Late Effects of Fast Neutrons and X-rays on Adult Rabbit Brain*.

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Irradiation of normal brain tissue is unavoidable in the treatment of certain types of cancer by radiotherapy. We have reported that the visual evoked potentials recorded from the rabbit gradually decreased over a long period of time after irradiation with 300 R of X-rays to the brain.1) Little attention has been devoted to the study of the functional changes in the brain after irradiation with fast neutrons. The present study was designed to explore the effects of neutron irradiation of the brain on the longevity and electrocorticograms (ECoGs) of the adult rabbit. The sleep-wakefulness cycle was used as a measure of the ECoGs. For comparative purposes, the effects of X-rays were also investigated.

 Eleven male Japanese white rabbits were obtained from Funabashi Farm Co., Ltd. at 4 months of age. Throughout the remainder of life they were individually caged and supplied 150 g of pellet food and 400 ml of tap water every morning. The animals were weighed and examined periodically, and food and water consumption was measured weekly. The procedures for the implantation of electrodes and the recordings of the ECoGs were described in a previous paper.1) Recordings of the ECoGs were continuous for 3 hours, starting at 10:00 am. Baseline recordings were made at weekly intervals for a period of about 2 months before irradiation. Recordings were also repeated at biweekly intervals until the animals died after irradiation. The neutrons (14 MeV mean energy) were produced by a bombarding a beryllium target with 30 MeV deuterons at the National Institute of Radiological Sciences, giving a dose rate of approximately 30 rad/min. There was about 3 per cent contamination with gamma rays. The X-rays were delivered by a 200 kVp 20 mA X-ray machine with 0.5 mm Cu and 0.5 mm Al filters. Target-to-skin distance was 30 cm and the size of the beam was 10 x 10 cm. The dose rate was 100 R/min. Animals to be irradiated were placed in a lucite box and exposed to a

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single dose of radiation directed to the dorsal surface of the head. The head, except for the region of the brain, was shielded with a steel plate for neutron irradiation and a 4 mm thick lead plate for X-ray irradiation.

Table 1 shows age at irradiation, dose and types of radiation and survival days after irradiation of individual rabbits of the control, neutron and X-ray groups. Part of the results of the control group study have been reported in a previous paper. 2) Mean survival days (±SD) after exposure were 210.3 ± 106.1 in the neutron group and 222.8 ± 103.2 in the X-ray group. No significant differences in survival times were observed between the 2 irradiated groups. These values were significantly shorter than those for the control group (P < 0.05). According to Ordy et al., adult male mice irradiated with 500 rad of deuteron to the brain showed significant life-shortening, 3) while Sato et al. 4) reported that in adult female mice irradiated with 800 R of X-rays to the head, life-shortening was not significant.

The ECoGs may be described by the 2 pattern designations of slow wave sleep (SWS) and wakefulness (W). High voltage and low activity periods were regarded as SWS, and low voltage and fast activity periods were defined as W (Fig. 1). The SWS cycle time and the SWS length of all of the ECoGs were calculated for individuals of each group. The proportion of the total SWS
time to the total recording time (TRT), SWS cycle time, and SWS length in the control group were variable from day to day in the same animals and from one animal to the next throughout the observation period. These were 35–55%, 5–20 min., and 5–10 min., respectively. These 3 values of the 2 irradiated groups before exposure were similar to those of control group. Most irradiated animals showed no change in the 3 values after exposure. The proportion of total SWS time to TRT of animal No. 668 tended to decreased 4 to 7 months after exposure. Eldred and Trowbridge\(^5\) reported that no remarkable change in the electroencephalogram was noted in most monkeys examined from a few hours to several months after whole body exposure to 400–800 R, until prior to death.

The general behavior of animals Nos. 637 and 808 seemed unchanged throughout observation period. They died suddenly without any weight loss. The 3 non-irradiated animals (Nos. 676, 682 and 715) and the 4 irradiated animals (Nos. 723, 738, 765 and 815) continued in almost good health until shortly before death, and then showed a reduction in food and water intake and a visible loss in body weight (Fig. 2). These animals died of general prostration. The body weight of animals Nos. 668 and 822 gradually decreased after irradiation. At death, these 2 animals showed considerable emaciation. Hopewell \textit{et al}\(^6\) reported that in adult rats irradiated with 3000 R of X-rays to the brain, body weight loss was observed in an interval of 3 to

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**Fig. 2.** Body weight of individuals of the control, neutron and X-ray groups as a function of age. Arrows show age at irradiation.
20 weeks prior to death.

In summary, the present study demonstrates that there were no differences between the effects of fast neutrons and X-rays on the longevity of the adult rabbit and that the sleep-wakefulness cycle of the ECoGs showed no changes after irradiation with fast neutrons or X-rays. Geraci et al.\textsuperscript{7} and Kogel et al.\textsuperscript{8} reported that the late effects of fast neutrons on the central nervous system were slightly larger than those of X-rays. These were for doses far greater than those used in this experiment and measured by incidence of paraplegia after irradiation of the spinal cord.

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