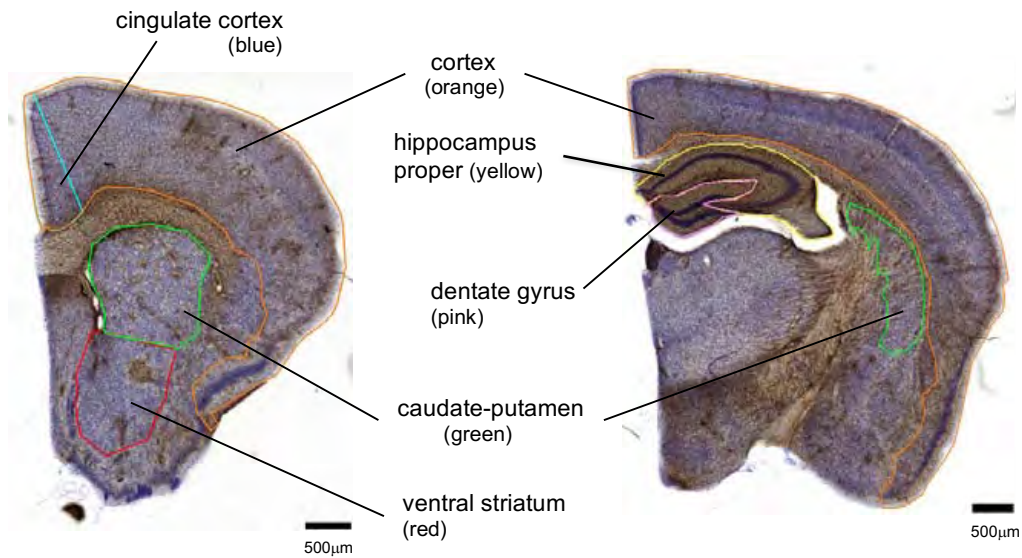


Figure S1: Definition of brain regional volumes and cortical thickness measurements

Analyses of brain regional volumes

Regional volumes were calculated from cerebrum (whole brain excluding the olfactory bulb, medulla, optic nerve and cerebellum), cortex, cingulate cortex, striatum (caudate putamen + ventral striatum), caudate-putamen, ventral striatum, hippocampus proper and dentate gyrus. The figure below indicates how these regions were delineated.



Analyses of cortical thickness

Cortical thickness measurements were taken perpendicularly to the pial surface (red line) at 3000 μm (yellow line), 6000 μm (green line) and 9000 μm (blue line) from the longitudinal fissure when all six cortical layers were present (from +1.6 mm to -4.6 mm from Bregma (see figure below)).

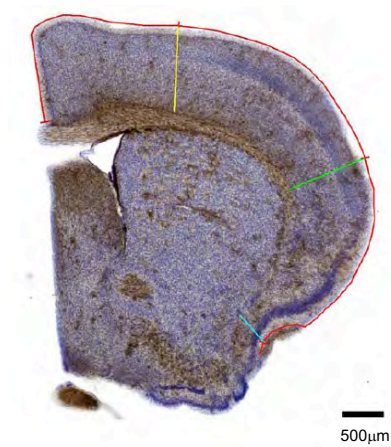


Figure S2: The effect of *Htt*^{Q111} genotype and diet on ferritin (A), GFAP (B), and NeuN (C) immunostaining.

A and B: Panels show delineation of ferritin-positive and GFAP-positive objects by CellProfiler 2.2.0. Left: inverted grayscale images (20x); middle: positive objects identified; right: overlay of positive objects with input image. Outlined in green are the positive objects included in the quantification; red outlines were omitted from the quantification. **C:** Representative images of the striata of 18- and 10-month mice immunostained with NeuN antibody (40x). Graphs for **A**, **B** and **C** show quantitative data from striata of 18-month *Htt*^{+/+} (N=5: 3 males, 2 females) and *Htt*^{Q111/+} (N=6: 3 males, 3 females) mice, and 10-month *Htt*^{+/+} and *Htt*^{Q111/+} mice fed either a medium fat diet (*Htt*^{Q111/+} N=6: 3 males, 3 females; *Htt*^{+/+} N=6: 3 males, 3 females) or high fat diet (*Htt*^{Q111/+} N=4: 2 males, 2 females; *Htt*^{+/+} N=6: 3 males, 3 females). Bars (mean \pm SD) show the number of ferritin-positive objects (A); the fraction of the striatal area occupied by GFAP-positive objects (B); the fraction of the striatal area occupied by NeuN-positive nuclei (C). Genotype (gt) p value in a 2-way ANOVA is shown.

