Table S1. Macroscopic lesions in hippocampus of FXTAS cases

Case Number	Macroscopic lesions
Case 1	Mild generalized atrophy and moderate dilation of lateral ventricles
Case 2	Unremarkable
Case 4	Mild increase in ventricular size and expansion of the cerebral white matter (edema)
Case 5	Decreased size of the hippocampus and marked diffuse ventriculomegaly
Case 6	White matter disease and mild ventricular dilation (MRI)
Case 7	Decreased size of the hippocampus and ventriculomegaly
Case 9	Moderate frontal gyral atrophy, multiple irregular soft regions of grayish discoloration – prominent in periventricular
Case 10	Left hemisphere shows marked decrease in ventricular size
Case 12	Marked decrease in the size of the amygdala and hippocampus, moderate ventricular dilation
Case 13	Moderate frontoparietal atrophy and ventricles decreased in size
Case 14	Mild frontal cortical atrophy
Case 15	Mild atrophy and scattered white matter disease (MRI)
Case 16	Moderate frontal cortical atrophy, moderate enlargement of ventricles, marked thinning of gray matter ribbon in all lobes to 2mm
Case 18	Diffuse frontoparietal and superior temporal gyral atrophy, mild edema, equivocal decrease in ventricular size
Case 19	Moderate frontoparietal and temporal lobe atrophy
Case 21	Atrophy of the rostral superior frontal gyrus, compressed ventricles, which are not clearly dilated, irregular small areas of grayish discoloration in white matter, which are not periventricular
Case 22	Mild frontal temporal-parietal atrophy, moderately dilated ventricles

Not applicable for cases 3, 8, 11, 17, 20, and 23 to 26.

Table S2. Neuropathology in hippocampus in 26 FXTAS cases

Case Number	Inclusions (neurons + astrocytes)	CA1 neuron cell drop	CA3 neuron cell drop	(S)	(G)	(PVC)	(Co)	(H)	(T)	(Cl)	(He)
Case 1	Yes	3	3	2	2	3	3	2	2	1	1
Case 2	Yes	3	1	2	2	2	1	1	1	2	1
Case 3	Yes	1	2	1	2	2	3	1	1	2	2
Case 3	No	3	2	4	2	2	3	1	2	2	1
Case 4	Yes	2	2	1	4	1	2	1	2	2	1
Case 5	Yes	3	3	1	2	2	1	1	2	2	1
Case 6	Yes	2	1	1	2	2	1	1	1	1	2
Case 7	Yes	3	3	1	1	2	2	1	2	2	1
Case 8	Yes	3	1	2	2	2	2	1	2	2	1
Case 9	Yes	3	3	1	3	2	1	1	2	2	1
Case 11	Yes	3	3	1	2	2	3	2	2	3	2
Case 12	Rare	2	3	3	1	2	2	2	2	2	2
Case 13	Rare	3	2	1	3	3	3	2	2	2	2
Case 14	Yes	3	1	2	2	3	2	1	2	2	1
Case 15	Yes	1	2	2	2	2	3	2	3	2	2
Case 16	No	2	1	1	2	2	1	1	1	2	1
Case 17	Yes	3	3	1	1	2	1	1	1	1	1
Case 18	Yes	3	-	3	2	2	1	1	2	2	1
Case 19	Yes	4	3	1	3	2	2	2	2	3	2
Case 20	Yes	4	2	3	2	2	2	1	2	2	2
Case 21	Yes	2	2	2	2	3	3	3	2	2	1
Case 22	Yes	3	2	1	3	3	1	2	3	2	1
Case 23	Yes	3	2	1	2	2	2	1	1	2	1
Case 24	Yes	3	3	1	1	2	1	2	2	1	2
Case 25	Yes	4	3	1	2	1	1	1	2	1	1
Case 26	Yes	3	2	1	2	2	1	1	1	2	1

Spongiosis (S), Gliosis (G), Perivascular cuffing (PVC), Congestion (Co), Microhemorrhage (H), Vessel wall thickness (T), Clearing (Cl), Hemosiderin (He); All scales of severity: normal or minimal abnormality (1), mild (2), moderate (3), extensive/severe (4). NA, tissue not available for analysis, either because specific samples were unavailable or because fixation artefacts precluded further analysis. Reference for NIA-Reagan criteria (Newell et al., 1999).

