ELSEVIER

European Journal of Pharmacology 343 (1998) 145–150

ejp

Antagonistic effects of β-phenylethylamine on quinpirole- and (−)-sulpiride-induced changes in evoked dopamine release from rat striatal slices

Shigeto Yamada *, Mutsuo Harano, Masatoshi Tanaka

Institute of Brain Diseases, School of Medicine, Kurume University, Asahi-machi 67, Kurume, Fukuoka 830, Japan

Received 7 August 1997; revised 11 November 1997; accepted 14 November 1997

Abstract

To assess the role of β-phenylethylamine in aspects of dopamine release, we measured the level of β-phenylethylamine in the rat striatum after killing the rats by microwave irradiation. We then investigated the effect of β-phenylethylamine on electrically evoked dopamine release from rat striatal slices in vitro. The striatal β-phenylethylamine level was 46.5 ± 3.5 ng/g wet tissue, equivalent to 0.3 μmol/l. Superfusion with low concentrations of β-phenylethylamine up to 1 μmol/l had no effect on spontaneous or electrically evoked dopamine release from striatal slices. Quinpirole reduced the evoked dopamine release from slices in a concentration-dependent manner. The quinpirole-induced reduction of evoked dopamine release was attenuated 30% by superfusion with 0.3 μmol/l β-phenylethylamine. Moreover, the (−)-sulpiride (0.1 μmol/l)-induced increase in evoked dopamine release was also attenuated by superfusion with 0.3 μmol/l β-phenylethylamine. These data indicate that submicromolar levels of β-phenylethylamine could modify the dopamine autoreceptor mediated changes in evoked dopamine release from rat striatal slices. © 1998 Elsevier Science B.V.

Keywords: β-Phenylethylamine; Dopamine release, electrically evoked; Quinpirole; (−)-Sulpiride

1. Introduction

β-Phenylethylamine is a trace amine in mammalian tissues with a chemical structure and pharmacological and behavioral effects, that closely resemble those of amphetamines (Wolf and Mosnaim, 1983). β-Phenylethylamine is synthesized in dopaminergic neurons of the nigrostriatal system (Greenshaw et al., 1986) and released by diffusion. The rate of diffusion is dependent on the rate of synthesis (Paterson et al., 1990; Juorio et al., 1991). Because of the low endogenous concentration of β-phenylethylamine in the brain (Durden et al., 1973; Saavedra, 1974; Reynolds et al., 1980; Huebert et al., 1994) and its relatively low potency in behavioral (Antelman et al., 1977; Dourish and Cooper, 1984) and pharmacological (Philips, 1986; Bailey et al., 1987) experiments, there has been much discussion as to whether endogenous β-phenylethylamine has any physiological role. However, the rate of synthesis of β-phenylethylamine in the rat brain is similar to that of dopamine and almost four times that of noradrenaline (Durden and Philips, 1980). Recently, it was reported that low doses of β-phenylethylamine cause ipsilateral rotational behavior in rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine system (Barroso and Rodrigez, 1996). Low dose β-phenylethylamine also causes substantial potentiation of the postsynaptic actions of dopamine and noradrenaline (Paterson et al., 1991). These data indicate that β-phenylethylamine undergoes extremely rapid turnover in the brain and may act in vivo as a neuromodulator (Paterson et al., 1990). However, little is known concerning how β-phenylethylamine affects dopaminergic transmission under physiological conditions. The present study was conducted to assess the effects of β-phenylethylamine on quinpirole-induced reduction and (−)-sulpiride-induced enhancement of electrically evoked dopamine release from striatal slices in rats, which represent the function of the release modulating dopamine autoreceptors (Arbilla and Langer, 1981;

* Corresponding author. Tel.: +81-942-353311; fax: +81-942-317708; e-mail: s-yamada@kurume.ktarn.or.jp

Yamada et al., 1993). The striatal level of endogenous β-phenylethylamine was also measured after killing of the rats either by decapitation or microwave irradiation.

