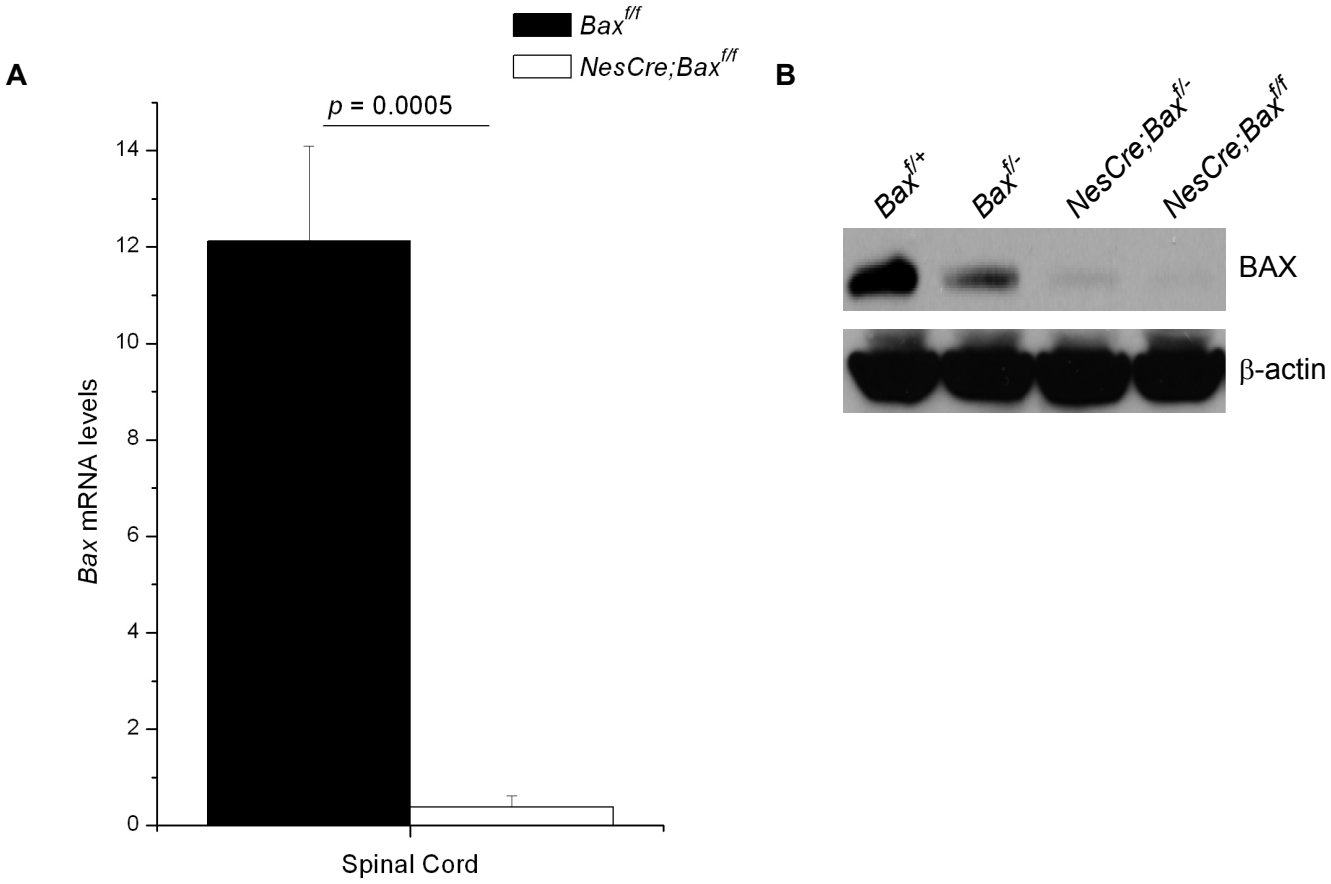