Table S3. Additional significant histopathology in hippocampus of 26 FXTAS cases

Case Number	Histopathology
Case 1	Atherosclerosis
Case 3	Neuropathology of Alzheimer's; no Lewy bodies; Lewy body disease
Case 4	Sever diffuse acute cerebral ischemic damage
Case 5	Scattered hypertrophic astrocytes with fibrillary processes, neurofibrillary tangles and beta-amyloid plaques
Case 10	Mild, patchy cerebrovascular aterosclerosis
Case 12	Diffuse, moderately severe ASD
Case 13	Tangles in hippocampus, no atherosclerosis
Case 15	Small vessel disease
Case 16	Pathologically met the criteria for Alzheimers; Prominent GVD and scattered plaques and tangles present in CA1
Case 17	Minimal patchy athersclerosis
Case 18	GFAP stain shows scattered reactive astrocytes, with patchy densities in deep white matter
Case 19	CA1 shows diffuse brick-red change in the neurons; acute ischemic damage to hippocampus
Case 20	Intermediate stage alzheimer's disease
Case 21	Biels stain shows small number of neuritic plaques in gray matter corresponding to aging. Loss of axons was seen in patchy areas of pallor in white matter, which corresponded to myelin loss. LFB-PAS showed decreased number of glial cells in these abnormal areas, moderate spotty athersclerosis
Case 22	Scant granulovacuolar degeneration

No additional or significant information for cases: 2, 6 to 9, 11, 14, 23 to 26.

Table S4. Number of total necrotic neurons (actual counts and percentages) in CA1&3 and DG1&2 subregions of FXTAS hippocampi.

Case Number	nN CA1	% nN CA1	nN CA3	% nN CA3	nN DG1	% nN DG1	nN DG2	% nN DG2
Case 1	1/60	1.5	1/35	2.85	0/67	0	1/90	0.9
Case 2	17/36	47.2	12/75	16	4/116	3.44	8/178	4.49
Case 3	0/94	0	3/40	7.5	0/28	0	1/122	0.8
Case 4	11/57	19.3	2/46	4.35	0/95	0	0/103	0
Case 5	4/75	5.3	6/52	11.53	1/95	1.05	3/169	1.77
Case 6	6/50	12	3/33	9.09	4/96	4.16	1/175	0.57
Case 7	3/68	4.4	5/60	8.33	4/106	3.77	2/102	1.96
Case 8	2/55	3.63	2/34	5.88	16/57	28.07	6/147	4.08
Case 9	3/59	5.08	5/60	8.33	0/139	0	0/99	0
Case 10	2/50	4	3/32	9.37	1/164	0.6	2/240	0.83
Case 11	2/60	3.33	7/28	25	0/105	0	3/78	3.85
Case 12	3/90	3.33	4/33	12.12	3/76	3.95	3/85	3.53
Case 13	0/58	0	1/48	2.08	2/65	3.07	1/128	0.78
Case 14	3/51	5.9	2/85	2.35	0/120	0	2/171	1.17
Case 15	13/151	8.6	7/44	15.9	8/118	6.77	2/51	3.92
Case 16	7/85	8.23	3/87	3.45	3/75	4	3/110	2.73
Case 17	1/35	2.8	0/37	0	1/149	0.67	2/124	1.6
Case 18	7/47	14.89	-	-	1/120	0.83	2/146	1.37
Case 19	4/24	16.6	0/39	0	1/59	1.69	2/218	0.92
Case 20	5/22	22.72	13/59	22.03	2/28	7.4	1/130	0.77
Case 21	6/85	7.06	3/47	6.38	3/175	1.7	16/180	8.88
Case 25	0/25	0	3/31	9.68	3/125	2.4	4/98	4.08
Case 26	8/52	15.38	6/55	10.9	2/112	1.78	3/96	3.13

The number of necrotic neurons were revealed as ratios of necrotic neurons per total number of neurons counted, and as percentage (%) of necrotic neurons. Necrotic neurons shown as nN CA1, nN CA3, nN DG1 and nN DG2; "-" Not available.