(R)-(−)-[77Br]4-Bromo-2,5-dimethoxyamphetamine Labels a Novel 5-Hydroxytryptamine Binding Site in Brain Membranes

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SUMMARY

(R)-(−)[77Br]4-Bromo-2,5-dimethoxyamphetamine [(R)-(−)[77Br]DOB] was synthesized to a high specific activity (1875 ± 50 Ci/mmol) and used to label membrane-associated recognition sites in rat brain. (R)-(−)[77Br]DOB displayed high affinity (Kd = 0.60 ± 0.08 nM) for a relatively low density of binding sites (Bmax = 1.2 ± 0.06 pmol/g of tissue) in rat cortical membranes as compared with [3H]ketanserin (Kd = 0.65 ± 0.1 nM; Bmax = 6.2 ± 0.6 pmol/g of tissue). Guanine, but not adenine, nucleotides were found to inhibit specific (R)-(−)[77Br]DOB binding. GTP (10−4 M) did not eliminate specific (R)-(−)[77Br]DOB binding but caused a competitive inhibition of the radioligand. Drug competition studies of 5-hydroxytryptamine (5-HT) and related agents indicate that both putative agonists and antagonists display nanomolar potency for these sites. A significant correlation (p < 0.01) exists between drug potencies for (R)-(−)[77Br]DOB-labeled sites and both 5-HT2 (r = 0.84) and 5-HT3 (r = 0.68) binding sites. However, the sites do not appear to be identical. Moreover, a significant correlation exists between drug potencies for (R)-(−)[77Br]DOB-labeled sites and human hallucinogenic drug potencies (r = 0.88; p < 0.01). We conclude that (R)-(−)[77Br]DOB labels a unique 5-HT recognition site in rat brain that does not coincide with previously described 5-HT binding site subtypes. The (R)-(−)[77Br]DOB site does not appear to be a high affinity “state” of the 5-HT2 receptor but may label a subset of heterogeneous 5-HT2 recognition sites.

(R)-(−)DOB is a potent human hallucinogen that selectively interacts with 5-HT receptors (1). Recently, (+)-[3H]DOB was synthesized and reported to label a high affinity “state” of the 5-HT2 receptor in the central nervous system (1–3). This conclusion was based on the fact that the affinity of a variety of 5-HT2 antagonists for the (+)-[3H]DOB site correlated with the affinity for the 5-HT2 receptor labeled by [3H]ketanserin. However, the site displayed nanomolar affinity for 5-HT, in contrast to the micromolar affinity displayed by 5-HT and 5-HT3 receptors, as defined in both radioligand studies using [3H]-antagonists (4, 5) and functional studies (6). In addition, the density of (+)-[3H]DOB sites represented approximately 5% of the density of 5-HT2 sites labeled by [3H]ketanserin in rat frontal cortex brain membranes. Unfortunately, the low specific activity of commercially available (+)-[3H]DOB (16 Ci/mmole) has hampered the extensive characterization of this potential important binding site.

In order to further investigate this site, we have developed a novel brominated radioligand of extremely high specific activity, (R)-(−)[77Br]DOB. Our preliminary analysis of this non-competitive compound revealed that it labeled a relatively low density of binding sites that did not appear to coincide with previously defined 5-HT binding site subtypes (7). We now report on the detailed characterization of this novel 5-HT binding site.

Materials and Methods

Radioligand binding assays were performed according to the methods of Titeler and colleagues (1–3) and Wang et al. (7). In brief, frozen rat brains were thawed from −70°C and brain regions were dissected. Tissues were homogenized in 20 volumes of 50 mM Tris-HCl (pH 7.7 at 25°C) and centrifuged at 45,000 × g for 10 min. The pellet was resuspended in Tris-HCl buffer and incubated for 10 min at 37°C. After a second centrifugation, the pellet was resuspended in 80 volumes of a buffer consisting of 50 mM Tris-HCl, 0.5 mM EDTA, 10 mM MgCl2, 0.1% acetic acid, and 10−4 M pargyline. The homogenates were immediately used in the binding assay.

