Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Dewan R, Chia R, Ding J, et al. Pathogenic Huntingtin repeat expansions in patients with Frontotemporal Dementia and/or Amyotrophic Lateral Sclerosis.

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Supplementary Methods and Materials

Description of clinical cases carrying pathogenic *HTT* repeat expansions

Patient #1
The patient developed neurologic symptoms at age 68. His neurologic examination was consistent with a diagnosis of FTD-PSP. There was no family history of neurological disease.

Patient #2
The patient developed behavioral changes at the age of 56, and she was diagnosed with behavioral variant FTD. By report, her elderly mother had been diagnosed with Alzheimer's disease.

Patient #3
The patient was a woman who developed language disturbances at age 57. She was subsequently diagnosed as having nonfluent primary progressive aphasia. There was no family history of neurological disease.

Patient #4
The patient was a 19-year-old woman who had presented with a two-year history of progressive academic performance decline, dysarthria, bradykinesia, and gait disturbance. Her speech had become progressively slurred and soft, and her handwriting had deteriorated. She did not report any falls, but she did have several episodes of syncope that were initially diagnosed as seizures. Cranial nerve examination revealed supranuclear vertical gaze palsy, masked facies, and dysarthria. She also was noted to have bradykinesia with cogwheeling in her upper limbs, and spasticity and hyperreflexia in the lower limbs. MRI of the brain showed basal ganglia iron deposition. She was started on Sinemet with no improvement. The patient's father was said to have a similar neurological syndrome consisting of cognitive decline, gait disorder, and dysarthria that started in his late twenties.

Patient #5
The patient developed symptoms of ALS at age 56 and died eleven years later of respiratory failure after a typical course of motor neuron disease.

Patient #6
The patient presented at the age of 44 with personality changes (short temper) and decreased initiative (apathy). His memory was intact, and neuropsychological evaluation was consistent with FTD. His father had speech loss and gait disturbance at age 40 and died from his illness at the age of 52.

Patient #7
This right-handed man presented with lower limb weakness at the age of 76. A sibling had been diagnosed with ALS. Neurological examination at the age of 84 revealed an ALS Functional Rating Scale of 17 (maximum score of the ALSFRS-R = 40). He had upper and lower motor neuron signs in the bulbar region, the upper limbs, and the lower limbs. Additionally, he was diagnosed with FTD. He was placed on non-invasive positive pressure ventilation for respiratory failure.

Patient #8
This patient was a man who developed a right foot drop at the age of 62. He was initially diagnosed with primary lateral sclerosis and had a baclofen pump implanted for the treatment of spasticity. His symptoms progressed, and the diagnosis was changed to ALS based on neurophysiological testing. Before death, he was unable to ambulate, used a motorized wheelchair, had limited hand movements, wore a cervical collar to correct head tilt, and used an eye gaze system to communicate. He died at the age of 70 due to respiratory failure.

Whole-genome sequencing

Genomic DNA was extracted from whole blood or cerebellar brain tissue using a Maxwell RSC Instrument (Promega Corp., Madison, WI, USA). PCR-free, paired-end, non-indexed libraries were constructed using the TruSeq PCR-free chemistry according to the manufacturer's instructions (Illumina Corp., San Diego, CA, USA). Sequencing was performed on an HiSeq X Ten sequencer (version 2.5 chemistry, Illumina) using 150 base pair (bp), paired-end cycles, applying a single sample to each lane.

Raw genome data in FASTQ file format were transferred to Google Cloud Storage. Paired-end sequences were processed by following the pipeline standard developed by the Centers for Common Disease Genomics (CCDG; https://www.genome.gov/27563570/). This standard allows for whole-genome sequence (WGS) data processed by different groups to generate 'functionally equivalent' results (PMID: 30279509). The GRCh38DH reference genome was used for alignment, as specified in the CCDG standard. For WGS alignments and processing, the Broad Institute's implementation of the functional equivalence standardized pipeline was used. This pipeline, which incorporates the GATK (2016) Best Practices (PMID: 25431634), was implemented in the workflow description language (WDL) for deployment and execution on the Google Cloud Platform. Single-nucleotide (SNV) and InDel variants were called from the processed WGS data following the GATK Best Practices using another Broad Institute workflow for joint discovery and Variant Quality Score Recalibration (VQSR). Both Broad workflows for WGS sample processing and joint discovery are publically available (https://github.com/gatk-workflows/broad-prod-wgs-germline-snps-indels). The average sequencing read-depth after

filtering by alignment quality was 35x, and mean coverage per genome was 36.3 (95% confidence interval: 29.3–43.3). All of the whole-genome sequence data (discovery and replication cohorts) were processed using the same pipeline. Genome data obtained from the Wellderly control cohort and the NIA control cohort were treated the same as the data generated for the dementia resource to ensure uniformity of processing.

