

AD-A253 183



NTATION PAGE

Form Approved
OMB No. 0704-0188

ed to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Ave. of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE 15 July 1992	3. REPORT TYPE AND DATES COVERED September 1989 - September 1991
4. TITLE AND SUBTITLE Isolation Suppresses both Immune and Neuroendocrine Functioning and Decreases the Locomotor Activity of Normal and Immunosuppressed C ₃ H/HeN Mice			5. FUNDING NUMBERS RCC - 4020
6. AUTHOR(S) Daniel L. Collins, Stuart J. Cohen, Dale F. Gruber, Michelle M. D'Alesandro, and G. Andrew Mickley			8. PERFORMING ORGANIZATION REPORT NUMBER AFRRI 3rd Annual Program Review
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Armed Forces Radiobiology Research Institute Bethesda, MD 20889-5145			
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) JUL 22 1992 S C D			10. SPONSORING/MONITORING AGENCY REPORT NUMBER
11. SUPPLEMENTARY NOTES An environmental variable, "isolation" had a dramatic influence on the behavioral, neuroendocrine, and immune systems of C ₃ H/HeN mice.			
12a. DISTRIBUTION/AVAILABILITY STATEMENT Unlimited			12b. DISTRIBUTION CODE Unlimited
13. ABSTRACT (Maximum 200 words) This inter-disciplinary experiment examined the dramatic influence that environmental variables can have on behavioral, neuroendocrine, and immune system parameters. In this study, we examined the effects of housing on locomotion, circulating lymphocytes, and catecholamines (i.e., Norepinephrine [N] and Epinephrine [E]) of 12-week-old female C ₃ H/HeN mice. Ten week old female C ₃ H/HeN mice (10/group) were either immunocompromised (following 0.5 Gy or 4.5 Gy ⁶⁰ Co gamma irradiation) or normal (sham-irradiated), and were housed in isolation (1/cage) or groups (10/cage) for 25 days following radiation exposure. All dependent variables were obtained on day 25 postirradiation.			
14. SUBJECT TERMS Isolation, Immune System, Neuroendocrine, Locomotor activity, Immunosuppression			15. NUMBER OF PAGES 5
			16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unclassified

92-19066



02 7 18 073

ISOLATION SUPPRESSES BOTH IMMUNE AND NEUROENDOCRINE FUNCTIONING AND DECREASES THE LOCOMOTOR ACTIVITY OF NORMAL AND IMMUNOSUPPRESSED C3H/HeN MICE. Daniel L. Collins, Stuart J. Cohen, Dale F. Gruber, Michelle M. D'Alesandro, and G. Andrew Mickley. Armed Forces Radiobiology Research Institute, Bethesda, MD 20814-5145.

This inter-disciplinary experiment examined the dramatic influence that environmental variables can have on behavioral, neuroendocrine, and immune system parameters. In this study, we examined the effects of housing on locomotion, circulating lymphocytes, and catecholamines (i.e., Norepinephrine [N] and Epinephrine [E]) of 12-week-old female C3H/HeN mice. Ten week old female C3H/HeN mice (10/group) were either immunocompromised (following 0.5 Gy or 4.5 Gy ⁶⁰Co gamma irradiation) or normal (sham-irradiated), and were housed in isolation (1/cage) or groups (10/cage) for 25 days following radiation exposure. All dependent variables were obtained on day 25 postirradiation.

Results

Spontaneous Locomotor Activity: Sham-irradiated, isolated mice were significantly less [$t(28)=11.41$, $P<0.001$] active (mean=26.03 cm) than sham-irradiated, group-housed mice (mean=43.94 cm). Isolated mice, irradiated at 0.5 Gy were significantly less [$t(28)=8.77$, $P<0.001$] active (mean=23.5 cm) than group-housed, irradiated (0.5 Gy) mice (mean=42.9 cm). Generally, as dose increased, locomotion decreased, and isolated mice exhibited less locomotion than group-housed mice. At 4.5 Gy, a counterintuitive finding occurred. Group-housed, irradiated mice were initially more active (mean=63.4 cm) than were the isolated, irradiated mice (mean=57.5 cm). However, after 4 minutes, the isolated, irradiated mice were "more active" (43.9 cm) than the group-housed (30.6 cm), irradiated mice; this effect continued for the duration of the experiment (mean=30.4 cm and 20.91 cm respectively), [$t(20)=11.98$, $P<0.001$]. Thus, group housed mice consistently demonstrated greater spontaneous activity at 0.0 Gy or 0.5 Gy, than did isolated mice. However, in the 4.5 Gy condition, the locomotor activity trend reversed 4 minutes into the experiment.

