*Pharmacology Biochemistry and Behavior*, Vol. 43, pp. 131–137, 1992
Printed in the U.S.A. 

0091-3057/92 $5.00 + .00


# 5-$HT_{1A}$ and 5-$HT_2$ Receptors Mediate Discrete Behaviors in the Mongolian Gerbil

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Received 4 October 1991

EISON, A. S. AND R. N. WRIGHT. *5-$HT_{1A}$ and 5-$HT_2$ receptors mediate discrete behaviors in the Mongolian gerbil.* PHARMACOL BIOCHEM BEHAV **43**(1) 131–137, 1992.—Although the ability of agonists at specific serotonin (5-HT) receptor subtypes to induce distinct behaviors has been well documented in the rat, similar studies have not been reported in the Mongolian gerbil. We have found that the 5-$HT_{1A}$/5-$HT_2$ agonist 5-methoxy,*N*-*N* dimethyltryptamine (5-MeODMT) (0.5–8 mg/kg, SC), the specific 5-$HT_{1A}$ agonist 8-hydroxy(di-*n*-propylamino)tetralin (8-OH-DPAT) (0.125–16 mg/kg, SC), and the 5-HT precursor L-5-hydroxytryptophan (L-5-HTP) (100–250 mg/kg, SC) all elicit a 5-HT syndrome in the gerbil. This syndrome, analogous to the 5-HT syndrome in the rat, consists of reciprocal forepaw treading (RFT), hindleg abduction (HA), body tremors (BT), and Straub tail (ST). The putative 5-$HT_{1A}$ antagonist NAN-190 (0.25–8 mg/kg, SC) when dosed 15 min prior to either 5-MeODMT (4 mg/kg, SC) or 8-OH-DPAT (16 mg/kg, SC) blocked both RFT and HA in a dose-dependent manner, suggesting these 5-HT syndrome behaviors are mediated via 5-$HT_{1A}$ receptor activation. We also identified a unique, dose-responsive behavior in the gerbil, induced selectively by 5-$HT_2$ agonists such as quipazine (2–16 mg/kg, SC) and (±)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) (0.125–8 mg/kg, SC). This reciprocal hindleg body scratch (RHBS) behavior is dose dependently inhibited by pretreatment with the selective 5-$HT_2$ antagonist ritanserin (0.0125–0.2 mg/kg, SC). RHBS behavior is also potently inhibited by pretreatment with the selective 5-$HT_{1A}$ agonist 8-OH-DPAT (0.005–0.04 mg/kg, SC), demonstrating a 5-$HT_{1A}$/5-$HT_2$ receptor subtype interaction. Simultaneous administration of the 5-$HT_2$ agonist DOI (1 mg/kg, SC) with 8-OH-DPAT (0.5 mg/kg, SC) significantly potentiated both RFT and BT behaviors of the 5-HT syndrome in gerbils, as has been reported in rats. Furthermore, pretreatment with the selective 5-$HT_2$ antagonist ritanserin (0.5 mg/kg, SC) resulted in nearly complete inhibition of the potentiation of RFT and BT by DOI and 8-OH-DPAT. Ritanserin pretreatment also shifted the dose–response curve for the 5-MeODMT-induced 5-HT syndrome to the right. These data suggest that 5-$HT_2$ receptor activation facilitates the expression of some 5-$HT_{1A}$ receptor-mediated behaviors of the 5-HT syndrome and may explain why 5-MeODMT has greater potency than 8-OH-DPAT in the gerbil.

5-$HT_{1A}$ receptors  5-$HT_2$ receptors  Serotonin syndrome  Mongolian gerbil  Reciprocal hindleg body scratch

SUBTYPES of the serotonin (5-HT) receptor have been described in the CNS and classified as being 5-$HT_1$-like, 5-$HT_2$, or 5-$HT_3$ (4). The 5-$HT_1$-like receptors have been further subdivided into 5-$HT_{1A}$, 5-$HT_{1B}$, 5-$HT_{1C}$, and 5-$HT_{1D}$ receptor subtypes [see Peroutka (18) for review]. In rodents, it has been possible to ascribe a number of behavioral responses to selective activation of these 5-HT receptor subtypes. For example, recent studies suggest that selective activation of 5-$HT_{1A}$ receptors in rats elicits the 5-HT behavioral syndrome (reciprocal forepaw treading, flat body posture, hindlimb abduction, lateral head weaving, Straub tail, tremor) (19) and lower-lip retraction (2), while 5-$HT_2$ receptor activation produces head-shakes (15) in rats and an ear-scratch response in mice (6).

