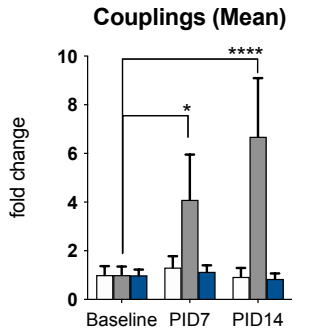


	Sham		SCI		SCI + Met	
Analysis	<i>Males</i>	<i>Females</i>	<i>Males</i>	<i>Females</i>	<i>Males</i>	<i>Females</i>
<i>Immediate Behaviour (Ladder)</i>	n=12	n=13	n=8	n=6	n=6	n=13
<i>Immediate Behaviour (Catwalk)</i>	n=7	n=6	n=11	n=7	n=8	n=9
<i>NSPC lineage tracking</i>	n=3	n=3	n=6	n=3	n=5	n=3
<i>OPC lineage tracking</i>	n=4	n=6	n=3	n=4	n=3	n=4
<i>Microglia analyses</i>	n=3	n=6	n=4	n=5	n=7	n=6
<i>Delayed Behaviour (Ladder)</i>	n=7	n=11	n=9	n=6	n=10	n=9
<i>Delayed Behaviour (Catwalk)</i>	n=7	n=11	n=9	n=6	n=10	n=9
	Vehicle			Met		
Analysis	<i>Males</i>	<i>Females</i>		<i>Males</i>	<i>Females</i>	
<i>In vitro analysis</i>	n=9	n=9		n=9	n=9	

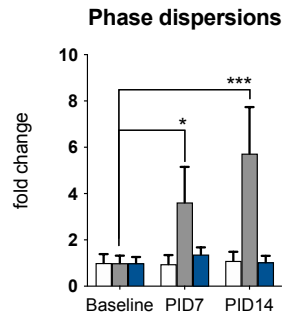
Supplemental Table 1: Summary of number of mice for all analyses

