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# Hallucinogenic drug interactions with neurotransmitter receptor binding sites in human cortex

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**Abstract.** The binding affinities of four hallucinogenic agents were analyzed at nine neurotransmitter binding sites in human cortex. *d*-Lysergic acid diethylamide (*d*-LSD), N,N-dimethyltryptamine (DMT), 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) and 1-(2,5-dimethoxy-4-bromophenyl)-2-aminopropane (DOB) display highest affinity for the recently identified "DOB binding site" labeled by $^{77}$Br-R(−)DOB. The phenalkylamines, DOI and DOB, display subnanomolar affinity for the $^{77}$Br-R(−)DOB-labeled site, whereas the indolealkylamines, *d*-LSD and DMT, display nanomolar affinity for this site. *d*-LSD was the most potent of the four hallucinogens at six of the other eight sites analyzed in this study. All four hallucinogens also display high affinity for the 5-hydroxytryptamine$_2$ (5-HT$_2$) receptor subtype, with potencies ranging from 4 to 360 nM. Marked differences in relative affinities were observed between the indolealkylamines and the phenalkylamines at the 5-HT$_{1A}$, 5-HT$_{1D}$, and DOB binding sites. These rank-order differences in affinities are likely to account for the differing effects of these agents in various biochemical and physiological assays.

**Key words:** Hallucinogens – Receptors – Human cortex

*d*-Lysergic acid diethylamide (*d*-LSD) represents the prototypical hallucinogenic agent. However, a number of other chemical structures also induce hallucinations in man. These agents can be divided into two general structural categories: indolealkylamines and phenalkylamines. N,N-Dimethyltryptamine (DMT) and *d*-LSD are examples of indolealkylamines, while 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) and 1-(2,5-dimethoxy-4-bromophenyl)-2-aminopropane (DOB) are examples of phenalkylamines. If hallucinosis derives from drug interactions with a single neurotransmitter receptor, then a common site of action for these two classes of hallucinogens must exist.

At the present time, a commonly accepted hypothesis of hallucinosis states that hallucinogenic agents act as agonists at the 5-hydroxytryptamine$_2$ (5-HT$_2$) receptor (Glennon et al. 1984; Glennon 1985). This theory is based largely on two main observations: human hallucinogenic dosages correlate with drug affinities for the 5-HT$_2$ receptor and certain 5-HT$_2$ antagonists are capable of blocking the discriminative cue properties of hallucinogens (Appel and Cunningham 1986; Glennon et al. 1986). However, hallucinogenic agents also display relatively high affinity for other neurotransmitter receptors in non-human brain membranes (Whitaker and Seeman 1977). Therefore, the present study was designed to analyze hallucinogenic drug interactions (i.e., *d*-LSD, DMT, DOB, DOI) with a series of neurotransmitter receptor binding sites in human cortical membranes.

In addition, the present study also determined the potencies of these agents for the "DOB binding site" in human brain membranes labeled by $^{77}$Br-R(−)DOB. This site was first labeled with $^3$H-DOB by Titeler and colleagues (Titeler et al. 1985; Lyon et al. 1987). The binding density in rat brain membranes was found to be 5% of the 5-HT$_2$ receptor density labeled with $^3$H-ketanserin. More recently, our laboratory (Wang et al. 1988) has used a novel radioligand, $^{77}$Br-R(−)DOB, to label the DOB site in rat cortex. The present study represents the first attempt to use $^{77}$Br-R(−)DOB to label the "DOB binding site" in human brain.

