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BRIEF COMMUNICATION

Automatically Determined Effects of Lithium, Scopolamine and Methamphetamine on Motor Activty of Rats

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WOLTHUIS, O. L., H. DE VROOME AND R. A. P. VANWERSCH. *Automatically determined effects of lithium, scopolamine and methamphetamine on motor activity of rats.* PHARMAC. BIOCHEM. BEHAV. 3(3) 515–518, 1975. – A device is described in which spontaneous motor activity of animals can be measured quantitatively in a capacitance field. By using multilevel detection in a homogeneous field the motions of the animals can be categorised according to their amplitudes and irrespective of the position of the animal in the cage. The effects of lithium ions, methamphetamine and scopolamine were assessed and compared with data in the literature.

Automatic activity measurements Rearing Methamphetamine Lithium Scopolamine

IN a detailed study Lát [6] has demonstrated the existence of a parabolic relationship between intra- and inter-individual differences in excitability level and speed of learning. Therefore, when the influences of drugs on learning behaviour are investigated [12], the effects of these compounds on motor activity should be measured and taken into account. The majority of devices used to measure activity (for review see [2]), however, given one overall score and the results obtained are not independent of the position of the animal in the cage.

The device proposed here is built on the same principle as the instrument used by Lát [6]. The essential difference is that in the present instrument two capacitor plates are used and the rat moves in a homogeneous electric field. The homogeneity of this field permits quantitative assessment of the vertical component of motor activity irrespective of the position or orientation of the animal in the cage. Moreover, the movements can be categorised into amplitude classes by means of multilevel detection.

We report here the activities of rats given lithium chloride, scopolamine and methamphetamine assessed by means of this apparatus.

METHOD

Animals

Male small Wistar (WAG) rats of 150–170 g body weight were brought from the breeding centre within the laboratory into the experimentation room 1 day prior to testing in order to allow them to begin adapting to the new environment. They were housed 6 to a cage. The relative humidity in the experimentation room was 50–60 percent, temperature 21–23°C, ambient noise 65–70 db and constant dim, indirect lighting was provided by a 75 W light bulb.

Drugs

The following drugs were administered: lithium chloride (Merck, Darmstadt, Germany), scopolamine hydrochloride (Brocades–ACF, Amsterdam, The Netherlands) and methylamphetamine hydrochloride (Burroughs Wellcome and Co, London, England). All drugs were injected subcutaneously (SC) in a volume 1 ml/kg body weight and dissolved in 0.9% NaCl. Control animals received solvent only.

Apparatus

One rat was placed into each of four identical glass cages (30 X 20 X 20 cm) provided with ventilation holes. The floor of each cage was covered with 180 g Tom Poes cat box absorbent (Quaker Oats Co, Rotterdam, The Netherlands). Each cage was placed between two parallel capacitor plates, 22 cm apart, made of aluminum sheet (50 X 40 X 0.15 cm). Each of the four measuring systems was situated in an essentially vibration free, electrically shielded box (80 X 80 X 80 cm).

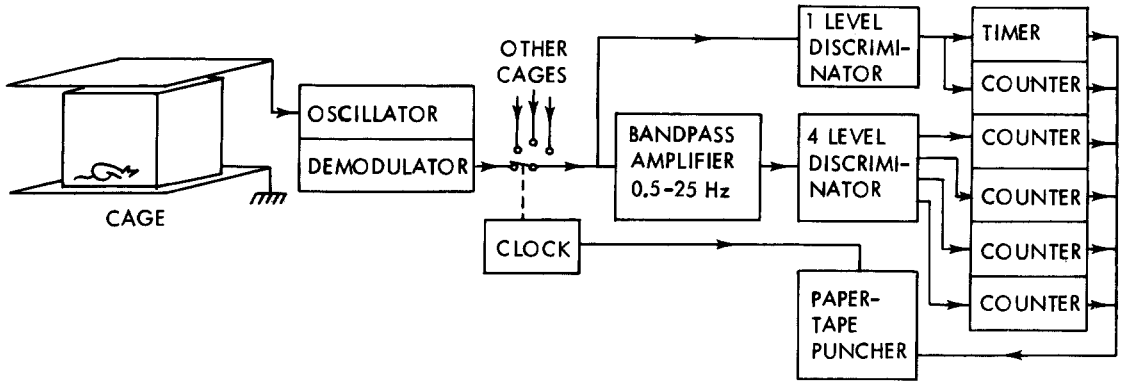

FIG. 1. A block diagram of the activity measurement device.

