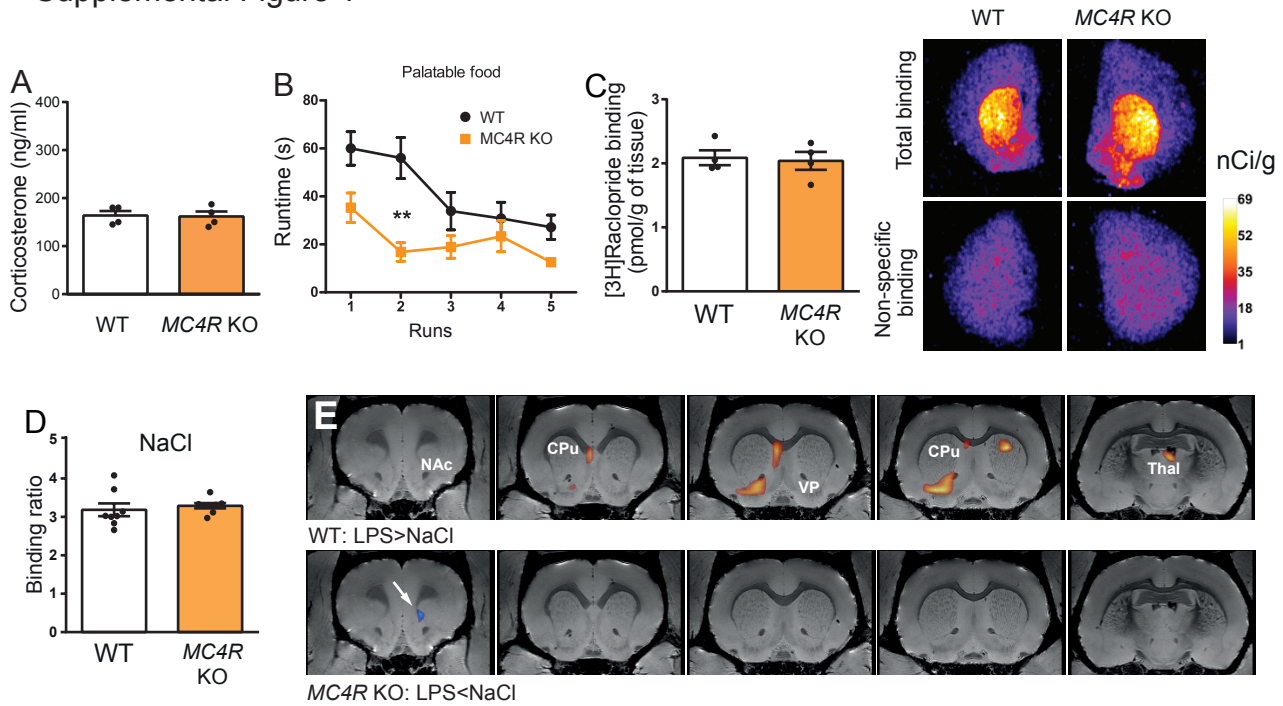


Supplemental Figure 1



**Supplemental Figure 1: Mice lacking MC4 receptors have an intact corticosterone response 2 hours after LPS, display normal reward-learning but have an inverted dopamine response to LPS.** (A), Mice with genetic deletion of MC4Rs, had an intact induction of HPA-axis as measured by blood corticosterone levels 2 hours post LPS i.p. compared to WT animals (n= 4, WT; 4, KO). (B), Mice lacking MC4Rs, were capable of learning an operant task to obtain Nutella as seen in the operant runway (n = 17, WT; 11, KO). (C) Ex vivo autoradiography assay with [3H]raclopride showed no difference in dopamine-receptor binding between WT and MC4R KO mice (n= 4, WT; 4, KO) (D) [11C]raclopride binding in WT and MC4R KO mice at baseline conditions (injected with NaCl). (E) WT animals had increased [11C]raclopride binding (orange labelling;  $p < 0.001$ ) in the dorsal and ventral striatum, lateral septum, ventral pallidum and medio-dorsal thalamic nucleus after LPS administration. No such increase was seen in MC4R KO mice. The MC4R KO mice instead displayed decreased [11C]raclopride binding (blue labelling;  $p < 0.001$ ) in a border-area between the ventral and dorsal striatum. The labeling is superimposed onto an MRI template. Results are displayed as mean  $\pm$  SEM. Statistical significance is illustrated as \*\*  $P < 0.01$ , ANOVA followed by Bonferroni's post hoc test.