The Serotonin 5-Hydroxytryptaphan\textsubscript{1A} Receptor Agonist, (+)8-Hydroxy-2-(di-\textit{n}-propylamino)-tetralin, Stimulates Sympathetic-Dependent Increases in Venous Tone during Hypovolemic Shock

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**ABSTRACT**

Adjuvant treatment of hypovolemic shock with vasoconstrictors is controversial due to their propensity to raise arterial resistance and exacerbate ischemia. A more advantageous therapeutic approach would use agents that also promote venoconstriction to augment perfusion pressure through increased venous return. Recent studies indicate that 5-hydroxytryptophan (5-HT\textsubscript{1A} receptor agonists increase blood pressure by stimulating sympathetic drive when administered after acute hypotensive hemorrhage. Given that venous tone is highly dependent upon sympathetic activation of \( \alpha_2 \)-adrenergic receptors, we hypothesized that the 5-HT\textsubscript{1A} receptor agonist, (+)8-hydroxy-2-(di-\textit{n}-propylamino)-tetralin (8-OH-DPAT), would increase venous tone in rats subject to hypovolemic shock through sympathetic activation of \( \alpha_2 \)-adrenergic receptors. Systemic administration of 8-OH-DPAT produced a sustained rise in blood pressure (\( \pm 4.4 \pm 3 \text{ mm Hg} \) 35 min after injection, \( P < 0.01 \) versus saline) and mean circulatory filling pressure (\( \pm 4.2 \pm 0.7 \text{ mm Hg} \), \( P < 0.01 \) versus saline) in conscious rats subjected to hypovolemic shock. An equipressor infusion of epinephrine failed to influence mean circulatory filling pressure (MCFP). Ganglionic blockade, \( \alpha_1 \)-, \( \alpha_2 \)-adrenergic receptor blockade prevented the rise in MCFP observed with 8-OH-DPAT, but only \( \alpha_1 \)-adrenergic receptor blockade diminished the pressor effect of the drug (\( P < 0.01 \)). 8-OH-DPAT raises blood pressure in rats in hypovolemic shock through both direct vascular activation and sympathetic activation of \( \alpha_2 \)-adrenergic receptors. The sympathoexcitatory effect of 8-OH-DPAT contributes to elevated venous tone through concurrent activation of both \( \alpha_1 \)- and \( \alpha_2 \)-adrenergic receptors. The data suggest that 5-HT\textsubscript{1A} receptor agonists may provide an advantageous alternative to currently therapeutic interventions used to raise perfusion pressure in hypovolemic shock.

Progressive and severe blood loss elicits a complex series of autonomic responses that help to maintain or restore arterial blood pressure. During the initial phase of blood loss, arterial baroreflex-mediated increases in sympathetic drive help to maintain arterial pressure. If blood loss continues, these compensatory responses suddenly abate resulting in a syncope-like episode characterized by low sympathetic activity and bradycardia (Schadt and Ludbrook, 1991). It is speculated that this latter phase may provide adaptive means to increase cardiac filling and to help maintain cerebral perfusion (Oberg and Thoren, 1970; van Lieshout et al., 2003). If hypotension persists, arterial baroreflex activity slowly recovers and progressive increases in sympathetic drive and tachycardia develop. The clinical features of this third phase of hemorrhage are commonly observed in patients who arrive in the emergency room after traumatic blood loss. Interventions at this stage must be rapid to prevent patients from progressing to a fourth, mostly irreversible stage of shock characterized by insensitivity to vasoconstrictors and high capillary permeability, both of which contribute to further maldistribution of blood volume and eventually death. Rapid reinfusion of volume is a universally accepted treatment of hypovolemic shock. However, the type of resuscita-