DATA QUALITY INSPECTED 8

Section For	
GRAB V	
TAB	
Source	
Justification	
By	
Distribution/	
Availability	
Dist	Avail and/or Special
A-1	

Neuroendocrine and Lymphocyte Values: The neuroendocrine values were differentially effected by dose and housing condition. Group-Housed mice (GHM) had a larger N/E ratio in the 0.0 Gy and 0.5 Gy conditions than did isolated mice (IM) (i.e., 0.0 Gy: GHM mean=2.6 vs IM mean=1.5; 0.5 Gy: GHM mean=3.6 vs IM mean=3.0). However, in the 4.5 Gy condition a reversal occurred. The N/E ratio of IM was larger (mean=5.1) than that of GHM (mean=3.9). The housing x dose catecholamine ratio reversal, in the 4.5 Gy condition, was due primarily to a massive (81%) decreased value of circulating epinephrine in the isolated mice. Thus, the reversal of locomotor activity in the 4.5 Gy condition may be associated with the circulating catecholamine levels (see Figure 1). Overall, lymphocyte suppression was greater in irradiated IM than in irradiated GHM (see Table 1).

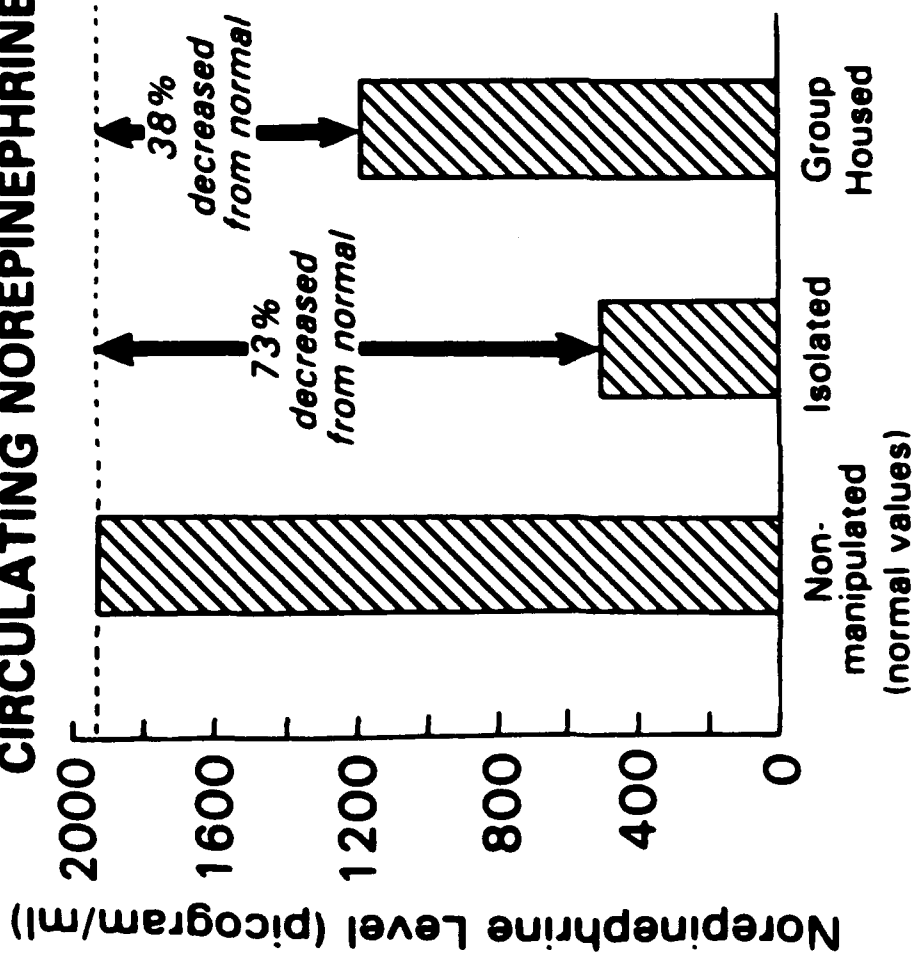
Discussion

In this study, we used an animal model to examine post-irradiation effects on the neuroendocrine system, the immune system, and spontaneous activity. Catecholamine ratios have frequently been used as a better comprehensive index for mental and physical stressors than the value of epinephrine or norepinephrine alone¹. Behavioral alterations, immunosuppression, or hormesis associated with irradiation are not new concepts^{2,3,4}. However, multi-modal studies that examined the effects of ionizing radiation on all of these variables using the same animal could not be found. Thus, this study is unique in its inter-disciplinary approach and suggests that the regulatory processes of the neuroendocrine system are influenced not only by exposure to immunosuppressive radiation but also by environmental factors, such as different housing conditions.

