Pharmacology Biochemistry & Behavior, Vol. 15, pp. 201–206, 1981. Printed in the U.S.A.

L-Tryptophan's Effects on Mouse Killing, Feeding, Drinking, Locomotion, and Brain Serotonin

JUDITH L. GIBBONS

Department of Psychology, St. Louis University, St. Louis, MO 63103

GORDON A. BARR AND WAGNER H. BRIDGER

Department of Psychiatry, Albert Einstein College of Medicine
1300 Morris Park Avenue, Bronx, NY 10461

AND

SARAH F. LEIBOWITZ

The Rockefeller University, New York, NY 10021

Received 9 February 1981

GIBBONS, J. L., G. A. BARR, W. H. BRIDGER AND S. F. LEIBOWITZ. *L-tryptophan's effects on mouse killing, feeding, drinking, locomotion, and brain serotonin.* PHARMAC. BIOCHEM. BEHAV. 15(2) 201–206, 1981.—Injections of the serotonin precursor *l*-tryptophan (25, 50, and 100 mg/kg IP), inhibited mouse killing behavior in rats, as indicated by a dose dependent increase in latencies to attack and kill mice. Tests in 24 hr food deprived rats revealed that feeding behavior was also significantly decreased by about 30% by tryptophan injections (50–100 mg/kg IP). Concomitant with the behavioral changes were increased levels of brain serotonin and its metabolite 5-hydroxyindoleacetic acid. Drinking, latencies to sniff mice, and ability to locomote on a rotating rod were not affected by *l*-tryptophan injections, although spontaneous activity in an open field was reliably reduced by 33% with a dose of 100 mg/kg. Thus, while the degree of selectivity for tryptophan's effects on behavior remains open to question, these findings are consistent with hypotheses of an inhibitory role for central serotonergic systems, particularly in mouse killing and feeding behaviors.

Tryptophan Serotonin Mouse killing behavior Feeding Drinking Rats Muricide

CENTRAL neuroanatomical systems which use serotonin (5-hydroxytryptamine, 5-HT) as a transmitter substance have been implicated in inhibiting a number of behaviors, including mouse killing [3,19] and feeding [5] in rats.

Evidence suggesting a role for the serotonergic projections of the dorsal raphe nucleus in mouse killing behavior (muricide) includes the induction or facilitation of killing by lesions of the dorsal raphe nucleus [35], maintenance on a tryptophan-free diet [18], and injections of the tryptophan hydroxylase inhibitor, para-chlorophenylalanine [16, 27, 34]. All of these manipulations decrease the activity of the 5-HT system and increase mouse killing. Conversely, mouse killing is suppressed by injections of 5-hydroxytryptophan (5-HTP), the immediate precursor of serotonin [21].

There is also some evidence that 5-HT systems may have an inhibitory role in feeding behavior. The drug fenfluramine, which releases 5-HT is a powerful anorectic (see [5,22] for reviews). Moreover, 5-HT itself, when applied directly to the paraventricular nucleus, suppresses feeding without an effect on general arousal level [23]. Intraperitoneal injections of the serotonin precursor 5-HTP also suppress feeding behavior (see [22] for a review).

Although 5-HTP has been shown to suppress both mouse killing and feeding behavior its action on central 5-HT systems may lack specificity. After peripheral administration of 5-HTP, serotonin is found in regions of brain which do not normally contain this transmitter [13]. *L*-tryptophan loading also increases brain 5-HT levels [12] and may do so in a more selective manner [1].

In the present studies, the effects of *l*-tryptophan injections were studied on a variety of measures, including mouse killing behavior, feeding, drinking, locomotor activity in an open field and on a rotarod, and on brain levels of serotonin and its metabolite 5-hydroxyindoleacetic acid (5-HIAA).

