are vast numbers of SA-residues present in the nervous system, estimated at 10^{11} per cell[19]. Good evidence for receptor action of sialocompounds has been presented for such bacterial toxins as tetanus and botulinum[20] and for lactins, viruses, mycoplasma, some hormones, and antibodies[21]. SA may also be involved in cationic binding of calcium, with an associated influence on neurotransmitter release and uptake[22].

Since DR a major constituent of DNA, the elevated DR-level in cerebellum would suggest a corresponding concentration of DNA in the cerebellum. The cerebellum contains exceptionally large amounts of DNA in the rat, rabbit and cat, with the amount exceeding that in the cerebral cortex by a ratio of more than 6 to 1[23]. This large amount is attributed to the extreme cell density of the cerebellar granular layer. Our research on rats is to our knowledge the first demonstration of genetic differences in brain SA and DR; such differences for SA confirm the speculation many years ago[24] that SA should be readily affected by genetic variables because gangliosides have a high degree of individual character, including the number of SA-residues. In subsequent research, we have replicated the differential distribution of both SA and DR in Wistar rats[25]. Moreover, the steady state concentration of both substances seems to be highly responsive to experimental variables; we have demonstrated significant effects of age and/or experience, and effects of both acute and chronic administration of ethanol[25].

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Thermoregulatory effects on the sheep of intracerebroventricular injections of L-glutamic acid

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Summary. L-glutamic acid injected in doses of 200–1000 nmoles · kg^{-1} into the cerebral ventricles of sheep had dose-dependent thermoregulatory effects: an increase in heat production and/or a decrease in respiratory frequency, and a rise in rectal temperature. A dose of 800 nmoles · kg^{-1} had effects comparable with those of a similar injection of 3 nmoles · kg^{-1} carbamylcholine.

When some of the putative transmitter substances are injected into a lateral cerebral ventricle of the unanaesthetized sheep through a previously implanted ventricular cannula, they cause distinct and quite regular patterns of change in the thermoregulatory effectors with resultant changes in rectal temperature (T_{re}) as summarized in the 1st 4 columns of the table[2–4]. These apparently orderly changes in effector activities have been interpreted as evidence that these substances, although applied in a rather gross and diffuse way, each act at particular points at the central nervous interface between the afferent paths from thermosensors and the efferent paths to thermoregulatory effectors.

Other possible transmitter substances tested in our laboratory at an early stage in this continuing study were: histamine, L-glutamic acid, taurine, glycine and γ-aminobutyric acid. At dose levels of up to 200 nmoles · kg^{-1} these substances were not found to cause thermoregulatory effects when injected into a lateral cerebral ventricle at 0 and 40 °C ambient temperature (T_a)[5]. In other species, however, some of these substances have been found to elicit thermoregulatory effects or, at least, to cause changes in body temperature when applied centrally[6,7]. The differences between the doses of 5-HT, CCh, NA and DA (table) which were required to elicit thermoregulatory effects could relate to differences in the rate and extent of diffusion into brain tissue from the ventricles, and differences in the accessibility of the target synapses, as well as to differences in receptor densities. We could, therefore, have missed the thermo-

Thermoregulatory changes induced by ICV injections of drugs

Responses	Drugs and doses 5-HT 40 nmoles · kg^{-1}	NA 100 nmoles · kg^{-1}	DA 200 nmoles · kg^{-1}	CCh 3 nmoles · kg^{-1}	Glut 800 nmoles · kg^{-1}
Panting (at high T_a)	↑	↓	↓	↓	↓
* Ear skin temperature	↑	↓	↓	↓	↓
Shivering (at low T_a)	↓	↓	↓	↑	↑
Rectal temperature (T_{re})	↓	↑↓ **	↑↓ **	↑	↑

5-HT, 5-hydroxytryptamine; NA, noradrenaline; DA, dopamine; CCh, carbamylcholine (carbachol); Glut, L-glutamic acid; T_a, ambient temperature; ↑, increase; ↓, decrease; * indicates state of peripheral vasomotor tone; ** ICV NA or DA causes a rise in T_{re} at high T_a and a fall in T_{re} at low T_a.

regulatory effects of some of these other putative transmitter substances because insufficient amounts were injected.

