

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 microcolorimetric 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).

References

- BRODY, M.J. & DIXON, R.L. (1964). Vascular reactivity in experimental diabetes mellitus. *Circulation Res.*, **14**, 494-501.
- CSEUZ, R., WENGER, T.L., KUNOS, G. & SZENTIVANY, M. (1973). Changes of adrenergic reaction pattern in experimental diabetes mellitus. *Endocrinology*, **93**, 752-755.
- DOTEVALL, G., FAGERBERG, S.E., LANGER, L. & WALAN, A. (1972). Vagal function in patients with diabetic neuropathy. *Acta med. scand.*, **191**, 21-24.
- WHEELER, T. & WATKINS, P.J. (1973). Cardiac denervation in diabetes. *Brit. med. J.*, **4**, 584-586.

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, fenflur-

amine, 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