METHOD

Animals

The animals were 100 male Long Evans hooded rats, obtained from Blue Spruce (Altamont, NY), weighing at least

TABLE 1

ATTACK AND KILL LATENCIES AFTER *L*-TRYPTOPHAN INJECTIONS

		Saline trial					*L*-tryptophan trial				
		1	2	3	4	5	1	2	3	4	5
Group 1											
(N=10, 25 mg/kg)	attack	22±10	18± 8	133±75	52± 22	67±41	15± 7	179±146	7± 3	16± 10	100± 72
	kill	25±10	49± 29	137±75	57± 22	76±24	18± 6	182±142	11± 2	20± 10	101± 72
Group 2											
(N=14, 50 mg/kg)	attack	18± 5	206±123	79±40	83± 36	209±97	258±137	344±171	298±171	411±201	353±172
	kill	23± 5	209±123	106±43	181±101	214±98	261±137	347±171	302±171	421±200	356±172
Group 3*											
(N=14, 100 mg/kg)	attack	51±35	72± 37	57±37	220±135	131±70	317±170	420±200	234±126	315±171	271±173
	kill	56±35	79± 38	60±38	224±135	136±70	321±169	425±200	239±125	323±171	274±173

Entries represent mean sec ± SEM.

*Latencies to attack and kill were significantly greater after 100 mg/kg *L*-tryptophan injections. There was not a significant interaction between trials and drug treatment.

350 g at the beginning of testing. Rats were housed individually in cages measuring 37.5×17.5×18.0 cm high, and were fed Teklad Mouse and Rat Diet (4% fat) laboratory chow and water ad lib except as described below. Rats were screened for mouse killing by placing a mouse in the home cage, and noting 24 hr later whether the mouse was dead or alive. In our hands approximately 50% of this strain of rats kill when tested in this manner.

Drugs

L-tryptophan methylester (Sigma) was dissolved in saline and injected IP in a volume of 1 ml/kg 60 min prior to behavioral tests or sacrifice for biochemical analysis.

Mouse Killing Tests

The test for mouse killing was a satiation test as previously described [16]. In this test a mouse was introduced into the home cage of the rat, and the rat's latencies to sniff, attack, and kill the mouse were recorded. Killed mice were removed immediately from the cage. If there was no kill in 30 min, the live mouse was removed. Sixty sec after the previous kill or removal of a live mouse, a second mouse was introduced. This procedure was continued for 5 mice or until a rat failed to kill 2 consecutive mice. A total of 38 killer rats were injected with one of three doses of *l*-tryptophan (25 mg/kg, N=10; 50 mg/kg, N=14; 100 mg/kg, N=14) and saline in a counterbalanced order with 2–4 days intervening between injections. Sixty min after each injection, rats were tested for mouse killing as just described.

Locomotor Activity

Two different measures were taken of effects of *l*-tryptophan on locomotor activity; these were spontaneous locomotion in the open field and performance on a rotarod task. To control for possible motor impairment by *l*-tryptophan, the rotarod test [11] was done on 19 rats, injected with either 100 mg/kg of *l*-tryptophan (N=10) or saline (N=9). Sixty min after injection the rat was placed on the rotarod (a 4.5 cm diameter rod, covered with hardware cloth, suspended 88 cm above the ground, rotated at 30 rpm). The amount of time the rat stayed on the rod was measured for a maximum of 120 sec.

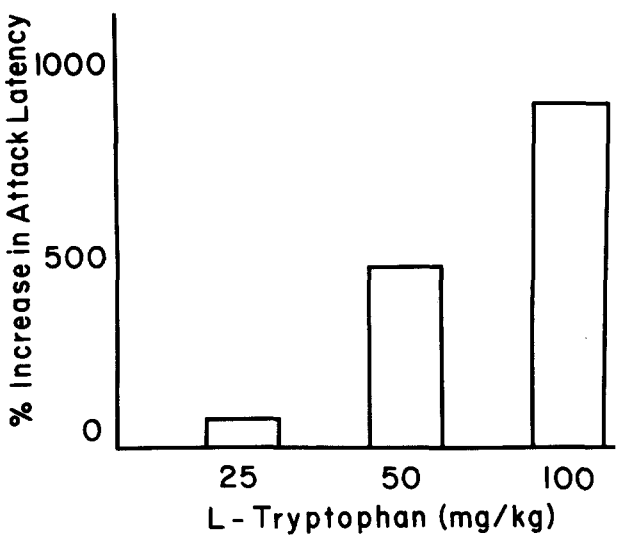

FIG. 1. Percent increase in attack latencies after injections of *L*-tryptophan, as compared to saline control tests. Latencies at 100 mg/kg dose significantly greater than saline, $p<0.05$.

