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Selective Effects of 8-OH-DPAT on Social Competition in the Rat

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WOODALL, K. L., A. M. DOMENEY AND M. E. KELLY. *Selective effects of 8-OH-DPAT on social competition in the rat.* PHARMACOL BIOCHEM BEHAV **54**(1) 169–173, 1996.—Previous research has demonstrated that dominant-subordinate relationships measured in small groups of rats competing for access to palatable food or fluids can be disrupted by both anxiolytic and anxiogenic drugs, and it has been proposed as a possible animal model of anxiety. The present study investigated the effects of the selective 5-HT_{1A} agonist 8-OH-DPAT on the rank order of triads of rats measured in terms of access to sweetened milk. The effect of 8-OH-DPAT on locomotor activity and intake of sweetened milk was also determined. 8-OH-DPAT (25 and 37.5 μg/kg) significantly increased the subordinate animals position in the social hierarchy without effect on the individual intakes of sweetened milk or locomotor activity. The same doses administered to dominant animals had no effect on any of the parameters measured. The 8-OH-DPAT-induced increase in social competition in subordinate rats was dissociable from effects on feeding behavior and locomotor activity. The results from this study provide further evidence that social competition in groups of rats may represent a model that can be used to detect drugs acting via receptor mechanisms believed to be implicated in anxiety.

Anxiety 8-OH-DPAT Social competition Rat

GROUPS of rats exposed to situations in which they are required to compete for limited access to palatable substances or fluid are shown to form stable hierarchies (11,12,23,25). These rank orders, consisting of dominant and subordinate animal in each social group, can be disrupted by administration of a number of pharmacological agents with anxiolytic properties. For example, administration of chlordiazepoxide to subordinate animals has been shown to increase their social rank order in a triad group competing for food (13). Further, increases in competition by subordinate rats for access to a sweetened milk solution have also been reported following treatment with chlordiazepoxide, buspirone, aldipem, and zoldipem (23). The ability of anxiolytic agents to modify social hierarchy rank has, therefore, led to the suggestion that the differential extent of competition shown by individual rats in the social group may be generated by different levels of anxiety (23,24). Additional evidence to support this theory has been obtained from studies that demonstrated that the anxiogenic compounds yohimbine, pentylenetetrazole, and FG7142 decreased the position of the dominant animal in the social hierarchy as measured by the extent of competition for sweetened milk (24). Thus, if basal levels of fear are higher in subordinate rats, this may provide a plausible explanation for the preferential effect of anxiolytic compounds on the social competition behavior of this subgroup.

Since the discovery that buspirone, a partial agonist at the 5-HT_{1A} receptor has anxiolytic activity in man (17), there has been a great deal of interest in the ability of animal models of anxiety to detect anxiolytic properties of agents acting via this receptor subtype. The outcome of such studies has frequently resulted in a perplexing array of data indicating both anxiolytic and anxiogenic effects for the same compound, e.g., 8-hydroxy 2(di-n-propylamino)tetralin (8-OH-DPAT), following single dose treatments (2,3,8,20,28). While such paradoxical effects may be related to use of single-dose administration this bidirectional behavioral effect has also been linked to differences in the experimental conditions and/or the animal model employed (19). Therefore, the relevance of the behavioral situation that is used to induce anxiogenesis may be a critical factor for the detection of these compounds. Because initial studies carried out by other workers have indicated that social competition is sensitive to both benzodiazepines and the novel anxiolytic buspirone, there is a possibility that it is a suitable model for detecting a wide range of pharmacological agents that possess anxiolytic activity.

The aim of this study was to further investigate the ability

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of putative anxiolytics to alter social hierarchies in rats competing for sweetened milk. The effect of 8-OH-DPAT, a selective 5-HT_{1A} agonist (29), on social competition in triads of rats competing for sweetened milk when administered to dominant and subordinate animals was determined. In addition, as 8-OH-DPAT is known to alter feeding and locomotor activity (30), the effect on changes in drinking behavior and on locomotor activity was determined to ensure that any changes in an animals rank position were due to selective changes on social competition.

METHOD

Animals

Male Lister Hooded rats (University of Bradford bred), weighing 271.8 ± 10.4 g at the start of the study, were used. Rats were housed in groups of three (triads) immediately after weaning and left for a period of 3 weeks prior to experimentation. Food (standard laboratory chow) and tap water was available ad lib.

