Pergamon

Pharmacology Biochemistry and Behavior, Vol. 49, No. 3, pp. 741–746, 1994
Copyright © 1994 Elsevier Science Ltd
Printed in the USA. All rights reserved
0091-3057/94 $6.00 + .00

0091-3057(94)00205-3

Food Carrying in Rats Is Blocked by the Putative Anxiolytic Agent Buspirone

HANS C. DRINGENBERG,[1] RICK A. KORNELSEN AND C. H. VANDERWOLF

Neuroscience Program, University of Western Ontario, London, Ontario, Canada, N6A 5C2

Received 11 November 1993

DRINGENBERG, H. C., R. A. KORNELSEN AND C. H. VANDERWOLF. *Food carrying in rats is blocked by the putative anxiolytic agent buspirone.* PHARMACOL BIOCHEM BEHAV 49(3) 741–746, 1994.—The effects of the putative anxiolytic agent buspirone on food-handling behavior of laboratory rats were investigated. Rats trained to travel from a covered shelter to a food source were provided with food pellets of six sizes. Smaller pellets were eaten at the exposed food source, whereas larger pellets were carried back to the shelter for consumption. Subcutaneous administration of buspirone hydrochloride (0.2–2.0 mg/kg) reduced carrying of larger food pellets in a dose-dependent manner. Instead, these pellets were also eaten at the exposed food source. Carrying was maximally suppressed 1 h after drug administration. Handling of smaller pellets, travel times, and eating times were not affected by buspirone. Similar results have previously been obtained with diazepam. Buspirone appears to exert its effects through 5-HT_{1A} and/or dopamine receptors, whereas diazepam interacts with benzodiazepine receptors. Thus, manipulations of distinct transmitter systems may have similar behavioral consequences on the food carrying responses of rats.

Anxiolytics Buspirone Defensive behavior Food carrying Foraging Rat Serotonin (5-HT)

THE FOOD-HANDLING behavior of animals is influenced by a variety of environmental factors that together determine the way an animal responds to a food item encountered during foraging excursions. It has been proposed that foraging animals trade off eating time against exposure and predation risk. The behavior of animals is organized such that eating or food intake is maximized and exposure risk is minimized (15,38).

A series of controlled laboratory experiments has elucidated some of the factors that influence the way rats handle food items encountered in their environment. When a foraging rat encounters a small food piece, it is immediately eaten at the location where the food is found. Larger food pieces, however, are taken to a shelter or home cage (45,47). Black-capped chickadees and grey squirrels displayed behaviors similar to those of laboratory rats when these animals encountered food items of varying sizes in natural foraging settings (17,18). Further investigations that dissociated food size and time to eat a food item showed that eating time is inversely related to the probability of eating in an exposed area (42). Also, food availability, travel distance and difficulty, ambient lighting, presence of a predator, and food deprivation all influence the food-handling behavior of laboratory rats (43,44). Thus, it appears that food handling in rats is controlled by a complex array of both environmental and internal stimuli to produce the most adaptive foraging behavior for the animal.

Protective food carrying can be manipulated using pharmacological agents. The anxiolytic drug diazepam (29) blocks a number of defensive behaviors in the rat, including food carrying to a shelter (22). This raises the question whether food carrying is sensitive to anxiolytics other than diazepam. In the present experiment, we tested whether the putative anxiolytic agent buspirone (8,12) resembles diazepam in reducing food carrying, or whether the distinct pharmacological properties of diazepam and buspirone, namely interactions with benzodiazepine receptors (33) for diazepam, and serotonergic (11,37) and dopaminergic (20,21) receptors for buspirone, may differentially affect food handling in laboratory rats.

METHOD

Animals and Materials

Male Long-Evans rats (n = 12; 250–300 g) were housed individually in hanging wire mesh cages in a colony room under a 12 L : 12 D schedule. Prior to training, the rats were placed on a restricted feeding schedule and their body weight

[1] Requests for reprints should be addressed to Hans C. Dringenberg, Neuroscience Program, Rm. 9334, Social Science Center, The University of Western Ontario, London, Ontario, Canada, N6A 5C2.

was maintained at approximately 90% of their normal body weight. Water was freely available.

