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Tonic Immobility in Domestic Fowl: Anticataleptic Effects of Quipazine[1]

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WALLNAU, L. B. *Tonic immobility in domestic fowl: Anticataleptic effects of quipazine.* PHARMAC. BIOCHEM. BEHAV. 12(3)347–352, 1980.—Quipazine, a putative serotonergic agonist, produced marked decreases in tonic immobility (TI) duration in doses of 5–25 mg/kg. Quipazine-treated animals required more elicitation attempts before displaying TI. Quipazine also blocked the haloperidol enhancement of tonic immobility. In a third experiment, quipazine produced stereotyped responses in chickens which yielded increases in activity on a stabilimeter platform. The results are discussed in terms of catalepsy and serotonergic and dopaminergic mechanisms.

Tonic immobility Catalepsy Stereotypy Activity Quipazine Haloperidol
Serotonergic system Dopaminergic system Raphe model Chickens

TONIC immobility (TI) is a cataleptic-like state that is elicited by a brief period of physical restraint. In the laboratory, under conditions of manual restraint, the animal initially struggles. These apparent escape attempts are short-lived and are followed by a motionless, often rigid posture which persists in absence of additional restraint. In domestic fowl, the response may last from a few seconds to over an hour and is characterized by tremors of the extremities, waxy flexibility, rigidity, decreased vocalization, eye closure, mydriasis, changes in heart and respiration rates, and decreased core temperature [16,17]. The response terminates abruptly and is often followed by escape and defensive reactions [16,17].

A serotonergic mechanism appears to be involved in tonic immobility [41]. Specifically, drugs which are known to directly inhibit central serotonergic neurons of the midbrain raphe nuclei (e.g., tryptophan, LSD, pargyline) in mammals [1–5], have been observed to enhance TI duration in avians [9, 18, 31]. Conversely, drugs (e.g., amphetamine) which activate raphe firing [15] produce short durations [8]. Wallnau and Gallup [41] have proposed a predictive framework for drug effects on TI, such that agents which either inhibit or activate raphe firing predict enhanced and abbreviated TI durations, respectively.

Serotonin (5-HT) and dopamine (DA) systems are known to interact for a number of behavioral phenomena including catalepsy [12, 22, 28]. These findings are consistent with anatomical data that demonstrate both 5-HT and DA input to mammalian striatal structures [7, 14, 29]. Similarly, homologous striatal areas in the avian brain (e.g., the nucleus basalis and paleostriatum augmentatum) contain high concentrations of 5-HT and DA [26, 27, 37, 39]. Thus it is not surprising, in light of serotonergic and dopaminergic participation in catelepsy [12, 22, 28] and the possible existence of parallel 5-HT and DA input to what appears to be the avian striatal system, that a recent finding implicates the involvement of a DA system in tonic immobility [40]. Haloperidol, a DA receptor antagonist, produced a marked increment in TI duration in doses of 1 and 2 mg/kg. On the other hand, apomorphine, a DA receptor agonist, attenuated immobility in doses ranging from 0.5 to 2 mg/kg and elevated locomotor activity and pecking, lending support to a competing response interpretation [40].

A number of investigations have reported that quipazine, a putative 5-HT receptor agonist [23,38], produces stereotyped behavior [13, 19, 21, 30], elevated locomotor activity [19,21], and also has anticataleptic effects [13,19]. With regards to the latter effect, it has been observed that quipazine blocks neuroleptic-induced catalepsy [13,19]. In order to assess the anticataleptic action of quipazine as well as possible 5-HT and DA interactions, the effects of quipazine and haloperidol on TI duration were examined. A third experiment examined the hyperactivity and stereotypy components of quipazine action on young avians.

EXPERIMENT 1

Quipazine, a putative 5-HT agonist, diminishes catalepsy in rats [13,19]. Since TI bears a striking resemblance to cataleptic states [17] and a serotonergic mechanism appears to participate in the response [41], the first experiment

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examined the effectiveness of varying doses of quipazine in reducing the duration and likelihood of tonic imobility.

METHOD

Animals

Thirty-six straight-run Production Red chickens were obtained one day after hatch from a commercial hatchery (Welp Inc.). The animals were group housed in heated brooders and maintained on a diet of Purina chick chow. Food and water were available continuously. Artificial illumination was provided in a daily photoperiod from 8 a.m. to 10 p.m. In order to prevent an attenuation of TI by familiarization and habituation to humans [35], exposure to humans was restricted to brief periods for routine daily care.

