Uses and Limitations of Photocell Activity Cages for Assessing Effects of Drugs

M. KRŠIAK*, HANNAH STEINBERG, and I. P. STOLERMAN

Department of Pharmacology, University College London

Received November 16, 1969

Abstract. The behaviour of rats placed in a new environment was determined simultaneously by photocells and by direct observation. Predictably, a typical photocell activity cage did not measure a simple or homogeneous pattern of behaviour even in undrugged animals: two components of behaviour, the number of walks across the cage and of rears onto the hind feet, were correlated with photocell counts, but grooming was not. Even this agreement between observation and automation broke down if dexamphetamine was given; the correlation between rears and photocell counts was reduced by graded doses of dexamphetamine and by dexamphetamine-amylobarbitone mixtures, and the stimulant effect of dexamphetamine on walks was greatly exaggerated by the photocells. Such discrepancies were much smaller with amylobarbitone alone. For the testing of drugs, the use of activity cages seems to be more limited than has sometimes been supposed. Complex changes of behaviour are masked by the relatively crude photocell counts, but they may be detected by standardised observation. Watching the animals might also help with the development of improved automatic devices.

 $Key\text{-}Words:$ Activity -- Screening -- Photocells and Observation -- Dexamphetamine -- Amylobarbitone -- Drug Combinations.

Introduction

The development of psychoactive drugs is heavily dependent on the initial screening tests in which behaviour is assessed by some form of automatic recording or by direct observation. Compounds are then either rejected or passed for fuller testing, and the efficiency of the screening test is therefore crucial for the entire programme but, as Kinnard and Watzman (1966) have pointed out, "It is ironic that, of all the procedures that comprise a screening program, these are the most critical, yet the least standardized, most highly individualized, and most vulnerable to environmental factors."

Photocell activity cages (Siegel and Steinberg, 1949) yield counts of the number of times that beams of light are broken by animals' movements, and have been much used in experiments with drugs (e. g. Winter

^{*} Present address: Institute of Pharmacology, Czechoslovak Academy of Sciences, Prague.

and Flataker, 1951; Dews, 1953; Cook *et al.,* 1955). However, little information is available about the kinds of behaviour actually picked up by photocells, or on how far observation and automation agree when directly compared. Finger (1969) has investigated activity during oestrus in rats and has found discrepancies between the results obtained with photocells and by direct observation. Furthermore, the correlations between the results obtained with different kinds of apparatus for measuring general activity have been generally found to be low; typically $r = 0.2$ (e.g. Eayrs, 1954; Tapp *et al.*, 1968).

The aim of the experiments described here was, first, to find out which components of the behaviour of undrugged control animals were measured by a typical photocell arrangement, and then to determine whether changes in the photocell counts due to "standard" drugs (dexamphetamine and amylobarbitone and combinations of these two), in a range of doses, adequately reflected changes in these components. A preliminary report of some of this work has been published (Kršiak *et al.,* 1968).

Methods

Subjects. Hooded rats aged about 120 days were used throughout. Between weaning and testing they were housed 16 to a cage in standard conditions with a regular day/night cycle, and were moved into the laboratory at least one week before the experiment.

Apparatus. The activity cage used is illustrated in Fig. 1. The interior dimensions were $27\times27\times27$ cm, and two photocells were mounted 4 cm above the floor. The light beams crossed in the centre of the cage, but double counts due to animals moving past both beams at once were prevented by a perspex column in the centre of the cage. The light transmitter units had infra-red filters in order to reduce any influence of the light on behaviour. The circuits used limited the maximum rate of counting to 2--3 counts per second.

The cage and the observer were in a sound-proofed room main. tained at $22^{\circ} + 1^{\circ}$ C; the number of interruptions of the light beams were recorded on digital counters in an adjoining room. Throughout the experiments, the combined counts from the 2 beams of each cage were recorded on the same counter.

Procedure. There were three separate experiments; the procedures for testing behaviour were similar throughout and only the drug treatments were different. Each rat was injected subcutaneously 35 min before a trial either with isotonic saline (0.2 ml/100 g body weight) or with a drug dissolved in saline. A trial consisted of placing a single experimentally naive rat in the cage for 10 min and recording its behaviour simultaneously by means of the photocells and by direct observation.