**ABBREVIATIONS:** 5-HT, 5-hydroxytryptophan; 8-OH-DPAT, (+)8-hydroxy-2-(di-\textit{n}-propylamino)-tetralin; MCFP, mean circulatory filling pressure; MAP, mean arterial pressure; L-659,066, (2R-trans)-N-(2-(1,3,4,7,12b-hexahydro-2'-oxo-spiro[2H-benzofuro(2,3-a)quinolizine-2,4'-imidazolidin]-3'-\textit{yl})ethyl) methanesulphonamide monohydrochloride; CVP, central venous pressure; HR, heart rate; VPP, venous plateau pressure; ANOVA, analysis of variance; Hex, hexamethonium chloride.
tion fluid used, as well as the amount and rate of reinfusion, remain controversial. Also controversial is the choice of vasocostrictor adjuvants used to help raise perfusion pressure. Epinephrine and other sympathomimetic agents are commonly given to support blood pressure during severe hypotensive shock when volume alone is insufficient to maintain pressure. However, catecholamine use is fraught with complications related to excessive vasoconstriction and exacerbation of ischemia as well as generation of arrhythmias (Meier-Hellmann et al., 1997). More recent evidence indicates that vasopressin and vasopressin analogs may be good alternatives to maintain arterial blood pressure in various types of shock (Kam et al., 2004). Although vasopressin is a highly potent arterial vasoconstrictor, it has virtually no vasoconstrictor effects on the venous vasculature (Warner, 1990). Theoretically, pressor agents that promote venous return and cardiac filling would provide a more favorable hemodynamic response than agents that act primarily by increasing arterial resistance. However, little is known about the veno-constrictor effects of pressor agents in hypovolemic shock.

We have shown that the 5-HT1A receptor agonist (+)-8-hydroxy-2-(di-n-propylamino)-tetralin (8-OH-DPAT) produces a potent sympathoexcitatory response in conscious rats when administered during the syncopal phase of blood loss (Scrogin, 2003; Osei-Owusu and Scrogin, 2004b). Preliminary data also indicate that 8-OH-DPAT is an effective pressor agent when administered to rats in hypovolemic shock (Henze et al., 2005). Venous tone is regulated largely by sympathetic drive (Pang, 2001). Therefore, we tested the hypothesis that 8-OH-DPAT increases arterial pressure during hypovolemic shock, in part, by stimulating sympathetic-mediated increases in venous tone through adrenergic receptor activation.

Materials and Methods

Animals

Male Sprague-Dawley rats weighing 310 to 360 g (Harlan, Indianapolis, IN) were maintained in the institutional animal facility under standard conditions (22 ± 2°C ambient temperature, 12:12 h light/dark cycle) with water and food provided ad libitum. All experiments were conducted in accordance with the Guide for the Care and Use of Laboratory Animals as adopted and promulgated by the National Institutes of Health.

Surgery

Four days prior to experiments, rats were anesthetized with sodium pentobarbital (60 mg/kg intraperitoneally; Sigma-Aldrich, St. Louis, MO) and instrumented with bilateral femoral arterial and unilemal femoral venous polyethylene catheters for measurement of arterial pressure, arterial blood withdrawal, and drug injections, respectively. Silastic tubing (o.d. 0.037 inches) was inserted into the thoracic vena cava via the femoral vein for measurement of central venous pressure. A saline-filled inflatable balloon-tipped catheter (Vesta, Inc., Franklin, WI) was inserted into the right atrium via the jugular vein to allow brief cessation of circulation for measurement of mean circulatory filling pressure (MCFP), an indirect measure of venous tone. All catheters were tunneled under the skin to exit at the nape of a neck.

Experimental Protocols

Hemorrhage Procedure. On the day of the experiment, animals were connected to the recording instrumentation while resting unrestrained in their home cage. Two measurements of baseline MCFP were taken 20 and 10 min prior to initiation of hemorrhage according to methods developed by Yamamoto et al. (1980). Hemorrhage was initiated using a modified Wiggers's model. Blood was withdrawn at a rate of 3.2 ml/kg/min for 6 min, after which the rate was reduced to 0.53 ml/kg/min for an additional 4 min. Over the following 15 min, small amounts of blood (0.1–0.25 ml) were withdrawn or infused manually to maintain mean arterial pressure (MAP) at 50 mm Hg. All blood volume manipulations were terminated 25 min after initiation of hemorrhage, after which blood pressure was allowed to fluctuate. MCFP measurements were performed 20, 30, 40, 50, and 60 min after initiation of blood withdrawal.

Study 1. Animals were randomly assigned to one of three experimental groups, all of which were given saline (150 µl i.v.) 15 min after the initiation of blood withdrawal to control for volume of drug injections used in later protocols. Ten minutes later, immediately after the termination of blood withdrawal, animals were given 8-OH-DPAT (9.85 µg/kg/150 µl i.v.; Sigma/RBI, Natick, MA) or saline. A third group received a variable infusion of epinephrine (2.5–1.0 µg/kg; Hospira, Inc., Lake Forest, IL), to match the blood pressure response of 8-OH-DPAT-treated rats. Arterial blood sampled 10 min after initiation of blood withdrawal (end of fixed-rate withdrawal) and 2 min after the last MCFP measurement were used for determination of hematocrit and total plasma protein concentration to assess the extent of hemodilution.