The testing apparatus consisted of a shelter attached to a wooden beam with a food receptacle placed at the end opposite to the shelter. The shelter was a wire mesh cage 25 × 18 × 18 cm, with an opening of 5 × 5 cm on one side to which the beam was attached. The cage was covered with dark cardboard except for the side opposite to the one with the opening. Thus, it was possible to observe a rat inside the cage. The wooden beam was 240 cm long, 9 cm wide, and was supported by legs 25 cm high. A small weighing dish in which food could be placed was located at the end of the beam.

Single cereal pellets (Post Honey Comb) were cut into smaller pieces of one of six sizes: 9 ± 1 mg (size 1); 24 ± 1 mg (size 2); 67 ± 4 mg (size 3); 96 ± 3 mg (size 4); 225 ± 8 mg (size 5); 405 ± 17 mg (size 6). The weights were determined by weighing 20 randomly chosen pellets of each size (means ± SEM are given).

Buspirone hydrochloride (Sigma Chemical Company) was dissolved in saline. Injections were given subcutaneously.

Procedure

For 1 week the rats were habituated to the test apparatus by placing them individually on the beam on which food pellets had been scattered at varying distances from the shelter. During the subsequent week, rats were familiarized to the testing procedure by placing them in the shelter and allowing them to retrieve food pellets of varying sizes from the receptacle at the end of the beam. By the end of the second week of pretraining, all rats would reliably leave the shelter and travel to the food receptacle to obtain food pellets.

The following doses of buspirone hydrochloride were used: 0.0 (i.e., saline vehicle only), 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.5, and 2.0 mg/kg. Six rats received these doses in ascending and six rats received these doses in descending order. The drug injection and behavioral testing were administered every second day.

Twenty minutes after receiving an injection, a rat was placed in the shelter and a food pellet was placed in the receptacle. The rat would leave the shelter and travel to the food receptacle where it took the food pellet into its mouth. The behavior of the rat subsequent to taking the food pellets was classified as: a) eat, the rat chewed and swallowed the pellet; b) sit, the rat sat on its hind feet, transferred the food pellet from its mouth to the forepaws, and ate it from its forepaws; c) carry, the rat carried the food pellet in its mouth back to the shelter where it was consumed. The behavior classification was recorded manually. Further, the following times were taken with stopwatches and recorded manually: a) eating time, time to eat a food pellet; b) carry time, time to carry a pellet to the shelter; c) return time, time taken to travel to the food source after leaving the shelter. A rat received a pellet of each size, one pellet at a time, to make six trials for each drug dose. The order of pellet presentation was randomized.

In an additional experiment, rats received a single injection of buspirone (1.5 mg/kg, SC, $n = 6$) or an equivalent volume of saline ($n = 6$). One hour after the injection and continuing in 1 h intervals until 3 h postinjection, a rat was given one trial with each of the pellet sizes 3-5. In all other aspects, the procedures for this experiment were equivalent to the ones outlined above.

Data are presented as mean ± SEM. For statistical treatment, a mixed design with one between factor and two within factors was used. The between factor had two levels (rats receiving ascending or descending drug doses) and the two within factors had nine and six levels (nine drug doses; six pellet sizes). Where appropriate, Newman-Keul's follow-up tests or Student's *t*-tests were performed. All data were analyzed using the software packages CLR Anova (Version 1.1, Clear Lake Research Inc.) and StatWorks (Version 1.1, Cricket Software Inc.).

RESULTS

As shown in Fig. 1, after encountering a food item, saline-injected rats tended to eat smaller pellets immediately (e.g., sizes 1 and 2), transferred medium sized pellets (size 3) from their mouth to their paws, and ate these pellets in a sitting posture, and carried large food pellets (sizes 4–6) to the shelter where they were eaten. Thus, in accordance with previous work (43,47), pellet size strongly influenced the food-handling behavior of the rats. Consequently, there were significant effects of pellet size on the occurrence of eats, sits, and carries, $F(5, 50) = 647.5$, 52.4, and 104.1; $p < 0.0001$, respectively).

