THERMAL CHANGES PRODUCED BY NOREPINEPHRINE APPLICATION IN THE PREOTIC AREA OF MONKEYS

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Summary : The effect of injection of norepinephrine in the anterior regions of hypothalamus on rectal temperature, skin temperature, heart rate and respiratory rate in rhesus monkeys was studied. The injection of 2 μg of norepinephrine in the preoptic area produced a fall in body temperature without any accompanying change in skin temperature, heart rate and respiratory rate. The findings suggest that the suppression of heat production may be responsible for the norepinephrine induced hypothermia in monkeys.

Key words : preoptic area norepinephrine rectal temperature skin temperature

INTRODUCTION

Norepinephrine (NE), its nerve terminals and receptors are present in the medial preoptic area (mPOA) (1, 8). NE produces hypothermia in several vertebrate species when injected into the mPOA (2, 3, 5, 9, 13). NE injected into the cerebral ventricle produced hypothermia in rhesus monkeys (10). There are only few studies dealing with the changes in temperature after administration of NE in the anterior region of hypothalamus in primates (11, 12, 16) Though they generally indicate a fall in body temperature, large doses (16) and multiple injections (11, 12) were employed in these studies. In the present study, the changes brought about in rectal temperature, skin temperature, heart rate and respiratory rate were simultaneously monitored after single injection of small doses of NE in a particular cannula in the anterior regions of hypothalamus.

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MATERIAL AND METHODS

The study was conducted on eight male rhesus monkeys (Macaca mullata), in the weight range 2.5 to 5.0 *kg*, which were trained for two weeks, before surgery, to sit on a restraining chair. Under sodium pentobarbitone (35 *mg/kg* body weight) anaesthesia, 21 gauge stainless steel guide cannulae, fitted with indwelling styli, were aseptically implanted into various regions of anterior hypothalamus (Fig. 1). Two cannulae (one on each side) were implanted in each animal.

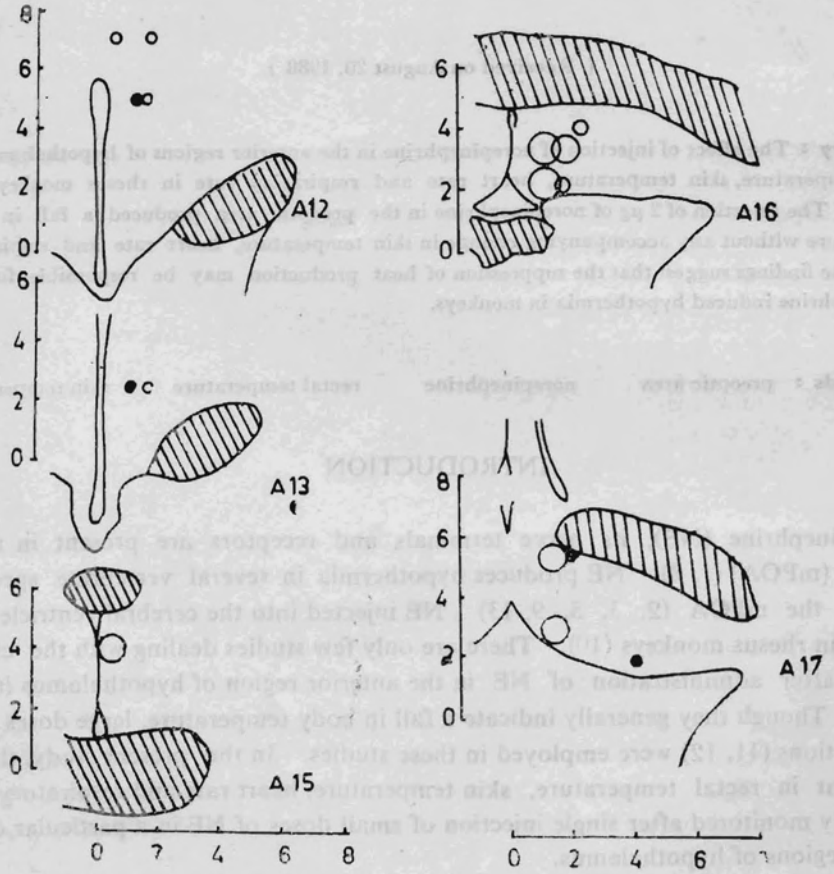

Fig. 1 : Outlines of the coronal section of rhesus monkey brain at A 12, 13, 15, 16 and 17 as per the atlas of Snider and Lee (15). Open circles indicate the sites from where hypothermic changes were obntained on administration of NE. Size of these circles indicate the magnitude of response. Filled circles indicate no response sites.

All experiments were conducted in an atmospheric temperature of 25-28°C. The body temperature was recorded by a flexible thermister probe moved 8 cm into the rectum (7). The skin temperature was also recorded with a thermister from the thigh about 5 cm above the knee. The heart rate was counted from the EKG recorded on a polygraph. Respiratory rate was counted by direct observation. The basal readings of rectal and skin temperature, heart rate and respiratory rate were noted at 10 minute intervals. The drug was injected only after the above mentioned parameters showed three consecutive stable readings.