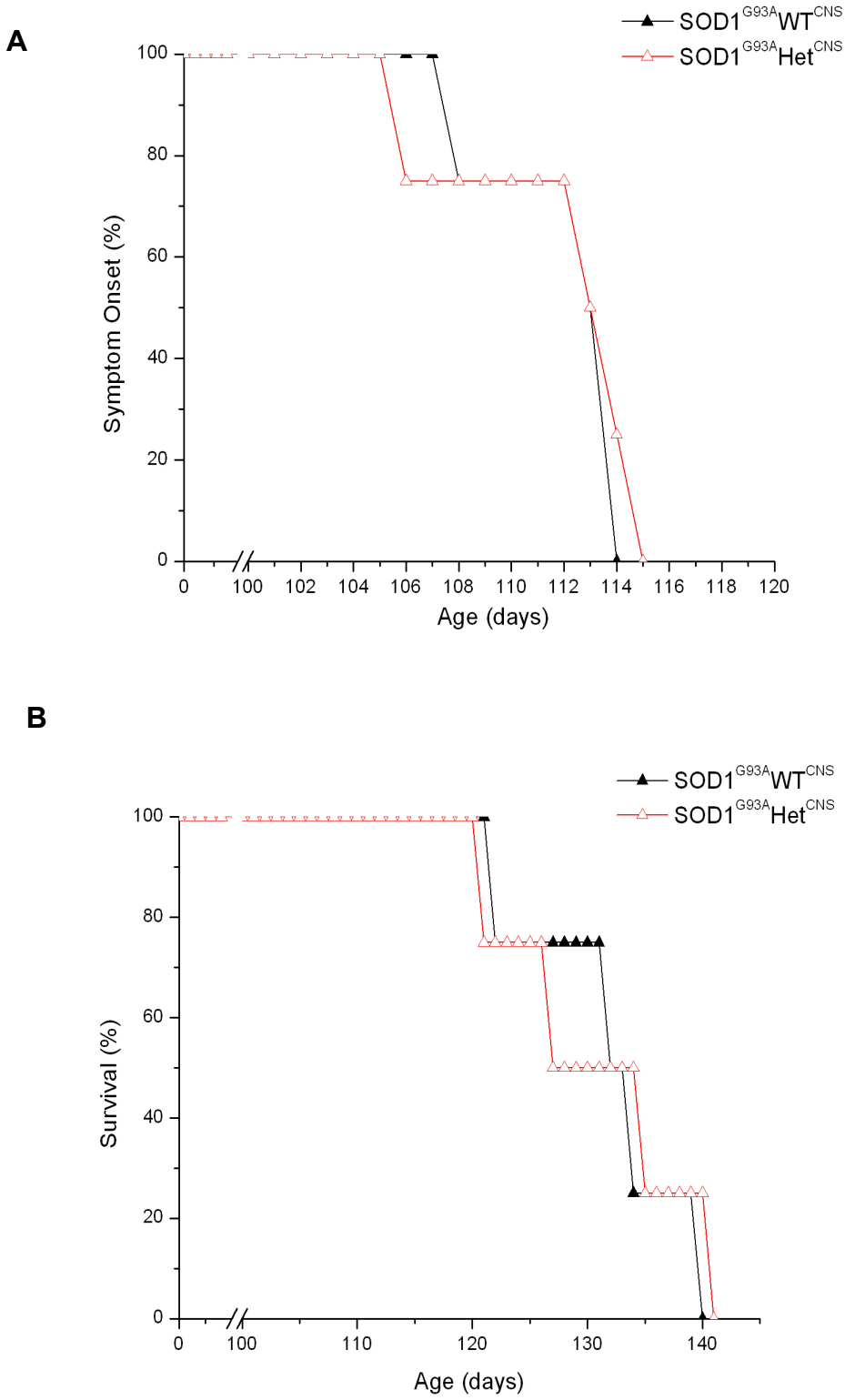
