

Supplementary Table 1. The comparative demographic and clinical profile of patient cohorts

	HC n=110	ALS-NEG n=133	ALS-C9 n=22	ALS-ATXi n=5	p - value
Age	59.2(10.5)	61.6(10.2)	56.4(8.9)	59.6(15.1)	.09
Gender -male	65(59%)	74(55%)	12(54.5%)	5(100%)	.25
Handedness – right n(%)	102 (92%)	124 (93%)	19 (86%)	4 (80%)	.50
Symptom onset – spinal n(%)	n/a	113 (85%)	16 (72%)	4 (80%)	.35
Symptom Duration (months)	n/a	19.6(9.2)	20.8(6.2)	18.8(5.9)	.82
ALSFRS-r (max.48)	n/a	36.8(6.6)	37.9(6.8)	35.8(3.7)	.73
Availability of cerebellar exam n(%)	n/a	101(75%)	19(86%)	4(80%)	.55
Comorbid FTD n(%)	n/a	15(11%)	13(59%)	1(20%)	.00*
Availability of ECAS n(%)	n/a	93(69%)	14(63%)	4(80%)	.73
Abnormal ECAS in those available n(%)	n/a	23(24%)	9(64%)	1(25%)	.01*

Supplementary Table 2. Cerebellar cortical thickness in healthy controls and ALS-ATXi

Cerebellar CT		Estimated marginal means \pm S.E. for groups		Statistics	
		HC N=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left Lobules ^a	I-II	1.416 \pm 0.033	1.715 \pm 0.158	$\eta^2 p = 0.030$	0.067
	III	3.213 \pm 0.035	3.438 \pm 0.169	$\eta^2 p = 0.015$	0.197
	IV	4.911 \pm 0.014	4.909 \pm 0.066	$\eta^2 p = 0.000$	0.973
	V	4.898 \pm 0.014	4.882 \pm 0.068	$\eta^2 p = 0.000$	0.818
	VI	4.978 \pm 0.010	4.939 \pm 0.050	$\eta^2 p = 0.005$	0.451
	VIIb	4.608 \pm 0.019	4.657 \pm 0.093	$\eta^2 p = 0.002$	0.604
	VIIIa	4.648 \pm 0.017	4.723 \pm 0.081	$\eta^2 p = 0.007$	0.371
	VIIIb	4.513 \pm 0.033	4.647 \pm 0.157	$\eta^2 p = 0.006$	0.407
	IX	3.569 \pm 0.042	3.833 \pm 0.202	$\eta^2 p = 0.015$	0.204
	X	2.491 \pm 0.043	2.829 \pm 0.205	$\eta^2 p = 0.023$	0.110
	Crus I	4.577 \pm 0.020	4.520 \pm 0.093	$\eta^2 p = 0.003$	0.557
	Crus II	4.366 \pm 0.026	4.271 \pm 0.123	$\eta^2 p = 0.005$	0.452
Right Lobules ^b	I-II	1.354 \pm 0.030	1.764 \pm 0.143	$\eta^2 p = 0.066$	0.006
	III	3.092 \pm 0.034	3.242 \pm 0.161	$\eta^2 p = 0.007$	0.363
	IV	4.771 \pm 0.017	4.702 \pm 0.083	$\eta^2 p = 0.006$	0.417
	V	4.751 \pm 0.018	4.653 \pm 0.086	$\eta^2 p = 0.011$	0.270
	VI	4.927 \pm 0.012	4.844 \pm 0.055	$\eta^2 p = 0.019$	0.143
	VIIb	4.787 \pm 0.016	4.782 \pm 0.078	$\eta^2 p = 0.000$	0.943
	VIIIa	4.641 \pm 0.016	4.713 \pm 0.077	$\eta^2 p = 0.008$	0.361
	VIIIb	4.572 \pm 0.025	4.762 \pm 0.121	$\eta^2 p = 0.021$	0.127
	IX	3.761 \pm 0.037	3.991 \pm 0.179	$\eta^2 p = 0.014$	0.211
	X	2.250 \pm 0.037	2.260 \pm 0.175	$\eta^2 p = 0.000$	0.956
	Crus I	4.636 \pm 0.021	4.604 \pm 0.102	$\eta^2 p = 0.001$	0.760
	Crus II	4.576 \pm 0.020	4.576 \pm 0.098	$\eta^2 p = 0.000$	0.996

Estimated marginal means \pm standard error for cortical thickness adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.919; F = 0.739; p = 0.710; $\eta^2 p = 0.081$. ^bWilks' Lambda = 0.859; F = 1.367; p = 0.194; $\eta^2 p = 0.141$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 3. Cerebellar grey matter volumes in healthy controls and ALS-ATXi

