terms of the chalone hypothesis, since fetal and newborn epidermis, although rich in Langerhans cells[6] and active G1 inhibitor, does not respond at all to the G1 chalone[16]. Finally, there is a large body of evidence that Langerhans cells originate from the mesenchyme rather than from ectodermal tissue; and this is certainly not in accordance with the concept that chalones are growth regulators which are synthesized by the same tissue they act upon.

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Topographic localisation of insulinogenic and insulinoprival areas in the hypothalamus

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Summary. Electrical stimulation of hypothalamic areas through stereotaxically implanted electrodes were carried out in conscious male rhesus monkeys. There was a significant increase in immunoreactive insulin (IRI) following lateral hypothalamus (LHA) stimulation. An opposite response was obtained from ventromedial hypothalamus (VMH). Thus, insulinogenic and insulinoprival responses were obtained from feeding and satiety, suggesting a significant role of insulin in the regulation of food intake.

Hypothalamic stimulation produces changes both in food intake and endocrinal-metabolic activity. The feeding and satiety behaviours are influenced by LHA and VMH[2]. The earlier studies have either been done to determine hypothalamo-hypophyseal interactions or hypothalamo-metabolic regulations[3-11]. The present study was undertaken to investigate the serum insulin (IRI) response following electrical stimulation of these as well as other areas of the brain.

Materials and methods. 8 male rhesus monkeys *(Macaca mulatta)* weighing between 5 and 7 kg were observed for 15 days in an air-conditioned laboratory maintained at a temperature of 26±1 °C. The monkeys were given a synthetic diet supplied by Hind Lever Ltd, India, which essentially has a carbohydrate content of 73.6%, protein 11.3% and fat 9.0%. The animals were restrained daily in a primate chair for a period of 1 h till they ceased to display signs of struggle or uneasiness. Subsequently, the blood samples were drawn after an overnight fast on alternate days for the determination of serum insulin.

Bipolar varnish insulated stainless steel electrodes made from 26-gauge were implanted stereotaxically in different parts of hypothalamus and cerebral cortex; the methodology has been discussed earlier[7]. The animals took 4-5 days to recover from the effects of surgery. Subsequently, the estimations of fasting serum insulin were obtained to confirm that these were in the preoperative range.

Electrical stimulation of VMH, LHA, preoptic (Po) and cerebral cortex (CC) was carried out on alternate days and changes in serum insulin were investigated. The stimulation was carried out for 30 min, using square wave pulses of 5.5-7.0 V, 0.5 msec duration and a frequency of 75 cycles/sec. The blood samples were drawn by putting an indwelling catheter in the saphenous vein before, during, immediately after and 120 and 210 min following the termination of electrical stimulation. Serum insulin was measured by radioimmunoassay[12], using dextran coated charcoal for separation of free and bound hormone. After the completion of the experiment, electrolytic lesions were produced

Effect of electrical stimulation of different hypothalamic areas and cerebral cortex on serum levels of insulin (μU/ml) in normoglycaemic monkeys

Time in min	0	10	20	30	120	210
Lateral hypothalamus	21.65±6.0 (8)	26.2±8.17 (6)	26.0±8.0 (6)	33.37±5.77** (8)	46.36±12.0* (8)	24.2±4.5 (8)
Ventromedial hypothalamus	38.7 ±5.2 (7)	32.0±2.0 (6)	33.6±7.2 (6)	29.5 ±4.8 (7)	26.1 ± 5.2* (7)	24.0±5.0* (7)
Preoptic	27.6 ±3.8 (6)	23.9±5.6 (5)	21.8±5.3 (5)	20.6 ±4.5 (6)	21.6 ± 5.2 (6)	21.8±5.2 (6)
Cerebral cortex	19.6 ±2.3 (5)	20.8±1.4 (5)	18.4±1.7 (5)	22.1 ±2.2 (5)	16.0 ± 2.0 (5)	20.8±2.5 (5)

Values are mean ± SE. Number of observations in parentheses. * $p<0.05$; ** $p<0.01$. Paired t-test was done for the log values between basal level (0 min) and subsequent time intervals taking only those animals for which observations at both these levels were available.

in the brain in anaesthetized animals by passing DC current of 4 mA for 30 sec through the implanted electrodes. The brain was then perfused with 10% formalin and histopathological verification of the electrodes site was confirmed subsequently.