Administration of buspirone resulted in a dose-dependent increase in the probability of pellets being consumed at the exposed food source, and a corresponding decrease in the probability of pellets being carried to the shelter for consumption (Fig. 2). Overall drug effects were significant for all three behaviors: eat, $F(8, 80) = 2.4$, $p = 0.023$; sit, $F(8, 80) = 9.2$, $p < 0.0001$; and carry, $F(8, 80) = 8.4$, $p < 0.0001$. However, for eating, Newman-Keul's tests revealed no significant differences except that the 0.8 mg/kg dose differed from the 1.2 and 1.5 mg/kg doses at $p < 0.05$. There was a pronounced and dose-dependent increase in the incidence of sits with increasing drug dose. Newman-Keul's tests showed that for the probability of sitting, the 1.2, 1.5, and 2.0 mg/kg doses were significantly different from the saline, 0.2, 0.4, and 0.8 mg/kg dose at $p < 0.01$ and from the 0.6 and 1.0 mg/kg doses at $p < 0.05$. Finally, with increasing drug doses, there was a clear, dose-dependent decline in the incidence of carries. Newman-Keul's tests showed that the 1.2, 1.5, and 2.0 mg/kg doses were significantly different from the saline, 0.2, and 0.4 mg/kg doses at $p < 0.01$. In addition, the 1.2 and 2.0 mg/kg doses also differed from the 0.6 and 0.8 mg/kg doses at $p < 0.01$.

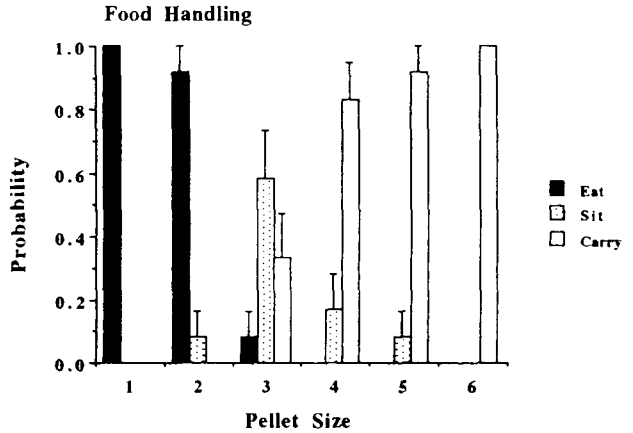

FIG. 1. Effect of pellet size on probability of eating, sitting, and carrying for saline injected rats ($n = 12$). With increasing pellet size, probability of eating decreased and carrying increased. Sitting occurred for medium-sized pellets.

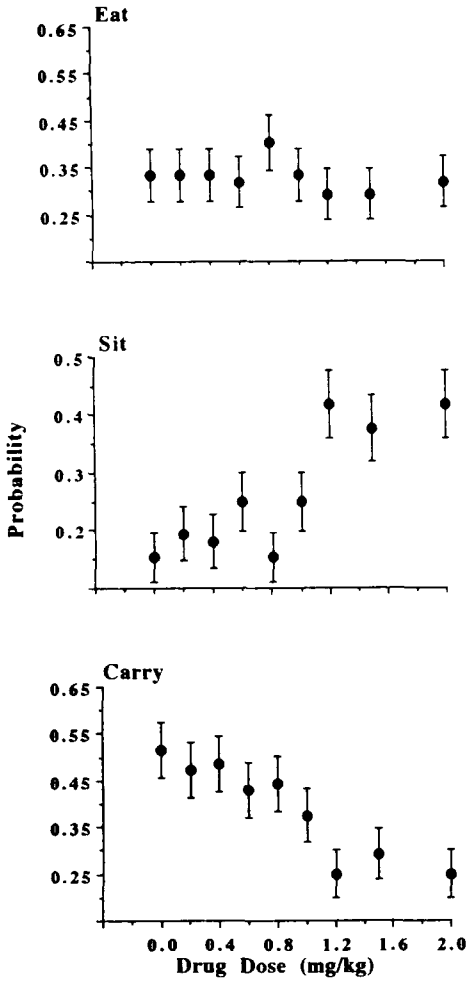

FIG. 2. Effects of saline and buspirone administration (0.2-2.0. mg/kg, SC) on probability of eating, sitting, and carrying across all six pellet sizes. There was no consistent effect of buspirone on eating probability. However, sitting probability was significantly increased and carrying probability significantly decreased with successively higher drug doses (see text).