Serotonin receptor subtype-mediated behavioral responses have been used to probe the "functional" status of these receptor subtypes and often parallel neurochemical or electrophysiological findings. Reduction in the frequency of head-shakes induced by 5-$HT_2$ agonists have been associated with decreased densities of central 5-$HT_2$ receptors (8). However, interesting species differences in 5-HT receptor subtype-mediated behaviors have been encountered. Administration of the selective 5-$HT_{1A}$ receptor agonist 8-hydroxy(di-*n*-propylamino)tetralin (8-OH-DPAT) results in the 5-HT syndrome in rats but produces head-shakes in pigs (14).

The behavioral consequences of selective activation of 5-HT receptor subtypes have not yet been fully described in the Mongolian gerbil. Examination of 5-HT-mediated behavioral responses in this species are of interest because: a) agents selective for 5-HT receptor subtypes such as the 5-$HT_2$ antagonist naftidofuryl and the 5-$HT_{1A}$ agonist 8-OH-DPAT exhibit a neuroprotective effect on ischemia-induced neuronal dam-

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age in the gerbil (3,9) and it would therefore be useful to determine the efficacy and specificity of serotonergic agents at 5-HT receptor subtypes in this species; and b) these investigations would expand upon our understanding of the behaviors induced by selective 5-HT receptor agonists and may provide insight into functionally relevant 5-HT receptor interactions.

While a preliminary report has described a behavioral response to the nonselective 5-$HT_{1A}$/5-$HT_2$ agonist 5-methoxy-*N,N*,dimethyl-tryptamine (5-MeODMT) in gerbils (5), we present an extensive characterization of 5-HT receptor subtype-mediated behavioral responses in this species, including an examination of 5-HT receptor subtype interactions.

## METHOD

### *Animals*

Male Mongolian gerbils (Tumblebrook Farm, West Brookfield, MA) weighing 40–60 g were used. Gerbils were group housed (eight per cage) and maintained on a 12L : 12D cycle in a temperature- and humidity-controlled room with food and water ad lib prior to testing.

### *Behavioral Observations*

Gerbils were first habituated to the test environment by placing them in individual clear Plexiglas chambers (34 × 28 × 17 cm) lined with woodshavings 30 min prior to treatment. Gerbils were injected with various doses of 5-$HT_{1A}$ receptor agonists: 8-OH-DPAT (0.125–16 mg/kg), buspirone (8–128 mg/kg), BMY 14802 (15–120 mg/kg), gepirone (8–128 mg/kg), 5-MeODMT (0.5–8 mg/kg), and L-5-hydroxytryptophan (L-5-HTP) (100–250 mg/kg) or saline (eight gerbils per group). Components of the 5-HT behavioral syndrome (reciprocal forepaw treading, hindleg abduction, body tremors, and Straub tail) were scored individually at 5-min intervals for 30 min beginning 5 min postinjection except L-5-HTP, which began 35 min postinjection. Each gerbil was rated on an intensity scale (0–3) based upon the method of Arnt and Hyttel (1) as absent (score 0), periodic (score 1), semicontinuous (score 2), or continuous (score 3), and scores were collected over the 30-min observation period. The total mean score (± SEM) for each treated group was subsequently calculated.

Immediately following administration of the 5-$HT_2$ agonists (±)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) (0.125–8 mg/kg) and quipazine (2–16 mg/kg), or saline, observations were then made to assess the frequency of the reciprocal hindleg body scratch response (RHBS). RHBS episodes were characterized as rapid scratching of the body with the hindlegs in a unilateral, alternating fashion. The RHBS response for each gerbil was scored for a 30-s period every 5 min for 30 min commencing 5 min postinjection. The total mean frequency (± SEM) for each treatment group over the 30-min observation period was calculated. In addition, animals were injected with the 5-$HT_{1B}$/5-$HT_{1C}$ agonist 1-(3-trifluoromethylphenyl)piperazine (TFMPP) (2–8 mg/kg) and the 5-$HT_{1B}$ agonist methoxy-3-(1,2,3,5-tetrahydropyridyl)indole succinate (RU 24969) (2–16 mg/kg) and observed for RHBS.

For drug antagonism studies, the 5-$HT_2$ antagonists ritanserin (0.0125–0.2 mg/kg) and emopamil (0.5–32 mg/kg) were injected 30 min prior to administration of DOI while the 5-$HT_{1A}$ agonists 8-OH-DPAT (0.0025–0.04 mg/kg) and gepirone (0.15–2.4 mg/kg) were injected 15 min prior to DOI. Similarly, the 5-$HT_{1A}$ antagonist 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine (NAN-190) (0.25–8 mg/kg) was administered 15 min prior to injection of 8-OH-DPAT (16 mg/kg) and 5-MeODMT (4 mg/kg). For drug interaction studies, doses of 8-OH-DPAT (0.25–4 mg/kg) were simultaneously coadministered with a dose of DOI (1.0 mg/kg). All pretreatment times and observation periods were based upon previous experiments (22) and pilot studies.