In order to measure spontaneous locomotor activity in the open field, ten rats were injected with *l*-tryptophan (100 mg/kg) or saline in a counterbalanced order with 2–4 days intervening between tests. Sixty min after injection, they were placed into one corner of an open field (90 cm square by 32 cm high with the floor marked by squares, 15 cm on a side). The number of squares entered in each of 5 min was recorded.

Feeding and Drinking

The effects of tryptophan injections on food and water intake in hungry animals were also studied. Twelve killer rats were tested with saline, and 3 doses of *l*-tryptophan (25,

TABLE 2

FOOD AND WATER INTAKE AFTER L-TRYPTOPHAN INJECTIONS

	Food intake (mean g chow ± SEM)			Water intake (mean ml water ± SEM)		
	1st interval	2nd interval	3rd interval	1st interval	2nd interval	3rd interval
Saline	5.0 ± 0.4	3.7 ± 0.4	3.5 ± 0.6	6.4 ± 0.9	4.7 ± 0.6	6.1 ± 1.0
L-tryptophan						
25 mg/kg	5.0 ± 0.4	3.2 ± 0.4	3.9 ± 0.5	6.2 ± 0.9	4.9 ± 0.6	7.5 ± 1.2
50 mg/kg	5.0 ± 0.4	3.5 ± 0.3	2.4 ± 0.3*	6.9 ± 0.6	5.3 ± 0.7	5.8 ± 0.8
100 mg/kg	3.7 ± 0.4*	2.7 ± 0.4*	3.7 ± 0.6	5.1 ± 0.4	5.7 ± 0.6	7.0 ± 1.1

The 1st and 2nd intervals were 30 min long, and the 3rd interval was 60 min long.
*Significantly different from saline, $p<0.05$.

50 and 100 mg/kg), according to a replicated Latin Square design with one week intervening between tests. For 24 hr before each test, rats were food deprived. Sixty min after an injection of drug or saline vehicle, measured amounts of food pellets and water were presented. These were removed and replaced after 1/2 hr, 1 hr and 2 hr. The differences between the amount given to the animal and the amount recovered was recorded as intake.

Serotonin and 5-HIAA Assays

Whole brain serotonin and 5-HIAA were measured in rats injected with *l*-tryptophan to verify that the tryptophan injections had been effective in altering brain biogenic amines. Nine rats injected with saline, 6 rats injected with *l*-tryptophan in a dose of 25 mg/kg, and 6 rats injected with *l*-tryptophan in a dose of 100 mg/kg were sacrificed by decapitation 60 min after injection; the brains were quickly removed from the skull and frozen in dry ice. The brains were stored at −50°C for a maximum of 2 weeks, before assaying fluorimetrically for 5-HT and 5-HIAA according to the method of Curzon and Green [10]. Recovery values averaged 99% for 5-HT and 70% for 5-HIAA.

Statistics

Latencies to sniff, attack, and kill in the mouse killing tests were transformed to logarithms of the form $x'=\log_{10}(x+10)$ before analysis. This transformation minimized heterogeneity of variance [20]. Data were then analyzed by the appropriate analysis of variance (ANOVA) or *t*-test.

RESULTS

Mouse Killing

L-tryptophan inhibited mouse killing by increasing the latencies to attack and kill mice. The attack and kill latencies over the five trials after saline and after *l*-tryptophan injections are presented in Table 1. Attack and kill latencies were highly correlated: r=.92 to .99 for the three groups. The inhibition of killing was a dose-related effect (see Fig. 1) with only the highest dose of *l*-tryptophan significantly different from saline. At this dose (100 mg/kg), both attack and kill latencies were significantly increased, $F(1,13)=4.88$, $p<0.05$ for attack; $F(1,13)=5.95$, $p<0.05$ for kill. There were no significant interactions between drug treatment and trial. Most mice were killed within the 30 min trial. After saline injections 99.5% of the 190 mice were killed. After *l*-tryptophan injections, 100% of the mice were killed at the lowest 25 mg/kg dose, 87% of the mice were killed at the 50 mg/kg dose, and 86% were killed at the 100 mg/kg dose. Sniff latencies were not affected by any dose of *l*-tryptophan.

