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BRIEF COMMUNICATION

Controlled Demonstration of Metrazol Kindling

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PINEL, J. P. J. AND K. F. CHEUNG. *Controlled demonstration of metrazol kindling.* PHARMAC. BIOCHEM. BEHAV. 6(5) 599–600, 1977. – Convulsive responses elicited in rats by intraperitoneal injections of metrazol were intensified following a series of metrazol injections administered once every three days. However, neither handling alone nor placebo injections increased the susceptibility of control rats to metrazol-induced convulsive symptoms. Thus, although increases in the susceptibility to metrazol seizures following periodic placebo injections have been reported by others, such increases do not appear to be a critical factor in metrazol kindling.

Seizures Rats Metrazol Kindling

PERIODIC injections of metrazol have been shown to produce a progressive increase in seizure susceptibility (kindling). For example, Mason and Cooper [2] found that a dose of metrazol which was initially subconvulsive would eventually elicit grand mal seizures in rats injected with it once every three days. However, recently Izquierdo, Fernandez, Oliveira, and Settineri [1] reported that increases in the susceptibility to metrazol seizures followed a series of daily placebo injections. Since placebo controls were included in neither the Mason and Cooper study nor in its replication by Pinel and Van Oot [3], the metrazol kindling in these studies may have been an artifact of the injection procedure rather than being a consequence of the metrazol per se.

METHOD

The animals were 57 male, 285–385 g, hooded rats purchased from the Canadian Breeding Farm and Laboratories, St. Constant, Quebec. Each rat was injected intraperitoneally with 20 mg/kg of metrazol and the incidence of each of four convulsive symptoms – (1) rhythmic ear twitches, (2) jaw clonus, (3) facial tremors, and (4) myoclonic body jerks – was assessed during the ensuing ten 1-min intervals. Each rat received a score for each symptom which was the number of 1-min intervals in which that symptom was observed at least once; thus the maximum score that each subject could obtain for each symptom was ten. The responses to this pretreatment injection were used as a basis for assigning the animals to three equivalent groups (n = 19). Three days later, and at 3-day intervals thereafter, the subjects in each of these groups received one of three treatments. Rats in the experimental group were injected every three days with metrazol (20 mg/kg); rats in the placebo control group were injected at 3-day intervals with an equal dose of isotonic saline; and rats in the second control group were handled similarly but not injected. This treatment regiment continued until Day 127 when all animals again received the standard 20 mg/kg injection of metrazol. Responses to this posttreatment metrazol injection were assessed by an experimenter unaware of each animal's experimental history.

RESULTS AND DISCUSSION

The responses of the animals in each of the three groups to the pretreatment and posttreatment metrazol injections are summarized in Fig. 1. It is readily apparent that the incidence of each of the four epileptic symptoms was increased appreciably by the intervening series of metrazol injections but not by either of the two control procedures ($p>0.1$). Thus, although animals were assigned to groups on the basis of their initial response to metrazol, planned comparisons indicated that by the end of the experiment each of the four symptoms was significantly more prevalent in the experimental group than in the controls combined (ear twitches, $F(1,54) = 13.76$, $p<0.0005$; jaw clonus, $F(1,54) = 9.94$, $p<0.003$; facial tremor $F(1.54) = 7.29$, $p<0.01$; myoclonus $F(1,54) = 11.52$, $p<0.002$). The responses to the treatment injections of metrazol were assessed after every third injection during the course of the experiment, and the results of these assessments are presented in Fig. 2 to illustrate the progressive development of symptoms within the experimental animals.

Although increases in the susceptibility to metrazol injections following periodic placebo injections have been reported by others [1], the present data indicate that such increases are not a critical factor in metrazol kindling.

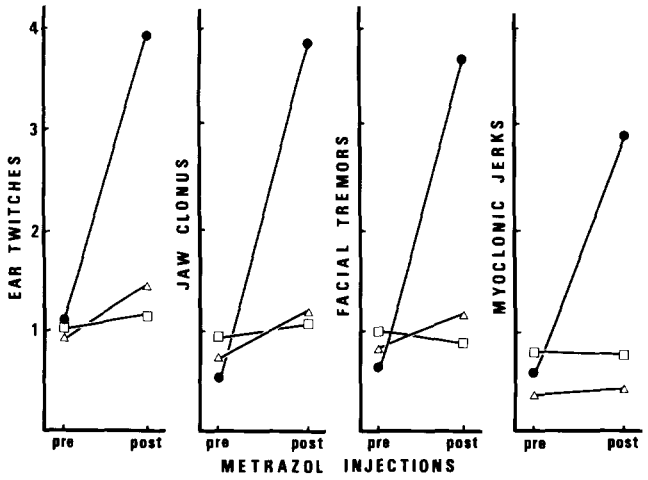

FIG. 1. Convulsive responses elicited by metrazol before and after a series of periodic metrazol injections (circles), placebo injections (squares), or control handling (triangles). Each point represents the mean number of ten 1-min postinjection periods in which a particular symptom was observed in animals of that group.

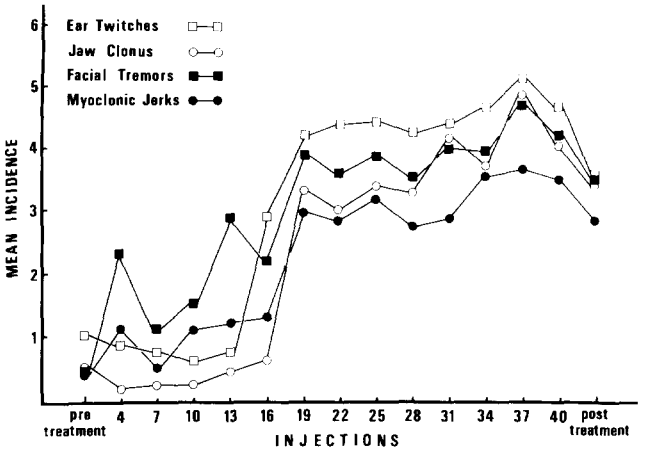

FIG. 2. Progressive increases in the incidence of epileptic symptoms elicited by a series of 43 metrazol injections. Each point represents the mean number of 1-min intervals in the 10 min following each injection during which a particular symptom was observed at least once.

REFERENCES

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