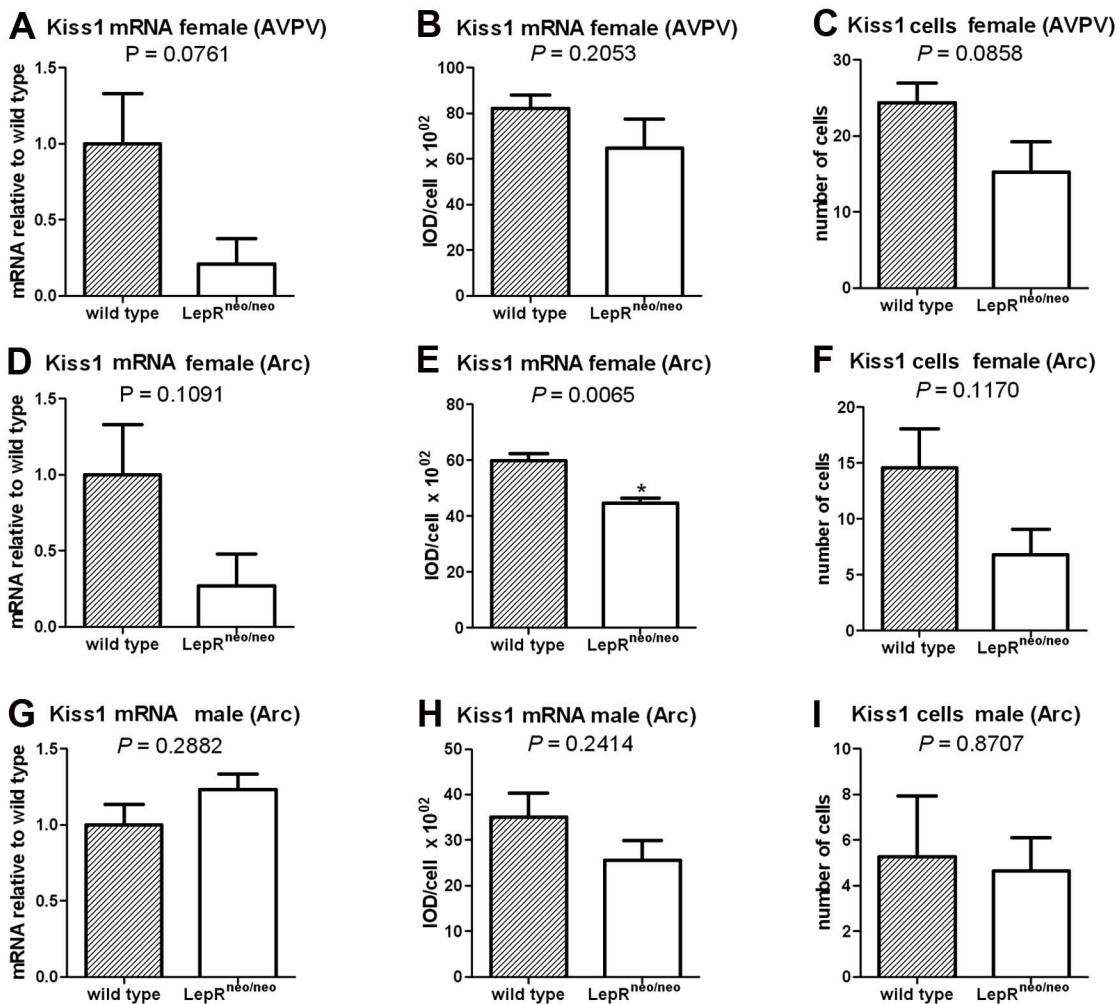


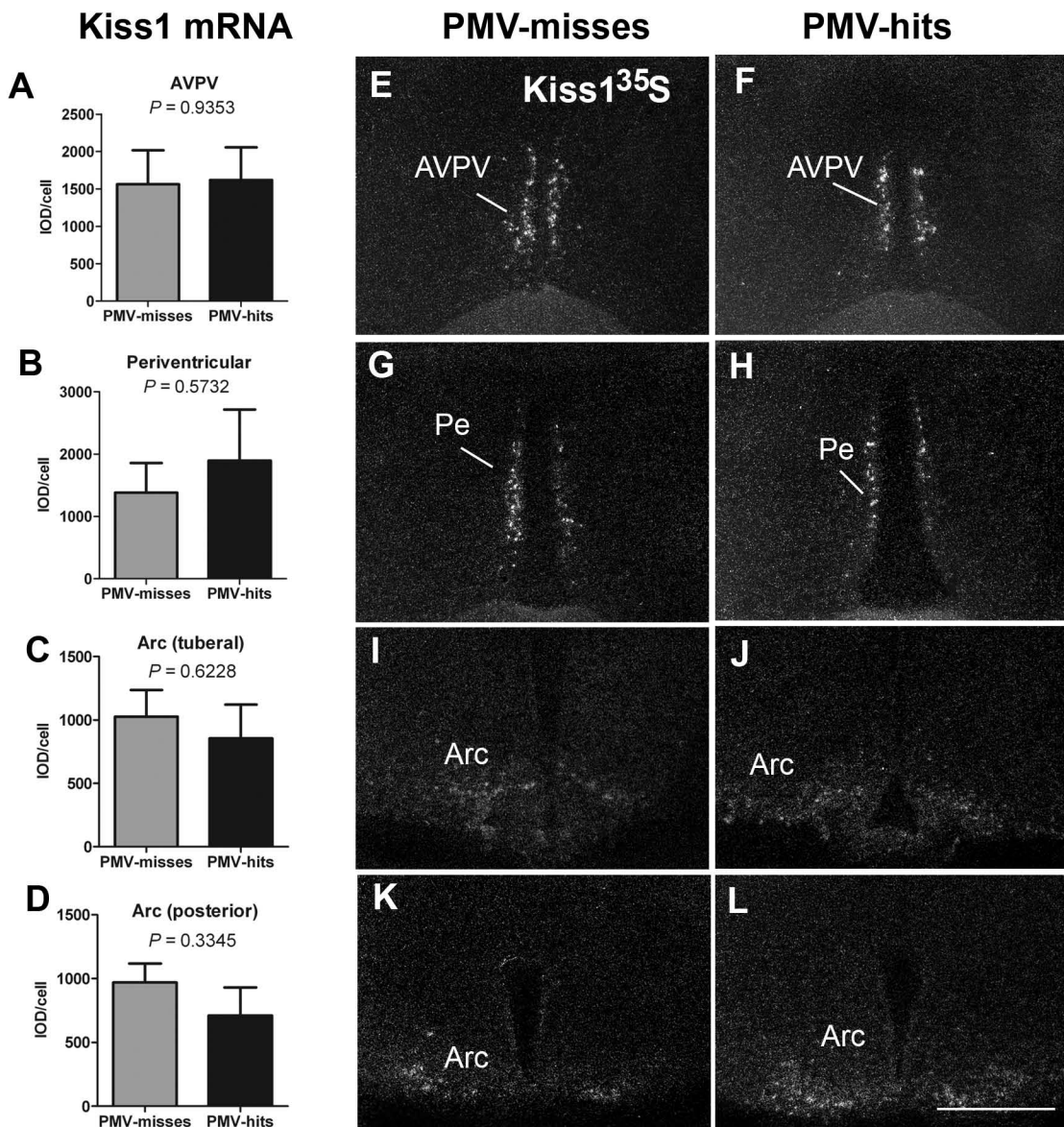
Supplementary Figure 1

Reactivation of LepRs in the PMV of LepR null male mice causes no changes in weight and morphology of reproductive organs. **A-B**, LepR^{neo/neo} male mice displayed an equivalent seminal vesicle (A) and testis (B) weight, compared to age-matched wild type mice. **C-D**, no changes were observed in seminal vesicle (C) and testis (D) weight comparing intact LepR^{neo/neo}, PMV-misses and PMV-hits. **E-G**, no difference was observed comparing testis cross-sectional area, number of seminiferous tubules and percentage of seminiferous tubules containing spermatids/sperm bundle. **H-J** brightfield photomicrographs showing sections of the testis from a wild type (H), a PMV-miss (I) and a PMV-hit. Seminiferous tubules showed a similar morphology comparing groups. They showed a clear lumen and apparent normal spermatogenesis and spermiogenesis. Virtually no significant occurrence of vacuolization or cell death was noticed. Leydig cells were apparently normal, with high cytoplasmic content suggestive of regular steroid production. Scale: 400 µm.



