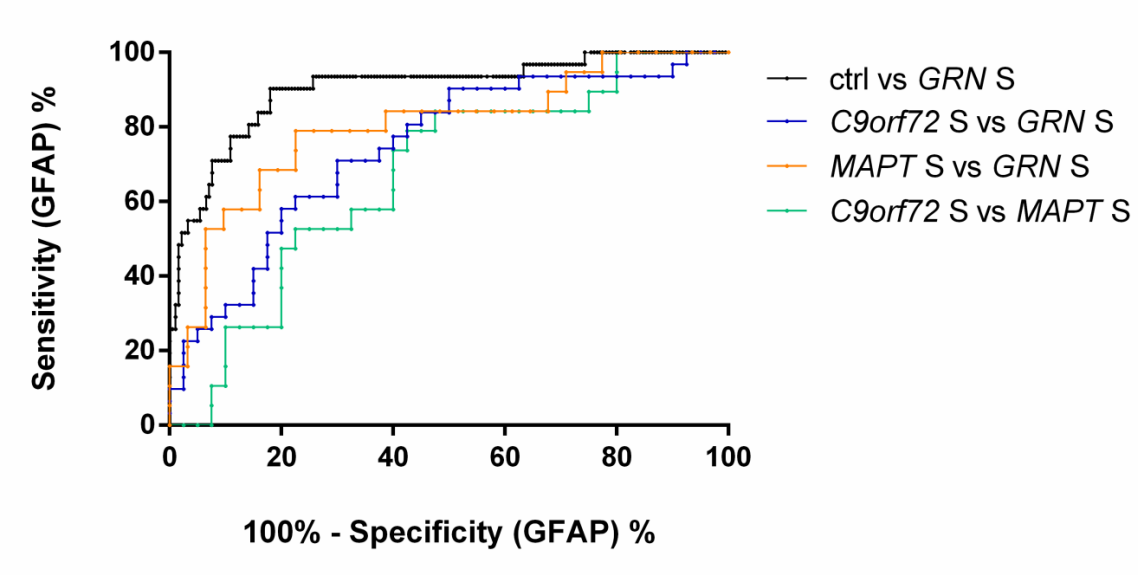
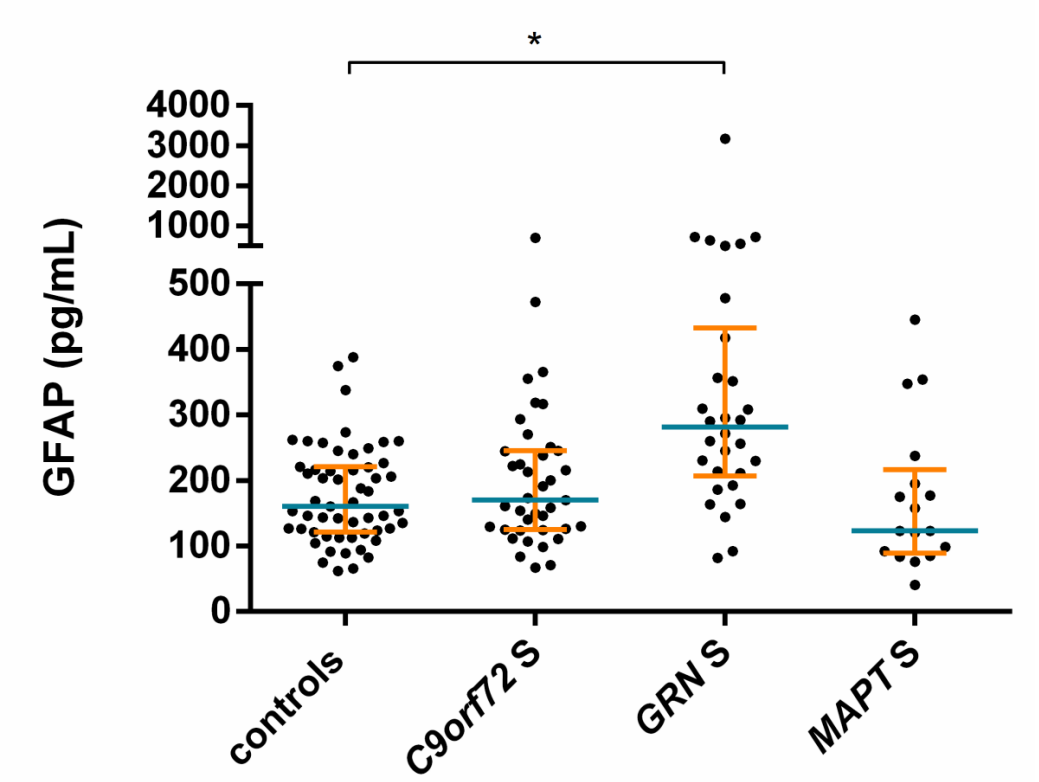
Supplementary Figure 1. Receiver operating characteristic curves showing the ability of GFAP to distinguish controls from symptomatic *GRN* mutation carriers and the symptomatic mutation carriers from one another.