TABLE 3

OPEN FIELD ACTIVITY AND ROTAROD TESTS AFTER L-TRYPTOPHAN INJECTIONS

	Saline	L-tryptophan 100 mg/kg
Rotarod task (sec on rod)	40 ± 13	39 ± 11
Open field (squares crossed in 5 min)	87 ± 18	58 ± 15*

*$p<0.05$ as compared to saline. Entries are means ± SEM's.

Ingestive Behaviors

L-tryptophan, at 50 and 100 mg/kg, significantly decreased food intake in 24-hr food deprived rats (Table 2). This was shown in a significant interaction between drug treatment and time period of testing, $F(6,66)=3.36$, $p<0.01$. A Dunnett's test showed that during the first two 30-min test periods, eating was reliably reduced when rats received 100 mg/kg of *l*-tryptophan, as compared to saline conditions. During the second hr of testing feeding was reliably reduced by 50 mg/kg *l*-tryptophan. Water intake was not affected by *l*-tryptophan injections (Table 2).

Locomotor Activity

Injections of *l*-tryptophan which significantly inhibited mouse killing behavior did not affect the rats' ability to locomote on rotating rod (Table 3). Rats injected with saline remained on the rod an average of 40 sec (SEM=13) and those injected with *l*-tryptophan (100 mg/kg) stayed on the rod an average of 39 sec (SEM=11).

However, when injected with *l*-tryptophan, rats showed reduced spontaneous activity in the open field (Table 3). When treated with 100 mg *l*-tryptophan/kg rats crossed an average of 33% fewer squares than when injected with saline,

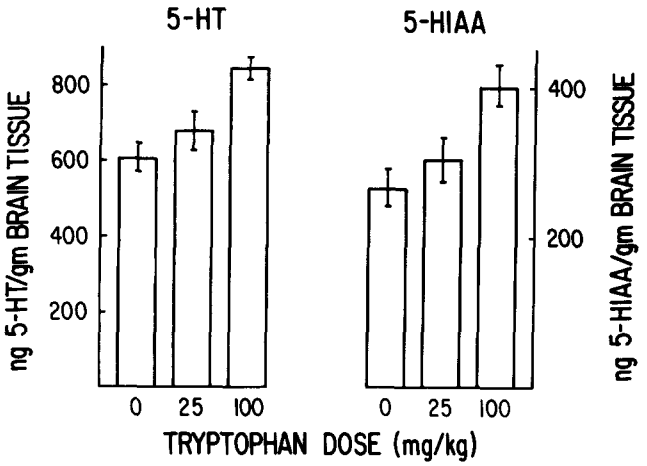

FIG. 2. Whole brain serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels following injection of *L*-tryptophan. Only at the higher dose of tryptophan (100 mg/kg) were levels significantly increased above saline controls.

$F(1,9)=9.03$, $p<0.05$. There was also a significant change over the five min of testing, $F(4,36)=7.81$, $p<0.05$, with activity decreasing over time for both drug and saline conditions.

Brain Serotonin and 5-HIAA

Significant increases of brain serotonin (38%) and 5-HIAA (49%) were demonstrated after injections of 100 mg/kg *l*-tryptophan, but not after injections of 25 mg/kg *l*-tryptophan (Fig. 2). The serotonin values were significantly different among the groups, $F(2,16)=9.26$, $p<0.01$, but Dunnett's *a posteriori* comparison showed that only the group which received 100 mg/kg *l*-tryptophan differed significantly from controls, $p<0.05$. Similarly, 5-HIAA significantly differed among the treatment groups, $F(2,16)=5.20$, $p<0.05$, and a subsequent comparison by Dunnett's test showed that only the group which received 100 mg/kg *l*-tryptophan had higher 5-HIAA levels, $p<0.05$.

DISCUSSION

Thus, in the present study, injections of *l*-tryptophan, the amino acid precursor of serotonin, inhibited mouse killing behavior in rats by selectively lengthening latencies to attack and kill mice. This result agrees with a preliminary report [8] showing tryptophan inhibits mouse killing and is consistent with other studies showing similar effects after injections of quipazine, a serotonin receptor agonist [33] and 5-HTP, the immediate precursor of serotonin [21].

