THE INFLUENCE OF HORMONAL STATE ON THE RESPONSE OF THE ISOLATED RABBIT OVIDUCT TO CATECHOLAMINES

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The histochemical demonstration of adrenergic innervation in the isthmus of the rabbit oviduct (Brundin, 1965) raises the possibility that these nerves are of significance in the control of egg transport. Since the rate of egg transport may be altered by the administration of both oestrogenic and progestational substances (see Chang & Harper, 1966; Kendle & Telford, 1970), several studies have been undertaken to investigate the possible interaction between hormonal state and nervous activity.

The results of one such recent study (Howe & Black, 1973) indicated that the muscular response to α- and β-adrenoceptor stimulation was dependent on oestrogen and progesterone. The present investigation extends these observations by using an in-vitro method to enable simultaneous recording of longitudinal and circular muscle activity under conditions of natural oestrogen and progesterone dominance. Uterine histology was also examined to enable the correlation of the results with the actual hormonal background at the time of autopsy.

Five mature New Zealand White does were used to provide tissue under endogenous oestrogenic domination. A further six were given 50 i.u. HCG (Pregnyl, Organon) intravenously and were killed 4 days later to provide tissue under endogenous progesterone domination. At autopsy, a portion of the uterus was removed from each animal and fixed in buffered formol. Sections were subsequently cut using a freezing microtome and stained with 0·1 % w/v methylene blue. The degree of endometrial proliferation was assessed according to the method described by McPhail (1934).

A standard length (5 cm) was taken from the uterine end of the left oviduct from each animal, and the tissue was suspended in an isolated organ bath containing Ringer's solution (sodium chloride, 0·9 %; potassium chloride, 0·042 %; calcium chloride, 0·024 %; sodium bicarbonate, 0·05 %; and glucose, 0·1 % w/v). The temperature was maintained at 37°C and the solution was oxygenated with a mixture of 95 % O₂: 5 % CO₂. The ampullary end of the portion of isthmus was tied round a cannula formed by bending a No. 12 hypodermic needle through 180° and removing the point. The uterine end of the tissue, which was then uppermost in the organ bath, was connected by
thread to an optical wedge transducer (Scientific and Research Instruments Ltd) to record longitudinal muscle activity. Ringer solution was pumped through the cannula into the oviduct at a rate of 0.59 ml/min, using a motorized syringe (Palmer Instruments). The resistance to flow was measured by a physiological pressure transducer (Bell and Howell) as an index of circular muscle activity.

Preliminary investigations on tissues from seven rabbits showing various degrees of endometrial proliferation from full oestrogenic to full progestational domination indicated that the in-vitro preparation was unsuitable for demonstrating the effects of $\beta$-adrenoceptor stimulation. This was possibly due to the spontaneous muscle tone being low in vitro so that further inhibition produced no apparent change. Inhibitory responses may be readily observed in vivo (see Howe & Black, 1973). These investigations also indicated that the $\alpha$-adrenoceptors present in the circular muscle layer were atypical as they were more sensitive to adrenaline than to noradrenaline. This is the reverse of the relative sensitivities of typical $\alpha$-adrenoceptors (Ahlquist, 1948). As a result of these investigations, adrenaline was chosen for further study.

Dose–response curves to adrenaline were determined for each of the eleven portions of oviduct. The curves were prepared by measuring longitudinal and circular muscle responses to four suitable concentrations of adrenaline introduced into the organ bath for a standard time, three or four replicate responses at each concentration being obtained. From these data, the slope of the log dose–response curve to adrenaline for each tissue was calculated.

Because of the variation in the degree of progestational domination indicated by the endometrial proliferation index, the results obtained were divided into three experimental groups. The results of two of these groups, oestrogen-dominated (McPhail scores \( \downarrow \)) and progesterone-dominated (McPhail scores 3 to 4) are summarized in Table 1. The significance of difference of mean slopes between these groups was determined using Student’s $t$ test.

The third group consisted of three animals whose uterine histology indicated incomplete progesterone dominance (mean McPhail score 2). The mean slopes of the log dose–response curves in the group were intermediate between those

**Table 1.** Slopes of the log dose–response curves to adrenaline on isolated oviducts from oestrogen- and progesterone-dominated rabbits

<table>
<thead>
<tr>
<th>Group</th>
<th>McPhail score</th>
<th>Slopes of log dose–response curves</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Circular muscle</td>
</tr>
<tr>
<td>Oestrogen-dominated</td>
<td>1</td>
<td>40-83</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>54-17</td>
</tr>
<tr>
<td>Progesterone-dominated</td>
<td>4</td>
<td>3-33</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>17-50</td>
</tr>
</tbody>
</table>

* Significantly different, 0.001 < $P$ < 0.01 ($t = 5.44$; d.f. = 6). N.S., not significantly different.
of the other two groups but, because of wide variation and the small number of estimates, they were not significantly different from either of the other group means.

The results given in Table 1 confirm the findings of previous workers (Howe & Black, 1973) that \( \alpha \)-adrenoceptor activity in the circular muscle layer is depressed by progestational domination. Despite the fact that only four replicates are included in each experimental group, the depression is statistically highly significant, provided that the animals are grouped according to their actual hormonal background. This was indicated by the McPhail score of uterine histology, and did not correspond exactly to the expected hormonal background on the basis of the treatment given.

The results further indicate that the depression of \( \alpha \)-adrenoceptor activity under progestational domination is confined to the atypical \( \alpha \)-adrenoceptors of the circular muscle layer, and is not due to a non-specific muscular depressant activity of progesterone as the responses of the longitudinal muscle are not affected. If these preliminary findings can be confirmed and extended to include other species, they are of potential practical application for the control of fertility. The main difficulty of applying drugs acting on the autonomic nervous system to fertility control is their widespread effects elsewhere in the body. If, however, the \( \alpha \)-adrenoceptors of the circular muscle of the oviduct are atypical, it is possible that selective agonists and antagonists may be developed to regulate the activity of this tissue only.

REFERENCES