Genomes were excluded from analysis for the following reasons: (1) high contamination rate (> 5% based on VerifyBamID freemix metric)[4], (2) excessive heterozygosity rate (exceeding +/- 0.15 F-statistic), (3) low call rate (≤ 95%), (4) discordance between reported sex and genotypic sex, and (5) duplicate samples (determined by pi-hat statistic). Samples with non-European ancestry based comparison of principal components analysis with the HapMap 3 Genome Reference Panel (Fig. S2) were flagged, but not excluded.[5,6]

Whole-genome sequence data was analyzed for pathogenic mutations in fifty genes associated with neurodegenerative diseases including *ALS2*, *APP*, *ATP13A2*, *ATXN2*, *BSN*, *C9orf72*, *CHCHD10*, *CHMP2B*, *CSF1R*, *DCTN1*, *DNAJC6*, *FBXO7*, *FIG4*, *FUS*, *GBA*, *GCH1*, *GRN*, *HNRNPA1*, *KIF5A*, *LRRK2*, *MAPT*, *MATR3*, *OPTN*, *PANK2*, *PARK2*, *PARK7*, *PFN1*, *PINK1*, *PLA2G6*, *POLG*, *PSEN1*, *PSEN2*, *RAB39B*, *SETX*, *SNCA*, *SOD1*, *SPG11*, *SPTLC1*, *SQSTM1*, *SYNJ1*, *TAF1*, *TARDBP*, *TBK1*, *TIA1*, *TUBA4A*, *UBQLN2*, *VAPB*, *VCP*, *VPS13C*, and *VPS35*.

Brain immunohistochemistry

Formalin-fixed, paraffin-embedded sections were prepared from postmortem brain regions and stained with Luxol fast blue counterstained with hematoxylin and eosin, and immunostained using polyclonal antibodies against huntingtin (2B4), p62, and 1c2 (see Table S3 for primary antibody conditions). The huntingtin/p62 dual stains were performed using a DAB and alkaline phosphatase dual staining system on a Leica Bond autostainer with a hematoxylin counterstain.

Repeat-primed PCR assay

The repeat-primed PCR assay to measure HTT CAG repeat length was performed using the Eppendorf Mastercycler pro thermal cycler (Fisher Scientific, Houston, TX, USA) in a final volume of 20µl containing 1X FailSafe Premix J (Epicenter, Madison, WI, USA), 1.0U Platinum TaqDNA polymerase (Invitrogen Corporation, Carlsbad, CA, USA), 0.5 µM Primer Mix containing 0.5 µmol/L each of forward primer 5′-ATGAAGGCCTTCGAGTCCCTCAAGTCC-3′, with a 5’ 6FAM fluorescent tag, and reverse primer 5′-CGGTGGCGGCTGTTGCTGCTGCTGCTGCTG-3′ (Eurofins Genomics LLC, Louisville, KY, USA), and 1µl of 15-25ng/µl genomic DNA. Cycling conditions were identical to those in Jama

et al (Jama, 2013 #3). The 5’ end of the reverse primer in this protocol contains 15 bp specific to the region in between the *HTT* CAG and CCG trinucleotide repeats, fully encapsulating the trailing CAA-CAG sequence and preventing against any changes in primer specificity due to loss of interruption (conversion to CAGCAG).

Fragment length analysis was performed on an ABI 3730xl genetic analyzer (Applied Biosystems Inc., Foster City, CA, USA), using a mixture of 2µl of repeat-primed PCR products, 0.5µl GeneScan 500 LIZ size standard (Thermo Fisher Scientific, Cincinnati, OH, USA) and 7.5µl HiDi formamide (Applied Biosystems Inc.). The mixture was heated at 95℃ for 3 minutes and then immediately cooled on ice for at least 5 minutes, prior to loading for capillary electrophoresis. Data was analyzed using GeneScan software (version 4, Applied Biosystems Inc.). Repeat expansions were quantifiable with a 3-bp periodicity.