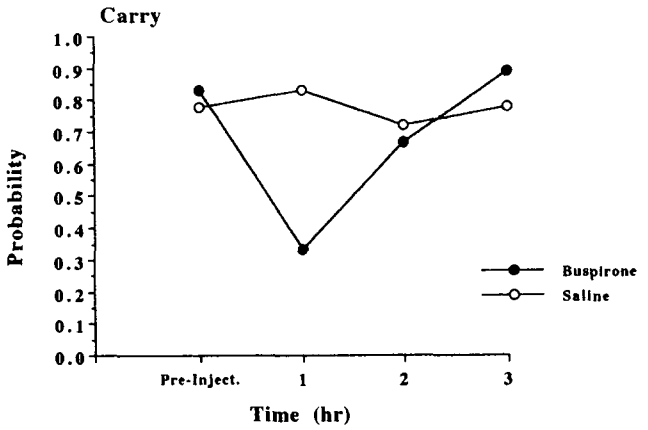

FIG. 3. Effect of a 1.5 mg/kg injection (SC) of buspirone (n = 6) or saline (n = 6) on carrying probability for pellet sizes 3-5. Buspirone decreased carrying probability 1 h after the injection. Two hours after drug administration, carrying probability for buspirone-injected rats had returned to saline levels.

When the effects of buspirone were analyzed for each pellet size, there were significant drug effects for sizes 3-6 for both sit and carry probability ($p < 0.03$). Thus, buspirone increased sits and decreased carries selectively for medium and large pellets, whereas small pellets were always eaten.

Ascending and descending buspirone doses had equivalent effects on all food-handling behaviors. Thus, there were no significant effects of injection schedule on either eat, sit, or carry probability, $F(1, 10) = 0.24$, 0.15, and 0.47, respectively; $p > 0.5$).

The effect of buspirone was most pronounced 1 h after administration of the drug. As shown in Fig. 3, a single 1.5 mg/kg injection produced a clear decrease in the carry probability for pellet sizes 3-5 1 h subsequent to the injection. After a further hour, carry probability had returned to saline control levels. The fact that buspirone, but not saline, reduced food carrying over time was highlighted in the significant drug by time interaction, $F(3, 30) = 8.54$, $p = 0.0003$. Further, comparisons of carry probability for each test time showed that only at 1 h after the injection was there a significant difference between the saline and buspirone treated rats, $F(1, 10) = 12.27$, $p = 0.006$, all other $p > 0.25$).

The effects of buspirone on eat, carry, and return time were analyzed only for pellet 6 because this was the only pellet carried sufficiently across all drug doses to yield sufficient data for reliable analyses. Buspirone administration had no effects on either eat, carry, or return times for this pellet. As shown in Fig. 4, it took a rat an average of approximately 80 s to eat a size 6 pellet, 3 s to carry it to the shelter, and 4 s to make the return trip from the shelter to the food source. None of these times were significantly altered by buspirone and comparisons of eat, carry, and return times after all buspirone doses to the saline condition failed to show any significant differences ($p > 0.05$, Student's t-test). The only exception was a significant difference between the carry times for the saline and 1.5 mg/kg buspirone conditions ($p = 0.017$).

The fact that travel and eat times were not altered by the administration of buspirone highlighted the fact that no sensory-motor impairments were apparent after buspirone administration. There was, however, a pronounced lack of activity in the home cage shortly after buspirone administration in the rage of 0.8-2.0 mg/kg. Within 5 min of an injection, the rat would lie down and spontaneous locomotor activity was virtually absent for variable time periods. If such a rat was removed from its home cage and placed on an open surface, however, it would immediately resume a normal upright posture and engage in sniffing, lateral head movements, scanning, and stepping.

