

Supplementary Figure Legends

Fig. S1: β -gal detection in $LRF^{-/-}$ adult brain sections shows a neuron-specific staining pattern.

(a) 50 μ m coronal sections of a $LRF^{-/-}$ mouse from rostral (i - olfactory bulb) to caudal (vi - cerebellum & brainstem) showing blue β -gal staining in areas dense in neuronal cell bodies. Error bar indicates 1mm. (b) Immunofluorescence staining of 50 μ m-thick adult hippocampal sections confirms the presence of β -gal protein (green) in CA1 and stratum radiatum (SR) of $LRF^{-/-}$ (right panel) but not WT (left panel) neuronal cells that express a neuronal-specific marker, MAP2 (red). Tissue sections were counter-stained with DAPI (blue). Scale bar indicates 50 μ m.

Fig. S2. Early growth measurements and adult weight analysis shows that mice lacking LRF are smaller in size than wild-type littermates. (a and b) $LRF^{+/+}$ (solid line with square), $LRF^{+/-}$ (dashed line with diamond), and $LRF^{-/-}$ (dotted line with triangle) were weighted daily for 21 days and then every second day for 4 more weeks. A repeated measures ANOVA on average weight gain over time was conducted. Sample sizes for $LRF^{+/+}$, $LRF^{+/-}$, and $LRF^{-/-}$ were 8, 11, and 20 respectively for males (a) and 13, 10, and 16 respectively for females (b). P values are indicated on graph. (c) Virgin adult mice weights at 24 weeks of age. A two-tailed t -test on average weight was conducted. Sample sizes for $LRF^{+/+}$, $LRF^{+/-}$, and $LRF^{-/-}$ were 22, 17, and 15 respectively for males and 12, 19, and 6 respectively for females. (“*” indicates $P<0.05$, and “***” indicates $P<0.001$). (d and e) Individual organs were weighed and graphed as proportion to total body weight. A two tailed t -test was used for statistical analysis. “*” indicates $P<0.05$. Sample sizes for $LRF^{+/+}$, $LRF^{+/-}$, and $LRF^{-/-}$ were 5, 4, and 4 respectively for males (d) and 7, 4 and 7 respectively for females (e).

Fig. S3: Tail suspension test for neurological impairment. **(a)** Photographic representation of hind limb clasping in $LRF^{-/-}$ mice compared to $LRF^{+/+}$ mice. **(b, c)** Tail suspension tests were conducted for male **(b)** and female **(c)** mice over the course of one minute. White bars indicate no clasping of the hind legs. Grey bars indicate clasping after 30 seconds of tail suspension, and black bars indicate clasping within the first 30 seconds of tail suspension. Sample sizes for $LRF^{+/+}$ (WT), $LRF^{+/-}$ (HET), and $LRF^{-/-}$ (KO) were 45, 52, and 33 respectively for males and 33, 61, and 21 respectively for females. (*) $P=0.0013$; (**) $P=0.0001$, (***) $P=8.41 \times 10^{-10}$ compared to $LRF^{+/+}$ in a Z test for proportions.