2. Materials and methods

2.1. DA release from striatal slices

Male Wistar rats weighing 250 to 300 g were used. The animals were housed in a light-, humidity- and temperature-controlled environment for more than 7 days before the experiments. They were killed by decapitation between 9.00 and 10.00 a.m. The brains were rapidly removed and the slices obtained were put in ice-cold Krebs solution aerated with 95% O_2 and 5% CO_2. Four slices, each 0.3 mm thick, were made with a Micro Slicer (Dohan EM. Co.) at A9760 to A7630, according to the atlas of Konig and Klippel (1963). One slice was used for control experiments (superfusion without drugs) and three were used for perfusion with β-phenylethylamine and/or quinpirole. The striatal tissue in the slices was punched out with a metal tube (3 mm inner diameter). One striatal slice was placed in a chamber made from a Plexiglass tube in which platinum electrodes had been mounted to stimulate the slice. The slice was then superfused with Krebs solution and aerated with 95% O_2 and 5% CO_2, at a flow rate of 0.7 ml/min, at 37°C. The composition of the Krebs solution (in mmol/l) was: NaCl, 118.0; KCl, 4.9; $NaHCO_3$, 25.0; NaH_2PO_4, 1.25; $CaCl_2$, 1.25; $MgCl_2$, 1.18 and glucose, 11.0, together with nomifensine (3 μmol/l). After 30 min of superfusion, electrical field stimulation was performed with platinum spiral electrodes set up at the end of the chamber. The stimuli were 20 mA rectangular pulses, 2 ms in duration, with a frequency of 1 Hz, applied for 2 min, 30 min (S1) and 62 min (S2) after the beginning of the superfusion. Various concentrations of β-phenylethylamine (0.1–1 μmol/l) with or without 1 μmol/l quinpirole, a dopamine D_2 receptor agonist, or 0.1 μmol/l (−)-sulpiride, a dopamine D_2 receptor antagonist, were added to the superfusion medium 15 min before S2. In another experiment, various concentrations of quinpirole (0.1, 0.3, 1 and 3 μmol/l) were added at 15 min before S2 to the superfusion medium with or without 0.5 μmol/l β-phenylethylamine. The superfusate was collected in tubes, as the 7-min fraction. Dopamine released into the superfusate was adsorbed onto alumina, eluted with 300 μl of 0.1 mol/l acetic acid and quantified by high performance liquid chromatography with electrochemical detection (HPLC-ECD). The HPLC method used has been described previously (Yamada et al., 1993). The dopamine release evoked during S1 and S2 was calculated by subtracting the spontaneous dopamine release from the total release. The spontaneous dopamine release during each stimulation, assessed from the sample collected during the 7-min period preceding each stimulation, was expressed as sp1 and sp2, respectively.

2.2. Determination of β-phenylethylamine level in the rat striatum

Rats were killed either by decapitation or by microwave irradiation. The microwave was set at 5 kW for a duration of 1.3 s. Each brain was quickly removed and the striatum was dissected, then stored at −80°C until analysis. Extraction of β-phenylethylamine from the striatum was performed with a previously reported method (Yamada et al., 1994a). In short, the striatal tissue was homogenized with 1 ml of 0.1 mol/l formic acid and centrifuged at $10\,000 \times g$ for 5 min. 50 ng of deuterium-labeled β-phenylethylamine was added to 0.5 ml of the supernatant as an internal standard and the mixture was kept at 5°C for 15 min for equilibration. Following the addition of 0.2 ml of 5 M NaOH, the sample was applied to an Extrelut column (3.5×1 cm, Merck) for 15 min, then eluted with 7 ml of ethyl acetate. The eluate was collected in a tube and evaporated under a gentle stream of dry nitrogen gas. The residue was then derivatized with 50 μl of pentafluoropropionate anhydrous at 60°C for 30 min. The solvent was evaporated to dryness with dry nitrogen gas and the sample was reconstituted with 20 μl of ethyl acetate. 1 μl of the solution was injected into a gas chromatography-chemical ionization-mass spectrometer (GC-CI-MS). GC-CI-MS analysis was carried out with a Hitachi M-80B (Hitachi, Japan) double-focused mass spectrometer interfaced to a data acquisition system. Isobutane served as the CI reagent gas (source pressure 4×10^{-6} Torr). Helium was used as the GC carrier gas (40 ml/min). The GC-MS interface oven and transfer line were set at 220°C. A megabore column (0.56 mm i.d., 15 m long, J&W Co.) coated with DB-1 was used. The oven temperature was maintained isothermally at 130°C. For the selected ion monitoring study, m/z 268 and 272 (MH^+ for β-phenylethylamine-pentafluoropropionate and d4-β-phenylethylamine-pentafluoropropionate) were monitored. Peak area measurements were used for the estimation of ion currents.

2.3. Data analysis

Values are expressed as ng of dopamine/mg protein in a slice per 7-min fraction or as the S2/S1 ratio (mean ± S.E.M.). The striatal level of β-phenylethylamine was expressed as ng/g wet tissue (mean ± S.E.M.). Statistical comparisons were performed using one way or two way analyses of variance (ANOVA), followed by Scheffe's *F*-test for the superfusion experiments and Student's *t*-test for the striatal level of β-phenylethylamine.