### *Drugs*

The following drugs were obtained from Research Biochemicals, Inc. (Natick, MA): DOI HCl, 8-OH-DPAT HBr, NAN-190, ritanserin, and TFMPP HCl. 5-MeODMT and L-5-HTP were obtained from Sigma Chemical Co. (St. Louis, MO). Buspirone, BMY 14802, emopamil, gepirone, and RU 24969 were provided by Bristol-Myers Squibb Company (Wallingford, CT). All drugs were dissolved in distilled water with the exception of 5-MeODMT, which was dissolved in 0.1 N HCl and brought to volume with distilled water. L-5-HTP was dissolved in warmed distilled water minimally acidified with 0.5 N HCl. All drugs were given subcutaneously in a volume of 2 ml/kg.

### *Statistical Analysis*

Statistical comparisons for syndrome data were made by the Mann–Whitney *U*-test (16). RHBS data were analyzed by Student's *t*-test or one-way analysis of variance (ANOVA) followed by Dunnett's *t*-test where appropriate. For dose-response data, $ED_{50}$ values were calculated by the method of Finney (7).

## RESULTS

### *5-HT Behavioral Syndrome*

As presented in Fig. 1, the gerbil 5-HT syndrome is dose dependent and can be induced by the 5-$HT_{1A}$/5-$HT_2$ agonist

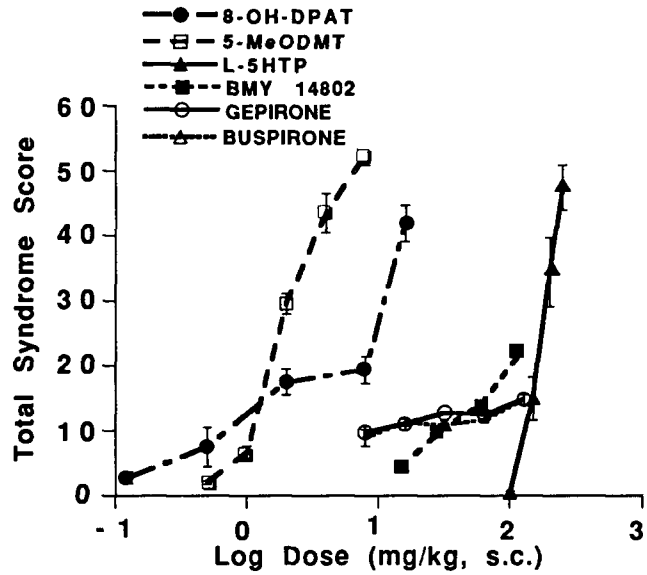


FIG. 1. Selected 5-$HT_{1A}$ agonists and L-5-HTP dose dependently induce the 5-HT syndrome in gerbils ($n$ = 8 per dose). The syndrome was scored at 5-min intervals for 30 min beginning 5 min after injection except L-5-HTP, which began 35 min postinjection. Total syndrome scores are expressed as mean ± SE. $ED_{50}$ values (mg/kg, SC; 5-MeODMT, 1.9; 8-OH-DPAT, 3.0; buspirone, 5.0; gepirone, 3.9; BMY 14802, 33; and L-5-HTP, 168) were generated using the Finney dose-response analysis method.