Cerebellar GM		Estimated marginal means \pm S.E. for groups		Statistics	
		HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left Lobules ^a	I-II	0.030 \pm 0.001	0.036 \pm 0.005	$\eta^2 p = 0.015$	0.202
	III	0.508 \pm 0.011	0.568 \pm 0.053	$\eta^2 p = 0.011$	0.270
	IV	2.093 \pm 0.032	2.031 \pm 0.153	$\eta^2 p = 0.001$	0.690
	V	3.608 \pm 0.043	3.507 \pm 0.208	$\eta^2 p = 0.002$	0.637
	VI	7.946 \pm 0.096	7.985 \pm 0.463	$\eta^2 p = 0.000$	0.934
	VII B	4.050 \pm 0.059	4.148 \pm 0.284	$\eta^2 p = 0.001$	0.736
	VIII A	4.951 \pm 0.060	5.730 \pm 0.290	$\eta^2 p = 0.059$	0.010
	VIII B	3.359 \pm 0.052	3.447 \pm 0.248	$\eta^2 p = 0.001$	0.729
	IX	2.690 \pm 0.044	2.846 \pm 0.210	$\eta^2 p = 0.005$	0.468
	X	0.587 \pm 0.007	0.533 \pm 0.036	$\eta^2 p = 0.019$	0.149
	Crus I	11.179 \pm 0.155	11.412 \pm 0.744	$\eta^2 p = 0.001$	0.760
	Crus II	6.936 \pm 0.098	7.081 \pm 0.472	$\eta^2 p = 0.001$	0.764
Right Lobules ^b	I-II	0.035 \pm 0.001	0.041 \pm 0.004	$\eta^2 p = 0.019$	0.145
	III	0.498 \pm 0.010	0.543 \pm 0.046	$\eta^2 p = 0.008$	0.334
	IV	1.962 \pm 0.028	1.708 \pm 0.133	$\eta^2 p = 0.031$	0.065
	V	3.330 \pm 0.043	3.233 \pm 0.208	$\eta^2 p = 0.002$	0.650
	VI	7.937 \pm 0.099	7.830 \pm 0.476	$\eta^2 p = 0.000$	0.827
	VII B	4.230 \pm 0.055	4.279 \pm 0.264	$\eta^2 p = 0.000$	0.854
	VIII A	4.851 \pm 0.060	5.286 \pm 0.287	$\eta^2 p = 0.020$	0.141
	VIII B	3.436 \pm 0.057	3.545 \pm 0.277	$\eta^2 p = 0.001$	0.701
	IX	2.854 \pm 0.044	3.032 \pm 0.210	$\eta^2 p = 0.006$	0.411
	X	0.585 \pm 0.007	0.528 \pm 0.035	$\eta^2 p = 0.022$	0.120
	Crus I	11.180 \pm 0.149	11.685 \pm 0.716	$\eta^2 p = 0.004$	0.493
	Crus II	7.120 \pm 0.108	7.419 \pm 0.519	$\eta^2 p = 0.003$	0.574

Estimated marginal means \pm standard error for GM volumes adjusted for age, gender and total intracranial volumes. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.880; F = 1.120; p = 0.353; $\eta^2 p = 0.120$. ^bWilks' Lambda = 0.875; F = 1.181; p = 0.307; $\eta^2 p = 0.125$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 4. Cerebellar white matter volume profiles in healthy controls and ALS-NEG and ALS-C9

