On-line Table 1. VBM results for volumes of GM and WM in 15 patients with HD ($P < .05$ FDR corrected)

	Cluster	Voxel		Coordinates (Local Maxima)			
	Size (mm^3)	T	$P_{FDR\text{-}corr}$	X	Y	Z	Areas
GM: Controls>HD	66,659	8.67	.000	14	7	4	R and L caudate, putamen, thalamus, insula, temporal superior gyrus
	7924	6.25	.000	39	−21	54	R precentral and postcentral gyri
	5571	5.21	.001	19	−64	27	R and L calcarine gyri, R cuneus and precuneus
	2534	6.92	.000	5	27	16	R and L anterior and middle cingulum
	2492	4.28	.004	−35	−85	10	L middle and superior occipital gyri
	2431	4.90	.001	47	−68	8	R middle temporal and middle occipital gyri
	2239	4.90	.001	29	−78	24	R middle and superior occipital gyri
	1693	4.71	.002	−15	−66	30	L calcarine gyrus, L cuneus and precuneus
	1171	4.51	.003	−41	−17	43	L precentral and postcentral gyri
WM: Controls>HD	1054	5.86	.010	12	5	−1	R internal capsule of genu
	963	5.18	.010	37	4	16	R frontal subcortical WM
	881	5.65	.010	−13	1	−1	L internal capsule of genu
	671	4.83	.014	−22	−20	23	L corticospinal tract (corona radiata)
	359	5.31	.010	23	−53	16	R splenium of corpus callosum
	108	5.20	.010	−37	6	12	L frontal subcortical WM

On-line Table 2: VBM results showing the significant ($P < .05$ FDR corrected) correlation between individual scores of motor deficit and cognitive tests and the areas of GM and WM losses in 15 HD gene carriers

	Cluster Size (mm^3)	Voxel		Coordinates (Local Maxima)			Areas
		T	$P_{FDR\text{-}corr}$	X	Y	Z	
GM							
Motor Scale	7451	9.69	.007	3	−15	4	R thalamus, putamen, caudate, and insula gyrus; L thalamus and caudate
Symbol Digit test	16626	10.35	.004	33	3	9	R putamen and insula, rolandic operculum, inferior operculum frontal, inferior triangularis frontal, inferior orbital frontal, superior temporal, and Heschl gyri
	8820	8.78	.004	18	1	16	R thalamus, caudate, amygdala, olfactory and medial orbital frontal gyri; L thalamus, caudate, olfactory, and anterior cingulum gyri
	10080	8.51	.004	−34	3	12	L insula, rolandic operculum, inferior operculum frontal, Heschl, superior temporal gyri, and L putamen and pallidum
	2385	8.29	.004	−14	−27	−13	L hippocampus, parahippocampal and lingual gyri; L cerebellar hemisphere 4–5
	2145	7.43	.005	53	−23	38	R postcentral, precentral, and supramarginal gyri
	1150	7.05	.005	19	−26	−11	R hippocampus, parahippocampal, lingual, precuneus, and posterior cingulum gyri
Stroop Color-Word	3319	9.45	.010	−35	38	18	L middle frontal, inferior triangularis frontal, and superior frontal gyri
Interference Test	14241	9.37	.010	37	4	13	R insula, rolandic operculum, inferior operculum frontal, Heschl, and superior temporal gyri; R putamen
	1292	9.00	.010	44	−16	36	R postcentral and precentral gyri
	11583	8.58	.010	−44	−14	11	L insula, rolandic operculum, inferior triangularis frontal, superior temporal, Heschl gyri; L putamen
	2885	8.28	.010	−7	−3	4	R caudate and thalamus; L caudate and thalamus
	3181	6.57	.010	12	−48	−27	R lingual gyrus; R cerebellar hemisphere 3–6; vermis 4–8
	1209	6.10	.010	−1	23	−7	R anterior cingulum, olfactory and medial orbital frontal gyri; L anterior cingulum and olfactory gyri
Verbal Fluency test	29848	17.21	.000	−29	−16	4	L insula, middle frontal, rolandic operculum, inferior triangularis frontal, inferior operculum frontal, precentral, superior temporal, and Heschl gyri; L putamen and pallidum
	45420	13.89	.000	50	−6	4	R insula, rolandic operculum, anterior cingulum, inferior operculum frontal, inferior triangularis frontal, medial orbital frontal, olfactory, superior temporal, and Heschl gyri; R putamen and caudate; L anterior cingulum, olfactory and medial orbital frontal gyri; L caudate
	4248	13.26	.000	53	−24	39	R postcentral, precentral, and supramarginal gyri
	3251	13.23	.000	−10	−32	−13	L hippocampus, parahippocampal, lingual, and fusiform gyri; L cerebellar hemisphere 4–5
WM							
Motor Scale	7185	9.40	.009	1	−15	−7	L superior corona radiata, corticospinal tract, and brain stem
	3070	8.02	.009	20	−15	21	R superior corona radiata, corticospinal tract, inferior fronto-occipital fasciculus
	1401	6.00	.011	12	−21	−43	Brain stem
	1102	4.79	.023	13	33	0	R inferior fronto-occipital fasciculus and genu of corpus callosum
Symbol Digit test	48865	9.70	.020	−40	27	27	L and R frontal subcortical WM, corticospinal tract, genu of corpus callosum, forceps minor, cingulum
	3626	5.83	.020	−44	−17	−22	L inferior and superior longitudinal fasciculi (temporal part)
	2667	4.84	.020	13	−53	−46	R middle cerebellar peduncle and R cerebellar WM
	1205	4.32	.023	−13	−45	−44	Inferior brain stem and L inferior and middle cerebellar peduncles, L cerebellar WM
Stroop Color-Word Interference test	18940	9.48	.014	40	13	15	R frontal subcortical WM, corticospinal tract, genu of corpus callosum, superior longitudinal fasciculus (temporal part)
	16744	6.97	.018	−31	35	4	L frontal subcortical WM, corticospinal tract, superior longitudinal fasciculus (temporal part)
	11724	5.75	.023	−16	−57	−29	L superior longitudinal fasciculus (temporal part), L middle cerebellar peduncles and L cerebellar WM
	11657	5.35	.023	22	−47	−27	R middle cerebellar peduncles and cerebellar WM
Verbal Fluency test	48865	9.70	.020	−40	27	27	L and R frontal subcortical WM, corticospinal tract, genu of corpus callosum
	3626	5.83	.020	−44	−17	−22	L inferior and superior longitudinal fasciculi
	2667	4.84	.020	13	−53	−46	Inferior brain stem and L inferior and middle cerebellar peduncles, L cerebellar WM
	1205	4.32	.023	−13	−45	−44	R middle cerebellar peduncles and cerebellar WM