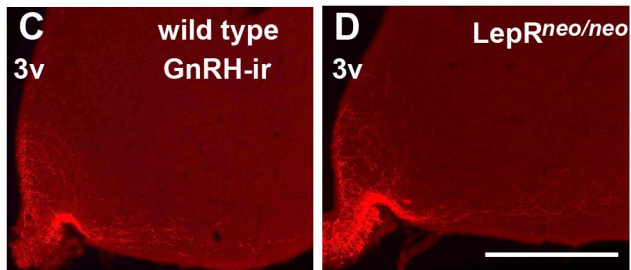
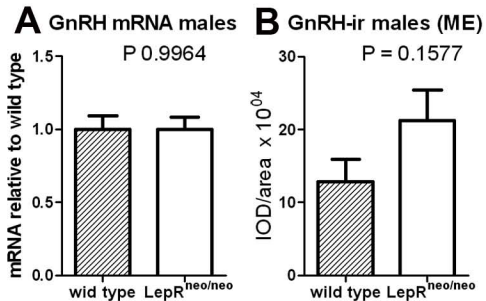
Supplementary Figure 2

Kiss1 gene expression in wild type and LepR null mice. Putative changes in Kiss1 gene expression was analyzed by quantitative real-time PCR (A, D, G), by quantification of the integrated optical density of Kiss1-positive cells after radiolabeled in situ hybridization (B, E, H), and by counting the number of Kiss1 expressing cells after radiolabeled in situ hybridization (C, F, I). **A-C**, LepR^{neo/neo} female mice show an apparent reduction, although not statistically significant, in the expression on Kiss1 mRNA in the anteroventral periventricular nucleus (AVPV) compared to wild type littermates. **D-F**, LepR^{neo/neo} female mice showed a reduction in the integrated optical density of individual Kiss1-positive cells in the arcuate nucleus (Arc) compared to wild type littermates. **G-I**, no changes in Kiss1 expression in the Arc was observed comparing male LepR^{neo/neo} and wild type littermates. * statistically different from wild-type mice.



Supplementary Figure 3

Reactivation of LepRs in the PMV of LepR *null* mice causes no change in *Kiss1* mRNA expression. **A-D**, bar graphs showing quantification of the integrated optical density of *Kiss1*-positive cells of PMV-hits ($n = 7$) and PMV-misses ($n = 6$). Analyses were performed in *Kiss1* neurons located in the anteroventral periventricular nucleus (E-F, AVPV), in the periventricular nucleus (G-H, Pe), and in two levels of the arcuate nucleus (Arc): tuberal (I-J) and posterior (K-L). Scale: 400 μ m.



Supplementary Figure 4

LepR *null* male mice show no difference in GnRH mRNA expression and GnRH immunoreactivity compared to wild type mice. **A-B**, male LepR^{neo/neo} and wild type mice display comparable expression of GnRH mRNA/cell and GnRH immunoreactivity (GnRH-ir) in the median eminence/mediobasal hypothalamus. **C-D**, fluorescent photomicrographs showing the similar pattern of GnRH-ir in the median eminence/mediobasal hypothalamus in male LepR^{neo/neo} and wild type mice. 3v, third ventricle. Scale: 400 μ m.