Study 2. Rats were subject to the hemorrhage protocol described above but were given the autonomic ganglionic blocker, hexamethonium chloride (30 mg/kg i.v.; Sigma), 15 min after the initiation of hemorrhage, followed 10 min later by either saline or 8-OH-DPAT (9.85 µg/kg/150 µl i.v.).

Study 3. Rats were treated as in study 2 but were pretreated with the a1-adrenergic receptor blocker, prazosin (25 µg/kg i.v.; Sigma), rather than hexamethonium.

Study 4. Rats were treated as in study 2 except they were pretreated with peripherally acting a2-adrenergic receptor blocker, L-659,066 (100 µg/kg i.v.; Merck & Co., Inc., Rahway, NJ), rather than hexamethonium.

Data Acquisition and Analysis. During all experiments, arterial and central venous pressures (CVPs) were recorded continuously on a Macintosh G4 PowerBook computer using PowerLab data acquisition software (Chart version 5.2.1; ADInstruments, Grand Junction, CO). Heart rate was calculated online using peak-to-peak detection of the arterial pulse pressure wave. Mean arterial pressure, heart rate (HR), and CVP were averaged within subject over 20-s segments and averaged within groups at 5-min intervals. MCFP was determined by initiating circulatory arrest by brief (~5 s) inflation of the balloon catheter. During balloon inflation, central venous pressure increased to a plateau level (VPP), whereas MAP decreased to a nadir, referred to as final arterial pressure. Mean circulatory filling pressure was calculated as VPP + 1/60(final arterial pressure − VPP). Total blood volume withdrawn during the course of hemorrhage was determined gravimetrically at the end of the hemorrhage period.

Two and three-way ANOVAs with repeated measures were used to determine effects of autonomic manipulations and 8-OH-DPAT or epinephrine treatment over time (from 25–60 min after start of hemorrhage) on hemodynamic parameters where appropriate. Separate one- and two-way ANOVAs were used to assess effects of pressor agents on MCFP or the effects of hexamethonium, prazosin, or L-659,066 treatment on MCFP responses to 8-OH-DPAT over time (from 20–60 min after start of hemorrhage). Significant main effects and interactions were followed up with Tukey/Kramer post hoc tests. Total blood loss was pooled across pretreatment groups. Total blood loss and change in hematocrit and plasma protein were analyzed by two-way ANOVA followed by Tukey/Kramer post hoc tests. Change in plasma protein and hematocrit of the two groups treated with L-659,066 were excluded from the ANOVA due to excessive variability.
Results

Statistical analyses showed no differences in hemodynamic responses to hemorrhage prior to drug treatment in any of the groups. Thus, BP, HR, and CVP data obtained prior to drug administration were pooled across groups for clarity of presentation and to assess the hemodynamic profile during the initial blood withdrawal period.

**Hemodynamic Effect of 8-OH-DPAT in Circulatory Shock.** The initial blood withdrawal (22.4 ml/kg) over the first 10 min of hemorrhage caused a precipitous drop in MAP (−70.4 ± 3.5 mm Hg), HR (−138 ± 23 beats per minute), and CVP (−1.5 ± 0.5 mm Hg). An additional 12.2 ± 1.0 ml/kg blood was withdrawn over the following 15 min to maintain MAP at 50 mm Hg. Heart rate reached a nadir 10 min after initiation of blood withdrawal but then began to rise steadily and stabilized near baseline by the end of blood withdrawal. Changes in CVP paralleled changes in MAP (Fig. 1).

Following termination of hemorrhage, 8-OH-DPAT administration caused a rapid rise in MAP that persisted throughout the 35-min posthemorrhage recording period. Heart rate and CVP were not affected by 8-OH-DPAT. Continuous infusion of epinephrine, titrated to match the pressor effect of 8-OH-DPAT, caused a distinct tachycardia during the early part of the infusion (Fig. 1).

