

## N O T I C E

THIS DOCUMENT HAS BEEN REPRODUCED FROM  
MICROFICHE. ALTHOUGH IT IS RECOGNIZED THAT  
CERTAIN PORTIONS ARE ILLEGIBLE, IT IS BEING RELEASED  
IN THE INTEREST OF MAKING AVAILABLE AS MUCH  
INFORMATION AS POSSIBLE

EFFECT OF HABITUATION ON THE SUSCEPTIBILITY OF THE RAT  
TO RESTRAINT ULCERS

M.S. Martin, F. Martin and R. Lambert

Translation of "Effet de l'habituatation sur la sensibilité du Rat à  
l'ulcère de contrainte", Comptes Rendus des Séances de la Société  
de Biologie et de ses Filiales, Vol. 164, No. 4, 1970, pp 826-828

(NASA-TM-76072) EFFECT OF HABITUATION ON  
THE SUSCEPTIBILITY OF THE RAT TO RESTRAINT  
ULCERS (National Aeronautics and Space  
Administration) 12 p HC A02/MF A01 CSCL 06C

N80-19748

Unclas  
14916

G3/51

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION  
WASHINGTON, D.C. 20546  
MARCH, 1980



EFFECT OF HABITUATION ON THE SUSCEPTIBILITY OF THE RAT  
TO RESTRAINT ULCERS

M.S. Martin, F. Martin and R. Lambert

Unité de Recherches de Physiopathologie Digestive, INSERM,  
Hôpital Edouard Herriot, Lyon

When a rat is subjected to repeated periods of restraint, two opposing factors intervene in the development of gastric lesions: the cumulative effect of the restraint tends to aggravate these lesions, and habituation to stress tends to minimize them (1). We attempted to dissociate the latter factor by habituating the rat to periods of restraint of too short a duration to give rise to ulcers, while respecting a sufficient interval between the periods of immobilization.

Materials and Method

We used 30 Wistar rats, 10 males and 20 females, weighing 200 to 270 grams. These animals we divided into two groups of 15 rats, evenly balanced in terms of sexes and weights. Restraint was always carried out in metal tubes (2), in an air-conditioned room at a temperature of 22°C.

The rats of the first group were habituated to conditions of restraint by 4 sessions of 6 hours each during which they were immobilized in metal tubes. These 4 sessions were spread over a period of 2 to 4 weeks, respecting an interval of 3 to 15 days (average, 6.6 days) between periods of restraint. Three days after the fourth session, the rats were subjected to a 24-hour period of restraint.

The rats of the second group were used as controls. They underwent no habituation sessions and were subjected directly, at the same time as the animals of the first group, to the 24-hour restraint period.

At the end of the 24-hour restraint period, the rats of both groups were sacrificed, using ether. The stomachs were examined. Only ulcerous lesions were taken into account. These lesions are considered severe when at least one of them has reached a diameter of 3 mm.

### Results

The table shows that the rats which were first habituated to restraint are less susceptible to ulcers than the control animals; this difference is significant ( $p < 0.05$ ). The difference is also very clear when we compare the animals which were affected by serious lesions. In this group in fact, we find only one rat habituated to restraint, as opposed to 8 control rats. Habituation of the rat, then, reduces both the occurrence and the severity of restraint ulcers.

We also noted differences in the behavior of two groups of rats with regard to restraint: the control rats spontaneously entered the restraint tube, while the habituated rats showed an increasingly marked unwillingness, betraying the memory of previous stress. However, defecation by the rats, a barometer of their emotional condition, gradually diminishes in the course of repeated restraint periods.

TABLE: COMPARISON OF THE OCCURRENCE OF ULCERS IN RATS HABITUATED TO RESTRAINT AND IN CONTROL ANIMALS

Series	Repeated restraint			Control group		
	No. of rats	No. of rats w/ulcers	No. of rats w/serious ulcers	No. of rats	No. of rats w/ulcers	No. of rats w/serious ulcers
1	5 f	3	1	5 f	4	4
2	5 m	0	0	5 m	3	1
3	5 f	1	0	5 f	3	3
Total	15	4 (27%)	1 (7%)	15	10 (67%)	8 (53%)

In each series the rats which were habituated to restraint developed ulcers less frequently than the control group.

### Discussion

The cumulative ulcerogenous effect of repeated restraint can predominate over habituation when the rat is subjected to long periods of immobilization, separated by short intervals (3). Bonfils (1), using 24-hour periods of restraint separated by free intervals of 48 hours, notes a progressive reduction of recent ulcers (effect of habituation) contrasting with an increase of healing lesions (cumulative effect). Guth and Mendick (4), subjecting rats to daily but brief periods of restraint (4 hours), observed as we did, a gradual reduction in the occurrence of ulcers.

In our experiment we attempted to completely dissociate the phenomenon of habituation from the cumulative effects of respecting an interval of three days between the last habituation session and the final period of restraint and by using, for habituation, 6-hour restraint periods. In our experimental conditions, a 6-hour restraint period may be considered as subliminal because it gives rise to a percentage of ulcer development of less than 10% (5).

The possibility of rats becoming habituated to restraint rules out, in practice, the use for restraint test purposes of an animal which has already been subjected to immobilization, even of short duration.

### Summary

The frequency and gravity of restraint ulcers are significantly diminished in rats which have previously been subjected to immobilization of short duration. The habituation of the rat to conditions of restraint probably explains this phenomenon.

#### REFERENCES

1. S. Bonfils, G. Lieffoghe, X. Gelle, M. Dubrasquet and A. Lambling, Rev. Franc. Et. Clin Biol., Vol. 5, p. 253, 1960.
2. M.S. Martin, F. Martin and R. Lambert, Digestion, Vol. 2, p. 253, 1969.
3. D.A. Brodie and H.M. Hanson, Gastroenterology, Vol. 38, p. 353, 1960.
4. P.H. Guth and P. Mendick, Gastroenterology, Vol. 46, p. 285, 1964.
5. C. André, M.S. Martin, R. Lambert, and F. Martin, C.R. Soc. Biol., Vol. 163, p. 162, 1969.