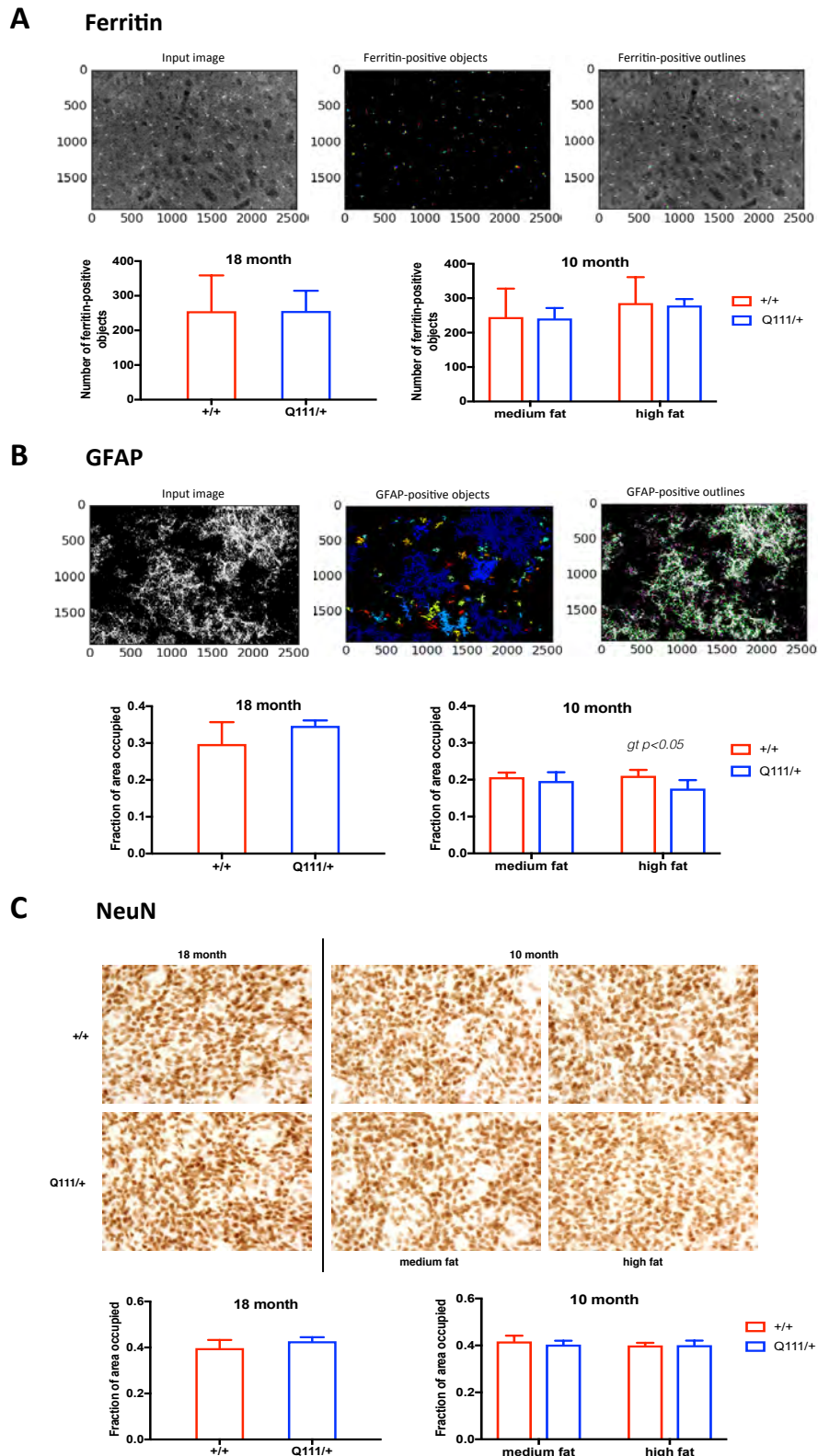


Figure S3: Brain regional volumes in 18-month *Htt*^{Q111/+} and *Htt*^{+/+} mice

Tukey box-and-whiskers plots showing brain regional volumes in 18-month *Htt*^{Q111/+} (N=6: 3 males, 3 females) and *Htt*^{+/+} mice (N=5: 3 males, 2 females). See Fig.S1 for the definition of these brain regions. 2-tailed unpaired Student's t-tests showed no significant differences in the volume of any brain region between *Htt*^{Q111/+} and *Htt*^{+/+} mice.