Balloon inflation prior to hemorrhage caused a large rise in CVP. In subsequent tests after blood loss, the rise in CVP was markedly attenuated and remained low throughout the posthemorrhage period in saline-treated rats. The rise in CVP during balloon inflation was exaggerated in hemorrhaged rats given 8-OH-DPAT (data not shown). This resulted in a significant elevation of MCFP that lasted throughout the recovery period. Epinephrine infusion had no effect on MCFP (Fig. 2).

**Effect of Autonomic Blockade on Hemodynamic Responses to 8-OH-DPAT.** Ganglionic blockade caused an immediate drop in pressure below the target MAP of 50 mm Hg (data not shown). This was quickly rectified by reinfusion of a small amount of shed blood. As a result, the total blood withdrawal needed to sustain hypotension was reduced in rats given hexamethonium (Table 1). Ganglionic blockade had a slight but nonsignificant tachycardic effect and did not influence CVP (data not shown).

Ganglionic blockade attenuated recovery of blood pressure following termination of hemorrhage. However, the immediate pressor response to 8-OH-DPAT was similar in intact and ganglionic-blocked rats compared with their respective control groups (Fig. 3, compare light- and dark-gray shaded areas). With time, the pressor response diminished in ganglionic-blocked animals (dark gray) but grew larger in intact animals (light gray). An overall ANOVA revealed a significant interaction among ganglionic blockade, 8-OH-DPAT treatment, and time (P < 0.01). Subsequent two-way ANOVAs performed at each time point showed significant interactions between ganglionic blockade and 8-OH-DPAT 50 and 55 min after the start of hemorrhage due to the waning pressor effect of 8-OH-DPAT after ganglionic blockade and the persistent pressor effect in intact animals. Heart rate and CVP were not significantly affected by 8-OH-DPAT in either intact or ganglionic-blocked rats (data not shown).

MCFP is directly affected by both blood volume and venous tone (Guyton et al., 1954). Since the total volume of blood withdrawn differed among rats given various pretreatments (i.e., hexamethonium, prazosin, L-659,066, or saline), MCFP was only compared between groups subjected to similar degrees of blood withdrawal, e.g., in study 2, only 8-OH-DPAT- and saline-treated rats subjected to ganglionic blockade were compared with one another, whereas animals with intact autonomic responses were compared in a separate analysis. In contrast to intact rats, 8-OH-DPAT did not increase MCFP after ganglionic blockade (Fig. 4).

**Effect of Prazosin on 8-OH-DPAT-Mediated Hemodynamics.** Blockade of peripheral α1-adrenergic receptors exacerbated the hemorrhage-induced hypotension resulting in less blood withdrawal over the course of hemorrhage (Table 1). Prazosin also attenuated recovery of blood pressure following termination of hemorrhage and completely blocked
the pressor effect of 8-OH-DPAT (Fig. 5). Prazosin had no effect on either HR or CVP (data not shown) but blocked the ability of 8-OH-DPAT to increase MCFP (Fig. 6).

**Effect of L-659,066 on 8-OH-DPAT-Mediated Hemodynamics.** Blockade of peripheral α₂-adrenergic receptors did not alter blood pressure prior to saline or 8-OH-DPAT administration. Consequently, total blood loss did not differ between rats pretreated with the α₂-adrenergic receptor antagonist and those pretreated with saline (Table 1). However, α₂-adrenergic receptor blockade did attenuate the recovery of blood pressure following termination of blood withdrawal and tended to accelerate decompensation in a subset of animals, leading to the increased blood pressure variability observed at the end of the recording period. The magnitude of the initial pressor response to 8-OH-DPAT was not affected by α₂-receptor blockade. Although the blood pressure profile observed after L-659,066 clearly resembled that observed after hexamethonium, there was no significant interaction between L-659,066 and 8-OH-DPAT treatment either as a whole or over time. L-659,066 raised HR and CVP immediately after injection but did not influence the HR or CVP response to 8-OH-DPAT (Fig. 7).

