LC and A2 areas. Most neuronal populations in the spinal IML cells are sympathetic preganglionic neurons[26]. Among PNMT-containing neurons in 5 areas examined, we could not find any significant change in both young SHR and KWR. The results are in accordance with the recent report[27] indicating no change in adrenaline contents in A1 and A2 areas of young SHR, since the distribution of PNMT activity in the rat brain correlates with that of adrenaline[28]. However, the early report[29] describes a significant elevation of PNMT activity in the A1 and A2 areas of young SHR. The discrepancy might be explained by strain difference in the onset of hypertension caused by long inbreeding at various sources. Indeed our preliminary study indicates elevation of PNMT activity in the A1 cell area of adult SHR at 25 weeks of age. The present results give no direct evidence suggesting the participation of adrenergic neurons in the brainstem and spinal areas in the development of hypertension in SHR.

The observed activation of noradrenergic neuronal activity in the LC, A2 and IML areas may be related to activation of synaptic neurons in sympathetic ganglia[5] and of peripheral sympathetics[3-5]. Since activation of the peripheral sympathetic nervous system disappeared at adult SHR, causal relationship of both is still doubtful[6]. However, when one can consider labile hypertension as an early sign of essential hypertension[30,31], the activation of the peripheral sympathetic nervous system in young SHR cannot be excluded as one of the causal factors inducing hypertension. It is clear that in young SHR the selective activation of noradrenergic neurons in the LC, A2 and IML areas initiates the peripheral sympathetic nervous activation, as an early sign of hypertension. Adrenergic neurons in the brainstem were not involved in the development of hypertension nor in the activation of the peripheral sympathetic nervous system of young SHR.

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The effects on thermoregulation of intracerebroventricular injections of L-aspartic acid in the sheep

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Summary. L-Aspartic acid was injected into a lateral cerebral ventricle of the sheep at ambient temperatures between 0° and 40 °C. Doses of 100 or 500 nmoles · kg^{-1} caused a rise in heat production and/or a decrease in heat loss; rectal temperature rose. Atropine sulphate attenuated or prevented these effects.

We have recently reported[1] that the injection of L-glutamic acid into the cerebral ventricular system of the sheep produces regular changes in the thermoregulatory effectors which result in a rise in rectal temperature (T_{re}). In view of the accumulating evidence[2,3] that L-aspartic acid may be involved in central nervous transmission we have tested the effect of intracerebroventricular (ICV) injections of this substance in similar experiments. A total of 30 experiments were done on 12 adult castrated male Welsh Mountain sheep, each fitted with a cannula aseptically implanted into one lateral cerebral ventricle. At least 7 days were allowed after surgery before experiments were begun. These were conducted in a temperature-controlled chamber at 0°, 7°, 20° or 40 °C. A dose of 100 or 500 nmoles · kg^{-1} L-aspartic acid was injected through the cannula in a volume of 0.15 ml sterile, pyrogen-free 0.9% saline; the drug was washed in with a further injection of 0.25 ml saline. In some experiments an injection of 20 or 40 nmoles · kg^{-1} atropine sulphate (in 0.15 ml) was given 10 min before the L-aspartic acid.

Rectal temperature (T_{re}), respiratory frequency (RF) and the temperature of the skin of the ears and flank (indicative

of the degree of peripheral vasomotor tone) were monitored for 1 h before and 2 h after the injections. In some experiments oxygen consumption ($\dot{V}_{O_2}$) was also measured.

Results. The effect of L-aspartic acid was to evoke changes which increased heat production and conservation and decreased heat loss, and this caused a rise in T_{re}. This general pattern was consistently seen but the extent of the changes depended on the ambient temperature (T_a). At 0° and 7 °C T_a 500 nmoles · kg^{-1} L-aspartic acid exerted little effect on RF which was already low, or on skin blood vessels which were fully constricted but it produced an increase in heat production, signalled by a rise in oxygen consumption, and a rise in T_{re}. Following the injection of 500 nmoles · kg^{-1} at 20 °C T_a, RF fell, the ears vasoconstricted and T_{re} rose. $\dot{V}_{O_2}$ was not monitored. A dose of 100 nmoles · kg^{-1} produced similar effects at this T_a but the changes were smaller and short lived. At T_a 40 °C, RF was of the order of 240 breaths · min^{-1} but on injection of 500 nmoles · kg^{-1} L-aspartic acid it immediately fell to 30–50 breaths · min^{-1} This resulted in a steep rise in T_{re}. After 20–30 min, RF rose above the pre-injection rate and T_{re} declined towards the normal value. At any one T_a the intensity of the changes produced by 500 nmoles · kg^{-1} L-aspartate was very similar to those produced by an ICV injection of 800–1000 nmoles · kg^{-1} L-glutamic acid but the effects did not last as long. The changes produced by L-aspartic acid at T_a 7°, 20° and 40 °C were greatly attenuated by the prior injection of 20 nmoles · kg^{-1} atropine sulphate; a dose of 40 nmoles · kg^{-1} atropine sulphate (tested at 20° and 40 °C T_a only) almost completely abolished the action of 500 nmoles · kg^{-1} L-aspartic acid.

