Effect of fenfluramine and norfenfluramine on glucose uptake by the isolated rat diaphragm

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It has been suggested that part of the action of fenfluramine is due to an increase in skeletal muscle uptake of glucose (Butterfield & Whichelow, 1968), but Garrow and his co-workers (1972) were unable to confirm this. We have investigated this effect on an *in vitro* preparation of rat hemidiaphragm, using the method described by Frayn & Adnit (1972). Campbell (1971) showed that norfenfluramine is the main metabolite of fenfluramine and the effect of this compound was also investigated.

The effects of both drugs were studied on the isolated rat diaphragm in the presence of 100 μU/ml insulin and in the absence of insulin. In the presence of insulin both fenfluramine and norfenfluramine caused a similar and significant increase in glucose uptake (Table 1). Diaphragms incubated in the absence of insulin did not show any significant increase in uptake. Measurement of the glycogen content after incubation did not show any significant changes in the drug treated diaphragms.

These results would suggest that fenfluramine and norfenfluramine in therapeutic concentrations influence peripheral glucose uptake.

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Table 1 Effect of fenfluramine and norfenfluramine on glucose uptake by the isolated rat diaphragm

	Fenfluramine						*Norfenfluramine*					
No insulin present												
Drug ng/ml	0	10	0	100	0	1000	0	10	0	100	0	1000
Mean glucose uptake*	5.3	4.9	5.4	6.0	6.1	6.2	7.4	7.6	7.1	7.5	8.1	7.6
Mean percentage change ±s.e. mean†		+2 ± 12		+16 ± 9		+14 ± 9		+10 ± 13		+7 ± 9		+6 ± 7
t		0.17		1.67		0.41		0.77		0.78		0.89
Significance *P*		N.S.		N.S.		N.S.		N.S.		N.S.		N.S.
With insulin 100 μU/ml												
Drug ng/ml	0	10	0	100	0	1000	0	10	0	100	0	1000
Mean glucose uptake*	7.1	8.4	6.9	9.3	8.7	11.1	7.2	8.5	6.4	8.2	8.2	10.4
Mean percentage change ±s.e. mean†		+22 ± 11		+42 ± 12		+29 ± 7		+19 ± 14		+30 ± 9		+13 ± 7
t		1.89		3.59		4.11		1.39		3.33		4.30
Significance *P*		0.1 > *P* > 0.5		0.01 > *P* > 0.001		0.01 > *P* > 0.001		N.S.		0.01 > *P* > 0.001		0.01 > *P* > 0.001

* Results expressed in mg glucose taken up/gram fresh weight of tissue in 90 minutes.
† All comparisons are made on a 'within rat' basis. Means of 10 experiments.
N.S. = not significant.

References

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