A block diagram of the device is shown in Fig. 1. The electronic detector consists of a fixed-frequency oscillator of 130 KHz and a resonance circuit of which the cage capacitor forms a part. Movements of the rat cause changes in the tuning of the resonance circuit, inducing changes in the output signal from this circuit. This signal is demodulated and amplified. A multiplexer selects the signal from one of the four cages at a time. The largest pulses in the selected signal, i.e. those exceeding 1 V, which correspond with rearing of the rat (see Results), are counted directly. Smaller signals first pass a band-pass filter (0.5–25 Hz) in order to eliminate drift and noise. After a further 20-fold amplification these signals are analysed by a 4 channel amplitude discriminator which distinguishes levels of 50, 150, 250 and 350 mV. Thus, 4 amplitude classes are separated; movements falling within these classes are registered on 4 separate counters. Finally, the cumulative time is registered that a signal exceeding 1 V (cumulative rearing time) is present.

During short term experiments (e.g. 1.5 hr) the data from the cages are successively sampled for one minute intervals and punched on paper tape together with the cage number, i.e. in 4 min all cages have been sampled for 1 min each. Analysis of the punched tapes is done by means of a Fortran II program on a PDP 8/1 computer. The data from multiple sets of 4 rats (usually 2 experimental and 2 control animals) can be grouped, averaged, statistically analysed and graphically displayed on a Tektronix 611 visual display unit and copied by a Tektronix 4601 hard copy unit. The copies obtained are essentially identical to Figs. 2 3 and 4.

Calibration

Calibration was done with an oscilloscope and a calibration device. The latter consisted of a 8 cm long metal rod of 4 mm dia. connected to a synchronous motor. The rod rotated in a windmill fashion in a plane at an angle of 60° with the horizontal plans. The rotation centre was 7.3 cm above the cage floor, the rotation speed was 1 rev/sec. Because one arm of the rotor was 1½ mm longer than the other, it was possible to adjust the amplifier so that only a Class 4 of amplitude signal was registered when the longer arm was moving upward whereas Class 1, 2 and 3 signals were registered when the longer as well as when the shorter arm was moving upward. Thus, in Class 4 half as many counts were registered as in the Classes 1, 2 and 3.

Procedure

Randomly chosen rats were taken out of their home cages and their activity was registered for 16 min. They were then quickly taken out of the glass cages, injected with drug or solvent and returned. The activity was subsequently measured during 80 min.

RESULTS

Measuring Technique

It was established that the glass cages were located in homogenous fields by placing the rotating calibration device at several places between the plates and registering the counts. The calibration was shown to be stable for at least 24 hr and diurnal rhythms in activity of rats could be recorded. For this stability, especially during long term experiments it was found to be essential that a good absorbent be used on the cage floor because wet paw marks on the walls of the glass cages lead to unpredictable disturbances of the measurements. The type of cat box absorbent used could absorb an amount of water equal to half its own weight and compared favorably with two other brands tested, with wood shavings or with multilayer filter paper. Moreover, it had no sharp edges which might affect the motor activity of the rat.

Attempts were made to correlate the signal changes with various types of behavioral activity. It was established by two methods that signals exceeding 1 V represented rearing: (1) slow-motion videorecordings of rats of 150–170 g body-weight showed that, when their heads passed through an imaginary horizontal plane 16 cm above the bottom of the glass cage, a signal larger than 1 V was generated; and (2) when rearing was prevented by mounting a ceiling 16 cm above the cage bottom, the signal output remained below 1 V. In addition, it was found that when lightly anaesthetised rats were put into the cages only counts of the lowest amplitude were scored; synchronously with the respiratory rhythms. Counts in Amplitude Class 1, therefore, represent mostly breathing. Counts in the Amplitude Classes 2, 3 and 4 (which, together with Class 1 were called horizontal movements in the figures) were difficult to categorise, because many types of behaviors induce the same changes in the electric field, however, by means of videorecordings it appeared that isolated movements of the

head (e. g. sniffing) or the extremities were scored mostly as amplitude 2, extensive movements made by rats remaining in one place (e.g. scratching and grooming) as Amplitude 3 and walking around in the cage as Amplitude 4 movements.

