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QUANTIFICATION OF BEHAVIOUR IN SOCIAL COLONIES OF RHESUS MONKEY

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Abstract : It is necessary to use experimental animals with behavioural, physiological and disease susceptibility pattern similar to man so that the results have a clinical predictive value. For such studies the non-human primate is the animal of choice. Rhesus monkey is a good choice for this purpose but information about its behaviour is fragmentary. In order to obtain a quantitative baseline data for psychopharmacological studies, a protocol has been developed to score various social and solitary behaviours in adult male and female rhesus monkeys. The study was conducted on rhesus monkeys in a social colony of one male and seven female living in a semi-restricted environment. The behavioural patterns were quantitated so as to compare effect on various components of behaviour. Aggressiveness and vigilance were prominent in the male while social affiliative behaviour was dominant in the female. Other behavioural responses were of similar magnitude in both sexes. It is however necessary to have data with some standard CNS active agents on these behavioural protocol. Therefore, initially the behavioural effects of amphetamine and haloperidol were studied. Significant effects observed following d-amphetamine (1-4 mg/kg, im); it induced dose dependent suppression of social behaviour (approach, contact, grooming), feeding, hypervigilance, stereotypy and oral hyperkinesia. On the other hand haloperidol (0.01-0.04 mg/kg, im) produced decrease in social and solitary behaviour and marked cataleptic posture. It is possible to quantitate drug effects on various aspects of behaviour of the rhesus monkey and to develop neuropsychitric models with the help of this protocol for use in study of drug effects on behaviour.

Key words : non-human primate, rhesus monkey, haloperidol, behaviour, amphetamine, social colony

INTRODUCTION

Several neurological disorders are associated with behavioural disturbances. Behavioural changes are also produced by centrally acting or even other classes of drugs. In addition, a number of industrial chemicals and xenobiotics can profoundly affect behaviour (1). To study the behavioural effects of drugs and toxins in

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experimental animals, it is, desirable that animal behaviour should closely resemble human behaviour. The non-human primate serves the purpose in the most satisfactory manner. Among the primates, rhesus monkey (Macaca mulatta) has been the most preferred, partly due to easy availability and reasonable life span. Rhesus monkeys are particularly noted for rich variety of social interactions in their natural habitat and in the laboratory setting, where they live in structurally organised social groups (2-4). Rhesus monkey should be a particularly good species for studies on drug induced alterations of social behaviour and preclinical evaluation of drugs. Studies of social behaviour in non-human primates have been interpreted as being directly homologous with those in man (5). Behavioural changes in rhesus monkey have also been proposed to serve as a model system in the study of psychotic behaviour (6-7). Only limited information is available regarding various components of social behaviour of the rhesus monkey specially in a group where a male lives with a group of female monkeys and their young progenies. It is necessary to quantitate the normal behaviour patterns of rhesus monkey living together in a social colony, and to obtain baseline data before using it for studying the behavioural effects of CNS active drugs. To study the CNS active drugs on these behavioural protocols, we have started with amphetamine (AMP) and haloperidol in rhesus monkey because dopamine (DA) has been implicated as one of the important neurotransmitters in the regulation of behaviour.

Amphetamine has profound effects on a wide range of psychological and behavioural processes (8), AMP research in both animals and humans has implicated a role for DA in behavioural disorders, including schizophrenia and obesity as well as in the medication of rewarding aspect of drugs of abuse (8–10). However, there is paucity of studies on AMP induced behaviour changes in non-human primates especially rhesus monkey. Therefore, in the present study, besides developing the behavioural protocol, the quantitative assessment of AMP and haloperidol induced effects on social, solitary and abnormal behavioural responses of rhesus monkey has been attempted.

METHODS

The subjects for the study were 3-5 year old adult rhesus monkeys weighing 4-6 kg. Each group comprised of eight monkeys (one male and seven females) who had lived together as a social colony. The colony was housed in a 20'×12'×8' cage throughout the study. The social and solitary behavioural patterns were studied. The monkeys were maintained under controlled conditions of temperature, humidity, air change and 12 hour light/darkness cycle. A balanced diet was provided in the morning and evening and water was available *ad libitum* through an automatic watering system. Animals were allowed 4-6 weeks time to stabilize their behaviour in the new sorrounding. To reduce the stress induced by handling and dosing to minimum, the animal was handled by a single experimenter. During the period of habituation, monkeys were caught and removed from the cage at least once a week and administered saline intramuscularly (im) or orally.

