recessive genetic trait remains the best available explanation for our results.

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Evidence for the Theory of Dual Hypothalamic Control of Ovulation

THE hypothalamus is rich in monoamines including serotonin (5-HT) and catecholamines (dopamine, adrenaline and noradrenaline). It has been reported that an injection of 5-HT into the third ventricle inhibits the secretion of gonadotrophins in cyclic and bilaterally ovariectomized rats[1–3] and elevated levels of 5-HT in the hypothalamus interfere with both gonadotrophically induced[4,5] and spontaneous ovulation[6,7]. On the other hand, intraventricular injection of dopamine[1] or its metabolite adrenaline[8] promotes gonadotrophin secretion and/or ovulation. On the basis of these and other results it has been postulated that the hypothalamus exerts a dual control over ovulation—its inhibitory influence being transmitted *via* a 5-HT pathway and a stimulatory one through a catecholaminergic (CA) pathway. It is believed that the balance between these contrasting influences determines the occurrence of ovulation—a certain critical balance in favour of the CA pathway promoting ovulation, and the opposite inhibiting it[6–11]. How these contrasting influences interact to regulate ovulation during the reproductive cycle is not known. We therefore injected monoamines or their antagonists into the third ventricle of immature rats primed with gonadotrophin and given a single injection of progesterone, and studied the effects of these procedures on ovulation. It is well documented that the facilitatory effect of progesterone on ovulation in such rats is exerted at the hypothalamic level, because barbiturates[12,13] or hypothalamic lesions[14] can block ovulation induced by progesterone.

Immature rats (65–70 g, 28-day-old) of the Sprague-Dawley strain were maintained under controlled conditions of light (on from 06.00–18.00 h) and temperature (71° F) and provided free access to food and water. Rats received a single subcutaneous injection of 5 IU of pregnant mare's serum gonadotrophin (PMSG, Equinex, Ayerst) in 0.1 ml saline at 11.00 h on day 29 followed by a single subcutaneous injection of 1.0 mg of progesterone (0.2 ml oil, Sigma Co.) 24 h later. Under our conditions the "critical period", that is, the period during which the neurogenic activation of the anterior pituitary occurs, extends from 14.00 h to 16.00 h on the day of progesterone injection as determined by pentobarbital sodium-induced inhibition of ovulation (unpublished data). On the following morning the animals were killed and both Fallopian tubes searched for ova. Rats were anaesthetized with ether on the morning or afternoon of the day of progesterone injection and placed in a stereotaxic instrument. Monoamines or their antagonists were injected into the third ventricle *via* a 27 gauge needle in a volume of 10 μl of vehicle composed of propylene glycol-saline (1 : 1, v/v). The sham operated animals received vehicle alone. When two different agents were administered they were given together in the same volume (10 μl). The position of the cannula was verified at autopsy in the initial experiment using thirty-five rats. Of these, only two of the cannulae were misplaced. In subsequent experiments, therefore, the position of the cannula was not verified.

Injection of PMSG alone failed to induce ovulation (group A, Table 1) but an additional injection of progesterone 24 h later induced a full ovulatory response in 100% of the animals (group B), thus confirming the well established facilitatory effect of progesterone on ovulation in these animals[12]. Intraventricular injection of vehicle alone 1–2 h after progesterone injection, that is, approximately 1 h before the onset of the "critical period" under our conditions, did not interfere with progesterone induced ovulation (group C) whereas an injection of an α-adrenergic blocker, phenoxybenzamine (group D), blocked the facilitatory effect of progesterone. When a β-adrenergic blocker, propranolol, was substituted it failed to inhibit ovulation (group E). These results demonstrate that the facilitatory effect of progesterone on ovulation is transmitted through an α-adrenergic pathway. Thus following progesterone injection the balance between 5-HT and CA systems must be in favour of the latter. If the balance between these contrasting influences is crucial in ovulation, then maintaining the balance in favour of the 5-HT system ought to interfere with the facilitatory effect of progesterone. This indeed proved to be the case as 100 μg of 5-HT creatinine sulphate (equivalent to 45 μg

Table 1 Effects of Intraventricular Injection of Monoamines and their Antagonists on Progesterone Induced Ovulation in Immature Rats primed with PMSG (Mean ± s.e.)

Group and treatment	Body weight at autopsy (g)	No. of rats ovulating / No. treated	Inhibition of ovulation (%)	Ova / Ovulating animal
(A) PMSG, 5 IU	76±1	0/10	100	0
(B) Control	80±1	11/11	0	10.0±0.8
(C) Sham control, 10 µl*	74±2	5/5	0	11.1±1.4
(D) Phenoxybenzamine, 100 µg†	76±1	1/5	80	13
(E) Propranolol, 100 µg†	79±2	5/5	0	8.6±1.8
(F) 5-HT, 100 µg	71±1	2/10	80	8.0±2.0
(G) 5-HT+LSD, 2 µg	78±2	10/10	0	10.1±0.9
(H) 5-HT+dopamine, 100 µg	72±2	9/10	10	10.3±0.7
(I) Starvation‡	61±1	6/6	0	9.2±0.8

All rats received 5 IU PMSG on day 29. In addition, groups B to I received 1 mg progesterone 24 h later, that is, at 11.00 h. Within 2 h after the steroid injection monoamines or their antagonists were microinjected into the third ventricle under ether anaesthesia. Tubal ova were counted at autopsy 48 h after PMSG injection.
* Vehicle alone.
† Given 1 h before progesterone, that is, at 10.00 h.
‡ Food was withdrawn following PMSG injection until autopsy but water was available.