Assays consisted of 100 μl of a solution of (R)-(−)[77Br]DOB (final

ABBREVIATIONS: DOB, 1-(4-bromo-2,5-dimethoxy-4-bromoamphetamine; 5-HT, 5-hydroxytryptamine; d-LSD, d-lysergic acid diethylamide; Gpp(NH)p, guanosine 5'-[(α,γ-imido)triphosphate; GTP-S, guanosine-5'-O-(3-thio)triphosphate; 8-OH-DPAT, 8-hydroxy-2-di-N-propylamino-tetralin; DOI, (±)-(2,5-dimethoxy-4-iodoamphetamine); 5-CT, 5-carboxyamidotryptamine.

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concentrations, 0.052–9.6 nM), 800 μl of tissue suspension, and 100 μl of buffer or displacing drug. Drugs were dissolved in buffer, except for (+)-butaclamol, which was dissolved to 10⁻³ M in ethanol and then diluted in buffer. After incubation at 25° for 30 min, the assay mixtures were rapidly filtered through no. 32 glass fiber filters (Schleicher and Schuell; Keene, NH) and washed twice with 5 ml of 50 mM Tris-HCl buffer. Specific binding was stable after incubation periods of approximately 15–60 min. Radioactivity was measured by liquid scintillation counting in 5 ml of Aquasol (New England Nuclear; Boston MA) at an estimated 80% efficiency. Specific binding was defined as the excess over blanks taken in the presence of 10⁻⁴ M DOI, a concentration of nonradioactive drug that displaces greater than 99% of specific radioligand binding. Competition experiments using (R)-(−)-[^77]BrDOB were performed using 0.08–2.7 nM of radioactive ligand. At these concentrations, 80–90% of the total binding was specific.

[^77]Br was synthesized by a high energy spallation reaction at Los Alamos National Laboratories (Los Alamos, NM) (8). (R)-(−)-[^77]BrDOB was synthesized to a radiochemical purity of greater than 99% by a modified Coenen synthesis (9, 10). The initial specific activity was determined by high pressure liquid chromatography ultraviolet quantitation. The specific activity was 375 Ci/mmol in the first synthesis and 1875 Ci/mmol in the second synthesis. The specific activity was corrected to allow for the decay of [^77]Br (t₁/₂ = 57 hr) for each experiment.

Drugs were obtained from commercial sources except for (+)-DOB, (−)-DOB, d-LSD, and (−)-dimethoxyamphetamine, which were obtained from the National Institute on Drug Abuse (Bethesda, MD). 5-CT was the generous gift of Dr. Roger Whiting of Syntex Corporation (Palo Alto, CA).

Results

Saturation analysis of specific (R)-(−)-[^77]BrDOB binding in rat brain membranes. Specific (R)-(−)-[^77]BrDOB binding to rat brain membranes was saturable and of high affinity. The experiment shown in Fig. 1A was performed using (R)-(−)-[^77]BrDOB with a specific activity of 450 Ci/mmol. At a concentration of 0.12 nM, specific binding accounted for 88% of total binding. Half-maximal specific binding was achieved at approximately 0.80 nM (R)-(−)-[^77]BrDOB, at which specific binding accounted for 84% of total binding. At the highest concentration of (R)-(−)-[^77]BrDOB analyzed in this single experiment (9.6 nM), specific binding represented 50% of total binding. The Scatchard analysis of these data (Fig. 1B) is consistent with a homogenous population of binding sites.

A total of eight saturation studies was performed in the present study. Scatchard analysis of the saturation data reveals a Kᵦ value of 0.60 ± 0.08 nM with a B_max value of 1.2 ± 0.2 pmol/g in rat cortical membranes. By contrast, saturation studies using [^3H]ketanserin in the same tissue (six experiments) reveal a Kᵦ value of 0.65 ± 0.1 nM and a B_max value of 6.2 ± 0.6 pmol/g of tissue. Thus, the density of (R)-(−)-[^77]BrDOB-labeled sites represents only 19% of the density of 5-HT₂ sites labeled by [^3H]ketanserin.

Regional studies were also performed using approximately 0.3 nM (R)-(−)-[^77]BrDOB. As shown in Table 1, the cortex displays the highest amount of specific (R)-(−)-[^77]BrDOB binding (100% = 0.52 ± 0.4 pmol/g) whereas the caudate has slightly less specific binding. The midbrain and hippocampus display intermediate amounts of specific (R)-(−)-[^77]BrDOB binding whereas the cerebellum has the least amount of specific binding. These findings are similar to the regional differences in (±)-[^3H]DOB binding that have been observed previously (3).