Supplementary Figure 2. Plasma GFAP in older (age > 51 years) gender-matched controls (n = 55) and symptomatic FTD mutation carriers for each gene: *C9orf72* (n = 39), *GRN* (n = 30) and *MAPT* (n = 17). Median designated by blue line; interquartile ranges indicated by orange error bars. * = significant differences. Mean age [standard deviation] in years: controls = 61.4 (6.9); *C9orf72* = 66.0 (6.2); *GRN* = 64.9 (6.7) and *MAPT* = 60.9 (6.7). Median GFAP [interquartile range] (pg/mL): controls = 160.4 (121.5 - 221.3); *C9orf72* = 170.5 (125.1 - 245.4); *GRN* = 281.2 (211.5 - 417.8) and *MAPT* = 123.3 (92.5 - 195.1).



Supplementary Table 1. Summary of cross-sectional imaging data at baseline. The whole brain and six cortical regions are expressed as a percentage of total intracranial volume. Values are displayed as medians with interquartile ranges. PS – presymptomatic; S – symptomatic.

	Controls	*C9orf72* PS	*C9orf72* S	*GRN* PS	*GRN* S	*MAPT* PS	*MAPT* S
Number of participants	171	72	34	83	24	34	14
Whole brain	80.7 (79.0 - 82.5)	79.6 (76.7 - 81.4)	72.4 (69.0 - 76.3)	80.8 (79.3 - 82.5)	71.1 (69.1 - 75.3)	81.2 (79.2 - 82.1)	72.2 (71.3 - 74.4)
Frontal	12.5 (12.0 – 13.0)	12.3 (11.8 - 12.8)	10.5 (9.7 - 11.2)	12.8 (12.1 - 13.2)	10.3 (9.8 - 11.1)	12.5 (12.1 - 12.9)	11.2 (11.0 - 11.5)
Temporal	8.5 (8.2 - 8.7)	8.3 (8.1 - 8.6)	7.6 (7.1 - 8.0)	8.6 (8.2 - 8.9)	7.7 (7.2 - 8.1)	8.6 (8.2 - 8.9)	6.3 (6.1 - 7.3)
Parietal	6.6 (6.3 - 6.9)	6.4 (6.1 - 6.7)	5.7 (5.3 - 5.9)	6.8 (6.4 - 7.0)	5.7 (5.3 - 6.2)	6.6 (6.3 - 6.9)	6.0 (5.7 - 6.4)
Occipital	5.1 (4.9 - 5.5)	5.0 (4.8 - 5.3)	4.5 (4.3 - 4.9)	5.2 (5.0 - 5.4)	5.0 (4.7 - 5.2)	5.1 (4.7 - 5.4)	4.9 (4.7 - 5.1)
Cingulate	2.0 (1.9 - 2.1)	2.0 (1.9 - 2.1)	1.8 (1.7 - 1.9)	2.0 (1.9 - 2.2)	1.7 (1.7 - 1.9)	2.0 (1.9 - 2.1)	1.8 (1.7 - 1.9)
Insula	0.8 (0.7 - 0.8)	0.7 (0.7 - 0.8)	0.5 (0.5 - 0.6)	0.8 (0.7 - 0.8)	0.6 (0.5 - 0.6)	0.8 (0.7 - 0.8)	0.5 (0.5 - 0.6)

Supplementary Table 2. Summary of longitudinal imaging data. The whole brain and six cortical regions are expressed as an annualized percentage rate of atrophy. Values are displayed as medians with interquartile ranges. PS – presymptomatic; S – symptomatic.