Cerebellar WM		Estimated marginal means \pm S.E. for groups			Statistics		
		HC n=110	ALS-NEG n=133	ALS-C9 n=22	Univariate effect size	HC vs ALS-NEG	HC vs ALS-C9
Left Lobules ^a	I-II	0.031 \pm 0.001	0.029 \pm 0.001	0.025 \pm 0.003	$\eta^2 p = 0.024$	0.494	0.051
	III	0.216 \pm 0.006	0.204 \pm 0.006	0.210 \pm 0.014	$\eta^2 p = 0.008$	0.437	1.000
	IV	0.328 \pm 0.007	0.320 \pm 0.006	0.293 \pm 0.016	$\eta^2 p = 0.015$	1.000	0.154
	V	0.592 \pm 0.013	0.572 \pm 0.012	0.549 \pm 0.030	$\eta^2 p = 0.009$	0.771	0.564
	VI	0.886 \pm 0.017	0.889 \pm 0.015	0.923 \pm 0.038	$\eta^2 p = 0.003$	1.000	1.000
	VIIIB	0.760 \pm 0.016	0.742 \pm 0.014	0.782 \pm 0.036	$\eta^2 p = 0.006$	1.000	1.000
	VIIIA	0.959 \pm 0.018	0.923 \pm 0.017	0.948 \pm 0.042	$\eta^2 p = 0.008$	0.457	1.000
	VIIIB	0.792 \pm 0.020	0.796 \pm 0.018	0.747 \pm 0.046	$\eta^2 p = 0.004$	1.000	1.000
	IX	0.888 \pm 0.025	0.867 \pm 0.023	0.813 \pm 0.057	$\eta^2 p = 0.006$	1.000	0.695
	X	0.057 \pm 0.003	0.052 \pm 0.002	0.043 \pm 0.006	$\eta^2 p = 0.022$	0.351	0.086
	Crus I	1.940 \pm 0.038	1.946 \pm 0.035	1.983 \pm 0.088	$\eta^2 p = 0.001$	1.000	1.000
Crus II	1.201 \pm 0.203	1.215 \pm 0.021	1.264 \pm 0.053	$\eta^2 p = 0.005$	1.000	0.815	
Right Lobules ^b	I-II	0.030 \pm 0.001	0.029 \pm 0.001	0.026 \pm 0.003	$\eta^2 p = 0.005$	0.682	0.255
	III	0.227 \pm 0.006	0.213 \pm 0.005	0.217 \pm 0.014	$\eta^2 p = 0.012$	0.074	0.501
	IV	0.350 \pm 0.008	0.324 \pm 0.007	0.292 \pm 0.017	$\eta^2 p = 0.045$	0.015	0.002
	V	0.669 \pm 0.014	0.681 \pm 0.013	0.656 \pm 0.031	$\eta^2 p = 0.003$	0.500	0.707
	VI	1.002 \pm 0.016	1.009 \pm 0.015	0.982 \pm 0.037	$\eta^2 p = 0.002$	0.768	0.624
	VIIIB	0.629 \pm 0.016	0.639 \pm 0.015	0.659 \pm 0.037	$\eta^2 p = 0.002$	0.644	0.466
	VIIIA	0.866 \pm 0.019	0.879 \pm 0.017	0.898 \pm 0.042	$\eta^2 p = 0.002$	0.600	0.487
	VIIIB	0.633 \pm 0.017	0.648 \pm 0.016	0.661 \pm 0.039	$\eta^2 p = 0.003$	0.520	0.510
	IX	0.835 \pm 0.023	0.816 \pm 0.021	0.800 \pm 0.053	$\eta^2 p = 0.002$	0.548	0.539
	X	0.071 \pm 0.003	0.070 \pm 0.003	0.069 \pm 0.007	$\eta^2 p = 0.000$	0.851	0.823
	Crus I	1.975 \pm 0.034	2.030 \pm 0.031	2.047 \pm 0.078	$\eta^2 p = 0.006$	0.240	0.401
Crus II	1.176 \pm 0.022	1.201 \pm 0.020	1.315 \pm 0.051	$\eta^2 p = 0.023$	0.409	0.014	

Estimated marginal means \pm standard error for WM volumes adjusted for age, gender and total intracranial volumes. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.905; F = 1.062; p = 0.384; $\eta^2 p = 0.049$. ^bWilks' Lambda = 0.904; F = 1.073; p = 0.370; $\eta^2 p = 0.049$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 5. Cerebellar white matter volume profiles in healthy controls and ALS-ATXi

Cerebellar WM		Estimated marginal means \pm S.E. for groups		Statistics	
		HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left Lobules ^a	I-II	0.031 \pm 0.001	0.031 \pm 0.005	$\eta^2 p = 0.000$	0.824
	III	0.218 \pm 0.005	0.211 \pm 0.025	$\eta^2 p = 0.001$	0.790
	IV	0.331 \pm 0.007	0.277 \pm 0.036	$\eta^2 p = 0.019$	0.143
	V	0.594 \pm 0.013	0.553 \pm 0.062	$\eta^2 p = 0.004$	0.512
	VI	0.893 \pm 0.015	0.925 \pm 0.073	$\eta^2 p = 0.002$	0.669
	VIIIB	0.764 \pm 0.017	0.748 \pm 0.081	$\eta^2 p = 0.000$	0.847
	VIIIA	0.967 \pm 0.020	1.024 \pm 0.096	$\eta^2 p = 0.003$	0.563
	VIIIB	0.804 \pm 0.019	0.727 \pm 0.092	$\eta^2 p = 0.006$	0.414
	IX	0.901 \pm 0.024	0.747 \pm 0.115	$\eta^2 p = 0.015$	0.193
	X	0.058 \pm 0.003	0.033 \pm 0.012	$\eta^2 p = 0.033$	0.056
	Crus I	1.945 \pm 0.037	2.105 \pm 0.179	$\eta^2 p = 0.007$	0.386
Crus II	1.203 \pm 0.023	1.254 \pm 0.111	$\eta^2 p = 0.002$	0.657	
Right Lobules ^b	I-II	0.030 \pm 0.001	0.021 \pm 0.005	$\eta^2 p = 0.021$	0.130
	III	0.230 \pm 0.005	0.242 \pm 0.025	$\eta^2 p = 0.002$	0.644
	IV	0.352 \pm 0.008	0.321 \pm 0.037	$\eta^2 p = 0.006$	0.416
	V	0.673 \pm 0.013	0.661 \pm 0.063	$\eta^2 p = 0.000$	0.852
	VI	1.010 \pm 0.016	1.059 \pm 0.076	$\eta^2 p = 0.004$	0.532
	VIIIB	0.631 \pm 0.015	0.680 \pm 0.073	$\eta^2 p = 0.004$	0.516
	VIIIA	0.874 \pm 0.020	0.884 \pm 0.096	$\eta^2 p = 0.000$	0.924
	VIIIB	0.644 \pm 0.015	0.558 \pm 0.074	$\eta^2 p = 0.012$	0.258
	IX	0.847 \pm 0.021	0.714 \pm 0.101	$\eta^2 p = 0.015$	0.201
	X	0.072 \pm 0.003	0.070 \pm 0.014	$\eta^2 p = 0.000$	0.879
	Crus I	1.980 \pm 0.029	2.236 \pm 0.140	$\eta^2 p = 0.028$	0.076
Crus II	1.174 \pm 0.022	1.257 \pm 0.104	$\eta^2 p = 0.005$	0.440	

