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BRIEF COMMUNICATION

Group Instability and the Social Response to Methamphetamine[1]

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SYME, L. A. AND G. J. SYME. *Group instability and the social response to methamphetamine.* PHARMAC. BIOCHEM. BEHAV. 2(6) 851–854, 1974. – The effects of methamphetamine on body contact and social distances in stable (familiar) and unstable (unfamiliar) groups of rats were investigated. Although there was no difference in body contact in the stable and unstable saline groups, methamphetamine reduced body contact significantly more in the unstable group than it did for its stable counterpart. Methamphetamine had no effect on social distance in the unstable group but decreased social distance in the stable group. Group stability may therefore be not only desirable but necessary, if the effects of drugs on social responses are to be meaningfully interpreted.

Group stability Photographs Methamphetamine Rat

WHILE there is some literature concerned with the effects of social variables on the response of animals to psychotropic drugs (e.g. [9]) only one study [22], using a non-social automated activity measure, has investigated the problems of social disruption occurring in the transfer of animals between the cage and test environment. Most studies confound two sources of behavioral influence in the experimental setting, social and environmental, by placing unfamiliar animals together in this setting and then observing an "unstable" group [19].

Investigations of the effects of drugs on simple social measures such as sociability (body contact and approach behavior and/or inter-animal distance), for example, have tended to confound such effects by providing stimulus animals which were previously unknown to their animals (e.g., [3,4]) and by testing them in social conditions differing from those in the cage environment [1, 8, 10, 15, 16].

Until now many studies employing social variables have adopted an "ethological" approach (e.g. [10,16]) using familiar or unfamiliar rats or mice and providing a verbal description of the social interaction between pairs of treated and untreated animals. However, this procedure involves the separation of partners for periods of up to 24 hours, thus ensuring the disruption (in this case short-term social isolation) necessary to produce observable social behavior. Other methods using social variables either observe the behavior of treated rats in unstable groups (e.g. [15]) or use group-housed rats but neglect to state whether familiar animals are present in the test setting (e.g. [20,21]).

Some recent methods of measuring "sociability" [19,21] do allow rats to be tested in the groups in which they have been caged. Consequently we can now ascertain the effects of group instability on social interactions in treated rats. In a previous study [19] a dosage of 2 mg/kg methamphetamine was used to produce an increase in psychomotor activity but not stereotyped behavior [2] in a group of familiar rats. This treatment decreased the amount of physical contact and affected social distances within the group 30–40 min after injection. The present study investigates whether this effect is modified in any way when the animals are tested in a group size consistent with that in

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which they were caged, but of an unstable constitution. Use of several dose levels was precluded by the number of animals available. However, while the desirability of such procedures is acknowledged, the expedient application of a single typical dosage to investigate a specific social parameter or a new method [13, 14, 19] may be justified.

METHOD

Animals

The animals were 28 male hooded rats of the New Zealand Black and White Strain derived from animals originally obtained from the Otago University Breeding Centre. These weighed 150–200 g at the time of the experiment and were selected from an experimental stock of 63 rats. All were housed in constant groups of 7 for a month before the experiment began. Food and water were freely available and the animals were maintained on a reversed light–dark schedule. Two of the groups were retained intact during testing and served as controls for the unstable group conditions. The two unstable groups were obtained by randomly selecting 2 rats from each of the remaining seven groups immediately before testing to form two groups of 7 animals in which all animals were unfamiliar to each other.

Apparatus

The apparatus used has previously been described in detail elsewhere [19]. Briefly, however, it consisted of a circular open field of 1.2 m diameter with an enclosing wall 0.4 m high. The floor and walls of this were painted brown and white painted lines divided the floor into 49 numbered sections of equal area and approximately equivalent shape. Illumination was provided by four 40 W fluorescent lamps placed around the perimeter but 1 m above the field. Photographs were taken manually by an observer situated above the field using a 35 mm camera and electronic flash. The flash did not appear to disturb the animals' activities.