	Controls	*C9orf72* PS	*C9orf72* S	*GRN* PS	*GRN* S	*MAPT* PS	*MAPT* S
Number of participants	102	38	15	46	14	24	4
Scan interval (years)	1.1 (1.0 - 1.2)	1.1 (1.0 - 1.2)	1.1 (0.9 - 1.2)	1.0 (1.0 - 1.1)	1.0 (1.0 - 1.1)	1.1 (1.1 - 1.1)	1.0 (1.0 - 1.4)
Whole brain	0.0 (-0.3 - 0.4)	0.5 (-0.1 - 1.0)	1.0 (-0.3 - 2.1)	0.2 (-0.2 - 0.5)	2.4 (1.2 - 3.0)	0.1 (-0.9 - 0.6)	0.7 (0.5 - 1.6)
Frontal	0.1 (-1.0 - 0.7)	0.2 (-0.6 - 1.1)	1.5 (-0.7 - 2.7)	0.2 (-0.7 - 0.6)	3.6 (0.9 - 9.1)	-0.3 (-2.3 - 1.2)	1.6 (0.6 - 4.5)
Temporal	-0.2 (-0.8 - 0.5)	0.5 (-0.4 - 1.1)	0.2 (-0.8 - 2.5)	0.2 (-0.5 - 0.7)	2.3 (1.6 - 4.4)	0.1 (-1.6 - 0.5)	0.6 (-0.2 - 1.5)
Parietal	0.1 (-1.0 - 1.2)	-0.1 (-1.3 - 1.3)	0.8 (-1.6 - 4.3)	0.5 (-0.3 - 1.4)	3.6 (0.9 - 5.6)	0.0 (-0.7 - 1.0)	0.6 (-0.1 - 3.3)
Occipital	0.6 (-0.7 - 1.7)	0.7 (-0.9 - 2.4)	1.0 (-2.4 - 2.2)	0.6 (-0.6 - 1.7)	1.1 (0.4 - 2.6)	-0.3 (-1.0 - 1.1)	1.8 (0.1 - 2.9)
Cingulate	0.2 (-1.0 - 0.8)	0.9 (-0.4 - 2.1)	0.8 (-0.5 - 2.2)	0.5 (-0.4 - 1.2)	3.4 (1.7 - 4.7)	-0.7 (-2.4 - 1.6)	2.5 (2.0 - 2.7)
Insula	0.0 (-1.4 - 1.3)	0.7 (-1.2 - 1.6)	-0.3 (-2.6 - 2.4)	0.6 (-0.4 - 1.7)	7.0 (1.7 - 10.8)	-0.1 (-1.4 - 1.8)	2.3 (1.5 - 3.5)

Supplementary Table 3. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma GFAP concentration and baseline brain and cortical regional volumes. PS – presymptomatic; S – symptomatic. Significant negative correlations shown in bold.

		***C9orf72* PS**	***C9orf72* S**	***GRN* PS**	***GRN* S**	***MAPT* PS**	***MAPT* S**
Whole brain	**r**	**-0.45**	-0.12	-0.21	-0.10	0.13	-0.23
	p-value	**<0.001**	0.507	0.054	0.630	0.465	0.436
Frontal	**r**	**-0.35**	-0.23	**-0.23**	-0.24	-0.09	-0.23
	p-value	**0.002**	0.183	**0.039**	0.255	0.606	0.427
Temporal	**r**	**-0.27**	-0.12	**-0.35**	-0.36	-0.05	-0.17
	p-value	**0.024**	0.489	**0.001**	0.082	0.782	0.563
Parietal	**r**	**-0.33**	-0.12	-0.09	-0.17	0.01	-0.47
	p-value	**0.005**	0.513	0.440	0.433	0.953	0.088
Occipital	**r**	-0.15	-0.15	0.00	-0.28	0.05	-0.43
	p-value	0.215	0.408	0.992	0.188	0.803	0.126
Cingulate	**r**	**-0.44**	-0.16	**-0.24**	-0.21	0.23	-0.27
	p-value	**<0.001**	0.383	**0.027**	0.318	0.200	0.358
Insula	**r**	**-0.26**	-0.28	**-0.27**	-0.18	0.06	-0.02
	p-value	**0.029**	0.105	**0.016**	0.402	0.719	0.958

Supplementary Table 4. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma GFAP concentration and longitudinal brain and cortical regional rates of atrophy. PS – presymptomatic; S – symptomatic. Significant positive correlations shown in bold.

		***C9orf72* PS**	***C9orf72* S**	***GRN* PS**	***GRN* S**	***MAPT* PS**	***MAPT* S**
Whole brain	**r**	0.03	0.05	0.02	0.07	-0.02	-0.40
	p-value	0.856	0.870	0.906	0.805	0.917	0.600
Frontal	**r**	-0.03	0.17	-0.08	0.20	-0.05	0.80
	p-value	0.870	0.541	0.608	0.493	0.828	0.200
Temporal	**r**	-0.26	0.03	0.13	**0.66**	0.12	-0.40
	p-value	0.121	0.920	0.373	**0.010**	0.577	0.600
Parietal	**r**	-0.09	-0.07	0.05	0.40	-0.17	0.40
	p-value	0.597	0.810	0.762	0.159	0.428	0.600
Occipital	**r**	0.14	-0.07	0.10	0.24	-0.54	0.80
	p-value	0.395	0.800	0.503	0.401	0.007	0.200
Cingulate	**r**	0.17	0.07	-0.17	0.55	-0.07	-0.40
	p-value	0.300	0.810	0.264	0.052	0.735	0.600
Insula	**r**	0.06	-0.03	0.15	0.18	-0.04	-0.80
	p-value	0.711	0.910	0.328	0.533	0.853	0.200

Supplementary Table 5. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma NfL concentration and both MMSE and FTLD-CDR sum of boxes. PS – presymptomatic; S – symptomatic. Significant negative correlations shown in bold.