Procedure

At 21 days of age, animals were randomly assigned to groups that received doses of 5, 10, or 25 mg/kg IP of quipazine maleate (Miles Laboratories). A fourth group received an equivalent volume (2 ml/kg) of distilled water which served as the vehicle. Following injection, each animal was placed in an individual holding box. Fifteen minutes following injection, each animal was transported in its holding box to a room and individually tested for tonic immobility. TI was elicited by manually restraining the animal on its right side on a table for 15 sec. The duration of immobility was timed by a stop-watch from the moment the animal was released until it successfully righted itself. If the initial induction attempt did not elicit the response, and animal was returned to the holding box for 60 sec and subsequently restrained again. This procedure was repeated until an animal exhibited TI or five unsuccessful induction attempts were made. Subjects that failed to display immobility after the fifth elicitation attempt were given duration scores of zero seconds. All testing was conducted between 10 a.m. and 4 p.m., with each group equally represented across time of day. Persons collecting data were kept uninformed of group designations.

RESULTS

Table 1 summarizes the results of the first experiment. A square-root transformation was performed on the duration data to alleviate skew and minimize heterogeneity of variance. Analysis of variance revealed an overall effect for dose, $F(3,32)=6.66$, $p<0.005$. An analysis of the trend components revealed significant linear, $F(1,32)=14.68$, $p<0.001$, and quadratic effects, $F(1,32)=5.28$, $p<0.05$. The nature of these trends were clarified by multiple post hoc comparisons using a Newman-Keuls test. The 5 mg/kg group differed from the vehicle control group ($p<0.05$) as did the two remaining drug groups ($p<0.01$). However, there were no differences among the three groups receiving quipazine. Thus all doses of quipazine were effective in reducing TI duration.

For the number of inductions required to elicit TI, analysis of variance was precluded because the control group showed no variability. All animals in this group displayed TI on the first induction attempt. Out of nine subjects each in the 0, 5, 10 and 25 mg/kg groups, 0, 6, 4 and 8 birds respectively, scored above the median (1.5) on inductions. A median test yielded a significant effect for dose, $\chi^2(3)=15.56$, $p<0.01$, indicating that quipazine birds required more induction attempts.

TABLE 1

THE EFFECT OF QUIPAZINE ON TONIC IMMOBILITY DURATION (SEC)

	Dose (mg/kg, IP)			
	0	5	10	25
Mean	761.22	393.00	96.67	20.22
Standard error	258.24	228.72	66.17	12.69

EXPERIMENT 2

Recent findings suggest dopaminergic participation in TI. Dopamine receptor blockade by haloperidol produced long TI durations and apomorphine, a DA receptor agonist, attenuated the response [40]. Quipazine, which abbreviated TI in Experiment 1, attenuates neuroleptic-induced catalepsy in rats [13,19]. In Experiment 2 an attempt was made to block the haloperidol enhancement of TI with quipazine.

METHOD

Animals

Thirty-two straight-run Production Red chickens were housed and maintained as described in Experiment 1.

Procedure

Previous investigations have found that stressful and aversive events that occur in close temporal proximity to TI elicitation will enhance response duration as a function of their intensity [16,34]. Thus, consistent with the possibility that a single injection can be mildly aversive, when two injections are administered shortly before TI induction the durations of TI for the double-injected controls are sometimes elevated [42]. In order to obviate the double-injection effect, which might otherwise mask the effects of other treatments, solutions were prepared so that each animal would receive only one injection. At 19 days of age each animal received an injection (IP) of either the vehicle, 2 mg/kg of haloperidol (McNeil Laboratories), 25 mg/kg of quipazine, or a solution containing both haloperidol and quipazine. Thus the design was essentially a 2×2 factorial employing haloperidol—no haloperidol and quipazine—no quipazine conditions. The vehicle for all injections contained 0.002 ml of warm lactic acid (USP) per ml of distilled water. All injection volumes were 1.6 ml/kg. Testing was conducted as described in Experiment 1. While previous findings revealed that haloperidol had optimal effects 30 min following administration [40], pilot data with the present colony of birds found that a 15 min injection-test interval was sufficient to produce the haloperidol enhancement.