<table>
<thead>
<tr>
<th>Total Blood Loss</th>
<th>Δ Hematocrit</th>
<th>Δ Plasma Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ml/kg</strong></td>
<td><strong>%</strong></td>
<td><strong>g/100 ml</strong></td>
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<tr>
<td>Saline + saline (10)</td>
<td>35.0 ± 0.10</td>
<td>-3.9 ± 0.9</td>
</tr>
<tr>
<td>Saline + 8-OH-DPAT (10)</td>
<td>36. ± 0.9</td>
<td>-0.47 ± 0.10</td>
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<tr>
<td>Epinephrine (8)</td>
<td>-6.3 ± 1.2</td>
<td>-0.61 ± 0.06</td>
</tr>
<tr>
<td>Hex + saline (8)</td>
<td>29.6 ± 0.10</td>
<td>-5.5 ± 0.5</td>
</tr>
<tr>
<td>Hex + 8-OH-DPAT (8)</td>
<td>-5.9 ± 0.7</td>
<td>-0.60 ± 0.06</td>
</tr>
<tr>
<td>Prazosin + saline (8)</td>
<td>25.9 ± 0.10</td>
<td>-6.3 ± 1.0</td>
</tr>
<tr>
<td>Prazosin + 8-OH-DPAT (9)</td>
<td>-4.4 ± 0.7</td>
<td>-0.43 ± 0.13</td>
</tr>
<tr>
<td>L-659,066 + saline (7)</td>
<td>34.3 ± 0.04</td>
<td>-1.0 ± 1.8</td>
</tr>
<tr>
<td>L-659,066 + 8-OH-DPAT (8)</td>
<td>-1.0 ± 1.7</td>
<td>-0.04 ± 0.31</td>
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</tbody>
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* P < 0.01 vs. saline pretreatment.
† P < 0.01 vs. L-659,066 pretreatment.

L-659,066 pretreatment blocked the effect of 8-OH-DPAT on MCFP (Fig. 8). L-659,066 itself appeared to lower MCFP compared with control animals despite a similar volume of blood withdrawal during hemorrhage (compare Figs. 2 and 8). However, hematocrit and plasma protein changes were highly variable in animals treated with L-659,066. Therefore, MCFP of saline- and L-659,066-treated rats was not directly compared.

**Fig. 1.** MCFP 10 min prior to hemorrhage and 20, 30, 40, 50, and 60 min after start of blood withdrawal (shaded box) in animals treated with saline, 8-OH-DPAT, or epinephrine. Data are group means ± S.E. Group n values are in parentheses. ***, P < 0.01 versus saline; †, P < 0.05 versus epinephrine.**

**Fig. 2.** MCFP 10 min prior to hemorrhage and 20, 30, 40, 50, and 60 min after start of blood withdrawal (shaded box) in animals treated with saline, 8-OH-DPAT, or epinephrine. Data are group means ± S.E. Group n values are in parentheses. ***, P < 0.01 versus saline; †, P < 0.05 versus epinephrine.

**Fig. 3.** MAP during hemorrhage (shaded box) and subsequent administration of hexamethonium chloride (Hex) or saline (15 min), followed by either 8-OH-DPAT or saline (25 min). Data are pooled prior to first injection, then divided into Hex-treated (closed triangles) and saline-treated (closed circles) groups following the first injection, and further divided into the four final groups following the second injection. Shading delineates pressor response to 8-OH-DPAT with respect to its appropriate control group in intact (light gray) and ganglionic-blocked (dark gray) animals. Darkest shading indicates overlap between pressor responses. Intact 8-OH-DPAT- and saline-treated group data taken from experiment 1 are included in analysis. Data are group means ± S.E. Groups n values are in parentheses. ***, P < 0.01, saline + 8-OH-DPAT versus saline; §§, P < 0.01, saline + 8-OH-DPAT versus Hex + 8-OH-DPAT; # and ##, P < 0.05 and 0.01, Hex + 8-OH-DPAT versus Hex + saline; ††, P < 0.01, Hex + saline versus saline.

**Fig. 4.** MCFP prior to hemorrhage and 20, 30, 40, 50, and 60 min after start of blood withdrawal in animals given saline or 8-OH-DPAT following ganglionic blockade with hexamethonium chloride. Data are group means ± S.E. Group n values are indicated in parentheses of legend.
Discussion

In the current study, 8-OH-DPAT elicited a significant pressor response when administered during hypovolemic shock. The pressor effect was mediated by a combination of direct- and sympathetic-dependent activation of $\alpha_1$-adrenergic receptors. 8-OH-DPAT produced a similar initial pressor effect in the absence of ganglionic blockade suggesting that the direct vascular effect of 8-OH-DPAT predominated immediately after drug treatment. The pressor effect waned after 20 to 25 min in animals subjected to ganglionic blockade but persisted in intact animals, indicating that the sympathetic component of the pressor response elicited a lasting hemodynamic effect.

