

Electronic Supplementary Material

Neuron loss and degeneration in the progression of TDP-43 proteinopathy

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Fig. S1

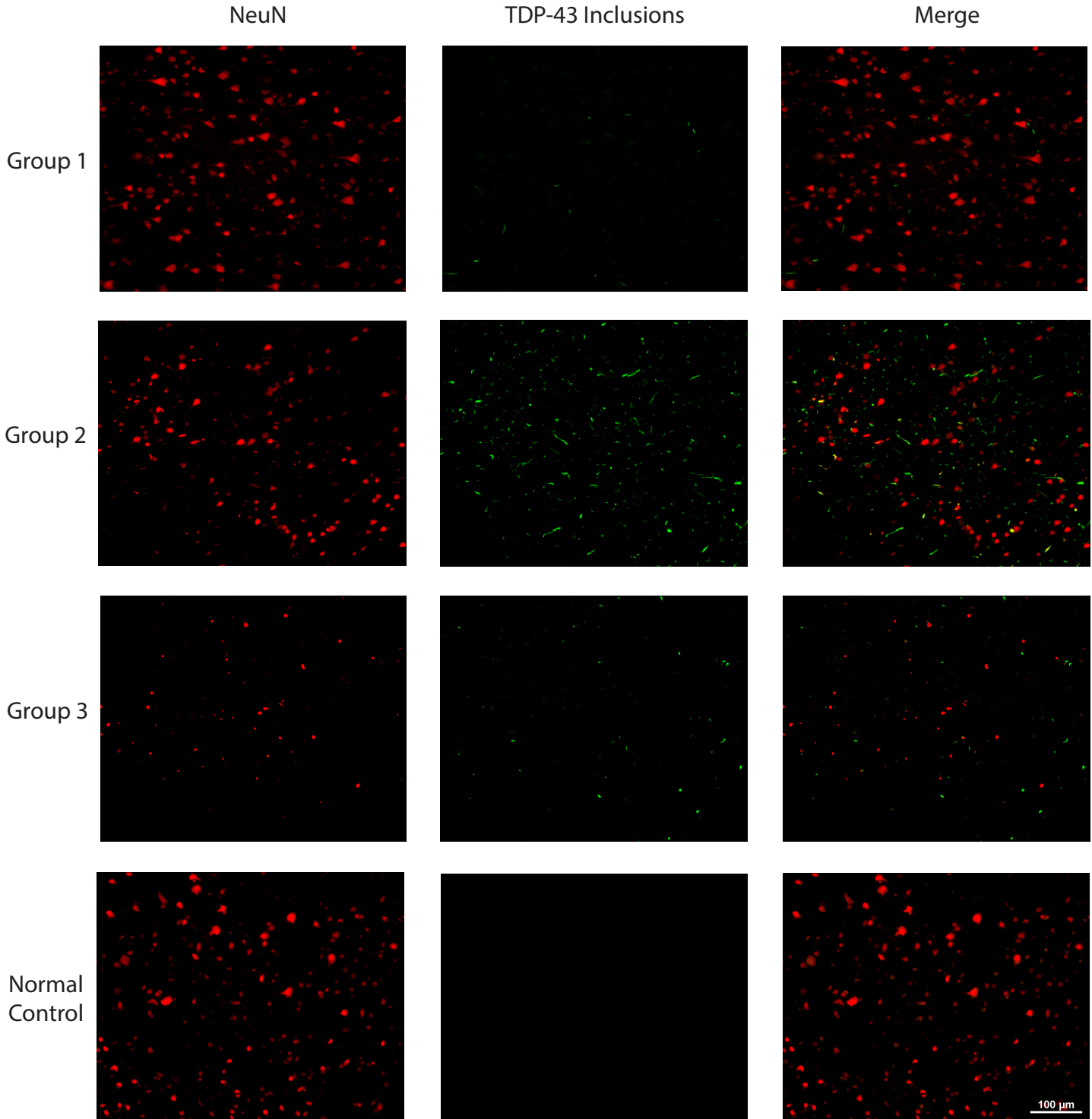