On-line Table 3. TBSS results: areas of increased MD in 15 patients with HD versus 15 healthy controls[a]

Cluster size (mm^3)	*P*	Coordinates (Local Maxima) X	Y	Z	Areas
12016	.000	44	−9	−30	R superior and inferior longitudinal fasciculi, inferior fronto-occipital fasciculus, external capsule and corticospinal tract
9283	.000	−37	−6	−27	L superior and inferior longitudinal fasciculi, inferior fronto-occipital fasciculus, external capsule and corticospinal tract
692	.003	−4	6	−10	Fornix
601	.003	51	−40	−14	R inferior longitudinal fasciculi and inferior fronto-occipital fasciculi
355	.006	15	14	28	R corona radiata
331	.006	−11	−14	−16	L corticospinal tract (cerebral peduncle)
316	.006	37	−43	−15	R inferior longitudinal fasciculus
290	.006	−29	−31	35	L subcortical frontoparietal WM
207	.010	14	−32	2	Fornix (crus)
177	.011	35	2	32	R subcortical frontal WM
148	.013	−11	6	2	L anterior limb of internal capsule and anterior thalamic radiation
142	.013	15	−53	24	R subcortical parietal WM
138	.014	23	−84	6	R inferior longitudinal fasciculus
128	.015	−11	−58	24	L subcortical parietal WM
120	.016	27	−86	12	R inferior longitudinal fasciculus
94	.023	28	−24	−1	R corticospinal tract (retrolenticular part of internal capsule)
92	.023	28	−26	38	R corticospinal tract (corona radiata)
90	.023	16	−8	52	R corona radiata
85	.024	−50	−35	−16	L subcortical temporal WM
78	.026	20	−25	48	R corticospinal tract (corona radiata)
75	.027	−16	−75	15	L subcortical occipital WM
69	.029	21	52	0	R forceps minor
63	.033	5	−24	−10	R anterior thalamic radiation
61	.035	14	−80	17	R subcortical occipital WM
58	.036	13	12	−4	R anterior limb of internal capsule
56	.038	37	−27	47	R corticospinal tract
54	.039	52	−6	19	R subcortical frontal WM
53	.040	16	−65	−2	R subcortical occipital WM
50	.042	−26	−22	8	L corticospinal tract (retrolenticular part of internal capsule)
49	.043	−37	−42	−16	L inferior longitudinal fasciculus
48	.043	−4	−25	−8	L anterior thalamic radiation
45	.045	−27	−69	19	L subcortical parietal WM
45	.045	24	−87	−2	R subcortical occipital WM

[a] MD: HD>controls.

On-line Table 4. TBSS results: correlation between decreased FA and Motor Scale score in 15 patients with HD

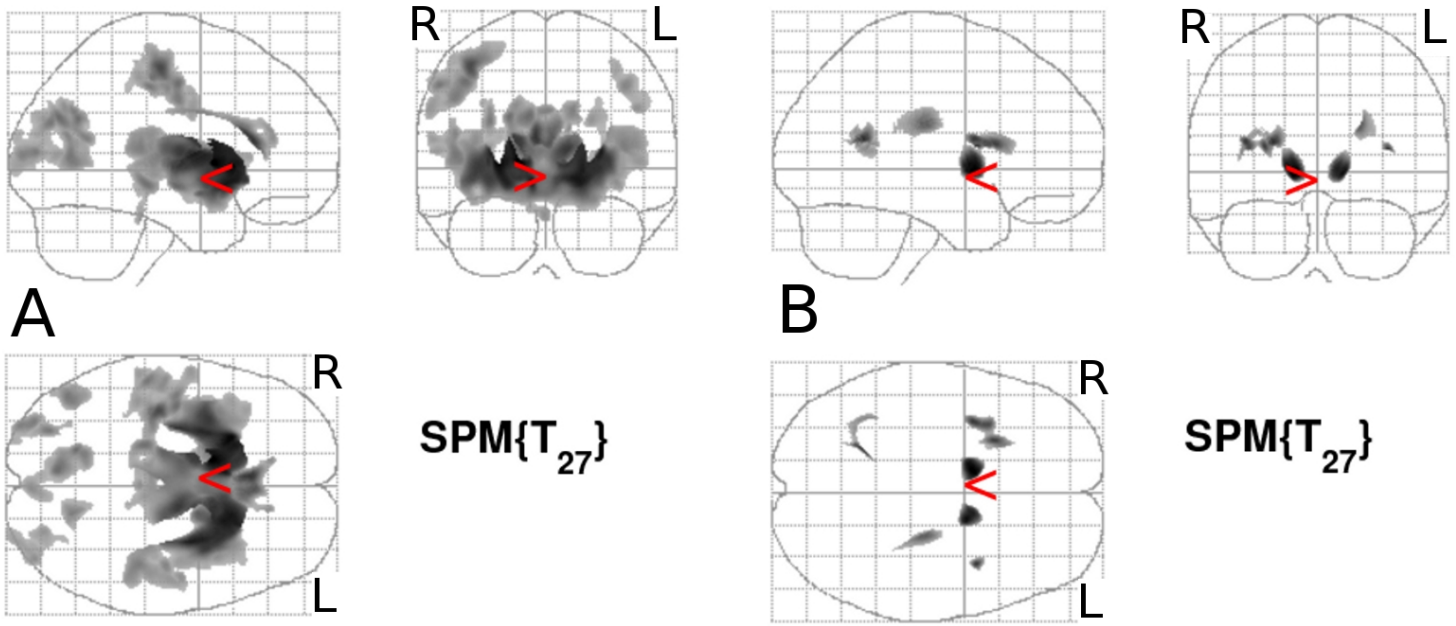
Cluster Size (mm^3)	*P*	Coordinates (Local Maxima) X	Y	Z	Areas
5306	.001	−34	−57	−3	Corpus callosum, forceps major, and L inferior fronto-occipital fasciculus
1161	.017	−16	32	−18	L inferior fronto-occipital fasciculus and forceps minor
1061	.020	36	−60	−3	Corpus callosum, forceps major, and R inferior fronto-occipital fasciculus