Estimated marginal means \pm standard error for WM volumes adjusted for age, gender and total intracranial volumes. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.921; F = 0.709; p = 0.739; $\eta^2 p = 0.079$. ^bWilks' Lambda = 0.904; F = 0.878; p = 0.572; $\eta^2 p = 0.096$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 6. Superior cerebellar peduncle (SCP) volumes in healthy controls, ALS-NEG and ALS-C9

	Estimated marginal means \pm S.E. for groups			Statistics	
	HC n=110	ALS-NEG n=133	ALS-C9 n=22	HC vs ALS-NEG	HC vs ALS-C9
SCP volume	260.202 \pm 5.246	250.211 \pm 4.778	238.923 \pm 12.069	0.491	0.325

Estimated marginal means \pm standard error for SCP volume adjusted for age, gender and total intracranial volume. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (not applicable): $F = 1.774$; $p = 0.172$; $\eta^2 p = 0.014$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 7. Superior cerebellar peduncle (SCP) volumes in healthy controls and ALS-ATXi

	Estimated marginal means \pm S.E. for groups	
	HC n=100	ALS-ATXi n=5
SCP volume	260.254 \pm 4.763	224.205 \pm 22.908

Estimated marginal means \pm standard error for SCP volume adjusted for age, gender and total intracranial volume. The comparison between HC and ALS-ATXi was not significant: $F = 2.363$; $p = 0.127$; $\eta^2 p = 0.021$.

Supplementary Table 8. Radial diffusivity (RD) in cerebro-cerebellar tractography in healthy controls and ALS-NEG and ALS-C9

Cerebro-cerebellar RD×10 ⁻³ values			Estimated marginal means ± S.E. for groups			Statistics			
			HC n=110	ALS-NEG n=133	ALS-C9 n=22	Univariate effect size	HC vs ALS-NEG	HC vs ALS-C9	
Left ^a	FPC	L1L	0.520 ± 0.006	0.529 ± 0.006	0.534 ± 0.006	η ² p = 0.038	0.984	0.373	
		L1R	0.508 ± 0.009	0.544 ± 0.010	0.552 ± 0.010	η ² p = 0.169	0.023	0.004	
	PPC	L1L	0.537 ± 0.006	0.546 ± 0.006	0.557 ± 0.006	η ² p = 0.081	0.944	0.065	
		L1R	0.540 ± 0.013	0.563 ± 0.013	0.589 ± 0.013	η ² p = 0.102	0.657	0.029	
	TPC	L1L	0.648 ± 0.020	0.697 ± 0.021	0.711 ± 0.021	η ² p = 0.078	0.288	0.096	
		L1R	0.709 ± 0.029	0.689 ± 0.031	0.746 ± 0.031	η ² p = 0.028	1.000	1.000	
	OPC	L1L	0.575 ± 0.013	0.584 ± 0.013	0.615 ± 0.013	η ² p = 0.078	1.000	0.095	
		L1R	0.635 ± 0.025	0.688 ± 0.026	0.658 ± 0.026	η ² p = 0.033	0.437	1.000	
	DRTC	L1L	0.592 ± 0.009	0.580 ± 0.009	0.603 ± 0.009	η ² p = 0.048	1.000	1.000	
		L1R	0.643 ± 0.020	0.721 ± 0.021	0.677 ± 0.021	η ² p = 0.100	0.032	0.433	
	Right ^b	FPC	R1R	0.504 ± 0.006	0.517 ± 0.006	0.535 ± 0.006	η ² p = 0.167	0.382	0.002
			R1L	0.543 ± 0.009	0.548 ± 0.009	0.547 ± 0.009	η ² p = 0.004	1.000	1.000
PPC		R1R	0.530 ± 0.008	0.536 ± 0.008	0.557 ± 0.008	η ² p = 0.092	1.000	0.056	
		R1L	0.593 ± 0.013	0.598 ± 0.014	0.590 ± 0.014	η ² p = 0.003	1.000	1.000	
TPC		R1R	0.632 ± 0.024	0.676 ± 0.024	0.690 ± 0.024	η ² p = 0.049	0.593	0.272	
		R1L	0.683 ± 0.019	0.671 ± 0.020	0.700 ± 0.020	η ² p = 0.018	1.000	1.000	
OPC		R1R	0.565 ± 0.014	0.587 ± 0.014	0.594 ± 0.014	η ² p = 0.034	0.868	0.484	
		R1L	0.617 ± 0.022	0.690 ± 0.023	0.665 ± 0.023	η ² p = 0.080	0.074	0.420	
DRTC		R1R	0.578 ± 0.010	0.599 ± 0.010	0.607 ± 0.010	η ² p = 0.064	0.464	0.151	
		R1L	0.650 ± 0.017	0.651 ± 0.018	0.674 ± 0.018	η ² p = 0.019	1.000	0.986	