Fig. S2

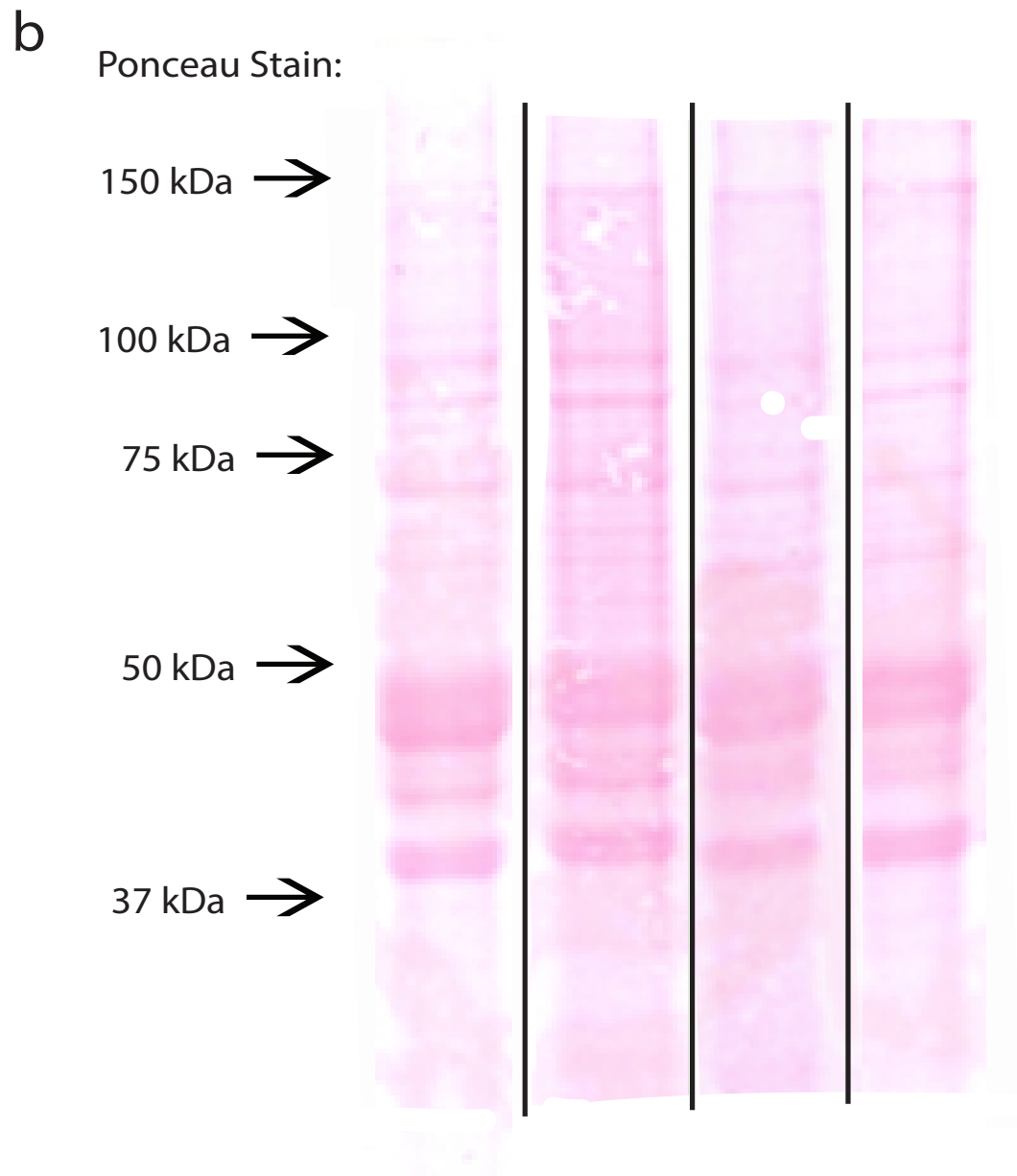
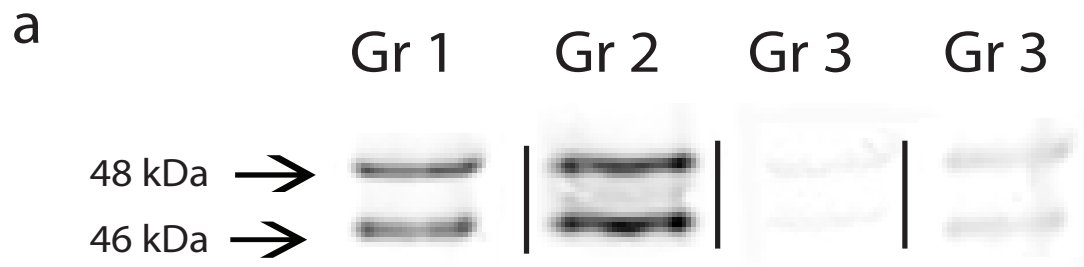
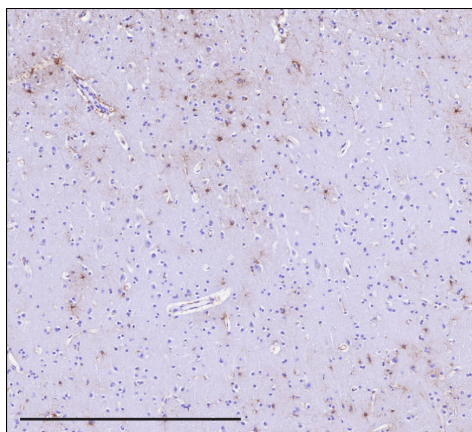
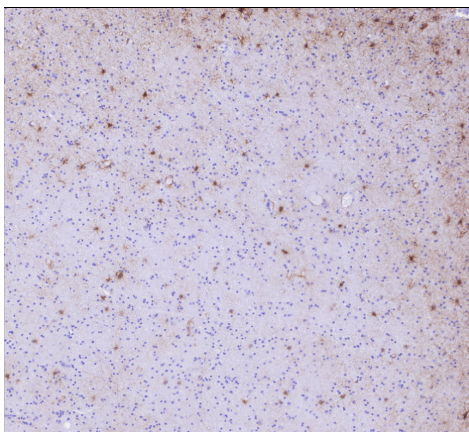