Concomitant with the decreased mouse killing were increases in brain serotonin and 5-HIAA. At the lower 25 mg/kg dose of *l*-tryptophan neither mouse killing latencies nor brain amine levels were changed. At the higher 100 mg/kg dose, brain serotonin and 5-HIAA levels were significantly increased and mouse attacking and killing inhibited. Increases in brain 5-HT and 5-HIAA after *l*-tryptophan injections have been reported previously by a number of investigators [12, 24, 36], and the magnitude of the present increases corresponds to these previous studies.

The correlation between the biogenic amine changes and mouse killing behavior supports the hypothesis of neurons using 5-HT as a transmitter being important in the inhibitory control of killing [3,19]. The hypothesis is also supported by previous studies showing increased killing after reduction of 5-HT functioning, for example, after neurotoxic or electrolytic lesions of raphe nuclei [7,31], maintenance on a tryptophan-free diet [17,18] or inhibition of 5-HT synthesis [16, 27, 34].

In the present study, *l*-tryptophan had a small but significant effect on food intake. During the first hour of testing after injection of 100 mg/kg *l*-tryptophan, food intake was reduced by 28%; during the second hour of testing after injection of a lower dose, 50 mg/kg, intake was reduced by 31% as compared to saline control trials. Reduced food intake after tryptophan injection was noted previously by Fernstrom and Wurtman [12], contrary to the negative finding of Weinberger *et al.* [36]. An additional report on tryptophan and food intake is that of Barrett and McSharry [4] who observed a synergistic action of a relatively low tryptophan dose (25 mg/kg), injected in combination with a monoamine oxidase inhibitor, in producing feeding suppression. This was associated with increased brain 5-HT levels. 5-Hydroxytryptophan, when injected IP or directly into the hypothalamus, has also been shown to suppress feeding behavior [6,23]. These data support the hypothesized role of brain serotonin in the suppression of food consumption (see [5,22] for reviews).

The further possibility that serotonin may be related to specific dietary preferences is suggested by the studies of Ashley and Anderson [2] and Wurtman and Wurtman [37]. However, in the present study only a high protein chow was offered and so selective preferences could not be discerned.

Mouse killing is believed to be a form of predatory aggression [29,30]; it has a complex relation to feeding [32]. The suppression of both feeding and mouse killing by *l*-tryptophan might suggest that the effects on killing were simply secondary to those on feeding; an anorectic rat might not be motivated to kill. Although this interpretation of the present results is plausible, it should be noted that other manipulations which reduce feeding, such as pilocarpine injections or maintenance on a tryptophan-free diet, can increase mouse killing behavior [14,18].

In general, injections of *l*-tryptophan have little or no effect on locomotor activity ([15] and review by Messing *et al.* [26]). The present results are consistent with these findings in that locomotion on a rotating rod was not affected by 100 mg/kg *l*-tryptophan. Spontaneous locomotion in the open field was, however, reduced by one-third after tryptophan injections. These differences are likely to be due to the difference in underlying mechanisms tapped by the two procedures. After injections of *l*-tryptophan rats may have the capacity to locomote normally, but may not be motivated to do so in an open field.

Parenteral injections of any drug including *l*-tryptophan might be expected to have a variety of physiological effects, both in the brain and the periphery. Moreover, even tryptophan's effects on brain serotonin might be expected to cause several behavioral changes since central 5-HT systems are widespread and have been linked not only to mouse killing [3,19] and to feeding [5] but to sleep [28], reduced pain sensitivity [25] and sexual behavior (e.g. [26]) as well. It has been suggested that these central 5-HT systems as a whole serve a general inhibitory function [9] mediating the "trophotropic" system of behavioral suppression and reduced responsiveness. However, the present studies do not provide total support for that hypothesis. In these studies

injections of *l*-tryptophan which increased brain 5-HT and 5-HIAA did not significantly change latencies to sniff mice, amount of water consumption in food deprived rats, nor ability to locomote on a rotarod. Thus, although stimulating the neural systems using 5-HT as a transmitter often results in behavioral suppression, there are important exceptions [26]. Moreover, techniques which differentiate separate parts of the 5-HT system have often shown that the subsystems have different functions [15,35]. Further studies will elucidate these more clearly, but among those functions are likely to be inhibitory control of mouse killing and feeding behavior.

