Cardiovascular sensitivity of experimentally diabetic and genetically obese pithed rats to autonomic agents

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The increased risk of autonomic malfunction associated with diabetes mellitus is now well established. Impaired vagal function has been demonstrated in diabetic patients by Dotevall, Fagerberg, Langer & Walan (1972) and Wheeler & Watkins (1973). Hyper-responsiveness to noradrenaline has been demonstrated in vascular tissue from experimentally diabetic animals, e.g. in perfused rat hindquarters by Brody & Dixon (1964) and in the isolated rabbit aorta by Cseuz, Wenger, Kunos & Szentivany (1973). In this communication a comparison between the differences in sensitivities of the cardiovascular systems of two week streptozotocin (60 mg/kg i.v.) and one week alloxan (50 mg/kg i.v.) diabetic CFE male rats and their untreated controls (10, 5 and 10 respectively) and between genetically obese (Zucker strain) and their non-obese litter mates (6 and 7 respectively) is presented. The animals were pithed and dose-response curves to noradrenaline, isoprenaline and acetylcholine constructed. Animals treated with the diabetogens were only considered diabetic if their blood glucose was found to be above 250 mg per 100 ml blood (estimation of blood glucose was by a micro-colorimetric copper reduction method). Falls in mean blood pressure caused by 1 and 3 μg/kg acetylcholine were significantly ($P < 0.05$) reduced in both diabetic groups compared with their controls. The genetically obese rats, however, appeared to have similar sensitivities to their non-obese litter mates. Rises in mean blood pressure caused by 100 ng, 300 ng, 1 μg and 3 μg/kg noradrenaline were all significantly ($P < 0.01$) reduced in the streptozotocin but not in the alloxan diabetic group. The pressor response to noradrenaline was similar in the obese group compared to their non-obese litter mates.

Changes in blood pressure due to isoprenaline were not significantly different in any of the three test groups compared with their controls. Changes could, however, have been obscured by the rather large standard errors obtained.

The lack of increased noradrenaline sensitivity in alloxan diabetic rats contrasts with the results of Brody & Dixon (1964).

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Inhibition of the effects of weight-reducing drugs in guinea-pigs by Vitamin C

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Administration of fenfluramine produces loss of weight and anorexia in guinea-pigs (groups of 5) on a scorbutogenic diet (Odumosu & Wilson, 1974). This effect occurs in consequence of the immediate tissue depletion of ascorbic acid produced by the drug. Its anti-obesity action is inhibited by administration of supplementary Vitamin C. The change in body weight and anorexia after administration of saline, fenfluramine, diethylpropion or mazindol were investigated over a period of 72 h, in guinea-pigs, after 24-h fasting. The drugs were given i.p. in doses of fenfluramine (F) 15 mg/kg, diethylpropion (D) 50 mg/kg, mazindol (M) 15 mg/kg, with or without Vitamin C 30 mg/kg s.c. Body-weight increased by 5% after 72 h in the guinea-pigs receiving saline. In those receiving Vitamin C, weight increased by 8%, confirming the finding of Williams & Hughes (1972). Fenfluramine (15 mg/kg) caused a 5% reduction in body weight after 7 h which had decreased to 6% by 24 hours. After 60 h the guinea-pigs in the F group had regained their initial weight. Administration of Vitamin C to guinea-pigs in the F group caused them to gain weight after 7 h so that the initial weight was regained after 48 hours. Mazindol caused 2% (not

significant) loss of weight which had been regained after 7 hours. After 72 h guinea-pigs in the M group were as heavy as the group receiving the Vitamin C supplement alone. Administration of Vitamin C to guinea-pigs in the M group completely inhibited weight loss.

Vitamin C had increased food intake to 140% of that in the saline treated group 2 h after its administration. Fenfluramine inhibited food intake for 5 h in the same fashion as mazindol and diethylpropion. After 48 h food intake was 85% of that in the saline treated group. Supplementary Vitamin C caused guinea-pigs in the D group to increase their food intake 1 h sooner than the F group. In the M group Vitamin C restored food intake to 60% of that in the saline group within 2 h of administration. Administration of Vitamin C can differentiate between the anti-obesity and anorectic actions of weight-reducing drugs. It inhibits the anti-obesity action, but has little effect on the anorectic action, of fenfluramine and diethylpropion. Vitamin C inhibits the anti-obesity action of mazindol and reduces its anorectic effect.

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Rat liver tryptophan pyrrolase activity in iron deficiency anaemia

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Liver tryptophan pyrrolase (TP) is one of the peripheral factors affecting 5-hydroxytryptamine (5-HT) synthesis (Badawy & Evans, 1974) and is inversely-related to brain (5-HT) concentration (Curzon, 1969). The haem activator of TP contains Fe, and we therefore examined the effect of iron deficiency on TP activity and on three of its regulatory mechanisms.

Male Wistar rats (Tucks, Rayleigh, Essex) were made mildly- or severely-Fe-deficient by the diet of McCall, Newman, O'Brien, Valberg & Witts (1962). Control rats received the same diet supplemented with Fe. The deficiency was verified by haematological tests. The determination of TP activity in the absence (holoenzyme) or the presence (total enzyme) of added haematin, and the doses of injected compounds have previously been described (Badawy & Evans, 1973). The haem-free apoenzyme was calculated by difference. The results in mildly- and severely-Fe-deficient rats, as well as in their respective controls, were similar and were therefore pooled.

Control rats ('A' groups) gave typical results

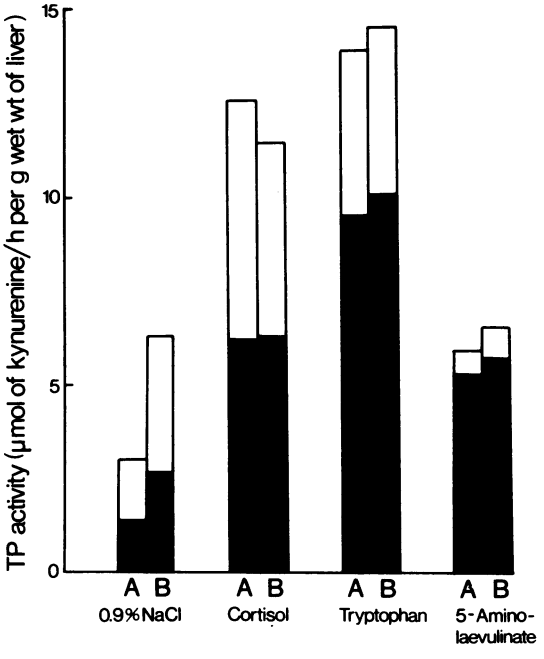

Figure 1 Comparison of tryptophan pyrrolase activities in iron-deficient and control rats.
The enzyme activity was determined at 4 h after intraperitoneal administration of various compounds. Closed columns represent holoenzyme whereas open ones apo-enzyme activity. The sum of the two columns gives the total activity. A, Control rats; B, iron-deficient rats.