Competition Procedure

On the first week of experimentation the triads of rats were familiarized with the testing box and the sweetened milk (Nestle's® sweetened condensed milk diluted with tap water; 1 : 2), which were used in the competition procedure. The testing box consisted of a clear perspex cage 59 × 38 × 30.5 cm (length × width × height) with a food container and drinking spout located on the end wall. The drinking spout was surrounded by a perspex tube (4.5 cm diameter), which ensured that only one animal was able to drink at a time. All animals were water deprived overnight (a period of 14 h), and the following day placed into the testing box and given access to the sweetened milk for a period of 15 min.

On the second week of testing the rats were no longer water deprived and were given access to the testing box and sweetened milk for 5 min. During the testing period the rats were observed every 5 s, and a note of which animal was drinking was made. This procedure was carried out twice a week for a period of 5 weeks. Any groups that did not show stable rank orders in terms of drinking bouts were eliminated from the study.

8-OH-DPAT (12.5, 25, 37.5, 50, 100, and 200 μg/kg, n = 8), or saline (n = 16) was administered to either the dominant or subordinate rat in each triad 15 min prior to testing. One dose of 8-OH-DPAT or saline was administered per week and, therefore, there was a 7-day period between different treatments. The two remaining rats in each triad were administered with saline.

All drug treatments were carried out in a randomised blind trial. Following the 8-OH-DPAT study all triads were tested for two trials to ensure that their rank orders returned to baseline levels.

Intake Studies

8-OH-DPAT (12.5, 25, 37.5, 50, 100, and 200 μg/kg), or saline (n = 8) was administered to each rat in each triad, 15 min prior to testing. One dose of 8-OH-DPAT or saline was injected in each test session. Rats were placed into individual holding cages and given unlimited access to sweetened milk solution for 30 min. During the first 5 min the amount of time each rat spent at the drinking spout was determined and the drinking bottles were weighed after the first 5 min and again at the end of the 30-min testing period to determine the amount consumed by each animal.

Locomotor Activity Studies

Locomotor activity was measured in photocell boxes 24 × 14 × 14 cm (length × width × height) at 5-min intervals for 30 min, 15 min after treatment of all rats (n = 8) with saline or 8-OH-DPAT (12.5, 25, 37.5, 50, and 100 μg/kg SC).

Drugs

8-OH-DPAT.HBr (Research Biochemical International) was dissolved in saline and weight adjusted to give free base weight (mg). All doses of 8-OH-DPAT and vehicle were injected subcutaneously in a volume of 1 ml/kg body weight.

Statistics

Data were converted to percentage drinking (proportion of time spent at the spout/total time) for each of the three rats in each group and the raw data analysed using one-way analysis of variance followed by Dunnett's t-test.

RESULTS

Establishment of Social Hierarchy

Of the groups tested in the study 80% competed for the sweetened milk and developed stable hierarchies. Each hierarchy consisted of a dominant, intermediate, and subordinate rat that had access to the drinking spout for 39.9 ± 0.9%, 31.1 ± 1.1%, and 19.4 ± 1.7% of the testing time respectively (Fig. 1).

Effect of 8-OH-DPAT on Social Competition

Treatment of the subordinate rat with 8-OH-DPAT 15 min prior to testing of social competition caused a significant in-

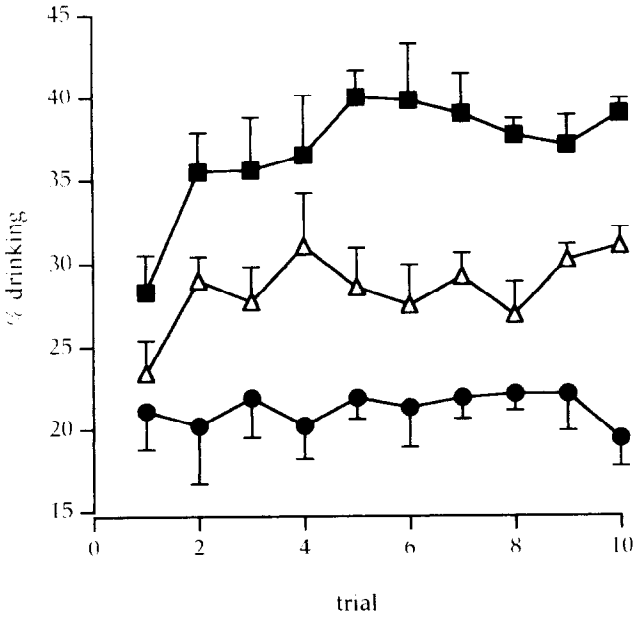

FIG. 1. The stablility of dominant (closed square), intermediate (open triangle), and subordinate (closed circle) rats (n = 8) competing for sweetened milk during 10 trials, over a 5-week testing period. All values are % drinking of the rats expressed as mean ± SEM.

