The β-Receptors in the Rat Pancreas

The stimulatory effect of isoproterenol (ISO) perfusion, a predominant β-stimulatory agent, upon insulin secretion in human beings has been reported by PORTE[1,2]. This stimulation was not accompanied by any hyperglycemia. MALAISSE et al.[3,4] have reported the effect of this drug in vitro, describing a blocking or stimulating action. The latter was obtained only when an α-blocking agent and glucose in a concentration of at least 100 mg/100 ml ($0.6 \times 10^{-2} M$ glucose) were present in the incubation medium together with ISO. The present investigation is intended to determine whether the pancreas response to ISO could be obtained under different experimental conditions as the previously reported.

Slices of rat pancreas (norvegicus male rats of about 100–150 g body weight) were incubated following a technique described in some previous reports[5]. After an equilibration period of 30 min in Krebs Ringer bicarbonate buffer (pH 7.4) with $0.3 \times 10^{-2} M$ glucose at 37 °C, the pancreas slices were placed in incubation flasks with 3 ml of the same buffer and incubated with continuous gassing, using a mixture of 95% oxygen and 5% carbon dioxide during 15 min (baseline). After this period, the slices were transferred to a second incubation medium (stimulation) with (a) $1.7 \times 10^{-2} M$ glucose or (b) $0.3 \times 10^{-2} M$ glucose plus 8.07×10^{-4} mM ISO. Release of insulin into the incubation medium (baseline and stimulation) was determined by the immunoassay method of HERBERT[6].

The results are summarized in the Table. In all cases the amounts of insulin are expressed in μU/mg of tissue/15 min.

These results show that when glucose in the medium increases from $0.3 \times 10^{-2} M$ to $1.7 \times 10^{-2} M$ a significant stimulation of the release of insulin from the pancreas was obtained. ISO, in the above mentioned concentration, was able to elicit an insulin response similar to the one observed with high glucose concentration.

On the basis of these results, several conclusions may arise: (a) the existence of β-receptors in the rat pancreas; (b) these receptors can be stimulated by ISO in the presence of low concentrations of glucose and in abscence of α-blockers; (c) release of insulin is obtained as a result of the stimulation of β-receptors[7].

Pancreas response. Insulin expressed in μU/mg tissue/15 min

Baseline	Response (test substance added)		Δ	P
$0.3 \times 10^{-2} M$ glucose	$1.7 \times 10^{-2} M$ glucose	$0.3 \times 10^{-2} M$ glucose + 8.07×10^{-4} mM ISO		
22.0 ± 2.1 (9)	41.0 ± 3.2 (9)		+ 19.0	< 0.01
21.2 ± 2.6 (7)		35.6 ± 1.9 (7)	+ 14.4	< 0.01

Figures represent mean value ± S.E.M. No. of cases in brackets.

Resumen. Se estudió el efecto del isoproterenol (ISO) sobre la secreción de insulina in vitro. Los resultados indican que el ISO es capaz de estimular la secreción de insulina en forma similar a la glucosa en altas concentraciones.

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Distribution of Noradrenaline in the Genital Organs of the Female Rat with a Remark on Dopamine in the Cervix and Vagina

Recent investigations have revealed a distinct adrenergic innervation to the different female reproductive organs of several mammals, e.g. rabbit[1], cat[2], guinea-pig[3] and human female[4]. Furthermore, a considerable variation of the amount of adrenergic innervation to various parts of the female genital tract has been demonstrated[5]. In contrast to the species mentioned, the female rat has been reported to receive adrenergic innervation to the genital organs almost exclusively as blood vessel innervation[6,7]. However, histochemical findings have indicated that at least the isthmic part of the rat oviduct may receive adrenergic nerves to the smooth muscular wall as well[6,8]. Because of this finding it seemed to be of interest to make a quantitative estimation of the adrenergic innervation to various parts of the female rat genital tract by determination of their noradrenaline (NA) content.

Material and methods. 60 adult female Sprague-Dawley rats weighing 180–250 g were used. No determination of the stage of estrus cycle was performed since it has been

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shown that the normal hormonal variations do not influence the endogenous NA content of the uterus[9,10]. The animals were killed by decapitation under light ether anaesthesia. The genital organs were rapidly removed, weighed and homogenized in 0.4 *N* perchloric acid. The following organs were taken: the ovary, the oviduct with 2 mm of the uterine horn, the rest of the uterine horn and the cervix with the adjacent $^1/_4$ of the vagina.