Check list of social, solitary and

abnormal behaviour technique was a modified version of the protocol of Schlemmer and Davis (11). The observations were carried out from an adjacent room with the help of two strategically placed 180° rotating video cameras with zoom lens, fixed in the behavioural chamber. Behavioural responses were also videotaped for analysis and record.

Data has been analysed for the following parameters selected as important indicators of social and solitary behavioural responses.

(A) Social behaviour

1. Social groom – Discrete picking or spreading of the hair of co-inhabitant
2. Approach – One monkey walks or runs towards other animals from a distant point (3 feet) to within an arm's length so it could touch the other animal or vice versa
3. Body jerk – Quick voluntary jerks of the body while the animal is looking directly at another animal in close proximity.
4. Huddle – When two animals are sitting together where at least one monkey's arm is embracing the other animal.
5. Contact – When the body of one animal is touching the body of another animal but no social interaction or huddling takes place.

(B) Aggressiveness

1. Threat – Eyebrows up, ear back, mouth open and only lower teeth are visualised, stares at another animal, some times accompanied by a specific low pitched vocalization.
2. Chase – Pursuit of another animal for purpose of attack.
3. Attack – Vigorous, hostile, biting and or/ hair pulling of another monkey.
4. Yield – Move away from a location, so that a more dominant monkey may occupy it.

(C) Solitary behaviour

1. Feeding habit – The patterns of manipulation and mastication of food.
2. Drinking habit – Drinking water from automatic watering system.
3. Locomotion – The number of ambulations from one point to a distant point (3 feet).
4. Self groom – Discrete picking or spreading of hair.
*5. *Scratch* – Scratching of a single specific location (for example scratching of the leg followed by scratching of the arm would be scored as two distinct scratches).
*6. *Vigilance* – The number of observed changes of visual field determined by head and eye movement.
7. Yawn – Involuntary wide opening of mouth for intake of air and both upper and lower teeth are visualized.
*8. *Vocalization* – The number of clearly audible sounds emanating from the observed animal.
9. Respiratory rate in sitting posture
10. Pupil Size
11. Salivation
12. Picking genitalia – Manipulation or grooming of genitals.
13. Lying down – Assumes horizontal position on the cage floor.
14. Resting with eye open – Maintaining a relaxed posture, initiating no active behaviour for 30-60 sec while eyelids remain open for more than 30 sec.
15. Resting with eye closed – Maintaining a relaxed posture initiating no active

behaviour for 30-60 sec while eyelids were shut for more than 30 sec.

*Scored by the frequency of occurance during each 60 sec observation interval. All other behaviour patterns were scored by the presence (1) or absence (0). Respiratory rate was counted with the help of stop watch, and size of the pupil was observed and graded as normal (N), dilated (D) or constricted (C).

Each monkey was observed in rotation for 1 min at every 10 min for 2 hrs. Scores of each behaviour from the twelve 1 min intervals were summed up for individual animals and represent the day's score for that monkey.

The monkeys were also observed at 4, 6, 8 and 24 hrs for any significant alteration in behaviour. Statistical analysis was performed for all behavioural data by using Mann-Whittney "U" Test.

Separate colonies of rhesus monkeys were treated with CNS active drugs intramuscularly as follows (a) received graded doses of AMP *per se* (b) received graded doses of haloperidol *per se*. Since the same animals were used for different doses in colonies (a & b), an interval of ten days was maintained between the two doses to wash out the effect of previous dose.

Amphetamine sulphate (Sigma Chemicals, USA) was dissolved in 0.09% saline and haloperidol injection (Searle Pharmaceuticals) were used.