Supplementary Figures

Figure S1. Flow chart outlining the study

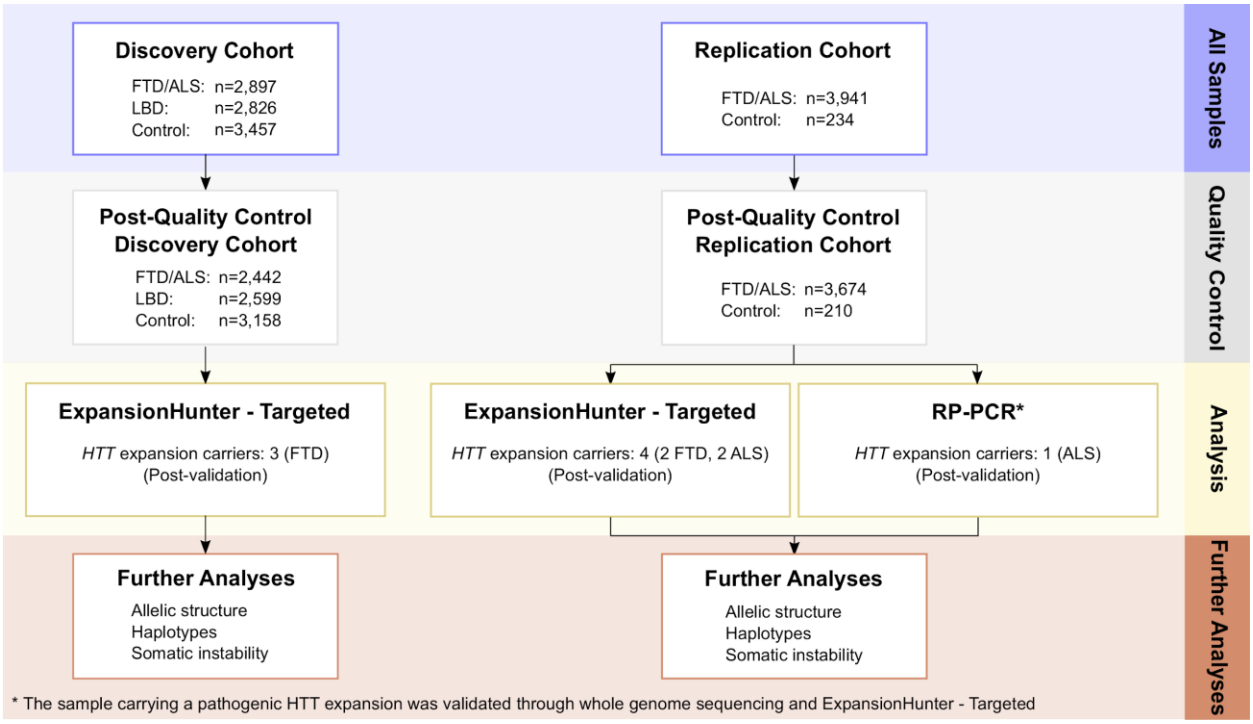


Figure S2. Ancestry determination using comparison of principal components analysis with the HapMap 3 Genome Reference Panel.[5]

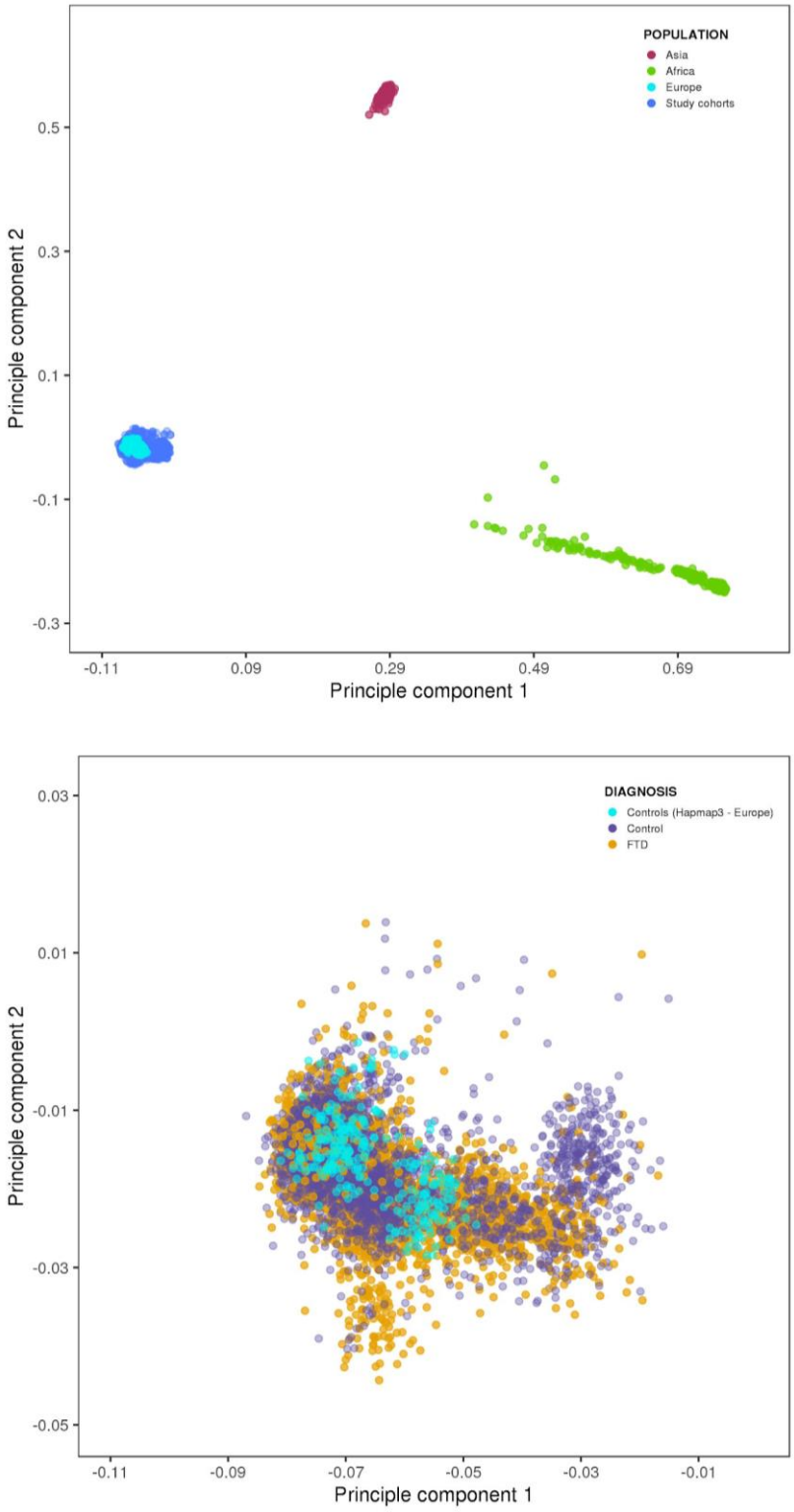


Figure S3. Chromatograms of repeat-primed PCR assay performed using samples carrying full-penetrance *HTT* pathogenic alleles.