Sympathetic-dependent activation of $\alpha_1$-adrenergic receptors mediated a significant amount of the compensatory vasoconstriction that developed following termination of blood withdrawal in control animals. This was evidenced by the lower blood pressure observed in prazosin-treated rats following termination of blood withdrawal despite their having had significantly less blood withdrawn than control animals.
only during infusion of norepinephrine (Ito and Hirakawa, 1984). Selective \( \alpha_1 \)-adrenergic agonists produce little increase in MCFP when infused into intact rats, whereas norepinephrine produces a potent, dose-dependent increase in MCFP (Pang and Tabrizchi, 1986). Studies in isolated mesenteric veins confirm that activation of \( \alpha_1 \)-adrenergic receptors may be necessary to observe a venoconstrictor effect of \( \alpha_2 \)-adrenergic receptors in some vascular beds. Specifically, clonidine and other \( \alpha_2 \)-adrenergic agonists alone do not produce mesenteric venoconstriction, but yohimbine, idazoxan, or rauwolscine inhibit venoconstriction caused by norepinephrine (G. Fink, unpublished data). Taken together, the data suggest that \( \alpha_1 \) and \( \alpha_2 \)-adrenergic receptor populations interact with one another to mediate sympathetic-dependent increases in venous tone.

Surprisingly, epinephrine did not affect MCFP despite its high affinity and agonist activity at both \( \alpha_1 \)- and \( \alpha_2 \)-adrenergic receptor subtypes. To our knowledge, the effect of epinephrine on MCFP has not previously been studied in mammals. Selective \( \beta \)-receptor agonists tend to increase MCFP in intact rats but produce a consistent decrease in MCFP when administered after blockade of sympathetic reflexes (Abdelrahman and Pang, 1990). Thus, the \( \beta \)-adrenergic properties of epinephrine may have antagonized its \( \alpha \)-adrenergic-mediated venoconstrictor effect. Alternatively, the venoconstrictor effect of epinephrine may have been masked by a concomitant loss of circulating blood volume due to increased capillary filtration. Although not significant, the fall in hematocrit tended to be larger with epinephrine infusion arguing against a greater loss of intravascular volume in this group.

Presumably, a peripherally acting agent with both \( \alpha_1 \) and \( \alpha_2 \) agonist activity, but little \( \beta \) activity such as norepinephrine would significantly increase venous tone during hemorrhage. As described above, norepinephrine has a potent effect on MCFP in intact animals. To our knowledge, no one has yet determined the effect of norepinephrine on MCFP in hemorrhage. Such studies are problematic because of norepinephrine’s propensity to exacerbate ischemia during hypovolemia. There were no outward signs of exacerbated ischemia in animals treated with 8-OH-DPAT. In accordance, preliminary evidence suggests that the 8-OH-DPAT does not exacerbate ischemic end-organ injury as assessed by hemorrhage-induced neutrophil activation in lung, kidney, or gut (Osei-Owusu and Scroggin, 2004a).

An increase in venous tone should result in an elevation in venous return and a rise in blood pressure if right atrial pressure is maintained. Surprisingly, neither ganglionic blockade nor \( \alpha_2 \)-receptor blockade had any apparent effect on the initial pressor response to 8-OH-DPAT despite their ability to block the 8-OH-DPAT-mediated rise in MCFP. However, it could be argued that the direct arterial vasoconstrictor effect of 8-OH-DPAT was exaggerated after ganglionic blockade due to the greater availability of adrenergic receptors. Pressor responses to norepinephrine are exaggerated in euolemic animals after ganglionic blockade (Rowe et al., 1979; Del Basso et al., 1983). The pressor response to 8-OH-DPAT-mediated sympathetic activation was also likely exaggerated during \( \alpha_2 \)-receptor blockade due to lack of \( \alpha_2 \)-adrenergic autoreceptor inhibition of catecholamine release. This view is supported by the greater HR rise observed during blood withdrawal in animals treated with L-659,066. Thus, we suspect that the rise in MCFP elicited by 8-OH-DPAT...
presumably due to their ability to inhibit glutamatergic neurotoxicity (Bienenberg and Burkhardt, 1990; Semkova et al., 1998). These characteristics, together with the data provided here, suggest that 5-HT1A receptor agonists may provide a beneficial alternative to currently used vasoconstrictors to raise pressure during hypovolemic shock.

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References


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