ACKNOWLEDGEMENTS

This research is based in part on a dissertation submitted to Carnegie-Mellon University by Judith L. Gibbons, in partial fulfillment of the requirements of the Ph.D. degree. A preliminary report of these data was presented at the 6th annual meeting of the Society for Neuroscience, Toronto, 1976 [17]. We are grateful to Dr. Nansie S. Sharpless for developing the procedures for measuring serotonin and 5-HIAA, to Gregg Tyler Schimmel for assistance in behavioral testing, to Mark Muehlbach and Earnestine Benford for editorial assistance and to Doris Winter for preparation of the manuscript. This investigation was supported in part by training grants MH 06418 and 1 T32 MH 15174-01 from the National Institute of Mental Health (J. L. G. and G. A. B.), a Sigma Xi Grant-in-Aid (J. L. G.), an NIH Biomedical Research Support Grant (G. A. B.), an NIH Research Grant MH22879 (S. F. L.), an Alfred P. Sloan fellowship (S. F. L.) and funds from the Whitehall Foundation (S. F. L.).

REFERENCES

1. Aghajanian, G. K. and I. M. Asher. Histochemical fluorescence of raphe neurons: selective enhancement by tryptophan. *Science* **172:** 1159–1161, 1971.
2. Ashley, D. V. M. and G. H. Anderson. Correlation between plasma tryptophan to neutral amino acid ratio and protein intake in the self-selecting weanling rat. *J. Nutr.* **105:** 1412–1421, 1975.
3. Barr, G. A., J. L. Gibbons and W. H. Bridger. Neuropharmacological regulation of mouse killing by rats. *Behav. Biol.* **17:** 134–159, 1976.
4. Barrett, A. M. and L. McSharry. Inhibition of drug-induced anorexia in rats by methysergide. *J. Pharm. Pharmac.* **27:** 889–895, 1975.
5. Blundell, J. E. Is there a role for serotonin (5-hydroxytryptamine) in feeding? *Int. J. Obesity* **1:** 15–42, 1977.
6. Blundell, J. E. and M. B. Leshem. The effect of 5-hydroxytryptophan on food intake and on anorexic action of amphetamine and fenfluramine. *J. Pharm. Pharmac.* **27:** 31–37, 1975.
7. Breese, G. R., B. R. Cooper, L. D. Grant and R. D. Smith. Biochemical and behavioral alterations following 5,6-dihydroxytryptamine administration into brain. *Neuropharmacology* **13:** 177–187, 1974.
8. Broderick, P., I. Sanghvi, V. Lynch and P. Cervoni. Antagonism of muricidal behavior in rats by lithium and tryptophan. *Pharmacologist* **20:** 171, 1978.
9. Brodie, B. B. and P. A. Shore. A concept for a role of serotonin and norepinephrine as chemical mediators in the brain. *Ann. N.Y. Acad. Sci.* **66:** 631–642, 1957.
10. Curzon, G. and A. R. Green. Determination of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in small regions of rat brain. *Br. J. Pharmac.* **39:** 653–655, 1970.
11. Dunham, N. W. and T. S. Miya. A note on a simple apparatus for detecting neurological deficits in rats and mice. *J. Pharm. Sci.* **46:** 208–209, 1957.
12. Fernstrom, J. D. and R. J. Wurtman. Brain serotonin content: physiological regulation by plasma neutral amino acids. *Science* **178:** 414–416, 1972.
13. Fuxe, J., L. L. Butcher and J. Engel. DL-5-hydroxytryptophan-induced changes in central monoamine neurons after peripheral decarboxylase inhibition. *J. Pharm. Pharmac.* **23:** 420–424, 1971.
14. Gay, P. E., R. C. Leaf and F. B. Arble. Inhibitory effects of pre- and posttest drugs on mouse killing by rats. *Pharmac. Biochem. Behav.* **3:** 33–45, 1975.
15. Geyer, M. A., A. Puerto, D. B. Menkes, D. S. Segal and A. T. Mandell. Behavioral studies following lesions of the mesolimbic and mesostriatal serotonergic pathways. *Brain Res.* **106:** 257–270, 1976.
16. Gibbons, J. L., G. A. Barr, W. H. Bridger and S. F. Leibowitz. Effects of para-chlorophenylalanine and 5-hydroxytryptophan on mouse killing behavior in killer rats. *Pharmac. Biochem. Behav.* **9:** 91–98, 1978.
17. Gibbons, J. L., G. A. Barr, W. H. Bridger and S. F. Leibowitz. Effects of PCPA, tryptophan, and a tryptophan free diet on mouse killing behavior of rats. *Soc. Neurosci. Abstr.* **2:** 465, 1976.
18. Gibbons, J. L., G. A. Barr, W. H. Bridger and S. F. Leibowitz. Manipulations of dietary tryptophan: Effects on mouse killing and brain serotonin in the rat. *Brain Res.* **169:** 139–153, 1979.
19. Katz, R. J. Role of serotonergic mechanisms in animal models of predation. *Prog. Neuropsychopharmac.*, in press, 1981.
20. Kirk, R. E. *Experimental Design: Procedures for the Behavioral Sciences.* Belmont, CA: Brooks/Cole, 1968.
21. Kulkarni, A. S. Muricidal block produced by 5-hydroxytryptophan and various drugs. *Life Sci.* **7:** 125–128, 1968.
22. Leibowitz, S. F. Neurochemical systems of the hypothalamus in control of feeding and drinking behavior and water-electrolyte excretion. In: *Handbook of the Hypothalamus,* Vol. 3, edited by P. J. Morgane and J. Panksepp. New York: Marcel Dekker, 1979.
23. Leibowitz, S. F. and P. J. Papadakos. Serotonin-norepinephrine interaction in paraventricular nucleus: antagonistic effects on feeding behavior in the rat. *Soc. Neurosci. Abstr.* **4:** 542, 1978.
24. Marsden, C. A. and G. Curzon. Studies on the behavioral effects of tryptophan and *p*-chlorophenylalanine. *Neuropharmacology* **15:** 165–171, 1976.
25. Messing, R. B. and L. D. Lytle. Serotonin-containing neurons: their role in pain and analgesia. *Pain* **4:** 1–26, 1977.
26. Messing, R. B., D. J. Pettibone, N. Kaufman and L. D. Lytle. Behavioral effects of serotonin neurotoxins: An overview. *Ann. N.Y. Acad. Sci.* **305:** 480–496, 1978.
27. Miczek, K. A., J. L. Altman, J. B. Appel and W. V. Boggan. Para-chlorophenylalanine, serotonin, and killing behavior. *Pharmac. Biochem. Behav.* **3:** 355–362, 1975.