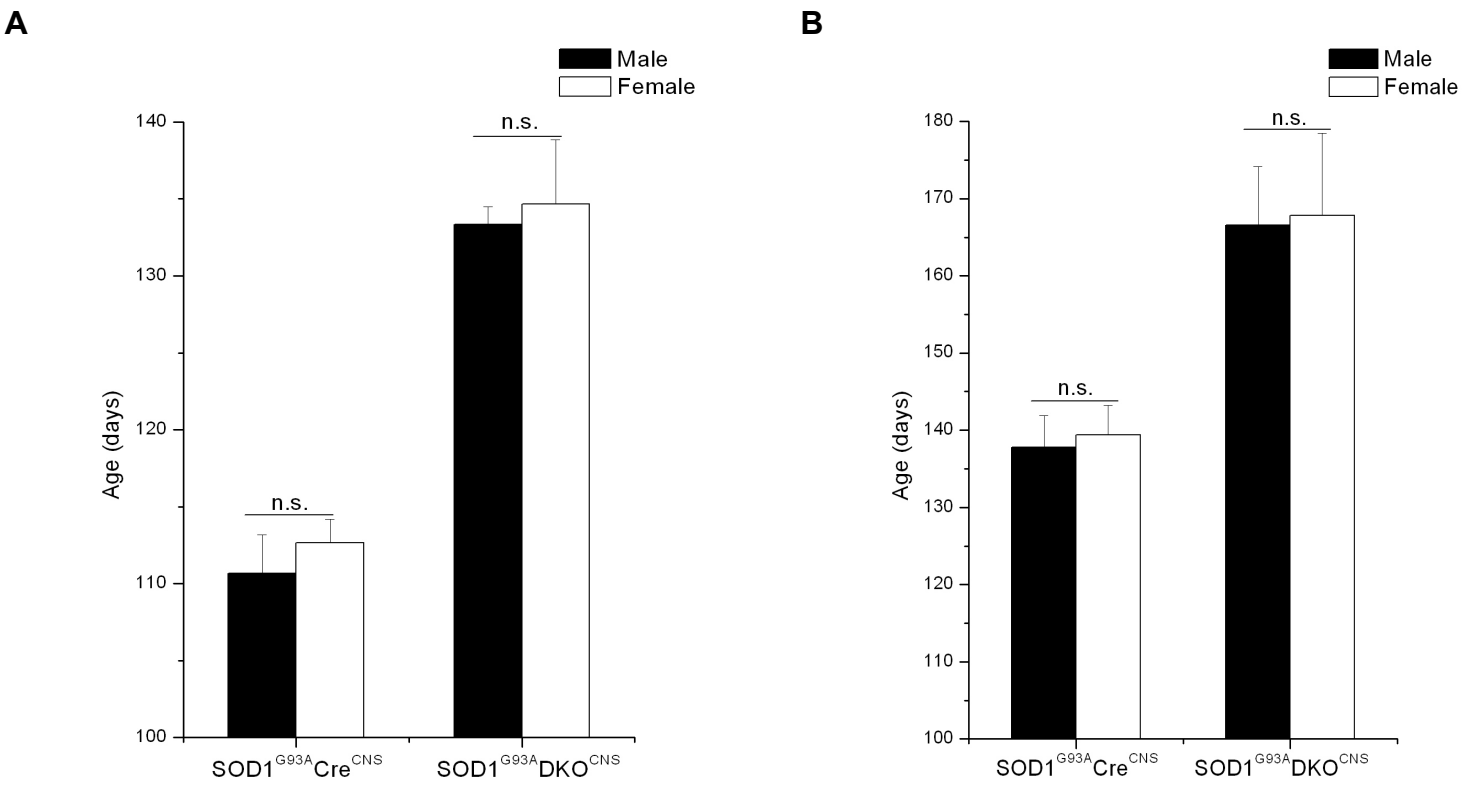


