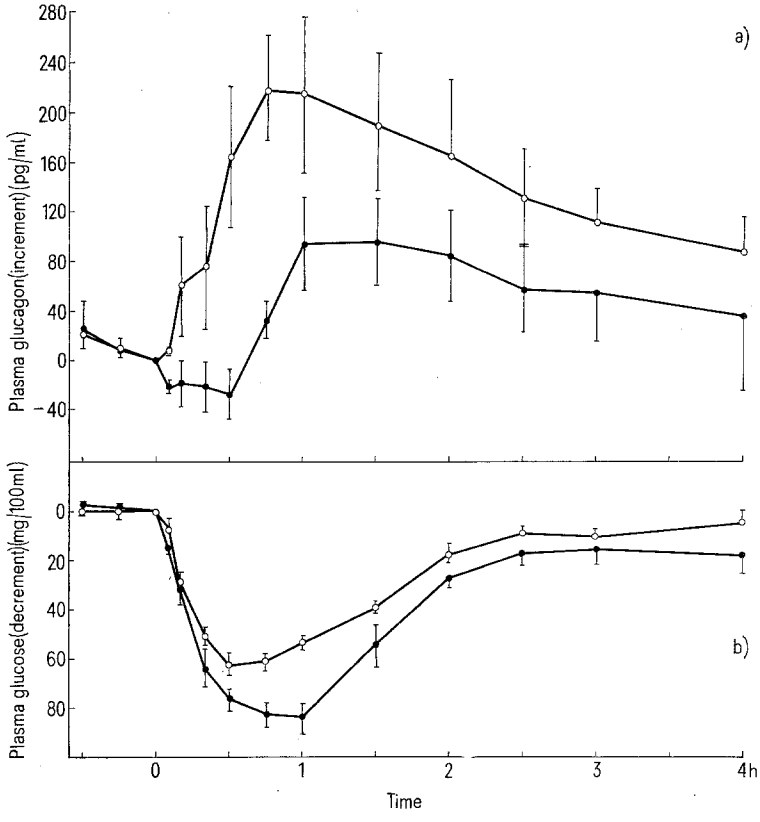


Fig. 2. Comparison of the changes in mean plasma glucagon (a) and glucose concentrations (b) in response to i.v. insulin (0.1 units/kg) at time = 0, in normal calves (○, $n = 4$) and calves with cut splanchnic nerves which were pretreated with atropine (0.2 mg/kg) (●, $n = 4$). Vertical bars: S.E. of each mean value.

relatively insensitive to changes in plasma glucose concentration. These results do, however, support the contention that a cholinergic mechanism is implicated in the release of glucagon which normally occurs in response to hypoglycaemia.

*Zusammenfassung.* Der durch Insulin herbeigeführte hypoglykämische Effekt wurde in Kälbern mit durchtrenntem Nervous splanchnicus durch Atropin verstärkt, wobei sich der Anstieg des Plasma-Glukagonwertes verzögerte und reduzierte. Es wird ein cholinergischer Mechanismus der Glukagonsekretion während der Hypoglykämie vermutet.

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## Changes in Body Temperature Produced by Injecting Prostaglandin $E_1$, EGTA and Bacterial Endotoxins into the PO/AH Region and the Medulla Oblongata of the Rat[1]

Heating and cooling of the medulla oblongata produces changes in body temperature[2,3] and behavior[3] similar to those produced by altering the temperature of the preoptic/anterior hypothalamic (PO/AH) temperature control region. These parallel effects of thermal stimulation of the 2 regions and the finding that the influence of medullary thermoresponsiveness does not depend upon mediation by the PO/AH region[3] suggest that the medulla contains a separate secondary thermosensitive mechanism for body temperature control. It is of interest to know if the 2 brain regions also respond in parallel fashion to certain chemical substances known to influence thermoregulation. Therefore, we compared changes in rectal temperature ($T_r$) produced by injecting prostaglandin $E_1$ ($PGE_1$), which is presumed to act as a mediator in thermoregulation[4,5], into the PO/AH region and medulla. EGTA and bacterial endotoxins, compounds which have been shown to cause hyperthermia after central or peripheral administration, were also injected.