NE (Arterenolol bitartrate, Sigma Chemicals) dissolved in pyrogen free saline, was administered unilaterally through an injector cannula as mentioned earlier (6). The NE ($2\mu g$ in 0.2 μl) was then delivered over a period of 2 min. The injector cannula was replaced by the stylus after a minute. The injection sites extended from the middle hypothalamus (at the level of ventromedial and dorsomedial nuclei) to anterior end of preoptic area (Fig. 1). After the experiment the brain site and the spead of injected material were verified histologically by injecting 0 2 μl of 2% ferric chloride. The monkeys were then deeply anaesthetised with sodium pentobarbitone and the brain was perfused through carotid arteries with 3% potassium ferrocyanide in formolsaline. Localised blue spot (produced by Prussian blue reaction) noticed on the histological section indicated the injection site.

The preinjection data of all the parameters were first analysed by two way analysis of variance to find out the significance of the variation of the basal readings. The results from eight sites which showed a drop of rectal temperature by 0.4°C or more were pooled together for analysis. The readings obtained in these animals at each ten mintue interval after injection were compared with preinjection readings using Dunnet's test.

RESULTS

A total of sixteen sites were studied in eight monkeys. The first step of the analysis revealed that there was no significant intragroup variation in the preinjection readings of all the parameters. The rectal temperature was the only parameter which showed any significant difference after the injection of NE (Fig. 2). The eight sites, which showed a drop of rectal temperature by 0.4°C or more, were located medially and extended from the anterior end of the preoptic area to the junction between dorsomedial nuclei and preoptic area. The sites lying posteriorly and laterally showed either a small drop or no change in rectal temperature (Fig. 1). The injection of NE in the mPOA produced a fall in rectal temperature which started immediately after the injection. The maximum fall was obtained around 30 min. after injection and came back to preinjection level by 90 min. There was no significant change in skin

temperature, heart rate and respiratory rate after NE injection in any of the brain sites studied.

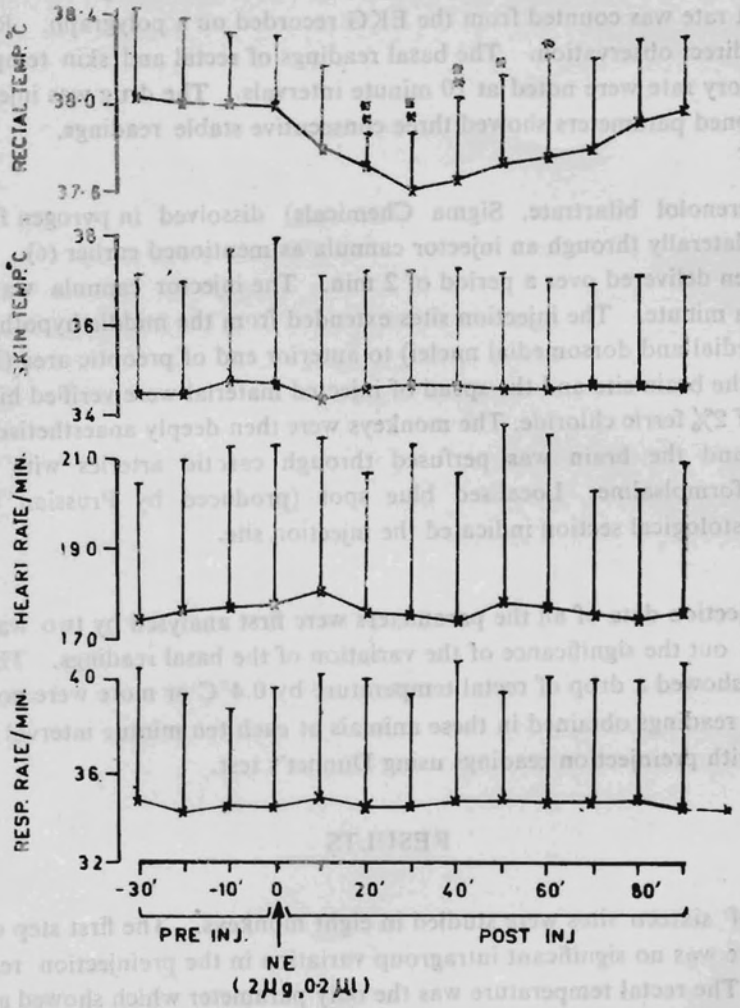

Fig. 2 : Effect of administration of Norepinephrine (NE) at medial preoptic area on rectal temperature, skin temperature, heart rate and respiratory rate (mean + SD). * $P<0.005$, ** $P<0.01$.

DISCUSSION

The results of this study show that the injection of NE in the preoptic area in rhesus monkeys produces a fall in body temperature which is similar in nature to that observed in

the other species (2, 3, 5, 9, 13). As the sites, which did not show any marked change, served as control, it was considered redundant, at this stage to have another control group of which received saline injection. It was suggested that vasodilation is one of the primary causes of NE induced fall in body temperature in rats and baboons (14, 16). Involvement of a hyperventilatory heat loss mechanism is also not indicated by the present results. It was suggested that heat production *per se* may be decreased after ventricular administration of NE (4). That may contribute towards the decreased body temperature after NE application at the preoptic area also. The heart rate is not altered, indicating the non-involvement of generalised autonomic response. Administration of a large volume of NE might have caused the changes in the heart rate which was reported by Toivola and Gale (16). It could also be possible that their study was conducted in a cold environment, as intraventricular administration of NE in low atmospheric temperature produces a fall in skin temperature (14). The simultaneous arousal response, which was observed in rats (6), was not observed in monkeys. It is difficult to observe arousal response in studies conducted in awake, alert monkeys during the day.

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