These results agree with the concept of Lands and others that there are different β-receptor mechanisms in different tissues but are difficult to reconcile with their simple two receptor hypothesis.

Department of Pharmacology,
Allen and Hanburys Ltd.,
Ware, Herts, U.K.

J. B. FARMER
G. P. LEVY

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Antagonistic effects of dopa and propranolol on brain glycogen

We have reported previously that propranolol raises the glycogen content of the brain (Estler & Ammon, 1966, 1967), but we could not decide whether this effect was attributable to the anti-adrenergic effect of propranolol, which, by lowering the cyclic 3′,5′-AMP content of the brain, should inhibit glycogen breakdown and favour glycogen synthesis, or to the central depressant properties of propranolol, described by Leszkovsky & Tardos (1965), Murmann, Almirante & Saccani-Guelfi (1966) and Estler & Ammon (1969), that could likewise depress glycogenolysis. A decision seemed to be possible, however, on the assumption that the blockade of the adrenergic receptors is competitive (Wang, 1967) and should be overcome by large amounts of catecholamines. Experiments were therefore made on mice treated simultaneously with propranolol, and dopa which was chosen since unlike catecholamines, it crosses the blood brain barrier and penetrates into the brain where it is converted to dopamine and noradrenaline (Hornykiewicz, 1966; Marley, 1966). Dopa should thus antagonize the anti-adrenergic effects of propranolol if given in sufficient amounts.

Female NMRI-mice, kept at 25°, were treated with (±)-propranolol (5 μg/g, i.p.) or with (±)-dopa (300 μg/g, i.v.) or with both. 30 or 60 min later they were killed by immersion in liquid air. The brains were removed while still frozen and glycogen was measured (Kemp & Kits van Heijningen, 1954). Motility was measured in circular activity cages (Estler & Ammon, 1969).

As in our previous experiments (Estler & Ammon, 1966, 1967), propranolol did not significantly affect the spontaneous motor activity of single mice, but the glycogen content of the brain was increased (Table 1). The behavioural effect of dopa may range from central stimulation to central depression, depending on the species, dose and experimental condition (Boissier & Simon, 1966; Hornykiewicz, 1966). In our experiments 300 μg/g of dopa much reduced the motor activity of mice and temporarily lowered the glycogen content of the brain, a decrease probably attributable to the glycogenolytic action of catecholamines derived from dopa. After 1 h, brain glycogen concentrations returned to normal. In this way the effects of dopa are in contrast to those of other central depressants, which raise the glycogen content of the brain (Ammon, Estler & Heim, 1965), but resemble those of ethanol

Table 1. *Effects of propranolol and dopa on motor activity and cerebral glycogen in mice*

Treatment	Spontaneous motor activity (Impulses/30 min) min after treatment 0–30	30–60	Cerebral glycogen (μmol glucose equivalents/g) min after treatment 0	30	60
Controls	138 ±11 (34)	73 ±11 (34)	6·36 ±0·20 (14)	—	—
(±)-Propranolol 5 μg/g, i.p.	134 ±17 (24)	60 ±11 (24)	—	6·85* ±0·23 (13)	7·60* ±0·28 (12)
(±)-Dopa 300 μg/g, i.v.	44* ± 6 (35)	25* ± 4 (35)	—	5·81* ±0·20 (12)	6·30 ±0·21 (12)
(±)-Propranolol 5 μg/g, i.p.+ (±)-Dopa 300 μg/g, i.v.	46* ± 7 (35)	23* ± 4 (35)	—	6·24† ±0·20 (14)	6·98*† ±0·20 (12)

Mean values and standard errors of the means (s.e.), number of animals in parentheses.
* Value significantly different from the control, $P \leqslant 0{\cdot}05$.
† Significantly different from mice treated with propranolol alone, $P \leqslant 0{\cdot}05$.

which depresses CNS function and transitorily decreases the cerebral glycogen content by releasing catecholamines from their stores (Ammon & others, 1965; Estler & Ammon, 1965). When given simultaneously with propranolol, dopa prevented the increase of the glycogen content within the first 30 min after its injection. Later, the glycogen rose at the same rate as in the animals treated with propranolol alone.

Our experiments show that the β-receptor blocking agent propranolol and the sympathomimetic drug dopa have similar effects on brain function but antagonistic effects on brain glycogen. It seems reasonable to assume that the glycogen metabolism of the brain is controlled by adrenergic mechanisms and that the increase of brain glycogen produced by propranolol is the result of the β-receptor blocking rather than the central depressant properties of propranolol.

Pharmakologisches Institut
der Universität Erlangen-Nürnberg,
Universitätsstr. 22,
D–8520 *Erlangen, Germany.*

C.-J. ESTLER
H. P. T. AMMON

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