

hemisphere in the same section from each group of animals (figure 1, A5, B5, C5, D5 and E5).

**Discussion.** The simultaneous injection of the 2-DG isotope tracer and the microspheres was chosen to gain insight into the earliest metabolic events that occur in the whole brain following embolization.

Quantitative use of this method necessitates that at least 30 to 45 min have elapsed after isotope injection to insure that the 2-DG glucose in the unmetabolized brain pool has undergone conversion to 2-DG-6-P. Also a steady state must exist from the time of 2-DG administration to the time of the animal's sacrifice to attain a completely accurate representation of 2-DG utilization and uptake. Consideration of these 2 theoretical limitations of this technique makes quantitative interpretation of the 15 and 30 min autoradiographs difficult; however, they are so different from controls that they suggest that there is a massive early non-utilization of glucose in these time periods. EEG and evoked potential responses recorded from rats which have undergone similar carotid embolization demonstrate marked physiological changes in the entire hemisphere<sup>5,7</sup>. Recent experimentation in the cat has demonstrated similar alterations of glucose metabolism in both the deep and cortical circulation<sup>6</sup>. These present experiments clearly

demonstrate shrinkage of zones of altered glucose utilization with time. I postulate is that the shrinkage of these zones is caused by collateral circulation which is stimulated by the glycolysis which occurs in an ischemic area<sup>5,7</sup>. The increased tracer accumulation seen at 30 min, 1 and 4 h is independent of increased blood flow due to collateral circulation unless this is also accompanied by an increased metabolic rate<sup>3</sup>.

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## Autonomic response of the fish to pyrogen

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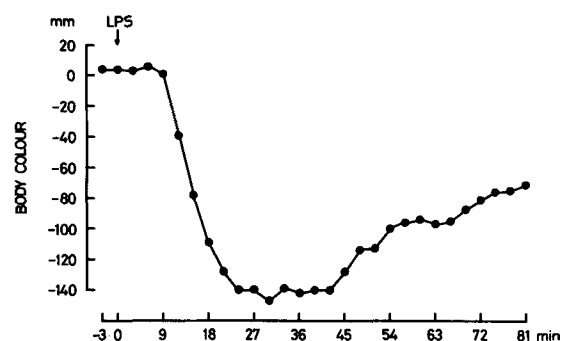
**Summary.** Lipopolysaccharide (LPS) applied to the anterior brainstem of the carp caused lightening of body colour. This indicates that an increase in set point temperature is responsible for increased cutaneous autonomic activity following LPS-administration.

Recently, pooled observations have clearly shown that the fish possesses the same central mechanism as that of homeotherms, for initiating temperature responses. Localized temperature displacement of the hypothalamus can elicit thermoregulatory behaviour by altering the thermopreferendum of the fish<sup>2-5</sup>, and also induces changes in autonomic functions<sup>6</sup>. We have confirmed the existence of such central mechanisms in the fish by experiments in which the cyprinid fishes changed their heart rate and body colour in response to selective thermal stimulation of the spinal cord<sup>7-9</sup>. This functional similarity of the central nervous system in the fish and homeotherms has been further demonstrated by behaviourally-acquired fever in the fish following pyrogen administration; a pyrogen-injected fish increased its thermopreferendum presumably due to an increase in the set point temperature<sup>10</sup>, as is actually the case for the homeotherms<sup>11-14</sup>. We report here that a pyrogen applied to the hypothalamus of the fish can also induce changes in cutaneous autonomic activity, besides an increase in behaviourally selected ambient water temperature.

We used gallaminized carp, *Cyprinus carpio*, of 24-27 cm length. Lipopolysaccharide (LPS) from *E. coli* UKT-B strain (0.02-0.5 µg in 0.1-0.2 ml fish saline) was applied manually to the anterior brainstem including the hypothalamus, while monitoring body colour of the tail region by means of a photoelectrical technique assessed to measure the intensity of reflected light from restricted body surface<sup>9</sup>. Body colour change of the carp is achieved by the pigmentary movements within the melanophores located in the skin areas. These pigmentary movements are controlled only through the single innervation by sympathetic ef-

ferents of the cutaneous region; excitation causes aggregation of the pigments, i.e. lightening, and inhibition causes dispersion of pigments within the melanophores, i.e. darkening of body colour<sup>15</sup>. Thus, body colour of the carp is an excellent indicator for examining the effect of pyrogen administration on the cutaneous sympathetic system.

