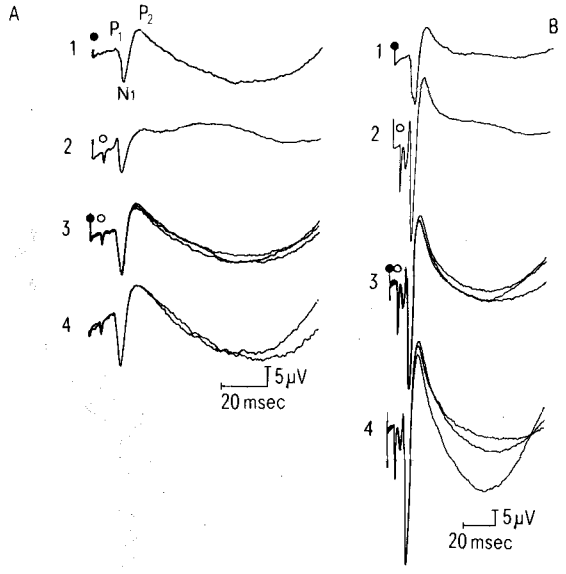

Interaction of human EESGs, recorded from the posterior epidural space at the T_{12} level, elicited by segmental and descending volleys at 2 intensities (1.2× threshold in A and 6.0× threshold in B). 1: EESG elicited by tibial nerve stimulation at the popliteal space. 2: EESG elicited by epidural stimulation of cervical cord at the C_6 level. 3: EESG elicited by both tibial nerve and cervical cord stimulations. The timing of the 2 stimuli was adjusted to produce the 2 EESGs at the same time period. 4: Simple summation of EESGs in 1 and 2. The closed and open circles represent the stimulus artifacts of tibial nerve and cervical cord stimulations, respectively. Each trace is a computer average of 25 responses. Upward deflection denotes positivity in all traces.

77.6±0.8%, respectively. By contrast, there was a linear addition of the initial spike potentials without occlusion.

A greater occlusion in the slow positive waves than in the negative waves, demonstrated in both weak and strong stimulations, may indicate that there are more common elements in the paths producing PAD than in those producing the synchronous interneuronal activities.[9,11]. This occlusion phenomenon may partially account for the inhibitory effect of descending volleys on sensory inputs, such as pain, at the spinal level in man.

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Effects of monochromatic X-radiation on the membrane of nodes of Ranvier under voltage and current clamp conditions*

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Summary. Monochromatic Ag-K_α-radiation decreased irreversibly the peak sodium current in nodes of Ranvier. This decrease occurs only with a delay of about 1000 sec after a threshold dose of about 8 kR has been reached. Potassium current and resting potential are practically not affected.

Ionizing radiation has been used to study the mechanism of excitation in nerve membranes by altering their electrical properties[2-11]. Some of the investigators[2,4,5,9,11] reported a temporary enhancement of excitability at X-ray doses of less than 10 kR, while others[3,6,8,10] demonstrated that radiation doses below 10 kR were ineffective in changing action potential (rate of rise, amplitude), conduction velocity or membrane resistance. At higher doses a decrease of excitability was observed by all investigators.

Non-ionizing radiation exerts specific effects on the electrical properties of excitable membranes. The results of the first voltage clamp analysis of UV-radiation on nerve membranes[12] and of subsequent investigations[13,14] showed that UV-radiation specifically blocks sodium channels of the nodal membrane without altering the resting potential and the potassium channels. The blocking effect appeared to be due to alteration of the gating system of the sodium channels[14].

Using radiation of different energy it could be anticipated that specific alterations on a macromolecular or intermolecular scale would lead to further insights on the mechanisms of the excitation process. A further purpose of this investigation was to solve the contradiction of the results cited above.

This study represents the first voltage clamp analysis of X-irradiation effects on ion permeabilities of the nerve membrane using monochromatic X-radiation. The experimental procedures were described in detail elsewhere[13,15]; single nerve fibres were dissected from the sciatic nerve of *Rana esculenta*[16] and voltage- or current clamped according to the method of Nonner[17]. Membrane currents or voltages were digitized and recorded on-line using a Honeywell DDP-516 processing computer, and stored on magnetic-tape for offline data evaluation. Monochromatic Ag-K_α radiation was produced by an X-ray diffraction tube (RDF-50, Ag anode; Philops) and a constant potential generator (PW-1140; Philips). K_α-radiation was isolated and focussed (beam width < 0.1 mm) by a precision quartz monochromator (GM-8; AEG-Telefunken). High precision focussing avoided irradiation of the internodes and thereby induction of injury currents. A dose range up to 20 kR was studied. In addition, X-radiation of continuous energy was produced by an X-ray inspection tube (MCN-161, 1 mm beryllium window; Philips) operat-

ed at 95 kV/30 mA. The irradiation of the internodes was avoided as far as possible by a sequence of lead diaphragms.