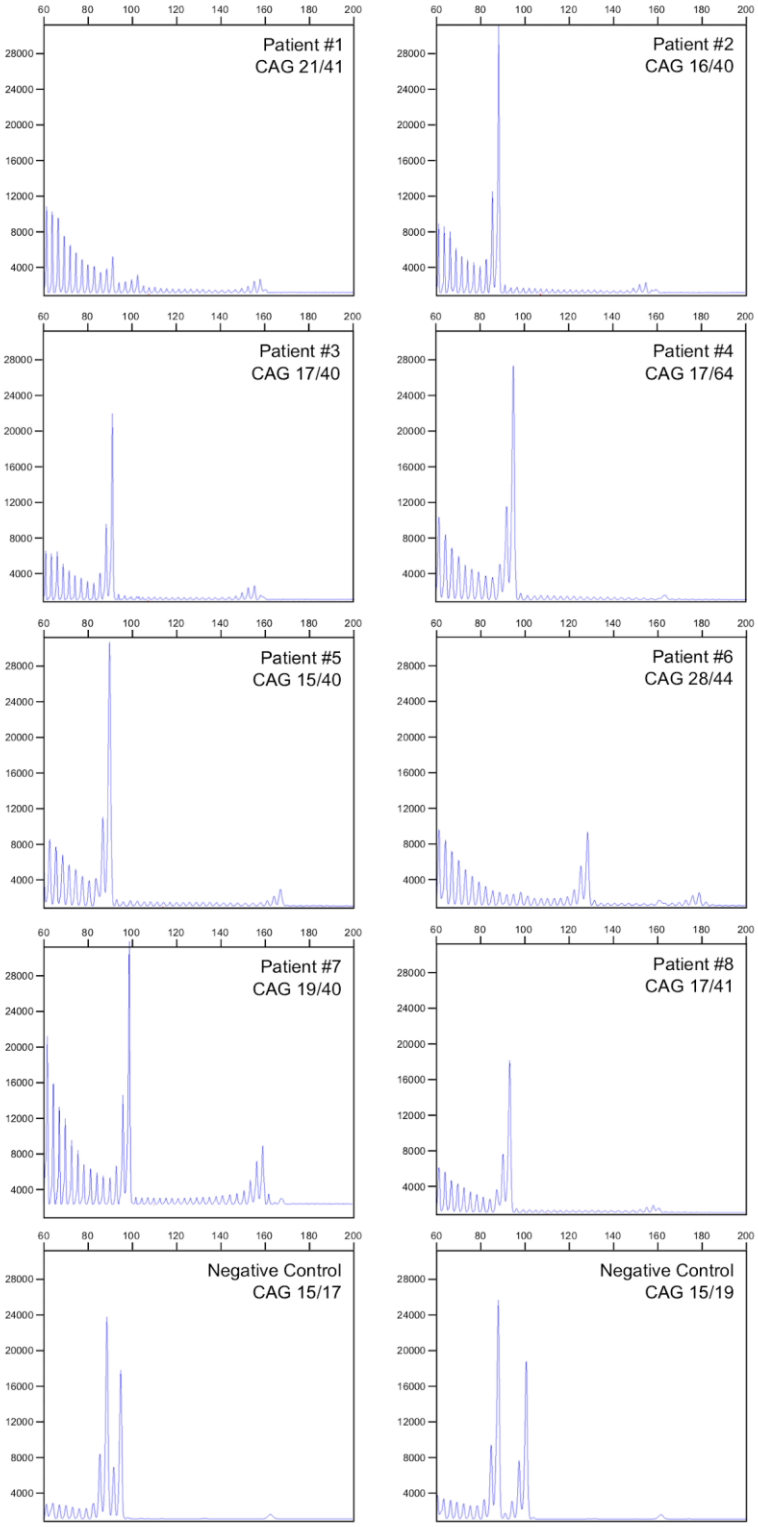


Figure S4. Chromatograms of repeat-primed PCR assay performed using samples from twenty-two brain and spinal cord regions obtained at the postmortem of patient #8.