Fig. 1. Plan of the activity cage; interruptions of the 2 beams of infra-red light were recorded on digital counters, and simultaneously various components of behaviour were scored by direct observation

Each rat was used once only and all trials took place between 1 and 5 p.m. In each experiment the allocation of rats to treatments was by a random method, the same experimenter observed of all the rats within each experiment, and scored three components of behaviour:

1. "Walks"--the number of times the rat moved, with all four feet, more than half-way across the space between any two opposite walls of the cage. The total time spent in walking was also recorded.

2. "Rears"--the number of times that the rat stood on its hind feet, with its head raised at least 15 cm above the floor of the cage. The total time of rearing was also measured.

3. "Grooming"--the time the rat spent washing or scratching, or manipulating in any other way any part of its body.

Experiment 1. Undrugged Rats. The aim was to determine which components of behaviour the photocells picked up when undrugged rats were tested. Sixteen male rats were given saline and were tested as described under *procedure.*

Experiment 2. Dexamphetamine. Forty female rats were allocated to 5 treatment groups, and were injected either with saline or with dexamphetamine sulphate $(0.25, 0.5, 1.0 \text{ or } 2.0 \text{ mg/kg})$; the doses were selected on the basis of earlier experiments with Y-mazes (Rushton and Steinberg, 1963) and of a preliminary experiment with the activity cage, as being within the range which produced clear effects on activity. By using a second counter for each cage the total photocell counts

during each 10-minute trial were recorded both at the fastest rate at which the recording equipment would respond (approximately 10 counts per second) and with a reduced rate $(2-3 \text{ counts per second})$, in order to determine whether this characteristic of photocell units might be important.

Experiment 3. Amylobarbitone and Amylobarbitone-Dexamphetamine Combinations. Sixty-four female rats were allocated to 8 treatment groups. Five of the groups were used to study dose-response relationships of amylobarbitone sodium and received either saline or a dose of amylobarbitone $(3.75, 7.5, 15.0 \text{ or } 30.0 \text{ mg/kg})$. The remaining three groups were given dexamphetamine (1.0 mg/kg), either alone or in combination with amylobarbitone (7.5 or 15.0 mg/kg). The doses were chosen on the basis of experiments with Y-mazes (Rushton and Steinberg, 1963, and 1967).

Results

Experiment 1. Undrugged Rats

The frequency measures (numbers of "walks" or of "rears") will be used throughout; the times spent walking and rearing, which were also recorded, were highly correlated with the corresponding frequency measures (typically, $r = 0.9$), and showed substantially similar drug effects. Variability also was similar for the two types of measure, and the frequency measures were finally chosen for full analysis only because they could be conveniently illustrated on the same scales as photocell counts. The behaviour of 15 of the 16 rats was scored simultaneously by two experienced observers and agreement between them was very close $(r = 0.966$ and 0.969, for walks and rears respectively, *dt* 13, $p < 0.001$ in both cases).

Scatter diagrams have been plotted (Fig. 2) to show how the numbers of "walks" and of "rears" are related to photocell counts $(r = 0.77$ and 0.80, for walks and rears respectively, df 14, $p < 0.001$ in both cases). The correlations are not significantly different from each other $(t = 0.20)$. The time spent "grooming" was not correlated with photocell counts $(r = -0.15)$. The correlation of walks with rears was 0.42, which is not statistically siguificant. Partial correlation coefficients for walks and rears with photocell counts were also high $(0.80 \text{ and } 0.83 \text{ respectively})$; that both walks and rears are correlated with photocell counts is probably not merely because they are correlated with each other.

Multiple linear regression analysis (using a library programme, BMD O2R) showed that the combination of walks and rears could account for 85% of the variance of the photocell counts. This close agreement between photocell counts and the observational measures is shown in 262 M. Kršiak, Hannah Steinberg, and I. P. Stolerman:

Fig.2. 16 control rats were tested individually for lOmin in the activity cage (experiment 1). The scatter diagrams illustrate the relations between photocell counts and two components of behaviour: both walks and rears were significantly correlated with photocell counts $(p < 0.001$ in both cases)

:Fig.3 a and b. The high correlation between photocell counts and combined walks and rears for control rats is shown in Fig.3a. Agreement was less marked when the results obtained by many untrained observers in separate experiments were included (Fig.3b). In both cases, the optimal combination of walks and rears was calculated by a muttiple regression technique

Fig.3a; the multiple regression coefficient (R) , which is isometric with the correlation coefficient (r) , was 0.93 for the 16 rats used in this experiment. The small remaining variance can be attributed either to behaviour measured by the photocells but not scored by observation, or to experi. mental errors.