RESULTS

Table 2 depicts the results. Due to heterogeneity of variance, a square-root transformation was performed on duration data. Analysis of variance yielded main effects for the

TABLE 2

THE EFFECTS OF QUIPAZINE (25 mg/kg, IP) AND HALOPERIDOL (2 mg/kg, IP) ON TONIC IMMOBILITY DURATION (SEC)

	Drug condition			
	Vehicle	Haloperidol	Quipazine	Quipazine/ haloperidol
Mean	614.25	1840.63	66.88	46.13
Standard error	211.75	390.53	35.04	18.16

TABLE 3

THE EFFECT OF QUIPAZINE ON THE NUMBER OF INDUCTION ATTEMPTS REQUIRED TO ELICIT TONIC IMMOBILITY

	Dose (mg/kg, IP)			
	0	10	25	50
Mean	1.2	2.4	4.4	4.6
Standard error	0.13	0.58	0.40	0.40

haloperidol condition, $F(1,28)=7.27$, $p<0.02$, and the quipazine condition, $F(1,28)=44.08$, $p<0.001$, which replicates previous findings ([40], Experiment 1). In addition there was an interaction for the two drug conditions, $F(1,28)=6.25$, $p<0.02$. Simple effects analyses elucidated the nature of this interaction. Birds in the haloperidol—no quipazine group showed longer reactions than animals receiving the vehicle, $F(1,28)=13.51$, $p<0.001$, but there was no difference between the no haloperidol—quipazine and haloperidol—quipazine groups, $F<1$. Thus while haloperidol enhanced TI for animals that did not receive quipazine, animals that received both haloperidol and quipazine had short durations like those that were injected with only quipazine.

In contrast to the first experiment, there were no effects for the number of inductions required to elicit TI. Thus in an attempt to replicate the effect of quipazine on number of inductions, 40 additional birds received either 0, 10, 25 or 50 mg/kg IP of quipazine in a distilled water vehicle at injection volumes of 5 ml/kg. The animals were tested for TI as described in the first experiment, but only the number of inductions required to elicit TI were recorded. Table 3 depicts the results. Analysis of variance indicated that quipazine animals required more elicitation attempts to display TI, $F(3,36)=15.85$, $p<0.001$, and the linear, $F(1,36)=38.66$, $p<0.001$, and quadratic, $F(1,36)=8.19$, $p<0.01$, components for dose were significant. Multiple comparisons by Newman-Keuls test revealed that birds in the 25 mg/kg and 50 mg/kg groups did not differ, but both groups did require more induction attempts than the 10 mg/kg ($p<0.01$) and control ($p<0.01$) groups. In addition, animals in the 10 mg/kg group differed from controls ($p<0.05$). Thus all doses of quipazine made animals more resistant to TI elicitation with optimal effects occurring at the higher doses.

EXPERIMENT 3

Informal observations of quipazine-injected animals following testing in the preceding experiments indicated that quipazine produced hyperactivity and stereotyped behavior. Animals intermittently displayed a squatting posture in which the head was held back and beak gaped. Wing abduction commonly accompanied this posture. Between the brief periods that this posture was exhibited, animals stood erect and frequently shifted weight alternately on each foot in a swaying motion. Along with this behavior, animals would occasionally lurch and dart forward with an apparent loss of balance. Although hyperactivity and stereotypy have been observed in quipazine-treated rats [13, 19, 21, 30], the effects are not analagous to those of dopaminergic agonists [13]. There appears to be qualitative differences for avians as well. Unlike chickens injected with quipazine, apomorphine-treated birds display loud chirping, intense bouts of pecking, crouching which usually precedes flight, and increased locomotion [11, 36, 40]. It has been suggested that apomorphine may reduce TI because the behavioral effects of the drug involve responses which would compete with or otherwise disrupt an immobile state [40]. Since the behavioral effects of quipazine were so pronounced, and a competing response interpretation might apply for quipazine as well, Experiment 3 assessed the effect of quipazine on overall activity using a stabilimeter.

METHOD

Animals

Sixteen straight-run Production Red chickens were housed and maintained as reported in the first experiment.

Apparatus

A Lafayette Instruments activity platform (model 86010) was used to assess general activity. The platform was equipped with an enclosure (30×30×30 cm) for containing the animals and was housed in a sound attenuated chamber. The gain control of the activity platform was adjusted to a setting of five and the activity switch was set on "slow". These settings would reliably register counts when animals shifted weight from foot to foot, pecked the enclosure, or walked. Activity counts were automatically tallied by electromechanical apparatus.

