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The Use of Doppler Shift Radar to Monitor Physiological and Drug Induced Activity Patterns in the Rat

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MARSDEN, C. A. AND B. KING. *The use of Doppler shift radar to monitor physiological and drug induced activity patterns in the rat.* PHARMAC. BIOCHEM. BEHAV. **10**(5)631–635, 1979.—Doppler shift radar was used to monitor circadian activity patterns in the rat and to study the behavioural effects of p-chloroamphetamine and d-amphetamine. Activity was classified in two ways:- (a) slow (non-locomotory) and high (locomotory) speed movements. (b) the number of starts of activity, within either the slow or high speed zones of activity during a pre-set time. p-Choloramphetamine (5 mg/kg) produced a biphasic activity response; an initial increase in continuous non-locomotory activity followed by a longer lasting increase in exploratory locomotion containing regular starts of activity. d-Amphetamine (2.5 mg/kg) produced an increase in both non-locomotory and locomotory movements but a marked reduction in starts of activity (i.e. continuous non-exploratory activity). The combination of information on the amount and pattern (starts) of activity allows a more detailed analysis of the effects of drugs on activity to be made than with existing automated methods.

Circadian rhythm Activity p-Chloroamphetamine d-Amphetamine

MANY psychoactive drugs not only induce changes in total motor activity but also produce a shift from one form of activity (e.g. normal exploratory behaviour) to another (e.g. continuous body movements without exploratory behaviour). Existing automatic activity monitors have only limited capabilities of differentiating between different types of activity—while some activity meters are able to separate activity into gross and fine movements they are unable to determine the pattern of activity in terms of the number of discrete bursts of activity within a set time. Such information is important if one wants to distinguish between normal exploratory and stereotyped behaviour.

The present paper describes a system using doppler shift radar which can analyse both the speed and time pattern of activity. To test the capabilities of the system the circadian activity pattern in the rat was monitored and a comparison made of the effects of p-chloroamphetamine and d-amphetamine on the pattern during the light period. p-Chloroamphetamine administration causes an initial release of 5-hydroxytryptamine (5HT) [6, 9] and amphetamine releases catecholamines [8].

Principle and Apparatus

The Actimat (Kinson Electronics, Wellington House, Eton Road, London NW3 4SY) uses the principle of doppler shift radar. This involves directing an extremely low energy microwave source (10.5 GHz) into an experimental area (60×70×65 cm. Fig. 1) and measuring and analysing the small frequency change of the reflected signal caused by movement. The traditional problems of interference from passing persons, fluorescent lighting and adjacent ventilation systems are eliminated by the use of a special enclosure (Fig. 1) which fully absorbs troublesome stray microwave radiation. An added avantage of the enclosure is that it can be used to provide a sound resistant environment with integral air exchange and controlled lighting. The 3 $\mu W/cm^2$ energy level of the beam is some 100 times lower than the U.K. health safety level for humans and has no effect on rodents. Another advantage of microwaves projected from above is that standard plastic animal housing with metal grille lids placed in the enclosure have little effect on the movement of the microwaves so long as the grille lids are not full of food. In the present experiments standard plastic cages were used with the food in hoppers inside the cage.

The frequency of the reflected signal is linearly related to the speed of movement of the animal and its amplitude proportional to the body area involved. In these experiments two frequency bands were used. Firstly 0.4 Hz to 4 Hz, which was used to monitor low speed activity, consisting largely of movements of the head and body without actual locomotion (based on direct behavioural observation). Sec-

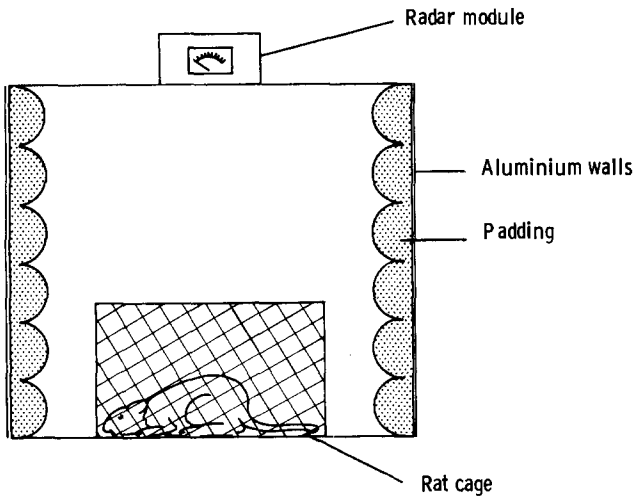

FIG. 1. Cross section diagram of the doppler radar module in position over the enclosure. The radar module is connected to a unit (not shown) containing the time base, sensitivity and start-time controls. The outputs of this unit are recorded on a microprocessor controlled programmable printer.