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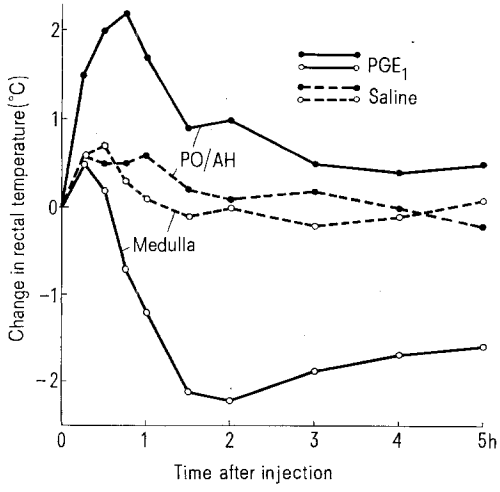
*Material and methods.* Male albino rats (300–400 g) were maintained at a room temperature of 21–23 °C. A single guide tube (0.016 in id) with an obturator was implanted in the PO/AH region in each of 20 rats and in the medulla oblongata of 15 others. The surgical procedures and stereotaxic coordinates were the same as those used to implant thermodes in previous experiments[3]. 7 to 10 days were allowed for recovery. Before making injections, $T_r$ was measured every 15 min with a thermistor probe (6 cm insertion) until the values recorded were consistent. Then the obturator was removed, and an injection cannula (0.012 in od) was inserted so that it extended 0.5 mm beyond the tip of the guide tube. 1 µl of nonpyrogenic saline or one of the other chemical agents was injected over a 30–50 sec period. The cannula was left in place for another 20–40 sec before removal. $T_r$ was then measured every 15 min for 1 h, at 30 min intervals during the 2nd h and at hourly intervals thereafter. The agents injected were: $PGE_1$ (95% pure); the chelating agent EGTA (Sigma) which, when injected into the posterior hypothalamus, produces a large rise in temperature[6]; typhoid vaccine (TV; Wyeth) which produces hyperthermia when placed in the PO/AH region[7,8]; and Piromen which causes fever when given peripherally. $PGE_1$ and EGTA were dissolved in nonpyrogenic saline just before injection. Injections were not repeated at intervals of less than 72 h. Locations of the injection sites were determined through standard histological procedures.

*Results.* $PGE_1$. $PGE_1$ injected into the PO/AH region caused a rise in $T_r$ (Figure). Maximum increases in $T_r$ (0.9–2.5 °C range) occurred 15–120 min after 1.0 µg was given. Both the magnitude of hyperthermia and the time to peak rise in $T_r$ were dependent upon the locus of the cannula tip. Injections within 0.8 mm of the midline produced the greatest increases in $T_r$ (1.7–2.5 °C) in the shortest intervals (15–60 min). Lower doses (0.01–0.5 µg) produced smaller and less reliable rises in $T_r$. There was no evidence of tolerance with repeated injections. No decreases in $T_r$ below saline control levels were recorded.




Changes in rectal temperature produced by injecting $PGE_1$ into the PO/AH region or the medulla oblongata in 2 unanesthetized rats resting in a neutral environment (23 °C).

On the other hand, injection of equal amounts of $PGE_1$ into the medulla lowered $T_r$ (Figure) in all rats. Maximum decreases as great as 2.2 °C occurred 1–5 h after injection and were seen consistently with up to 5 repetitions of the dose. Smaller doses of $PGE_1$ (0.01–0.5 µg) were less consistent in lowering $T_r$. All injection sites were within the region of the medulla where thermal stimulation alters $T_r$[3].