Nucleotide effects on specific (R)-(−)-[^77]BrDOB binding. The results of studies examining 10⁻⁴ M nucleotide effects on (R)-(−)-[^77]BrDOB binding are given in Table 2. GTP and its nonhydrolyzable analogues GppNHp and GTPγS have the greatest effect on the specific binding of (R)-(−)-[^77]BrDOB. These nucleotides (10⁻⁴ M) significantly inhibit specific (R)-(−)-[^77]BrDOB binding by 63–75%. The inhibitory effect of GDP is slightly less pronounced (49%) but is still significantly different from control values (p < 0.01). By contrast, GMP and the adenine nucleotides are markedly less effective in modulating specific (R)-(−)-[^77]BrDOB binding. These nucleotides have no significant effect on the specific binding of (R)-(−)-[^77]BrDOB at a concentration of 10⁻¹ M.

This decrease in binding appears to be due to an affinity shift with no change in site density, as shown by Scatchard analysis. For example, the effect of GTP on the affinity and density of (R)-(−)-[^77]BrDOB-labeled binding sites was determined in rat cortex. Under control conditions in this series of experiments (three experiments), the Kᵦ value of (R)-(−)-[^77]BrDOB was 0.60 ± 0.08 nM with a B_max value of 1.4 ± 0.1 pmol/g of tissue. In the presence of 10⁻⁴ M GTP, the Kᵦ is slightly increased to 0.92 ± 0.1 nM whereas the B_max is essentially unchanged at 1.1 ± 0.1 pmol/g of tissue. The ability of GTP to alter the Kᵦ of (R)-(−)-[^77]BrDOB is best observed in the presence of 10⁻¹ M GTP. Under this condition, the Kᵦ for (R)-(−)-[^77]BrDOB is 1.6 ± 0.4 nM with a B_max value of 1.2 ± 0.2 pmol/g of tissue. A representative experiment is shown in Fig. 2.

Drug competition studies with (R)-(−)-[^77]BrDOB-labeled binding sites in rat cortex. The results of drug competition studies using (R)-(−)-[^77]BrDOB are listed in Table 3. (−)-DOB is the most potent displacing agent (Kᵦ = 0.62 ± 0.1 nM) and is an order of magnitude more potent than (+)-DOB (Kᵦ = 18 ± 9 nM). Specific (R)-(−)-[^77]BrDOB binding is also displaced by nanomolar concentrations of 5-HT, metergoline, and a number of putative 5-HT₂-selective antagonists. By contrast, the 5-HT₁A-selective agent 8-OH-DPAT, the 5-HT₁B agent RU 24969, the 5-HT₁D agent 5-CT, and the 5-HT₃-selective agonist 5C-NMS were significantly less potent at (R)-(−)-[^77]BrDOB-labeled sites.

Representative drug competition curves are shown in Fig. 3. 5-HT, d-LSD, and ketanserin are inactive in competing for specific (R)-(−)-[^77]BrDOB binding at concentrations below 10⁻⁸ M. Monophasic competition is apparent at drug concentrations between 10⁻⁸ and 10⁻⁷ M. In the experiment shown in Fig. 3, 5-HT is slightly more potent than d-LSD and ketanserin. The slopes of the three competition curves are nearly identical and represent Hill slopes of approximately unity.

Correlation of drug affinities for (R)-(−)-[^77]BrDOB-labeled sites and drug affinities for 5-HT₂ and 5-HT₁C binding sites. Drug affinities for (R)-(−)-[^77]BrDOB-labeled sites were compared with drug affinities for 5-HT and 5-HT₁C binding sites as defined in previous studies. As shown in Fig. 4A, a significant correlation exists between drug Kᵦ values for (R)-(−)-[^77]BrDOB-labeled sites in rat cortex and 5-HT₁C binding sites (r = 0.64; p < 0.01; slope = 0.98; n = 19). Despite the statistical significance of this correlation, a number of apparent discrepancies should be noted. For example, the affinity of 5-HT for (R)-(−)-[^77]BrDOB-labeled sites (3.5 nM) is 2 to 3 orders of magnitude more potent than its affinity (562–30,000 nM) for [^3H]ketanserin-labeled 5-HT₂ sites in rat cortex as reported in multiple laboratories (11, 12). Conversely, the affinity of chlor-
promazine for (R)-(−)-[^7]BrDOB-labeled sites (70 nM) is more than an order of magnitude less potent than its affinity for [3H]ketanserin-labeled 5-HT₂ sites (2.8 nM) in rat cortex (3).

