

**Fig. S1. Neuronal vacuolization and axonal spheroids characterize sialin<sup>-/-</sup> mouse CNS tissue.** (A) Toluidine blue stained sections of P21 cerebellum (top) and ventral cervical spinal cord (bottom) from control (left) and sialin<sup>-/-</sup> (right) mice. Arrows identify neurons containing cytoplasmic vacuoles found in sialin<sup>-/-</sup> mouse tissue. Note the rarity of the darkly staining myelin structures (arrowheads) in the cerebellar white matter and spinal cord from the sialin<sup>-/-</sup> mice (B) Electron micrographs of P21 cerebellum (top) and spinal cord (bottom) from control (left) and sialin<sup>-/-</sup> (right) mouse tissue. Arrows identify Purkinje cells (top) and motor neurons (bottom) containing electron lucent vacuoles. (C) Cross section of P21 sialin<sup>-/-</sup> optic nerve shows electron dense axonal spheroids in both myelinated (arrow) and unmyelinated axons. WM = white matter, G = granule cell layer, P = Purkinje cell layer, M = molecular cell layer. Scale bars are as follows: (A) 25  $\mu\text{m}$  (top), 50  $\mu\text{m}$  (bottom), (B) 10  $\mu\text{m}$ , (C) 2  $\mu\text{m}$ .

**Fig. S2. Sialin<sup>-/-</sup> mouse myelin segment analysis.** Representative coronal sections of P18 sialin<sup>-/-</sup> mouse brains immunostained for MBP. (A) Individual myelin segments originating from a single striatal oligodendrocyte can be identified. Note the oligodendrocyte process (arrowheads) originating from the MBP<sup>+</sup> cell body and leading to a clusters of myelin segments cut in cross-section. (B) Longitudinal sections of myelin segments in the corpus callosum. Individual myelin segments were identified by scrolling through z stacks of images and length of each myelin segment was measured using Image J software. Arrowheads demarcate the ends of a representative myelin segment. Scale bar is 25  $\mu\text{m}$ .

**Fig. S3. Analysis of optic nerve oligodendrocyte morphology and myelin structure.**

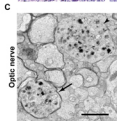
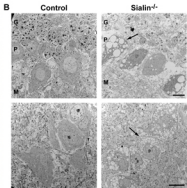
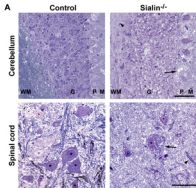
Ultrastructure of P21 control and sialin<sup>-/-</sup> optic nerves. (A) A P21 sialin<sup>-/-</sup> optic nerve

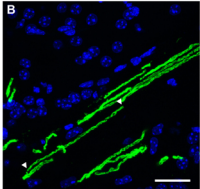
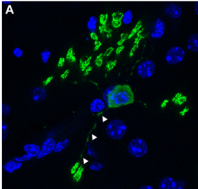
longitudinal section demonstrates a node (N) flanked by paranodes (P). Axonal accumulation of membranous organelles can be seen in the node and adjacent paranodal regions. (B) A heminode formed by a single paranode. (C-E) Cell bodies of individual oligodendrocytes defined by clumped chromatin adjacent to the nuclear envelope, the dark cytoplasm, prominent rough endoplasmic reticulum and lack of intermediate filaments (Peters, 1991). Representative oligodendrocyte from a control optic nerve (C) and a typical oligodendrocyte from a *sialin*<sup>-/-</sup> optic nerve (D) appear similar. Rare *sialin*<sup>-/-</sup> oligodendrocytes containing electron lucent vacuoles (E, arrow) were found. Scale bars are as follows: (B) 0.5  $\mu\text{m}$  and (E) 5  $\mu\text{m}$ .

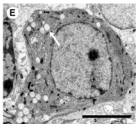
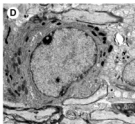
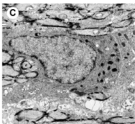
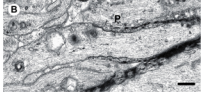
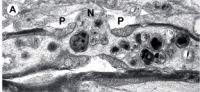
**Fig. S4. Decreased number of post-mitotic oligodendrocytes in *sialin*<sup>-/-</sup> mice optic nerves.**

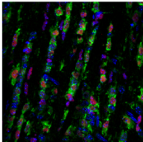
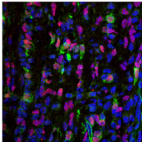
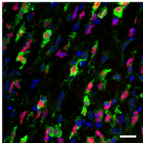
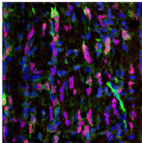
Longitudinal sections of optic nerves from P7 (left) and P15 (right) control (top) and *sialin*<sup>-/-</sup> (bottom) mice. Oligodendrocyte lineage cells are labeled with antibodies recognizing Olig2 (red) and CC1 (green). Nuclei are counterstained with DAPI (blue). P7 optic nerves show increased cell density, less organization and fewer CC1+ cells than P15 optic nerves. Chains of oligodendrocytes are evident in P15 control optic nerves. Scale bar is 20  $\mu\text{m}$ .

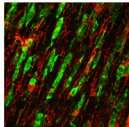
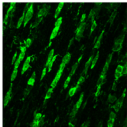
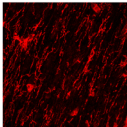
**Fig. S5. Optic nerves from *sialin*<sup>-/-</sup> mice show normal OPC staining, but decreased numbers of oligodendrocytes.** Representative longitudinal sections of P21 optic nerves from control (top) and *sialin*<sup>-/-</sup> (bottom) mice immunolabeled for NG2 (red) and CC1 (green). NG2 staining is similar in control and *sialin*<sup>-/-</sup> nerves while the number of CC1 cells is reduced in *sialin*<sup>-/-</sup> optic nerves. Scale bar is 20  $\mu\text{m}$ .







**P7****P15****Control****Sialin<sup>-/-</sup>**

**NG2****CC1****Merge****Control****Sialin<sup>-/-</sup>**