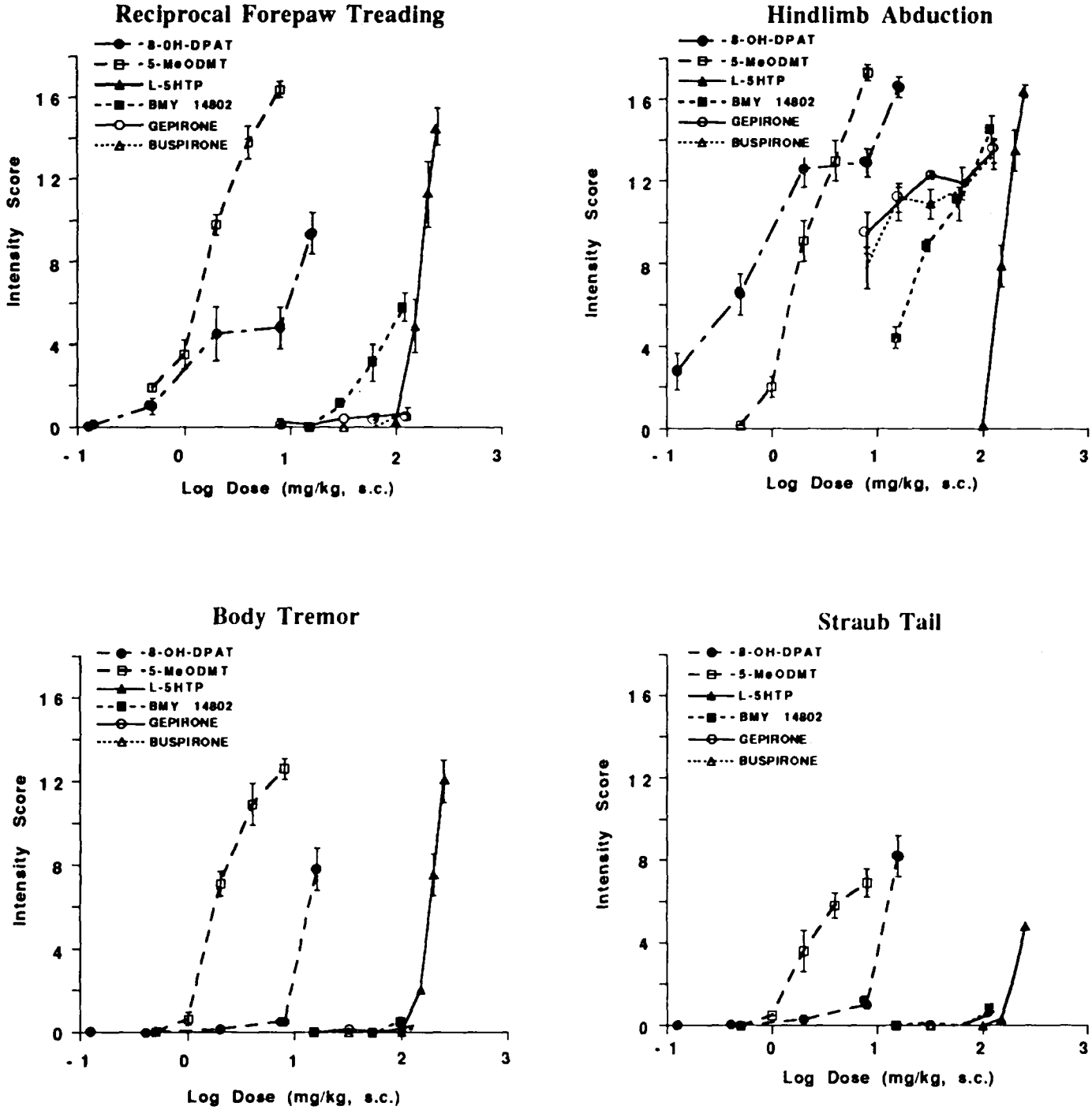


FIG. 2. Components of the 5-HT syndrome in gerbils are dose dependently induced by selected 5-$HT_{1A}$ agonists and L-5-HTP. The syndrome was scored at 5-min intervals for 30 min beginning 5 min postinjection except L-5-HTP, which began 35 min postinjection. Total 30-min scores for each component are expressed as mean ± SE based upon eight gerbils per dose.

5-MeODMT, the selective 5-$HT_{1A}$ agonist 8-OH-DPAT, the 5-$HT_{1A}$ partial agonists buspirone, gepirone, and BMY 14802, and the 5-HT precursor L-5-HTP. The most prominent and dose-responsive features of the 5-HT behavioral syndrome were reciprocal forepaw treading, hindleg abduction, body tremor, and Straub tail (Fig. 2). Of the 5-HT agonists tested, 5-MeODMT was most potent in eliciting the 5-HT behavioral syndrome. Rank order potencies were 5-MeODMT > 8-OH-DPAT > gepirone = buspirone > BMY 14802 > L-5-HTP (Fig. 1). Flat body posture was also observed consistently following administration of all 5-HT agonists but was not dose dependent and was therefore not quantified in these experiments. The putative 5-$HT_{1A}$ antagonist NAN-190, while itself devoid of stimulatory action, blocked, in a dose-dependent

