Fibroblast Growth Factor 19 Alters Excitablilty in the Dorsal Motor Nucleus of the Vagus

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Abstracts will be considered for both poster and platform presentations

Neurophysiology

According to the CDC, there are more than 30 million Americans living with diabetes. Most diabetes research focuses on defects in insulin and glucose metabolism, but emerging evidence suggests that the brain plays an underappreciated role in systemic glucose regulation. One such homeostatic regulatory center is the brainstem dorsal vagal complex (DVC) which monitors metabolic status through both vagal afferent neural and humoral signals including glucose, insulin, and leptin. Parasympathetic motor neurons in the DVC respond to this information by altering vagal output to regulate pancreatic hormone release and hepatic glucose production. Fibroblast growth factor 19 (FGF19) has potent, insulin-independent antidiabetic effects when injected intracerebroventricularly, though the mechanisms of action are unknown. This information, together with the fact that FGF19's receptor/co-receptor combination is present in the DVC, suggests that this area is a prime candidate for the observed antidiabetic effects. Here, patch-clamp electrophysiology was used to measure the effects of FGF19 on action potential (AP) frequency and synaptic current sin vagal motor (i.e., DMV) neurons in brainstem slices from mice. Application of FGF19 (230 pM) either increased (33%), decreased (50%) or caused no change in AP firing in DMV neurons. The frequency of spontaneous synaptic currents was also altered, and FGF19 also caused significant outward or inward whole-cell currents in most DMV neurons. Evidence that FGF19 alters voltage-gated and rectifying potassium currents in DMV neurons is under investigation. These cellular effects are consistent with the hypothesis that FGF19 modifies parasympathetic output to the viscera and could contribute to the peptide's effects on metabolism. Studies aimed at understanding the anti-diabetic effects of FGF19 in the DVC are underway.