These results were then combined with those from the 16 saline controls of experiments 2 and 3 and also with 21 other saline rats tested in undergraduate classes. The correlations of walks and rears with photo. cell counts were then somewhat lower (0.69 and 0.62) but still significant df 51, $p < 0.001$ in both cases). The lower values are probably a consequence of including results obtained by untrained observers. The correlation between the two observational measures, walks and rears, was significant with the much larger number of rats now included $(r = 0.51, df 51, p < 0.001)$. Nevertheless, the partial correlation coefficients of walks and rears with photocells remained significant $(r = 0.55, dt 50, p < 0.001$ and $r = 0.42, dt 50, p < 0.01$. The multiple regression equation was: Photocell counts $= 29.7 + 0.70$ ("Walks") + 0.74 ("Rears"). The effectiveness of this equation is illustrated in Fig. 3 b : with this larger number of rats the multiple regression coefficient (R) $= 0.75.$

Experiment 2. Dexamphetamine

In order to reduce the heterogeneity of variance, all the results from this experiment and from experiment 3 were subjected to a square root transformation before statistical analysis. A similar transformation had not been considered necessary for analysing the results of experiment 1 and in any case had negligible effects when applied later as a check. One-way analyses of variance and regression analyses of dose-response relationships were performed throughout.

Dexamphetamine increased the total number of photocell counts during the 10 min trial (Fig.4a). The maximum number of counts under dexamphetamine was approximately double the number under saline. The linear component of the upward trend with dose was highly significant $(p < 0.001)$. A significant quadratic component $(p < 0.05)$ gives statistical support to the levelling of the dose-response curve at doses of 1.0 to 2.0 mg/kg. The results were also analysed separately for the first and second halves of the 10 min trial (Fig. 5a). Under saline, photocell counts were lower in the second half of the trial than in the first, and it was there that the effect of dexamphetamine was clearest; in both parts of the trial dexamphetamine raised the number of photocell counts to about 85 in 5 rain (cf. Tedeschi et *al.,* 1964).

The numbers of "slow" photocell counts (maximum rate $2-3$ /sec) were only slightly below the numbers of "fast" counts (maximum 10/sec); reducing the rate of counting did not therefore change the dose-response relationship for dexamphetamine (Fig.4a). The variability within groups was also similar for fast and slow counts at all dose levels. For example, after 0.25 mg/kg of dexamphetamine, the mean fast count was 127.3/10 min (s.d. 35.4) and the mean slow count was 119.4 (s.d. 33.8).

The effects of dexamphetamine on the numbers of walks and of rears are illustrated in Fig. 4a; on neither measure were the effects of the drug as marked as on photocell counts. The increase in walks is highly significant, but the tendency for the curve to level off at the higher doses was

Fig.4a and b. Ten groups of 8 rats were injected subcutaneously either with saline or a dose of a drug 35 min before a 10 min trial in the activity cage. After dexamphetamine, marked discrepancies occurred when the results with photocells were compared with observation. (Fig. 4 a, experiment 2), but agreement was close after amylobarbitone (Fig.4b, experiment 3). Photocell counts were recorded both at the highest rate at which the circuits could respond ("fast" counts) and with the maximum possible counting rate deliberately reduced to $2-3$ counts/second ("slow" counts), but the results did not differ

not (Table 1). Rears increased only slightly with dose, and even the linear trend did not reach an acceptable level of significance ($p < 0.1$). Time spent grooming on the other hand decreased sharply with dose (Fig. 6).

Walks and rears were combined at each dose according to the multiple regression equation determined in experiment 1 from a total of 53 control rats. Fig.4a shows that even the increase in walks and rears combined was less marked than the increase in photocell counts, and that this discrepancy increased steadily with doses up to 1.0 mg/kg. At that dose the effect of dexamphetamine on photocell counts exceeded its effect on walks and rears combined by 45% . Further analyses showed that the discrepancy was concentrated in the second half of the trial, where it reached 70% ; it has already been established (Fig.5a) that this was precisely where, on the basis of photocell counts, dexamphetamine appeared to have the most marked effects.