## Materials and methods

Radioligand binding studies were performed as described previously (Peroutka and Snyder 1979; Heuring and Peroutka 1987; Wang et al. 1988). Briefly, human brain samples from adult patients who died from non-neurological diseases were obtained at autopsy from the Department of Pathology, Stanford University Medical Center, the National Neurological Research Bank, or the Canadian Brain Tissue Bank. Tissue samples were rapidly frozen and stored at −70° C until needed. On the day of study, the samples were thawed in Tris-HCl buffer. Tissues were homogenized in 20 volumes Tris-HCl buffer (pH 7.7 at 25° C) using a Brinkmann Polytron and then centrifuged in an IEC B20A centrifuge at 49000 *g* for 10 min. The supernatant was discarded and the pellet was resuspended in the same volume of Tris-HCl buffer and incubated at 37° C for 10 min prior to a second centrifugation at 49000 *g* for 10 min. The final pellet was resuspended in 80 volumes of Tris-HCl buffer containing 10 μM pargyline, 4 mM calcium chloride and 0.1% ascorbic acid. The buffer used for the DOB site analysis consisted of 50 mM Tris-HCl, 0.5 mM EDTA, 10 mM $MgCl_2$, 0.1% ascorbate, and 10 μM pargyline. The suspensions were immediately used in the binding assay. Radioligand binding studies consisted of 0.1 ml $^3$H-radioligand

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(0.3 nM $^3$H-8-OH-DPAT; 1.4 nM $^3$H-5-HT; 0.4 nM $^3$H-spiperone; 0.6 nM $^3$H-WB 4101; 1.5 nM $^3$H-rauwolscine; 0.2 nM $^3$H-dihyroalprenolol hydrochloride (DHA); 3–8 pM $^{77}$Br-R(−)DOB; 0.1 nM $^3$H-quinuclidinyl benzilate (QNB); 0.1 nM $^3$H-flunitrazepam), 0.1 ml buffer or displacing drug and 0.8 ml tissue suspension. Following incubation at 25° C for 30 min, the assays were rapidly filtered under vacuum through #32 glass fiber filters (Schleicher and Schuell; Keene, NH) with two 5 ml washes using 50 mM Tris-HCl buffer. Radioactivity was measured by liquid scintillation spectroscopy in 5 ml 3a70 Counting Cocktail (Research Products International; Mt. Prospect, IL) at 54% efficiency. $^{77}$Br-R(−)DOB radioactivity was measured at 80% efficiency. Specific binding was defined as the excess taken over blanks in the presence of $10^{-5}$ M 5-HT for 5-HT$_{1A}$ and 5-HT$_{1D}$ sites, $10^{-6}$ M cinanserin for 5-HT$_2$ sites, $10^{-6}$ M DOI for DOB sites, $10^{-6}$ M prazosin for alpha$_1$-adrenergic sites, $10^{-4}$ M yohimbine for alpha$_2$-adrenergic sites, $10^{-6}$ M propranolol for beta-adrenergic sites, $10^{-6}$ M scopolamine for muscarinic cholinergic sites, and $10^{-6}$ M diazepam for benzodiazepine sites.

All drugs were diluted and dissolved in assay buffer. Drug sources were as follows: $^3$H-5-HT (20 Ci/mmol), $^3$H-spiperone (21.4 Ci/mmol), $^3$H-WB 4101 (17.6 Ci/mmol), $^3$H-rauwolscine (78.5 Ci/mmol), $^3$H-dihydroalprenolol hydrochloride (DHA) (99.9 Ci/mmol), $^3$H-quinuclidinyl benzilate (QNB) (30.1 Ci/mmol), $^3$H-flunitrazepam (78 Ci/mmol) (Dupont – New England Nuclear, Boston, MA); $^3$H-8-OH-DPAT (100 Ci/mmol; Research Products International Corp., Mount Prospect, IL); $^{77}$Br-R(−)DOB (1875 Ci/mmol; generous gift of Dr Chester A. Mathis, UC Berkeley); 5-HT, diazepam, DMT, scopolamine, yohimbine (Sigma Chemical Co., St Louis, MO); *d*-LSD, DOB, DOI (National Institute on Drug Abuse, Bethesda, MD); cinanserin (E.R. Squibb & Sons, Inc., Princeton, NJ); prazosin (Pfizer Inc., New York, NY); propranolol (Ayerst Lab. Inc., New York, NY).