ondly 4–100 Hz, representing the high speed activity zone, which was mainly normal exploratory behaviour with movement around the cage. Within these two zones, activity was quantified in two ways (a) the seconds spent in each zone during a pre-set time period, referred to as activity counts, with each count representing 1 sec of activity. Over a pre-set period the count totals represented the fraction of the total time spent by the animal in each zone of activity (b) the number of starts of activity that occurred within each zone during the pre-set time period. A start of activity in these experiments was defined as activity in that zone following 10 sec of no activity in that zone. Monitoring starts of activity allows time dependent patterns of behaviour to be demonstrated. The doppler radar module was connected to a unit containing the time base, sensitivity and start-time controls. The outputs of this unit was recorded on a microprocessor controlled programmable printer (Kinson Electronics).

Animals and Drugs

In all experiments male Wistar rats (220–240 g) singly housed were used and maintained on a 12 hr light-dark cycle with food (Oxoid 41B) and water ad lib.

p-Chloroamphetamine (5 mg/kg) and d-amphetamine (2.5 mg/kg) were dissolved in 0.9% saline and administered

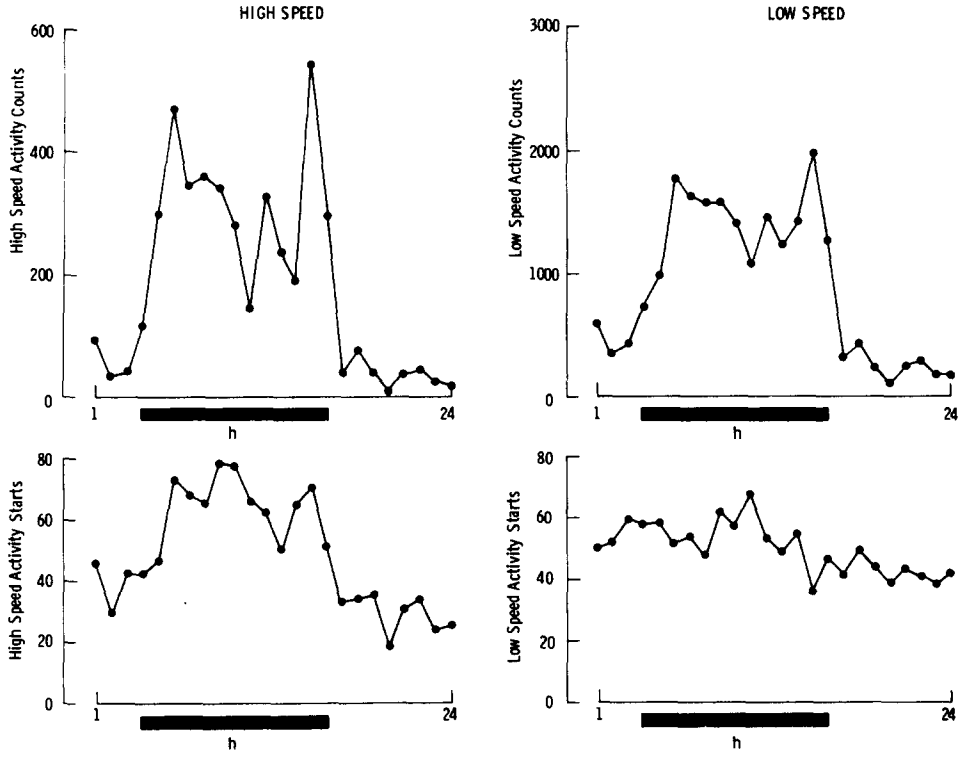

FIG. 2. Circadian changes in the level and pattern of activity within the slow and high speed activity zones. The results are the mean of 6 experiments each experiment involving one rat. Note the clear circadian changes in the high speed zone (exploratory locomotory activity) both in terms of the level (counts) and pattern (starts). The changes in the slow speed zone (non-locomotory activity) are less marked and there is no clear circadian pattern in the starts of activity in this zone.