Estimated marginal means ± standard error for radial diffusivity adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (left hemisphere): ^aWilks' Lambda = 0.552; F = 1.869; p = 0.022; η²p = 0.257, ^bWilks' Lambda = 0.643; F = 1.336; p = 0.172; η²p = 0.198. Bold p-values are significant at p < 0.05, after Bonferroni correction for multiple comparisons. Partial η² effect size is interpreted as small (η²p = 0.01), medium (η²p = 0.06) or large (η²p = 0.14).

Supplementary Table 9. Axial Diffusivity (AD) in cerebro-cerebellar tractography in healthy controls and ALS-NEG and ALS-C9

Cerebro-cerebellar AD×10 ⁻³ values			Estimated marginal means ± S.E. for groups			Statistics		
			HC n=110	ALS-NEG n=133	ALS-C9 n=22	Univariate effect size	HC vs ALS-NEG	HC vs ALS-C9
Left ^a	FPC	L1L	1.092 ± 0.007	1.097 ± 0.007	1.083 ± 0.007	η ² p = 0.027	1.000	1.000
		L1R	1.090 ± 0.011	1.110 ± 0.012	1.092 ± 0.012	η ² p = 0.025	0.716	1.000
	PPC	L1L	1.114 ± 0.006	1.120 ± 0.007	1.113 ± 0.007	η ² p = 0.009	1.000	1.000
		L1R	1.122 ± 0.016	1.143 ± 0.016	1.137 ± 0.016	η ² p = 0.015	1.000	1.000
	TPC	L1L	1.108 ± 0.023	1.159 ± 0.024	1.173 ± 0.024	η ² p = 0.061	0.412	0.181
		L1R	1.167 ± 0.035	1.147 ± 0.036	1.207 ± 0.036	η ² p = 0.022	1.000	1.000
	OPC	L1L	1.117 ± 0.012	1.118 ± 0.012	1.127 ± 0.012	η ² p = 0.006	1.000	1.000
		L1R	1.153 ± 0.035	1.182 ± 0.036	1.141 ± 0.036	η ² p = 0.010	1.000	1.000
	DRTC	L1L	1.116 ± 0.010	1.105 ± 0.010	1.138 ± 0.010	η ² p = 0.076	1.000	0.432
		L1R	1.158 ± 0.020	1.197 ± 0.021	1.166 ± 0.021	η ² p = 0.030	0.565	1.000
Right ^b	FPC	R1R	1.060 ± 0.009	1.073 ± 0.009	1.079 ± 0.009	η ² p = 0.036	0.911	0.420
		R1L	1.119 ± 0.010	1.105 ± 0.011	1.105 ± 0.011	η ² p = 0.019	1.000	1.000
	PPC	R1R	1.090 ± 0.008	1.110 ± 0.008	1.106 ± 0.008	η ² p = 0.050	0.283	0.506
		R1L	1.163 ± 0.017	1.151 ± 0.017	1.154 ± 0.017	η ² p = 0.004	1.000	1.000
	TPC	R1R	1.064 ± 0.031	1.144 ± 0.033	1.142 ± 0.033	η ² p = 0.061	0.245	0.275
		R1L	1.153 ± 0.024	1.128 ± 0.025	1.153 ± 0.025	η ² p = 0.011	1.000	1.000
	OPC	R1R	1.092 ± 0.015	1.110 ± 0.016	1.115 ± 0.016	η ² p = 0.018	1.000	0.914
		R1L	1.138 ± 0.026	1.211 ± 0.027	1.174 ± 0.027	η ² p = 0.054	0.185	1.000
	DRTC	R1R	1.087 ± 0.012	1.123 ± 0.013	1.127 ± 0.013	η ² p = 0.091	0.128	0.082
		R1L	1.122 ± 0.018	1.151 ± 0.019	1.174 ± 0.019	η ² p = 0.059	0.839	0.156