DISCUSSION

Laboratory rats, squirrels, and a number of bird species all consume smaller food items in open, exposed locations, whereas larger items are taken to a sheltered place for consumption. Thus, animals optimize food intake and minimize exposure and predation risk (17,18,36,38,43). In the present study, administration of buspirone significantly reduced the carrying of large food items to a covered shelter for consumption. Instead, these food items were consumed at the food source, that is, in an open, exposed locale. Buspirone did not

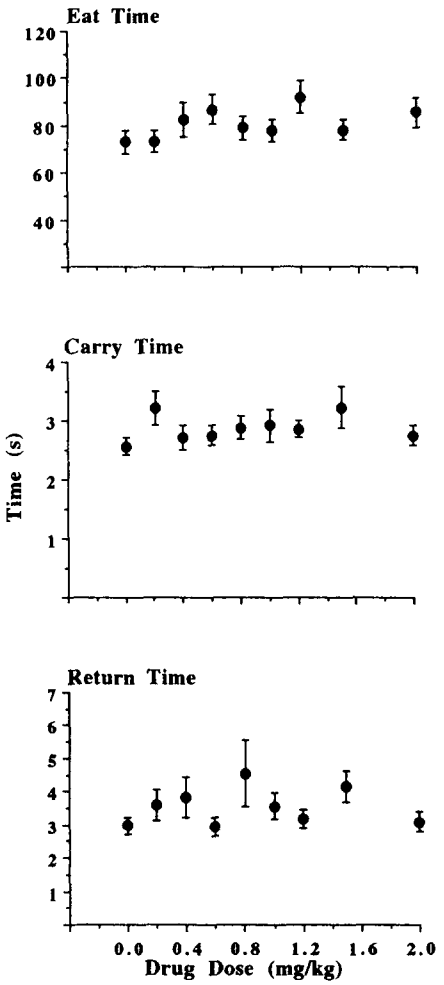

FIG. 4. Effects of saline and buspirone administration (0.2–2.0 mg/kg, SC) on eating, carrying, and returning times for size 6 pellets. Buspirone had no effects on any of these times.

affect the way rats responded to small food items that were always eaten immediately, or midsized items that were always picked up and consumed from the forepaws at the food source. Also, the time to eat a large pellet, carry it to the shelter, and return from the shelter to the food source were not affected by buspirone.

The fact that many aspects of the food-carrying behavior were consistent across the saline and all buspirone doses suggests that the present results were not due to some general alteration of the way food items or eating times were perceived which, in turn, could affect the handling of food items (42). Also, even though high buspirone doses reduced carrying of the large pellets, carrying of these pellets still occurred. Thus, the drug treatment did not interfere with locomotion or food carrying per se. Instead, the likelihood of rats to perform of a specific motoric response to large food items was reduced.

Although the limited duration of the experiment precludes any firm conclusions, we did not note the development of any tolerance to buspirone. The response to a given dose of buspirone was not significantly affected by previous experience (or no experience) with the drug. This finding is consistent with clinical data indicating that tolerance to buspirone may not develop (7,34). The lack of order-of-dose effects also suggests that possible holdover effects of buspirone treatment were minimal because it may be expected that these would increase the effect of doses that followed large doses.

Buspirone increases eating (3) and cork gnawing (27) in the rat, and it is possible that this may influence food-handling behaviors. However, the reduced food carrying reported here may not be due to a general effect of buspirone on eating. Increasing appetite or eating by decreasing body weight increases food hoarding (6,19). Also, in the food-carrying paradigm used here, food deprivation does not alter the carrying of food items of varying sizes (47). Thus, an increase in appetite or eating cannot satisfactorily account for the reduction in food carrying apparent after buspirone treatment.