Fig. S3

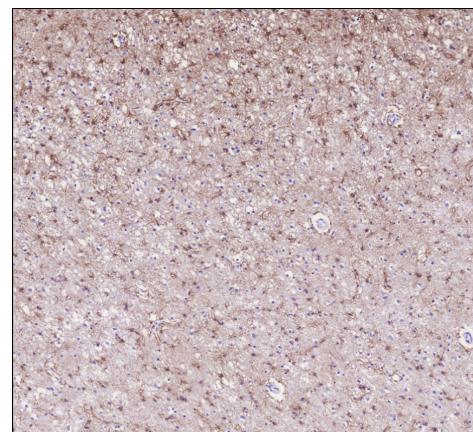
Group 1



Group 2



Group 3



GFAP

Fig. S4

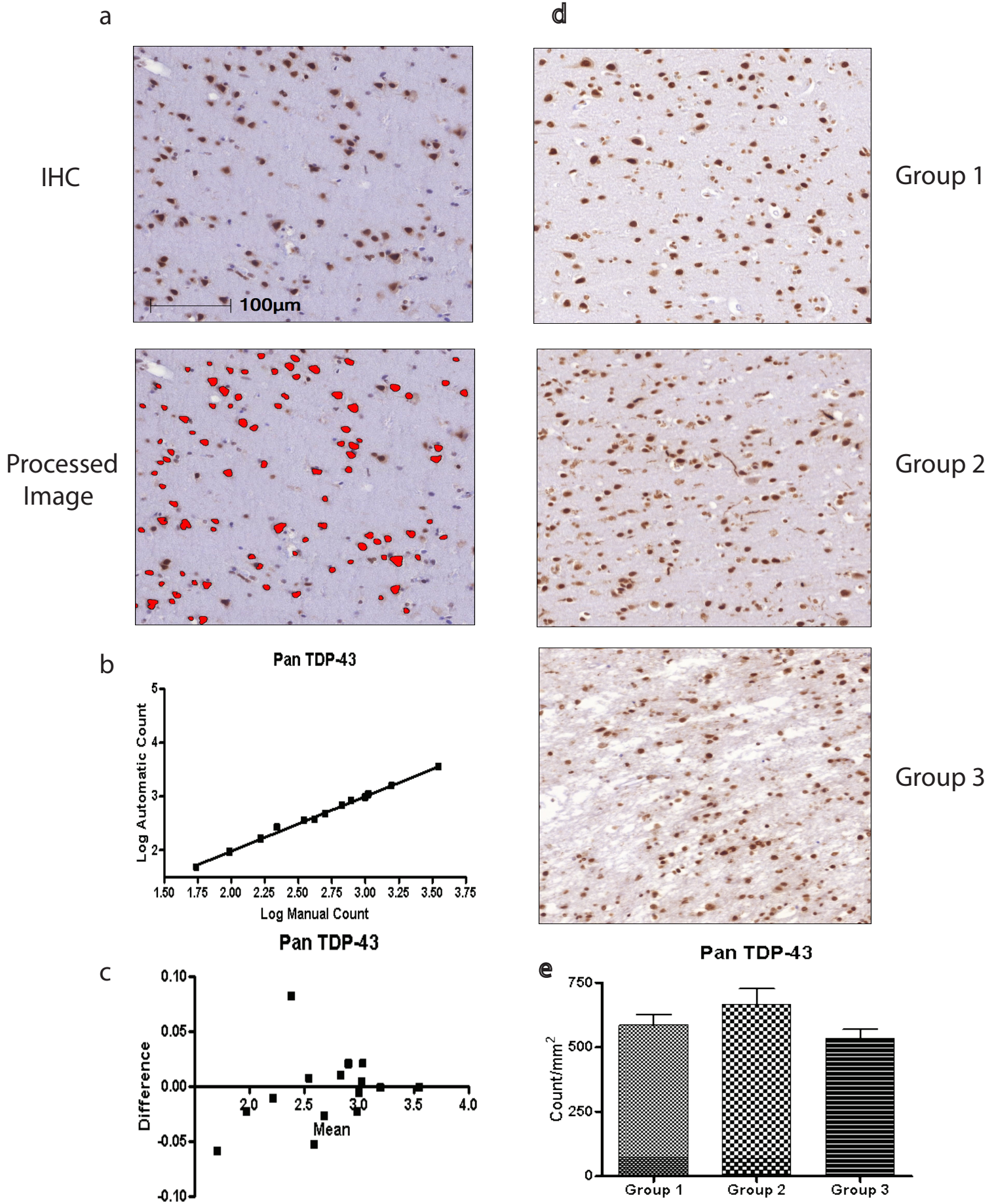


Table S1 Focused analyses of bvFTLD-TDP recapitulate spread of pathology and genetic differences.

Measure	Estimate	Standard Error	Chi-Squared with DF=1 (P-Value)	OR (95% CI)	Chi-squared (DF) (P-Value)
Phase					
I ¹	-2.057	0.658	9.78 (0.0018)	0.13 (0.04-0.46)	
II ²	-0.422	0.421	1.01 (0.3160)	0.66 (0.29-1.50)	6.70 (2)
III/IV ³	2.478	0.527	22.09 (<0.0001)	11.92 (4.24-33.52)	(0.0352)
Mutation					
Non-C9/GRN ⁴	0.492	0.860	0.33 (0.5675)	1.64 (0.30-8.82)	
<i>C9orf72</i> ⁵	-1.721	0.664	6.72 (0.0095)	0.18 (0.05-0.66)	5.45 (2)
<i>GRN</i> ⁶	1.230	0.996	1.52 (0.2169)	3.42 (0.49-24.07)	(0.0656)

¹Phase III/IV is reference group.

²I is reference group.

³II is reference group.

⁴*GRN* is reference group.

⁵Non-C9/GRN is reference group.

⁶*C9orf72* is the reference group.

*GEE using a proportional odds model for Group 1-2 based on 80 observations. I- orbital frontal cortex; II- mid-frontal, anterior cingulate, entorhinal and superior temporal cortices; III- motor, sensory, and angular cortices; IV- visual cortex. Regions III and IV are combined due to small number of observations in each region.

Table S2 Focused analyses of non-bvFTLD-TDP recapitulate spread of pathology and genetic differences.

Measure	Estimate	Standard Error	Chi-Squared with DF=1 (P-Value)	OR (95% CI)	Chi-squared (DF) (P-Value)
Phase					
