

The effect of ototoxic drugs on the acoustic startle reaction of the rat

E.S. HARPUR (introduced by P.F. D'ARCY)

Department of Pharmacy, The Queen's University of Belfast, N. Ireland

In a previous communication (D'arcy & Harpur, 1973) it was shown that i.v. administration of either ethacrynic acid or frusemide significantly reduced noise-induced startle response in mice. However, new studies on mice, to which kanamycin, neomycin, streptomycin or combinations of these drugs were chronically administered i.p., did not show a greater reduction of startle in the drug-treated animals compared with saline-treated controls.

In further experiments rats were individually tested for acoustic startle reaction in a ventilated perspex box suspended within a sound-resistant case (background noise 51 ± 2 dB re 0.0002 dyn/cm²). The box allowed penetration of pure tone stimuli, generated by an audio oscillator and fed, via a 15 W amplifier, to a speaker mounted on the outer case. Tone length was controlled by an electronic switch. Startle reaction was detected by a piezoelectric strain gauge and measured on a pen recorder.

Each rat was exposed to five stimuli of 240 ms duration at 5 s intervals. Habituation, or some other factor (possibly increasing age), caused a reduction in startle between tests even when the interval was several days or weeks. This agreed with the results of studies of the effect of interstimulus interval on habituation retention of rat acoustic startle reaction (Moyer, 1963; Davis, 1970).

When groups of Wistar albino rats were given daily s.c. injections of saline, kanamycin (250 mg/kg) or neomycin (50 mg/kg) and tested,

at intervals, for startle reaction to a 3 kHz tone (90 dB re 0.0002 dyn/cm²) the mean responses of all groups were reduced. However, when the stimulus frequency was raised to 8 kHz the responses of both the control and the neomycin-treated groups were restored to pre-drug levels while the response of the kanamycin-treated group was further reduced. This could indicate that the diminution in response of only the kanamycin treated animals was not due to habituation.

Habituation may be avoided by withholding exposure to acoustic stimuli until the animals have been intoxicated with the drug. The startle responses of groups of Lister hooded rats to an 8 kHz tone (90 dB re 0.0002 dyn/cm²) were first assessed after 35 days of drug administration s.c. as follows: (a) saline; (b) kanamycin (500 mg/kg/day); (c) neomycin (100 mg/kg/day); (d) neomycin (50 mg/kg/day) with kanamycin (250 mg/kg/day). The mean response of the group treated with the high dose of kanamycin (b) was very significantly smaller ($P < 0.001$) than that of the controls. The mean responses of the other groups were not significantly different from the control group. This result was indicative of severe kanamycin-induced deafness.

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References

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