Estimated marginal means ± standard error for axial diffusivity adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.666; F = 1.216; p = 0.256; η²p = 0.184, ^bWilks' Lambda = 0.723; F = 0.953; p = 0.524; η²p = 0.150. Partial η² effect size is interpreted as small (η²p = 0.01), medium (η²p = 0.06) or large (η²p = 0.14).

Supplementary Table 10. Fractional anisotropy (FA) values for the cerebro-cerebellar tracts in healthy controls and ALS-ATXi

Cerebro-cerebellar FA values			Estimated marginal means \pm S.E. for groups		Statistics		
			HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi	
Left ^a	FPC	L1L	0.453 \pm 0.005	0.462 \pm 0.009	$\eta^2 p = 0.030$	0.388	
		L1R	0.466 \pm 0.005	0.450 \pm 0.012	$\eta^2 p = 0.052$	0.252	
	PPC	L1L	0.446 \pm 0.003	0.436 \pm 0.008	$\eta^2 p = 0.043$	0.299	
		L1R	0.453 \pm 0.005	0.455 \pm 0.012	$\eta^2 p = 0.002$	0.841	
	TPC	L1L	0.353 \pm 0.006	0.378 \pm 0.013	$\eta^2 p = 0.104$	0.101	
		L1R	0.340 \pm 0.009	0.313 \pm 0.021	$\eta^2 p = 0.050$	0.262	
	OPC	L1L	0.415 \pm 0.005	0.424 \pm 0.011	$\eta^2 p = 0.018$	0.504	
		L1R	0.389 \pm 0.010	0.390 \pm 0.022	$\eta^2 p = 0.000$	0.985	
	DRTC	L1L	0.396 \pm 0.005	0.392 \pm 0.012	$\eta^2 p = 0.003$	0.798	
		L1R	0.381 \pm 0.008	0.364 \pm 0.018	$\eta^2 p = 0.027$	0.414	
	Right ^b	FPC	R1R	0.451 \pm 0.004	0.450 \pm 0.010	$\eta^2 p = 0.000$	0.938
			R1L	0.447 \pm 0.005	0.451 \pm 0.011	$\eta^2 p = 0.004$	0.751
PPC		R1R	0.440 \pm 0.005	0.446 \pm 0.012	$\eta^2 p = 0.011$	0.607	
		R1L	0.426 \pm 0.005	0.418 \pm 0.012	$\eta^2 p = 0.017$	0.517	
TPC		R1R	0.342 \pm 0.006	0.339 \pm 0.015	$\eta^2 p = 0.001$	0.867	
		R1L	0.352 \pm 0.007	0.354 \pm 0.017	$\eta^2 p = 0.00$	0.905	
OPC		R1R	0.410 \pm 0.008	0.417 \pm 0.020	$\eta^2 p = 0.004$	0.755	
		R1L	0.394 \pm 0.009	0.355 \pm 0.021	$\eta^2 p = 0.096$	0.115	
DRTC		R1R	0.391 \pm 0.005	0.389 \pm 0.012	$\eta^2 p = 0.001$	0.911	
		R1L	0.356 \pm 0.008	0.347 \pm 0.018	$\eta^2 p = 0.010$	0.619	

Estimated marginal means \pm standard error for fractional anisotropy adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.522; F = 1.468; p = 0.238; $\eta^2 p = 0.478$, ^bWilks' Lambda = 0.801; F = 0.397; p = 0.929; $\eta^2 p = 0.199$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 11. Axial Diffusivity (AD) in cerebro-cerebellar tractography in healthy controls and ALS-ATXi

