Supplementary Material

Slice Recordings: Mice were deeply anesthetized with isoflurane and intracardially perfused with ice-cold high-sucrose solution that had been oxygenated with 95% O_2-5% CO_2. After removing the brain, it was immediately placed in the same oxygenated high-sucrose slice solution. Coronal brain slices from motor cortex (300 μm thick) were cut with a Vibratome (Leica VT1000S; Leica Microsystems, Buffalo Grove, IL) and transferred to an incubating chamber containing artificial cerebrospinal fluid (in mM): 130 NaCl, 3 KCl, 1.25 NaH_2PO_4, 26 $NaHCO_3$, 2 $MgCl_2$, 2 $CaCl_2$, and 10 glucose oxygenated with 95% O_2-5% CO_2 (pH 7.2-7.4, osmolality 290-310 mOsm, at 31±2ºC for 20 min), followed by exposure to room temperature. Recordings began after 1 h. CPNs from layer II/III and V were visualized using a 40x water-immersion lens on an Olympus microscope (BX50WI) equipped with infrared video microscopy (QICAM-IR Fast 1394; QImaging, Surrey, BC, Canada). Whole-cell patch clamp recordings from slices were obtained with a MultiClamp 700A amplifier (Molecular Devices, Sunnyvale, CA) and pClamp software (version 10.3). For voltage clamp recordings, patch pipettes (3-5 MΩ) were filled with a Cs-methanesulfonate-based internal solution containing (in mM): 130 Cs-methanesulfonate, 10 CsCl, 4 NaCl, 1 $MgCl_2$, 5 MgATP, 5 EGTA, 10 HEPES, 5 GTP, 10 phosphocreatine, and 0.1 leupeptin (pH 7.2 with CsOH, 270 mOsM). For current clamp recordings, a K-Gluconate-based internal solution was used (in mM): 112.5 K-gluconate, 4 NaCl, 17.5 KCl, 0.5 $CaCl_2$, 1 $MgCl_2$, 5 ATP, 1 NaGTP, 5 EGTA, 10 HEPES, pH 7.2 (270–280 mOsm). The patch pipette also contained biocytin (0.2%) for further morphological analysis of recorded cells.

Morphology: R6/2 mice and WT littermates (P60) were perfused and the brains stained for NeuN. Brains fixed with phosphate-buffered 4% paraformaldehyde were cryoprotected in 20% buffered sucrose and cryostat cut at 30 μm. The free-floating sections were processed for NeuN following the Mouse on Mouse (M.O.M.) Immunodetection Kit protocol (Vector Laboratories) and incubated in NeuN antisera (mouse anti-neuronal nuclei, Chemicon International, Temecula, CA, catalog number MAB377) at a 1:1000 dilution. Sections were further processed with a DAB substrate kit (Vector ABC Elite Mouse kit) and developed in 0.5 mg/ml 3,3'-diaminobenzidine tetrahydrochloride (DAB) and 0.01% hydrogen peroxide. The tissue was mounted on coated slides, dehydrated and cover slipped with DePeX mounting medium.