## Results

### *Drug interactions with 5-hydroxytryptamine binding site subtypes*

Drug competition studies were used to determine the $IC_{50}$ values of the four hallucinogenic agents at putative 5-HT binding sites in human cortex (Table 1). The indolealkylamines (*d*-LSD and DMT) display high affinity (<200 nM) for both 5-HT$_{1A}$ and 5-HT$_{1D}$ binding sites. By contrast, the phenalkylamines (DOI and DOB) display affinities

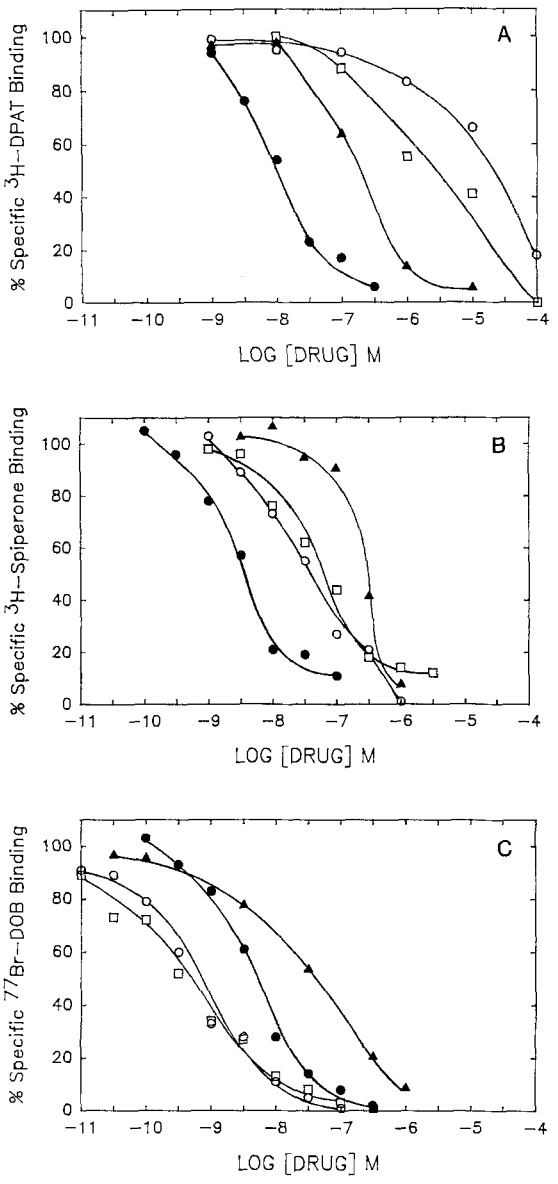


**Fig. 1A–C.** *d*-LSD, DMT, DOB, and DOI competition studies with 5-HT binding site subtypes in human cortex. Radioligand studies were performed as described in Materials and methods. Data shown are the results of a single experiment performed in triplicate. Each experiment was repeated three to five times. Drugs analyzed are ● *d*-LSD, ▲ DMT, ○ DOI and □ DOB. **A** Competition curves for the 5-HT$_{1A}$ site labeled by $^3$H-8-OH-DPAT. **B** Competition curves for the 5-HT$_2$ site labeled by $^3$H-spiperone. **C** Competition curves for the "DOB binding site" labeled by $^{77}$Br-R(−)DOB

**Table 1.** Hallucinogenic drug interactions with human 5-HT binding site subtypes. Radioligand binding assays were performed using human cortex membranes as described in Materials and methods. $IC_{50}$ values were determine dusing log probit analysis. Values shown are the means ± standard errors of three to five experiments, each performed in triplicate

| Human binding site | Radioligand | $IC_{50}$ values (nM) | | | |
|---|---|---|---|---|---|
| | | *d*-LSD | DMT | DOI | DOB |
| 5-HT$_{1A}$ | $^3$H-8-OH-DPAT | 7±2 | 170±9 | 19000 ±3000 | 9000 ±800 |
| 5-HT$_{1D}$ | $^3$H-5-HT | 56±16 | 138±1 | 2400 ±700 | 2800 ±500 |
| 5-HT$_2$ | $^3$H-Spiperone | 4±0.2 | 360±20 | 32 ±3 | 41 ±7 |
| DOB | $^{77}$Br-R(−)DOB | 4±0.5 | 12±1 | 0.4±0.1 | 0.2±0.01 |