On-line Table 5. TBSS results: correlation between decreased FA and Stroop Color-Word Interference test score in 15 patients with HD

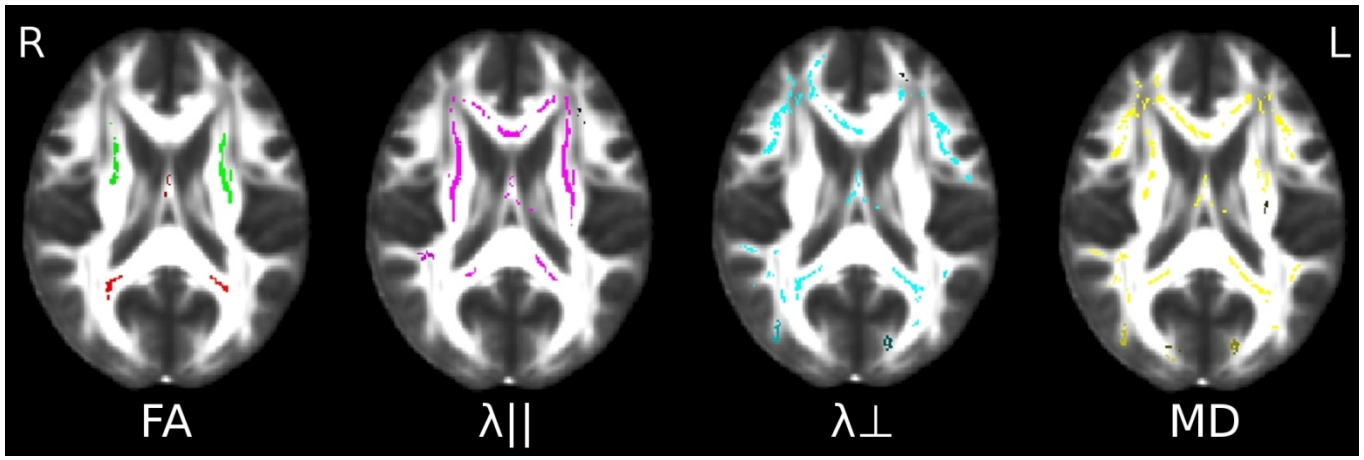
Cluster Size (mm^3)	*P*	Coordinates (Local Maxima) X	Y	Z	Areas
1287	.011	−16	31	−16	L inferior fronto-occipital fasciculus and forceps minor
1107	.015	5	26	8	Genu and body of corpus callosum
899	.022	17	29	−16	R inferior fronto-occipital fasciculus and forceps minor

On-line Table 6. TBSS results: correlation between decreased FA and Symbol Digit test score in 15 patients with HD