A slightly higher correlation coefficient \((r = 0.68; p < 0.01; \text{slope} = 0.80; n = 14)\) is observed between drug affinities for (R)-(−)-[^7]BrDOB-labeled sites in rat cortex and 5-HT₁c binding sites (Fig. 4B). Again, however, the two sites are not identical, inasmuch as drugs such as spiperone (1200 nM) (11) and ketanserin (98 nM) (13) are significantly less potent at 5-HT₁c sites than at (R)-(−)-[^7]BrDOB-labeled sites. Metergoline (0.51 nM) (11), on the other hand, is more potent at 5-HT₁c than at (R)-(−)-[^7]BrDOB binding sites. In addition, DOB has been reported to have an affinity of 69 nM for 5-HT₁c binding sites (14). Moreover, 5-HT₁c sites are found in extremely high density in the choroid plexus, whereas we failed
Fig. 2. GTP effects of (R)(−)[3H]DOB saturation studies in rat cortical membranes. Radioligand binding assays were performed as described in Materials and Methods. Nonspecific binding was determined in the presence of 1 μM (±)-DOI. The Scatchard data are taken from a single experiment, performed in triplicate. The experiment was repeated three times, with similar results.

TABLE 3

Drug affinities for (R)(−)[3H]DOB-labeled sites in rat cortex

Radioligand binding assays were performed as described in Materials and Methods. Values given are the means ± standard errors of three to six experiments, each performed in triplicate.

<table>
<thead>
<tr>
<th>Radioligand</th>
<th>Kᵦ (nM)</th>
</tr>
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<tbody>
<tr>
<td>1. (-)-DOB</td>
<td>0.62 ± 0.1</td>
</tr>
<tr>
<td>2. (±)-DOI</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td>3. Methylone</td>
<td>2.7 ± 0.5</td>
</tr>
<tr>
<td>4. (-)-dimethoxyethyl amphetamine</td>
<td>3.1 ± 0.6</td>
</tr>
<tr>
<td>5. 5-HT</td>
<td>3.5 ± 0.8</td>
</tr>
<tr>
<td>6. Spiperone</td>
<td>3.8 ± 2</td>
</tr>
<tr>
<td>7. Mesulergine</td>
<td>4.5 ± 0.9</td>
</tr>
<tr>
<td>8. Ketanserin</td>
<td>4.8 ± 0.7</td>
</tr>
<tr>
<td>9. d-LSD</td>
<td>4.8 ± 0.6</td>
</tr>
<tr>
<td>10. (-)-dimethoxymethyl amphetamine</td>
<td>6.4 ± 1</td>
</tr>
<tr>
<td>11. Methiothepin</td>
<td>6.5 ± 3</td>
</tr>
<tr>
<td>12. Cinanserin</td>
<td>7.2 ± 0.6</td>
</tr>
<tr>
<td>13. (+)-DOB</td>
<td>18 ± 9</td>
</tr>
<tr>
<td>14. Psilocin</td>
<td>19 ± 6</td>
</tr>
<tr>
<td>15. m-chlorophenylpiperazine</td>
<td>22 ± 3</td>
</tr>
<tr>
<td>16. Psilocybin</td>
<td>25 ± 4</td>
</tr>
<tr>
<td>17. (+)-Butaclamol</td>
<td>29 ± 10</td>
</tr>
<tr>
<td>18. Quipazine</td>
<td>31 ± 1</td>
</tr>
<tr>
<td>19. Tryptamine</td>
<td>49 ± 10</td>
</tr>
<tr>
<td>20. Chlorpromazine</td>
<td>70 ± 40</td>
</tr>
<tr>
<td>21. RU 24969</td>
<td>91 ± 3</td>
</tr>
<tr>
<td>22. 5-CT</td>
<td>320 ± 80</td>
</tr>
<tr>
<td>23. Mescaline</td>
<td>440 ± 100</td>
</tr>
<tr>
<td>24. (±)-3,4,5-trimethoxyamphetamine</td>
<td>450 ± 100</td>
</tr>
<tr>
<td>25. (±)-2,5-dimethoxyamphetamine</td>
<td>580 ± 100</td>
</tr>
<tr>
<td>26. 8-OH-DPAT</td>
<td>2,700 ± 300</td>
</tr>
<tr>
<td>27. (-)-Butaclamol</td>
<td>10,000 ± 2,000</td>
</tr>
<tr>
<td>28. ICS 205-930</td>
<td>17,000 ± 6,000</td>
</tr>
</tbody>
</table>