**Table 2.** Hallucinogenic drug interactions with human neurotransmitter binding sites. Radioligand binding assays were performed using human cortex membranes as described in Materials and methods. $IC_{50}$ values were determined using log probit analysis. Values shown are the means ± standard errors of three to five experiments, each performed in triplicate

| Human binding site | Radioligand | $IC_{50}$ values (nM) | | | |
|---|---|---|---|---|---|
| | | *d*-LSD | DMT | DOI | DOB |
| $Alpha_1$-adrenergic | $^3$H-WB-4101 | 500 ± 200 | 4400 ± 700 | 12000 ± 500 | 11000 ± 500 |
| $Alpha_2$-adrenergic | $^3$H-Rauwolscine | 19 ± 2 | 1200 ± 400 | 1900 ± 90 | 4000 ± 400 |
| Beta-adrenergic | $^3$H-DHA | 600 ± 80 | > 100000 | 3800 ± 800 | 5700 ± 1000 |
| Muscarinic cholinergic | $^3$H-QNB | > 100000 | 88000 ± 10000 | 4700 ± 400 | 10000 ± 2000 |
| Benzodiazepine | $^3$H-Flunitrazepam | > 100000 | > 100000 | > 100000 | > 100000 |

greater than 2000 nM at the 5-$HT_{1A}$ and 5-$HT_{1D}$ binding site subtypes. A representative competition study of the hallucinogens at 5-$HT_{1A}$ sites labeled by $^3$H-8-OH-DPAT is shown in Fig. 1 A.

All four hallucinogens display high affinity for the 5-$HT_2$ receptor site labeled by $^3$H-spiperone (Table 1 and Fig. 1 B). Potencies range from 4 to 360 nM, with *d*-LSD displaying the highest affinity and DMT displaying the lowest affinity for this receptor. The phenalkylamines, DOB and DOI, display an intermediate affinity for the 5-$HT_2$ binding site.

The four hallucinogens are most potent at the "DOB binding site" in human cortex labeled by $^{77}$Br-R(−)DOB (Table 1 and Fig. 1 C). The phenalkylamines DOB (0.20 ± 0.01 nM) and DOI (0.40 ± 0.10 nM) display subnanomolar affinity for the DOB site. Their affinity for this site is two orders of magnitude greater than for the 5-$HT_2$ receptor. *d*-LSD is equipotent (4 nM) at the "DOB binding site" and the 5-$HT_2$ receptor, while DMT displays 30-fold higher affinity for the DOB site (12 ± 1 nM) as compared with the 5-$HT_2$ binding site (Table 1).

*Drug interactions with other neurotransmitter binding sites*

*d*-LSD displays high affinity (19 ± 2 nM) for $alpha_2$-adrenergic binding sites in human cortex labeled by $^3$H-rauwolscine (Table 2). *d*-LSD also displays submicromolar affinity for $alpha_1$-adrenergic and beta-adrenergic receptor sites. DMT is considerably less potent (approximately 100-fold) than *d*-LSD at both the $alpha_2$-adrenergic receptor and the beta-adrenergic receptor. The phenalkylamines (DOI and DOB) display micromolar or greater affinity for the five neurotransmitter binding sites listed in Table 2. All four hallucinogens are essentially inactive at the muscarinic cholinergic binding site labeled by $^3$H-QNB and the benzodiazepine binding site labeled by $^3$H-flunitrazepam.