Procedure

Testing was carried out between 2 p.m. and 3 p.m. The rats in the first stable group were injected with the same dosage of methamphetamine as used in our previous study (2 mg/kg i.p.) and were placed individually in 18 × 18 × 18 cm holding cages for 30 min prior to testing. Similarly, the second stable group was injected with an equivalent volume of isotonic saline and placed in holding cages for 30 min before testing. Members of the unstable groups were taken from their home cages, injected with methamphetamine or saline and, as with the stable groups, were placed in holding cages for 30 min before testing.

Each group was then placed in the open field and allowed to roam freely for 1 min, after which time photographs were taken every 30 sec for a 10-min period. In this way, 20 photographs of the distribution of each group were obtained. The differences in the fur markings of each rat proved to be distinctive enough for the individual recognition of each rat.

Analysis

The position of each animal was noted for each of the 20 photographs. Three social measures were then obtained for each animal in each photograph. The first two measures were of the average distance of each animal from each of its groupmates, calculated from the mid-points of each occupied segment. A linear distance measure [1, 8, 11] involved calculation of the shortest distances between each rat and every other in the group. Using this measure there was a maximum number of 6 segments between a pair of rats (1.03 m between midpoints). However the use of a linear measure provides a distorted picture of the distribution of animals since rats show wall-hugging behavior in the open field [17]. Therefore the convention adopted for the second distance measure was to regard the distance between two rats in perimeter segments as being the shorter distance between the two, as calculated between midpoints around the perimeter, allowing a maximum distance of 12 segments (1.68 m between midpoints of segments around the circumference of the field). The distance between a rat in the inner segments of the field and another in a segment on the perimeter was calculated as the linear distance between the two, since there is no evidence to suggest that the center rat will move to the perimeter at any particular point. The convention adopted does provide an increase in the sensitivity of social distance measures which are usually confined to a relatively small area, in that the range of possible distances is increased from the diameter to nearly half the circumference of the field (since midpoints of outer segments are used the maximum distance is, in fact, $5/6\pi r$).

Finally, a proximity measure was obtained by counting for each rat in every photograph the number of animals with which it was in physical contact. This is probably the most powerful measure of the three used here, in that it is not known how close a rat must be to another before it is a relevant stimulus in a dynamic group situation such as that produced by the present method [17].

RESULTS

The median values for each condition and the probabilities associated with between-group comparisons are shown in Table 1. These medians were obtained from the mean frequencies of the number of animals each animal was found to be in contact with and the mean social distance between each animal and every other rat over the 20 photographs. A non-parametric mode of analysis was adopted since the perimeter–distance measure can only be regarded as ordinal. All probabilities were derived from the Mann-Whitney U test.

Although group instability did not have a significant effect on the amount of physical contact under the saline conditions, the methamphetamine-treated unstable group showed significantly less contact than the stable drug-treated group. Both methamphetamine groups had significantly less body contact than their controls.

The distance measures demonstrated identical effects. Although the median inter-individual distances were lowered by methamphetamine in both cases for the stable group, no significant effect on either measure was shown for the unstable group. On both distance measures the saline-treated unstable group had a significantly lower inter-animal distance than its stable counterpart. This observation was reversed, however, in the methamphetamine groups on the perimeter distance measure.

DISCUSSION

These results support the contention that group insta-

TABLE 1

MEDIAN VALUES FOR EACH CONDITION AND THE PROBABILITIES ASSOCIATED WITH BETWEEN-GROUP COMPARISONS (MANN-WHITNEY U TEST, TWO-TAILED). OBTAINED FROM THE AVERAGE SOCIAL DISTANCE AND AVERAGE NUMBER OF ANIMALS IN CONTACT PER PHOTOGRAPH.

Measure	Saline	Methamphetamine	*p*
Proximity			
Stable	0.95	0.40	0.002
Unstable	0.90	0.25	0.002
p	NS	0.02	
Linear Distance (cm)			
Stable	60.98	55.47	0.004
Unstable	55.28	56.62	NS
p	0.002	NS	
Perimeter Distance (cm)			
Stable	70.78	60.94	0.002
Unstable	63.20	63.27	NS
p	0.002	0.04	

bility can influence reaction to drugs in a social setting [22] and extend this to social responses.