Fig. 3. Drug competition studies versus specific (R)(−)[3H]DOB binding in rat cortical membranes. Radioligand binding assays were performed as described in Materials and Methods. Nonspecific binding was determined in the presence of 1 μM (±)-DOI. Data shown are the results of a single experiment, performed in triplicate. Each experiment was repeated 3–6 times. Drugs analyzed were 5-HT (■), d-LSD (▲), and ketanserin (○).

Fig. 4. Correlation of drug potencies for (R)(−)[3H]DOB-labeled sites and drug potencies for 5-HT₁₂ and 5-HT₁c binding sites. Drug affinities (Kᵦ, nM) for (R)(−)[3H]DOB-labeled sites were obtained from Table 3. A. Drug affinities for 5-HT₁₂ binding sites were obtained from Lyon et al. (3), Hoyer et al. (11), and Glennon et al. (20). B. Drug affinities for 5-HT₁c binding sites were obtained from Lyon et al. (3), Hoyer et al. (11), and Pazos et al. (13).

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\[ K_D (\text{nM}) \]

\[ B_{\text{max}} \ (\text{pmoles/g}) \]

- **CONTROL** 0.56 1.4
- +10⁻⁵ GTP 1.20 1.4
- +10⁻⁴ GTP 2.80 1.5

\[ r = 0.68 \]

\[ p < 0.01 \]

\[ 1 \]

Unpublished observations.
Correlation of drug affinities for (R)-(−)-[^7Br]DOB-labeled sites and human hallucinogenic dosages. As shown in Table 3, a number of hallucinogenic agents display high affinity for (R)-(−)-[^7Br]DOB-labeled binding sites. A significant correlation exists (r = 0.89; p < 0.01; slope = 0.93; n = 11) between drug affinities for these sites in rat cortex and the average dosage that has been reported to induce hallucinations in humans (15–17). As illustrated in Fig. 5, 10 of the 11 hallucinogenic agents lie near the linear regression line. The single exception is d-LSD; the drug is significantly less potent at (R)-(−)-[^7Br]DOB binding sites than might have been predicted on the basis of the affinities displayed by the other hallucinogenic agents.

Discussion

The major finding of the present study is that (R)-(−)-[^7Br]DOB specifically labels a distinct and unique population of 5-HT recognition sites in rat brain. The sites labeled by (R)-(−)-[^7Br]DOB do not appear to correspond to previously defined 5-HT₁, 5-HT₂, or 5-HT₃ binding subtypes because, for example, they display nanomolar affinity for both 5-HT₁ and spiperone (17). 8-OH-DPAT, RU 24969, 5-CT, and ICS 205-930 (which display high affinity for 5-HT₁A, 5-HT₁B, 5-HT₁D, and 5-HT₃ sites, respectively) all display relatively low affinities for the sites labeled by (R)-(−)-[^7Br]DOB. Although a significant correlation is observed between drug affinities for (R)-(−)-[^7Br]DOB binding sites and drug affinities for both 5-HT₁ and 5-HT₃ binding sites, the correlation appears to be based on the similarities between these sites on their exact correspondence.

The pharmacological characteristics of the (R)-(−)-[^7Br]DOB binding sites appear to be identical to those of the sites labeled by (+)-[^3H]DOB (1–3). In contrast to our interpretation of the data, Lyon et al. (3) concluded that (+)-[^3H]DOB labels a “high affinity agonist state” of the 5-HT₁ receptor. A number of facts were cited by these authors to support this hypothesis. For example, presumed agonists, but not antagonists, discriminate two subpopulations of 5-HT₁ receptors labeled by [^3H]ketanserin based on the analysis of drug competition curves (18). However, the ability to discriminate two subpopulations of [^3H]ketanserin-labeled 5-HT₁ recognition sites is not agonist specific. For example, trifluoromethylpiperazine displays a 10-fold selectivity for the “high” versus “low” affinity component of [^3H]ketanserin binding, yet trifluoromethylpiperazine is actually a pure antagonist of the 5-HT₁ receptor when analyzed using biochemical models of 5-HT₁ receptor function such as phosphoinositide turnover (19).