TABLE 1

NAN-190 ANTAGONISM OF 5-MeODMT- AND 8-OH-DPAT-INDUCED SEROTONIN SYNDROME

| 5-HT Agonist | NAN-190 (mg/kg) | Serotonin Syndrome Score | | | | |
|---|---|---|---|---|---|---|
| | | Forepaw Treading | Hindlimb Abduction | Body Tremors | Straub Tail | Total |
| 5-MeODMT (4 mg/kg) | Vehicle Control | 11.0 ± 0.6 | 12.9 ± 0.9 | 12.1 ± 0.8 | 2.8 ± 0.7 | 38.2 ± 2.3 |
| | 0.25 | 7.5 ± 0.4* | 7.8 ± 0.5* | 7.9 ± 0.9* | 1.8 ± 0.5 | 24.9 ± 1.7* |
| | 1 | 3.0 ± 0.6* | 0.5 ± 0.4* | 2.6 ± 0.8* | 0.2 ± 0.2† | 6.4 ± 1.3* |
| | 4 | 1.8 ± 0.8* | 0.1 ± 0.1* | 4.1 ± 1.0* | 0.2 ± 0.2† | 6.2 ± 1.5* |
| 8-OH-DPAT (16 mg/kg) | Vehicle Control | 9.6 ± 0.3 | 18.0 ± 0 | 8.0 ± 1.2 | 5.2 ± 0.6 | 40.9 ± 1.7 |
| | 0.5 | 8.6 ± 0.8 | 14.9 ± 0.6* | 3.6 ± 0.8† | 3.4 ± 0.7 | 30.5 ± 2.2* |
| | 2 | 4.9 ± 0.9* | 6.9 ± 1.5* | 0.5 ± 0.3* | 0.4 ± 0.2* | 12.6 ± 2.5* |
| | 8 | 1.2 ± 0.4* | 1.6 ± 0.8* | 0* | 0.1 ± 0.1* | 3.0 ± 1.1* |

NAN-190 administered SC 15 min prior to SC injection of 5-HT agonist. Scores are mean ± SE of eight gerbils per group.
*$p \leq 0.01$, †$p \leq 0.05$, vs. vehicle control, Mann–Whitney *U*-test, two tailed.

manner, the 5-HT behavioral syndrome induced by 5-MeODMT and 8-OH-DPAT (Table 1). Pretreatment with the 5-$HT_2$ antagonist ritanserin failed to alter the 8-OH-DPAT-induced 5-HT syndrome (data not shown) but resulted in a rightward shift of the dose–response curve for 5-MeODMT (Fig. 3). Ritanserin pretreatment shifted the dose–response curve for the 5-MeODMT-induced syndrome to the right largely by attenuation of reciprocal forepaw treading and body tremor behaviors.

*RHBS*

In time course studies, the peak of RHBS responding induced by DOI administration occurred at 30–40 min postdosing and declined thereafter during the 2-h observation period (Fig. 4A). The 5-$HT_2$ agonists DOI and quipazine both induced the reciprocal hindleg body scratch response in a dose-dependent manner (Fig. 4B). DOI was more potent than quipazine in electing the RHBS response ($ED_{50}$ = 0.38 and 1.7 mg/kg, respectively). In contrast, RHBS behavior was not observed following administration of 5-MeODMT, 8-OH-DPAT, buspirone, gepirone, BMY 14802, or the 5-$HT_{1B}$ agonist RU 24969. The 5-$HT_{1B}$/5-$HT_{1C}$ agonist TFMPP (8 mg/kg) marginally elicited RHBS (3.7 ± 0.9) when compared to the same dose of DOI (95 ± 4), while the 5-HT precursor, L-5-HTP, did not produce RHBS in the dose ranges examined. The selective 5-$HT_2$ antagonist ritanserin dose-dependently inhibited the RHBS response induced by DOI (2.0 mg/kg) with a 50% inhibition dose ($ID_{50}$) of 0.037 mg/kg SC (Fig. 5). Similarly, emopamil, another 5-$HT_2$ antagonist, inhibited the RHBS in a dose-dependent manner ($ID_{50}$ = 2.3 mg/kg, SC; Fig. 5).

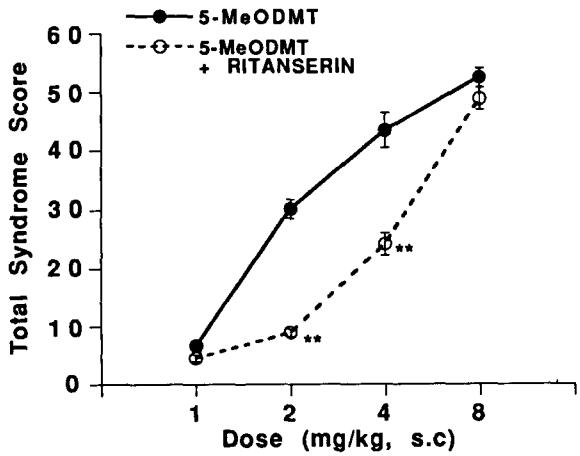


FIG. 3. Dose-dependent blockade of the 5-MeODMT-induced 5-HT syndrome by ritanserin. Gerbils were pretreated with ritanserin (0.5 mg/kg, SC) or vehicle 30 min prior to 5-MeODMT administration. Data are expressed as mean ± SE of total syndrome score ($n$ = 8 per dose). **$p < 0.01$, significantly different from 5-MeODMT alone. Mann–Whitney *U*-test, two tailed.