crease in their access to the drinking spout at 25 and 37.5 μg/kg SC compared to saline-injected controls, $F(6, 63) = 23.4$, $p < 0.001$. The increase in drinking by the subordinate animals was accompanied by decreases in access to the drinking spout of both dominant and intermediate animals, although this was not significant. At doses of 100 and 200 μg/kg SC access to the spout of the subordinate rats was significantly decreased, $F(6, 63) = 23.4$, $p < 0.001$; however, at these doses the animals exhibited a flattened body posture characteristic of 8-OH-DPAT behavioral syndrome (28) (Fig. 2). At 100 μg/kg SC the decreased access to the sweetened milk by subordinate rats was accompanied by a significant increase in drinking of the intermediate rats, $F(6, 63) = 2.5, p < 0.01$.

As shown in Fig. 3, treatment of the dominant rat with 8-OH-DPAT 15 min prior to testing of social competition did not significantly increase levels of social competition at any of the doses tested. At doses of 100 and 200 μg/kg SC access to the drinking spout of the dominant rats was significantly decreased, $F(6, 63) = 20.7$, $p < 0.001$, as animals exhibited the 8-OH-DPAT behavioral syndrome.

Following treatment with 8-OH-DPAT the hierarchies in all triads returned to stable levels consistent with those observed immediately prior to drug treatment.

Effect of 8-OH-DPAT on Intake of Sweetened Milk

Administration of 8-OH-DPAT 15 min prior to the determination of individual access to sweetened milk did not significantly modify the amount (g) consumed by the dominant, intermediate, or subordinate rats at doses of 12.5 to 50 μg/kg SC. At 100 and 200 μg/kg SC all of the animals exhibited 8-OH-DPAT behavioral syndrome and drinking was significantly decreased, $F(7, 55) = 110.1, p < 0.001$ (Table 1).

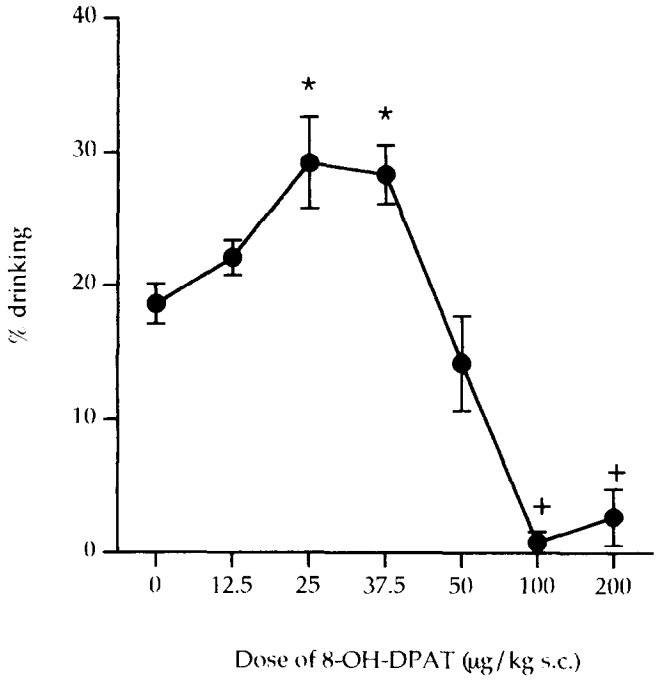

FIG. 2. The effect of 8-OH-DPAT, 12.5–200 μg/kg SC ($n = 8$) on the access to sweetened milk of the subordinate member of triads of Lister Hooded rats compared to saline-injected controls ($n = 16$). All values are % drinking of the subordinate animals expressed as mean ± SEM. Data were analyzed using one-way ANOVA followed by Dunnett's t-test, $^*p < 0.001$ increased compared to controls, $^+p < 0.001$ decreased from controls.