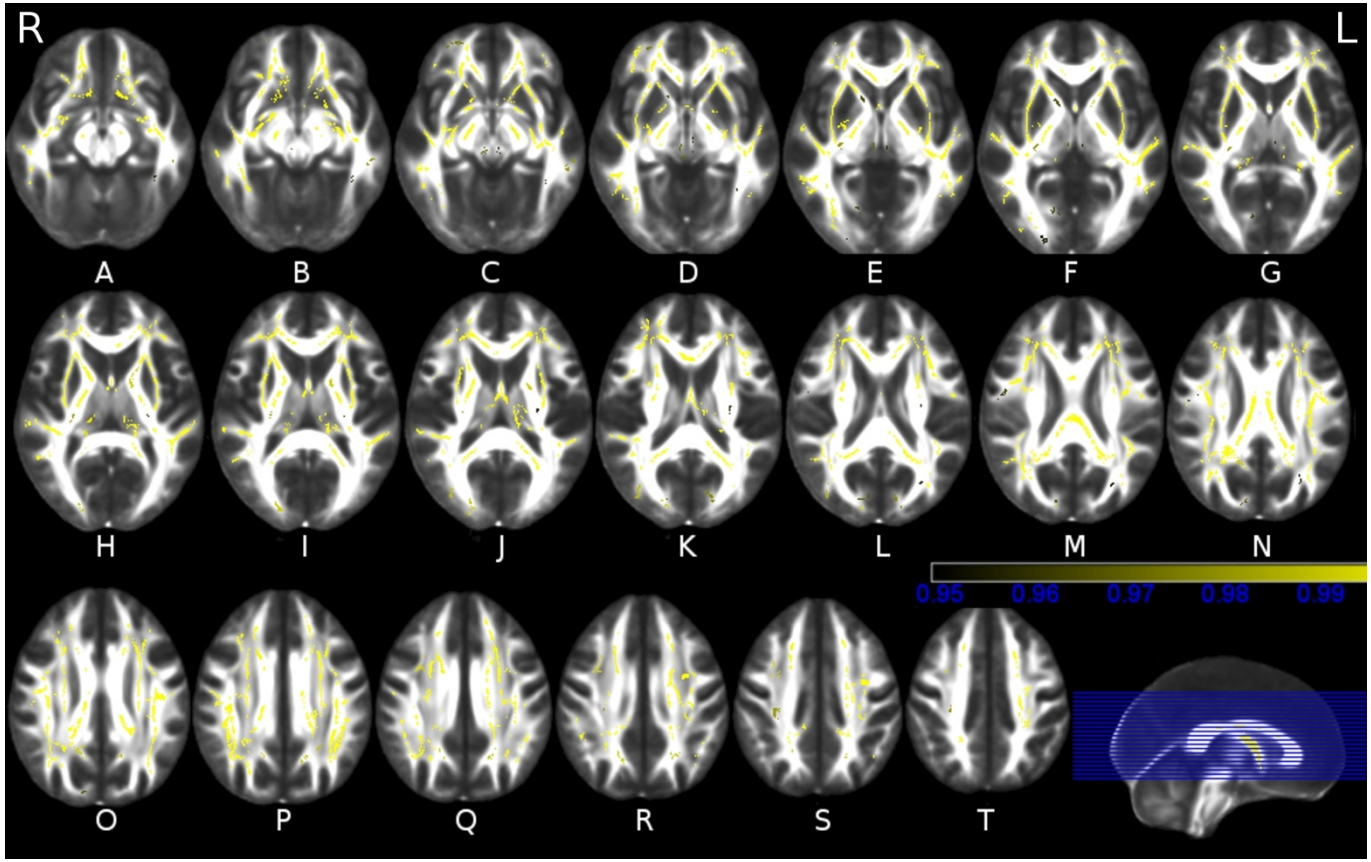
Cluster Size (mm^3)	*P*	Coordinates (Local Maxima) X	Y	Z	Areas
4767	.003	−12	40	−17	Corpus callosum, R corona radiata, and L and R inferior fronto-occipital fasciculi
652	.047	−31	−69	1	L inferior fronto-occipital fasciculus and forceps major



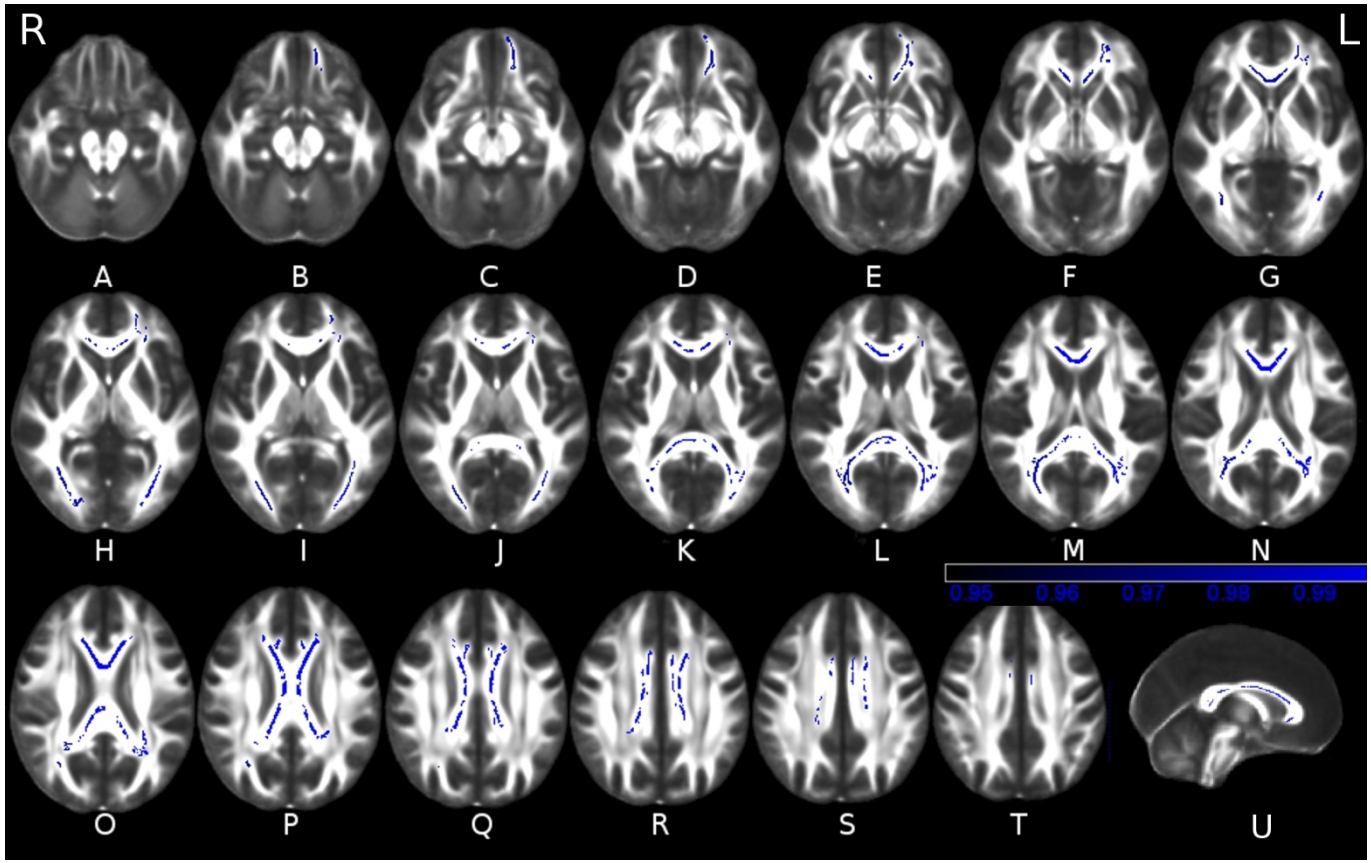
Supplementary Figure 1 (A-D): VBM analysis in HD gene carriers vs healthy controls. Maps of the t-value (voxel analysis at $p<0.05$ corrected for multiple comparisons) represented as glass brain (A,B) showing areas of GM (A) and WM (B) losses in HD gene carriers as compared to healthy controls. See Supplementary Table 1 for details.