RESULTS

In the present study, quantitative assessment of normal behavioural responses was carried out in adult male and female rhesus monkeys living together in a social colony. A summary of the results has been given in Table I. Some differences were observed between the two sexes while scores of other parameters were identical. It was observd that in the male monkeys, the body jerk and aggressiveness were prominent in social behaviour. In aggressiveness, threat is quite frequent. The attack is often preceeded by a chase, which may be mild, in which hair and tail pulling of another monkey, or severe, in which vigorous biting were observed. In solitary behaviour, vigilance, yawning and picking of genitalia are prominent as compared to the female monkey. On the other hand in female monkey, social groom, huddle, contact and yield are prominent. In social groom, the female monkeys not only perform discrete picking or spreading of the hair of the female monkeys, but they also do grooming of male monkey. The social groom behaviour was not observed with male monkeys. The female monkeys preferred to sit together and occassionally one monkey's arm is touching the body of another animal for social action or huddling, which showed a prominent affilative behaviour.

Besides this, female monkeys move away from a location, so that male monkey may occupy that location. This indicates a yielding behaviour. The other behavioural responses were of similar magnitude in both the sexes. Besides social and solitary behaviour we also observed an abnormal behaviour in three female i.e. a homosexual behaviour in which female monkey mounts on another co-inhabitant of same sex with pelvic thrusts.

During menstruation and pregnancy, the social behaviour (approach, huddle) were

TABLE I : Quantitative assessment of normal behavioural responses in male and female monkey.

Behavioural responses	*median score (Range)*	
	Male (n=7)	*Female (n=7)*
I. Social behaviour		
Social groom	0 (0)	3**(1–4)
Approach	2 (0–4)	2 (1–3)
Body jerk	2**(0–3)	0 (0)
Huddle	0 (0–1)	2** (1–3)
Contact	0 (0–1)	2** (1–4)
II. Aggressive behaviour		
Threat	2**(1–3)	0 (0)
Chase	1 (1–2)	0 (0)
Attack	1 (1–2)	0 (0–1)
Yield	0 (0)	2**(0–2)
III. Solitary behaviour		
Feeding	2 (1–3)	2 (1–3)
Drinking	2 (1–3)	1 (0–2)
#Locomotion	8 (7–12)	8 (5–10)
Self groom	1 (0–2)	1 (0–2)
#Scratch	2 (0–4)	2 (0–3)
#Vigilance	10**(8–14)	6 (4–8)
#Yawn	2**(1–3)	(0–1)
#Vocalization	0 (0–1)	0 (0–1)
Picking genitalia	1*(0–2)	0 (0)
Lying down	0 (0–3)	1 (0–2)
Resting with eye open	6 (4–7)	7 (5–8)
Resting with eye closed	0 (0–2)	1 (0–3)
Respiration/min	39.2 + 1.02	

*P<0.05; **P<.001
Using Mann-Whitney U Test.
# Indicates the mean frequency of occurence during each 60 sec observation interval.

TABLE II : Effect of amphetamine on behavioural responses of rehsus monkey.

Behavioural responses	*Median score (n=5) Amphetamine mg/kg im, per se*			
	Control	*1*	*2*	*4*
Social				
1. Approach	2	2	1*	0*
3. Contact	2	2	1*	0*
Solitary				
3. Feeding/Drinking	2	2	0*	0*
4. Grooming	2	2	1*	0*
5. Vigilance	10	20*	29*	44*
8. Respiratory rate	39.2+1.02	41.5+1.2	47.9*+ 1.1	52.0*+ 1.42
Abnormal				
9. Stereotypy	0	0	2@	4@
10. Oral hyperkinesia	0	0	2@	3@

*P<0.01, Significant difference from control.
@Score : Frequency of occurence per min

1	1–3
2	4–6
3	7–12
4	more than 12

significantly decreased. As pregnancy advanced, the lying and resting behaviour were significantly increased, as compared to control female rhesus monkeys.

Effect of amphetamine

Graded doses of AMP (1-4 mg/kg, im) induced alteration in normal social and solitary behavioural patterns and also produced certain abnormal behaviour. AMP in a dose of 2 and 4 mg/kg, im significantly suppressed approach, contact and grooming and also induced a decrease in feeding behaviour. AMP (4 mg/kg, im) also induced a significant increase in respiratory rate, as compared to control. Further, hypervigilant, stereotyped behaviour and oral hyperkinesia were observed. The onset of action was 30 min after drug administration, peak effect was observed at 45-60 min and the effect lasted for 6 hr (Table II).