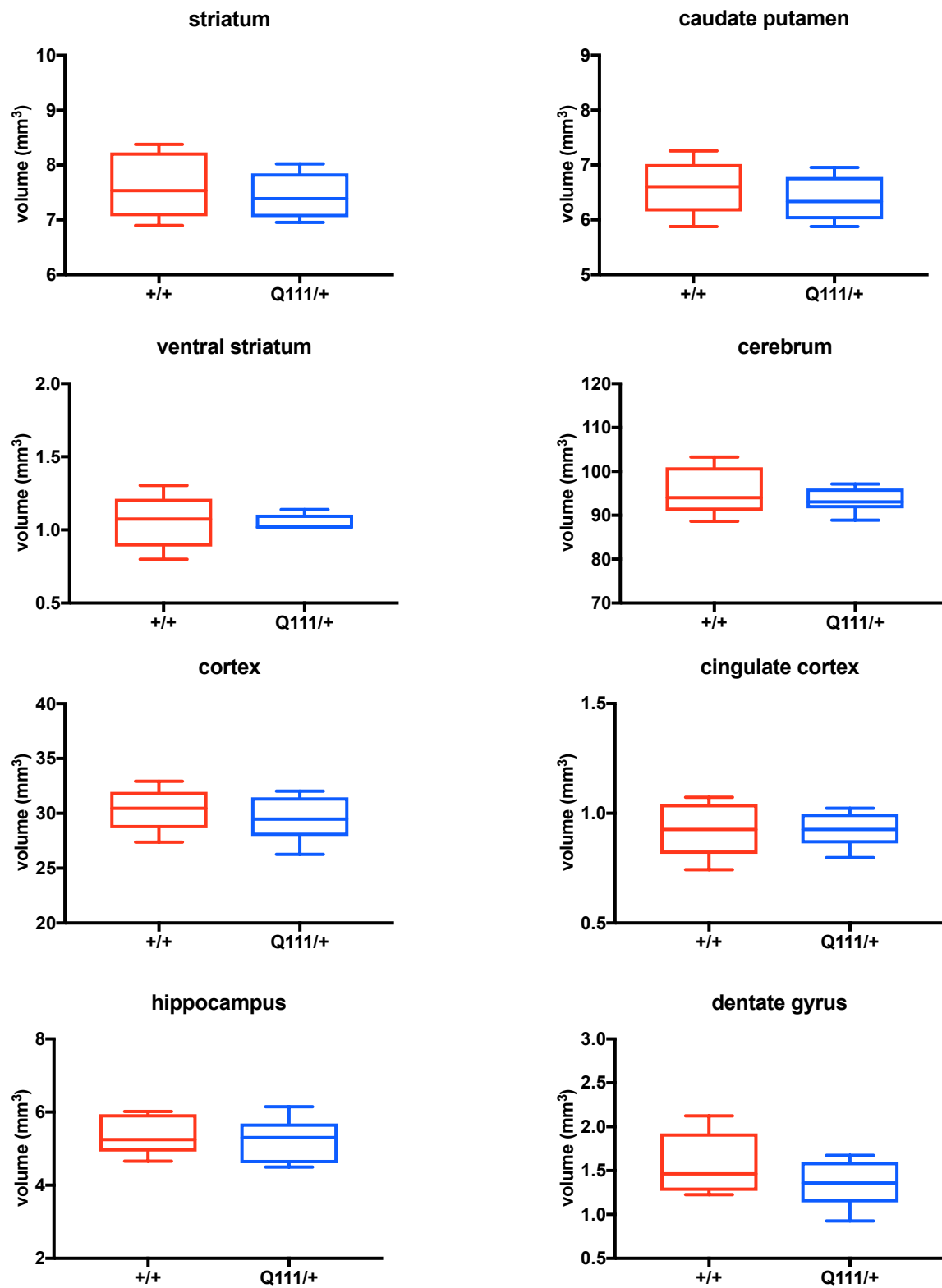


Figure S4: Cortical thickness measurements in 18-month *Htt^{Q111/+}* and *Htt^{+/+}* mice

Tukey box-and-whiskers plots showing examples of cortical thickness measurements taken at 3000 μm , 6000 μm and 9000 μm from the longitudinal fissure, and +1.6 to -3.8 mm from Bregma (Br) in 18-month *Htt^{Q111/+}* (N=6: 3 males, 3 females) and *Htt^{+/+}* (N=5: 3 males, 2 females) mice. Note that in some sections, measurements could not be accurately determined, resulting in a lower "N" at some locations.