In a recent reinvestigation we have found that histamine has a distinct excitatory action on all 3 autonomic thermoregulatory effectors: respiratory frequency, peripheral vasoconstriction, and heat production by shivering[8]. Taurine, although only in very high doses, has yet another distinct set of effects: it inhibits all 3 autonomic thermoregulatory effector functions. We have now reinvestigated the thermoregulatory effects of L-glutamic acid at different ambient temperatures and report as follows.

Results. At 20 °C T_a an intracerebroventricular (ICV) injection of 200 nmoles · kg^{-1} caused vasoconstriction of the ears, a small depression of respiratory frequency (RF) and a rise in T_{re}. At dose levels of 800–1000 nmoles · kg^{-1} these effects were greater. At 10 °C T_a an ICV injection of 800–1000 nmoles · kg^{-1} into the shorn sheep resulted in the rapid onset of visible shivering. At the same time there was an increase in oxygen consumption and a large rise in T_{re}. At 40 °C T_a an ICV injection of 800–1000 nmoles · kg^{-1} caused a fall in RF and, again, an increase in T_{re}.

As the table indicates the thermoregulatory effects of ICV injections of 800 nmoles · kg^{-1} of L-glutamic acid are virtually the same as those previously recorded in response to an ICV injection of 3 nmoles · kg^{-1} of carbachol, although they are of a shorter duration. As with carbachol[9], the thermoregulatory effects were attenuated by a prior ICV injection of the muscarinic receptor-blocker, atropine sulphate in a dose of 20 nmoles · kg^{-1}.

Discussion. There is no clear evidence that glutamate functions in the brain as a true synaptic transmitter substance, although when applied iontophoretically to cells in the CNS it has been reported[10] to excite many of them irrespective of their responsiveness to other putative transmitter substances. In view of this alleged non-specific excitatory effect of glutamate, the patterned thermoregulatory effects of large doses of L-glutamic acid injected into the cerebral ventricles of the sheep were unexpected. There is no doubt about the classification of the observations reported here: glutamate has an effect identical to that of acetylcholine plus eserine, or of carbachol, similarly applied at much lower concentrations. Glutamate could be acting as a cholinomimetic on ACh-receptors or it could be stimulating, directly or indirectly, the cholinergic neurones on the pathway responsible for exciting heat production and inhibiting heat loss. Why, in these experiments, the excitatory action of glutamate should be confined to this one pathway is not clear.

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Études des variations quantitatives du passage de la ferritine au niveau de la membrane basale glomérulaire en fonction du temps et sous l'influence de la théophylline

Time and theophylline influence on the quantitative variations of the glomerular basement membrane ferritin pathway

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Summary. A fine quantitative evaluation of ferritin aggregates in rat GBM permits to counts 5.08 ± 1.51 and 18.30 ± 3.21 g/cm², respectively 30 and 60 min after ferritin injection; likewise, 30 min after ferritin administration, 5.08 ± 1.51 and 17.11 ± 3.9 g/cm², respectively in normal and theophylline-treated animals.

L'utilisation de nombreux traceurs protéiques a permis de mieux comprendre le cheminement des macromolécules au niveau des différents éléments structuraux du filtre glomérulaire, mais aucune théorie ne s'est encore imposée parmi les divers schémas proposés[1–3]. Malgré les nombreux travaux réalisés dans ce domaine, aucun auteur n'a étudié quantitativement la répartition du traceur au sein des structures, comme le précise Karnovsky[1]: «toute tentative de quantification est difficile et n'a guère été essayée».

Nous présentons une méthode de comptage qui permet de déterminer la densité des grains de ferritine au sein d'une structure glomérulaire particulièrement intéressante, la membrane basale glomérulaire. Nous pouvons ainsi suivre les variations quantitatives du passage transglomérulaire du traceur, soit en faisant varier le temps séparant l'injection de la ferritine du sacrifice de l'animal, soit en modifiant les paramètres hémodynamiques glomérulaires par perfusion de théophylline.

Matériel et méthode. 9 rats mâles, de souche Wistar, pesant 250 g, anesthésiés à l'uréthane, sont perfusés avec du sérum physiologique à la vitesse de 0,15 ml/min (sauf les rats Th 30 qui reçoivent la même perfusion à laquelle on ajoute de la théophylline à 3 mg/ml). A la 15e min, 1,25 ml d'une solution de ferritine à 50 mg/ml (N.B.C., Cleveland)

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