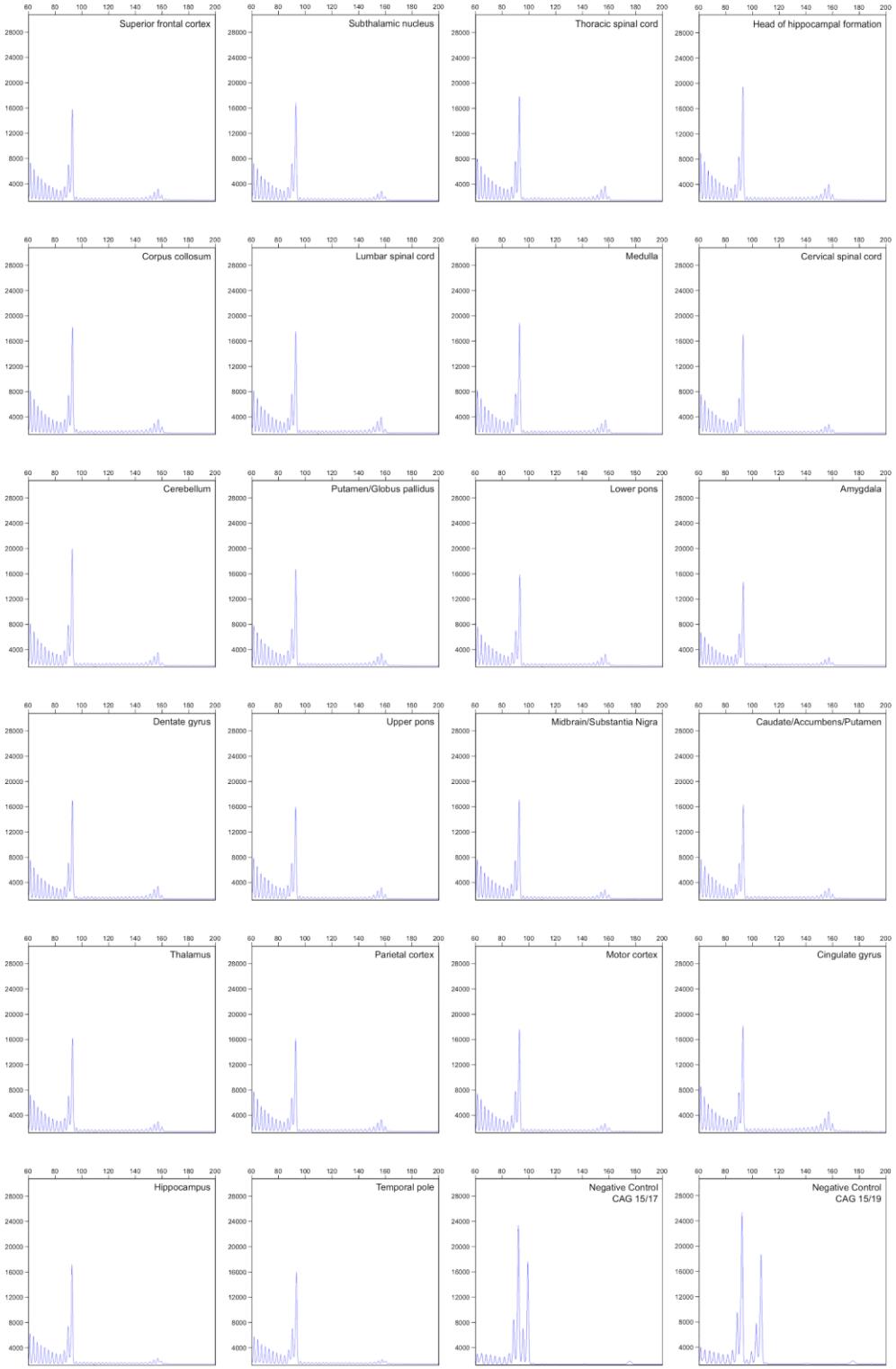


Figure S5. Instability index performed using samples from twenty-two brain and spinal cord regions obtained at the postmortem of patient #8. The index was generated from 'bulk' genomic data represented in the repeat-primed PCR using the method described by Lee and colleagues.[7]

