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Reserpine induction of mouse killing in nonkiller rats

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Seventy-five nonkiller male rats were divided into two groups, 38 animals receiving 3 mg/kg reserpine and the other 37 receiving saline. Fifty percent of the reserpine-treated animals showed mouse killing, whereas none of the other animals did so. Mouse-kill responses were already exhibited within 32 h after treatment, while the animals were still heavily sedated.

Much experimental work has been done on the pharmacological inhibition of aggressive behavior, e.g., the tranquilizing effects of reserpine upon various forms of aggressive behavior. Thus, Tedeschi, Mucha, Cook, Mattis, and Fellows (1959) found an inhibitory effect of reserpine upon footshock-induced aggressive behavior in male mice, and a similar effect was shown for isolation-induced fighting (Valzelli, Giacalone, & Garattini, 1967; Yen, Stanger, & Millman, 1959). The aggressiveness of rhesus monkeys toward humans was reported to be strongly reduced by reserpine administration (Plummer, Earl, Schneider, Trapold, & Barrett, 1954). Finally, clinical studies indicate a diminished aggressive behavior of psychiatric patients toward the nursing staff (Kline & Stanley, 1955; Mielke, 1956).

On the other hand, reserpine fails to inhibit the mouse-kill response in rats (Karli, 1959a, b). The present experiment will show that, in fact, reserpine induces mouse killing in a large proportion of nonkiller rats.

METHOD

One-hundred and five male Wistar rats weighing about 350 g were individually caged, with constant access to food and water. In four preexperimental tests of 24 h, all animals were screened with respect to mouse-killing behavior. Thirty "killers" were excluded from further experimentation, and the remaining 75 subjects were divided into two groups: 38 animals received 3 mg/kg reserpine (Serpasil, CIBA) in saline subcutaneously, and the other 37 received .9% saline only.

The mouse-kill tests consisted of presenting two mice to the subjects for 30 min. Each animal was tested at 1, 2, 4, 8, 12, 16, 24, 32, 40, 52, and 72 h following the injection. At least one mouse had to be killed for a given test to be scored as positive for killing. The statistical analysis of the results was done with the G-test (Woolf, 1956).

RESULTS

The reserpine-treated animals were heavily sedated, and had diarrhea and ptosis. Nevertheless, 50% of the reserpine-treated animals responded to mice introduced in the home cages at least once with a killing response, whereas none of the animals of the control group did ($F = 22.15$, $p < .001$).

Figure 1 presents the cumulative data of the reserpine- and saline-treated animals. Most animals continued to kill even after the sedating effect of reserpine had disappeared. This effect was seen up to 3 months following reserpine administration, at which time testing was discontinued.

DISCUSSION

The results of this experiment show that a large percentage of a group of nonkiller rats can, within 32 h, be transformed into mouse killers by a single injection of reserpine. Because the subsequent incidence of mouse killing in many rats exceeds several weeks, it seems highly unlikely that the effect can be attributed to a correspondingly prolonged action of reserpine. Possibly, learning factors are involved in these behavioral changes.

Several experiments suggest an inhibitory role of both noradrenalin and serotonin in the regulation of the mouse-kill response. Inhibition of mouse killing is seen following systemic administration of amphetamine, MAO-inhibitors or tricyclic anti-

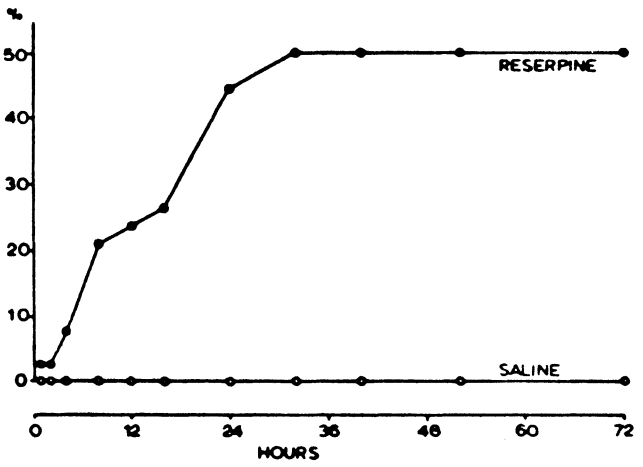

Figure 1. Cumulative percentage of animals killing at various intervals following administration of reserpine and saline.

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depressants or of 5-hydroxytryptophan (Horovitz, Ragozzino, & Leaf, 1965; Karli, 1959b; Kulkarni, 1968). The supposition has been made that the amygdaloid nuclei play a role in this inhibitory effect of monoamines upon mouse killing (Horovitz, Piala, High, Burke, & Leaf, 1966; Leaf, Lerner, & Horovitz, 1969). This is supported by data on the inhibition of mouse killing by implantation of noradrenalin in the medial and central nuclei of the amygdala. Since reserpine results in a depletion of noradrenalin and serotonin stores, the facilitatory effect of reserpine upon mouse killing described in this paper could be explained by a weakening of this monoaminergically mediated inhibitory system.

Reserpine also results in an increase of acetylcholine in the hypothalamus and the other parts of the brain (Giarman & Pepeu, 1962; Malhotra & Pundlik, 1959). There is, in fact, also evidence for a cholinergic regulation of mouse killing. Thus, implantation of cholinomimetics or choline-esterase inhibitors into the lateral hypothalamus both facilitated the mouse-kill response in killer rats and induced killing in nonkiller rats (Bandler, 1970; Smith, King, & Hoebel, 1970). It has been suggested that, because of the inhibition of mouse killing by antidepressants, there might be some pharmacological parallel between mouse killing by rats and human depressions (Horovitz et al., 1965; Leaf et al., 1969). The severe depressions seen in some reserpine treated patients (Archor, Hanson, & Gifford, 1955; Harris, 1957; Muller, Pryor, Gibbons, & Orgain 1955), together with the induction of mouse killing by reserpine, give further support to the idea of developing an animal model of human depression (McKinney & Bunney, 1969).

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