I ¹	-0.863	0.347	6.18 (0.0129)	0.42 (0.21-0.83)	
II ²	-0.139	0.448	0.10 (0.7566)	0.87 (0.36-2.10)	10.22 (2)
III/IV ³	1.002	0.282	12.67 (0.0004)	2.72 (1.57-4.73)	(0.0060)
Mutation					
Non-C9/GRN ⁴	1.143	0.551	4.30 (0.0380)	3.14 (1.07-9.23)	
<i>C9orf72</i> ⁵	-0.796	0.488	2.66 (0.1028)	0.45 (0.17-1.17)	4.62 (2)
<i>GRN</i> ⁶	-0.347	0.543	0.41 (0.5235)	0.71 (0.24-2.05)	(0.0991)

¹Phase III/IV is reference group.

²I is reference group.

³II is reference group.

⁴*GRN* is reference group.

⁵Non-C9/GRN is reference group.

⁶*C9orf72* is the reference group.

*GEE using a proportional odds model for Group 1-2 based on 193 observations. I- orbital frontal cortex; II- mid-frontal, anterior cingulate, entorhinal and superior temporal cortices; III- motor, sensory, and angular cortices; IV- visual cortex. Regions III and IV are combined due to small number of observations in each region.

Table S3 Superior temporal cortex tissue recapitulates genetic differences in FTLT-DTP.

		Group			
		1	2	3	Total
Mutation Status	Count Total % Col % Row %				
	Non-C9/GRN	11 19.3% 64.7% 39.3%	12 21.1% 66.7% 42.9%	5 8.8% 22.7% 17.9%	28 49.1%
	<i>C9orf72</i>	2 3.5% 11.8% 11.8%	4 7.0% 22.2% 23.5%	11 19.3% 50.0% 64.7%	17 29.8%
	<i>GRN</i>	4 7.0% 23.5% 33.3%	2 3.5% 11.1% 16.7%	6 10.5% 27.3% 50.0%	12 21.1%
	Total	17 29.8%	18 31.6%	22 38.6%	57

*A 2-sided Fisher's exact test finds a significantly different distribution of Groups in the three mutation statuses (p=0.018).