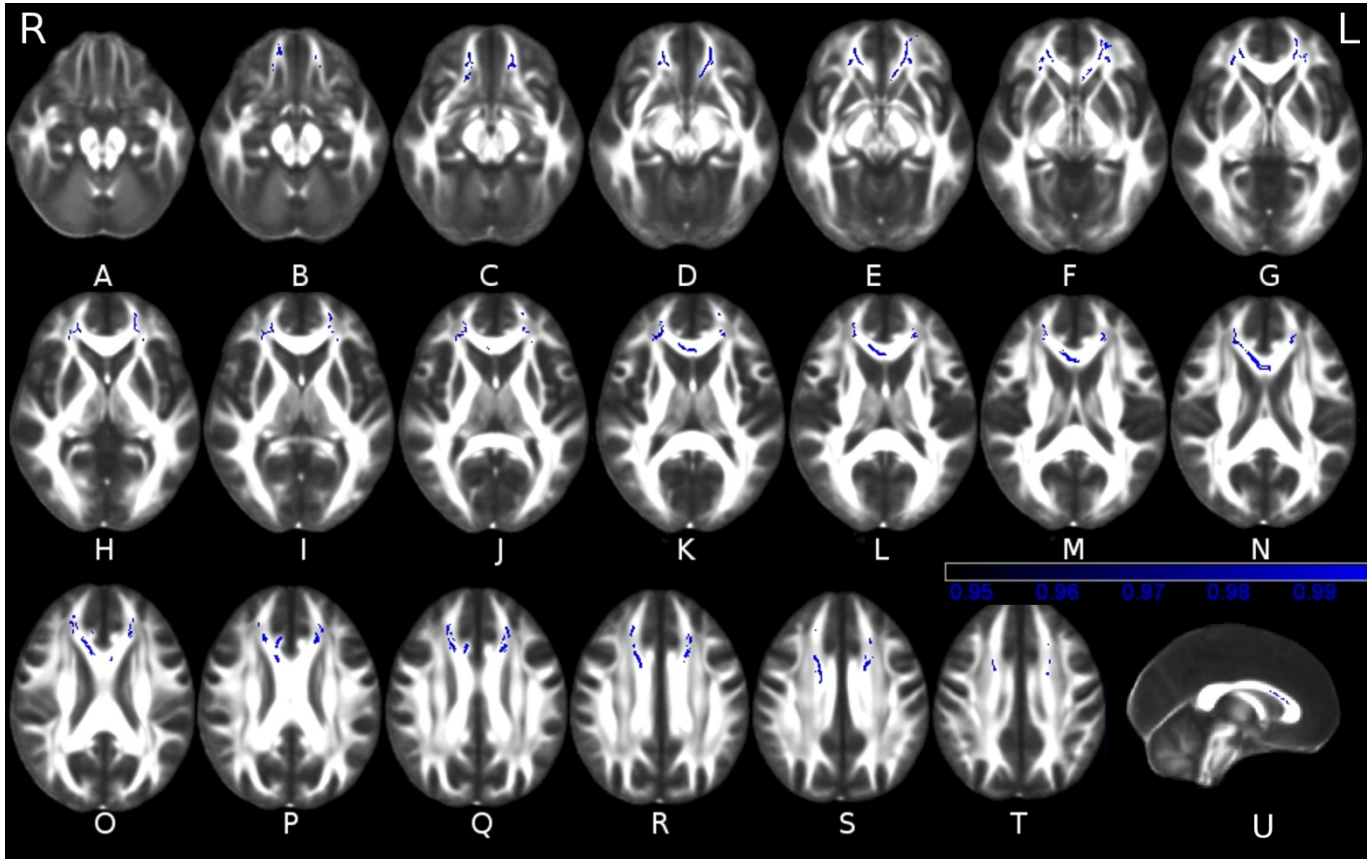
Supplementary Figure 2: TBSS analysis of FA, λ||, λ⊥ and MD maps in HD gene carriers vs healthy controls. Maps of the t-value ($t>3$ with $p<0.05$ corrected for multiple comparisons) at a mid-ventricular level showing in red the areas of significantly decreased FA in the lateral portions of the posteriors corpus callosum and anterior fornix and in green the areas of significantly increased FA in the supralenticular frontal WM comprising the corticospinal tracts, anterior thalamic radiations and superior fronto-occipital fasciculus. A corresponding increase of the greatest eigenvalue is shown in pink by λ|| map, while the λ⊥ map shows its increase in sky blue only in the areas of decreased FA and elsewhere. The map of MD shows in yellow the areas of increased MD which are widespread and corresponds to those of altered FA and beyond.