Supplemental Figure 1
Efficient *Cre* Mediated Deletion of *Bax*$^{f/f}$ from the Central Nervous System. **(A)** Relative *Bax* mRNA levels from the spinal cord of *Nestin Cre* (*NesCre*) positive versus *NesCre* negative *Bax*$^{f/f}$ mice determined by quantitative RT-PCR; *n*=3, unpaired two-tailed Student *t*-test. **(B)** Whole spinal cord extracts from 6-week old mice of indicated genotypes were immunoblotted with antibodies agains BAX and β-actin. RT-PCR, reverse transcription polymerase chain reaction; f, flox.

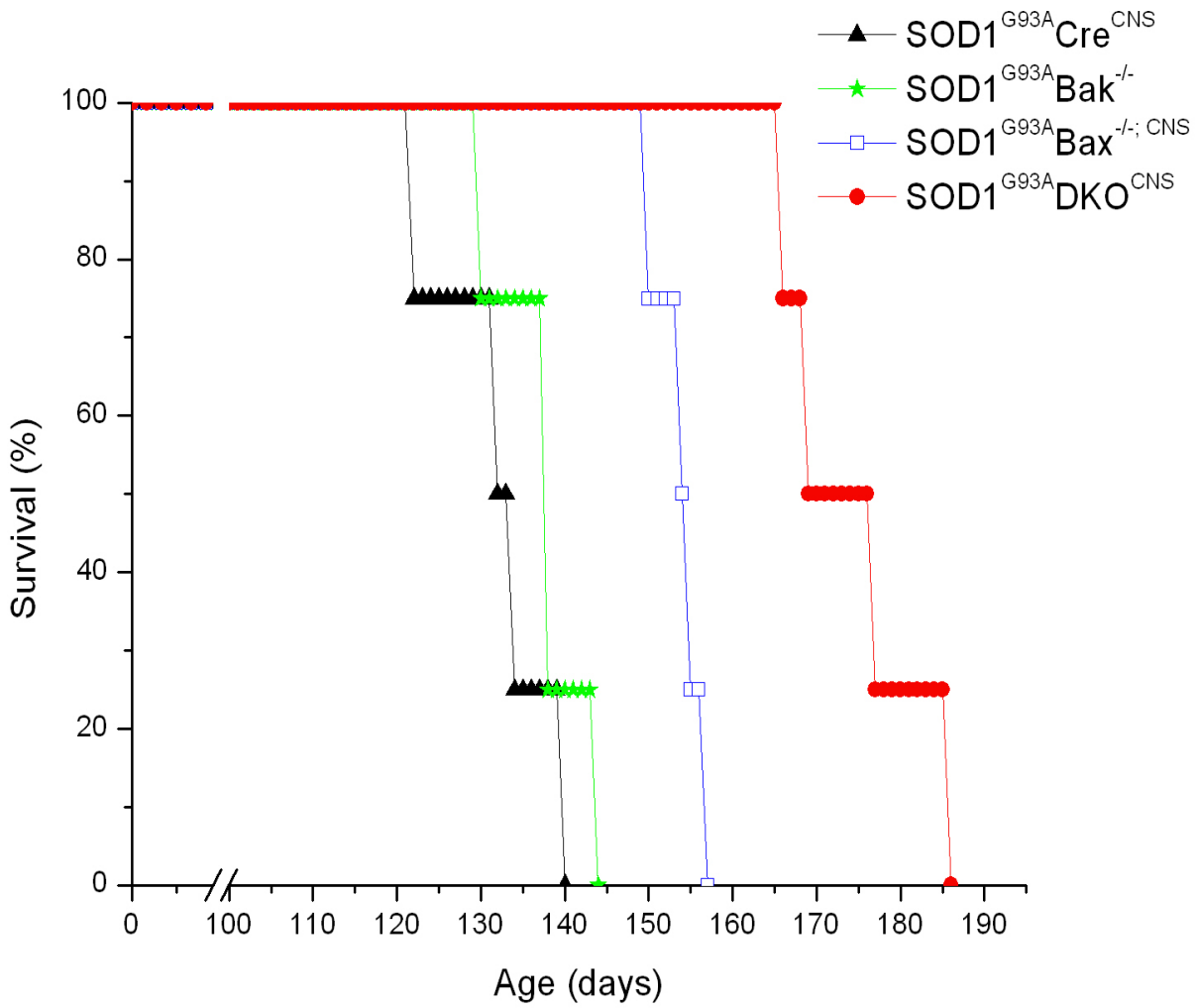


Supplemental Figure 2
No difference in symptom onset or survival between SOD1^{G93A} wildtype (WT) and SOD1^{G93A} Bax/Bak heterozygous (Het) mice. (**A**) Symptom onset in SOD1^{G93A}WT^{CNS} (112.5 ± 3.3) and SOD1^{G93A}Het^{CNS}(112 ± 4.1); p=0.86 (not statistically significant), n=4, unpaired two-tailed Student t-test. (**B**) Survival in SOD1^{G93A}WT^{CNS} (132 ± 7.5) and SOD1^{G93A}Het^{CNS} (131 ± 8.8); p=0.8 (not statistically significant), n=4, logrank test. WT were considered mice that contained both wildtype alleles for *bax* and *bak*, whereas heterozygous mice contained only one functional allele of *bax* and *bak*. All mice express *NesCre*. WT, wildtype; Het, heterozygous.