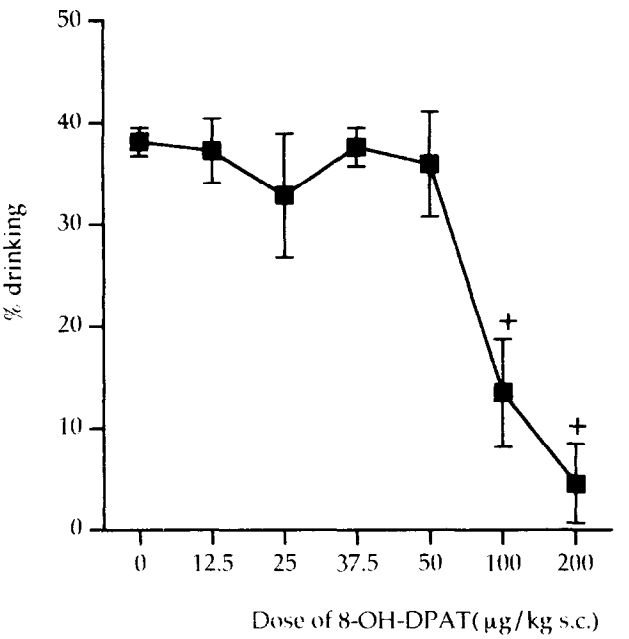

FIG. 3. The effect of 8-OH-DPAT, 12.5–200 μg/kg SC ($n = 8$) on the access to sweetened milk of the dominant member of triads of Lister Hooded rats compared to saline-injected controls ($n = 16$). All values are % drinking of the dominant animals expressed as mean ± SEM. Data were analyzed using one-way ANOVA followed by Dunnett's t-test, $^+p < 0.001$ decreased compared to controls.

Effect of 8-OH-DPAT on Locomotor Activity

There was no significant change in the locomotor activity of the dominant, intermediate, or subordinate rats when tested 15 min after treatment with 8-OH-DPAT (Table 2).

DISCUSSION

In this study 80% of the groups tested exhibited hierarchies that were stable over a period of several months, and this is similar to the percentage of stable hierarchies formed in studies by Gentsch et al. (1988) and Joly and Sanger (1991) (11,23). During this time, the percentage success rate of dominant, intermediate, and subordinate rats obtaining sweetened milk remained relatively constant. This is in contrast to previous work using competition for sweetened milk, which showed that over a 3-month period the hierarchy positions of each triad were reinforced such that the subordinate rats eventually gained little or no access to the milk for the whole of the 5-min testing period (23). A possible reason for the differences observed between these two studies may relate to the different strain of rats used, Wistar rats compared to Lister Hooded used in the present study.

Joly and Sanger (1991) have shown that anxiolytics can increase social competition when administered to subordinate rats competing for a palatable substance (23). In this study the lowest doses of 8-OH-DPAT increased the access of subordinate animals to sweetened milk. 8-OH-DPAT is a selective agonist at the 5-HT_{1A} receptor and has conflicting effects de-

TABLE 1

THE EFFECT OF 8-OH-DPAT ON THE INTAKE OF SWEETENED MILK

Dose of 8-OH-DPAT	$D_{5\,min}$	$I_{5\,min}$	$S_{5\,min}$	$D_{30\,min}$	$I_{30\,min}$	$S_{30\,min}$
Saline	7.5 ± 0.5	7.3 ± 0.6	7.1 ± 1.1	13.6 ± 0.5	13.5 ± 0.8	12.6 ± 1.1
12.5	6.5 ± 0.6	6.9 ± 0.7	6.0 ± 0.5	11.1 ± 1.0	13.1 ± 0.6	13.8 ± 0.6
25	6.3 ± 0.8	6.8 ± 0.7	7.1 ± 0.3	12.5 ± 0.8	12.6 ± 0.8	13.0 ± 0.4
37.5	7.1 ± 0.7	6.5 ± 0.6	7.9 ± 0.7	12.4 ± 0.5	13.9 ± 1.6	13.5 ± 0.8
50	7.6 ± 0.6	6.9 ± 0.6	7.6 ± 0.4	14.8 ± 0.6	12.9 ± 0.4	13.1 ± 0.8
100	0.4 ± 0.3*	0.4 ± 0.4*	0.1 ± 0.1*	0.6 ± 0.3*	0.6 ± 0.4*	0.5 ± 0.3*
200	0 ± 0*	0 ± 0*	0 ± 0*	0 ± 0*	0 ± 0*	0 ± 0*