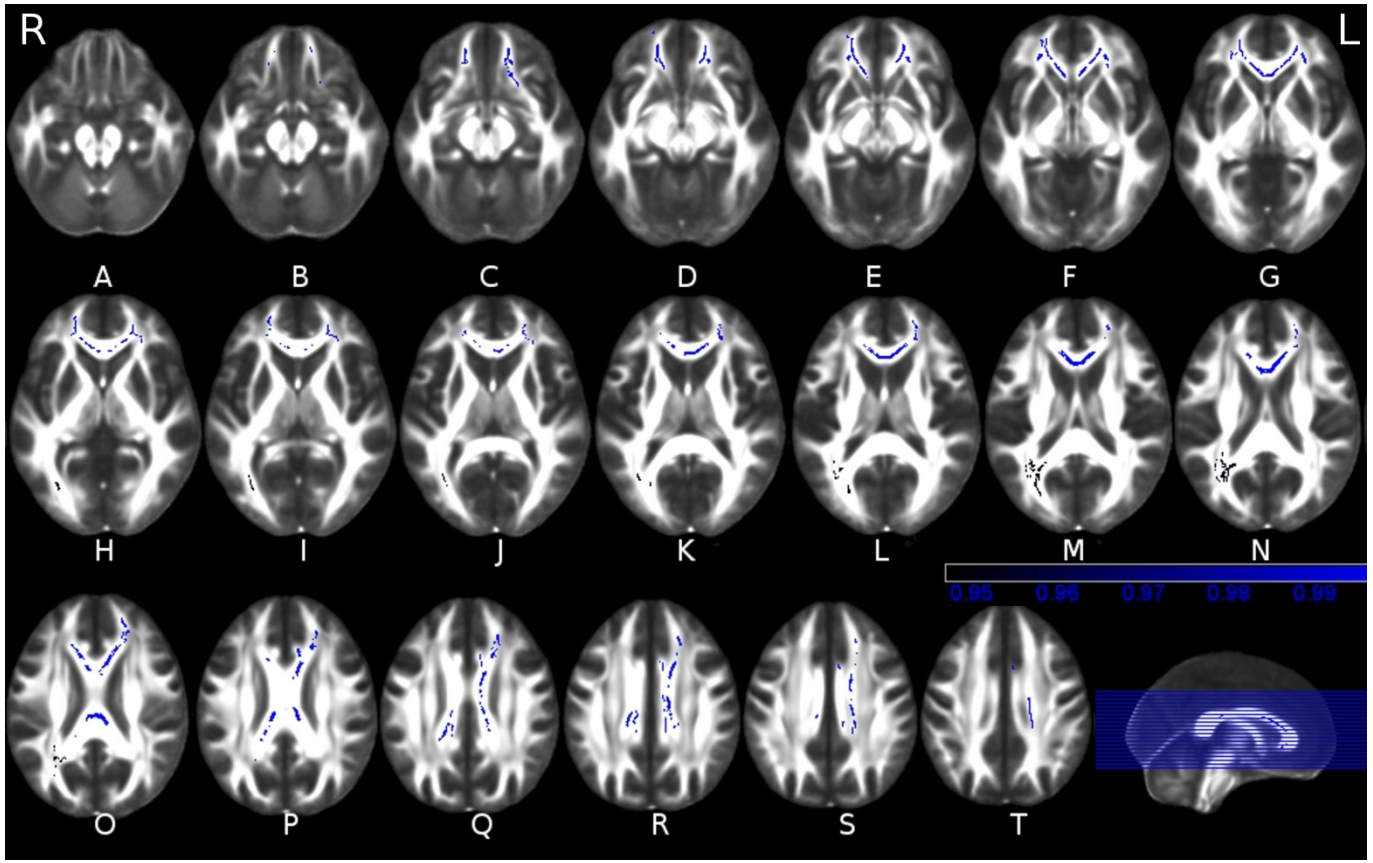
Supplementary Figure 3 (A-T): TBSS analysis of MD maps. Maps of the t-value ($t>3$ with $p<0.05$ corrected for multiple comparisons) showing in yellow the areas of significantly increased in WM in HD gene carriers as compared to controls. These include multiple association tracts and the corpus callosum. Note the involvement of arciform fibres and of the cerebral peduncles (B,C) (colour bar indicates 1-p values).