Results and discussion. In the present study, serum from monkeys after the electrical stimulation of the LHA, VMH, Po and CC were investigated for their insulin content. The table shows a significant increase in IRI following LHA stimulation. Expressing the prestimulation basal IRI (0 min) as 100%, the mean IRI at 10, 20, 30, 120 and 210 min was +121%, +120%, +154%, +214% and +112% respectively. An opposite response was obtained from VMH; the corresponding mean IRI values were −82.6%, −86.8%, −76.0%, −67.0% and −62.0% respectively. The stimulation of control electrode in the CC as well as that in the Po area did not result in any significant change in the levels of IRI. The functional reciprocity between 'feeding' (LHA) and 'satiety' (VMH) areas was also observed in the case of insulin, in addition to the reciprocity in feeding behaviour. Thus, insulinogenic and insulinoprival responses were obtained following the stimulation of 'feeding' and 'satiety' centres in the hypothalamus, suggesting a significant role of insulin in the regulation of food intake.

Idahl and Martin[13] and Martin et al.[14] reported that mouse ventrolateral hypothalamus releases a humoral factor in vitro which stimulates insulin secretion from islets of Langerhans. The extract from LHA stimulated, while that from VMH inhibited insulin secretion. Our results (in vivo) find support from those performed in vitro by Idahl and Martin[13] and Martin et al.[14]. Thus our findings suggest a close relationship between feeding behaviour and insulin secretion.

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CNS stimulation effect on the sexual maturation of the female rat[1]

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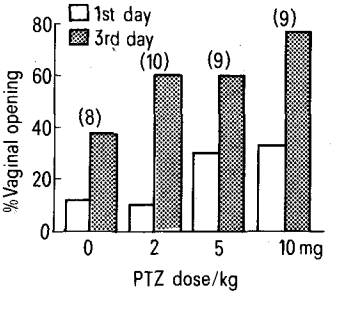
Summary. In the immature rat, CNS stimulants administration to pregnant mare serum gonadotropin (PMSG) primed rats resulted in significant ($p < 0.01$) ovarian and uterine hypertrophy when compared to animals treated with PMSG only. Meanwhile precocious puberty was produced by pentylenetetrazol treatment alone. The results of this experiment may indicate that administration of CNS stimulants has a specific action on the release of endogenous gonadotropin.

The involvement of the CNS in sexual puberty has been recognized for many years[4]. The immature hypophysis has been shown to contain significant quantities of gonadotropins, however, this gonadotropin is secreted in limited quantities during prepubertal life; hence the immature pituitary is capable of supporting reproductive function prior to the puberty[5]. It has been documented that hippocampus or pyriform lobe damaged during infancy (1 week) caused diminished gonadol development[6]. Precocious puberty was also recorded following the neural isolation of the medial basal hypothalamus[7]. Meanwhile, testosterone administration was found to induce precocious puberty in the female rat. This effect has been shown to be mediated by the hippocampus[8]. Recently, neural excitation with amino acids has been implicated in the regulation of gonadotropin secretion and the control of reproductive function in man[9]. The purpose of this investigation was to illustrate the effect of various CNS stimulant drugs on the hypertrophy of the ovary and uterus following the administration of PMSG and/or testosterone to the female immature rats.

Methods. Immature female Sprague Dawley rats with an average b.wt of 50–60 g were obtained from the Southern Animal farms, Alabama, at the age of 22 days. They were maintained on a 14 h:10 h light: dark cycle, with a controlled temperature of 23±1 °C and were fed with Purina rat chow and water ad libitum. In the 1st study, 8 groups of rats were utilized; each group was made up of 8 rats. Treatment was begun at the age of 23 days for the period of 3 days. Pregnant mare serum gonadotropin (20 IU PMSG, Sigma), theophylline (10 mg/kg, Nutritional Biochemical Corporation), picrotoxin (5 mg/kg, Pfaltz and Bauer, Inc.), testosterone (Δ^4-androsten-17B-o1-3 one; 5 mg/kg; Sigma) and pentylenetetrazol (pentamethylene-



Effect of 0 mg, 2 mg, 5 mg, and 10 mg/kg of pentylenetetrazol treatment on vaginal opening. Numbers within the bars indicated number of animals used.