## Discussion

The major finding of the present study is that hallucinogens interact differentially with a number of biogenic amine neurotransmitter binding sites in human cortical membranes. The indolealkylamines (*d*-LSD, DMT) display high affinity (≤ 360 nM) for all four of the 5-HT binding site subtypes analyzed (5-$HT_{1A}$, 5-$HT_{1D}$, 5-$HT_2$, "DOB binding site"). *d*-LSD also displays high affinity for $alpha_2$-adrenergic receptors. By contrast, the phenalkylamines (DOI, DOB) display nanomolar affinity only for the 5-$HT_2$ binding site and the "DOB binding site". The characterization of differential hallucinogenic drug affinities for multiple human binding sites should prove to be a useful tool for determining the receptor subtypes active in various effector systems.

Differential effects of indolealkylamines and phenalkylamines have been noted in multiple systems. Electrophysiological studies have shown that indolealkylamines, but not phenalkylamines, directly inhibit the intrinsic firing of dorsal raphe units in rat (Aghajanian et al. 1970; Haigler and Aghajanian 1973) and cat (Trulson et al. 1981). Biochemical studies have demonstrated the indolealkylamines suppress 5-HT metabolism and decrease levels of 5-hydroxyindoleacetic acid (Freedman et al. 1970) and increase synaptosomal levels of 5-HT (Halaris 1982). In these studies, phenalkylamines did not produce these effects. Similarly, indolealkylamines, but not phenalkylamines, display relatively high affinity for 5-$HT_{1A}$ and 5-$HT_{1D}$ binding sites in human brain. The differential effects of the indolealkylamines and phenalkylamines in each of these models makes it unlikely that their similar hallucinogenic effects are mediated by these receptor systems.

Glennon et al. (1984) have suggested that a single receptor, the 5-$HT_2$ receptor, mediates hallucinogenic effects in the human. In terms of human hallucinogenic dosages, *d*-LSD (0.05–0.1 mg) is an order of magnitude more potent than DOI or DOB (0.8–2 mg), while DMT (parenteral dose = 75–100 mg) is two orders of magnitude weaker than DOI or DOB (Glennon and Rosecrans 1982; Glennon et al. 1984). If hallucinosis is caused by drug interactions with a single receptor, then potencies of hallucinogenic agents at this receptor should correlate with the rank order of their human doses. Based on the analysis of the nine binding sites analyzed in the present study, the 5-$HT_2$ receptor does appear to be the most likely candidate for a single-receptor theory of hallucinosis. Indeed, Glennon et al. (1984) have shown a significant correlation between the human doses of 15 hallucinogens and their $K_i$ values for the 5-$HT_2$ receptor in the rat.

Glennon and colleagues have further hypothesized that hallucinosis occurs as a result of direct agonist effects at the 5-$HT_2$ receptor. In support of this theory, they have shown a correlation between $K_i$ values for a number of hallucinogens and discriminative cue $ED_{50}$ values using DOM as the training drug (Glennon et al. 1984). These data are supported by other discriminative cue studies (Glennon et al. 1983; Colpaert et al. 1985; Nielsen et al. 1985; Appel and Cunningham 1986). However, non-hallucinogenic drugs such as lisuride (White and Appel 1982),

yohimbine (Colpaert 1984) and fenfluramine Winter 1980) also generalize to hallucinogenic cues. Furthermore, spiperone (Colpaert et al. 1982), a potent 5-$HT_2$ antagonist, is not able to block hallucinogenic cues.