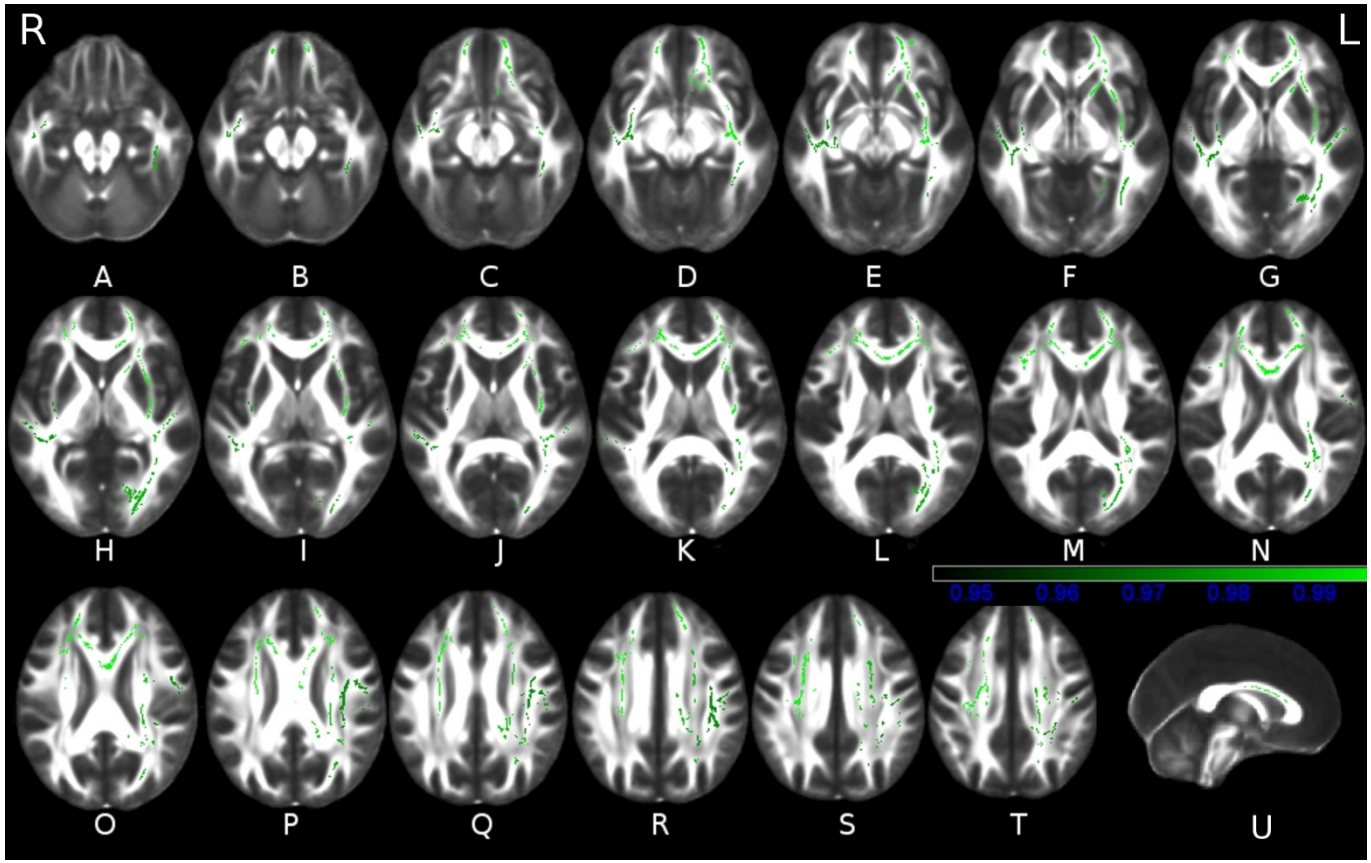
Supplementary Figure 4 (A-U): TBSS correlation results in HD gene carriers. Blue shows the areas where FA inversely correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the motor scale of the UHDRS. Note the predominant location within (head, body and splenium) (U) and beside the corpus callosum (colour bar indicates 1-p values) of the significant clusters.



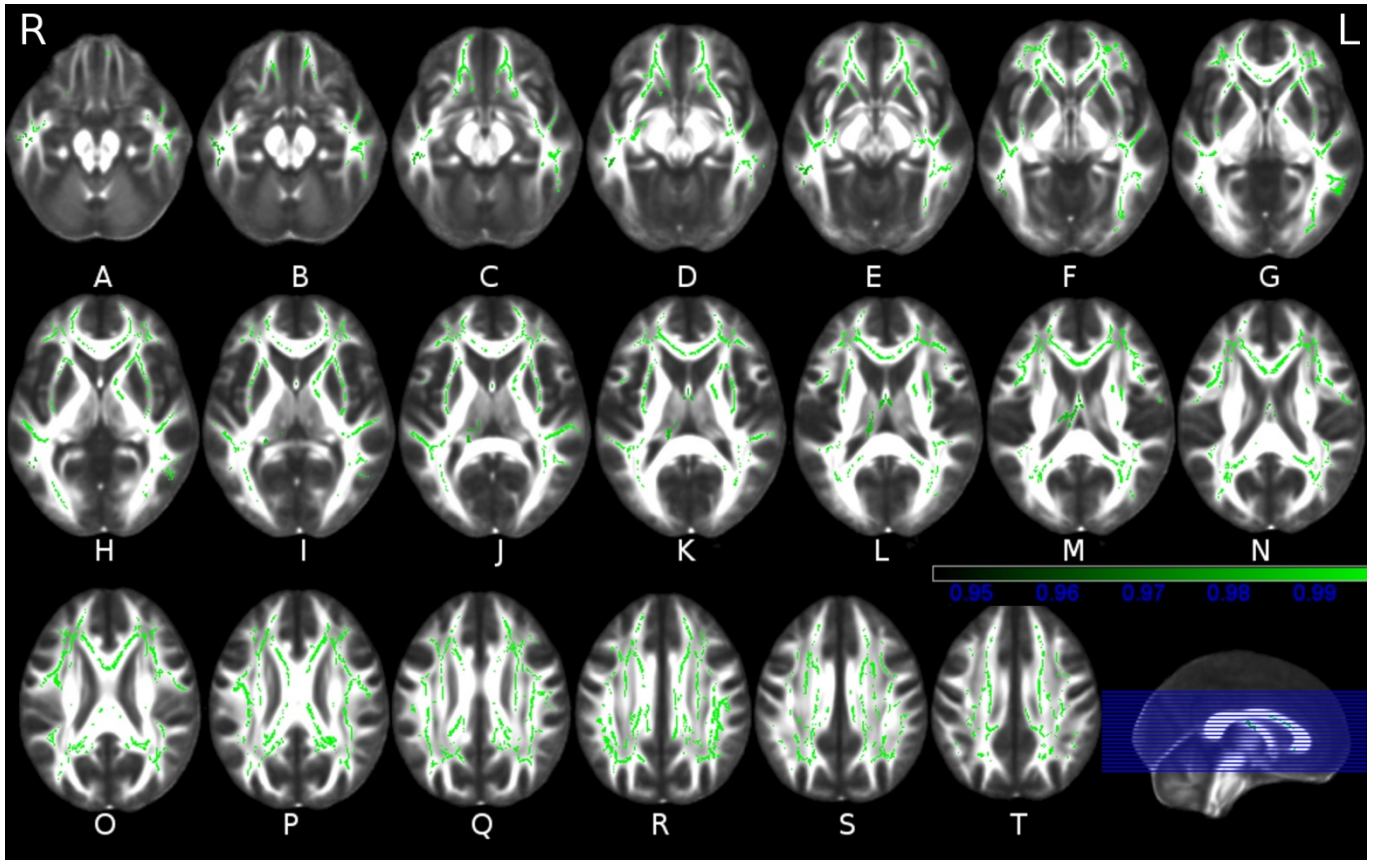
Supplementary Figure 5 (A-U): TBSS correlation results in HD gene carriers. Blue shows the areas where FA correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the Stroop test results. Note the restriction of the areas to the frontal lobes and to the anterior portion of the corpus callosum body (U) (colour bar indicates 1-p values).



