view of the similarity of these strains with respect to salt sensitivity, baroreceptor function and cardiac catecholamine turnover[9].

The mechanism for the impaired handling of an acute salt load by SBH rats remains to be clarified. Differences in GFR during acute volume expansion are unlikely, as renal function of SBH and SBN rats is comparable under steady state conditions (in preparation). Other proposed mechanisms for sodium retention by SBH are increased proximal tubular reabsorption mediated by activation of alpha adrenergic receptors[10], increased fractional reabsorption along the thick ascending limb of the loop of Henle mediated by ADH[11] or prostaglandin[12] and increased distal tubular sodium reabsorption[13].

The significance of the impaired response to acute saline loading in the Sabra hypertension-prone rats remains unknown. Future attempts to elucidate the mechanism of this phenomenon may shed more light on its relevance to the development of hypertension.

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Regional distribution of thiamin pyrophosphokinase in rat brain

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Summary. The highest specific activity of thiamin pyrophosphokinase was found in the cerebellum, and lower activity in cerebral cortex and midbrain. The regional difference in the enzyme activity was similar to that in thiamin content and the influx rate in rat brain, suggesting that the enzyme is involved in the thiamin transport.
Key words. Thiamin; thiamin pyrophosphokinase; cerebellum.

Thiamin pyrophosphokinase is an enzyme responsible for synthesis of thiamin pyrophosphate which acts as a coenzyme, and the brain enzyme has been purified from rat[1,2] and pig[3-5]. It is thought to be involved in membrane transport of thiamin in brain[6] and in intestine[7,8], though some studies[9-11] are against this idea. Rindi et al.[12,13] have recently reported that there is a significant difference in total thiamin content and the turnover rate among various regions of rat brain. In this paper, we determined the activity of thiamin pyrophosphokinase in different regions of rat brain in order to speculate about the possible involvement of the enzyme in the transport of thiamin in brain.

Materials and methods. Sprague-Dawley rats weighing about 250 g were decapitated and the brains were dissected according to the method of Glowinski and Iversen[14]. The tissue was homogenized in 10 volumes of 0.02 M Tris-HCl (pH 7.4)/2 mM 2-mercaptoethanol/1 mM EDTA and the homogenate was centrifuged at 100,000 × g for 1 h. The supernatant was used as the enzyme source. Thiamin pyrophosphokinase activity was determined by the method of Deus[15] with minor modification as follows. 1) 0.1 M Tris-HCl buffer (pH 7.5) was used instead of 0.1 M glycylglycine buffer (pH 7.3). 2) After the reaction, thiamin and thiamin pyrophosphate were separated by paper electrophoresis as described previously[16]. Under the conditions used, the activity was linear with respect to protein concentration and reaction time. Protein was determined by the method of Lowry et al.[17].

Results and discussion. The specific activity of thiamin pyrophosphokinase in different regions of rat brain is shown in the table. The highest activity was observed in the cerebellum, and lower activity in midbrain and cerebral cortex. The finding correlates well with the in vivo analysis of thiamin metabolism of rat brain reported by Rindi et al.[12,13]. They[12] demonstrated that there were differences in total thiamin content and the influx fractional rate constant among the regions of rat brain: the order of total thiamin content was cerebellum > striatum, pons, midbrain, medulla and hypothalamus > cerebral cortex > spinal cord, and that of the influx fractional rate constant was cerebellum > hypothalamus, pons and medulla > striatum, spinal cord and midbrain > cerebral cortex. Furthermore, they[13] have more recently found that rat cerebellum exhibits the highest level of thiamin pyrophosphate and the shortest turnover time for thiamin pyrophosphate. On the whole, the regional distribution of thiamin pyrophosphokinase activitiy described here is similar to that of total thiamin content and the influx rate constant. These

Thiamin pyrophosphokinase activity in different regions of rat brain

Regions	Thiamin pyrophosphokinase activity (nmol/mg protein/h)
Cerebellum	2.00 ± 0.06 (9)
Striatum	1.42 ± 0.19 (4)
Medulla oblongata	1.27 ± 0.09 (4)
Spinal cord	1.26 ± 0.17 (4)
Hippocampus	0.93 ± 0.19 (4)
Hypothalamus	0.87 ± 0.06 (4)
Cerebral cortex	0.79 ± 0.06 (9)
Midbrain	0.71 ± 0.11 (4)

Each value is mean ± SEM of the number of experiments shown in brackets.