Drug Effects

A dose of 2 mg/kg methamphetamine causes an increase in the number of rearings (Fig. 2). Since the cumulative rearing time is unaffected during the first 48 min after the injection, it can be deduced that during that period the duration of each rearing is shorter. Further it can be seen that predominatly the larger, i.e. the Amplitude 3 and 4 movements, are increased whereas the Amplitude 1 movements are slightly but significantly decreased. Scopolamine (1 mg/kg) causes mainly an increase in movements of Amplitude 2, 3 and 4 without a concomitant increase in rearing (Fig. 3), whereas 85 mg/kg lithium chloride leaves movements of Amplitude 2, 3 and 4 relatively unaffected but causes a reduction of rearing to almost zero (Fig. 4). The dose of 42.5 mg/kg lithium chloride causes no significant changes in motor activity.

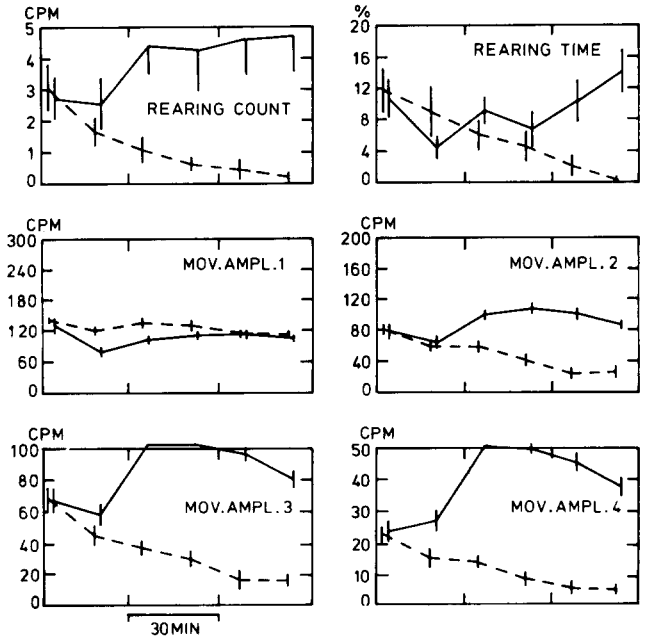

FIG. 2. The effects of 2 mg/kg methamphetamine SC on spontaneous motor behavior as a function of time. The dashed lines represent the mean (± S.E.) activities of 7 saline treated animals, the solid lines those of 7 methamphetamine treated animals. Injections were given immediately following the first measurements. The top left graph shows the number of rearings per min (cpm) averaged during 16 min periods, the top right graph the time spent in an upright position, expressed as a percentage of those 16 min periods. The lower graphs represent horizontal movements of increasing amplitudes, movement amplitude 4 being the largest. The graphs demonstrate that methamphetamine increases the number of rearings, whereas rearing time during the first 50 min has hardly changed. Moreover it can be seen that especially the horizontal movements with large amplitudes have increased.

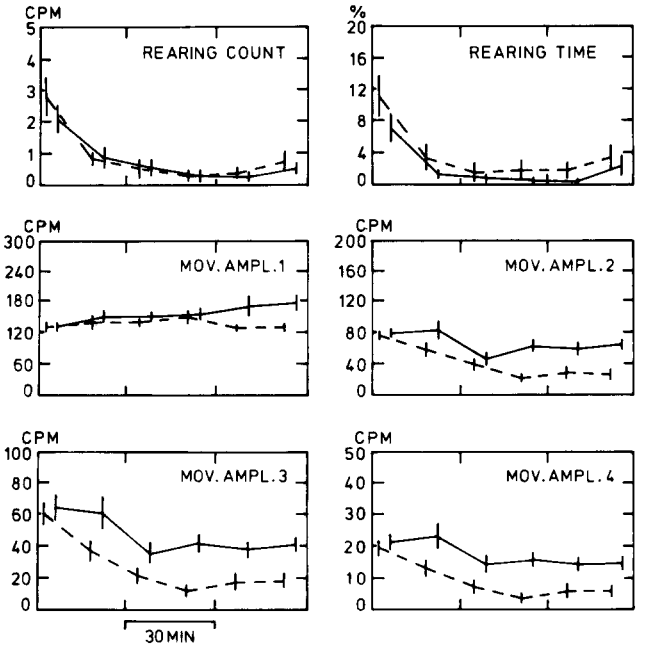

FIG. 3. The effects of 1 mg/kg scopolamine SC on spontaneous motor activity. The mean values (± S.E.) of 9 saline treated (dashed line) and 9 scopolamine treated (solid line) animals are shown. Scopolamine affects mainly the large amplitude horizontal movements (lower two graphs) and causes, in contrast to methamphetamine, no concomitant increase in rearing. For further details see Fig. 2.

