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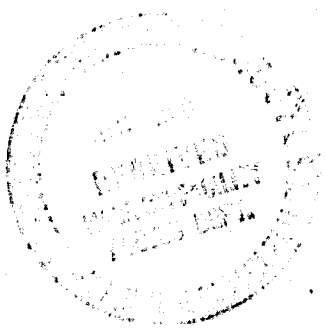
EFFECT OF PSYCHOTROPIC DRUGS ON GASTRIC ULCERS INDUCED BY IMMOBILIZATION. INCREASED PROTECTIVE EFFECT OF AMITRIPTYLINE CAUSED BY CHLORDIAZEPOXIDE

J. E. Blum and A. Huerlimann

Translation of "Zur Beeinflussung der durch Immobilisation ausgeloesten Magenulcera durch Psychopharmaka: Verstaerkung der Schutzwirkung von Amitriptylin durch Chlordiazepoxid," Medicina et Pharmacologia Experimentalis, Vol. 15, No. 6, 1966, pp 615-617.



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16. Abstract

Amitriptyline, but not chlordiazepoxide, protects rats from the occurrence of gastric erosions and ulcers following immobilization. When, however, chlordiazepoxide is given together with amitriptyline the protective effect of the latter is markedly increased.

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EFFECT OF PSYCHOTROPIC DRUGS ON GASTRIC ULCERS INDUCED BY IMMOBILIZATION. INCREASED PROTECTIVE EFFECT OF AMITRIPTYLINE CAUSED BY CHLORDIAZEPOXIDE

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Several hours of immobilization produce erosion and ulceration in the rat stomach [1, 2]. They are probably the consequence of a "stress reaction" (Selye) which is also probably responsible in humans for ulcers that occur following psychic trauma, burns and infections. In this context corticoid treatment promotes the occurrence of erosion [3]. /615*

The assumption of a central origin for erosions following immobilization in rats would require that, in addition to drugs that affect the stomach in a peripheral way, those drugs that have a central effect may also affect the occurrence of such mucosa erosions. The effect of atropine and neutralizing substances is well known [2, 4]. Many drugs that work on the central nervous system have autonomic effects, so that it is difficult to decide whether a protective effect is due to a peripheral or central action. This is not parallel with the central depressive effect [1].

Our study showed a protective effect for various psychotropic drugs that have an anticolinergic effect, as for example amitriptyline, in respect to erosions and ulcerations in the rat gastric mucosa due to immobilization. Other drugs with practically no autonomic effect, such as chlordiazepoxide, were ineffective in the experiment. However chlordiazepoxide had the capability of strengthening the effect of amitriptyline. We have no explanation for this phenomenon but we would like to report it briefly.

Method /616

The experiment was done on male albino rats weighing 60-70 g and belonging to our own closed, randomized Fuellinsdorf breed. 10 animals at a time were immobilized

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* Numbers in the margin indicate pagination in the foreign text.

for 16 hours following 48 hours of fasting with superficial ether anesthesia using the method of Bonfils [1] and Hanson and Brodie [2]. Then the animals were sacrificed with ether and the gastric mucosa examined with the naked eye for the presence or absence of erosions.

The animals being treated were given the preparations subcutaneously 30 minutes prior to the beginning of immobilization. Preparations used were amitriptyline hydrochloride and chlordiazepoxide hydrochloride.

Results

All the animals that were not treated presented usually a number of erosions with one possible exception. Chlordiazepoxide had no effect even in large, highly sedative doses. The protective effect of amitriptyline depended upon the dosage. When it was given simultaneously with chlordiazepoxide the protective effect was greater than for amitriptyline alone:

Preparation	Dose in mg/kg subcut.	Protective effect (Number of animals from a group of 10 showing no erosion)	Protective dose of amitriptyline calculated on half the animals showing no erosion
Controls		0 0	
Chlordiazepoxide	5 10 50	0 0 0	
Amitriptyline	2,5 5 7,5 10	2 5 8 9	4,6 mg/kg s.c.
Amitriptyline (A) + Chlordiazepoxide (C)	A 1,25 + C 0,5	1	
	A 2,5 + C 1	5	2,7 mg/kg s.c.
	A 5 + C 2	8	

The dosage effect curves for amitriptyline alone and when combined with chlordiazep-/617 oxide are regressive straight lines running parallel in a statistically reliable way

($p < 0.01$; correlation coefficient $r_{AC} = r_A = 0.99$; regression coefficient $b_{AC} = b_A = 11.8$ [1].

The results show that doses of chlordiazepoxide, which are ineffectual by themselves, reinforce the protective effect of amitriptyline over a wide dosage range approximately 1.7 times (1.52-1.82 in a reliable range of 95%).

Footnote

1. The statistical calculations were graciously performed by W. J. Ziegler.

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