Other experimental evidence suggests that hallucinogens may not be direct-acting agonists at the 5-$HT_2$ receptor. Recent studies in our laboratory (Pierce and Peroutka 1987; unpublished observations) determined the ability of *d*-LSD to affect $5HT_2$-mediated phosphatidylinositol (PI) turnover in rat cortex (Conn and Sanders-Bush 1984, 1985; Kendall and Nahorski 1985). Nanomolar concentrations of *d*-LSD did not stimulate PI turnover yet significantly inhibited the stimulatory effect of micromolar concentrations of 5-HT on PI turnover. DOB and DOI, on the other hand, acted as partial agonists of the 5-$HT_2$-mediated turnover of PI in rat cortical slices. In addition, we have observed that $10^{-4}$ M GTP does not affect *d*-LSD competition with 5-$HT_2$ receptors labeled by $^3$H-ketanserin, a finding which suggests that *d*-LSD is not acting as an agonist at this receptor (Battaglia et al. 1984). Therefore, although the rank-order potencies of the four hallucinogens at the 5-$HT_2$ receptor in human brain does appear to correlate with human dosages, further studies are needed to determine whether the drugs share a similar pattern of agonist versus antagonist effects at this receptor site.

Another possible candidate for a single receptor site which mediates hallucinosis is the recently identified "DOB binding site" labeled by $^3$H-DOB (Titeler et al. 1985; Lyon et al. 1987) or $^{77}$Br-R(−)DOB (Wang et al. 1988). The four hallucinogens display the highest affinity for this site as compared to the other eight binding sites examined in the present study. However, *d*-LSD has a 10-fold lower affinity for this binding site than DOB or DOI, in contrast to its being 10-fold more potent as a human hallucinogen. Nonetheless, the high affinity of the four hallucinogens for the "DOB binding site" suggests that it plays a role in some of the physiological effects of hallucinogens.

In conclusion, the four hallucinogens analyzed in the present study interact differentially with a variety of binding sites in human brain. It is conceivable that a single receptor subtype mediates hallucinosis. If so, the 5-$HT_2$ receptor and the "DOB bindig site" are likely candidates, since all four hallucinogens display high affinity for these sites. Alternatively, an as yet undefined single receptor site may mediate hallucinosis. On the other hand, it is possible that hallucinogens might exert their effects by modulating neuronal function via multiple receptors. Future studies using novel radioligands (e.g., $^{77}$Br-R(−)DOB) and human positron emission tomography (PET) may be useful in elucidating the mechanism of action of hallucinogenic drugs in man.

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## References

Aghajanian GK, Foote WE, Sheard MH (1970) Action of psychotogenic drugs on single midbrain raphe neurons. J Pharmacol Exp Ther 171:178–187

Appel JB, Cunningham KA (1986) The use of drug discrimination procedures to characterize hallucinogenic drug actions. Psychopharmacol Bull 22:959–967

Battaglia G, Shannon M, Titeler M (1984) Guanyl nucleotide and divalent cation regulation of cortical $S_2$ serotonin receptors. J Neurochem 43:1213–1219

Colpaert FC (1984) Cross generalization with LSD and yohimbine in the rat. Eur J Pharmacol 102:541–544

Colpaert FC, Niemegeers CJE, Janssen PAJ (1982) A drug discrimination analysis of lysergic acid diethylamide (LSD): in vivo agonist and antagonist effects of purported 5-hydroxytryptamine antagonists and of pirenperone, a LSD antagonist. J Pharmacol Exp Ther 221:206–214

Colpaert FC, Meert TF, Niemegeers CJE, Janssen PAJ (1985) Behavioral and 5-HT antagonist effects of ritanserin: a pure and selective antagonist of LSD discrimination in rat. Psychopharmacology 86:45–54

Conn PJ, Sanders-Bush E (1984) Selective 5-$HT_2$ antagonists inhibit serotonin stimulated phosphatidylinositol metabolism in cerebral cortex. Neuropharmacology 23:993–996

Conn PJ, Sanders-Bush E (1985) Serotonin-stimulated phosphoinositide turnover: mediation by the $S_2$ binding site in rat cerebral cortex but not in subcortical regions. J Pharmacol Exp Ther 234:195–203

Freedman DX, Gottlieb R, Lovell RA (1970) Psychotomimetic drugs and brain 5-hydroxytryptamine metabolism. Biochem Pharmacol 19:1181–1188