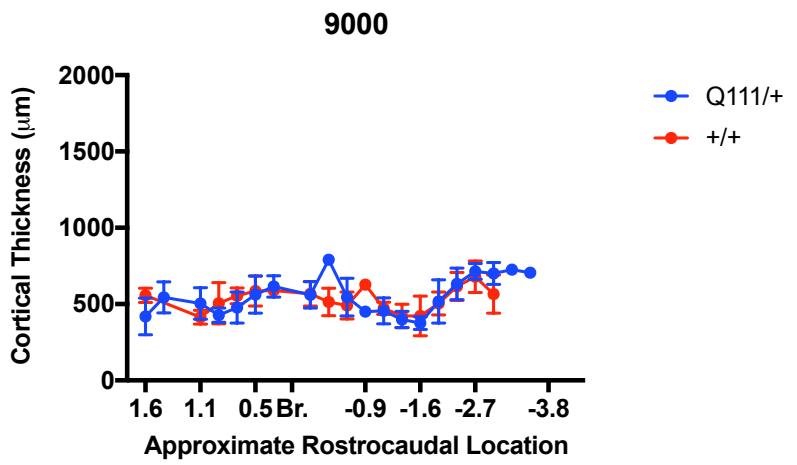
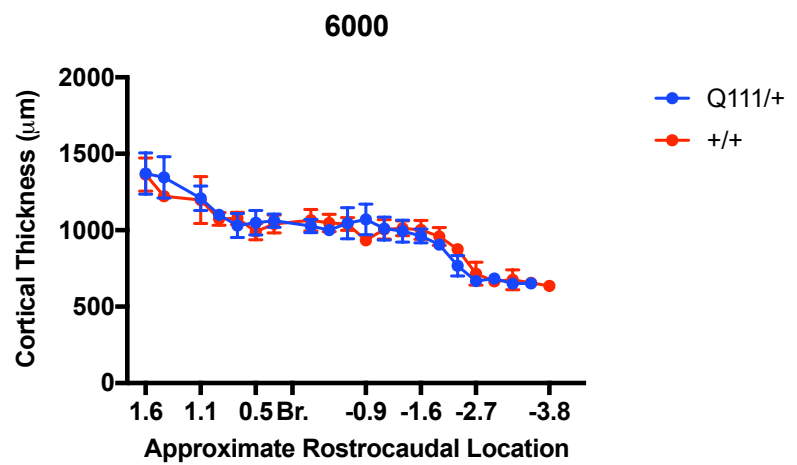
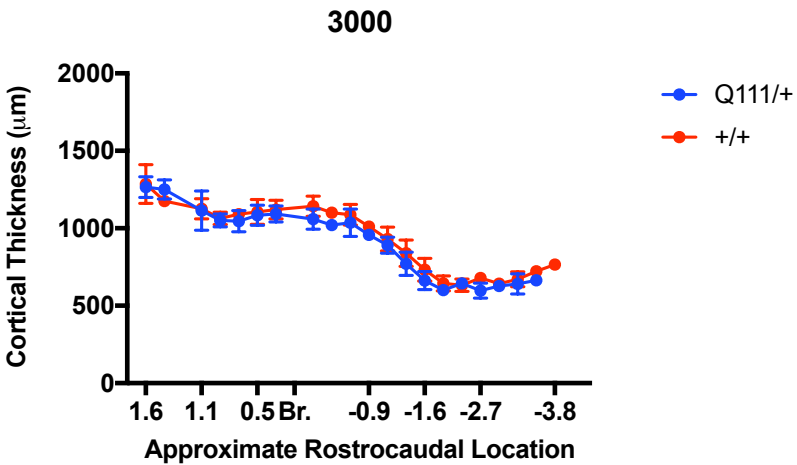


Figure S5: Cortical thickness measurements in 10-month *Htt^{Q111/+}* and WT mice on medium and high fat diets

Tukey box-and-whiskers plots showing cortical thickness measurements taken at 3000 μm , 6000 μm and 9000 μm from the longitudinal fissure, and +1.6 to -3.8 mm from Bregma (Br) in 10-month *Htt^{Q111/+}* mice fed either a medium fat diet (*Htt^{Q111/+}* N=6: 3 males, 3 females; *Htt^{+/+}* N=6: 3 males, 3 females) or high fat diet (*Htt^{Q111/+}* N=4: 2 males, 2 females; *Htt^{+/+}* N=6: 3 males, 3 females). Note that in some sections, measurements could not be accurately determined, resulting in a lower "N" at some locations.