An alternative method of looking at the validity of the photocell counts is to calculate correlations between the various measures at each

Fig. 5a and b. Photocell counts during different periods of the 10 min trial. Counts were most markedly increased by dexamphetamine during the second haft of the trial in the activity cage (a) . The action of amylobarbitone changed from stimulant early in the trial to predominantly depressant by the end (b)

dose. However, for reliable estimates of the value of the correlation coefficient, more than the 8 subjects tested at each dose are needed. In an attempt to overcome this difficulty the correlation coefficients for pairs of doses were pooled according to a method described by Snedecor and Cochran (1967). Thus, correlations were calculated for "low" doses $(0.25 \text{ and } 0.5 \text{ mg/kg})$, and "high" doses $(1.0 \text{ and } 2.0 \text{ mg/kg})$ of dexamphetamine (Table 2). Correlations after saline were calculated by combining in the same way the data from the 8 rats injected with saline in this experiment with those from the corresponding 8 rats in experiment 3. The correlations so calculated closely agree with those from experiment 1. Table 2 shows that while the correlation of photocell counts with walks remained high regardless of the dose of dexamphetamine, the correlation with rears fell to zero after the "high" doses. This suggests that what photocells measure in drugged animals may be different from what they measure in saline animals.

Experiment 3.

$Amylobarbitone and Amylobarbitone = Dexamphetamine Combinations$

The relations between doses of amylobarbitone and all the measures were in the form of an inverted "U". Small doses increased and the largest dose depressed all measures. Fig.4b shows that photocell counts increased with dose, reaching a peak at 7.5 mg/kg, and then declined. The statistical significance of a dose-response relationship of this form can be tested by the quadratic component of the overall between-doses variance; for example, for photocell counts the F ratio of that component was 22 (Table 1). That the facilitating effects were most pronounced

in the first half of the trial can be seen in Fig. 5 a ; only in the second half of the trial did even the largest dose have an appreciable depressant action. Slight ataxia was observed with 15 mg/kg and severe ataxia with 30 mg/kg , and this appeared substantially constant throughout the trial.

A more detailed breakdown of the results with amylobarbitone $(Fig.5b)$ shows that initially the drug acted as a stimulant at all doses tested. As the trial proceeded, this effect occurred only at progressively smaller doses and it seems possible that over even longer periods the drug might manifest only a depressant action. Photocell counts seem quite suitable for studying such changing patterns of drug effects over time.

Doses up to 15mg/kg increased the number of walks (Fig.4b), whereas 30 mg/kg was depressant. Rears also increased, but the peak effect occurred at 8.75 mg/kg, the smallest dose used. Larger doses progressively reduced the number of rears, which fell almost to zero at 30 mg/kg ($F_{\text{Lin}} = 22.18$, $p < 0.001$, as compared with $F_{\text{Lin}} = 1.22$ for walks). Fig. 6 shows that time spent grooming fell $(p < 0.001$, with the

Fig.6. Dexamphetamine depressed the time spent grooming during a 10 min trial in the activity cage, as did amylobarbitone (except at the smallest dose). Effects such as these are not detected by the photocells and appear quite different in their dose response-relationships from effects on walks and rears

largest dose omitted because of a marked fall in variance), except at the smallest dose, where there was a non-significant increase $(t = 1.52,$ df 16, $p < 0.1$).

Combining walks and rears according to the multiple regression equation for saline rats (experiment 1) produced a dose-response curve almost identical with that for photocell counts (Fig.4b). Slight discrepancies occurred at 7.5 and 15.0 mg/kg, where the photocells fractionally over-estimated relative to walks and rears combined, but even at the largest, severely depressant dose there was close agreement between the measures.

The correlations between measures were little affected by amylobarbitone over the range of doses used. As in experiment 2, pooled correlations for "low" and "high" doses were calculated (Table 2).