EGTA. When injected into the PO/AH region, doses of 1–5 µg of EGTA always caused a rapid rise (1.0–1.5 °C) in $T_r$ followed by a return to baseline within 1 h. The shortest time to peak response (15 min) was seen in animals with cannulas placed near the midline. Rats with lateral placements showed peak responses at 30–45 min post-injection. Similar doses of EGTA placed in the medulla produced 2 types of effects on $T_r$: either a rise of 1.4–1.5 °C within the 1st h or a fall of 1.0–1.3 °C 2–4 h after the injection.

Bacterial endotoxins. There were no parallel changes when bacterial pyrogens were injected into the PO/AH region and the medulla. 1 µl of TV injected into the PO/AH region produced no significant change in $T_r$. The same dose in the medulla lowered $T_r$ (−1.7– −2.6 °C) in 3 animals but had no influence on $T_r$ in 6 others. 1 µl of Piromen increased $T_r$ (0.8–2.1 °C) with a maximum at 1–2 h post-injection when placed in the PO/AH region but did not significantly change $T_r$ when placed in the medulla.

*Discussion.* The results showed no clear parallel between the effects on $T_r$ produced by injecting hyperthermogenic agents into primary (PO/AH) and secondary (medulla) temperature control regions of the brain. Except for EGTA which increased $T_r$ in rats with PO/AH cannulas and in a few rats with medullary cannulas, there were no similarities in the responses. The dissimilarities in the effects of chemical injections contrast with the parallel changes in $T_r$ and behavioral thermoregulation produced by heating and cooling the 2 brain regions[3]. This contrast suggests that the thermoregulatory systems of the PO/AH region and medulla oblongata are organized in one way with respect to responsiveness to thermal stimuli and in quite different ways with respect to responsiveness to the chemical compounds. One of the most remarkable results in the present experiments was that opposite effects on $T_r$ were produced by injecting $PGE_1$ into the PO/AH region and into the medulla. The rise in $T_r$ caused by $PGE_1$ in the PO/AH region is in agreement with results obtained with the cat[9] and rabbit[10]. The fall in $T_r$ when $PGE_1$ was placed in the medulla has not been reported before and was unexpected. Results of other experiments in which $PGE_1$ was injected into the cerebral ventricles of unanesthetized cats, rabbits and rats[4,5] raised the possibility that it might serve as a mediator in normal thermoregulation[4]. The present findings indicate that $PGE_1$ injected into 2 brain regions which are known to be thermoresponsive can influence temperature. If $PGE_1$ does play a role as a mediator of thermoregulation, its function in the medulla must be antagonistic to its function in the PO/AH region: to lower body temperature rather than to raise it. The possibility that $PGE_1$ in the medulla has a role in thermoregulation is made more plausible by findings that the medulla normally contains small amounts of $PGE_1$[11] and that iontophoretic application of this agent alters spontaneous firing of neurons in the reticular substance of the lower brainstem[12].

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*Résumé.* La prostaglandine $E_1$ a causé de l'hyperthermie si on l'injectait dans la région préoptique /hypothalamique antérieure/ des rats et de l'hypothermie au niveau de la région médullaire oblongue. L'EGTA, le Piromen et le vaccin typhoïdes ont rarement causé des changements parallèles dans la température rectale si on les injectait dans les deux régions cérébrales.

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## Two Types of Response Patterns from Cat Retinal Ganglion Cells to Moving Stimuli

Recent studies[1-3] have shown that on center (and off center) retinal ganglion cells of cats can be separated into two types. The first or sustained type responds to a step input of light with a high frequency burst of spikes followed by a maintained firing level which is considerably higher than the spontaneous level. This maintained level lasts for the duration of the stimulus. The second or transient type responds to the same stimulus also with a high frequency burst of spikes, but the firing level decays rapidly to a firing close to the spontaneous level. The two types also respond differently at stimulus off; the sustained type shows a strong and long-lasting inhibition while the transient type shows a weak and short-lasting inhibition.