observations suggest that thiamin pyrophosphokinase activity is responsible for the regional distribution of thiamin content, thiamin influx and thiamin pyrophosphate turnover in rat brain. In relation to the thiamin transport, our preliminary experiments showed that thiamin uptake into rat brain synaptosomes was inhibited by pyrithiamin, an inhibitor of thiamin pyrophosphokinase, and it did not show a saturability with respect to external thiamin concentration (data not shown). Furthermore, the thiamin uptake into cerebellar synaptosomes was higher than that into cortical synaptosomes (data not shown). These findings suggest that the thiamin uptake occurs by a facilitated diffusion in which thiamin pyrophosphokinase activity is involved. In view of the recent finding[18] that a thiamin pyrophosphate binding protein is present in the soluble fraction, the possibility is that a soluble thiamin binding protein might exist as a carrier for thiamin transport and its complex with thiamin would be the actual substrate for the thiamin pyrophosphate synthesis. If so, thiamin pyrophosphokinase activity would be directly coupled to the transport system for thiamin. Obviously further studies are required.

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α-Particle track autoradiographic study of the distribution of a [^{211}At]-astatinated drug in normal tissues of the mouse

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Summary. The microscopic distribution of the potential endoradiotherapeutic drug, 6-[^{211}At]-astato-2-methyl-1,4-naphthoquinol bis (diphosphate salt) in normal tissues of the mouse has been studied by α-particle track autoradiography. The uptake into critical radiosensitive tissues, especially bone marrow, colon and lung, was low.
Key words. Mouse; endoradiotherapy; α-particle track autoradiography; 6-[^{211}At]-astato-2-methyl-1,4-naphthoquinol bis (diphosphate salt).

This is an account of an autoradiographic study of the distribution of the potential α-emitting endoradiotherapeutic drug, 6-[^{211}At]-astato-2-methyl-1,4-naphthoquinol bis (diphosphate salt), abbreviated 6-[^{211}At]-astato-MNDP (fig. 1), in normal tissues of the mouse. Preliminary results of this development for experiments in mice with a transplanted chemically induced adenocarcinoma of the rectum are described[2]. Since then, the results of therapeutic experiments in mice have been reported[3-5].

Materials and methods. Astatine is the highest member of Group VIIB in the Periodic Table. It has only radioactive isotopes and the most suitable of these, $^{211}_{85}$At, has a radioactive half-life 7.21 h. The ranges of the α-particles of ^{211}At in unit density tissue are either 55 μm corresponding to energy 5.87 MeV for 42% of the disintegrations or 80 μm corresponding to energy 7.45 MeV for approximately 58% of the disintegrations. ^{211}At was prepared by the nuclear reaction ^{209}Bi(α, 2n) ^{211}At in the Nuffield 1.52 m cyclotron at Birmingham University, U.K., using a 28 MeV external α-particle beam. The compound 6-[^{211}At]-astato-MNDP was synthesized initially via a chloromercuri-intermediary[6] but more recently by an in vacuo heterogeneous isotopic exchange process with 6-iodo-MNDP[7]. The final astatinated product was purified by ion-exchange chromatography; 6-[^{211}At]-astato-MNDP was not carrier-free; its specific activity was approximately 50 μCi/mmole (6-iodo-MNDP). The resulting solution of 6-[^{211}At]-astato-MNDP was buffered to pH 7.4 and then sterilized by membrane filtration (Millipore 0.22 μm) for injection. Dose aliquots were determined by measurement of the 77–92 keV ^{211}Po K (K-L, M, N) X-rays using a 2 in NaI (TL) well crystal.

Male C57BL mice, of weight 25–30 g, bearing a single 0.5–0.8 g transplanted CMT-93 rectal adenocarcinoma[8] in the flank, were used in this study. 1 h prior to the injection of 6-[^{211}At]-astato-MNDP, mice received a s.c. injection of potassium perchlorate (10 mg kg^{-1}) in order to block thyroid function, and so prevent the uptake of any free ^{211}At. Animals received a single i.p. injec-

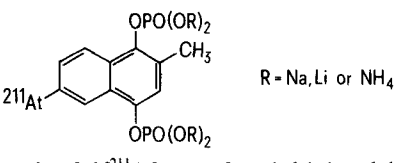

Figure 1. Formula of 6-[^{211}At]-astato-2-methyl-1,4-naphthoquinol bis (diphosphate salt), abbreviated 6-[^{211}At]-astato-MNDP.