Cerebro-cerebellar AD×10 ⁻³ values			Estimated marginal means ± S.E. for groups		Statistics	
			HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left ^a	FPC	L1L	1.092 ± 0.0075	1.073 ± 0.011	η ² p = 0.087	0.136
		L1R	1.089 ± 0.007	1.077 ± 0.016	η ² p = 0.016	0.528
	PPC	L1L	1.114 ± 0.004	1.103 ± 0.010	η ² p = 0.037	0.336
		L1R	1.122 ± 0.018	1.167 ± 0.042	η ² p = 0.036	0.342
	TPC	L1L	1.108 ± 0.015	1.096 ± 0.034	η ² p = 0.004	0.755
		L1R	1.156 ± 0.029	1.274 ± 0.068	η ² p = 0.090	0.129
	OPC	L1L	1.116 ± 0.009	1.102 ± 0.020	η ² p = 0.014	0.561
		L1R	1.146 ± 0.022	1.181 ± 0.051	η ² p = 0.016	0.532
	DRTC	L1L	1.118 ± 0.009	1.101 ± 0.022	η ² p = 0.021	0.475
		L1R	1.164 ± 0.014	1.065 ± 0.033	η ² p = 0.221	0.013
Right ^b	FPC	R1R	1.060 ± 0.006	1.045 ± 0.014	η ² p = 0.040	0.316
		R1L	1.117 ± 0.009	1.115 ± 0.021	η ² p = 0.000	0.928
	PPC	R1R	1.091 ± 0.005	1.097 ± 0.013	η ² p = 0.008	0.667
		R1L	1.158 ± 0.016	1.197 ± 0.038	η ² p = 0.033	0.365
	TPC	R1R	1.061 ± 0.019	1.095 ± 0.045	η ² p = 0.018	0.503
		R1L	1.154 ± 0.023	1.174 ± 0.052	η ² p = 0.005	0.734
	OPC	R1R	1.093 ± 0.013	1.094 ± 0.031	η ² p = 0.000	0.988
		R1L	1.137 ± 0.020	1.113 ± 0.048	η ² p = 0.008	0.655
	DRTC	R1R	1.087 ± 0.012	1.108 ± 0.027	η ² p = 0.018	0.509
		R1L	1.121 ± 0.021	1.224 ± 0.049	η ² p = 0.125	0.071

Estimated marginal means ± standard error for axial diffusivity adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.462; F = 1.864; p = 0.129; η²p = 0.538, ^bWilks' Lambda = 0.682; F = 0.745; p = 0.676; η²p = 0.318. Partial η² effect size is interpreted as small (η²p = 0.01), medium (η²p = 0.06) or large (η²p = 0.14).

Supplementary Table 12. Radial diffusivity (RD) in cerebro-cerebellar tractography in healthy controls and ALS-ATXi

Cerebro-cerebellar RD×10 ⁻³ values			Estimated marginal means ± S.E. for groups		Statistics	
			HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left ^a	FPC	L1L	0.520 ± 0.006	0.499 ± 0.011	$\eta^2 p = 0.112$	0.088
		L1R	0.506 ± 0.007	0.523 ± 0.017	$\eta^2 p = 0.032$	0.375
	PPC	L1L	0.536 ± 0.004	0.539 ± 0.010	$\eta^2 p = 0.003$	0.791
		L1R	0.539 ± 0.013	0.565 ± 0.031	$\eta^2 p = 0.022$	0.464
	TPC	L1L	0.648 ± 0.012	0.612 ± 0.028	$\eta^2 p = 0.051$	0.257
		L1R	0.700 ± 0.027	0.814 ± 0.063	$\eta^2 p = 0.094$	0.119
	OPC	L1L	0.575 ± 0.009	0.560 ± 0.020	$\eta^2 p = 0.017$	0.512
		L1R	0.630 ± 0.021	0.646 ± 0.048	$\eta^2 p = 0.004$	0.768
	DRTC	L1L	0.593 ± 0.021	0.585 ± 0.022	$\eta^2 p = 0.004$	0.768
		L1R	0.648 ± 0.018	0.618 ± 0.042	$\eta^2 p = 0.017$	0.519
Right ^b	FPC	R1R	0.503 ± 0.005	0.497 ± 0.011	$\eta^2 p = 0.009$	0.634
		R1L	0.541 ± 0.008	0.537 ± 0.017	$\eta^2 p = 0.002$	0.845
	PPC	R1R	0.528 ± 0.006	0.526 ± 0.014	$\eta^2 p = 0.001$	0.865
		R1L	0.590 ± 0.014	0.622 ± 0.032	$\eta^2 p = 0.030$	0.391
	TPC	R1R	0.633 ± 0.017	0.654 ± 0.039	$\eta^2 p = 0.010$	0.624
		R1L	0.684 ± 0.019	0.676 ± 0.045	$\eta^2 p = 0.001$	0.880
	OPC	R1R	0.566 ± 0.012	0.561 ± 0.027	$\eta^2 p = 0.001$	0.872
		R1L	0.615 ± 0.016	0.644 ± 0.036	$\eta^2 p = 0.020$	0.481
	DRTC	R1R	0.578 ± 0.010	0.594 ± 0.024	$\eta^2 p = 0.016$	0.528
		R1L	0.646 ± 0.022	0.738 ± 0.052	$\eta^2 p = 0.086$	0.138

Estimated marginal means ± standard error for radial diffusivity values adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (neither hemisphere): ^aWilks' Lambda = 0.582; F = 1.148; p = 0.389; $\eta^2 p = 0.418$, ^bWilks' Lambda = 0.688; F = 0.725; p = 0.692; $\eta^2 p = 0.312$. Bold p-values are significant at p < 0.05, after Bonferroni correction for multiple comparisons. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$).