Procedure

At 26 days of age, subjects were matched for weight and half of the matched pairs received 25 mg/kg IP of quipazine while the remaining animals received an equivalent volume (2 ml/kg) of the distilled water vehicle. Animals were placed in holding boxes for 10 min prior to testing. At test time animals were placed individually in the platform enclosure. Activity counts were recorded for 5 two-min blocks of time. The platform was cleaned following the removal of each subject. Observers viewed the animals through a small window in the chamber and took informal notes.

RESULTS

Figure 1 illustrates the results. Analysis of variance revealed that animals receiving quipazine displayed more activity than vehicle-injected birds, $F(1,14)=32.50$, $p<0.001$, and activity increased across time blocks, $F(4,56)=10.67$, $p<0.001$. The drug condition interacted with time, $F(4,56)=5.39$, $p<0.001$, and this interaction was decomposed into trend components. Specifically there was a sig-

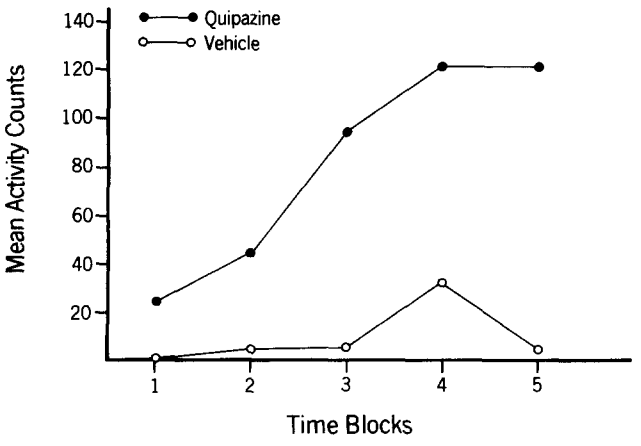

FIG. 1. The effect of quipazine (25 mg/kg, IP) on activity as a function of blocks (2 min each) of time.

nificant drug × time linear interaction, $F(1,14)=22.62$, $p<0.001$, reflecting the monotonic increase in activity across time for the quipazine-treated birds and relatively little change for animals in the control group. Informal observations indicated that activity recorded by the apparatus for quipazine-injected animals consisted primarily of the stereotyped swaying behavior, and short periods of lurching and darting forward. All but one of the quipazine birds exhibited the swaying and weight shift pattern, and all subjects in this group displayed the squatting posture accompanied by wing abduction. In contrast, recorded activity of the vehicle subjects primarily involved occasional locomotion and flight.

DISCUSSION

Quipazine has been observed to reduce neuroleptic-induced catalepsy [13,19]. Consistent with these data, and the apparent DA participation in TI [40], quipazine reduced TI duration, made animals more difficult to immobilize, and blocked the haloperidol enhancement of tonic immobility. It has been reported that quipazine, in addition to having serotonergic action, inhibits DA uptake in rat striatal tissue *in vitro* [32]. In agreement with this finding and the apomorphine attenuation of TI [40], one might interpret the quipazine reduction of immobility in terms of its putative activation of a DA mechanism. However, the results and observations of Experiments 2 and 3 are inconsistent with a DA interpretation of the quipazine effect. If quipazine reduced TI by activating the DA system through reuptake inhibition, then haloperidol should have blocked the quipazine reduction of TI duration. In contrast, examination of the interaction of drug conditions revealed that quipazine blocked the haloperidol potentiation of immobility, with quipazine—haloperidol animals displaying low durations comparable to those of animals that received only quipazine.

Quipazine has also been observed to produce stereotyped behavior in rats [19,21], suggesting DA receptor activation, however these behavioral effects do not appear to be analogous to those elicited by DA receptor agonists such as apomorphine [13]. Similarly, quipazine produced stereotyped behavior and elevated activity in chickens (Experiment 3), but it was noted that these behaviors differed *qualitatively* from those exhibited in young avians following apomorphine administration [11, 36, 40]. This observation suggests that quipazine does not primarily interact with DA receptors in avians. In fact, the behavioral effects of quipazine observed in Experiment 3 closely resemble those reported for avians following activation of serotonergic mechanisms [9,24].

