## MECHANISMS FOR REGULATION OF TOTAL BODY SALT CONTENTS BY SALT

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## Summary

The aim of this study was to define mechanisms for regulation of total body salt contents by salt. Salt intake causes an increase in body fluid and atrial pressure, resulting in secretion of atrial natriuretic peptide (ANP). ANP is now known to be a member of family of the natriuretic peptide system, since B-type (BNP) and C-type natriuretic peptide (CNP) have been isolated. ANP and its family may play role in regulation of total body salt contents by control of NaCl movement across the intestine as well as renal function, because the intestine is indispensable site for salt homeostasis as well as the kidney. Salt intake also causes an increase in Na concentration of portal vein, which elicits hepato-intestinal reflex and hepato-renal reflex.

Intravenous infusion of ANP (300ng/kg/min) suppressed net absorption of salt across the jejunum but not the ileum in the dog. Net absorption of salt across the jejunum was also suppressed by BNP and CNP. ANP and BNP augment natriuresis but not CNP. To define these functional differences of ANP family, we studied production of cyclic GMP ( $_{\rm C}$ GMP) at the jejunal, ileal, renal and femoral regions by infusion of ANP family. ANP produced  $_{\rm C}$ GMP at the jejunal region far greater than the ileal region. This difference in  $_{\rm C}$ GMP production may be the cause of the regional difference of ANP action. BNP and CNP did not produce  $_{\rm C}$ GMP at the jejunal region. Therefore, ANP suppresses jejunal absorption via the  $_{\rm C}$ GMP-producing receptors, and BNP and CNP may be via the non- $_{\rm C}$ GMP-producing receptors.

We studied the effect of intraportal infusion of 9%NaCl, 6.5%LiCl or 50 %glucose in a dose of 0.02ml/kg/min on net absorption of salt across the jejunum in dogs. NaCl infusion suppressed the absorption, but not LiCl and glucose. Thus, the Na receptors in the portal vein can be excited by an infusion of this amount of NaCl solution, but the osmoreceptors cannot be stimulated. The response was blocked by sectioning the hepatic nerves or by administration of atropine. Thus, an afferent limb of this reflex system is the hepatic nerves, and an efferent limb is the cholinergic nerve fibers.

Intraportal infusion of 9%NaCl, 6.5%LiCl or 50%glucose (0.15ml/kg/min) increased osmolality by 10.2mOsmol/kg and simultaneously suppressed renal nerve activity to 70% of control in rabbits. Intraportal infusion of 9%NaCl (0.04ml/kg/min) increased osmolality of portal venous blood by 3mOsmol/kg and plasma Na concentration (pNa) by 0.5meq/l and suppressed renal nerve activity (hepato-renal reflex). However, intraportal infusion of 6.5%LiCl and 50%glucose in the same dose as NaCl failed to suppress renal nerve activity. Thus, the Na receptors in the portal vein can be excited by an increase in pNa by 0.5meq/l but the osmoreceptors cannot be stimulated by an increase in osmolality by 3mOsmol/kg. Intraportal infusion of 9%NaCl (0.15ml/kg/min) stimulates both Na receptors and osmoreceptors. The threshold of the Na receptors is lower than the osmoreceptors. An afferent limb of the reflex is the hepatic nerves and an efferent limb is the renal nerves.

In conclusion, ANP secreted by salt intake suppresses jejunal salt absorption and augments natriuresis in a feedback fashion, and intraportal Na concentration increased by salt intake does in a feedforward fashion.