28. Morgane, P. J. and W. C. Stern. Chemical anatomy of brain circuits in relation to sleep and wakefulness. In: *Advances in Sleep Research*, Vol. 1, edited by E. Weitzman. New York: Spectrum Publications, 1974.
29. Moyer, K. E. Kinds of aggression and their physiological basis. *Commun. Behav. Biol.* **2:** 65–87, 1968.
30. O'Boyle, M. Rats and mice together: The predatory nature of the rat's mouse killing response. *Psychol. Bull.* **81:** 261–269, 1974.
31. Paxinos, G. and D. M. Altrens. 5-7-Dihydroxytryptamine lesions: effects on body weight, irritability, and muricide. *Aggress. Behav.* **3:** 107–118, 1977.
32. Polsky, R. H. Hunger, prey feeding, and predatory aggression. *Behav. Biol.* **13:** 81–93, 1975.
33. Rodriguez, R. and E. G. Pardo. Quipazine, a new type of antidepressant agent. *Psychopharmacologia* **21:** 89–100, 1971.
34. Sheard, M. H. The effect of p-chlorophenylalanine on behavior in rats: Relation to brain serotonin and 5-hydroxyindoleacetic acid. *Brain Res.* **15:** 524–528, 1969.
35. Waldbillig, R. J. The role of the dorsal and median raphe in the inhibition of muricide. *Brain Res.* **160:** 341–346, 1979.
36. Weinberger, S. B., S. Knapp and A. J. Mandell. Failure of tryptophan load-induced increases in brain serotonin to alter food intake in the rat. *Life Sci.* **2:** 1595–1602, 1978.
37. Wurtman, J. J. and R. J. Wurtman. Fenfluramine and fluoxetine spare protein consumption while suppressing calorie intake by rats. *Science* **190:** 1178–1180, 1977.