Suitable mixtures of dexamphetamine and amylobarbitone produced more walking and rearing and less grooming than any dose of either drug given separately (Fig.7), which is consistent with earlier findings with exploratory behaviour (Rushton and Steinberg, 1963, 1967, and to be published; Bradley *et al.,* 1968; Kumar, 1968) and with learned behaviour (e.g. Rutledge and Kelleher, 1965; Weiss and Laties, 1964). Precise comparisons are difficult because the behaviour and measures

Fig.7. Separate groups of 8 rats were injected subcutaneously 35 min before a 10 min trial in the activity cage with either saline or a dose of amylobarbitone, in all cases combined with dexamphetamine 1.0 mg/kg (experiment 3). It can be seen that photocell counts "followed" the dose-response curve for walks and not that for rears

	Saline	Dexamphetamine		Amylobarbitone	
		"Low" Doses $(0.25$ and $0.5 \,\mathrm{mg/kg}$	"High" Doses $(1.0 \text{ and }$ $2.0 \,\mathrm{mg/kg}$	"Low" Doses $(3.75$ and 7.5 mg/kg	"High" Doses $(15.0 \text{ and }$ $30.0 \,\mathrm{mg/kg}$
PC/Walks	0.69	0.87	0.82	0.94	0.94
PC/Rears	0.79	0.59	-0.11	0.71	0.69

Table 2. *Correlation coefficients (r) , each based on 16 rats, between photocell counts (PC)* and direct observation: values of (r) above 0.62 are statistically significant $(p < 0.01)$. *Dexamphetamine, especially in "high" doses, reduces the correlation between photocell counts and rears, but does not affect the correlation between photocell counts and walks.*
Annual hard in the new substantial effects on either relationship. *Amylobarbitone has no substantial effects on either relationship*

taken varied, but the effective dose ranges in the Y-maze and the activity cage seem closely comparable. The effects of the mixtures were approximately equal to the sum of the effects of the constituent drugs; for example, after dexamphetamine 1 mg/kg combined with amylobarbitone 7.5 mg/ kg, the mean numbers of photocell counts, walks and rears were 143, 87 and 56 respectively, as compared with numbers of 157, 99 and 39 calculated by adding the effects of the two constituents to the saline score. In order to examine these results more closely, two-factor analyses of variance were calculated, with the two drugs as the factors. Both doses of amylobarbitone increased the numbers of photocell counts and of walks $(F_{\text{Lin}} = 8.04$ and 8.25 for photocell counts and walks respectively, d^t 1,42, $p < 0.01$ in both cases), as did the dose of dexamphetamine $(F = 25.21$ and 24.70, *dt* 1,42, $p < 0.001$; the interactions between the measured effects of the two drugs were not significant ($F = 0.77$ and 0.81, dt 2.42). However, rears increased only with the smaller dose of amylobarbitone, and, after *15mg/kg,* fell to the level obtained with dexamphetamine alone ($F_{quad} = 10.31, df \, 1.42, p < 0.01$). As walks and rears are both measured by photocells (experiment 1), one would have expected photocell counts to remain constant as the dose of amylobarbitone was increased from 7.5 to 15.0 mg/kg, but in fact the photocells "followed" the increase in walks. However, this ceases to be surprising if one takes into account the information (experiment 2) that after $1-2$ mg/kg of dexamphetamine the photocells measured only walks and not rears. Conversely, from the rise in the photocell count with the mixture containing 15 mg/kg of amylobarbitone one could not have inferred that the number of rears had actually changed in the opposite direction (Fig. 7).

Discussion

The results suggest that simple two-beam photocell activity cages can give a good indication of the walking and rearing of undrugged rats, but not necessarily of the behaviour of drugged rats; the photocell counts gave an exaggerated impression of the effects of dexamphetamine on walking and rearing. It has sometimes been suggested that mainly walking is picked up by such photocell counts (cf. Watzman *et al.,* 1966), but our results show that rearing can also be detected, though it cannot be discriminated unless specially designed equipment is used (e.g. Lát, 1964; Tedeschi *et al.,* 1964). Walks and rears were not found to be highly correlated with each other and might therefore be expected to respond differentially to extraneous stimuli such as drugs (cf. Fig. 7). Even dexamphetamine, a "standard" drug, disrupted the correlation between photocell counts and rears (Table 1). For similar reasons measures of behaviour which involve both walking and rearing components, such as "sniffing" (Bindra and Baran, 1959) or specially devised compound indices of activity (Morrison and Lee, 1968), may therefore in some circumstances give equivocal results.

270 M. Kršiak, Hannah Steinberg, and I. P. Stolerman:

The present results confirm earlier findings (Bindra and Baran, 1959 ; Heimstra, 1962; Morrison and Lee, 1968) that the effects of drugs on grooming can be very different from their effects on walking and rearing. Such effects are not detectable by the usual type of photocell counts; they merely confirm that general activity is not a unitary variable and that the effects of treatments depend on exactly which components are measured (see reviews by Cofer and Appley, 1964; Gross, 1968).