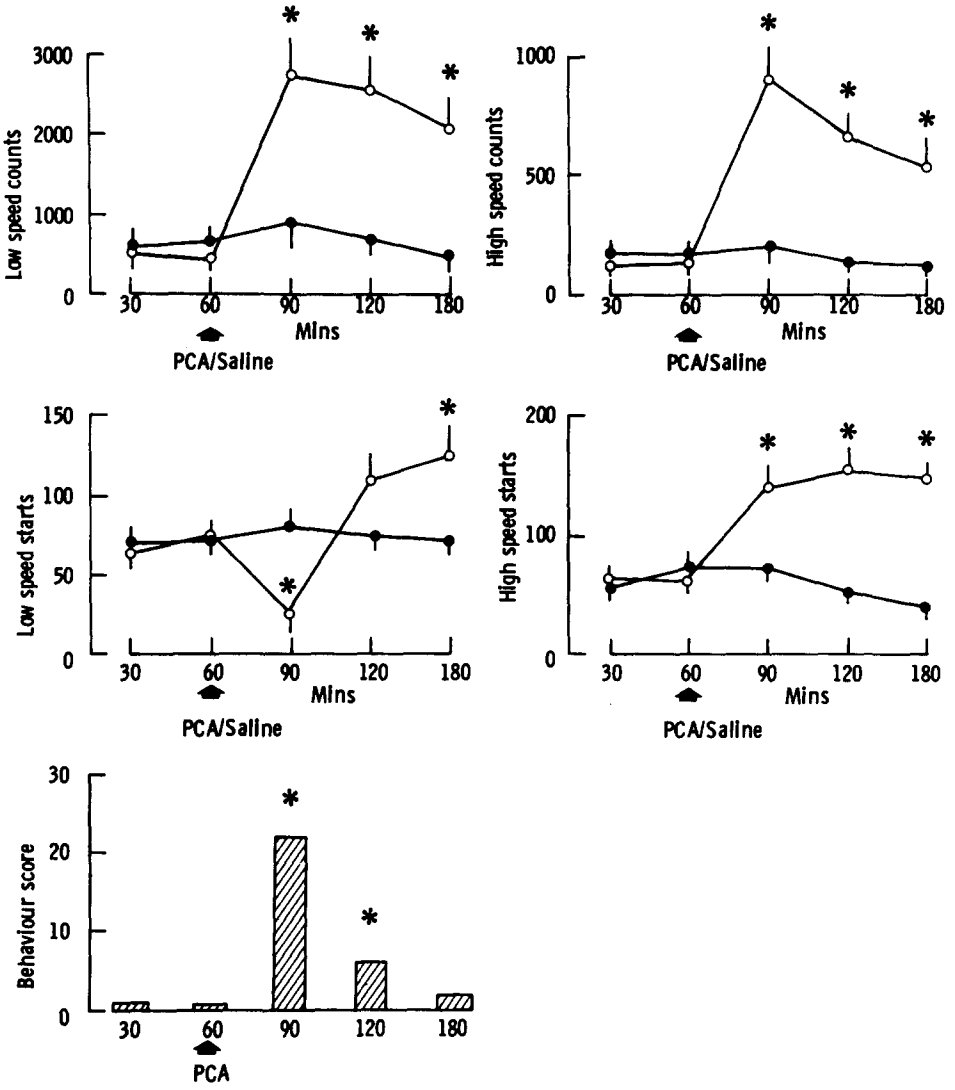

FIG. 3. Effects of p-chloroamphetamine (5 mg/kg ○——○) and 0.9% saline (2 mls/kg ●——●) on slow and high speed activity counts and starts. Injections were made 90 min after the start of the light period and activity monitored for 60 min before injection. Behaviour was scored every 5 min and is given as the mean total score/30 mins. Note the two phases of the activity response produced by p-chloroamphetamine. The initial marked rise in slow speed activity is accompanied by a decrease in slow speed starts and associated with the maximum increase in behaviour score indicating continuous non-locomotory movements. From 30 min the initial response is replaced by an increase in exploratory locomotory behaviour (large high speed activity counts together with increased starts). Results are the mean of 6 experiments±SE, in both drug and saline treated groups, each experiment involving 1 rat. Differences in activity analysed by student t-test and behaviour score by the Mann Whitney U test $^*p<0.01$.