Consumption of sweetened milk (g) during 5 and 30 min free access by dominant (D), intermediate (I), and subordinate (S) rats 15 min after treatment of 8-OH-DPAT (12.5–200 μg/kg SC). All values are mean ± SEM (n = 8) for all groups and statistical analysis was performed using one-way ANOVA followed by Dunnetts t-test. *$p < 0.001$.

pending on whether it acts via presynaptic or postsynaptic receptors (21). Previous research has suggested that at relatively low doses (60 μg/kg or less), 8-OH-DPAT acts via inhibitory presynaptic receptors (21). The effect of activating presynaptic receptors is to reduce the firing of 5-HT neurones via a negative feedback system (21). As decreased levels of 5-HT are generally thought to decrease levels of anxiety (22), the increase seen in rank order of the subordinate rats in this study could be due to a decrease in their levels of fear in the competitive situation. The induction of the 8-OH-DPAT behavioral syndrome, for example, the adoption of a flat body posture, at the higher doses tested is probably due to activation of postsynaptic 5-HT_{1A} receptors. 8-OH-DPAT behavioral syndrome closely resembles 5-HT behavioral syndrome seen when 5-HT levels are increased following treatment with 5-HT precursors or 5-HT agonists (30).

The doses of 8-OH-DPAT that disrupted the dominant–subordinate relationship when administered to the subordinate animal had no effect when administered to the dominant rat. If the increased competition is due to a decrease in fear of the subordinate animals an increase in rank order by dominant animals would not be expected as their basal levels of fear would be relatively low.

It must also be considered that the effect of 8-OH-DPAT on social competition in the rat may reflect an antidepressant potential. 5-HT_{1A} agonists such as gepirone and ipsapirone have been shown to be effective in the treatment of depression in clinical trials (1,16). In addition, 5-HT_{1A} agonists have been active in certain animal models used to detect antidepressants. For example ipsapirone, buspirone, and 8-OH-DPAT are effective in the learned helplessness model of depression (7,15, 26). Indeed, animal models for detection of antidepressant action based on social dominance in groups of rats have been proposed. A number of reports have used observations based on the agonistic interactions that occur between animals for assessing dominance, e.g., direct social encounters that end in a submissive posture by one animal (18,27). Chronic treatment of subdominant rats with the antidepressants clomipramine and mianserin has been reported to increase their relative rank positions in the hierarchy (27). One explanation for anxiolytics increasing hierarchical separation in a competition situation and chronic treatment with antidepressants increasing hierarchical separation in measures of agonistic behavior is that anxiolytic drugs act by disinhibiting previously suppressed behaviors and antidepressants increase aggressive behavior when it is not suppressed (27). It is clear that more work is needed to clarify the differences between effects of drugs on dominance measured by competition and agonistic interactions.

Another possible explanation is that alterations in the dominant–subordinate relationship following treatment of the subordinate rat with 8-OH-DPAT are due to changes in feeding behavior. A number of 5-HT_{1A} receptor agonists have been

TABLE 2

THE EFFECT OF 8-OH-DPAT ON LOCOMOTOR ACTIVITY

Dose of 8-OH-DPAT	$D_{5\,min}$	$I_{5\,min}$	$S_{5\,min}$	$D_{30\,min}$	$I_{30\,min}$	$S_{30\,min}$
Saline	37.8 ± 5.6	39.0 ± 6.1	42.5 ± 6.3	77.3 ± 13.7	100.9 ± 27.7	84.6 ± 12.3
12.5	33.5 ± 4.7	36.1 ± 5.0	38.9 ± 5.1	89.8 ± 14.3	82.3 ± 9.5	82.0 ± 6.5
25	35.7 ± 5.6	33.5 ± 3.7	35.9 ± 4.4	83.3 ± 7.7	82.0 ± 7.4	79.5 ± 6.4
37.5	39.8 ± 5.5	36.8 ± 4.4	37.8 ± 3.6	86.1 ± 13.2	67.5 ± 7.3	84.0 ± 5.6
50	30.3 ± 6.0	33.4 ± 5.5	41.4 ± 4.5	78.1 ± 11.9	78.1 ± 8.9	73.6 ± 5.4
100	19.0 ± 4.7	17.9 ± 3.2	24.1 ± 5.4	49.3 ± 7.7	47.6 ± 6.7	52.9 ± 9.1