These results suggest that injected L-aspartic acid, like injected L-glutamic acid, exerts an effect on the hypothalamic pathways between cold sensors and heat production (and conservation) effectors. The fact that the effect of both amino acids is blocked by atropine sulphate may indicate that their site of action is at, or before, the postulated[4,5] cholinergic synapse on this pathway. Such an interpretation should, however, be accepted with caution since there is evidence that atropine can block amino acid receptors as well as muscarinic receptors[6]. Caution is also necessary in accepting these results as evidence of a physiological role of endogenous aspartic and glutamic acid in thermoregulation but they suggest such a possibility.

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Lipoprotein lipase activator deficiency in very low density lipoproteins in rat nephrotic syndrome

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Summary. Marked urinary loss of lipoprotein lipase activator in experimental rat nephrotic syndrome may be partly responsible for its deficiency in plasma very low density lipoproteins.

Normally, circulating triglycerides which are primarily transported in the very low density lipoproteins (VLDL) are metabolized to glycerol and fatty acids by 2 important processes. These are a) an enzyme system of lipoprotein lipases (LPL) and b) a group of apolipoproteins which are constituents of the protein moiety of VLDL. The C apolipoproteins play a major role in the activity of LPL with apolipoprotein CII (apoCII) as the principal activator peptide. C apolipoproteins are transported in high density lipoproteins (HDL) and VLDL. VLDL contain B and C apolipoproteins. C apolipoproteins disassociate from VLDL during their catabolism, are transferred to HDL, and the VLDL is converted at least in part to the B apoprotein containing low density lipoproteins (LDL)[2]. HDL acts as a 'reservoir' of apoCII activator peptide[3]. Exogenous and endogenous hypertriglyceridemia is associated with redistribution of apoCII from HDL to chylomicrons[3] and VLDL[4]. The long half life (8–10 h) of C peptides compared to the relatively short half life of B apoprotein of VLDL (10 min) suggests that C peptides cycle between HDL and VLDL and chylomicrons[5,6].

We have previously studied an experimental rat model of hyperlipoproteinemia[7]. In these rats, the nephrotic syndrome (proteinuria, edema and hyperlipoproteinemia) was induced with a single injection of puromycin aminonucleoside. The model disease in rats mimics the disease in humans in that severe atherosclerosis occurs in association with the hyperlipoproteinemia[8,9]. In these nephrotic rats we have shown a) urinary loss of HDL, b) activation of LPL in vitro with hydrolysis of triolein to fatty acids and glycerol and c) an alteration in the composition of urinary HDL compared to its composition in the plasma. Based on these observations we have hypothesized that urinary loss of HDL and activator peptides in the nephrotic syndrome may be associated with an inadequate supply of activator for newly formed VLDL[7]. In order to test this hypothesis the following experiment was performed in which were included measurements of plasma VLDL activator activity and urinary loss of LPL activator in the puromycin aminonucleoside nephrotic syndrome rat model.

Materials and methods. 14 Sprague-Dawley rats, 240–280 g in weight were used. In 7 rats nephrotic syndrome was induced with a single jugular vein injection (under ether anesthesia) of the aminonucleoside of puromycin 6-dimethylamino-9 (3-amino 3′-deoxy-D-B-ribofuranosyl-purine), 10 mg/100 g rat weight as described previously[7]. 7 control rats were given a single jugular vein injection of saline. The rats were placed in metabolic cages. 7 days after injection, the rats were fasted except for water and urine was collected over 17 h. Blood samples in EDTA (1 mg/ml) were obtained by intracardiac puncture and plasma separated at 4 °C by centrifugation. The urine and plasma from each group of 7 rats were separately pooled so as to obtain sufficient material for analysis.

VLDL was isolated from plasma by ultracentrifugation using a L5-50 Beckman ultracentrifuge and a 40.3 rotor for 22 h[10]. The supernate from the 1st ultracentrifugation was layered with 0.15 M sodium chloride in 0.01 M EDTA and respun again for 22 h. VLDL protein[11], total plasma cholesterol and triglycerides, were quantitated using Lipid