

# PNAS

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Supplementary Information for

Chronic G<sub>q</sub> signaling in AgRP neurons does not cause obesity

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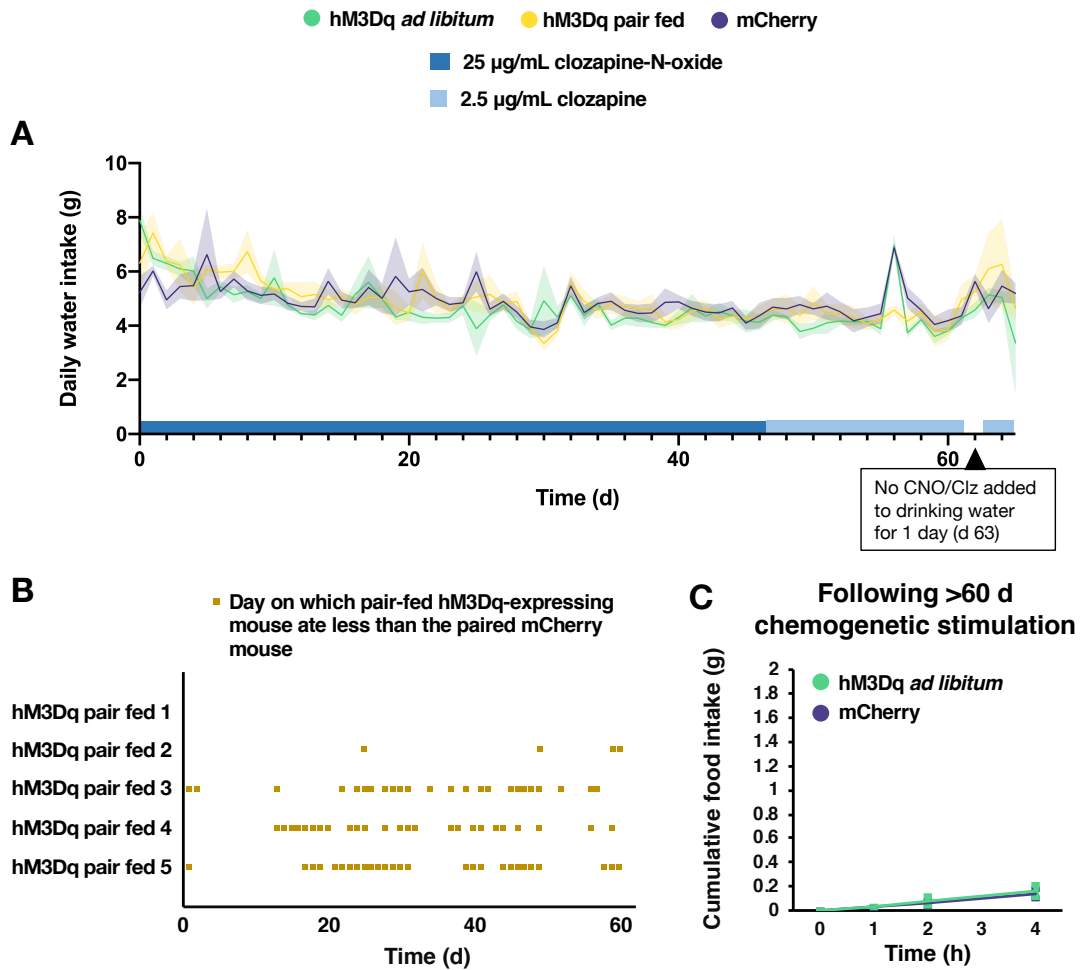
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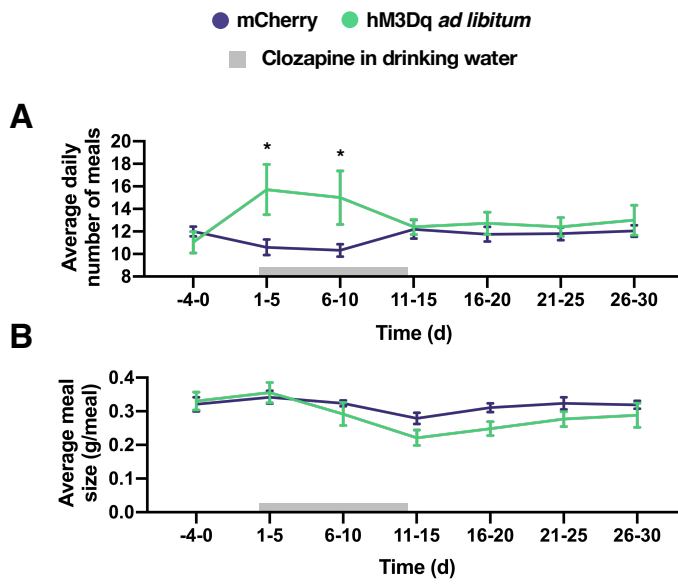
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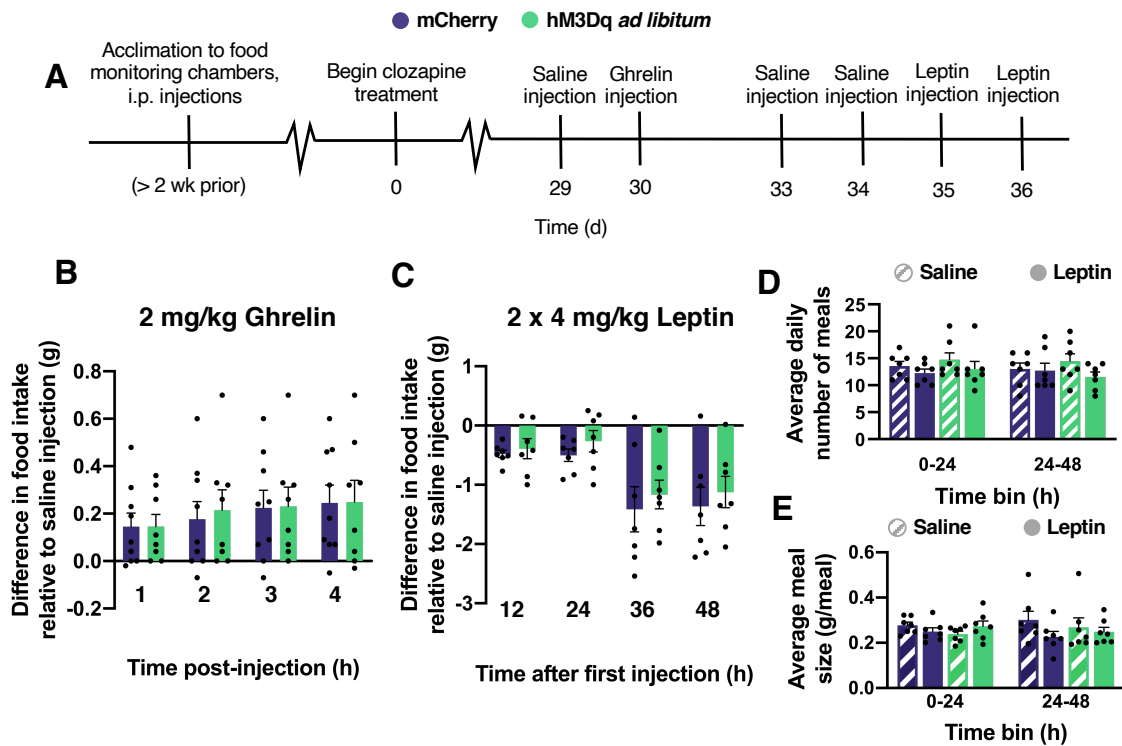
Figures S1 to S3