A typical result of effects of monochromatic X-irradiation on peak sodium and steady state potassium currents is shown in the figure 1. The ionic currents decreased spontaneously at a certain rate (rundown usually observed in dissected nerve fibres). During the irradiation period of 1300 sec (5 R/sec indicated by a horizontal bar plus arrow) no significant change was detected; however, after a delay of about 700 sec after cessation of the X-irradiation a sudden decrease of the peak sodium current occurred (figure, B) which was never observed without irradiation. Evaluation of 6 experiments revealed that the rapid decrease of the peak sodium current started always 800–1000 sec after reaching a threshold X-ray dose of 6–10 kR independent of the duration of the irradiation period. Thus, the onset of the irradiation-induced decrease of sodium current would occur during or after the irradiation, depending on duration and dose rate of the X-irradiation. In 5 single nerve fibres irradiated with doses below 10 kR no significant alteration of the peak sodium current was found. The steady state potassium current was much less affected than the peak sodium current (figure, A).

The steady state inactivation of the Na system (as measured by the ratio of the peak sodium currents at a test voltage, preceded or not by a hyperpolarizing prepulse) was also rapidly decreased with a delay of approximately 1000 sec after reaching the threshold irradiation dose (figure, C).

Additional current clamp experiments showed consistently delayed decreases in rate of rise and height of action potential but no significant changes in resting potential.

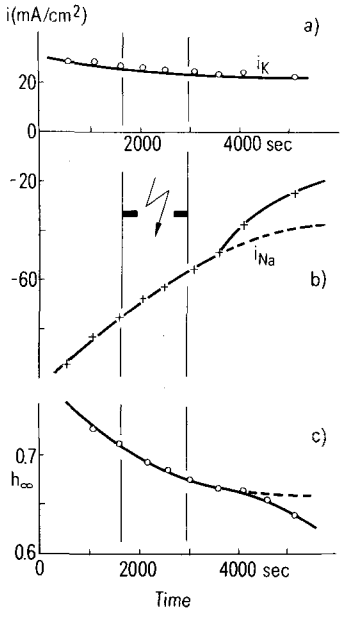
For comparison with results of other authors 11 X-irradiation experiments were carried out using a continuous X-ray energy spectrum (max. 95 keV). The results of 6 experiments employing irradiation doses greater than 10 kR were most similar to those described above. Though the applied dose rate (55 R/sec) was about 1 order of magnitude higher, the radiation-induced decrease of the sodium current started to develop only with a delay of approximately 1200 sec after reaching the threshold dose of around 10 kR, which is similar to the delay of 800–1000 sec seen in the experiments with monochromatic X-irradiation. 5 fibres irradiated with doses less than 10 kR exhibited no radiation-induced effects.

These results support earlier reports[3,6,8,10] that X-irradiation reduces excitability by blocking of sodium channels; temporary increases of excitability as described by other authors[2,4,5,9,11] were never detected. These were most probably artifacts produced by injury currents as was already demonstrated by Booth et al.[18] in UV-irradiation experiments.

Phenomenologically, X-radiation induces similar effects to those of UV-radiation: irreversible reduction of sodium current, decrease of the steady state sodium inactivation, little change of potassium current and practically no influence on resting potential. However, unlike the immediate onset of the effects of UV-radiation, X-irradiation effects occur only after reaching a threshold dose, and this with a delay of around 1000 sec.

A delay in the development of the radiation effects could be explained either by a multi-photon process or by slow chemical reactions leading to the final block of sodium channels. The latter case appears to be more likely because the radiation-induced decrease of current can even occur after the X-irradiation is turned off (figure), and the delay appears to be independent of dose rates differing by an order of magnitude.

Apparently X-radiation does not directly affect excitability. Therefore the expectation that high energy radiation would offer a tool for specifically changing structure/function relations in ionic conductances was not fulfilled. X-irradiation leads to the indirect destruction of ionic channels, where sodium channels appear to be more sensitive than potassium channels.



Effects of monochromatic X-radiation. *A* Steady-state K currents (○) were measured at the end of 20-msec testpulses to +30 mV. *B* Na peak currents (+) were measured during test potentials to −10 mV preceded by 50-msec prepulses to −120 mV. *C* Steady-state Na inactivation (0) was determined from the ratio of Na peak currents measured during testpulse without and with prepulses. Holding potential, −70 mV; temperature, 15 °C.

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