		***C9orf72* PS**	***C9orf72* S**	***GRN* PS**	***GRN* S**	***MAPT* PS**	***MAPT* S**
MMSE	**r**	**-0.33**	**-0.35**	-0.12	-0.35	0.18	-0.45
	p-value	**0.004**	**0.031**	0.124	0.084	0.323	0.105
FTLD-CDR	**r**	-0.06	0.10	0.19	0.32	0.25	**0.79**
	p-value	0.676	0.648	0.134	0.126	0.248	**0.021**

Supplementary Table 6. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma NfL concentration and baseline brain and cortical regional volumes. PS – presymptomatic; S – symptomatic. Significant negative correlations shown in bold.

		***C9orf72* PS**	***C9orf72* S**	***GRN* PS**	***GRN* S**	***MAPT* PS**	***MAPT* S**
Whole brain	**r**	**-0.53**	-0.03	**-0.35**	-0.25	-0.13	-0.19
	p-value	**<0.001**	0.855	**0.001**	0.243	0.478	0.523
Frontal	**r**	**-0.51**	-0.23	**-0.30**	**-0.46**	-0.21	-0.18
	p-value	**<0.001**	0.181	**0.006**	**0.024**	0.237	0.533
Temporal	**r**	**-0.37**	0.02	**-0.48**	0.11	-0.14	-0.22
	p-value	**0.001**	0.900	**<0.001**	0.613	0.425	0.446
Parietal	**r**	**-0.51**	-0.07	**-0.36**	-0.17	-0.07	-0.33
	p-value	**<0.001**	0.685	**0.001**	0.416	0.686	0.246
Occipital	**r**	**-0.33**	0.03	-0.09	0.02	-0.16	-0.13
	p-value	**0.005**	0.860	0.423	0.942	0.380	0.659
Cingulate	**r**	**-0.49**	0.02	**-0.37**	-0.12	-0.29	-0.30
	p-value	**<0.001**	0.909	**0.001**	0.582	0.096	0.303
Insula	**r**	**-0.47**	-0.08	**-0.32**	**-0.50**	-0.13	0.06
	p-value	**<0.001**	0.634	**0.004**	**0.012**	0.456	0.840

Supplementary Table 7. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma NfL concentration and longitudinal brain and cortical regional rates of atrophy. PS – presymptomatic; S – symptomatic. Significant positive correlations shown in bold.

		***C9orf72* PS**	***C9orf72* S**	***GRN* PS**	***GRN* S**	***MAPT* PS**	***MAPT* S**
Whole brain	**r**	0.17	-0.28	0.16	**0.63**	-0.10	0.20
	p-value	0.317	0.315	0.280	**0.016**	0.639	0.800
Frontal	**r**	-0.10	0.17	-0.15	**0.79**	-0.27	**1.00**
	p-value	0.545	0.541	0.311	**0.001**	0.210	**<0.001**
Temporal	**r**	-0.17	-0.01	0.29	**0.54**	-0.08	0.20
	p-value	0.317	0.980	0.051	**0.047**	0.722	0.800
Parietal	**r**	-0.09	0.05	0.21	0.41	-0.21	0.80
	p-value	0.607	0.870	0.159	0.144	0.314	0.200
Occipital	**r**	-0.12	0.15	0.00	0.08	-0.35	**1.00**
	p-value	0.479	0.585	0.991	0.782	0.099	**<0.001**
Cingulate	**r**	0.15	-0.23	0.01	0.41	-0.15	0.20
	p-value	0.354	0.413	0.960	0.162	0.498	0.800
Insula	**r**	-0.01	-0.08	0.25	**0.63**	-0.07	-0.40
	p-value	0.934	0.791	0.099	**0.016**	0.731	0.600

Supplementary Table 8. Spearman's correlation coefficients (r, and p value) assessing the relationship between plasma NfL concentration and age. Significant correlations shown in bold.

		Controls	*C9orf72* PS	*C9orf72* S	*GRN* PS	*GRN* S	*MAPT* PS	*MAPT* S
Age	**r**	**0.64**	**0.64**	0.05	**0.74**	0.10	**0.60**	-0.31
	p-value	**<0.001**	**<0.001**	0.767	**<0.001**	0.596	**<0.001**	0.201