*Interaction Studies*

As presented in Fig. 6, the 8-OH-DPAT-induced 5-HT behavioral syndrome was markedly potentiated by simultaneous treatment with DOI. The dose of DOI used (1.0 mg/kg, SC) did not elicit reciprocal forepaw treading, hindleg abduction, body tremor, or Straub tail, but it did elicit low body posture. Pretreatment with the 5-$HT_2$ antagonist ritanserin blocked the DOI-induced facilitation of 8-OH-DPAT behavioral syndrome (Table 2). The selective 5-$HT_{1A}$ agonists 8-OH-DPAT and gepirone reduced the RHBS response induced by DOI (2.0 mg/kg) in a dose-dependent manner with 8-OH-DPAT being more potent than gepirone in this regard ($ID_{50}$ = 0.014 and 0.40 mg/kg, respectively; Fig. 7).

## DISCUSSION

The ability of 5-$HT_{1A}$ agonists to induce the typical components of the 5-HT syndrome in rats (19) and mice (20) has previously been described. In this study, we demonstrated that administration of 5-$HT_{1A}$ agonists produces a robust behavioral syndrome in the Mongolian gerbil. The 5-HT behavioral syndrome in gerbils is similar to that observed in rats and mice, consisting of reciprocal forepaw treading, hindleg abduction, body tremor, and Straub tail. Unlike the 5-HT syndrome in rats (19), flat body posture, while routinely observed, was not dose dependent. The gerbil 5-HT syndrome was induced by the selective 5-$HT_{1A}$ agonist 8-OH-DPAT and 5-$HT_{1A}$ partial agonists (buspirone, gepirone, and BMY 14802) with rank order potencies paralleling the efficacy of

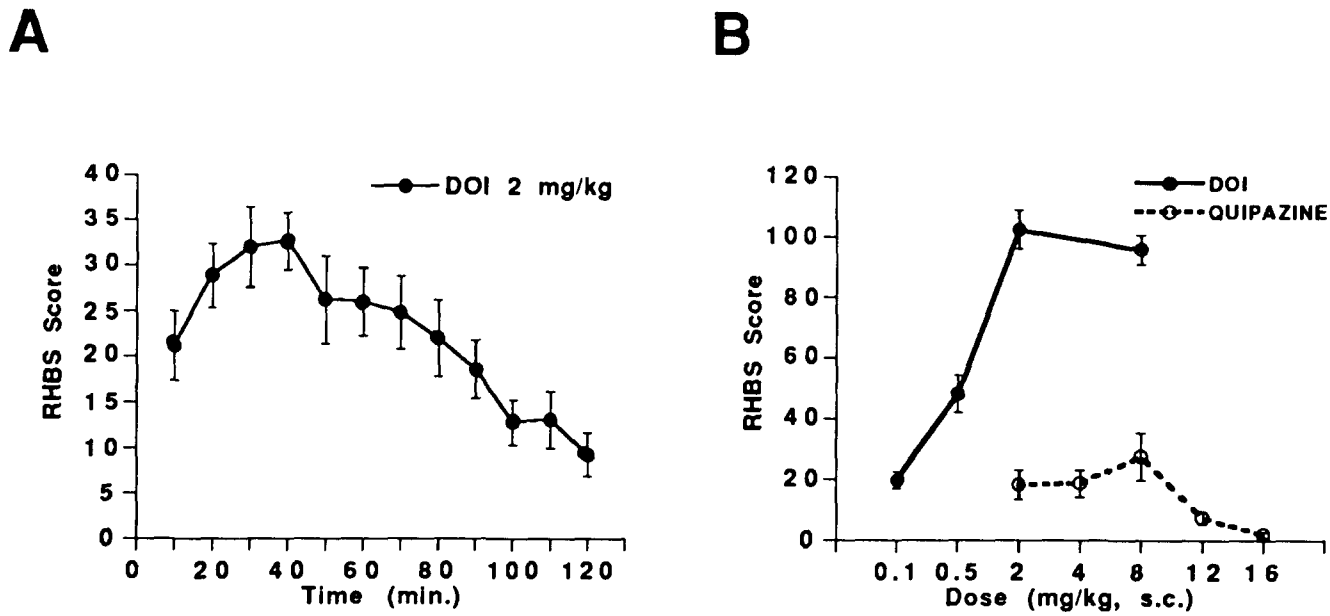


FIG. 4. (A) Time course of RHBS frequency following administration of DOI (2 mg/kg, SC; $n = 8$) in gerbils. The frequency of RHBS episodes was determined during 30-s observation periods every 5 min beginning 5 min after injection. Total RHBS scores (mean ± SE) are presented for 10-min intervals. (B) The 5-$HT_2$ agonists DOI and quipazine induce the reciprocal hindleg body scratch (RHBS) in gerbils. The frequency of RHBS episodes was determined during 30-s observation periods every 5 min for 30 min beginning 5 min postinjection. Total RHBS scores are expressed as mean ± SE based upon eight gerbils per dose.

these agents at postsynaptic 5-$HT_{1A}$ receptors [(21); F. D. Yocca, personal communication].