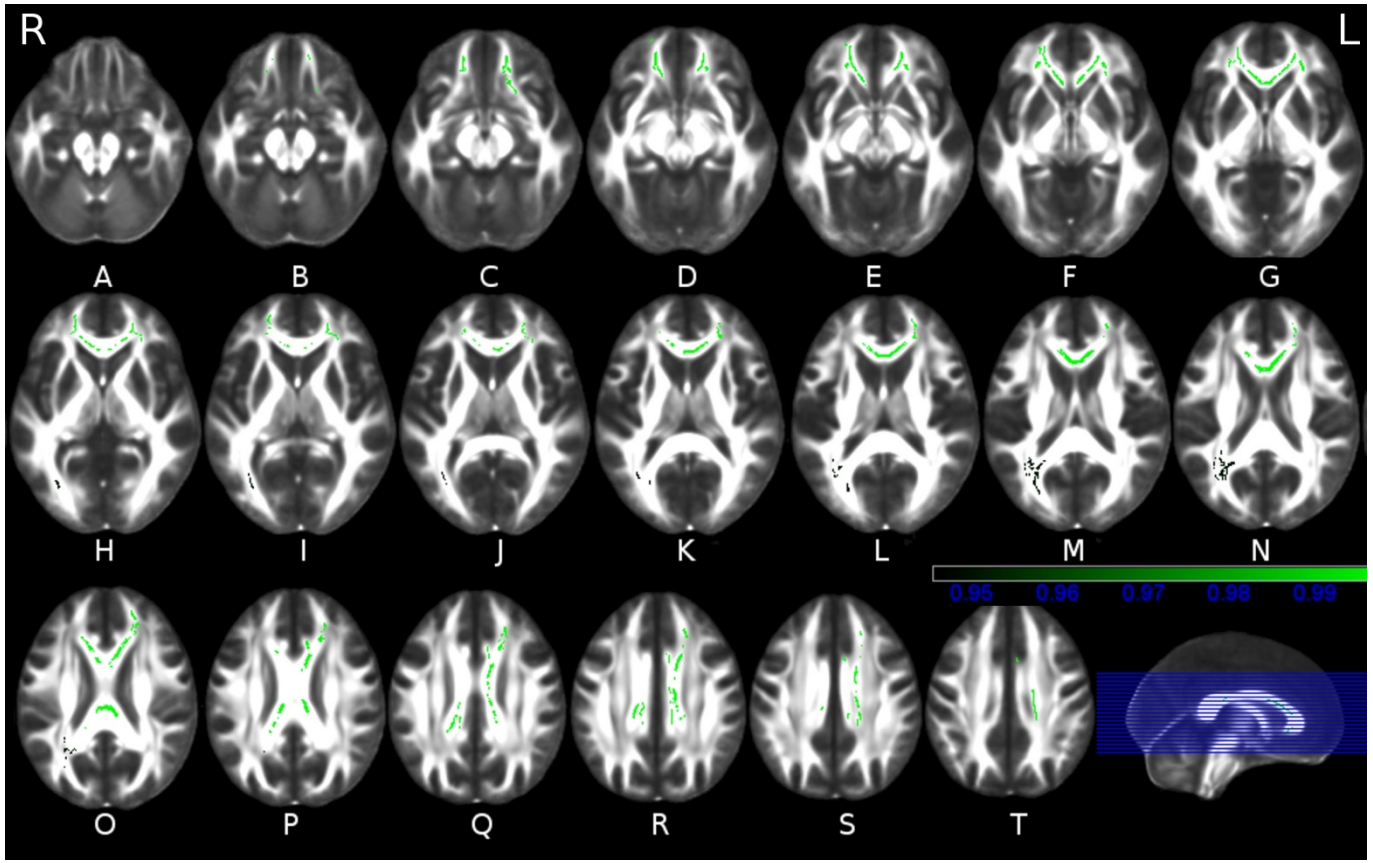
Supplementary Figure 6 (A-U): TBSS correlation results in HD gene carriers. Blue shows the areas where FA correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the individual scores in the Symbol Digit test (colour bar indicates 1-p values). The clusters in the corpus callosum (U) are localized in the anterior and posterior portion of the body and in the head.



Supplementary Figure 7 (A-U): TBSS correlation results in HD gene carriers. Green shows the areas where MD correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the individual motor score (colour bar indicates 1-p values). The clusters in the corpus callosum (U) are localized in the body.



Supplementary Figure 8 (A-T): TBSS correlation results in HD gene carriers. Green shows the areas where MD inversely correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the individual scores in the Verbal Fluency test (colour bar indicates 1-p values).



Supplementary Figure 9 (A-T): TBSS correlation results in HD gene carriers. Green shows the areas where MD inversely correlates ($t>3$ with $p<0.05$ corrected for multiple comparisons) with the individual scores in the Symbol Digit test (colour bar indicates 1-p values).