To the extent that quipazine primarily activates, either directly or indirectly, 5-HT receptors [10, 23, 30, 38], the results of Experiment 2 suggest a possible serotonergic-dopaminergic interaction in the modulation of TI duration. Previous studies have indicated that 5-HT and DA participate in neuroleptic-induced catalepsy. For example, 5-HT depletion by *p*-chlorophenylalanine or midbrain raphe lesions blocks haloperidol-induced catalepsy [12, 22, 28]. Also pretreatment with LSD, which is known to inhibit activity of raphe neurons [2,4], reduces neuroleptic-induced catalepsy [22]. Thus catalepsy produced by neuroleptics such as haloperidol may depend in part on the functional integrity of the 5-HT system. A putative serotonergic-dopaminergic interaction for TI is also consistent with anatomical data in avians in that areas of the avian brain thought to have striatal function have high concentrations of 5-HT and DA [26, 27, 37, 39]. Additional work is necessary to determine the exact role of these structures for TI.

It is difficult to interpret the quipazine reduction of TI in terms of a previously proposed midbrain-raphe model [41]. Since quipazine is a putative 5-HT receptor agonist, one might predict that it would reduce impulse flow of 5-HT neurons (e.g., [25]) perhaps via autoreceptors or indirectly via collaterals, and thus increase TI [41] in contrast to the marked reduction that actually was observed. However, preliminary findings have failed to demonstrate an effect of quipazine on raphe firing rate [10]. It is interesting that recent work has found that combined administration of tryptophan and the MAO inhibitor pargyline produces short durations of TI [9], while separately these drug manipulations inhibit raphe activity [1, 3, 5] and enhance TI duration [9, 18, 31]. The quipazine reduction of TI also parallels the combined effect of tryptophan and MAO inhibition in that both treatments produce a hyperactivity syndrome consisting of stereotyped behaviors and postural effects in both mammals and avians [9, 20, 21, 24]. Quipazine effects may resemble those of combined 5-HT manipulations due to the multiple effects quipazine may have on the serotonergic system. That is, quipazine may inhibit monoamine oxidase [21], block 5-HT reuptake [25], or promote 5-HT release [30] in addition to directly stimulating 5-HT receptors [23,38].

Aghajanian and Wang [6] have suggested a dissociation between drug effects on raphe firing and postsynaptic consequences of these manipulations. For example, drugs that produce a direct inhibition of raphe would presumably reduce 5-HT transmission and as a result release postsynaptic neurons from tonic inhibition. On the other hand, a drug that facilitates 5-HT transmission in addition to inhibiting raphe firing would have the opposite postsynaptic effect. With this proposal in mind, it has been suggested [9] that tryptophan and MAO inhibitors, when administered separately may inhibit raphe firing directly or by collaterals intrinsic to raphe [6] and result in decreased 5-HT input to postsynaptic receptors. However, when tryptophan and MAO inhibition are combined, 5-HT may be elevated beyond its intraneuronal storage capacity and, as suggested by Grahame-Smith [20], "spill over" onto postsynaptic receptor sites. Thus while direct inhibition of raphe would reduce postsynaptic effects of 5-HT and increase TI duration, manipulations which facilitate synaptic transmission or postsynaptic effects of

5-HT (e.g., a "spill over" following combined tryptophan and pargyline administration) would reduce TI. Consistent with this interpretation are the findings that d-amphetamine [8] and peripherally administered 5-HT [31], which augment raphe activity [15,33] and presumably increase postsynaptic stimulation, and quipazine which may act directly on postsynaptic receptors [23,38], all reduce TI duration. Thus a reformulation of the midbrain-raphe model of TI should shift the emphasis from drug effects on raphe activity per se to the postsynaptic consequences of serotonergic manipulations.

NOTE ADDED IN PROOF

Consistent with a serotonergic interpretation of the quipazine effect, recent work has found that pretreatment with cinanserin (50 mg/kg IP, 60 min prior to quipazine), a putative 5-HT receptor blocker, prevented the quipazine reduction of TI and quipazine-induced stereotypy.

