Supplementary Material 1

Supplementary Methods

Genotyping of mice

Approximately 1-2 mm of tail tip was clipped from each animal at P2-4. DNA was extracted by incubating each sample at 75°C for 5 minutes followed by 95°C for 10 minutes (deactivation step) with 20 µL 5X PCRBIO Rapid Extract Buffer A (1u/µL), 10 µL 10X PCRBIO Rapid Extract Buffer B (PCR Biosystems, USA) and 70 µL PCR grade water. The volume was then adjusted by adding 900 µL PCR grade water followed by centrifugation at 16000g for 1 minute. The supernatant containing mouse DNA was collected and kept at -20°C until use.

1 µL DNA sample solution was amplified in 20 µL PCR reaction mixture containing 0.4 µL each of: 25 µM forward primer (AGT CTG TAC CAG GCA GAA CTT G) and reverse primers (Rwt: CCC TGA GAT GTG GGT GAA TAG; Rmut: AGA CTG CCT TGG GAA AAG CG), 10 µL taq mix red (PCR Biosystems, USA) and 7.8 µL Rnase-free PCR grade water. The reaction condition included an activation step at 94°C for 2 minutes followed by 15 cycles of denaturation (94°C for 2 seconds), annealing (65°C for 15 seconds) and extension (68°C for 21 seconds); and another 15 cycles of denaturation (94°C for 15 seconds), annealing (60°C for 15 seconds) and extension (72°C for 21 seconds) which was followed by a final extension at 72°C for 2 minutes.

After the reaction was complete, samples (10 µL) were loaded in 2% agarose gel (stained with 2 µL Syber Safe DNA gel stain, Invitrogen, USA) in 1X TAE (Promega, USA) buffer and run for 2 minutes at 70V in a gel electrophoresis apparatus (BIORAD, USA). The gel was then observed under a UV transilluminator (Syngene, UK; Figure S1).

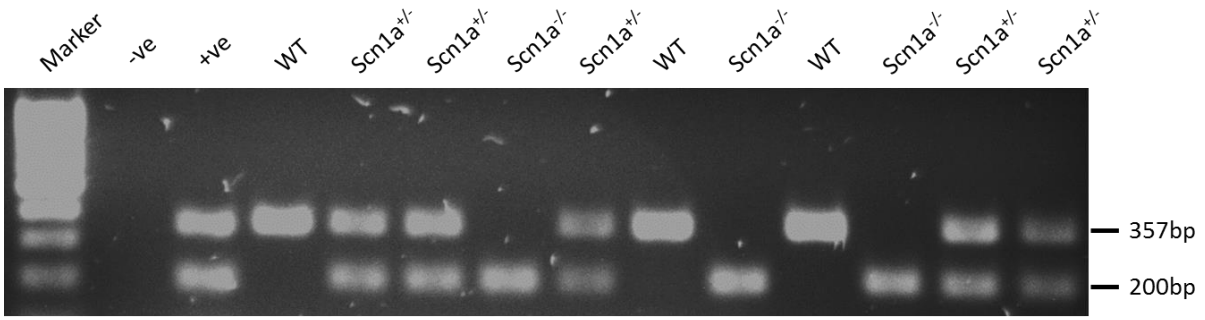

Figure S1. Example result from PCR used for genotyping animals produced via breeding of the 129S-*Scn1a*$^{tm1Kea/Mmjax}$ transgenic mouse line. Mouse tail DNA was amplified with primers for the *wild type* (*WT*) and mutated (*Scn1a*$^{-/-}$) *Scn1a* alleles. The presence of a 357bp band indicates the *WT* allele, and a 200bp band indicates the *Scn1a*$^{-/-}$ allele. -ve: negative control; +ve: positive control.

