Secretin: classically a gut hormone, recently a neuropeptide, and now a pituitary hormone to regulate water homeostasis

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Secretin is the first hormone discovered, and has recently been shown to function also as a neuropeptide. In this lecture, I will provide evidences indicating its role to regulate body fluid homeostasis. Regulation of body fluid and solute concentrations is critical to recovery from intracellular and extracellular dehydration. In either case, both physiological and behavioral responses, including release of the antidiuretic hormone vasopressin (VP) to prevent further water loss in the kidney and the dipsogenic peptide angiotensin II (ANGII) to increase fluid intake, are essential for constant body fluid content maintenance. The role of secretin in renal water reabsorption have remained controversial until our recent data showing that secretin acts via a VP-independent mechanism to stimulate aquaporin water channel surface presentation and expression in kidney tubules. Regarding the source of secretin, we show secretin release from the posterior pituitary into circulation upon water deprivation or direct electrical stimulation of the PVN. In the hypothalamus, increased expressions of the secretin, its receptor, and VP genes are observed upon water deprivation. In addition, intracerebroventricular secretin injection revealed that secretin could stimulate VP expression in the hypothalamus and VP release into systemic circulation. Since secretin is an upstream stimulator of VP, it is possible that secretin also performs function in the lamina terminalis, the present study provides evidence revealing that secretin is a neuroactive peptide that exerts direct actions on VP expression and release, and the control of water drinking behavior in mice. More importantly, we show that the presence of a functional secretin and secretin receptor system is essential to mediating the osmoregulatory effects of ANGII, hence, secretin is potentially the missing link that connects ANGII with its effects in the central nervous system. Taken together, secretin functions at multiple levels to regulate water balance in our body.