intraperitoneally (2 mls/kg). Controls were given 0.9% saline 2 mls/kg. Rats were assigned to drug and saline treated groups (6 rats/group). Each rat received either one of the drugs or saline 90 min after the lights went on. No animal received more than one injection. Activity was monitored for 60 min before injection and for up to 120 min after injection using 30 min time periods. The activity of a further 6 rats was monitored individually for 72 hr using 60 min time periods. Differences between drug and saline treated rats were analysed using the Student t-test.

Behaviour Score

The behaviour response produced by p-chloroamphetamine was scored using a 0–3 rating scale previously described [2] of the following behavioural features: Lateral head weaving, forepaw treading, hindlimb abduction and straub tail. Behaviour was scored every 5 min before and after injection and results given are the 30 min mean total behavioural score. Differences between the pre-and post-injection scores were analysed by the Mann Whitney U test.

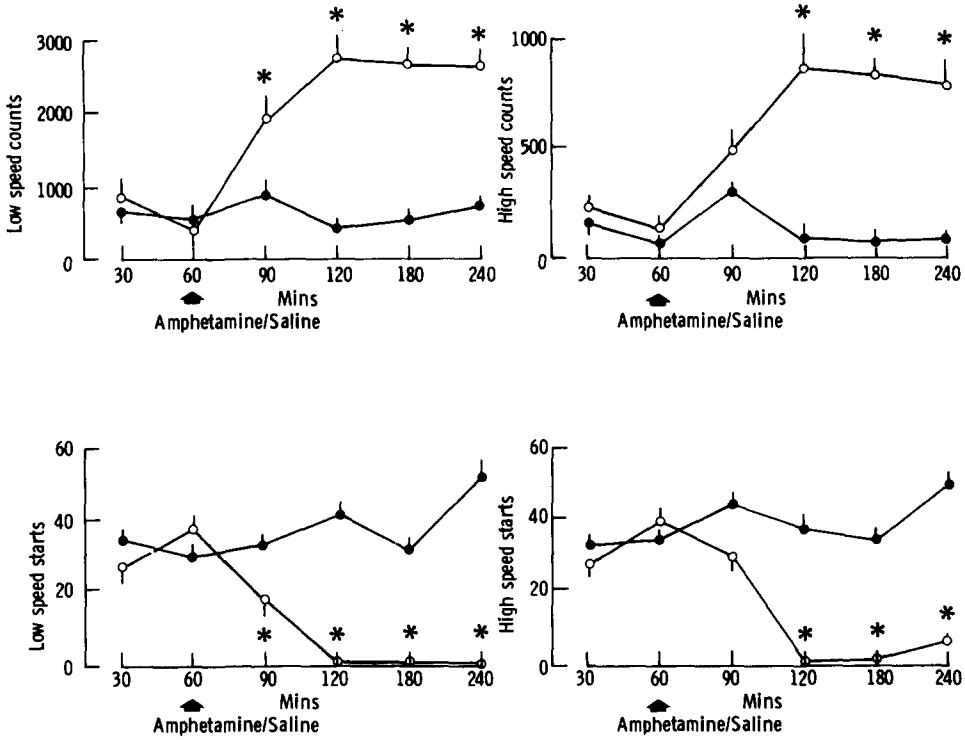

FIG. 4. Effects of d-amphetamine (2.5 mg/kg ○——○) and 0.9% saline (●——●) on slow and high speed activity and starts. Injections were made 90 min after the start of the light period and activity monitored for 60 min before injection. Note the prolonged rise in counts and decrease in starts in both activity zones. Results are the mean of 6 experiments±SE, in both drug and saline treated groups, each experiment involving 1 rat. Differences analysed by Student t-test $^*p<0.01$.