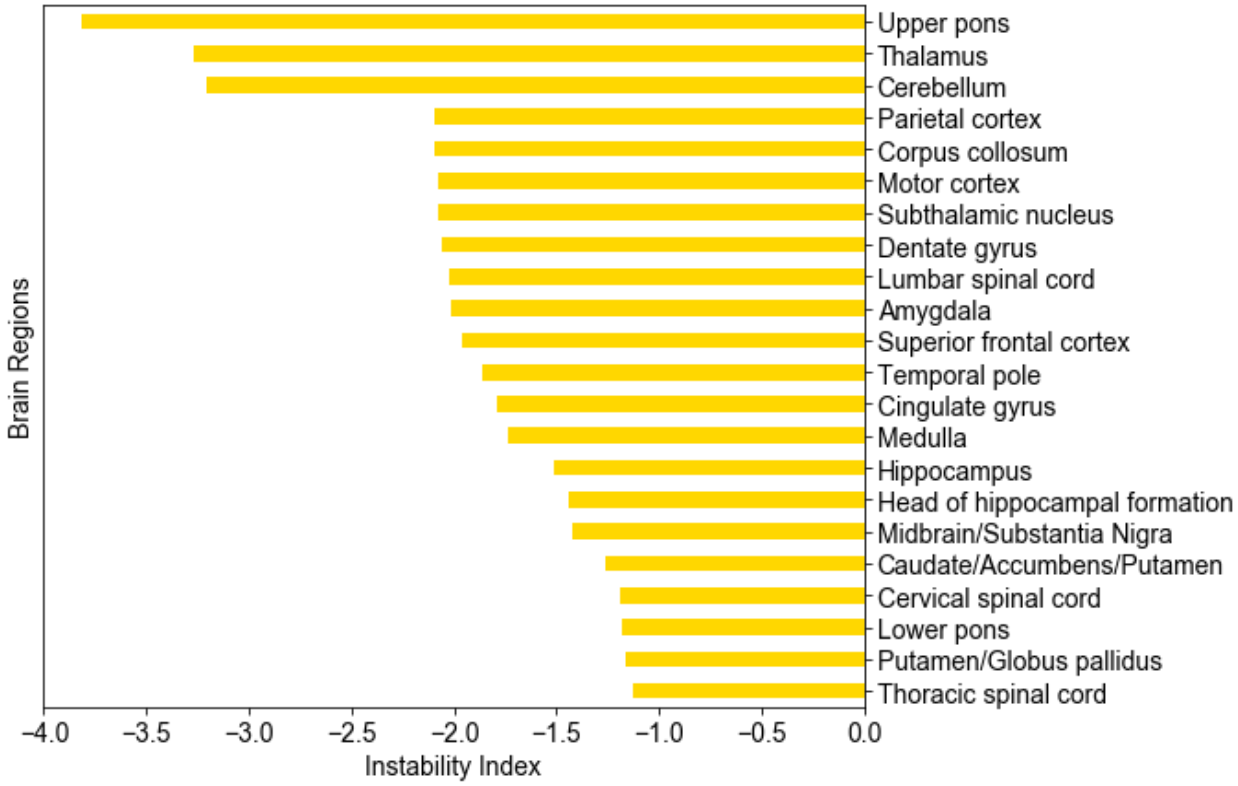
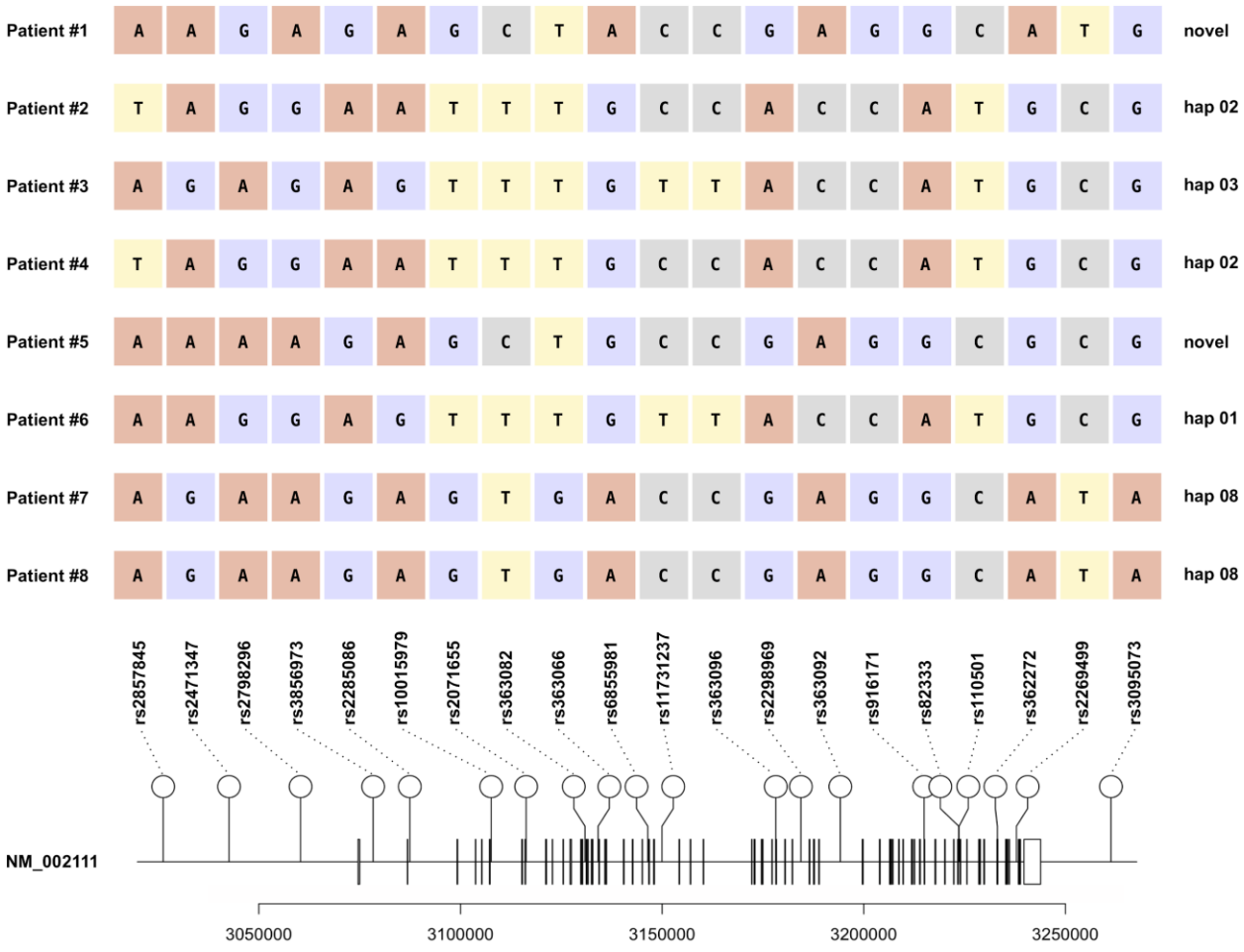