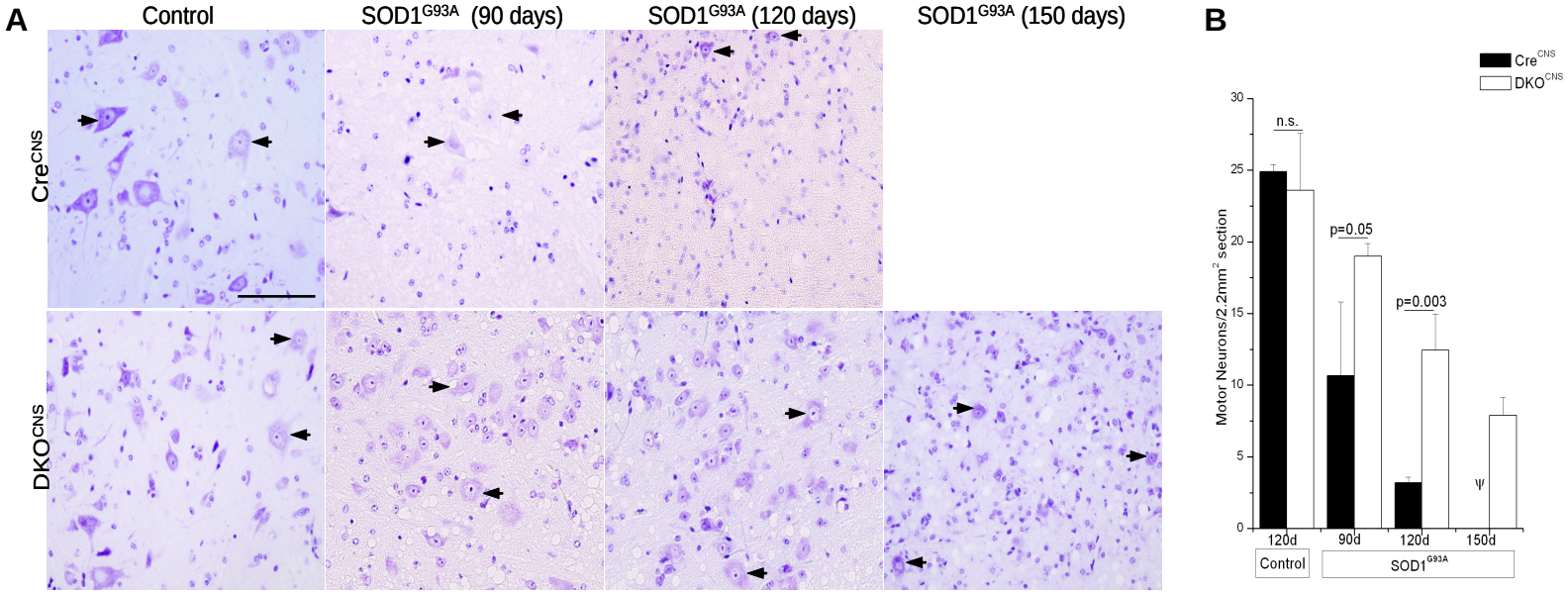


Supplemental Figure 3

Gender does not affect symptom onset or survival. (**A**) Symptom onset in SOD1^{G93A}Cre^{CNS} males (110 ± 5.1 days) versus females (113.3 ± 1.7 days) and SOD1^{G93A}DKO^{CNS} males (136 ± 5 days) versus females (134.7 ± 4.2 days). n.s., not statistically significant, *n*=3, unpaired two-tailed Student *t*-test. (**B**) Survival in SOD1^{G93A}Cre^{CNS} males (137.8 ± 4.1 days) versus females (139.4 ± 3.8 days) and SOD1^{G93A}DKO^{CNS} males (166.6 ± 7.6 days) versus females (167.8 ± 10.7 days). *n.s.,* not statistically significant, *n*=5, unpaired two-tailed Student *t*-test.

