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The Effect of Ethanol on Wheel Running in Rats

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DUNCAN, P. M. AND A. M. BAEZ. *The effect of ethanol on wheel running in rats.* PHARMAC. BIOCHEM. BEHAV. **15**(5) 819–821, 1981.—Rats were given IP injections of ethanol at 0, 400, 800 and 1200 mg/kg. Their activity in running wheels was recorded for one hour post-injection. Ethanol at 800 and 1200 mg/kg depressed running. This effect was greatest during the first 15 min post-injection when activity levels were highest in the nondrugged condition. No evidence of an ethanol-produced increase in running was seen. The monotonic, dose-related activity decrement with no biphasic effect from ethanol in wheel running is similar to some reports of this drug's effect on rats in other paradigms, such as food-motivated operant responding and spontaneous motor activity.

Ethanol Wheel running Activity level

AT high doses, ethanol, like other "CNS depressants" produces sleep, coma, and death in all species of animals in which its effects have been investigated. At doses which do not produce sleep, ethanol usually produces a dose-related decrease in the vigor or rate of occurrence of ongoing behavior. Two examples of behavior which is so "depressed" by ethanol are operant responding for food (in rats [4,5], in pigeons [8,11], in monkeys [2]), and "spontaneous motor activity" (in rats [4, 5, 9, 17], in mice [10]). Ethanol sometimes has a "biphasic" effect in that at low to moderate doses it can produce increases in activity level. This activity-increasing effect has been observed in monkeys [2], rats [3,14], gerbils [15], and in mice [6], but seems to be quite situation-specific and seen more generally in some species than in others.

The rate of ongoing activity of rodents can also be measured in the running wheel. This apparatus has been used extensively (cf. [7]) to study diurnal cycles, anticipation of feeding, effects of food and water deprivation, lesions of various brain structures, and to some extent to investigate drug effects (e.g., [13]). The effect of ethanol on rats' wheel running has not been previously studied. Pettijohn [15] found a biphasic ethanol dose-response effect in Mongolian gerbils. Low to moderate (800, 1600 mg/kg) ethanol doses caused increased running, whereas higher doses (2400 mg/kg) reduced wheel revolutions. The purpose of the present experiment was to determine dose-response relations between ethanol treatment and wheel running in rats.

METHOD

Animals

Eleven male rats of the Long-Evans strain were used. Their age at the start of the experiment was approximately 180 days and mean weight was approximately 400 g. The rats were housed in individual cages with light onset at 0600 and dark onset at 1800. They had continuous access to Purina lab chow and water, except during hour-long sessions in running wheels. Ambient temperature was maintained at 21 degrees Centrigrade.

Aparatus

Six standard Wahman running wheels, diameter 35.5 cm, were used. Each rat was always run in the same wheel. Each wheel revolution acuated an electromechanical counter located in an adjacent room.

Procedure

The rats were housed in the laboratory for two weeks before the start of data collection for adaptation to the dark-light cycle, handling, the injection procedure, and daily running sessions. On each of 10 weekdays prior to data collection each rat was weighed and placed in a running wheel for 30 min. For each of the last five of these adaptation days the running period was preceded by an IP injection of normal saline at a volume of four ml per kg of body weight. Twenty percent (volume/volume) ethanol solution for injection was prepared by diluting 95 percent ethanol with normal saline. Ethanol doses of 0, 400, 800, or 1200 mg/kg were given via IP injections between one and five min before each rat was placed in its wheel. The total wheel revolutions occurring during each of the subsequent four 15-min periods were recorded. Each rat received all four ethanol doses (including the four ml/kg saline injection), which were administered in a counterbalanced sequence over eight data collection days. Each rat received all four doses on two different days, so all data presented represent the mean of two running sessions. On days immediately following injection-data collection days rats were given a running session, but no injections were administered and no data were collected. Running sessions were conducted between 1500 and 1700 hours.

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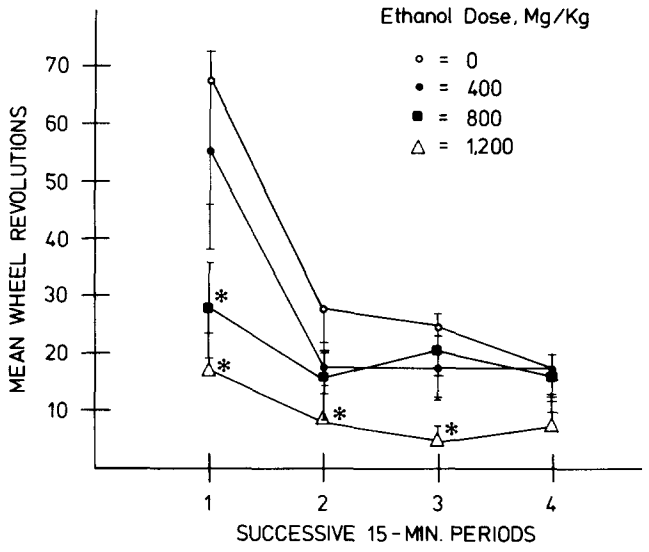

FIG. 1. Means and SEM of wheel revolutions during 4 successive 15-min intervals after ethanol or saline injection. Asterisks indicate significant differences ($p<0.05$) from saline treatment at the comparable time interval N=11.