**Fig. S1.** Effects of chronic AgRP neuronal activation. (A) Daily water intake during CNO/Clz treatment (Mixed effects model: Time:  $F(7.967, 101.5)=6.305$ ,  $p<0.0001$ ; Group:  $F(2, 13)=0.439$ ,  $p=0.654$ ; Interaction:  $F(7.967, 101.5)=6.305$ ,  $p=0.052$ ). (B) Plot marking days on which individual pair-fed hM3Dq-expressing mice ate less food than the paired control mouse. (C) Food intake after CNO injection after >60 d CNO/Clz treatment.



**Fig. S2.** Chronic AgRP neuronal activation alters meal size. (A) Average daily number of meals prior to, during, and after 10 d Clz treatment, indicated by gray bar on abscissa (2-way ANOVA: Interaction:  $F(6,48) = 6.224$ ,  $p < 0.0001$ ; Time:  $F(6,48) = 1.196$ ,  $p = 0.325$ ; Group:  $F(1,8) = 1.485$ ,  $p = 0.258$ ; \* marks Sidak's multiple comparison significance). (B) Average meal size prior to, during, and after 10 d Clz treatment, indicated by gray bar on abscissa (2-way ANOVA: Interaction:  $F(6,48) = 3.216$ ,  $p = 0.0098$ ; Time:  $F(2.604, 20.83) = 13.85$ ,  $p < 0.0001$ ; Group:  $F(1,8) = 1.085$ ,  $p = 0.328$ ).



**Fig. S3.** Chronic  $G_q$  signaling in AgRP neurons does not alter leptin or ghrelin sensitivity. (A) Experimental design schematic. (B) Difference in cumulative food intake between ghrelin and saline injections (2-way ANOVA: Interaction:  $F(3,45)=0.1697$ ,  $p=0.9163$ ; Time:  $F(2,234,33.52)=4.224$ ,  $p=0.0198$ ; Group:  $F(1,15)=0.01465$ ,  $p=0.9053$ ). (C) Difference in cumulative food intake between leptin and saline injections (2-way ANOVA: Interaction:  $F(3,36)=0.119$ ,  $p=0.949$ ; Time:  $F(1.239,14.87)=19.28$ ,  $p=0.0003$ ; Group:  $F(1,12)=0.553$ ,  $p=0.472$ ). (D) Meal number after saline and leptin injections (2-way ANOVA: Interaction:  $F(9,96)=1.615$ ,  $p=0.1217$ ; Time:  $F(3,96)=198.5$ ,  $p<0.0001$ ; Group:  $F(3,96)=1.690$ ,  $p=0.174$ ). (E) Meal size after saline and leptin injections (2-way ANOVA: Interaction:  $F(3,48)=0.654$ ; Time:  $F(1,48)=0.006$ ,  $p=0.941$ ; Group:  $F(3,48)=1.389$ ,  $p=0.257$ ).