Figure S6. Occurrence of known haplotypes across the *HTT* locus in the FTD/ALS patients carrying full penetrance repeat expansions. Haplotypes were defined by Chao and colleagues.[8]



Supplementary Tables

Table S1. Demographic and clinical features of samples included in the analysis.

	FTD (n = 1,476)	**ALS (n = 1,065)**	**LBD (n = 2,599)**	**Control (n = 3,158)**
Female (%)	678 (46.0%)	490 (46.0%)	1,649 (63.4%)	1,483 (47.0%)
Age (IQR)	65.2 (58.0–71.0)	65.6 (59.0–73.0)	74.7 (68.0–82.0)	77.0 (69.0–86.0)
Site of onset				
Cognitive (%)	1,476 (100%)	2 (0.2%)	2,599 (100.0%)	-
Bulbar (%)	-	322 (30.2%)	-	-
Spinal (%)	-	603 (56.6%)	-	-
Family history (%)	67 (4.5%)	111 (10.4%)	240 (9.2%)	-
C9orf72 carrier	50 (3.4%)	104 (9.8%)	-	-

FTD, frontotemporal dementia; ALS, amyotrophic lateral sclerosis; LBD, Lewy body dementia; IQR, interquartile range; *C9orf72* carrier status is based on repeat-primed PCR and ExpansionHunter – Targeted; Site of onset is missing for 138 ALS cases. *C9orf72* status is missing for 6 ALS and 22 FTD cases. The contributing study sites and consortia for these samples were: Pitie-Salpetriere Hospital (Paris), University of Thessalia (Volos), Dublin Brain Bank (Dublin), University of Torino (Torino), University Hospital of Cagliari (Cagliari), University of Bari (Bari), University of Luxembourg (Luxembourg City), Hospital de Sant Pau (Barcelona), University Hospital Mutua de Terrassa (Barcelona), Biobanc-Hospital Clinic - IDIBAPS (Barcelona), Hospital Universitario "Marques de Valdecilla" (Santander), King's College London (London), University College London (London), Imperial College London (London), University of Bristol Brain Bank (Bristol), Newcastle University (Newcastle upon Tyne), The University of Manchester (Manchester), McGill University (Montreal), University of Toronto (Toronto), Virginia Commonwealth University (Richmond, VA), Banner Sun Health Research Institute (Phoenix, AZ), Rush Alzheimer's Disease Center (Chicago, IL), Northwestern University (Evanston, IL), Parkinson's Disease Biomarker Program, Fox Investigation for New Discovery of Biomarkers Program, Indiana University School of Medicine (Indianapolis, IN), National Institutes of Health (Bethesda, MD), New York University Langone Medical Center (New York, NY), Icahn School of Medicine at Mount Sinai (New York, NY), National Cell Repository for Alzheimer's Disease (Indianapolis, IN), University of California San Diego (San Diego, CA), University of California (Irvine, CA), North American Brain Expression Consortium, NINDS Biorepository at Coriell Institute (Camden, NJ), University of Maryland Brain Bank (Baltimore, MD), University of Kansas Medical Center (Kansas City, KS), University of Michigan Brain Bank (Ann Arbor, MI), Mayo Clinic (Jacksonville, FL), Mayo Clinic (Rochester, MN), Brigham & Women's Hospital (Boston, MA), Scripps Translational Science Institute (La Jolla, CA), Johns Hopkins University (Baltimore, MD), Oregon Health & Science University Brain Bank (Portland, OR), and Baltimore Longitudinal Study on Aging (Baltimore, MD).

Table S2. Primer sequences and conditions used for the repeat-primed PCR.[9]

Primers	Sequence
Forward	6FAM-ATGAAGGCCTTCGAGTCCCTCAAGTC
Reverse	ATGAAGGCCTTCGAGTCCCTCAAGTC

Thermocycling conditions were as follows: 95℃ for five minutes, then 35 cycles consisting of 94℃ for one minute, 64℃ for one minute, 72℃ for two minutes, followed by a final extension stage of 72℃ for fifteen minutes.

Table S3. Conditions used for immunohistochemistry staining of brain and spinal cord tissue.