RESULTS

By the end of the adaptation period individual rats' daily running patterns had stabilized, varying no more than 10 percent in total revolutions between successive adaptation days. A general pattern of running was seen, in that most occurred during the first 15-min interval, followed by a progressive decline in wheel revolutions in the subsequent interval. This within-session decline in activity was seen reliably during the 30-min adaptation sessions, and during the 60-min saline treatment sessions.

Although partial wheel revolutions could actuate the counters, such "wheel-rocking" behavior was rarely seen, and thus the counter totals accurately indicated the amount of actual running behavior.

Although individual rats' daily total amounts of running were quite stable across latter adaptation sessions, there was considerable variation among animals. Activity levels after saline treatment ranged from 16 to 198 revolutions during the first 15-min, and from 49 to 451 revolutions over the entire 1-hr session.

The mean numbers of wheel revolutions which occurred during the four 15-min recording intervals after each of the three ethanol doses and the saline treatment are presented in Fig. 1, which indicates that ethanol produced a monotonic dose-related decrement in wheel-running. These data were anlayzed by means of a four (ethanol doses) by four (successive 15-min recording intervals) ANOVA for repeated measures on two variables. The main effect of ethanol was significant, $F(3,30)=7.65$; as was the main effect of time intervals, $F(3,30)=10.58$; and the drug-dose by time interval interaction, $F(9,90)=6.17$; $p<0.001$ for all three F values. The differences between amounts of running after saline treatment compared to that recorded after each ethanol dose for each of the four time intervals were analyzed by means of Dunnet's test. All ethanol-saline differences designated here as significant were at the $p<0.05$ level. The 400 mg/kg dose did not significantly decrease running, and the 800 mg/kg dose produced a significant decrement only during the first recording interval. The 1200 mg/kg ethanol dose significantly depressed running during the first three of the four successive 15-min intervals. The significant main effect of time intervals was due to the time-related running decrement seen after all drug and saline treatments. The significant dose by time interaction effect apparently resulted because the drug-produced decrement was largest in the first recording interval, when the greatest amounts of running occurred in the saline condition.

DISCUSSION

Under the conditions of this experiment, ethanol produced a dose-related decrement in wheel running, with no evidence of the biphasic effect (which would have included increases in running at low doses) reported by Pettijohn [15] for the Mongolian gerbil. The most obvious difference between the present experiment and the Pettijohn study is the species investigated. In both experiments nocturnal rodents were treated with identical ethanol doses during the light phase of the diurnal cycle. The rats used in the current experiment were mature, and in the absence of ethanol treatment ran somewhat less than is typical of younger, lighter rats. However, rate-increasing effects are generally easiest to demonstrate against a relatively low non-drugged baseline rate [16]. Rats in the present experiment received repeated ethanol injections and thus were to some degree ethanol-tolerant. The effects Pettijohn reported were seen in gerbils not previously exposed to ethanol. However, no consistent running increases were seen in rats receiving their initial ethanol treatment, so drug tolerance is not likely to have obscured a rate-increasing effect.

Drug effects on wheel running in rats have apparently not been investigated extensively, if at all. Both wheel running and "spontaneous motor activity" (as detected by a stabilimeter, photocells, or an Animex-type device) are types of ongoing activity which are probably related, but certainly are not identical. For example, vigorous grooming and exploratory rearing are motor activities which actuate a sensitive stabilimeter, but are not recoreded as "activity" in a running wheel which is rotated only by walking or running. It is not surprising that the effects of some experimental manipulations (e.g., brain lesions, water deprivation) produce different effects in rats when tested in running wheels, compared to the effects on motor activity measured by other methods (cf. [7].

Although wheel running behavior is not completely identical to locomotor activity which occurs in other types of apparatus, the depressant-only effects seen here have also been reported in several other studies of rat "spontaneous motor activity" when ethanol was administered at similar doses [4, 5, 9, 17].

Any generalization about similarity between ethanol's effect on wheel running and on SMA in rats is however limited in view of reports that ethanol sometimes does produce increases in rats SMA at low to moderate doses [3,14]. The variables which determine whether ethanol produces an increase in rat SMA are not readily identifiable. Specific configuration and size of the test apparatus may be important, since ethanol produces increased ambulation with some reliability in the "open-field" apparatus (e.g., [1]). Gener-

alization about drug effects on SMA levels is further complicated by reports that the occurrence and degree of a "drug effect" on rats' activity may depend on how the behavior is detected and quantified. These differences have been observed when 'SMA' was detected simultaneously in the same rats by photocells and by the "Animex" device [12].

The present experiment identifies a set of conditions under which no increase in wheel running was produced by ethanol. Additional research may determine under what, if any, conditions ethanol does increase wheel running in rats.

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