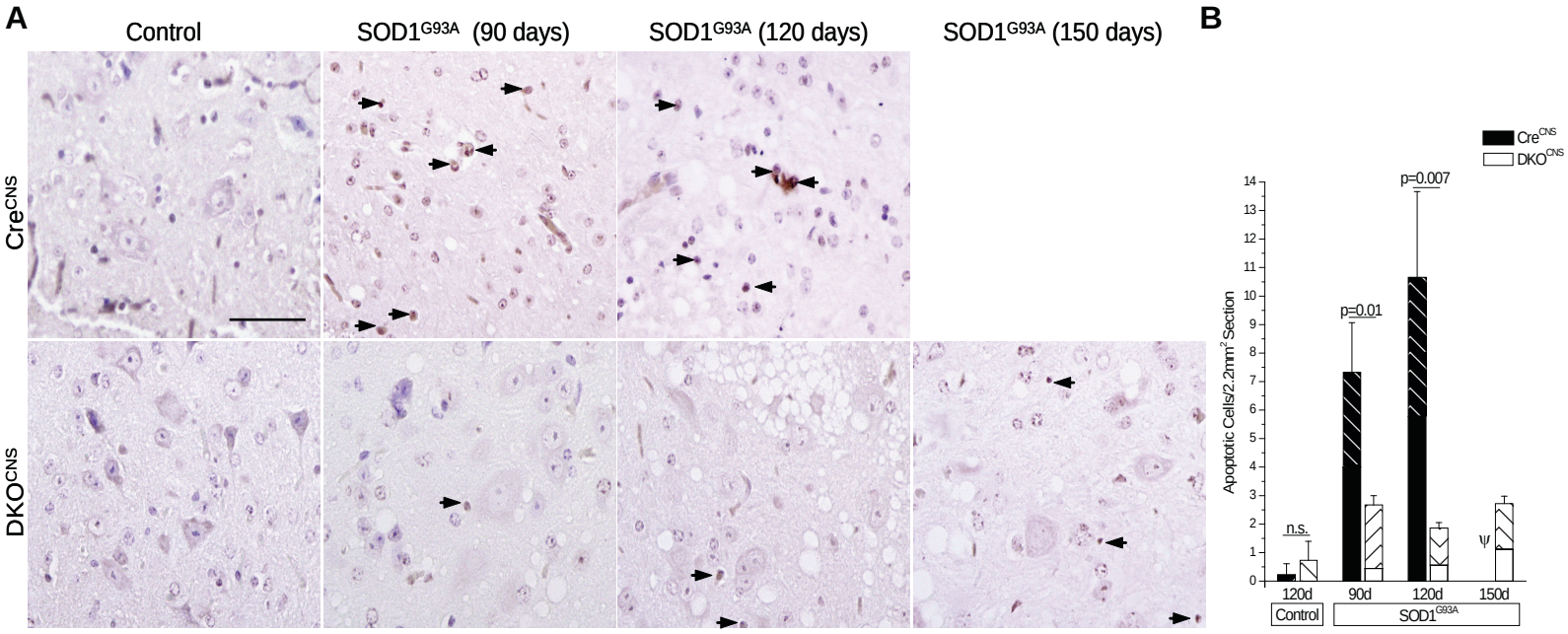


Supplemental Figure 4
Modest protection in lifespan of SOD1^{G93A}Bak$^{-/-}$ or SOD1^{G93A}Bax$^{-/-;CNS}$ mice compared to SOD1^{G93A}DKO^{CNS}. Survival in SOD1^{G93A}WT^{CNS} (132 ± 7.5 days), SOD1^{G93A}Bak$^{-/-}$ (137.5 ± 5.7 days), SOD1^{G93A}Bax$^{-/-;CNS}$(154 ± 2.9 days), and SOD1^{G93A}DKO^{CNS} (174 ± 9 days). Bak$^{-/-}$ and Bax$^{-/-;CNS}$ versus DKO^{CNS} are p=0.008 and p=0.04, respectively, n=4, logrank test. DKO, double knockout.