REFERENCES

1. Aghajanian, G. K. and H. J. Haigler. Direct and indirect actions of LSD, serotonin and related compounds on serotonin-
2. Aghajanian, G. K., W. E. Foote and M. H. Sheard. Lysergic acid diethylamide: Sensitive neuronal units in the midbrain raphe. *Science* **161:** 706–708, 1968.
3. Aghajanian, G. K., A. W. Graham and M. H. Sheard. Serotonin-containing neurons in brain: Depression of firing by monoamine oxidase inhibitors. *Science* **169:** 1100–1102, 1970.
4. Aghajanian, G. K. and J. H. Haigler. Direct and indirect actions of LSD, serotonin and related compounds on serotonin-containing neurons. In: *Serotonin and Behavior,* edited by J. Barchas and E. Usdin. New York: Academic Press, 1973, pp. 263–266.
5. Aghajanian, G. K. and H. J. Haigler. L-tryptophan as a selective histochemical marker for serotonergic neurons in single-cell recording studies. *Brain Res.* **81:** 364–372, 1974.
6. Aghajanian, G. K. and R. Y. Wang. Physiology and pharmacology of central serotonergic neurons. In: *Psychopharmacology: A Generation of Progress,* edited by M. A. Lipton, A. DiMascio and K. F. Killam. New York: Raven Press, 1978, pp. 171–183.
7. Andén, N. E., A. Carlsson, A. Dahlström, K. Fuxe, N. A. Hillarp and K. Larsson. Demonstration and mapping out of nigro-neostriatal dopamine neurones. *Life Sci.* **3:** 523–530, 1964.
8. Boren, J. L. and G. G. Gallup, Jr. Amphetamine attenuation of tonic immobility. *Physiol. Psychol.* **4:** 429–432, 1976.
9. Boren, J. L., G. G. Gallup, Jr., S. D. Suarez, L. B. Wallnau and G. J. Gagliardi. Pargyline and tryptophan enhancement of tonic immobility: Paradoxical attenuation with combined administration. *Pharmac. Biochem. Behav.* **11:** 17–22, 1979.
10. Briggs, I. Actions and interactions of iontophoretically applied quipazine and monoamines on brain stem neurones. *Expl Brain Res.* **23:** 28, 1975.
11. Cheng, H. C. and P. Long. Dopaminergic nature of apomorphine-induced pecking. *Eur. J. Pharmac.* **26:** 313–320, 1974.
12. Costall, B., D. H. Fortune, R. J. Naylor, C. D. Marsden and C. Pycock. Serotonergic involvement with neuroleptic catalepsy. *Neuropharmacology* **14:** 859–868, 1975.
13. Costal, B. and R. J. Naylor. The role of the raphe and extrapyramidal nuclei in the stereotyped and circling responses to quipazine. *J. Pharm. Pharmac.* **27:** 368–371, 1975.
14. Davies, J. and P. Tongroach. Neuropharmacological studies on the nigro-striatal and raphe-striatal system in the rat. *Eur. J. Pharmac.* **51:** 91–100, 1978.
15. Foote, W. E., M. H. Sheard and G. K. Aghajanian. Comparison of effects of LSD and amphetamine on midbrain raphe units. *Nature* **222:** 567–569, 1969.
16. Gallup, G. G., Jr. Animal hypnosis: Factual status of a fictional concept. *Psychol. Bull.* **81:** 836–853, 1974.
17. Gallup, G. G., Jr. and J. D. Maser. Tonic immobility: Evolutionary underpinnings of human catalepsy and catatonia. In: *Psychopathology: Experimental Models,* edited by J. D. Maser and M. E. P. Seligman. San Francisco: Freeman, 1977, pp. 334–357.
18. Gallup, G. G., Jr., L. B. Wallnau, J. L. Boren, G. J. Gagliardi, J. D. Maser and P. H. Edson. Tryptophan and tonic immobility: Effects of dietary and systemic manipulations. *J. comp. physiol. Psychol.* **91:** 642–648, 1977.
19. Grabowska, M., L. Antkiewicz and J. Michaluk. A possible interaction of quipazine with central dopamine structures. *J. Pharm. Pharmac.* **26:** 74–76, 1974.
20. Grahame-Smith, D. G. Studies *in vivo* on the relationship between brain tryptophan, brain 5-HT synthesis and hyperactivity in rats treated with a monoamine oxidase inhibitor and L-tryptophan. *J. Neurochem.* **18:** 1053–1066, 1971.
21. Green, A. R., M. B. H. Youdim and D. G. Grahame-Smith. Quipazine: Its effects on rat brain 5-hydroxytryptamine metabolism, monoamine oxidase activity and behaviour. *Neuropharmacology* **15:** 173–179, 1976.
22. Gumulka, W., W. Kostowski and A. Czlonkowski. Role of 5-HT in the action of some drugs affecting extrapyramidal system. *Pharmacology* **10:** 363–372, 1973.
23. Hong, E., L. F. Sancilio, R. Vargas and E. G. Pardo. Similarities between the pharmacological actions of quipazine and serotonin. *Eur. J. Pharmac.* **6:** 274–280, 1969.
24. Jacobs, B. L. An animal model for studying central serotonergic synapses. *Life Sci.* **19:** 777–786, 1976.
25. Jacoby, J. H., R. A. Howd, M. S. Levin and R. J. Wurtman. Mechanisms by which quipazine, a putative serotonin receptor agonist, alters brain 5-hydroxyindole metabolism. *Neuropharmacology* **15:** 529–534, 1976.
26. Juorio, A. V. and M. Vogt. Monoamines and their metabolites in the avian brain. *J. Physiol.* **189:** 489–518, 1967.
27. Karten, H. J. and J. L. Dubbeldam. The organization and projections of the paleostriatal complex in the pigeon (*Columba livia*). *J. comp. Neurol.* **148:** 61–90, 1973.
28. Kostowski, W., W. Gumulka and A. Czlonkowski. Reduced cataleptogenic effects of some neuroleptics in rats with lesioned midbrain raphe and treated with p-chlorophenylalanine. *Brain es.* **48:** 443–446, 1972.
29. Lorens, S. A. and H. C. Guldberg. Regional 5-hydroxytryptamine following selective midbrain raphe lesions in the rat. *Brain Res.* **78:** 45–56, 1974.
30. Malick, J. B., E. Doren and A. Barnett. Quipazine-induced head-twitch produced by serotonin receptor activation in mice. *Fedn Proc.* **34:** 801, 1975.
31. Maser, J. D., G. G. Gallup, Jr. and L. E. Hicks. Tonic immobility in chickens: Possible involvement of monoamines. *J. comp. physiol. Psychol.* **89:** 319–328, 1975.
32. Medon, P. J., J. L. Leeling and B. M. Phillips. Influence of quipazine, a potential anti-Parkinsonian agent on the uptake of ^{3}H-dopamine and ^{3}H-serotonin into rat striatal tissue *in vivo*. *Life Sci.* **13:** 685–691, 1973.
33. Mosko, S. and B. L. Jacobs. Effect of peripherally administered serotonin on the neuronal activity of midbrain raphe neurons. *Brain Res.* **79:** 315–320, 1974.