Glennon RA (1985) Involvement of serotonin in the action of hallucinogenic drugs. In: Green AR (ed) Neuropharmacology of serotonin. Oxford University Press, Oxford, pp 253–280

Glennon RA, Rosecrans JA (1982) Indolealkylamine and phenalkylamines hallucinogens: a brief overview. Neurosci Behav Rev 6:489–497

Glennon RA, Young R, Rosecrans JA (1983) Antagonism of the effects of the hallucinogen DOM and the purported 5-HT agonist quipazine by 5-$HT_2$ antagonists. Eur J Pharmacol 91:189–196

Glennon RA, Titeler M, McKenney JD (1984) Evidence for 5-$HT_2$ involvement in the mechanism of action of hallucinogenic agents. Life Sci 35:2505–2511

Glennon RA, Titeler M, Young R (1986) Structure-activity relationships and mechanism of action of hallucinogenic agents based on drug discrimination and radioligand binding studies. Psychopharmacol Bull 22:953–958

Haigler HJ, Aghajanian GK (1973) Mescaline and LSD: direct and indirect effects on serotonin-containing neurons in brain. Eur J Pharmacol 21:53–60

Halaris AE (1982) Nerve terminal effects of indoleamine psychotomimetics on 5-hydroxytryptamine. Neurosci Behav Rev 6:483–487

Heuring RE, Peroutka SJ (1987) Characterization of a novel $^3$H-5-hydroxytryptamine binding site subtype in bovine brain membranes. J Neurosci 7:894–903

Kendall DA, Nahorski SR (1985) 5-hydroxytryptamine-stimulated inositol phospholipid hydrolysis in rat cerebral cortex slices: Pharmacological characterization and effects of antidepressants. J Pharmacol Exp Ther 233:473–479

Lyon RA, Davis KH, Titeler M (1987) $^3$H-DOB (4-bromo-2,5-dimethoxyphenylisopropylamine) labels a guanyl nucleotide-sensitive state of cortical 5-$HT_2$ receptors. Mol Pharmacol 31:194–199

Nielson EB, Ginn SR, Cunningham KA, Appel JB (1985) Antagonism of the LSD cue by putative serotonin antagonists: relationship to inhibition of in vivo $^3$H-spiroperidol binding. Behav Brain Res 16:171–176

Peroutka SJ, Snyder SH (1979) Multiple serotonin receptors: differential binding of $^3$H-5-hydroxytryptamine, $^3$H-lysergic acid diethylamide and $^3$H-spiroperidol. Mol Pharmacol 16:687–699

Pierce PA, Peroutka SJ (1987) Correlation of psychotropic drug effects at neurotransmitter receptors with phosphatidylinositol hydrolysis in rat cerebral cortex. Soc Neurosci Abstr 13:801

Titeler M, Herrick K, Lyon RA, McKenney JD, Glennon RA (1985) $^{3}$H-DOB: a specific agonist radioligand for 5-$HT_2$ serotonin receptors. Eur J Pharmacol 117:145–146

Trulson ME, Heym J, Jacobs BL (1981) Dissociations between the effects of hallucinogenic drugs on behavior and raphe unit activity in freely moving cats. Brain Res 215:275–293

Wang SSH, Mathis CA, Peroutka SJ (1988) R(−)$^{77}$Br-2,5-Dimethoxy-4-bromoamphetamine ($^{77}$Br−DOB): a novel radioligand which labels a 5-hydroxytryptamine binding site subtype. Psychopharmacology 94:431–432

Whitaker PM, Seeman P (1977) Hallucinogen binding to dopamine/neuroleptic receptors. J Pharm Pharmacol 29:506–507

White FJ, Appel JB (1982) Training dose as a factor in LSD-saline discrimination. Psychopharmacology 76:20–25

Winter JC (1980) Effects of the phenethylamine derivatives, BL-3912, fenfluramine, and Sch-12679, in rats trained with LSD as a discriminative stimulus. Psychopharmacology 68:159–162

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