The generality of our findings might be questioned on the grounds that often groups of e.g. 5 mice are tested simultaneously in a cage, whereas we have used single rats. Nevertheless, the classification and measures of behaviour obtained by our observations were such as to maximise correlations with photocell counts; the behaviour of groups of mice, including social interactions which have been shown to be determinants of drug effects (Chance, 1946; Heimstra, 1962), would probably be even less adequately measured by photocell counts.

There seems little doubt that the photocell system used in the present experiments was representative in the sense that the drugs used had effects on photocell counts which are consistent with earlier work. For example, suitable doses of dexamphetamine have long been known to be stimulant both in photocell cages (Dews, 1953) and in activity wheels (Tainter, 1943). In our experiments the numbers of walks and of rears were only slightly increased by dexamphetamine, as previously found by direct observation of Y-mazes (Rushton and Steinberg, 1963 and to be published). Discrepancies arose between observation and photocell counts, in the direction of over-estimation of activity by the photoceils, and this was most marked in the second half of the trial, just where the drug had the clearest effect on photocell counts. These discrepancies may have occurred because these larger doses of dexamphetamine can induce qualitative changes in behaviour (Tainter, 1943; Randrup, Munkvad and Udsen, 1963; Lát, 1964); instead of the normal well coordinated locomotion the rats were engaging in apparently aimless activity (Chance and Silverman, 1964), continually sniffing, swinging their heads vertically or horizontally, and stepping on the spot (Rushton and Steinberg, 1963).

With amylobarbitone, throughout the range of doses used, agreement between observation (combined walks and rears) and automation was striking. The relation between dose of amylobarbitone and grooming was of rather different form, and it was hardly surprising that the photocells did not reflect this because under non-drug conditions grooming and photocell counts are not correlated. Amylobarbitone usually depresses photocell counts when the doses are large and produce marked ataxia (Cook et *al.,* 1955; Rushton and Steinberg, 1963), which is confirmed by

the present findings with the 30 mg/kg dose. That smaller doses of barbiturates can have a stimulant action has been known for some time (Brown, 1960; Read *et al.,* 1960; Kinnard and Carr, 1961; Rushton and Steinberg, 1963) and essentially similar effects of a range of doses of amylobarbitone have been shown on several measures in the present experiments. Although amylobarbitone can reduce fear (Miller, 1964), recent work suggests that the increased locomotion which it produces in a new environment may be due to a separate action (Kumar, 1968). Various characteristics of the test environment can affect the action of barbiturates (Janků and Kršiak, 1966); that both "stimulant" and "depressant" drugs in some doses appear to have similar effects in particular test situations need no longer cause surprise, and illustrates once again the inadequacy of such a rudimentary classification.

The results of our experiments with drugs illustrate how the theoretical limitations of photocell counts can in practice give misleading results. For some drugs, such as amylobarbitone, this distortion seems minimal, and photocells therefore seem valid for assessing dose and time relations (cf. experiment 3). The use of photocells, or of other automatic devices which have been specially designed to measure particular components of behaviour, such as rearing, (Tedeschi *et al.*, 1964; Lát, 1964), or the investigation of a circumscribed area (Berlyne, 1955; Kumar 1969) is also different in principle from the more usual approach of trying to make the apparatus as sensitive as possible to *all* types of movements, and need not be subject to the pitfalls discussed here.

The limitations of activity cages are therefore greater than has sometimes been supposed; the degree to which they mask or distort complex changes in behaviour varies with different drugs and cannot be predicted. Kinnard and Watzman (1966) have concluded that further increases in the complexity (and cost) of existing kinds of automatic equipment are unlikely to overcome such limitations; it remains to be seen whether recently described methods (e.g. Svensson and Thieme, 1968) are able to discriminate better between the types and the finer characteristics of the movements picked up. No doubt activity cages will continue to be widely used, but it seems that for most purposes more meaningful information can be obtained from detailed and standardisedobservational procedures (possibly abstracted from those described by Silverman, 1965 ; Chance, 1968 ; Irwin, 1968). In more general terms, we arc supporting a "criterion behaviour" approach (Russell, 1960; Steinberg, 1962), and are arguing that one should not use techniques merely because they are sensitive to existing drugs and yield neat, "objective" and quantitative results. Detailed observation of what the animals are actually doing seems to be essential for evaluating and developing automatic recording devices.