We have examined the responses of retinal ganglion cells of cats to moving stimuli and have found 2 types of response patterns; the type 1 on-center units show a decrease in the firing rate (inhibition) prior to the excitation from the receptive field center (RFC); the type 2 on-center units do not show the decrease prior to the excitation[4]. We wish to present evidence that these 2 types correspond to the sustained and transient types and to point out that the differences can be accounted for by a difference in the spatial arrangement of the center and surround components of the receptive field (RF).

Recordings were made from single optic tract fibres from lightly anesthetized cats with lacquer-coated microelectrodes. The preparation of the animal and recording system have been presented in detail earlier[5]. The stimulus was a square or slit of light moved across the visual field at a constant velocity of 3.6°/sec. The data were analyzed on a PDP-8 computer to give average response histograms.

Average response histograms from a type 1 on-center unit which shows the inhibition prior to the excitation from the RFC are shown in the left column of Figure 1. The stimulus was a 0.7° square which moved at a constant velocity of 3.6°/sec across the RF. The numbers at the left represent the stimulus intensity in log threshold unit, i.e., 0.4 represents a stimulus 0.4 log units above threshold. With a stimulus 0.4 log units above threshold, the firing rate increases from the spontaneous level (40 spikes/sec) to a maximum of 200 spikes/sec as the stimulus passes into the center of the RFC. As the stimulus moves out of the RFC the firing level drops to 25 spikes/sec before returning to the spontaneous level. With the stimulus intensity 1.2 log untis above threshold, there is a decrease in the firing rate just prior to the excitation from the RFC. This inhibition arises from the antagonistic surround of the RF. At 2.0 log units above theshold, the degree of inhibition prior to the excitation is stronger.

Average response histograms from a type 2 unit are shown in the right column of Figure 1. The response

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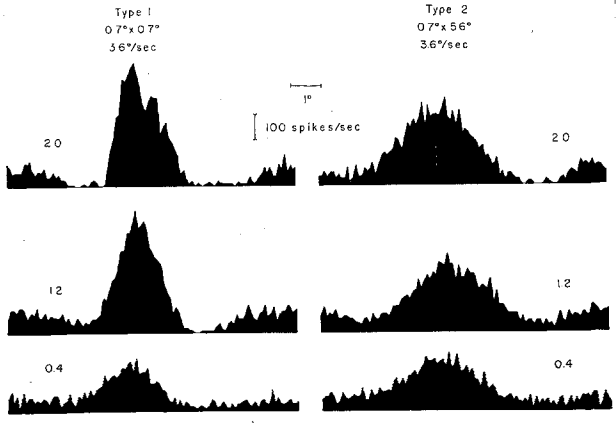


Fig. 1. Average response histograms of type 1 and type 2 on center units. The numbers on the left represent the stimulus intensity in log threshold units. The stimulus was a 0.7° square for the type 1 unit and a 0.7° × 5.6° vertical slit for the type 2 unit. Background luminance was −1.0 log ftl.

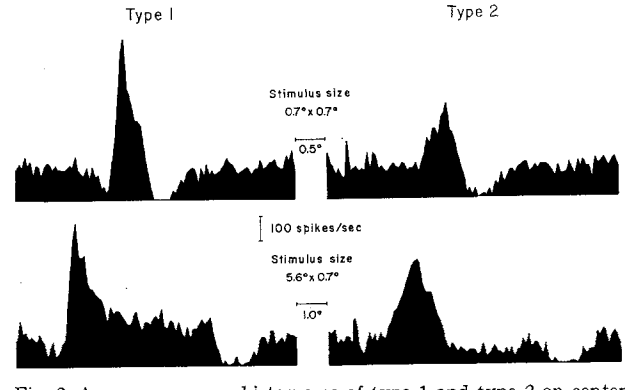


Fig. 2. Average response histograms of type 1 and type 2 on center units. The responses to 0.7° square are shown in the upper row while the responses to a 5.6° × 0.7° horizontal slit are shown in the lower row. The stimulus was 2.0 log units above threshold for all responses. Background luminance was −1.0 log ftl.