

Water intake increases GLP-1 gene expression in the nucleus of the solitary tract

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Introduction

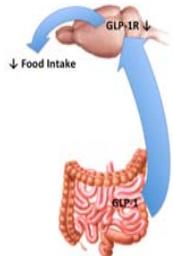
Glucagon-like peptide-1 (GLP-1) is produced in the intestine and brain. Drugs that target the GLP-1 system are used to treat diabetes and have shown some promise for the treatment of obesity. The GLP-1 system also appears to play an important role in fluid intake. It is unknown, however, if GLP-1 that is produced by the body is influenced during fluid intake or if the behavioral effects observed are artifacts of the administered drugs. We therefore tested if manipulations in fluid balance affected production of the GLP-1 precursor protein, proglucagon, or the GLP-1 receptor (GLP-1R). As a positive control, we measured proglucagon and GLP-1R in food deprived rats with or without access to food.

Methods

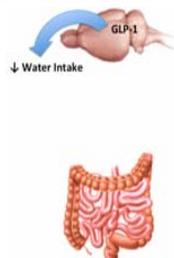
Subjects. Male, Sprague Dawley rats (325-349 g) were purchased from Harlan Laboratories (Indianapolis, IN). Rats were allowed to habituate to the colony for 1 week

Data analysis. Statistical testing was performed using Statistica (version 9.0, Statsoft, Tulsa, OK). Experiment 1 was analyzed by T-test, Experiment 2, 3, and 4 were analyzed by one-way ANOVA. Significant main or interaction effects ($p < 0.05$) were further analyzed using Newman-Keuls post hoc tests.

Food Intake and GLP-1



Water Intake and GLP-1



Experiment I

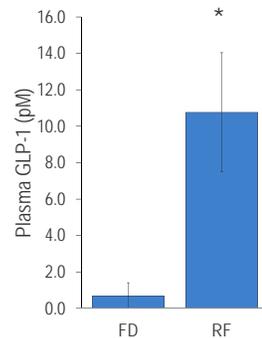


Figure 1. Effect of food intake on plasma GLP-1. Animals were food deprived for 24 hrs. After which, animals were returned food for periods of 0 and 30 min. Trunk blood was collected and analyzed by ELISA for GLP-1. Rats that ate had an increase of plasma GLP-1. * $p < 0.05$

Experiment II

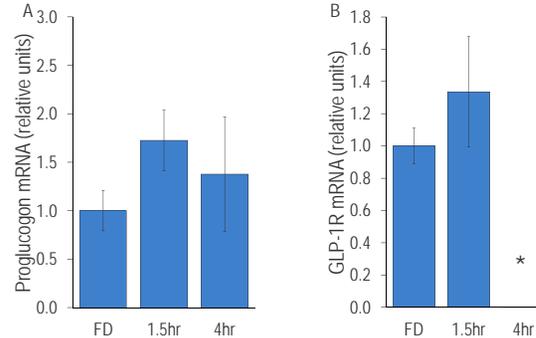


Figure 2. Effect of food intake on proglucagon mRNA and GLP-1. Animals were food deprived for 24 hrs. After which, animals were returned food for periods of 0, 1.5, and 4 hrs. Tissue was then collected from the nucleus of the solitary tract in the hindbrain. Collected tissue was then analyzed for proglucagon and GLP-1 receptor mRNA by quantitative PCR. (A) There was no effect between food deprived and re-fed rats on proglucagon mRNA. (B) Rats that were allowed to eat for 4 hrs had a decrease of GLP-1R mRNA. * $p < 0.05$

Experiment III

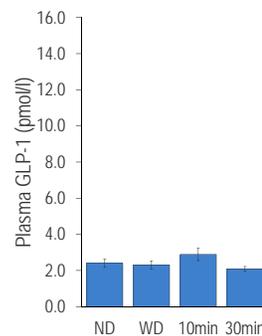


Figure 3. Effect of water intake on plasma GLP-1. Animals were water deprived for 24 hrs. After which, animals were returned water for periods of 0, 10, and 30 min. As a control, an additional group was never water deprived. Trunk blood was collected and analyzed by ELISA for GLP-1. There was no effect of water intake on plasma GLP-1.

Experiment IV

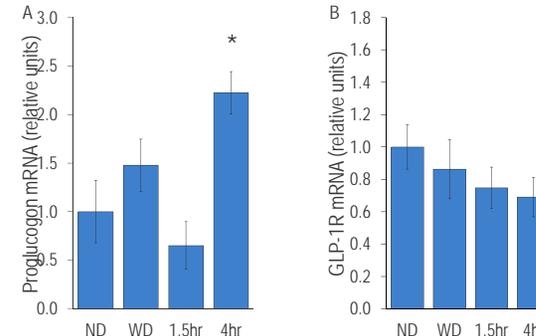


Figure 4. Effect of water intake on proglucagon mRNA and GLP-1. Animals were water deprived for 24 hrs. After which, animals were returned water for periods of 0, 1.5, and 4 hrs. As a control, an additional group was never water deprived. Tissue was collected from the nucleus of the solitary tract in the hindbrain. Collected tissue was then analyzed for proglucagon and GLP-1 receptor mRNA by quantitative polymerase chain reaction. (A) Rats that were allowed to drink for 4 hrs had an increase of proglucagon mRNA. * $p < 0.05$. (B) There was no effect of water intake on GLP-1R mRNA.

Summary and Conclusions

➤ Plasma content of GLP-1 of food deprived rats was significantly higher in re-fed than those continuously deprived rats

➤ Although there was no change in proglucagon mRNA in food deprived and re-fed rats, there was a significant decrease in GLP-1 receptor for rats who were re-fed for 4 hrs

➤ In contrast to the effect after food intake, there was no effect of water intake to plasma GLP-1

➤ Deprivation with subsequent intake caused a significant increase in proglucagon in the nucleus of the solitary tract for rats allowed to drink for 4 hrs

○ There was, however, no change in the GLP-1 receptor

➤ These data are the first to demonstrate a change in central GLP-1 after fluid intake

➤ There are key differences in the regulation of GLP-1 after food or water intake.

Acknowledgements

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