Effects of High NaCl and High KCl Diet on Hepatic Na⁺- and K⁺- Receptor Sensitivity
and Expression of NKCC1 in Rats

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Summary
We have demonstrated that Na⁺ and K⁺ receptors exist in the hepatoporal region plays an
important role in regulating body fluid homeostasis. These receptors sense Na⁺ and K⁺ concentration
via the bumetanide-sensitive Na⁺-K⁺-2Cl⁻ cotransporter (NKCC1) and transduce to electrical activity
of the hepatic nerve, and project to the nucleus solitary tract, area postrema, paraventricular
hypothalamic nucleus, and supraoptic nucleus. Then reflexively control renal excretory and intestinal
absorptive functions. It has been reported that high or low Na⁺ and high or low K⁺ diet affected the
expression of Na⁺ and K⁺ transporter in the intestine and kidney. These changes in expression might
contribute to regulating body fluid homeostasis by altering amounts of absorption and excretion.
Accordingly, there is a possibility that alternation of oral intake of Na⁺ or K⁺ alters NKCC1 expression
in the liver. To test this hypothesis, we investigated the effects of high NaCl and high KCl diet on
sensitivity of the hepatic Na⁺ and K⁺ receptor and the expression of NKCC1 in the liver of Sprague-
Dawley rat. The rats were randomly assigned to the 3 experimental groups and put on normal diet (Na⁺
0.3 %, K⁺ 0.8 %), high NaCl diet (Na⁺ 3 %, K⁺ 0.8 %), and high KCl diet (Na⁺ 0.3 %, K⁺ 8 %) for 4
weeks (from 7-weeks old to 11-weeks old). While measuring hepatic afferent nerve activity,
hypertonic NaCl solutions (0.375 M, 0.75 M, and 1.5 M) and isotonic KCl + NaCl solutions (25 mM
KCl + 125 mM NaCl, 50 mM KCl + 100 mM NaCl, and 100 mM KCl + 50 mM NaCl) were injected
as bolus doses of 0.1, 0.2, 0.5, and 1.0 ml/kg via the portal venous catheter. In response to injections,
hepatic afferent nerve activity increased in a Na⁺ or K⁺ concentration dependent manner. Under
intakes of high NaCl or high KCl diet for 4 weeks, the responses of hepatic afferent nerve activity
were significantly attenuated compared to those on normal diet. RT-PCR and Western blot were used
to measure the NKCC1 mRNA and protein expression, respectively. In both high NaCl and high KCl
diet groups, the level of NKCC1 mRNA expression was significantly lower than normal diet (1.13 ±
0.15 in normal diet, 0.67 ± 0.40 in high NaCl diet and 0.64 ± 0.11 in high KCl). Furthermore,
the expression of NKCC1 protein was also significantly depressed by high NaCl diet and KCl diet (2075 ±
202 in normal diet, 1016 ± 113 in high NaCl diet and 866 ± 209 in high KCl). These results suggest
that intakes of high NaCl or high KCl diet decrease the expression of NKCC1 in the liver and it may
cause the attenuation of hepatic Na⁺- and K⁺-receptor sensitivity.