A second major observation that Titeler et al. (2) used to support their hypothesis that [^3H]DOB labeled a “high affinity agonist state” of the 5-HT₁ receptor was the effect of 10⁻⁴ M GTP on [^3H]ketanserin-labeled binding sites. Although 10⁻⁴ M GTP had no significant effect on [^3H]ketanserin binding, it did cause a “shift” of putative agonist potencies. In addition, an increase was observed in the Hill slope of the putative agonist competition curves versus [^3H]ketanserin. They suggested that 10⁻⁴ M GTP effectively eliminated the “high affinity agonist state” of the 5-HT₁ receptor (18) with a shift of these sites into a “low affinity agonist state.” By contrast, the present data demonstrate that 10⁻⁴ M GTP does not eliminate (R)-(−)-[^7Br]DOB binding in rat cortex. This concentration of nucleotide appears to induce an approximately 3- to 5-fold decrease in the affinity of (R)-(−)-[^7Br]DOB without changing the density of the binding sites (Fig. 2).

A third fact cited by Titeler and colleagues (1–3) to support their hypothesis was that antagonist potencies at 5-HT₁ sites correlate significantly with their affinity for (R)-(−)-[^7Br]DOB-labeled sites. They did not include drugs that they considered to be “agonists” at the 5-HT₁ receptor. Because the agonist versus antagonist properties of drugs are difficult, and perhaps impossible, to determine from radioligand studies, all drugs were included in the correlations reported in the present report. As noted above, the Kᵢ values for the drugs analyzed in the present study were found to significantly “correlate” with their affinity for both the 5-HT₁ and 5-HT₁c binding sites. In contrast to the conclusion of Titeler and colleagues, we suggest that this correlation implies a similarity, rather than an identity, between the binding sites.

Therefore, we would like to offer an alternative hypothesis to the suggestion of Titeler and colleagues (i.e. that DOB labels a “high affinity agonist state” of the 5-HT₁ receptor). Our conclusion is based on an interpretation of both our own data using (R)-(−)-[^7Br]DOB and the extensive and important work of Titeler and colleagues using (±)-[^3H]DOB. We believe that the available data concerning the unique pharmacological properties of these sites indicate that, at the present time, they should be considered a novel and distinct subset of 5-HT binding sites (17). Furthermore, the pharmacological similarity of these sites to both the 5-HT₁c and 5-HT₂ receptors suggests that the sites labeled by (R)-(−)-[^7Br]DOB may be structurally similar to these other 5-HT receptor subtypes. Additional radioligand, functional, and molecular biological studies are needed before the sites labeled by (R)-(−)-[^7Br]DOB can be more definitively categorized. Given the controversies surrounding the nomenclature of 5-HT recognition sites, it may be best to refer to this site as the “DOB binding site” until such studies are completed.

Another potentially important observation in the present study is the significant correlation that exists between drug affinities for the (R)-(−)-[^7Br]DOB binding site and human hallucinogenic dosages. This correlation has also been reported recently by Titeler et al. (12). In addition, Glennon and Rose-
studies that cannot coincide with the "DOB binding site" described in the present report nor with the 5-HT₁, 5-HT₂, or 5-HT₃ classification system. More recently, Glennon et al. (20) reported a significant correlation between human hallucinogenic doses and 5-HT₂ receptor affinity. Therefore, the (R)-(–)–[77Br]DOB binding site represents the third putative 5-HT receptor for which a significant correlation with hallucinogenic doses has been documented. Although the mechanism of action of hallucinogenic drugs in humans remains unknown, these data suggest that each of the three sites may play a role in the pathophysiology of hallucinosis.

Finally, a central feature of this study was the use of a 77Br-labeled ligand. High specific activity 77Br should facilitate the analysis of radioligand binding in low density regions and/or tissues. In addition, short-lived positron-emitting isotopes of bromine may also be useful in positron emission tomographic scanning techniques. 77Br itself is not appropriate for such studies due to its low positron emission abundance, but the isotope 82Br may be useful as an in vivo radiolabel in human positron emission tomograph studies of hallucinogens. The use of such radiolabeled hallucinogens holds great promise for further study of the mechanism of hallucinogenic drug actions in man.

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References


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