Buspirone interacts with both serotonergic 5-HT_{1A} receptors (11,37) and dopamine autoreceptors (20,21). Serotonergic mechanisms have been proposed to play a role in anxiety [see (32) for a review], and a case has been made that it may be the serotonergic system that plays a primary role in mediating the anxiolytic action of buspirone (2,5,34,35). Whether the effect of buspirone to reduce food carrying is related to its anxiolytic action, however, is questionable. Buspirone is effective in reducing anxiety only in some animal models of anxiety (5,26, 30) and does not appear to act as an anxiolytic, or has effects much smaller than those obtained with more conventional anxiolytics, in several other animal models (9,13,14,26). Even the effect of the more conventional anxiolytic diazepam to block food carrying has been interpreted as a possible change in the perception of pellet size or time required to consume a food item, or as a suppression of movement components involved in food carrying, rather than as a consequence of reduced anxiety (22). Also, for buspirone to produce anxiolytic effects in humans, several weeks of buspirone treatment are required (16). Thus, the immediate behavioral change reported here apparent after only a single dose of buspirone may not be related to the anxiolytic actions of this drug.

Both buspirone (present study) and diazepam (22) block food carrying, that is, these drugs alter a specific aspect of food handling behavior, namely the motoric response to large food items. The fact that manipulations of both GABA and serotonergic/dopaminergic transmission block food carrying suggests that there may be a common mechanisms through which buspirone and diazepam exert their effects. It has been suggested that the behavioral effects of these drugs are, at least partially, mediated by the hippocampus because they both reduce hippocampal theta frequency (4,23,24). Consistent with this notion, high densities of 5-HT_{1A} binding sites and mRNA (25,28), as well as benzodiazepine receptors (1) and GABAergic interneurons (31) are found in the hippocampus. Further, the effects of diazepam and buspirone on food carrying are mimicked by hippocampal lesions (46). Alternatively, buspirone also acts at the level of the dorsal raphe where it inhibits neuronal discharge (37). This reduction in activity of raphe neurons may not be linked to changes in hippocampal theta frequency, however, because theta activity is not substantially altered by inhibition of serotonin synthesis or neurotoxic lesions of the raphe nuclei (40).

As already mentioned, it is questionable whether the results obtained here are related to a reduction in anxiety levels. Hippocampal theta frequency and amplitude are related to size and vigor of movement pattern, as well as to the initiation of movement (10,41,48). Thus, it is tempting to speculate that reduced hippocampal theta frequency after buspirone admin-

istration may affect the priming or initiation of the movement sequence involved in carrying a food item back to a shelter. However, in other animal models of anxiety, disinhibition and increased motor activity such as punished licking have been noted after buspirone administration (5). It may be some movement types (type 1 behaviors such as walking) depend more heavily on hippocampal circuits than others (type 2 behaviors such as licking, chewing, and grooming) (39). Clearly, whether the hippocampus is involved in mediating some of the behavioral effects of anxiolytics remains to be established.

ACKNOWLEDGEMENTS

The research was supported by a grant from the Canadian Natural Sciences and Engineering Research Council to C.H.V. H.C.D. is supported by an Ontario Graduate Scholarship.