Supplementary Table 13. Cerebellar peduncle profiles in healthy controls and ALS-ATXi

Anatomical region	Diffusivity index	Estimated marginal means \pm S.E. for groups		Statistics	
		HC n=110	ALS-ATXi n=5	Univariate effect size	HC vs ALS-ATXi
Left Superior Cerebellar Peduncle	FA	0.599 \pm 0.004	0.577 \pm 0.020	$\eta^2 p = 0.011$	0.273
	AD $\times 10^{-3}$	1.365 \pm 0.007	1.344 \pm 0.035	$\eta^2 p = 0.003$	0.573
	RD $\times 10^{-3}$	0.473 \pm 0.006	0.499 \pm 0.028	$\eta^2 p = 0.008$	0.358
Right Superior Cerebellar Peduncle	FA	0.591 \pm 0.004	0.564 \pm 0.020	$\eta^2 p = 0.016$	0.180
	AD $\times 10^{-3}$	1.372 \pm 0.007	1.363 \pm 0.033	$\eta^2 p = 0.001$	0.789
	RD $\times 10^{-3}$	0.488 \pm 0.006	0.524 \pm 0.028	$\eta^2 p = 0.015$	0.203
Left Inferior Cerebellar Peduncle	FA	0.483 \pm 0.004	0.481 \pm 0.018	$\eta^2 p = 0.000$	0.917
	AD $\times 10^{-3}$	1.079 \pm 0.005	1.072 \pm 0.025	$\eta^2 p = 0.001$	0.778
	RD $\times 10^{-3}$	0.494 \pm 0.004	0.506 \pm 0.021	$\eta^2 p = 0.003$	0.568
Right Inferior Cerebellar Peduncle	FA	0.480 \pm 0.004	0.464 \pm 0.018	$\eta^2 p = 0.006$	0.399
	AD $\times 10^{-3}$	1.080 \pm 0.005	1.074 \pm 0.026	$\eta^2 p = 0.001$	0.800
	RD $\times 10^{-3}$	0.491 \pm 0.005	0.512 \pm 0.022	$\eta^2 p = 0.008$	0.340
Middle Cerebellar Peduncle	FA	0.502 \pm 0.004	0.511 \pm 0.017	$\eta^2 p = 0.002$	0.601
	AD $\times 10^{-3}$	1.052 \pm 0.005	1.043 \pm 0.023	$\eta^2 p = 0.001$	0.695
	RD $\times 10^{-3}$	0.454 \pm 0.004	0.440 \pm 0.019	$\eta^2 p = 0.005$	0.469

Estimated marginal means \pm standard error for diffusivity values (FA, AD, RD) adjusted for age and gender. Post-hoc univariate comparisons across groups were only considered significant if the multivariate omnibus test reached significance (not applicable): Wilks' Lambda = 0.849; F = 1.154; p = 0.321; $\eta^2 p = 0.151$. Partial η^2 effect size is interpreted as small ($\eta^2 p = 0.01$), medium ($\eta^2 p = 0.06$) or large ($\eta^2 p = 0.14$). HC- Healthy Control, FA – Fractional Anisotropy, AD – Axial diffusivity, RD – Radial diffusivity

Additional details on genetic analyses

In addition to screening for GGGGCC repeat expansions in *C9orf72* and CAG trinucleotide expansions in *ATXN2*, whole-genome sequence data (1) or targeted DNA sequence data (2) were also evaluated in each participating patient. Sequence data was assessed for quality, aligned to the GRCh37 reference genome and variants were called, annotated and analysed using cutadapt V.1.9.1 (3), SAMtools V1.7 (4), Picard V.2.15.0 (<http://picard.sourceforge.net/>), Plink V.1.9 (5), R V.3.2.3 (<http://www.r-project.org/>), SnpEff V.4.3 (6) and Gemini V.0.20.1 (7). Samples were compared to 135 Irish controls sequenced as described previously (1). Samples were screened for protein-altering, exonic or splice-site variants present in 32 genes linked to ALS in the ALS online database (ALSod) (8) (*ALS2*, *ANG*, *ATXN2*, *CHCHD10*, *CHMP2B*, *DAO*, *DCTN1*, *ELP3*, *ERBB4*, *FIG4*, *FUS*, *HNRNPA1*, *MATR3*, *NEFH*, *NEK1*, *OPTN*, *PFN1*, *PRPH*, *SARM1*, *SETX*, *SIGMAR1*, *SOD1*, *SPAST*, *SPG11*, *SQSTM1*, *TAF15*, *TARDBP*, *TBK1*, *UNC13A*, *UBQLN2*, *VAPB*, *VCP*).

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