Further, the postsynaptic 5-$HT_{1A}$ antagonist NAN-190 (12) dose dependently blocked the syndrome induced by 8-OH-DPAT and 5-MeODMT, suggesting that these behavioral responses are mediated by 5-$HT_{1A}$ receptors. The failure of ritanserin to attenuate behavior elicited by 8-OH-DPAT further supports mediation by 5-$HT_1$ receptors.

Administration of the 5-$HT_2$ agonists DOI and quipazine produced a dose-dependent increase in the reciprocal hindleg body scratch, a behavior not previously described in this species. This reciprocal hindleg body scratch behavior may be analogous to another scratch behavior elicited by 5-$HT_2$ receptor stimulation in rodents, the ear-scratch response in mice (6). The ability of the 5-$HT_2$ antagonists ritanserin (11) and emopamil (17) to inhibit DOI-induced RHBS provides addi-

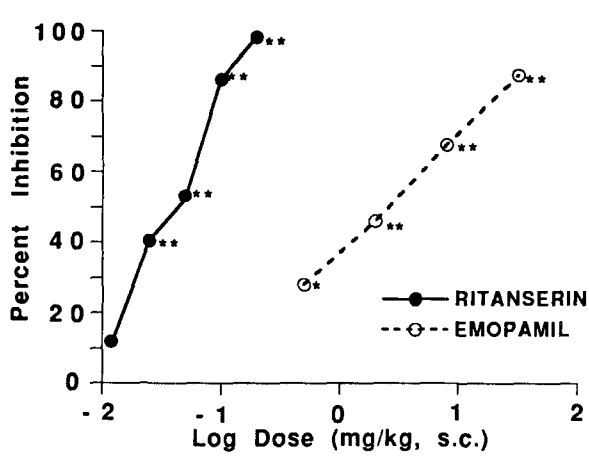


FIG. 5. Ritanserin and emopamil dose dependently antagonize the RHBS induced by DOI (2 mg/kg, SC). Gerbils were pretreated with ritanserin, emopamil, or vehicle 30 min prior to DOI administration. Data are expressed as percent inhibition of total RHBS episodes as compared to vehicle-treated controls ($n = 8$ per dose). *$p < 0.05$ or **$p < 0.01$ significantly different from vehicle control, two-tailed Dunnett test.

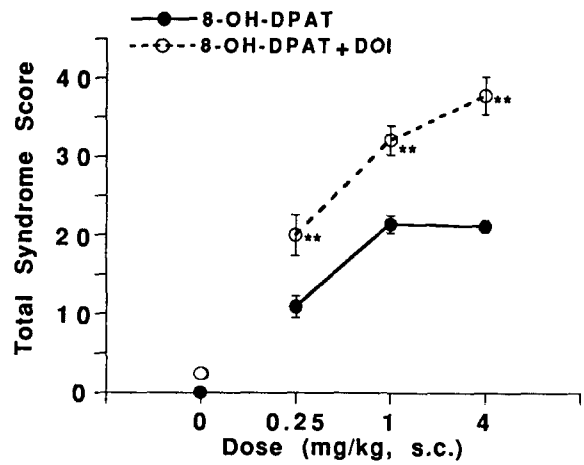


FIG. 6. Effect of 8-OH-DPAT alone and in combination with DOI (1 mg/kg, SC) on the 5-HT syndrome in the gerbil. The 5-HT syndrome was scored on an intensity scale (0–3) at 5-min intervals for 30 min beginning 5 min postinjection. Scores were collected over the 30-min observation period for each gerbil. Each point represents the mean ± SE of data from eight gerbils. **$p < 0.01$ significantly different from 8-OH-DPAT alone, two-tailed Mann-Whitney $U$-test.

TABLE 2

RITANSERIN ANTAGONIZES DOI FACILITATION OF THE 8-OH-DPAT-INDUCED SEROTONIN SYNDROME

| | DOI + 8-OH-DPAT Syndrome Score | | | | |
|---|---|---|---|---|---|
| | Forepaw Treading | Hindlimb Abduction | Body Tremors | Straub Tail | Total |
| Vehicle control | 9.2 ± 1.0 | 8.8 ± 0.8 | 5.1 ± 0.8 | 0 | 23.1 ± 2.1 |
| Ritanserin (0.5 mg/kg) | 2.6 ± 0.6* | 9.6 ± 0.4 | 0* | 0 | 12.6 ± 0.3* |

Ritanserin administered SC 30 min prior to the simultaneous administration of DOI 1 mg/kg SC and 8-OH-DPAT 0.5 mg/kg SC. Scores are mean ± SE of eight gerbils per group.

