Changes in Brain Self-Stimulation Rates After Exposure to X-Irradiation

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Abstract □ Alterations in the pressing rate of hypothalamic self-stimulating rats were observed after ionizing radiation. Total-body 600-r X-irradiation would increase, decrease, or not alter the mean pressing rate with generally little change in the daily rate deviation. While there is a correlation between structure and pressing rate, the agreement between irradiation response and hypothalamic structure is not complete. Electrodes in the median forebrain bundle produced no change in pressing rate after irradiation. Head irradiation mainly increased the daily deviation without changing the mean. The whole body irradiation effects are probably not direct.

Keyphrases □ Brain self-stimulation rates—X-irradiation effect □ Electrode position, brain—self-stimulation effect □ Lever pressing rate—self-stimulation determination □ X-irradiation, whole body, head—effect comparison

Electrical self-stimulation is a motivational test which may estimate anatomical correlates of integrative psychological processes (1, 2). However, it has been shown that lever-pressing rates vary greatly, 400–6,000 presses/hr., depending upon the nuclei within which the electrode is placed. It has also been shown that whole-body X-irradiation produces an inconstant effect on the rate of self-stimulation even when the electrodes are implanted in the same hypothalamic nuclei; arcuatus hypothalamic, dorsomedialis hypothalamic, and area lateralis hypothalamic (3). In view of these differences in response, the authors have investigated other brain areas from which low and high self-stimulation rates have been obtained (1, 2) to ascertain the effect of whole-body X-irradiation upon their response.

MATERIALS AND METHODS

Twenty-two female rats, Charles River CD strain, weighing 270 to 350 g., had a bipolar electrode implanted in the hypothalamus following the technique of Haley *et al.* (4, 5). Each animal had a daily 1-hr. session in the apparatus described by Farmer *et al.* (6). Each lever press consisted of sine wave 60-c.p.s. stimulus of 0.25-v. peak to peak maximum duration of 450 msec., and optimum current to produce the maximum pressing rate for each animal. This varied from 30–90 μamp., with some rats sensitive to changes of 2 μamp. A mean lever-pressing rate and its standard deviation were established, and then the animals were conditioned to their various experimental conditions until their pressing rates were approximately their original mean and deviation. Animals fulfilling this criteria were grouped as follows: 16 whole-body irradiated and six head irradiated. Other conditioned rats, as controls, were tested for extended time periods and showed no progressive changes in mean and standard deviation. The 600-r radiation dose was administered with an industrial unit employing the following technical factors: 250 kvp.; 15 ma.; FOD 70 cn.; filters—0.21 mm. Cu inherent, 0.5 mm. Cu, and 1.06 Al added; HVL 1.95 Cu; dose rate measured in air 23.0–24.2 r/min. The animals were rotated during irradiation. The machine was calibrated before and after irradiation with a thimble r-meter[1] and during exposure with a Radacon unit.[2]

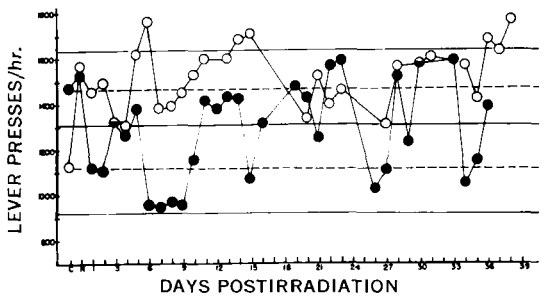

Figure 1—*Effect of 600-r total-body X-irradiation on hypothalamic self-stimulation in the rat. This figure shows the results of two typical rats (○, WB-44; ●, WB-17). Note the responses are just opposite during the first 12 postirradiation days and then fluctuate for the balance of the observation period. C, control values are represented by the dotted line (mean) and solid lines (standard deviation). These were determined over a 6-week time period, R, response immediately after irradiation. The rats were confined for 30 min. in the radiation boxes prior to runs only through the second day postirradiation.*

IRRADIATION EFFECTS

The rats' response to whole-body irradiation could be divided into three groups based on alterations in the mean pressing rate. Seven rats showed significant increases postirradiation, seven showed decreases, and two showed no alteration. Results of two typical rats are shown in Fig. 1 for the first 39 days postirradiation. The rats with approximately the same pressing rate had opposite effects, one WB-44 had approximately a 2-*SD* increase in the mean pressing rate with about the same standard deviation as in the preirradiation period, while the other WB-17 had a 1.5-*SD* decrease in mean rate with slightly greater than normal deviation. Several of the rats were tested through 81 days postirradiation, with little alterations in the basic shifts. There was a tendency to return to a normal or slightly greater than normal pressing rate with time. While a few rats showed a progressive decrease at later time periods, these alterations could be correlated to slight loosening of the electrode which results in brain damage and stimulation of adjacent brain areas. Under such circumstances the electrical stimulus becomes painful and the animals react by decreasing their lever-pressing rates. The electrode positions in the hypothalamus are seen in Fig. 2. Animals with the electrode in the median forebrain bundle had a pressing rate of about 3,500, while the lowest rates, below 1,000, were seen in the animals with the electrodes closest to the third ventricle.

