THE METABOLIC EFEECTS OF VILOXAZINE IN OBESE RATS

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In a previous communication (Kirby et al, 1978) we described the ability of the antidepressant drug viloxazine to lower body weight in obese rats. In this paper we present the results of further studies on the metabolic changes accompanying this fall in weight.

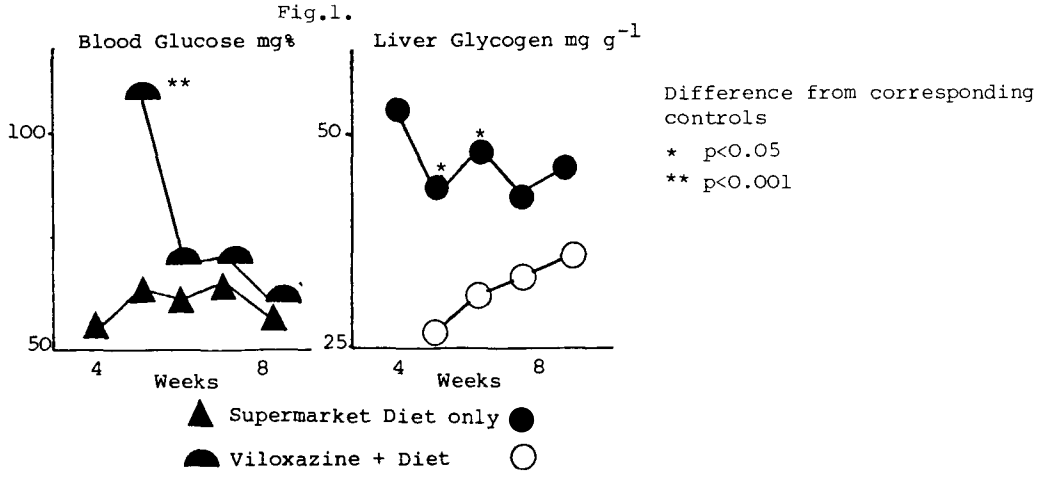
Groups of 6 female Wistar rats (University of Bath strain) weighing 200±10g were allowed free access to a varied diet of 'supermarket' foods, as described in detail elsewhere (Pleece et al, 1978). After 8 weeks, body weight increased by 135±9g. In contrast, in animals recieving viloxazine in the drinking water, starting at week 4 at a dose of 80mg.kg^{-1} and increasing by week 7 to 240mg.kg^{-1} the increase was only 92±8g. As expected, blood concentration of total lipid and cholesterol increased in animals fed the supermarket diet (789±78mg.100ml^{-1} & 55±5mg.100^{-1} respectively compared to values of 515±55 and 38±5 in pellet-fed controls).

Viloxazine administration induced a sustained fall in serum lipids (581±57mg.100 ml^{-1} compared to 789±78 at 8 weeks) indicating that the fall in body weight produced by the drug is caused by decreased food intake rather than mobilisation of fat stores. Introduction of viloxazine into the drinking water also produced an immediate increase in blood glucose and a corresponding decrease in liver glycogen (Fig. 1) indicating a mobilisation of glycogen stores.

Serum free and total tryptophan (TRY) concentrations did not change during development of obesity. However, administration of viloxazine at week 4 produced an immediate and sustained increase in free TRY (5.7±0.9µg.ml^{-1} compared to 2.9±0.6 in controls) followed by a similar increase in total TRY.

Free fatty acids are known to compete with TRY for binding sites on serum albumin. In decreasing body weight and total serum lipids, it might be predicted that viloxazine would increase bound TRY at least transiently. However, in our experiments, significant changes were first observed in free TRY. Further, the increase in free and total TRY was sustained over the 4 week treatment period; if viloxazine increased free TRY in serum by preventing passage of the amino acid into brain tissue, rapid increase in TRY metabolism by liver pyrrolase would be expected to reverse the change.

Fig.1.



Kirby, M.J., Pleece, S.A., Redfern, P.H. (1978) J.Pharm.Pharmac. 30: P36
Pleece, S.A., Kirby, M.J., Redfern, P.H. (1978) Br.J.Pharmac. 64: P442