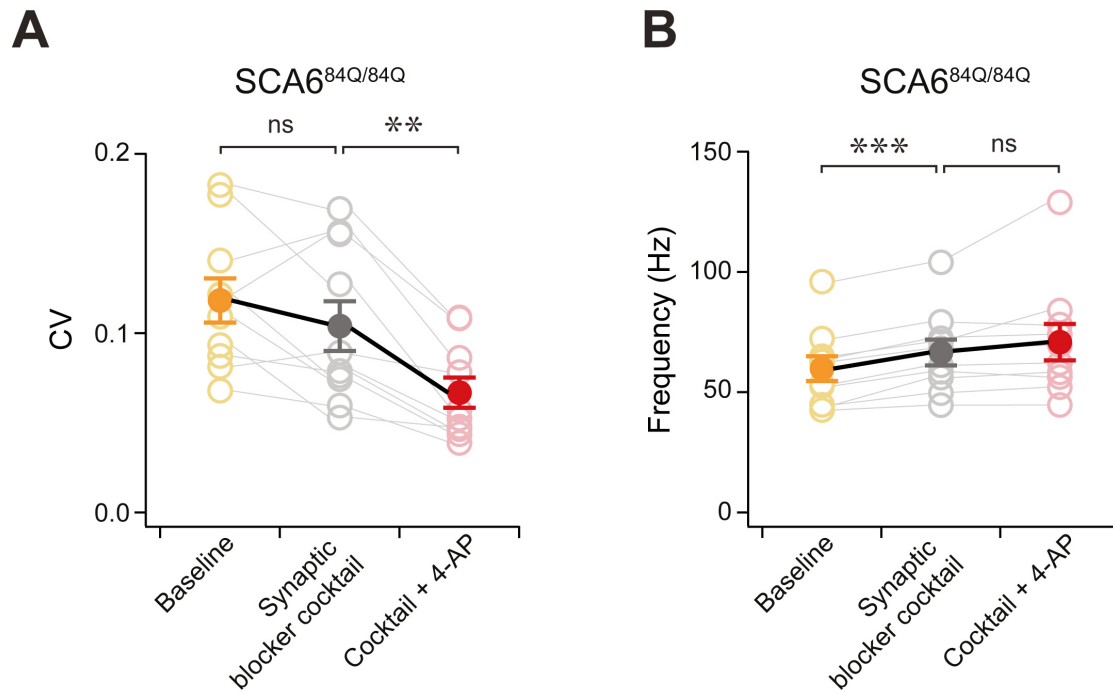


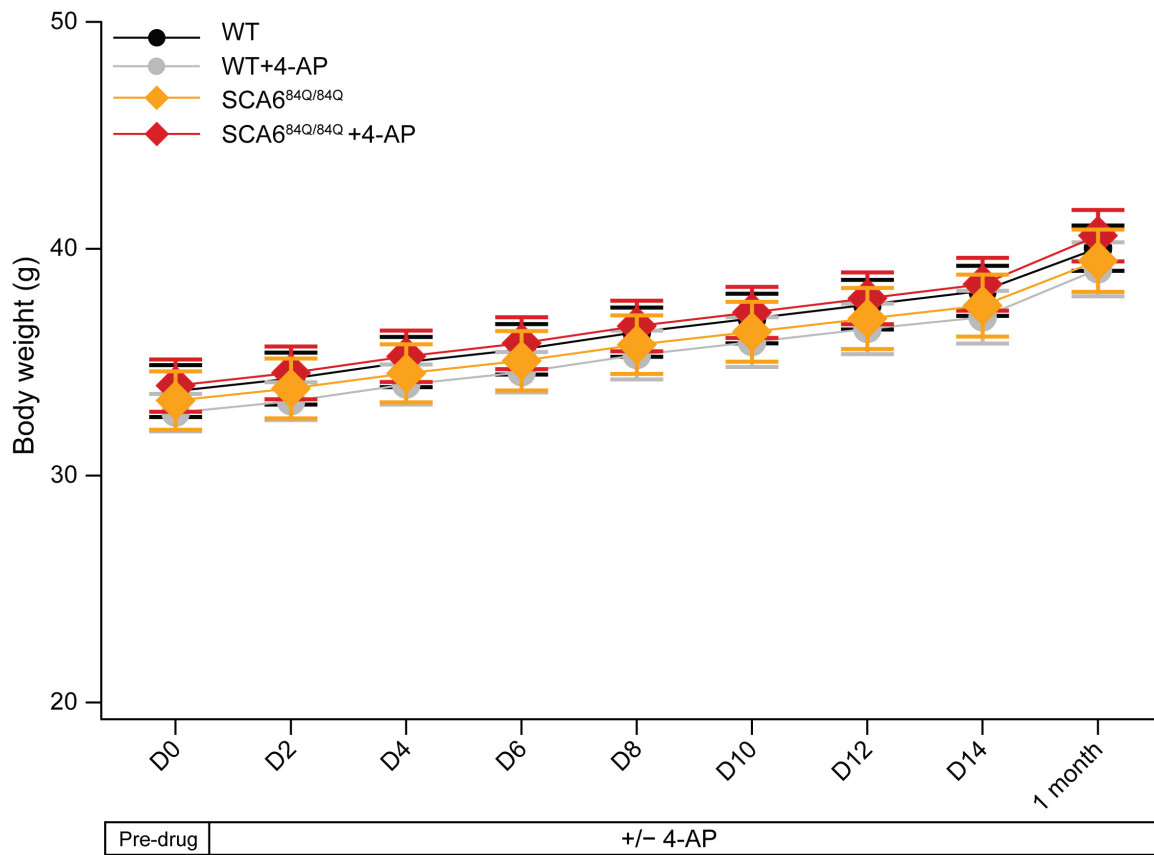
**4-aminopyridine reverses ataxia and cerebellar firing  
deficiency in a mouse model of spinocerebellar ataxia type 6**

Sriram Jayabal<sup>1,2</sup>, Hui Ho Vanessa Chang<sup>3</sup>, Kathleen E. Cullen<sup>3</sup>, and Alanna J. Watt<sup>1,\*</sup>

***Supplementary Information***



**Supplementary Figure 1. 4-AP does not act on presynaptic currents to increase Purkinje cell firing precision.** (A) A cocktail of synaptic blockers of fast excitatory (AMPA, NMDA) and inhibitory (GABA<sub>A</sub>) transmission did not alter firing precision (as measured by CV,  $P = 0.14$ ), while the further addition of 4-AP increased the regularity of Purkinje cell firing ( $P = 0.0008$ ;  $N = 10$  Purkinje cells from  $N = 3$  SCA6<sup>84Q/84Q</sup> mice; paired Student's  $t$  test, Bonferroni corrected, significance level  $\alpha = 0.025$ ). (B) Synaptic blockade increased firing rate in 7-month-old SCA6<sup>84Q/84Q</sup> mice (grey markers,  $P < 0.0001$ ), which is not altered after the subsequent application of synaptic blocker cocktail + 4-AP (red markers,  $P = 0.14$ ). Paired Student's  $t$  test, Bonferroni corrected, significance level  $\alpha = 0.025$ . \*\*  $P < 0.001$ ; \*\*\*  $P < 0.0001$ .



**Supplementary Figure 2. 4-AP administration does not affect weight of mice.** Mice were weighed on alternating days as a means of assessing their health either with 4-AP in their drinking water or without. Weight was indistinguishable across genotype and condition at all days measured (WT with vehicle: unfilled circles, N = 11; WT + 4-AP: black circles, N = 11; SCA6<sup>84Q/84Q</sup> with vehicle: orange diamonds, N = 9; SCA6<sup>84Q/84Q</sup> + 4-AP: red diamonds, N = 9; ANOVA fit model,  $F_{27,330} = 0.7209$ ,  $P = 0.847$ ; not significantly different at 3 months, data not shown,  $P = 0.36$ ).