57) Selective reduction of enhanced sodium appetite of SHR by chronic intracerebroventricular administration of α -human atrial natriuretic polypeptide (α -hANP). Hiroshi Itoh¹, Kazuwa Nakao^{1,2}, Goro Katsuura³, Narito Morii¹, Shozo Shiono¹, Makoto Sakamoto¹, Akira Sugawara¹, Takayuki Yamada¹, Yoshihiko Saito¹, Masami Eigyo³, Akira Matsushita³, and Hiroo Imura¹. 12nd Division, Department of Medicine, Kyoto University School of Medicine, 2Radioisotope Research Center, Kyoto University, Kyoto, 3Shionogi Research Laboratories, Osaka.

PURPOSE: Enhanced "need-free" sodium appetite of SHR has been reported and focused in the context of the contributory effect of excessive sodium intake to the development of hypertension. We have demonstrated that atrial natriuretic polypeptide (ANP) is widely distributed in the brain with the highest concentration in the hypothalamus and septum, the center of water and electrolyte balance and blood pressure control, by radioimmunoassay (1,2) and immunohistochemistry (2,3) and also reported the inhibitory effect of centrally administered ANP on water drinking induced by angiotensin II or water deprivation in rats (4). In this study, we have investigated the effect of centrally infused ANP on sodium appetite of SHR compared with WKY to elucidate the role of ANP as a neuropeptide. **PROCEDURE:** A free-choice, two-bottle preference test using 0.30 M NaCl solution and tap water was performed: intakes of 0.30 M NaCl solution, water and total fluid (0.30 M NaCl solution + water) were measured every day and preference rates for 0.30 M NaCl (the rate of 0.30 M NaCl solution to total fluid consumed) were calculated. Blood pressure was determined every two days by the tail cuff method. After 2-day control period, the intracerebroventricular (i.c.v.) infusion began and continued for 7 days. SHR were divided into three groups; group I (n=7) received isotonic saline as a vehicle, group II (n=9) received 100 ng/hr of α -hANP and group III (n=10) received 500 ng/hr of α -hANP, WKY were divided into two groups; group I (n=9) received saline and group II (n=7) received 500 ng/hr of α -hANP. **RESULTS:** In control period, SHR consumed significantly larger volume of hypertonic saline and total fluid and manifested a nearly seven-fold higher preference rate for 0.30 M NaCl compared with WKY. In SHR, chronic i.c.v. administration of α -hANP both with the dose of 100 ng/hr and 500 ng/hr suppressed intakes of 0.30 M NaCl and total fluid without any effect on water intake; cumulative intakes during the infusion of both group II and III were significantly suppressed compared with that of group I depicted on the table, and consequently preference rates for 0.30 M NaCl were significantly reduced from the corresponding control values in group II (39.9 $\pm$ 5.7% to 27.9 $\pm$ 2.7%, P<0.05) and group III (44.3 $\pm$ 5.7% to 29.9 $\pm$ 3.6%, P<0.025). In WKY, there were no effects of the infusion on the drinking behavior. Blood pressure was not altered either in SHR or in WKY during the infusion. **DISCUSSION:** These results reveal that chronic infusion of α -hANP preferentially reduces intake of hypertonic saline of SHR and decreases preference rate for 0.30 M NaCl. This selective attenuation of sodium appetite, along with our finding on the altered ANP level in the hypothalamus and septum in SHR (5), indicates the possible involvement of brain ANP in exaggerated sodium appetite of SHR and suggests the role of brain ANP as a body fluid and blood pressure modulating neuropeptide. **REFERENCES:** 1.Morii et al. BBRC 127:413,1985. 2.Kawata et al. Neuroscience in press,1985. 3. Kawata et al.Histochemistry83:1 1985. 4.Nakamura et al.Neurosci Lett 58:1,1985. 5.Morii et al. J. Hypertension in press, 1986.

Strain	Treatment group	No. of rats	Cumulative Intakes (ml/100g body weight) of		
			Water	0.30M NaCl solution	Total fluid
SHR	Group I (Saline)	7	46.0 $\pm$ 2.3	28.6 $\pm$ 4.1	74.6 $\pm$ 3.7
	Group II (α -hANP 100ng/hr)	9	43.9 $\pm$ 1.4	17.5 $\pm$ 2.2*	61.4 $\pm$ 2.2*
	Group III (α -hANP 500ng/hr)	10	43.4 $\pm$ 2.4	18.7 $\pm$ 2.4*	62.1 $\pm$ 2.7*
WKY	Group I (Saline)	9	58.0 $\pm$ 2.9	4.1 $\pm$ 1.2	62.1 $\pm$ 2.5
	Group II (α -hANP 500ng/hr)	7	58.0 $\pm$ 3.2	4.3 $\pm$ 1.6	62.3 $\pm$ 2.9

Values are the means $\pm$ S.E. of 7-day observation during the intracerebroventricular infusion (1 μ l/hr). Significantly different from saline-group: *P<0.05.