Acknowledgements. We thank Prof. H. O. Schild for discussion, Dr. R. Rushton, Mr. R. Bryant, Mr. B. Hutchings, Miss S. Theobald and Miss M. Dorr for help with the experiments and Miss C. Duncan for statistical advice.

The work was supported by grant no. MH-03313 from the National Institute of Mental Health, U.S. Public Health Service, by a grant from the Smith Kline and French Foundation, and one of us (M.K.) was the holder of a Riker International Fellowship in Pharmacology.

References

- Berlyne, D. E.: The arousal and satiation of perceptual curiosity in the rat. J. comp. physiol. Psyehol. 48, 238--246 (1955).
- Bindra, D., Baran, D.: Effects of methylphenidylacetate and chlorpromazine on certain components of general activity. J. exp. Anal. Behav. 2, 343--350 (1959).
- Bradley, D. W. M., Joyce, D., Murphy, E. H., Nash, B. M., Porsolt, R. D., Summerfield, A., Twyman, W. A.: Amphetamine-barbiturate mixture: effects on the behaviour of mice. Nature (Lond.) 220, 187-188 (1968).
- Brown, B.: CNS drug actions and interactions in mice. Arch. int. Pharmacodyn. 128, 391--414 (1960).
- Chance, M. R. A. : Aggregation as a factor influencing the toxicity of sympathomimetic amines in mice. J. Pharmacol. exp. Ther. $87, 214-219$ (1946).
- -- Ethology and psychopharmacology. Psychopharmacology: Dimensions and Perspectives, pp. 283-318. Joyce, C. R. B. (Ed.) London: Tavistock Publications 1968.
- -- Silverman, A. P.: The structure of social behaviour and drug action. Animal Behaviour and Drug Action, pp. 65-79. Steinberg, H., A. V. S. de Reuck, and J. Knight (Eds). London: Churchill 1964.
- Cofer, C. N., Appley, M. H.: Motivation: Theory and Research, pp. 269-301. London: Wiley 1964.
- Cook, L., Weidley, E. F., Morris, R. W., Mattis, P. A. : Neuropharmacological and behavioural effects of chlorpromazine (thorazine hydrochloride). J. Pharmacol. exp. Ther. 113, 11 (1955).
- Dews, P. B.: The measurement of the influence of drugs on voluntary activity of mice. Brit. J. Pharmacol. 8, 46--48 (1953).
- Eayrs, J. T,: Spontaneous activity in the rat. Brit. J. Anim. Behav. 2, 25--30 $(1954).$
- Finger, F. W.: Estrus and general activity in the rat. J. comp. physiol. Psychol. 68, 461--466 (1969).
- Gross, C. G.: General activity. Analysis of Behavioral Change, pp. 89-106, Weiskrantz, L., (Ed.). London: Harper & Row 1968.
- Heimstra, N. W.: Social influence on the response to drugs: I. Amphetamine sulphate. J. Psychol. 53, 233-244 (1962).
- Irwin, S. : Comprehensive observational assessment: 1A. A systematic quantitative procedure for assessing the behavioral and physiologic state of the mouse. Psychopharmacologia (Berl.) 13, 222-257 (1968).
- Janků, I., Kršiak, M.: Proc. Europ. Soc. for the Study of drug Toxicity, 8, 86-92. Excerpta Medica International Congress No. 118 (1966).
- Kinnard, W. J., Carr, C. J.: A preliminary procedure for the evaluation of central nervous system depressants. J. Pharmacol. exp. Ther. 121, 354-361 (1961).
- -- Watzman, N.: Techniques utilised in the evaluation of psychotropic drugs on animal activity. J. Pharm. Sci. 55, 995-1012 (1966).
- Kršiak, M., Steinberg, H., Stolerman, I. P.: Discrepancies in results obtained with activity cages and by observation. Brit. J. Pharmacol. 34, $684P-685P$ (1968).
- Kumar, R.: Psychoactive drugs, exploratory activity and fear. Nature (Lond.) 218, 665--667 (1968).
- **--** Exploration and latent learning: differential effects of dexamphetamine on components of exploratory behaviour in rats. Psychopharmacologia (Berl.) 16, $54-72$ (1969).