*$p \leq 0.01$ vs. vehicle control, Mann-Whitney $U$-test, two tailed.

tional evidence that this behavior may be mediated by 5-$HT_2$ receptors. While often used as a selective 5-$HT_2$ agonist, DOI also exhibits appreciable affinity for 5-$HT_{1C}$ sites (13). However, treatment with the 5-$HT_{1B}$/5-$HT_{1C}$ agonist TFMPP and the 5-$HT_{1B}$ agonist RU 24969 did not produce significant RHBS, lending additional support to the hypothesis that the RHBS is 5-$HT_2$ mediated. Interestingly, the indolealkylamine hallucinogen 5-MeODMT did not induce RHBS in gerbils. While 5-MeODMT possesses affinity for 5-$HT_2$ receptors, it also binds to other 5-HT receptors including 5-$HT_{1A}$ receptors (10). Based upon the dual pharmacology of 5-MeODMT (5-$HT_{1A}$ and 5-$HT_2$ agonism), it is possible that: a) 5-MeODMT may be more efficacious in the 5-HT syndrome than 8-OH-DPAT due to a facilitatory effect mediated by its intrinsic 5-$HT_2$ component and b) 5-MeODMT may fail to elicit RHBS due to an inhibitory effect mediated by its intrinsic 5-$HT_{1A}$ component. The first of these possibilities is supported by the observation that the dose-response curve for the 5-MeODMT-induced 5-HT syndrome is shifted to the right by pretreatment with the 5-$HT_2$ antagonist ritanserin (Fig. 3).

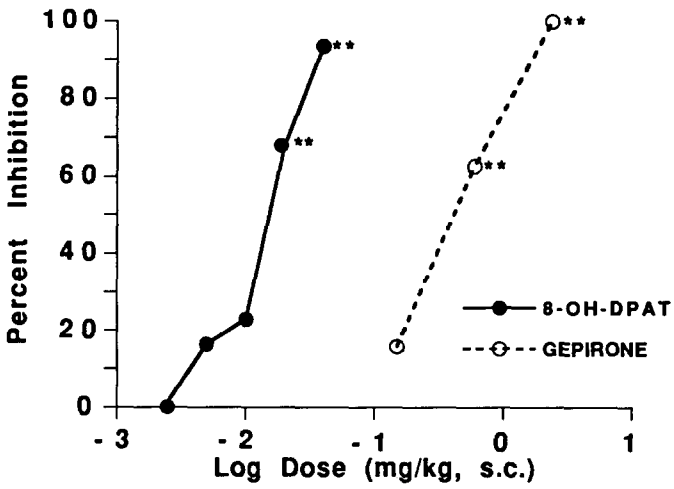


FIG. 7. 8-OH-DPAT and gepirone dose dependently antagonize the RHBS induced by DOI (2 mg/kg, SC). Gerbils were pretreated with 8-OH-DPAT, gepirone, or vehicle 15 min prior to DOI administration. Data are expressed as percent inhibition of RHBS episodes as compared to vehicle-treated controls ($n$ = 8 per dose). **$p < 0.01$ significantly different from vehicle control, two-tailed Dunnett test.

The present results indicate that in the gerbil [as in the rat; (1,6,22)] there is an interaction between 5-$HT_{1A}$ and 5-$HT_2$ receptors. Like the 5-$HT_2$-mediated head-shake response in rats, the RHBS response elicited by DOI was dose dependently inhibited by the 5-$HT_{1A}$ agonists 8-OH-DPAT and gepirone. Further, the 8-OH-DPAT-induced 5-HT behavioral syndrome in both rats and gerbils is potentiated by cotreatment with DOI. Importantly, in the present study the DOI-induced facilitation of 8-OH-DPAT-induced syndrome was blocked by pretreatment with the 5-$HT_2$ antagonist ritanserin (Table 2).

In summary, the present findings demonstrate that selective agonists for 5-HT receptor subtypes (5-$HT_{1A}$ and 5-$HT_2$) elicit distinct behaviors in the Mongolian gerbil and that interactions among these receptor subtypes appear similar to those observed in other rodent species. As serotonergic agents with neuroprotective effects (e.g., emopamil, 8-OH-DPAT) significantly alter 5-HT-mediated behavior, these behaviors might serve as a useful model to characterize the serotonergic efficacy of antiischemic agents in the species most often utilized for neuroprotection studies.

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