For the proximity measure, group instability accentuated the response to methamphetamine, even when there was no observable difference in contact behavior between stable and unstable groups in the placebo condition. Rats treated with methamphetamine in the unstable group were significantly less sociable on the contact measure than those in the stable drug condition.

Overall, the observed behavior of the treated animals is compatible with previous findings [15,20] which show that amphetamine increased locomotor activity and disturbed the contact behavior of groups of rats treated with a similar dosage to that used in the present study. For instance, Tikal and Benešová [20] found that 1.25 mg/kg amphetamine increased the number of active/contact postures while 2.5 and 5 mg/kg increased the number of active/isolated postures. However, because of serious differences or omissions in procedural descriptions it is difficult to generalise further between the two studies. Generally, in studies investigating the effects of amphetamine on social behaviors [3, 15, 16] animals are unfamiliar in the test situation, so that no comparison with the stable social condition of the present study is permitted, and frequently animals have been housed individually which provides greater variability in the drug response [6,7]. The work which should allow useful comparison with the present results [20,21] used rats of both sexes with no reference to how these were grouped in the experiment or analysis [20] or "monosexual" groups with no information regarding the possible influence of sex differences on the results obtained [5, 6, 9]); "female animals tend to be more reactive than males" [6].

On the social distance measures group instability obscured the effects of methamphetamine which were observed in the stable group. To clarify this statement it is instructive to observe the effects of instability on the spatial behavior of the saline controls. For both social distance measures the unfamiliarity of group members significantly decreased the distance between them. But this did not occur for the rats treated with methamphetamine. On the linear distance measure there was no significant difference between the stable and unstable groups, while on the perimeter distance measure the unstable group was significantly more dispersed, or socially isolated, than the stable group.

Both the contact and perimeter measures in this study produced results consistent with those obtained previously with a stable group of rats [19] in that this typical dosage of methamphetamine not only decreased social contact but also reduced social distances. In contrast to our earlier study, however, methamphetamine decreased inter-individual social distances rather than increased them, as was previously the case. The difference can probably be attributed to the greater huddling behavior of the saline controls in the earlier study [19]. Since these animals were of a different strain and younger than those used here this is not a surprising result. Even so, the lack of reliability in the direct distance measure supports the view that social distances are best calculated in terms of the animals' natural spatial behavior. In the open-field situation groups of rats prefer the perimeter segments [12,17] and, where square or rectangular fields are used (e.g. [12, 15, 19, 20]), the corner areas. Position preferences may also be influenced by cage dimensions and the shape and size of the field [18].

One other important aspect of the results concerns the differing outcomes for the contact and social distance measures. Firstly, group instability decreased social distance but not contact behavior in the placebo group. Secondly, methamphetamine decreased contact behavior but also decreased social distance in the stable group.

The first difference can probably be explained by the unfamiliarity of the animals which promoted a slight inter-animal exploratory response and thus a shorter social distance. The unfamiliar control animals may have explored the novel environment less than they would have in the presence of cagemates; that is, the stable group only experienced environmental novelty.

The second difference (the opposite effect of methamphetamine on contact and social distance measures) is not as easily explained. The effect cannot be attributed to increased center occupancy [19] since both perimeter and direct distances decreased. Methamphetamine perhaps decreased contact behavior in familiar animals but increased sensitivity to the less extreme social index, that of inter-animal distance. This would seem reasonable from previous results [20] showing a lower dosage than that used here to increase social contact but a higher dosage to increase active/isolated responses. The behavior of the rats in the present study could represent a middle stage in the social effects of methamphetamine, when the animals have decreased their contact behavior but are still socially interested, this being reflected in the lower inter-animal distance.

Consequently, despite earlier reports of a high correlation between contact and social distance [11] the two measures should be considered separately. While physical contact can be regarded as the primary index of sociability it is necessary to discover the different properties of the two measures which allow them to vary independently after drug administration.

Finally it is evident that the use of socially unstable groups did modify the effect of methamphetamine on social behavior. Studies investigating the effects of drugs on social responses should, therefore, be aware of the influence of this variable in the interpretation of results. The incorporation of both socially stable and unstable groups should be helpful when determining the broad social effect of drugs on behavior.

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