

Supplementary Table S3. Summary of neuroimaging findings related to *SOD1* mutations

Reference	Modality	Study design	Population	Findings
Müller et al. (2020)	Diffusion MRI	Cross-sectional	15 <i>SOD1</i> -ALS, 27 <i>C9orf72</i> -ALS (4 with bvFTD), 32 HC	<i>SOD1</i> -ALS compared to HC showed no FA reductions along the corticospinal tract, frontal or prefrontal brain areas.
Agosta et al. (2018)	Structural MRI	Cross-sectional	20 <i>SOD1</i> -ALS, 11 sporadic ALS, 33 HC	No differences were found in cortical thickness between <i>SOD1</i> -ALS, sporadic ALS and HC. Cervical cord atrophy was greater in <i>SOD1</i> -ALS than in sporadic ALS.
	Diffusion MRI	Cross-sectional	20 <i>SOD1</i> -ALS, 11 sporadic ALS, 33 HC	Both sporadic ALS and <i>SOD1</i> -ALS showed lower FA in corticospinal tracts compared to HC, but corticospinal tract integrity was more preserved in <i>SOD1</i> -ALS compared to sporadic ALS.
	Task-free fMRI	Cross-sectional	20 <i>SOD1</i> -ALS, 11 sporadic ALS, 33 HC	Sporadic ALS compared to HC showed increased connectivity within SMN, whereas <i>SOD1</i> -ALS showed similar SMN connectivity to HC.
Menke et al. (2016)	Structural MRI	Cross-sectional	12 presymptomatic (10 <i>SOD1</i> , 2 <i>C9orf72</i>), 12 sporadic ALS, 12 HC	Presymptomatic carriers compared to HC showed no differences in cortical gray matter volume, cortical thickness and subcortical gray matter structure volume.
	Diffusion MRI	Cross-sectional	12 presymptomatic (10 <i>SOD1</i> , 2 <i>C9orf72</i>), 12 sporadic ALS, 12 HC	Presymptomatic carriers compared to HC showed no differences in FA and RD.
	Task-free fMRI	Cross-sectional	12 presymptomatic (10 <i>SOD1</i> , 2 <i>C9orf72</i>), 12 sporadic ALS, 12 HC	Sporadic ALS but not presymptomatic carriers showed SMN alterations compared to HC. Both groups showed increased precuneus-cingulate-middle frontal network connectivity.
Blain et al. (2011)	Diffusion MRI	Cross-sectional	7 <i>SOD1</i> -ALS, 21 sporadic ALS, 20 HC	<i>SOD1</i> -ALS compared to HC showed no differences within corticospinal tracts, whereas sporadic ALS showed lower FA and RD.
Carew et al. (2011a)	¹ H MRS	Cross-sectional	4 presymptomatic <i>SOD1</i> , 29 HC, 23 patients with ALS	Presymptomatic <i>SOD1</i> showed reduced NAA/Cr and NAA/mI ratios in the cervical spinal cord relative to healthy controls.
Vucic et al. (2010)	Diffusion MRI	Cross-sectional	7 presymptomatic <i>SOD1</i> , 7 HC	No differences between presymptomatic <i>SOD1</i> and HC in FA, trace apparent diffusion coefficient, parallel diffusivity, or perpendicular diffusivity.
Stanton et al. (2009)	Diffusion MRI	Cross-sectional	6 <i>SOD1</i> -ALS, 20 sporadic ALS, 21 HC	<i>SOD1</i> -ALS had higher FA than sporadic ALS in the body of the corpus callosum, corona radiata and occipitotemporal and occipitoparietal white matter.
Ng et al. (2008)	Diffusion MRI	Cross-sectional	8 presymptomatic <i>SOD1</i> , 13 HC	Presymptomatic <i>SOD1</i> compared to HC showed reduced FA, increased tensor trace, and increased RD in the posterior limb of the internal capsule.
Turner et al. (2007a)	Structural MRI	Cross-sectional	7 <i>SOD1</i> -ALS, 23 sporadic ALS, 28 HC	<i>SOD1</i> -ALS compared to HC showed pronounced grey matter loss within the anteromedial frontal lobes, while sporadic ALS showed gray matter loss confined to the medial motor and premotor cortices.
Turner et al. (2007b)	[¹¹ C]WAY100635 PET	Cross-sectional	11 <i>SOD1</i> -ALS, 21 sporadic ALS, 19 HC	Sporadic and <i>SOD1</i> -ALS showed reduced [¹¹ C]WAY100635 binding compared to HC, but the reduction was more pronounced in sporadic ALS.

Turner et al. (2005)	[¹¹ C]flumazenil PET	Cross-sectional	2 presymptomatic <i>SOD1</i> , 10 <i>SOD1</i> -ALS, 24 sporadic ALS, 24 HC	Both sporadic and <i>SOD1</i> -ALS showed reduced [¹¹ C]flumazenil binding compared to HC. Sporadic ALS had reduced binding in premotor regions, motor cortex, and posterior motor association areas, while <i>SOD1</i> -ALS was associated with lower binding in the left frontotemporal junction and anterior cingulate.
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FTD, frontotemporal dementia; bvFTD, behavioral variant FTD; ALS, amyotrophic lateral sclerosis; HC, healthy control; SMN, sensorimotor network; FA, fractional anisotropy; RD, radial diffusivity; NAA, N-acetylaspartate; Cr, creatine; ml, myoinositol