34. Nash, R. F. and G. G. Gallup, Jr. Effect of different parameters of shock on tonic immobility. *Behav. Meth. Res. Instrum.* **7:** 361–364, 1975.
35. Nash, R. F. and G. G. Gallup, Jr. Habituation and tonic immobility in domestic chickens. *J. comp. physiol. Psychol.* **90:** 870–876, 1976.
36. Osuide, G. and P. O. Adejoh. Effects of apomorphine and its interaction with other drugs in the domestic fowl. *Eur. J. Pharmac.* **23:** 56–66, 1973.
37. Pscheidt, G. R. and B. Haber. Regional distribution of dihydroxyphenylalanine and 5-hydroxytryptophan decarboxylase and of biogenic amines in the chicken central nervous system. *J. Neurochem.* **12:** 613–618, 1965.
38. Rodriguez, R., J. A. Rojas-Ramirez and R. R. Drucker-Colin Serotonin-like actions of quipazine on the central nervous system. *Eur. J. Pharmac.* **24:** 164–171, 1973.
39. Spooner, C. E. and W. D. Winters. Distribution of monoamines and regional uptake of DL-norepinephrine-7-H^3 and dopamine-l-H^3 in the avian brain. *Pharmacologist* **8:** 189, 1966.
40. Wallnau, L. B., C. L. Carnrike, Jr. and G. I. Dewey. Tonic immobility: Effects of dopamine receptor blockade and stimulation. *Pharmac. Biochem. Behav.* **10:** 177–181, 1979.
41. Wallnau, L. B. and G. G. Gallup, Jr. A serotonergic, midbrain-raphe model of tonic immobility. *Biobehav. Rev.* **1:** 35–43, 1977.
42. Wallnau, L. B. and G. G. Gallup, Jr. Morphine potentiation of tonic immobility: Effects of naloxone, PCPA, and 5,6-DHT. *Pharmac. Biochem. Behav.* **10:** 499–504, 1979.