REFERENCES

1. Braestrup, C; Albrechtsen, R.; Squires, R. F. High densities of benzodiazepine receptors in human cortical areas. Nature 269: 702–704; 1977.
2. Charney, D. S.; Woods, S. W.; Krystal, J. H.; Heninger, G. R. Serotonin function in human anxiety disorders. Ann. NY Acad. Sci. 600:558–573; 1990.
3. Clark, M.; Fletcher, A. Does buspirone elicit feeding by a similar mechanism to that of 8-OH-DPAT ? Br. J. Pharmacol. 89:863P; 1986.
4. Coop, C. F.; McNaughton, N. Buspirone affects hippocampal rhythmical slow activity through serotonin$_{1A}$ rather than dopamine D_2 receptors. Neuroscience 40:169–174; 1991.
5. Eison, A. S.; Eison, M. S.; Stanley, M.; Riblet, L. A. Serotonergic mechanisms in the behavioral effects of buspirone and gepirone. Pharmacol. Biochem. Behav. 24:701–707; 1986.
6. Fantino, M.; Cabanac, M. Body weight regulation with a proportional hoarding response in the rat. Physiol. Behav. 24:939–942; 1980.
7. Feighner, J. P. Buspirone in the long-term treatment of generalized anxiety disorders. J. Clin. Psychiatry 48 Suppl. 12:3–6; 1987.
8. Feighner, J. P.; Merideth, C. H.; Hendrickson, G. A. A double-blind comparison of buspirone and diazepam in outpatients with generalized anxiety disorder. J. Clin. Psychiatry Suppl. 43:103–107; 1982.
9. File, S. E. The neurochemistry of anxiety. In: Burrows, G. D.; Norman, T. R.; Davies, B., eds. Antianxiety agents. Amsterdam: Elsevier; 1984:13–32.
10. Frederickson, C. J.; Whishaw, I. Q. Hippocampal EEG during learned and unlearned behavior in the rat. Physiol. Behav. 18: 597–603; 1977.
11. Glaser, T; Traber, J. Buspirone: Action on serotonergic receptors in calf hippocampus. Eur. J. Pharmacol. 88:137–138; 1983.
12. Goldberg, H. L.; Finnerty, R. Comparison of buspirone in two separate studies. J. Clin. Psychiatry Suppl. 43:87–91; 1982.
13. Goldberg, M. E.; Salama, A. I.; Patel, J. B.; Malick, J. B. Novel non benzodiazepine anxiolytics. Neuropharmacology 22:1499–1504; 1983.
14. Howard, J. L.; Pollard, G. T. Effects of buspirone in the Geller-Seifter conflict test with incremental shock. Drug Dev. Res. 19: 37–49; 1990.
15. Krebs, J. R.; McCleery, R. H. Optimization in behavioral ecology. In: Krebs, J. R.; Davies, N. B., eds. Behavioral ecology (2nd ed.). Sunderland, MA: Sinauer; 1984:91–121.
16. Lickey, M. E.; Gordon, B. Medicine and mental illness. New York: W. H. Freeman; 1991:294.
17. Lima, S. L. Maximizing feeding efficiency and minimizing time exposed to predators: A trade-off in the black-capped chickadee. Oecologia 66:60–67; 1985.
18. Lima, S. L.; Valone, T. J.; Caraco, T. Foraging-efficiency-risk trade-off in the grey squirrel. Anim. Behav. 33:155–165; 1985.
19. McCleary, R. A.; Morgan, C. T. Food hoarding in rats as a function of environmental temperature. J. Comp. Psychol. 39: 371–378; 1946.
20. McMillen, B. A. Buspirone and the dopaminergic system. In: Tunnicliff, G.; Eison, A. S.; Taylor, D. P., eds. Buspirone: Mechanisms and clinical aspects. San Diego: Academic Press; 1991:163–176.
21. McMillen, B. A.; Matthews, R. T.; Sanghera, M. K.; Shepard, P. D.; German, D. C. Dopamine receptor antagonism by the novel anti-anxiety drug, buspirone. J. Neurosci. 3:733–738; 1983.
22. McNamara, R. K.; Whishaw, I. Q. Blockade of hoarding in rats by diazepam: An analysis of the anxiety and object value hypotheses of hoarding. Psychopharmacology (Berlin) 101:214–221; 1990.
23. McNaughton, N.; Richardson, J.; Gore, C. Reticular elicitation of hippocampal slow waves: Common effects of some anxiolytic drugs. Neuroscience 19:899–903; 1986.
24. McNaughton, N.; Sedgwick, E. M. Reticular stimulation and hippocampal theta rhythm in rats: Effects of drugs. Neuroscience 3: 629- 632; 1978.
25. Pazos, A.; Palacios, J. M. Quantitative autoradiographic mapping of serotonin receptors in the rat brain: I. Serotonin-1 receptors. Brain Res. 346:205–230; 1985.
26. Pich, E. M.; Samanin, R. Disinhibitory effects of buspirone and low doses of sulpiride and haloperidol in two experimental anxiety models in rats: Possible role of dopamine. Psychopharmacology (Berlin) 89:125–130; 1986.
27. Pollard, G. T.; Howard, J. L. Cork gnawing in the rat as a screening method for buspirone-like anxiolytics. Drug Dev. Res. 22:179–187; 1991.
28. Pompeiano, M.; Palacios, J. M.; Mengod, G. Distribution and cellular location of mRNA coding for 5-HT$_{1A}$ receptor in the rat brain: Correlation with receptor binding. J. Neurosci. 12:440–453; 1992.
29. Randall, L. O.; Heise, G. A.; Schallek, W.; Bagdon, R. E.; Banziger, R.; Boris, A.; Moe, R. A.; Abrams, W. B. Pharmacological and clinical studies on valium, a new psychotherapeutic agent of the benzodiazepine class. Curr. Ther. Res. Clin. Exp. 3:405–425; 1961.
30. Riblet, L. A.; Taylor, D. P.; Eison, M. S.; Stanton, H. C. Pharmacology and neurochemistry of buspirone. J. Clin. Psychiatry Suppl. 43:11–16; 1982.
31. Seress, L.; Ribak, C. E. GABAergic cells in the dentate gyrus appear to be local circuit and projection neurons. Exp. Brain Res. 50:173–182; 1983.
32. Soubrie, P. Reconciling the role of central serotonin neurons in human and animal behavior. Behav. Brain Sci. 9:319–364; 1986.
33. Squires, R. F; Braestrup, C. Benzodiazepine receptors in rat brain. Nature 266:732–734; 1977.
34. Taylor, D. Serotonin agents in anxiety. Ann. NY Acad. Sci. 600: 545–557; 1990.
35. Traber, J.; Glaser, T. 5-HT$_{1A}$ receptor related anxiolytics. Trends Pharmacol. Sci. 8:432–427; 1987.
36. Valone, T. J.; Lima, S. L. Carrying food items to cover for consumption: The behavior of ten bird species feeding under the risk of predation. Oecologia 71:286–294; 1987.
37. Vandermaelen, C. P.; Matheson, G. K.; Wilderman, R. C.; Patterson, L. A. Inhibition of serotonergic dorsal raphe neurons by systemic and iontophoretic administration of buspirone, a non-benzodiazepine anxiolytic drug. Eur. J. Pharmacol. 129:123–130; 1986.
38. Vander Wall, S. B. Food hoarding in animals. Chicago: Univ. Chicago Press; 1990.
39. Vanderwolf, C. H. Cerebral activity and behavior: Control by