Effects of head irradiation are shown in Fig. 3. In general, there was little change in the mean pressing rate, but the standard deviation increased. Figure 3 also shows the normal extreme in pressing

[1] Victoreen.
[2] Radacon.

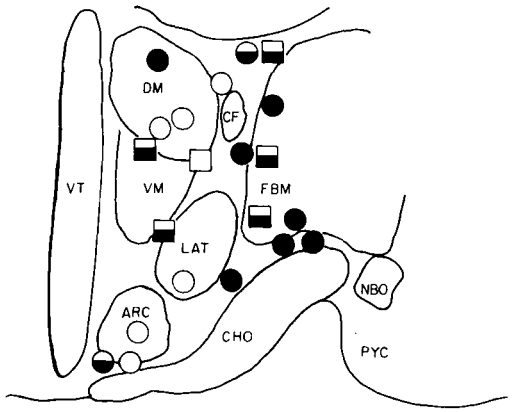

Figure 2—*Hypothalamic electrode position of irradiated rats used in the self-stimulation experiments. Key:* ○, ◒, ● = *WBR (whole body irradiated);* □, ◘, ■ = *HR (head irradiated);* ○, □ *decreased;* ◐, □ = *no change;* ●, ■ = *increase (all these refer to the change in the mean pressing rate over the first several days postirradiation). Schema of the hypothalamus is modified from Massopust (7). VT, third ventricle; DM, dorsomedial nucleus; VM, ventromedial nucleus; ARC, arcuata nucleus; LAT, lateral nucleus; CF, column of the fornix; FBM, medial forebrain bundle; CHO, optic chiasm; NEO, supraoptic nucleus; PYC, pyriform cortex.*

rates of the rats used in these experiments. The upper curve shows a rat with an electrode in the median forebrain bundle with a mean control rate of 3,800 (3,500–4,100) presses/hr. Other rats in this group had mean rates as low as 3,200 presses/hr. Irradiation increased the pressing rate to 4,400 and with time decreased it to 3,000. Other animals with similar electrode implants had mean control pressing rates of 900, 1,500, and 1,800/hr. The lower curve in Fig. 3 shows the animal with the 900 (800–1,000)/hr. rate. There is little change in lever-pressing rate throughout the observation except for the decrease on Day 1 and the increase on Day 8.

No overt behavioral alterations from normal occurred with either whole-body or head irradiation at this dosage, 600 r.

DISCUSSION

The mean self-stimulation rate of 900–3,800 presses/hr., depending on the electrode location in various regions of the hypothalamus, agrees with that found in other studies (1, 2, 4). As was found in a previous study (3), whole-body irradiation may produce opposite effects even though the electrodes are apparently in the same nuclei. However, this finding is not universal, since in some structures, as the median forebrain bundle, the response is fairly constant. With whole-body irradiation, the apparent pattern is one of decrease in rate in nuclei near the third ventricle to no change and an increase in rate as moved laterally. An interesting observation is that whole-body irradiation tends to change the mean rate but not the daily deviation, while head irradiation increases the deviation but does not alter the mean. This dichotomy does not usually occur in irradiation, as partial body irradiation has no effect to the same effect when compared to whole-body irradiation. This observation does not indicate whether the irradiation-induced changes are direct or indirect, although it implies not direct. In a group of 15 rats implanted for body irradiation, none trained to criteria; so no information was gained on direct body irradiation.

Stressful states, as confinement, may also produce reasonably

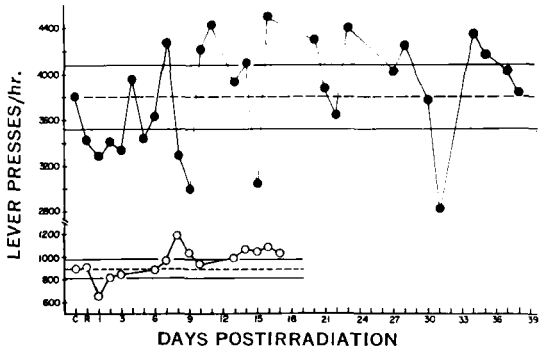

Figure 3—*Effect of 600-r head X-irradiation on hypothalamic self-stimulation. This figure shows the results of two typical rats (●, H-10;* ○, *H-15); also the normal extreme in pressing rates is represented. C, control values are represented by the dotted line (mean) and solid lines (standard deviation). Controls were determined over a 6-week time period. R, response immediately after irradiation. The rats were confined for 30 min. in the radiation boxes prior to runs only through the second day postirradiation.*

permanent alterations in subsequent pressing rates. This was particularly the case with rats confined for partial body irradiation. While a few rats were affected for only a few days, the vast majority took 20 to 30 trial days before their rates approached their normal control values; and some rats, even after ceasing this conditioning state, failed to return to previous levels.

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