support for a change-of-function effect. However, p.Gly1537Ser was absent from 101 additional ET cases, and sequencing SCN4A in a further 22 familial cases identified no additional candidate variants. Thus, despite strong segregation and functional evidence within the pedigree, the association remained family-specific and lacked independent replication.

27	Chao et al.	No ET-specific functional experiments performed.	HTRA2 encodes a mitochondrial serine protease involved in mitochondrial protein quality control and cellular stress/apoptotic pathways.	HTRA2 p.G399S was absent from all 468 ET cases, 778 PD cases and 14 ET/PD cases and was detected in only one healthy control. The study therefore did not replicate the previously reported association of HTRA2 p.G399S with hereditary ET or combined ET/PD and concluded that the variant is extremely rare and does not appear to play a major role in ET or PD in this Asian population.
28	Zhang et al.	RT-PCR confirmed gene TCP10L and CFAP298-TCP10L expression in control human cerebellum. p.Arg90Gln variant was not specifically tested.	TCP10L is a primate-specific nuclear protein implicated in transcriptional regulation.	WGS of a multigenerational Caucasian Canadian family identified a single rare candidate variant, TCP10L p.Arg90Gln, shared by all 3 confirmed ET/ET-plus cases and absent from 5 unaffected relatives. The variant was extremely rare (gnomAD NFE MAF 1.5×10^{-5}) and TCP10L expression was demonstrated in human cerebellum. However, the variant was identified in only one family, lacked independent replication and lacked variant-specific functional validation. The authors therefore proposed TCP10L for further genetic and functional investigation rather than

				establishing it as an ET gene.

29	Sánchez et al.	HEK293 cells, p.G171A produced approximately 3-fold lower SORT1 mRNA ($p<.0001$) and approximately 2-fold lower sortilin protein ($p<.05$) compared with WT. Mutant cells also showed significantly increased p75NTR mRNA, although the observed increase in apoptosis was not statistically significant. PGRN levels were unchanged.	SORT1 encodes sortilin, a VPS10-domain receptor involved in intracellular trafficking and signal transduction and binding proNGF/proBDNF.	WES identified the rare SORT1 p.Gly171Ala variant in two definite ET cases from one Spanish family. Functional experiments demonstrated reduced SORT1 mRNA and sortilin protein and increased p75NTR expression. However, an unaffected 43-year-old relative also carried the variant, and no additional p.G171A carriers or other candidate SORT1 variants were identified during follow-up screening. Thus, despite substantial functional evidence, the human genetic evidence remained family-specific and unreplicated.

30	Chen et al.	No ET-specific functional experiments performed.	PITX3 is a transcription factor important for midbrain dopaminergic neurons,	Neither of the two PD-associated PITX3 variants was significantly associated with ET in 200 Chinese Han cases and 426 controls. rs3758549 approached but did not reach significance at the allele level (T allele 14.0% ET vs 18.3% controls; p=.058), while rs4919621 was clearly negative (p=.537). Genotype and haplotype analyses were also negative. The study therefore provides no evidence that these two PITX3 variants contribute materially to ET susceptibility in this Chinese Han cohort.
31	Leng et al.	No new experimental functional study was performed for ET in this paper.	SCN11A encodes Nav1.9, a tetrodotoxin-resistant voltage-gated sodium channel preferentially expressed in peripheral nociceptive neurons that regulates resting neuronal excitability	SCN11A p.Arg225Cys was identified in a single four-generation Chinese family characterised by childhood familial episodic pain followed by adult-onset ET-like tremor. The variant was present in all 8 affected tested relatives and absent from 5 unaffected relatives. Although previous experimental studies established R225C as a gain-of-function Nav1.9 variant, the same variant had previously been reported in familial episodic pain without ET. The findings therefore support

				SCN11A-related episodic pain with an associated tremor phenotype in this family, rather than establishing SCN11A as a general ET gene.
32	Chen et al.,	No ET-specific functional experiments performed.	MAPK/ERK5 signalling and transcriptional regulation / neuronal development.	Three individual SNPs showed nominal ET associations after age/sex adjustment—TOX3 rs3104767 (OR 1.93, p=.007), MAP2K5/SKOR1 rs6494696 (OR 2.32, p=.032) and 2p14 rs6747972 (OR 1.66, p=.019)—but all lost significance after Bonferroni correction. In contrast, the five-SNP MAP2K5/SKOR1 GCGGG haplotype was more frequent in ET than controls (31.9% vs 15.5%; OR 1.96, 95% CI 1.37–2.81; p<.001), remaining significant in the <80-year subgroup. However, this was a small, single-centre study with substantial age/sex differences between cases and controls and no independent ET replication.

33	Diez-Fairen et al.	"No ET-specific functional experiments performed.	NA	SNP-based narrow-sense ET heritability was estimated at 75.5% (SE ±0.075, $p<2\times10^{-16}$), whereas dominance variance was not significant ($\delta^2=-0.003$, SE=0.0008). Chromosomes 6 and 21 showed the greatest regional heritability estimates. PD and RLS genetic risk scores did not significantly predict ET, and no genetic correlation with 832 tested traits survived Bonferroni correction. The study therefore supports an important additive genome-wide genetic contribution to ET, consistent with many variants of individually small effect.

Supplementary Table 7. Summary of Key Findings and Overall Evidence Strength of Included Studies.

Study	Study design / population	Principal findings	Contribution to evidence synthesis
Yan et al., 2020	Candidate-gene sequencing; 238 Chinese ET cases and 272 controls	FUS rs1052352 associated with ET; no support for previously proposed TENM4 or HTRA2causative variants	Adds an isolated candidate association for FUS and negative/conflicting evidence for TENM4/HTRA2
Liao et al., 2022	Large GWAS/meta-analysis; 7,177 ET cases and 475,877 controls of European ancestry	Five genome-wide significant loci; rs17590046 (PPARGC1A-region) supported a previous GWAS signal; SNV-based heritability 18.29%; cerebellar/axonogenesis enrichment	Strengthens evidence for a common-variant contribution to ET and provides further support for the PPARGC1A-region signal