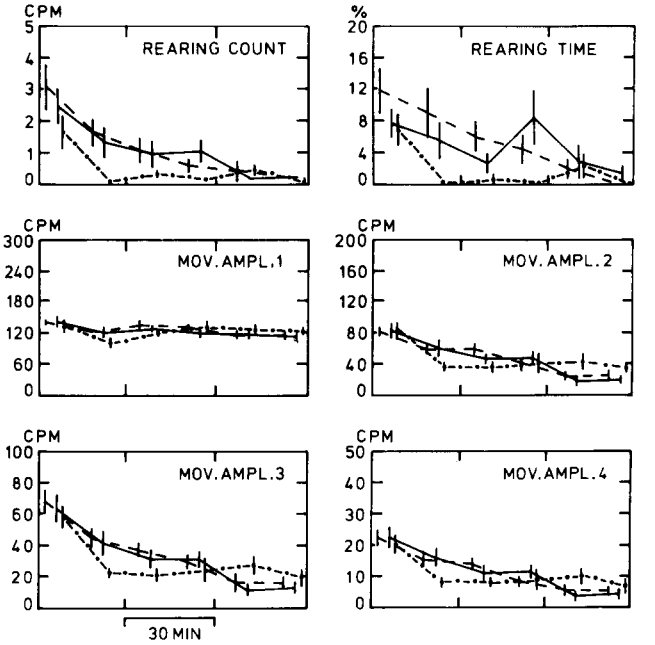

FIG. 4. The effects of 42.5 mg/kg (solid line) and 85 mg/kg (dash-point-dash line) lithium chloride SC compared with the effects of saline (dashed line). Each group consisted of 7 rats and the mean values (± S.E.) are represented in the graphs. The graphs show that the lower dose of lithium chloride causes no significant changes. The higher dose reduces rearing activity to zero, without a clearcut effect on horizontal movements. For further details see Fig. 2.

DISCUSSION

A device is described in which the vertical component of activity of rats can be measured in a quantitatively meaningful manner because the animal moves in a homogeneous field. Measurements, therefore, are irrespective of the position of the subject in the cage. The homogeneity makes a categorisation of activity possible on the basis of the vertical components of the movements of the animal. The present apparatus offers some advantages over instruments published in the literature. With the exception of the ultrasonic devices, which seem to have some problems of their own [2], most of these devices measure only overall activity. The system described here can easily be calibrated to accommodate bigger or smaller rats. Although the frequency and, if necessary, the sequence of the movements of certain amplitudes can be registered, the correlation between vertical amplitude and type of behavioral activity remains difficult to pin down, with the exception of rearing and breathing. Our identification of Amplitude 2, 3 and movements as sniffing, grooming and walking respectively should be treated with some caution and was merely meant to give an approximation of the types of movements measured.

Most of the effects of amphetamines are well known (see review by Grossman and Sclafani, [3]) and will not be discussed in this paper. However, it seems worthwhile to note that our data agree well with those of a recent elaborate study by Norton [8], who counted in (time lapse) photographic frames the frequency, duration and the sequence of a number of well-defined behavioural acts and found that amphetamine caused changes in the frequencies of these acts and shortening of each act. This supports our finding that the number of rearings increases but that each rearing is shortened. Also, our data, confirm Norton's findings that mainly the larger movements (such as walking and turning) were increased, whereas the smaller movements were less affected.

Scopolamine induces an increase in gross motor activity [1, 7, 10]. Our data are in agreement with those of a recent ethological study by van der Poel [9], who reported an increase in omnidirectional horizontal exploratory activity. The absence of a concomitant increase in rearing shown in the present experiments suggests that scopolamine causes a change in exploratory patterns.

Johnson and Wormington [4] and Johnson [5] found that lithium ions selectively depress rearing activity. Steinberg [11], who used photocell activity cages, seriously doubted the validity of these results since she found no effects of lithium in otherwise untreated animals. Our results fully agree with those of Johnson and Wormington [4] and indicate that the selective effects of lithium on rearing can be unequivocally demonstrated provided a proper detection method is employed.

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