of 5-HT) injected 1 h before the critical period blocked progesterone induced ovulation (group E). Conversely, by shifting the balance of monoamines in favour of CA, ovulation ought to be restored even in the presence of high levels of 5-HT. The inhibitory effect of 5-HT was completely blocked by a simultaneous injection of LSD (group G), a potent antagonist of 5-HT[15], or by dopamine (group H). These data should not necessarily be interpreted to mean that dopamine as such overcomes the inhibitory effect of 5-HT. It is equally possible that its metabolites adrenaline or noradrenaline may be involved. The possibility that the intraventricularly administered monoamines act on the pituitary can be excluded because monoamines do not inhibit the response of the pituitary to gonadotrophin releasing factors *in vitro*[16], nor do they significantly affect discharge of gonadotrophins from the pituitary when infused directly into the portal vessels in the pituitary stalk[3]. Body weight was unaffected by these treatments, so the nonspecific stress of the drugs cannot account for the observed effects. In fact, starving the animals beginning at the time of PMSG injection until autopsy, which caused a considerable loss of weight, failed to interfere with the facilitatory effect of progesterone on ovulation (group I).

Our results provide evidence for the first time that the inhibitory effect of 5-HT on ovulation can be overcome by a catecholamine and suggest that the balance between these contrasting influences is crucial in ovulation. These findings further reinforce the theory of dual hypothalamic control of ovulation postulated earlier[6].

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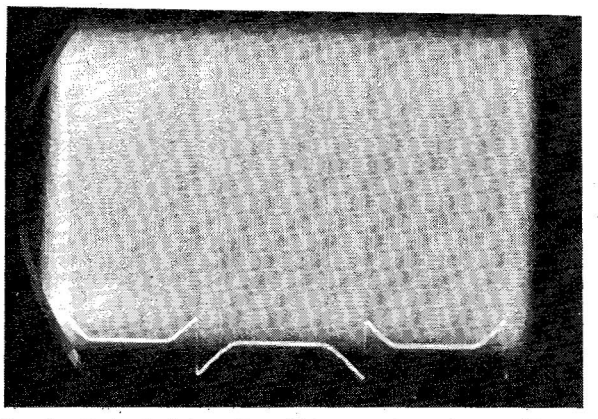

Fig. 1 Lateral interaction between channels sensitive to luminance. This figure illustrates the well-known enhancement of brightness produced when a given luminous area is flanked by regions whose luminance profile is as shown at the foot. (Downward deflexion represents increased luminance.) The role of the transition regions in generating the illusion is strikingly demonstrated by covering them with strips of plain paper.

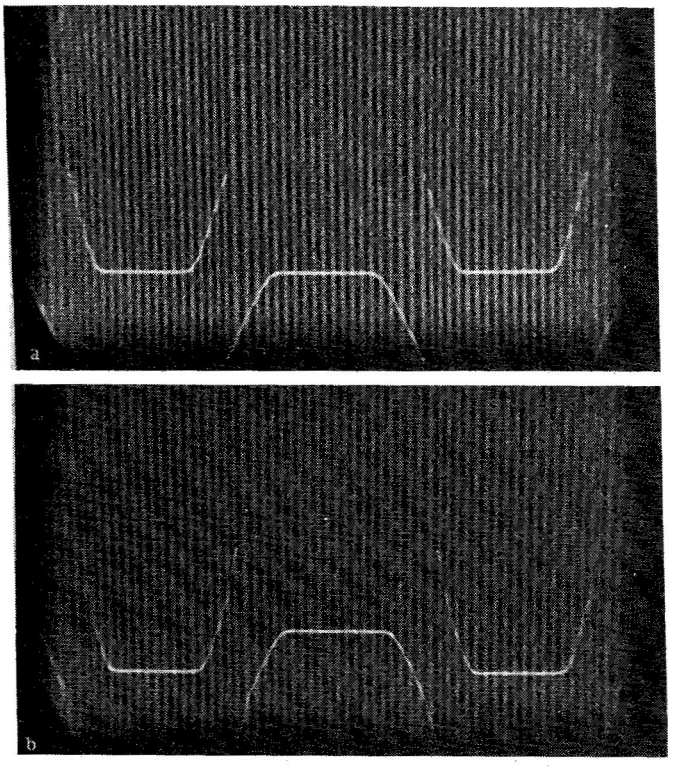

Fig. 2 Lateral interaction between channels sensitive to texture density. (a) The texture density (spatial frequency) of each pattern of lines is modulated in the same way as luminance was in Fig. 1. The height of the superimposed oscilloscope trace is linearly related to spatial frequency (upward deflexion for increased frequency). Closely analogous contrast enhancement effects can be observed. (b) By adding a central "pedestal" to the controlling waveform, the effect can be annulled and so quantified.

Lateral Interaction between Neural Channels sensitive to Texture Density?

A NUMBER of well-known visual phenomena, including Mach Bands[1] and the related illusion[2] shown in Fig. 1 are interpretable as evidence of lateral interaction between adjacent neural channels sensitive to retinal luminance. Inhibitory interaction would lead to disproportionate weight being given to sharp discontinuities in luminance. This can be taken to explain why the middle panel in Fig. 1 (when viewed from the right distance) is seen as brighter overall than its neighbours, though objectively all three have the same luminance at their centres. The limited retinal range of the interactive process responsible is shown by the gradual disappearance of the illusion as the viewing distance is increased.

Gibson[3] and others have shown psychophysically that the gradient of density of visual texture is an important clue to the orientation in depth of textured surfaces. This suggests that the visual nervous system might also have a gradient-enhancing process acting among elements sensitive to density of texture[4]. If so, one might expect analogous border contrast effects to those of Fig. 1 in the spatial-frequency domain giving rise to illusory spatial frequency shifts near discontinuities of texture density. In the experiments to be described these expectations were confirmed.