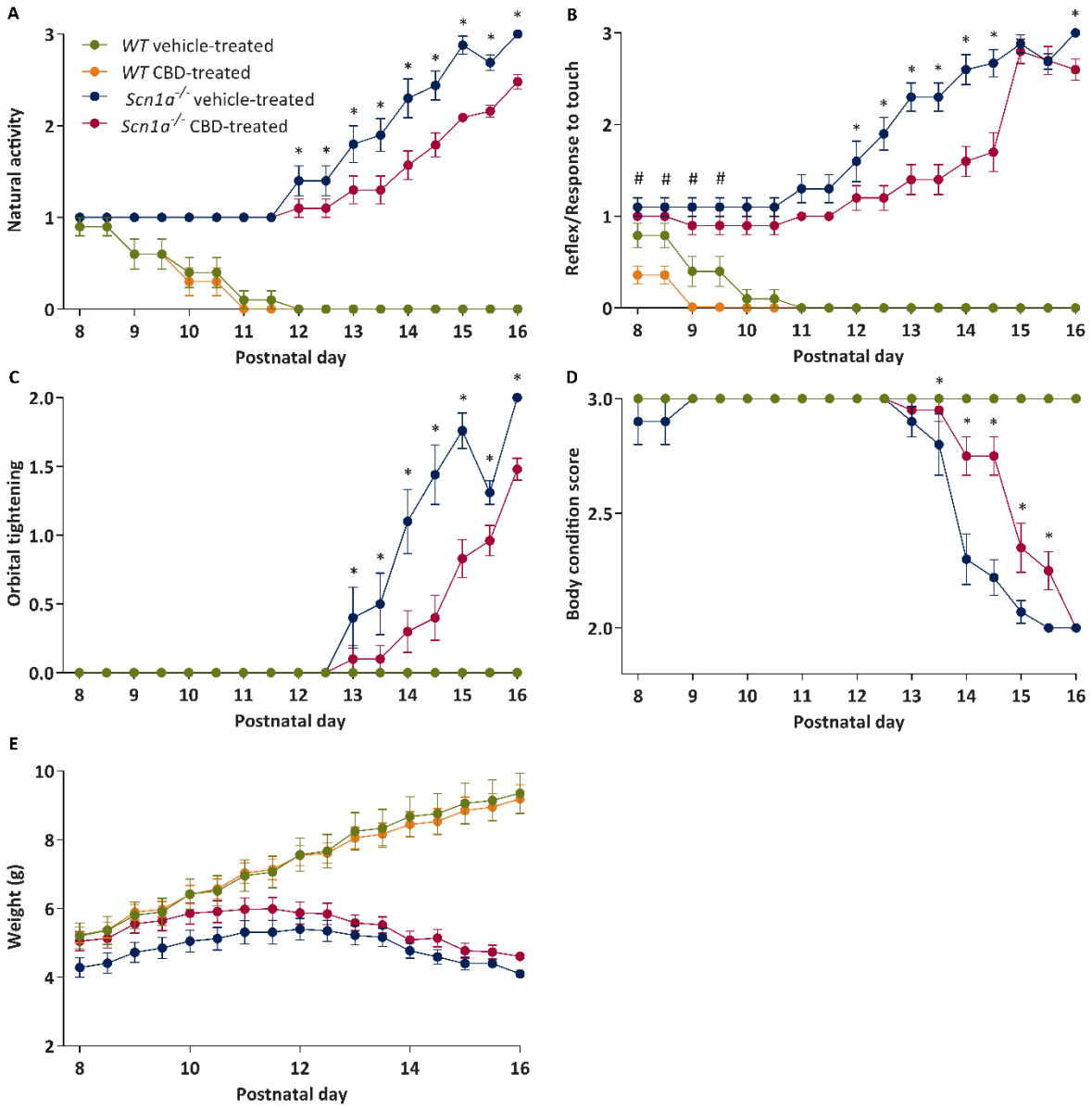

Figure S2. Plots showing chronic administration of CBD to wild type (*WT*) and *Scn1a*$^{-/-}$ mice on different welfare scores and weight change. **A**. Natural activity (NA) scores of *WT* vehicle-treated, *WT* CBD-treated, *Scn1a*$^{-/-}$ vehicle-treated and *Scn1a*$^{-/-}$ CBD-treated mice from postnatal day 8 (P8) onwards (n=10/group). CBD had no effect on NA score of *WT* mice. CBD significantly improved the NA score in *Scn1a*$^{-/-}$ mice from P12 onwards compared to the vehicle-treated *Scn1a*$^{-/-}$ mice. **B**. Reflex/response to touch (RT) scores. CBD significantly improved the RT score in *WT* mice from P8 to P9.5 compared to the vehicle-treated *WT* mice. CBD significantly improved the RT score in *Scn1a*$^{-/-}$ mice from P12 to P14.5 and on P16

compared to the vehicle-treated *Scn1a*$^{-/-}$ mice. **C.** Orbital tightening (OT) scores. CBD had no effect on OT score of *WT* mice. CBD significantly improved the OT score in *Scn1a*$^{-/-}$ mice from P13 onwards compared to the vehicle-treated *Scn1a*$^{-/-}$ mice. **D**. Body condition (BC) scores. CBD had no effect on BC score of *WT* mice. CBD significantly improved the BC score in *Scn1a*$^{-/-}$ mice from P13.5 to P15.15 compared to the vehicle-treated *Scn1a*$^{-/-}$ mice. **E.** Weight. CBD had no effect on weight in *WT* mice compared to the vehicle-treated *WT* mice. No three-way interaction of treatment×genotype×time was observed on weight. Data are expressed as mean ± SEM; data were analysed by a three-way ANOVA with Bonferroni's *post hoc* test; #$p<0.05$; *$p<0.05$; # represents *WT* vehicle-treated vs *WT* CBD-treated; * represents *Scn1a*$^{-/-}$ vehicle-treated vs *Scn1a*$^{-/-}$ CBD-treated.