Effect of haloperidol

Graded doses of haloperidol (0.01–0.04 mg/kg, im) produced dose dependent decrease in contact, body jerk, locomotion and vigilance and there was an increase in resting activity which denotes a sedative effect. Higher dose of haloperidol (0.04 mg/kg, im) produced marked cataleptic posture and the monkey maintained an abnormal posture for more than 20 min. The effect of haloperidol lasted up to 6 hr (Table III).

TABLE III : Effect of haloperidol on behavioural responses of rhesus monkey.

Behaviour responses	*Medial score (n=5)*			
	Haloperidol mg/kg, im. per se			
	Control	*0.01*	*0.02*	*0.04*
Social				
1. Contact	2	2	1*	0*
Solitary				
3. Locomotion	9	8	5*	2*
4. Vigilance	10	9	7*	5*
5. Resting with eye closed	0	0	1	3*
6. Stare	0	0	4*	6*
Abnormal				
7. Catalepsy	0	0	1	4@

*P<0.01, Significant difference from control.
@Score :
1 = Unnatural stance for less than 5 min.
2 = Unnatural stance for < 10 min.
3 = unnatural stance for < 20 min.
4 = Unnatural stance for 20 min.

DISCUSSION

Study of behaviour, particularly of the non-human primates, under the effect of drugs is of great help in understanding their effect in humans and occupies an important place in drug development programme. Compared to the extensive data on the anatomical, physiological and other

characteristics of these monkeys, relatively little is known about drug effects on primate behaviour, partly because quantification of results is difficult.

Considering the importance of studying primate behaviour, the first necessary step was to develop an experimental protocol for quantitative assessment of normal social and solitary behavioural patterns in rhesus monkey living together in a social colony. In the present study the normal social and solitary behaviour responses were observed in male and female adult monkeys in order to generate baseline data. It was observed that certain parameters of social behaviours like body jerk, threat (aggressiveness) and of solitary behaviour–vigilance (alertness), picking of genitalia and yawning are prominent in male monkeys. Similarly, social groom, huddle, contact and yield were dominant in female monkeys. The adult female showed a higher incidence of affiliative social behaviour than adult male. Male monkeys are more dominant and aggressive. Adult male tends to lunge, approach and chase more often than females. In a colony thé animals rested in small clusters, and are usually sexually segregated. Females of all ages rest together, only infant male sleep with the female. The small group may breakup suddenly and become alert in presence of external sound or object. Male monkeys usually slept alone.

In female monkeys, during menstruation and pregnancy the social behaviour was markedly decreased, and as pregnancy advances they prefer to spend most of the time lying or resting. Therefore, experiments with drugs should not be conducted during these periods. The decrease in social behaviour may be due to horomonal changes. It is not uncommon for macaques to mount members of the same sex. It has been hypothesized that this action aids in establishment and reaffirmation of dominance status within social groups (12). This condition may not be pathological but it is abonormal in the sense of not being species typical.

Rhesus monkey has been used for study of drug effects but such studies have generally been done on animals housed singly (13, 14). The present study provided quantitative paramaters of social activities in a group of animals living together as an unit.

Furthermore, by using this protocol, behavioural responses of CNS active durgs i.e amphetamine and haloperidol, were also studied in order to identify the profile of newer CNS active compounds and for comparative evaluation with the existing drugs. In the present study, AMP not only induced abnormalities in motor behaviour and stereotypy, but also caused major disruption of normal affiliative behaviour i.e. social cohesiveness, which is reflected by approach, contact and social groom. All these responses were significantly suppressed by AMP indicating a social withdrawal. Thus the effects of AMP on locomotor responses (hypervigilance and stereotypy) and on affiliative behaviour (social withdrawal) observed in the present study resemble those reported in AMP induced psychosis in human (8). Similarly, haloperidol produced a decrease in social and solitary behaviour along with cataleptic posture in monkeys. These alterations in

social and solitary behavioural responses and catalepsy were also observed in rodents and in human beings (15, 16).

Thus the study of behaviour, particularly of the non-human primates, under the effect of different centrally acting drugs is one of the most important steps in understanding effects of drugs in human and occupies an important place in new drug development programme.

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