References

1. Krahenbuhl, G.S., Marett, J.R., King, N.W. (1977). Catecholamine excretion in T-37 flight training, Aviation Space and Environmental Medicine, 48, 405-408.
2. Kimeldorf, D.J. and Hunt, E.L. (1965). Ionizing radiation: Neural function and behavior, Academic Press, New York.
3. Cohen, J.J. (1987). Conference on radiation hormesis: An overview, Health Physics, 52,(5), 519.
4. Luckey, T.D. (1989). Hormesis for Health Physicists, The Health Physics Newsletter, Vol XVII,(9), 1-5.

EFFECTS OF HOUSING ON CIRCULATING NOREPINEPHRINE



EFFECTS OF HOUSING ON CIRCULATING EPINEPHRINE

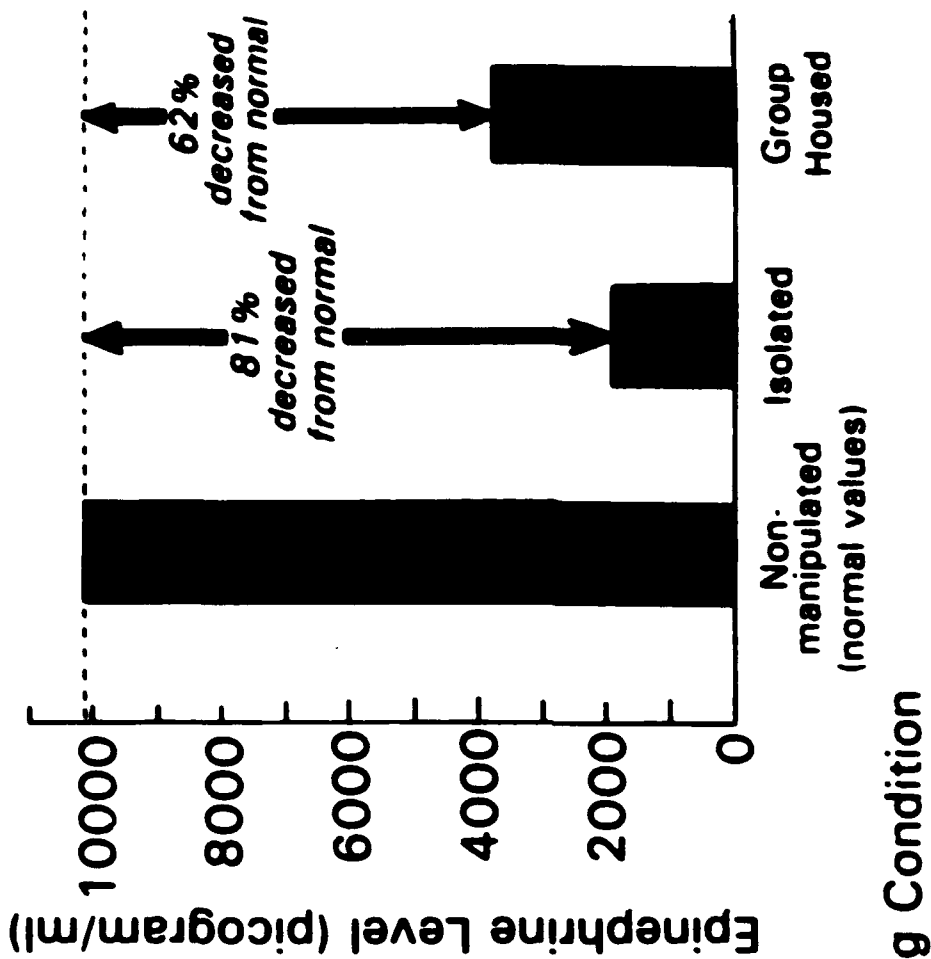


Figure 1

Figure 1: The neuroendocrine values were differentially effected by dose and housing condition. The housing and 60 Cobalt gamma irradiation conditions resulted in substantially reduced circulating values of norepinephrine and epinephrine from normally housed/nonmanipulated mice. Across doses, blood samples showed that the catecholamines of isolated mice were more divergent from normal values, than were the catecholamines of group housed mice.

LYMPHOCYTE SUPPRESSION IN ISOLATED OR GROUP HOUSED IRRADIATED MICE

Table 1	Gy			Mean
	0	0.5	4.5	
Isolated	1.0	2.0	1.0	1.3
Group Housed	2.2	1.4	1.0	1.5
Mean	1.6	1.7	1.0	

All values are $n \times 10^3$

Lymphocyte suppression was greater in isolated, irradiated mice than in group housed, irradiated mice. However, this effect was minimized as it appears that hormesis occurred in the isolated 0.5 Gy condition but not in any other condition.