Effect of 8-OH-DPAT (12.5–100 μg/kg SC) on locomotor activity measured at 5- and 30-min intervals of dominant (D), intermediate (I), and subordinate (S) rats compared to saline-injected controls. Values are mean ± SEM (n = 8) for all groups. Statistical analysis was performed using one-way ANOVA followed by Dunnetts t-test.

shown to increase feeding in animals (4,6,14), and 8-OH-DPAT has been shown to increase the intake of sweetened milk in the rat (5). The increase in feeding by 8-OH-DPAT is observed at low doses, and it is thought to be due to activation of presynaptic receptors (4). It has also been proposed that 8-OH-DPAT may increase the rewarding properties of food because opiate and dopamine antagonists block 8-OH-DPAT-induced feeding, although 8-OH-DPAT itself does not bind with high affinity to either opiate or dopamine receptors (9,10). However, in this study when rats were given unlimited access to sweetened milk there was no significant increase in intake by the dominant, intermediate, and subordinate rats at moderate doses of 8-OH-DPAT. This seems to suggest that the 8-OH-DPAT-induced increase in social competition is not due to an increase in drinking per se.

It has been reported that 8-OH-DPAT can cause increased locomotion (30), which may affect interactions between rats in a competitive situation. However, in this particular study there were no significant increases in locomotor activity following treatment with any of the doses of 8-OH-DPAT used.

The results from this study show that 8-OH-DPAT can increase social competition by subordinate rats at relatively low doses that do not affect drinking behavior or locomotor activity. This provides further evidence that social competition in the rat may be modified by a drug that exerts its effects through 5-HT mechanisms.