RESULTS

Circadian Rhythm

The doppler radar system clearly differentiated between high levels of activity in the dark and low levels in the light period (Fig. 2). The results showed a circadian pattern in both the high and low speed activity zones though the pattern was more marked in the high speed (locomotory behaviour) zone. Within the high speed zone the activity counts during the dark period showed a biphasic pattern which was much less apparent in the low speed counts (Fig. 2). During the light period there was not a continuous phase of inactivity, as there were characteristic starts of high speed activity (locomotion) both shortly after the lights went on and shortly before they went off. The patterns of activity within the zones indicated that in the high speed zone starts of activity clearly followed the activity counts while in the low speed zone there was no clear relationship (Fig. 2).

Effects of p-Chloroamphetamine (5 mg/kg) and d-Amphetamine (2.5 mg/kg)

p-Chloroamphetamine administration increased low speed activity counts but markedly decreased low speed activity starts at 30 min indicating an initial period of continuous slow speed movements (Fig. 3). While the increase in low speed counts was seen throughout the 90 min experiment the starts of slow speed activity returned to near normal values at 60 mins and were significantly increased at 90 mins. High speed activity counts also increased and this was maintained over the 90 min and was accompanied by a progressive increase in starts of high speed activity (Fig. 3). The highest behaviour score was at 30 min—the time at which there was a significant increase in low activity counts but a significant decrease in low activity starts (Fig. 3).

d-Amphetamine (2–5 mg/kg) significantly increased high and low activity counts and significantly decreased starts (Fig. 4).

DISCUSSION

The main objective of these experiments was to determine whether the use of doppler shift radar would allow one to obtain information on the type of activity and not just the amount of activity. The results indicate that the ability to determine patterns of activity gives an important new dimension to automated activity measurement techniques.

The marked circadian variation of activity in the rat is in agreement with results obtained using existing activity monitors (e.g. [1, 4]) and wheel running and stabilimeter cages in mice and rats (e.g. [3, 7]). The additional information obtained from monitoring starts of activity within the two zones showed that high activity in the high speed zone was associated with many short lasting starts of activity. The starts of activity however, in the low speed zone were not clearly related to the activity counts. This indicates that locomotory behaviour shows a clear diurnal pattern. Non-locomotory movements however show marked circadian

variations in intensity but not in the number of starts of activity indicating it is the duration, not the number, of each non-locomotory movement that varies in response to time of day. This combination of information on amount and starts of activity can be used to differentiate with greater subtlety the type of activity drugs induce. Direct observation of rats given p-chloroamphetamine, a drug that initially releases neuronal 5-HT followed by long-lasting decrease in brain 5HT [9] show an initial behavioural response consisting of repetitive lateral head weaving, hind limb abduction, forepaw treading and straub tail [2,10]. This behavioural response, assessed by the behavioural score in the present experiments was associated with an increase in low speed activity counts and a decrease in starts of low speed activity. The administration of p-chloroamphetamine was also associated with an increase in high speed activity counts and starts of high speed activity (Fig. 3). From direct observation the monitored response in the high speed zone was associated with enhanced exploratory and running behaviour which was apparent from about 30 min and lasted until about 120 min after giving the drug. Thus p-chloroamphetamine produced a biphasic behavioural response consisting of a phase of repetitive mainly non-locomotory movements which began shortly after administration, followed by a longer lasting period of increased exploratory behaviour. This biphasic response could be monitored by doppler radar. A similar biphasic response is produced by α-methyltryptamine, another drug which increases the release of presynaptic 5HT [5]. Stereotyped behaviour produced by d-amphetamine was clearly demonstrated by the doppler radar system as increased counts in the high and low speed zones associated with a marked decrease in starts of activity within the two zones indicating the continuous nature of the response (Fig. 4).

In summary an activity monitor able to measure both slow and fast speed activity and the number of bursts of activity in the respective speed zones is described. The system is able to distinguish between continuous (stereotyped) and normal exploratory behaviour. The use of doppler shift radar with the start facility to monitor patterns of activity should provide important information about physiological and drug induced changes in behaviour.

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