Antibody	**Company**	**Catalogue number**	**Dilution**	**Primary antibody incubation time (minutes)**	**Protocol and dilution**	**Platform**
Huntingtin/ p62 double stain	Millipore/ Abcam	MAB5492/ ab207305	1:2000	32/24	64 min (CC1)	Roche Ventana Instrument
Rabbit Anti-Ubiquitin	Dako	Z0458	1:2000	21 hrs	--	Manual
Anti-polyglutamine-Expansion Diseases Marker Antibody, clone 5TF1-1C2	Millipore Sigma	MAB1574	1:500	21 hrs	--	Manual
Anti-phospho TDP-43 (pS409/410)	Cosmo Bio Co., Ltd	CAC-TIP-PTD-M01	1:2000	21 hrs	pretreat 10min boil citrate buffer, pH 6.0	Manual

Table S4. Results of ExpansionHunter – Targeted applied to whole genome sequence data for ten disease causing repeat expansions that have been previously experimentally validated.

Gene	Chr	Inheritance*	Lower Bound	Control Pathogenic / Total	Control Pathogenic Freq	FTD Pathogenic / Total	FTD Pathogenic Freq	ALS Pathogenic / Total	ALS Pathogenic Freq	LBD Pathogenic / Total	LBD Pathogenic Freq
AR	X	XL	37	10/3157	0.003168	3/1377	0.002179	3/1065	0.002817	6/2599	0.002309
AR Female	X	XL	37	2/1665	0.001201	1/634	0.001577	1/490	0.002041	2/903	0.002215
AR Male	X	XL	37	8/1454	0.005502	2/743	0.002692	2/575	0.003478	4/1603	0.002495
ATN1	12	AD	48	0/3158	0	0/1377	0	0/1065	0	0/2598	0
ATXN1	6	AD	39	14/3158	0.004433	6/1377	0.004357	4/1065	0.003756	16/2599	0.006156
ATXN3	14	AD	52	0/3158	0	0/1377	0	0/1065	0	0/2599	0
C9ORF72	9	AD	30	5/3158	0.001583	59/1377	0.042847	108/1065	0.101408	6/2599	0.002309
DMPK	19	AD	50	4/3158	0.001267	2/1377	0.001452	1/1065	0.000939	2/2599	0.00077
FMR1	X	XL	200	0/3158	0	0/1377	0	0/1065	0	0/2599	0
FMR1 Female	X	XL	200	0/1665	0	0/634	0	0/490	0	0/903	0
FMR1 Male	X	XL	200	0/1455	0	0/743	0	0/575	0	0/1603	0
FXN (hom)	9	AR	66	0/3158	0	0/1377	0	0/1065	0	0/2599	0
HTT (CAG)	**4**	**AD**	**40**	**0/3158**	**0**	**3/1377**	**0.002179**	**0/1065**	**0**	**0/2599**	**0**
PHOX2B	4	AD	25	776/3158	0.245725	296/1377	0.21496	251/1065	0.235681	542/2599	0.208542

* Modes of inheritance: x-linked (XL), autosomal dominant (AD), autosomal recessive (AR); homozygous (hom) refers to biallelic expansion in genes with autosomal recessive

Supplementary References

1. Li H, Durbin R. Fast and accurate short read alignment with Burrows-Wheeler transform. Bioinformatics 2009;25(14):1754–60.

2. DePristo MA, Banks E, Poplin R, et al. A framework for variation discovery and genotyping using next-generation DNA sequencing data. Nat Genet 2011;43(5):491–8.

3. Poplin R, Ruano-Rubio V, DePristo MA, et al. Scaling accurate genetic variant discovery to tens of thousands of samples [Internet]. Available from: http://dx.doi.org/10.1101/201178

4. Jun G, Flickinger M, Hetrick KN, et al. Detecting and estimating contamination of human DNA samples in sequencing and array-based genotype data. Am J Hum Genet 2012;91(5):839–48.

5. International HapMap 3 Consortium, Altshuler DM, Gibbs RA, et al. Integrating common and rare genetic variation in diverse human populations. Nature 2010;467(7311):52–8.

6. Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: rising to the challenge of larger and richer datasets. Gigascience 2015;4:7.

7. Lee J-M, Zhang J, Su AI, et al. A novel approach to investigate tissue-specific trinucleotide repeat instability. BMC Syst Biol 2010;4:29.

8. Chao MJ, Gillis T, Atwal RS, et al. Haplotype-based stratification of Huntington's disease. Eur J Hum Genet 2017;25(11):1202–9.

9. Jama M, Millson A, Miller CE, Lyon E. Triplet repeat primed PCR simplifies testing for Huntington disease. J Mol Diagn 2013;15(2):255–62.

10. Dolzhenko E, Deshpande V, Schlesinger F, et al. ExpansionHunter: a sequence-graph-based tool to analyze variation in short tandem repeat regions. Bioinformatics 2019;35(22):4754–6.

11. Dolzhenko E, van Vugt JJFA, Shaw RJ, et al. Detection of long repeat expansions from PCR-free whole-genome sequence data. Genome Res 2017;27(11):1895–903.