- Lat, J.: The spontaneous exploratory reactions as a tool for psychopharmacological studies. A contribution towards a theory of contradictory results in psychopharmacology. Pharmacology of Conditioning, Learning and Retention. Mikhel' son, M. Ya., and V. G. Longo (Eds). London: Pergamon 1964.
- Miller, N. E.: The analysis of motivational effects illustrated by experiments on amylobarbitone. Animal Behaviour and Drug Action, pp. 1--18. Steinberg, H., A. V. S. de Reuck, and J. Knight (Eds). London: Churchill 1964.
- Morrison, C. F., Lee, P. N.: A comparison of the effects of nicotine and physostigmine on a measure of activity in the rat. Psychopharmacologia (Berl.)18, 210--221 (1968).
- Randrup, A., Munkvad, I., Udsen, P.: Adrenergie mechanisms and amphetamine induced abnormal behaviour. Aeta pharmaeol. (Kbh.) 20, 145--157 (1963).
- Read, G. W., Cutting, W., Fiirst, A. : Comparison of excited phases after sedatives and tranquilizer. Psychopharmacologia (Berl.) 1, 346--350 (1960).
- Rushton, R., Steinberg, H.: Mutual potentiation of amphetamine and amylobarbitone measured by activity in rats. Brit. J. Pharmacol. 21, 295--305 (1963).
- **--** Drug combinations and their analysis by means of exploratory activity in rats. Neuropsychopharmaeology, pp. 464--470. H. Brill, J. O. Cole, P. Deniker, H. Hippius, P. B. Bradley (Eds). Amsterdam: Exeerpta Mediea 1967.
- Russell, R. W. : An approach to the development of animal screening techniques in psychopharmaeology. U.S. Public Health Service Fsyehopharmacology Service Center Bulletin, 1-7 (December, 1960).
- Rutledge, C. 0., Kelleher, R. T. : Interactions between the effects of methamphetamine and pentobarbital on operant behavior in the pigeon. Psyehopharmacologia (Berl.) 7, 400--408 (1965).
- Siegel, P. S., Steinberg, M.: Activity level as a function of hunger. J. comp. physiol. Psychol. 42, 413--416 (1949).
- Silverman, A. P.: Ethological and statistical analysis of drug effects on the social behaviour of laboratory rats. Brit. J. Pharmacol. 24, 579--590 (1965).
- Snedeeor, G. W., Coehran, W. G. : Statistical methods, 6th Edtn. Ames (Iowa) : The Iowa State University Press 1967.
- Steinberg, H.: Experimental methods in psychopharmacology, pp. 78--87. Recent Advances in Pharmacology. Robson, J. M., and R. S. Staey (Eds). London: Churchill 1962.
- Tainter, M. L.: Effects of certain analeptic drugs on spontaneous running activity of the white rat. J. comp. Psyehol. 86, 143--155 (1943).
- Tapp, J.T., Zimmerman, R. S., D'Enearnacao, P. S. : Intercorrelational analysis of some common measures of rat activity, Psyehol. Rep. 28, 1047--1050 (1968).
- Tedesehi, D. M., Fowler, P. J., Cromley, W. H., Pauls, J. F., Eby, R. Z., Fellows, E. J. : Effects of centrally acting drugs on confinement motor activity. J. Pharm. Sci. 53, 1046-1050 (1964).

274 M. Kršiak et al.: Uses and Limitations of Photocell Activity Cages

- Svensson, T. H., Thieme, G.: An investigation of a new instrument to measure motor activity of small animals. Psychopharmacologia (Berl.) 14, 157--163 (1969).
- Watzman, N., Barry, M., Kinnard, W. J., Buckley, J. P.: Comparison of different photobeam arrangements for measuring spontaneous activity of mice. J. Pharm. $\mathrm{Sci.}$ 55, 907 $-$ 909 (1966).
- Weiss, B., Laties, V. G : Effects of amphetamine, chlorpromazine, pentobarbital, and ethanol on operant response duration. J. Pharmacol. exp. Ther. 144 , $17-23$ (1964).
- Winter, C.A., Ylataker, L.: The effect of cortisone, desoxycorticosterone, and adrenocorticotrophic hormone upon the response of animals to analgesic drugs. J. Pharmacol. exp. Ther. $103, 93-105$ (1951).

Dr. Hannah Steinberg University College London Department of Pharmacology Gower Street London W.C.1/England