A

Combined

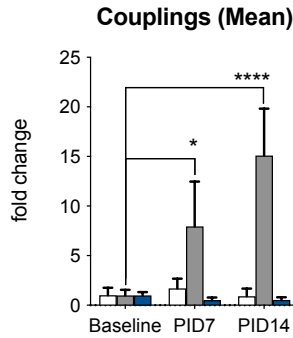


B

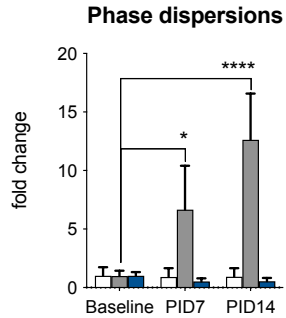


C

Females

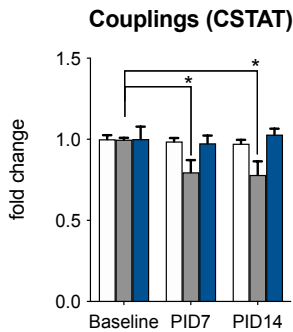


D

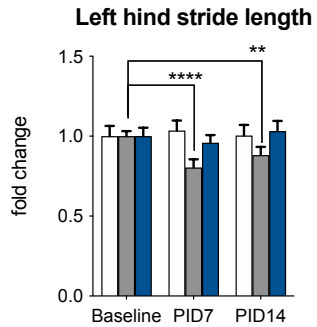


E

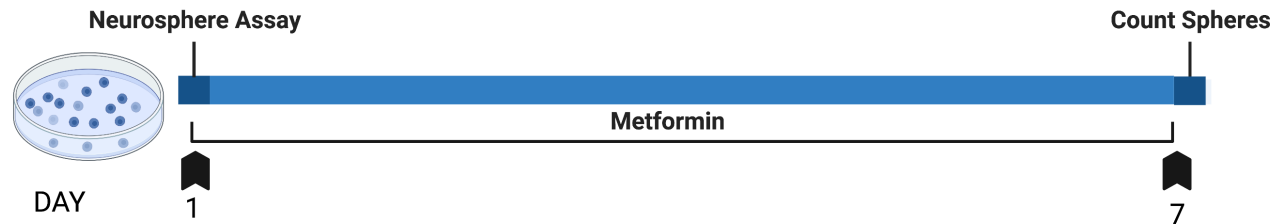
Males



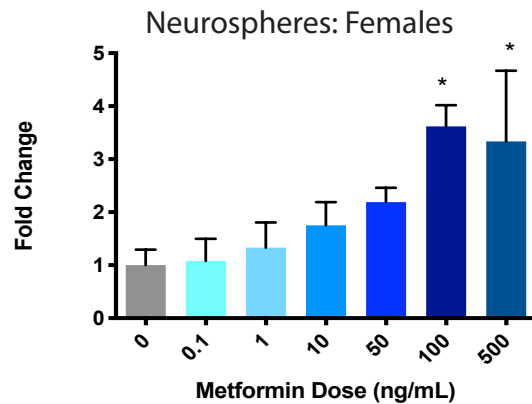
F



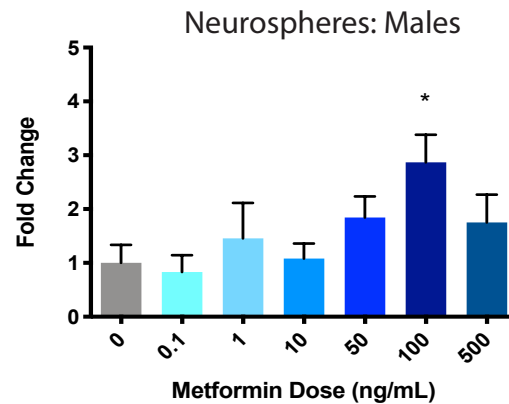
A

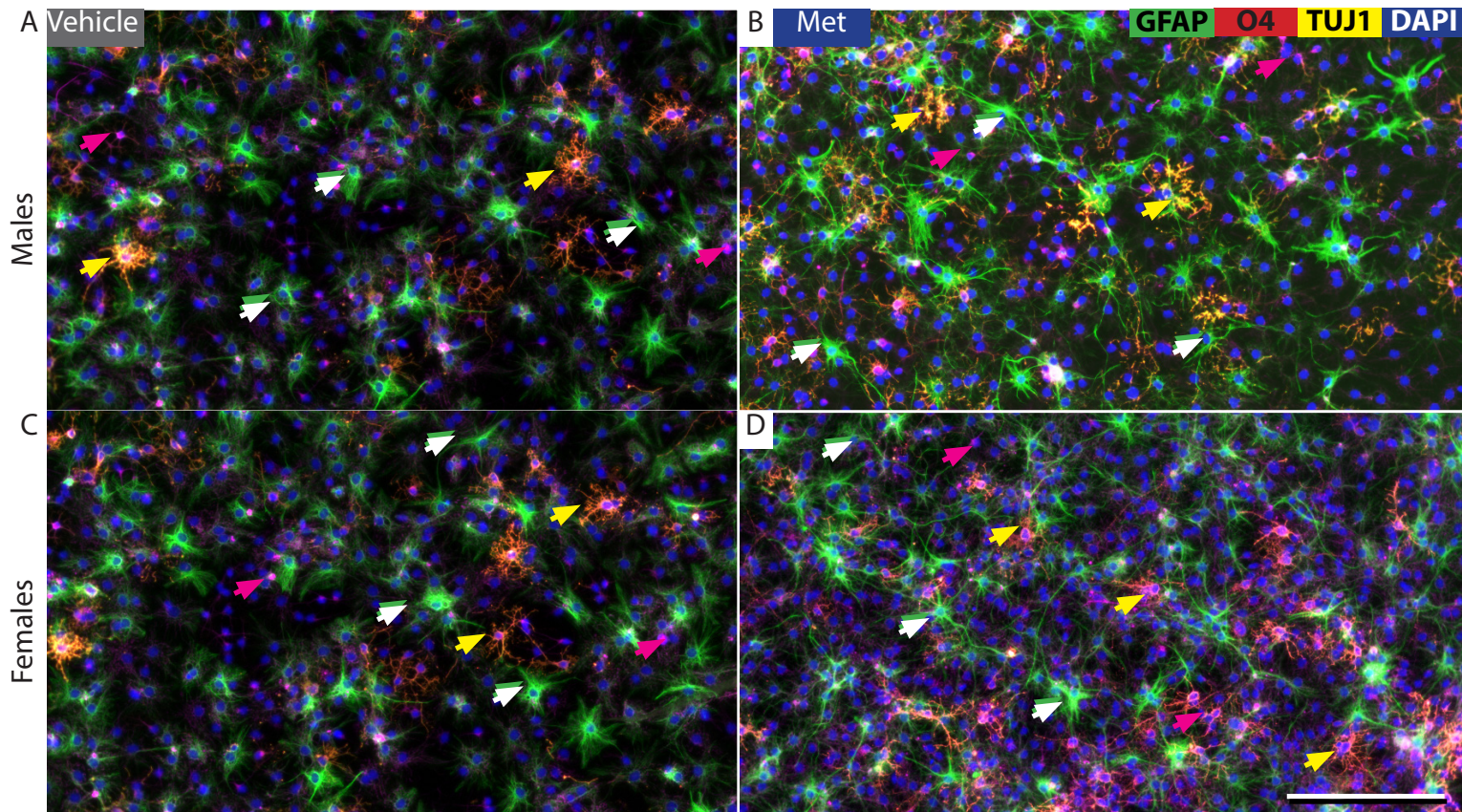


B

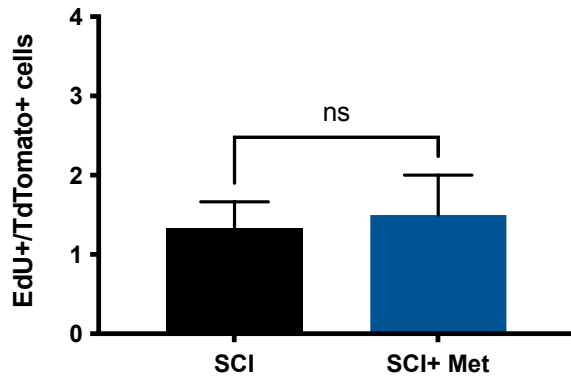


C

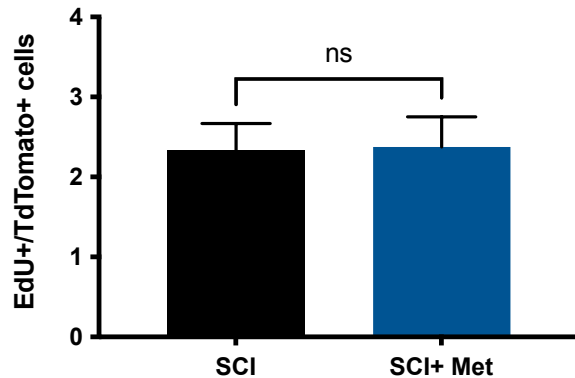




A **Females:** EdU+/TdTomato+ cells in dorsal cord



B **Males:** EdU+/TdTomato+ cells in dorsal cord



Supplemental Fig 1: Immediate metformin improves gait following SCI. Deficits in gait were observed in SCI mice in our acute studies. Mice that received metformin treatment (SCI+Met) were not impaired in any of these gait parameters at PID7 or PID14. **(A,B)** In our combined groups, mean couplings **(A)** and phase dispersion **(B)** were significantly impaired in SCI, but not SCI+Met mice. **(C, D)** Females had significant deficits in mean couplings **(C)** and phase dispersion **(D)** in SCI, but not SCI+Met mice. **(E,F)** Males demonstrated significant deficits in couplings (CSTAT) **(E)** and left hind stride length **(F)** in SCI, but not SCI+Met mice. Data are presented as mean \pm SEM; n=18-25/group including males and females; in data split by sex, n=6-11/group. *p<0.05.

Supplemental Fig. 2: *In vitro* dose-response curves for metformin. **(A)** *In vitro* experimental timeline. **(B)** *In vitro* delivery of metformin in females reveals a significant increase in the number of neurospheres at both 100ng/mL and 500ng/mL. **(C)** In males, a significant increase in the number of neurospheres is observed at 100ng/mL metformin. n=9 mice/group *p<0.05

Supplemental Fig. 3: Neurospheres are multi-potent in both males and females in the presence or absence of metformin. **(A)** male, vehicle. **(B)** male, metformin. **(C)** female, vehicle. **(D)** female, metformin. Scale bar in D= 200 μ m, n=12 neurospheres/group from 9 mice.

Supplemental Fig. 4: Rare Edu+/TdTomato+ cells are observed in the dorsal spinal cord in females and males. (A,B) There is no significant difference in Edu+/TdTom+ cells in the dorsal (injured) spinal cord in females (A) or males (B) between SCI and SCI+Met treated mice. Data are presented as mean \pm SEM; n=3-4 mice/group.