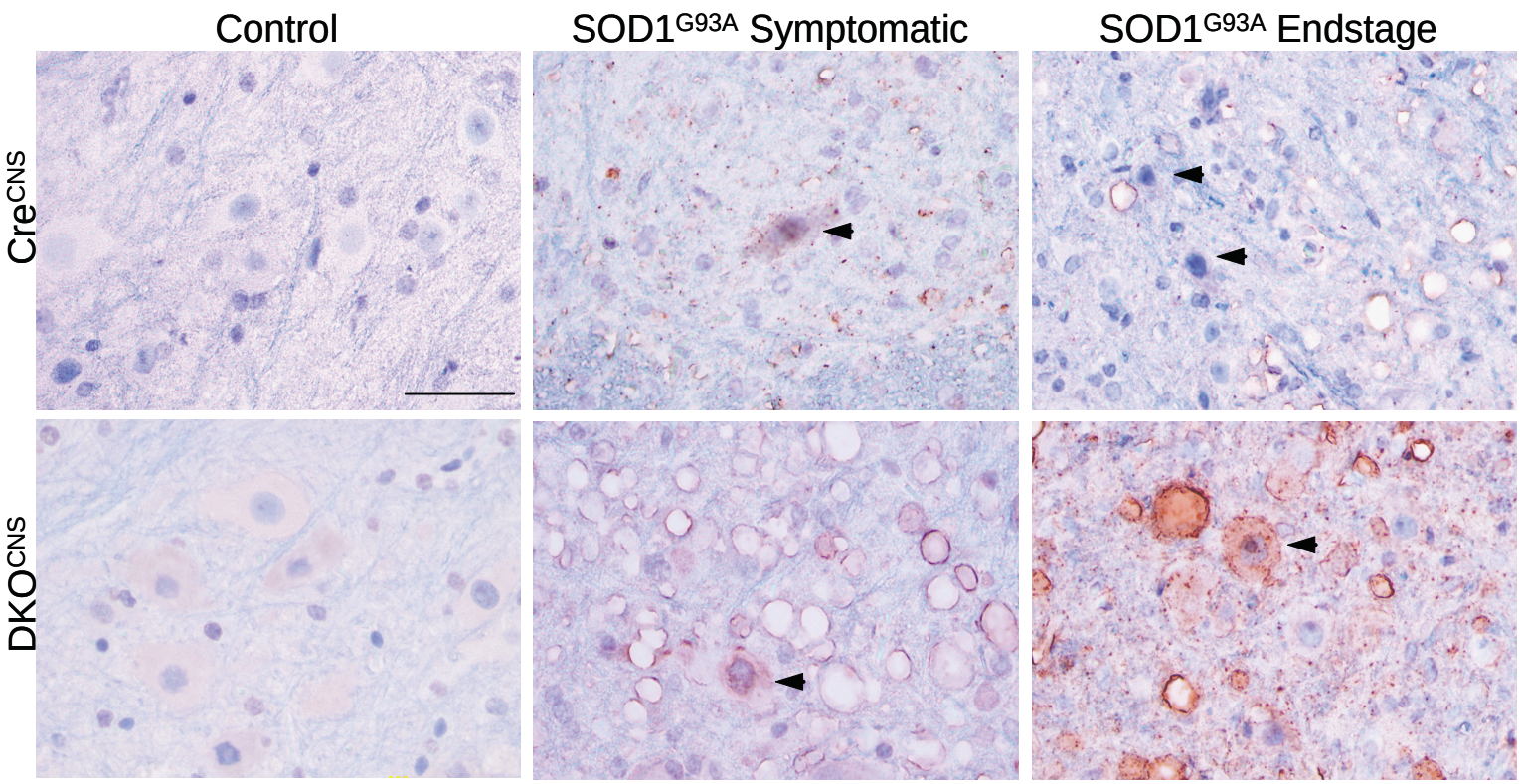
Supplemental Figure 5

Deletion of Bax/Bak preserves motor neurons. For (**A**), control mice were harvested at 120 days (d) of age; symptomatic at 90d or 90d/120d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively; and endstage at 120d or 150d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively (**A**) Representative cresyl violet stains of the anterior horn region of spinal cords from the indicated genotypes. Arrowheads indicate motor neurons. Scale bar: 200 µm. (**B**) Quantitation of anterior horn motor neurons from control and $SOD1^{G93A}$ mice using cresyl violet staining. For quantitation data, *n*=3 analyzed via Student's t-test. DKO, double knockout; ψ, all mice deceased at indicated timepoint; n.s., not statistically significant.



Supplemental Figure 6

Deletion of Bax/Bak promotes motor neuron survival. For (**A**), control mice were harvested at 120 days (d) of age; symptomatic at 90d or 90d/120d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively; and endstage at 120d or 150d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively (**A**) Representative TUNEL stains of the anterior horn region of spinal cords from the indicated genotypes. Arrowheads indicate positive staining. Scale bar: 100 μm. (**B**) Quantitation of apoptotic cells from control and $SOD1^{G93A}$ mice using TUNEL staining. Solid colors represent motor neurons and hatched pattern represents all other cell types. For quantitation data, *n*=3 analyzed via unpaired two-tailed Student's *t*-test. DKO, double knockout; ψ, all mice deceased at indicated timepoint; n.s., not statistically significant.



Supplemental Figure 7
SOD1 aggregates in both Cre^{CNS} and DKO^{CNS} neurons. Representative spinal cord anterior horn sections stained with antibody to SOD1 from the indicated genotypes. Arrowheads indicate examples of SOD1 aggregates within motor neurons. Control was taken at 120 (d) days of age; symptomatic was taken at 90 d and 120 d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively; and endstage was taken at 120 d and 150 d for $SOD1^{G93A}Cre^{CNS}$ and $SOD1^{G93A}DKO^{CNS}$, respectively.
Scale bar: 100 µm.