Because of the small amounts of NA expected, organs from 19–21 animals were pooled together in 3 experiments. The samples were passed through columns of alumina (0.5 × 0.8 cm) and eluted with 0.25 *N* acetic acid. The catecholamines were determined fluorimetrically according to CHANG[11].

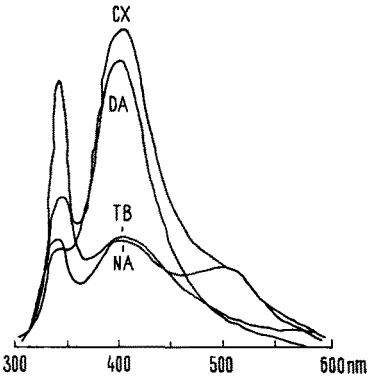
Results. The results are presented in the Table and the Figure. The NA is expressed as μg free base/g wet tissue weight.

With the method of CHANG[11], it is possible to determine NA and dopamine (DA) selectively in the same sample because of the great difference in activating and fluorescence wave-lengths of the corresponding fluorophores (NA 390/500, DA 330/400, uncorrected instrumental values). When read at the DA wave-lengths, a significant difference from the tissue blank value was obtained in the cervix-vagina sample (Figure). This corresponds to a DA content of about 0.27 μg/g. Traces of DA were also found in the sample from the uterine horn but not from those from the ovary or oviduct.

Discussion and conclusions. From the present results it is obvious that NA is unevenly distributed in the genital tract of the female rat with the largest amounts occurring in the oviduct. A distinct adrenergic innervation of the isthmic part of the rat oviduct has recently been reported[8]. These observations together further support the possibility of an adrenergic influence on rat oviduct function similar to that of the rabbit[12].

Comparatively large amounts of NA were also found in the samples from the cervix and upper part of vagina as compared to those of the uterine horns. Partly this NA could derive from ganglionic cells in the cervical area[5]. A similar difference in NA content between the cervix and the corpus of the human uterus has recently been reported[4]. The fairly low amounts of NA found in the uterine horns speak against a major adrenergic influence on uterine activity in this species. Earlier studies on the uterine content of NA in the rat show higher values, about 0.25 μg per g[9,13,14]. However, in these studies no separation was evidently made between cervical and uterine horn specimens.

The unexpected finding of DA in the cervical region of the rat is noteworthy in view of the fact that the female genital organs of other species studied (cat, rabbit, guinea-pig and human) have been found to lack measurable amounts of DA[5]. The origin of the DA found in the rat cervical region is at present obscure. However, fluorescent cells containing an unidentified monoamine have been reported to occur in the vicinity of adrenergic ganglia[5,15–17]. Furthermore, unpublished observations have revealed the presence of non-neuronal, intensively fluorescent cells in the cervical region of the female rat[18]. Since no peripheral dopaminergic neurons have been described so far, these cells may be the origin of the demonstrated DA. The functional implication of this finding is unknown[19].



Fluorescence spectrum of dopamine standard 0.1 μg (DA), noradrenaline standard 0.1 μg (NA), extract from the cervix (CX) and the corresponding tissue blank (TB). Activating wave-length 330 nm.

Noradrenaline distribution in the genital organs of the female rat

Sample	Noradrenaline μg/g			
	Ovary	Oviduct	Uterine horn	Cervix and vagina
I	0.13 (40)	0.09 (40)	0.28 (40)	0.24 (40)
II	0.13 (42)	0.07 (42)	0.32 (42)	0.26 (42)
III	0.11 (38)	0.06 (38)	0.31 (38)	–

No. of pooled organs in brackets.

Zusammenfassung. Durch Bestimmung des organeigenen Noradrenalingehalts wird die adrenergische Innervation der weiblichen Geschlechtsorgane der Ratte untersucht. Die Hauptmenge des Noradrenalins (0,3 μg/g) wird im Tuba uterina gefunden, der vierfache Betrag von Uterusinhalt. Daneben wurde Dopamin in Cervix und Vagina nachgewiesen.

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