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Control of Vasopressin Permeability across Blood Vessels by Proteases

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Summary

Systemic osmotic homeostasis is regulated mainly by neuroendocrine system of arginine-vasopressin (AVP) in mammalians. AVP is synthesized within the hypothalamic nuclei, transported into the neurohypophysis (NH) via axonal terminals, and released into blood circulation upon osmotic stimulation. In the present study, we investigated whether or not the serine proteases, tissue plasminogen activator and plasminogen, are responsible for AVP release and permeability in the NH. Confocal laser microscopic observation revealed that the immunoreactivity of tissue plasminogen activator (tPA) was seen specifically at neurosecretory granules of AVP-positive magnocellular terminals and that of plasminogen was seen at microvessels in the mouse NH. Electron microscopic immunohistochemistry further showed specific localization of tPA at neurosecretory granules of magnocellular terminals. tPA knockout (KO) mice but not plasminogen ones revealed lower ability in secreting AVP into the blood circulation upon an acute osmotic stimulation by using hypertonic 3% NaCl. The recombinant tPA was able to release AVP from isolated NH. Both tPA and plasminogen KO animals showed lower ability in secreting AVP into the blood circulation upon a chronic osmotic stimulation or water deprivation. Morphometric quantitative analysis demonstrated that chronic osmotic stimulation degraded laminin of neurohypophysial microvessels in WT mice but not in plasminogen KO ones. Laminin is known to be a critical modulator for vessel permeability of various substances. In conclusion, we suggest that AVP secretion is critically regulated by tPA- dependent receptor mediated processes of AVP release from terminals as rapid regulatory mechanism, and AVP permeability across blood vessels is regulated by plasminogen-dependent laminin degradation.