REFERENCES

1. Amsterdam, J. D.; Berwish, N.; Potter, L.; Rickels, K. Open trial of gepirone in the treatment of major depressive disorder. Curr. Ther. Res. 41:185–193; 1987.
2. Critchley, M. A. E.; Handley, S. L. Effects in the X-maze anxiety model of agents acting at 5-HT_1 and 5-HT_2 receptors. Psychopharmacology (Berlin) 93:502–506; 1987.
3. Critchley, M. A. E.; Njung'e, K.; Handley; S. L. Actions and some interactions of 5-HT_{1A} ligands in the elevated X-maze and effects of dorsal raphe lesions. Psychopharmacology (Berlin) 106: 484–490; 1992.
4. Dourish, C. T. 5-HT receptor subtypes and feeding behaviour. In: Bradley, P. B.; Hanley, S. L.; Cooper, S. J.; Key, B. J.; Barnes, N. M.; Coote, J. H., eds. Advances in the biosciences. Vol. 85. Serotonin, CNS receptors and brain function. UK: Pergamon Press; 1992:179–202.
5. Dourish, C. T.; Cooper, S. J.; Gilbert, F.; Coughlan, J.; Iverson, S. D. The 5-HT_{1A} agonist 8-hydroxy 2(di-n-propylamino)tetralin (8-OH-DPAT) increases consumption of palatable wet mash and liquid diets in the rat. Psychopharmacology (Berlin) 94:58–63; 1988.
6. Dourish, C. T.; Hutson, P. H.; Curson, G. Low doses of the putative serotonin agonist 8-hydroxy 2(di-n-propylamino)tetralin (8-OH-DPAT) elicits feeding in the rat. Psychopharmacology (Berlin) 86:197–204; 1985.
7. Drugan, R. C.; Crawley, J. N.; Paul, S. M.; Skolnick, P. Buspirone attenuates learned helplessness behaviour in rats. Drug Dev. Res. 10:63–67; 1987.
8. Dunn, R. W.; Corbett, R.; Fielding, S. Effects of 5-HT_{1A} receptor agonists and NMDA receptor antagonists in the social interaction test and elevated plus maze. Eur. J. Pharmacol. 169:1–10; 1989.
9. Fletcher, P. J. Dopamine receptor blockade in nucleus accumbens or caudate nucleus differentially affects feeding induced by 8-OH-DPAT injected into dorsal or median raphe. Brain Res. 552:181–189; 1991.
10. Fletcher, P. J. Opiate antagonists inhibit feeding induced by 8-OH-DPAT: Possible mediation in the nucleus accumbens. Brain Res. 560:260–267; 1991.
11. Gentsch, C.; Lichtsteiner, M.; Feer, H. Competition for sucrose-pellets in triads of male Wistar rats: The individuals' performance are differing but stable. Behav. Brain Res. 27:37–44; 1988.
12. Gentsch, C.; Lichtsteiner, M.; Feer, H. Competition for sucrose-pellets in triads of male Wistar rats: Effects of three serotonergic drugs. Prog. Neuropsychopharmacol. Biol. Psychiatry 12:639–651; 1988.
13. Gentsch, C.; Lichtsteiner, M.; Feer, H. Competition for sucrose-pellets in triads of male Wistar rats: Effects of acute and chronic chlordiazepoxide. Psychopharmacology (Berlin) 100:530–534; 1990.
14. Gilbert, F.; Dourish, C. T. Effects of the novel anxiolytics gepirone, buspirone and ipsapirone on free feeding and feeding induced by 8-OH-DPAT. Psychopharmacology (Berlin) 93:349–352; 1987.
15. Giral, P.; Martin, P.; Soubrié, P. Reversal of helpless behaviour in rats by putative 5-HT_{1A} agonists. Biol. Psychiatry 23:237–242; 1988.
16. Glaser, T. Ipsapirone, a potent and selective 5-HT_{1A} receptor ligand with anxiolytic and antidepressant properties. Drugs Future. 13:429–439; 1988.
17. Goldberg, H. L.; Finnerty, R. J. The comparative efficacy of buspirone and diazepam in the treatment of anxiety. Am. J. Psychiatry 136:1184–1187; 1979.
18. Grant, E. C.; Chance, M. R. A. Rank order in caged rats. Anim. Behav. 6:183–194; 1958.
19. Handley, S. L. Future prospects for the pharmacological treatment of anxiety. CNS Drugs 2:397–414; 1994.
20. Handley, S. L.; McBlane, J. W. 5-HT drugs in animal models of anxiety. Psychopharmacology (Berlin) 112:13–20; 1993.
21. Hutson, P. H.; Dourish, C. T.; Curzon, G. 8-hydroxy 2(di-n-propylamino)tetralin (8-OH-DPAT)-induced hyperphagia: Neurochemical and pharmacological evidence for an involvement of 5-hydroxytryptamine somatodendritic autoreceptors. In: Dourish, C. T.; Ahlenius, S.; Hutson, P. H., eds. Brain 5-HT_{1A} receptors. New York: Ellis Horwood; 1987:211–232.
22. Iverson, S. D. 5-HT and anxiety. Neuropharmacology 23:1553–1560; 1985.
23. Joly, D.; Sanger, D. J. Social competition in rats: A test sensitive to acutely administered anxiolytics. Behav. Pharmacol. 2:205–213; 1991.
24. Joly, D.; Sanger, D. J. Social competition in rats can be attenuated by anxiogenic drugs. Behav. Pharmacol. 3:83–88; 1992.
25. Kostowski, W.; Plewako, P.; Bidzinski, A. Brain serotonergic neurons: Their role in a form of dominance-subordination behaviour in rats. Behaviour 33:365–371; 1984.
26. Martin, P.; Beninger, R. J.; Hamon, M.; Puech, A. J. Antidepressant-like action of 8-OH-DPAT, a 5-HT_{1A} agonist in the learned helplessness paradigm: Evidence for a postsynaptic mechanism. Behav. Brain Res. 38:135–144; 1990.
27. Mitchell, P. J.; Redfern, P. H. Chronic treatment with clomipramine and mianserin increases the hierarchical position of subdominant rats housed in triads. Behav. Pharmacol. 3:239–247; 1992.
28. Moser, P. C. An evaluation of the elevated plus-maze test using a novel anxiolytic buspirone. Psychopharmacology (Berlin) 99:48–53; 1989.
29. Perouka, S. J. 5-Hydroxytryptamine receptor subtypes: Molecular, biochemical and physiological characterisation. Trends Neurosci. 11:496–500; 1988.
30. Tricklebank, M. D. The motor and discriminative stimulus properties of 8-OH-DPAT and their relationship to activation of the putative 5-HT_{1A} receptor. In: Dourish, C. T.; Ahlenius, S.; Hutson, P. H., eds. Brain 5-HT_{1A} receptors. New York: Ellis Horwood; 1987:140–151.