central cholinergic and serotonergic systems. Int. Rev. Neurobiol. 30:225–340; 1988.
40. Vanderwolf, C. H.; Baker, G. B.; Dickson, C. Serotonergic control of cerebral activity and behavior: Models of dementia. Ann. NY Acad. Sci. 600:366–383; 1990.
41. Whishaw, I. Q. A simple behavioral paradigm for the study of type Ihippocampal rhythmical slow activity (RSA) frequency shifts. Physiol. Behav. 29:751–753; 1982.
42. Whishaw, I. Q. Time estimates contribute to food handling decisions by rats: Implications for neural control of hoarding. Psychobiology 18:460– 466; 1990.
43. Whishaw, I. Q.; Dringenberg, H. C. How does the rat (*Rattus norvegicus*) adjust food-carrying responses to the influences of distance, effort, predatory odor, food size, and food availability? Psychobiology 19:251–261; 1991.
44. Whishaw, I. Q.; Gorney, B. P.; Dringenberg, H. C. The defensive strategies of foraging rats: A review and synthesis. Psychol. Rec. 41:185–205; 1991.
45. Whishaw, I. Q.; Nicholson, L.; Oddie, S. D. Food pellet size directs hoarding in rats. Bull. Psychon. Soc. 27:57–59; 1989.
46. Whishaw, I. Q.; Oddie, S. D.; McNamara, R. K.; Harris, T. L.; Perry, B. S. Psychophysical methods for study of sensory-motor behavior using a food-carrying (hoarding) task in rodents. J. Neurosci. Methods 32:123–133; 1990.
47. Whishaw I. Q.; Tomie, J. Food-pellet size modifies the hoarding behavior of foraging rats. Psychobiology 17:93–101; 1989.
48. Whishaw, I. Q.; Vanderwolf, C. H. Hippocampal EEG and behavior: Changes in amplitude and frequency of RSA (theta rhythm) associated with spontaneous and learned movement patterns in rats and cats. Behav. Biol. 8:461–484; 1973.