LPS-administration to the anterior brainstem invariably caused body colour to be lightened (table and figure). Lightening began with a mean latency of 14.9 min, reached the maximal response after 48.0 min and recovered by 50%



Body colour lightening induced by LPS. Ordinate shows body colour measured every 3 min and abscissa shows time course. Negative values for body colour indicate lightening of body colour. The reference body colour level, 0 on the ordinate, was taken as the mean level during 4 min before LPS administration. Result from the carp numbered 3 in the table.

Effect of LPS administration on body colour of the carp

Number	Length (cm)	Weight (g)	LPS ( $\mu$ g)	Body colour change		50% recovery (min)	Visceral temperature ( $^{\circ}$ C)
				Latency (min)	Peak (mm, min)		
1	27.0	505.0	0.02	15.5	— 48.0	27.0	20.6
2	26.0	510.0	0.02	5.0	— 48.0	24.0	20.8
3	25.5	420.0	0.02	7.0	— 141.9	38.0	23.4
4	27.0	540.0	0.50	18.0	— 99.5	112.0	20.9
5	25.0	515.0	0.10	29.0	— 62.0	39.0	21.5
$\bar{x}$	26.1	498.0	0.13	14.9	— 79.9	48.0	21.4
$S\bar{x}$	$\pm 0.4$	$\pm 1.8$	$\pm 0.08$	$\pm 3.8$	$\pm 16.2$	$\pm 14.6$	$\pm 0.5$

Body colour was evaluated semiquantitatively as mm of recorder deflexion. Negative values for body colour indicate lightening of body colour.

in 59.3 min. Application of only fish saline to the anterior brainstem induced no significant responses in body colour. Febrile properties of the LPS used was examined in five rabbits: i.v. injection of 0.2  $\mu$ g/ml per kg LPS induced an increase in rectal temperature by over 2.0 $^{\circ}$ C within 3 h.

It is possible that 'excitatory paling' of body colour as an arousal reflex is induced by nonspecific effects on the telencephalon during LPS-treatment. Such an excitatory paling, however, can be discriminated from LPS-induced lightening, because the former change begins and recovers relatively quickly, and is smaller in amplitude. The activity of cutaneous sympathetic efferents were deduced to be increased during body colour lightening, according to the functional property of effector neurones for body colour. Likewise, in the mammal, the activity of cutaneous sympa-

thetic efferents is thought to be increased during pyrogen-induced fever because there is vasoconstriction to reduce heat loss from the skin<sup>16,17</sup>.

If LPS increases a set point temperature in the thermoregulatory centre, the response should be predictable, viz., like that caused by cold stimulation. In fact, cold stimulation of the skin<sup>18,19</sup> and the spinal cord<sup>9</sup> induces lightening of body colour in the fish. Therefore, the present results could be taken to indicate that an increase in set point temperature is responsible for increased cutaneous autonomic activity following LPS-administration. In conclusion, the present investigation has provided further evidence that the fish has the same central mechanism as that of homeotherms for temperature responses, both in behaviour and in autonomic functions.

- 1 We express thanks to Dr S. Kanoh, National Institute of Hygienic Sciences, Osaka, Japan, for supplying the LPS.
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## Organization of the mammalian red nucleus and its interconnections with the cerebellum

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**Summary.** The red nucleus in monkeys and rats consists of a magnocellular, rubrospinal portion which receives its cerebellar information from the nucleus interpositus, and a parvocellular, rubroolivary portion which receives cerebellar afferents from the nucleus lateralis. Distinct interpositorubrospinal and dentatorubroolivary projections are therefore common to these 2 species.

Although the interconnections of the mammalian red nucleus (RN) and the cerebellum have been the subject of investigation for many years, certain details of their organization have only recently become apparent. In the cat, a somatotopically organized projection from the anterior interposed nucleus (NIA) terminates within all but the rostralmost portion of the RN<sup>1,2</sup> while the lateral (dentate) nucleus (NL) projects only to the rostral area which is

devoid of NIA input<sup>2,3</sup>. The RN of the cat is not well suited to a study of the functional organization of this centre, however, because it is not clearly divided into magnocellular and parvocellular portions<sup>4</sup>, i.e. large and small cells are interspersed throughout most of its rostrocaudal extent. It was therefore undertaken to study the organization and connections of the RN in the monkey and the rat in which this centre is more clearly polarized<sup>5-8</sup> and to compare their