Gut-Brain Axis and Neuroendocrinology: Translation to Addiction Medicine

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The reward properties of natural and chemical reinforcers are mediated via multiple and complex pathways in the brain. There is an underlying disruption in reward processing in animal models of addiction and individuals with alcohol and substance use disorders (ASUD). This raises the possibility that endocrine signals from the gut traditionally known to regulate appetite and food intake may play an important role in reward regulation as well as in development of ASUD, therefore representing promising novel targets in medication development. Dr. Leggio on behalf of his research team and collaborators, will present recent translational data on systems related to the gut-brain axis and to neuroendocrine pathways. An example is the work on the stomach-derived hormone ghrelin in ASUD. Preliminary clinical studies indicate that there is a relationship between endogenous blood ghrelin levels, drinking status and craving for alcohol in patients with AUD. A double-blind placebo-controlled human laboratory study demonstrated that intravenous administration of exogenous ghrelin resulted in acute increase of cue-induced alcohol craving in a simulated bar-lab setting. More recently, another double-blind placebo-controlled human laboratory study indicated that intravenous administration of exogenous ghrelin results in increased alcohol self-administration and differentially modulates brain activity during alcohol versus food cues while patients are performing a fMRI-based reward task. Together, these findings suggest that blocking the ghrelin receptor may be a novel pharmacological approach to treat AUD. Specific to this discussion, two additional sets of data will be presented: 1) recent ongoing efforts toward the development of a novel ghrelin receptor knock-out rat model; and 2) recent human preliminary data testing a novel ghrelin receptor inverse agonist in individuals with AUD. In conclusion, this line of research supports additional efforts aimed to investigate whether the ghrelin system may represent a novel potential target for medication development for addictions.

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