3. Results

3.1. Effects of β-phenylethylamine on dopamine release from the striatal slices

The spontaneous release of dopamine was 0.32 ± 0.01 ng/mg protein per 7-min fraction (mean ± S.E.M., $n = 16$, where n represents the number of slices taken from eight

Table 1
Effects of 2-phenylethylamine on dopamine release from rat striatal slices

PEA concentration		Basal DA release		Evoked DA realease
μM	*n*	sp2/sp1 ratio	*n*	S2/S1 ratio
0	16	1.04 ± 0.03	16	1.13 ± 0.05
0.1	9	1.06 ± 0.06	9	1.02 ± 0.03
0.3	16	1.07 ± 0.014	16	1.18 ± 0.04
1	16	1.12 ± 0.03	16	1.11 ± 0.06
10	6	1.37 ± 0.04*	6	0.82 ± 0.05*

PEA, 2-phenylethylamine; DA, dopamine.
Value is mean ratio ± S.E.M., *n* represents the number of slices from 3 to 8 rats.
* $P < 0.05$, compared to the control ratio.

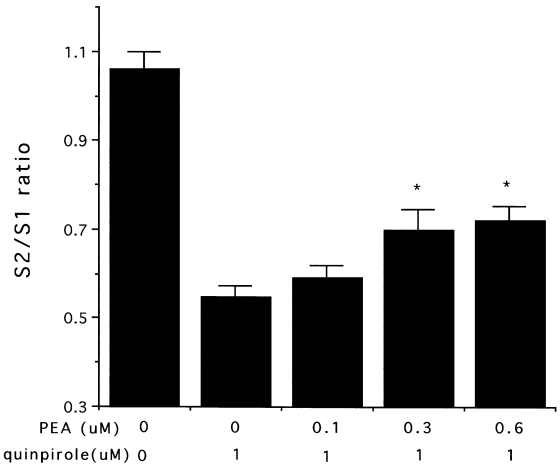

Fig. 1. Effects of β-phenylethylamine on the quinpirole-induced reduction of evoked dopamine release from striatal slices in the rat. The quinpirole-induced reduction of evoked dopamine release was attenuated by superfusion with β-phenylethylamine (one-way ANOVA $F(3, 27) = 6.01$, $P = 0.003$; * $P < 0.05$, compared to quinpirole group, Scheffe's test, $n = 7–8$ in each group, *n* represents number of slices taken from 4 animals). Values are mean ± S.E.M. of S2/S1 ratios.

animals). Electrical stimulation induced a significant increase in dopamine release, five-fold greater than the spontaneous release (1.67 ± 0.24 ng/mg protein per fraction). The control S2/S1 value was 1.13 ± 0.05. The spontaneous dopamine release from the striatum was unchanged by concentrations of β-phenylethylamine up to 1 μmol/l, but was increased by superfusion with β-phenylethylamine concentrations higher than 10 μmol/l (Table 1). The evoked dopamine release was not changed by superfusion with low concentrations of β-phenylethylamine (0.1 to 1 μmol/l, Table 1). The dopamine D2 receptor agonist, quinpirole (0.1 to 3 μmol/l), reduced the evoked dopamine release from striatal slices in a concentration dependent manner (96.3% of control for 0.1 μmol/l; 61.1% for 0.3 μmol/l; 55.6% for 1 μmol/l; 58.3% for 3 μmol/l). This reduction in evoked dopamine release was attenuated when the slice was superfused with 0.5 μmol/l of β-phenylethylamine (95.7% of control for 0.1 μmol/l quinpirole; 72.4% for 0.3 μmol/l; 69.8% for 1 μmol/l; 68.1% for 3 μmol/l) (two way ANOVA, treatment, $F(1, 40) = 17$, $P = 0.00015$, Table 2). Moreover, the quinpirole (1 μmol/l)-induced reduction of evoked dopamine release was also attenuated by superfusion with β-phenylethylamine (0.1 to 0.6 μmol/l, ANOVA, $F(3, 27) = 6.01$, $P = 0.003$, Fig. 1). The dopamine receptor antagonist, (−)-sulpiride (0.1 μmol/l), enhanced the evoked dopamine release by 188%. This effect was significantly attenuated by superfusion with 0.3 μmol/l β-phenylethylamine or 1 μmol/l β-phenylethylamine (ANOVA $F(2, 21) = 6.58$, $P = 0.006$, Fig. 2).

Table 2
Effects of 2-phenylethylamine on quinpirole-induced reduction of evoked dopamine release from rat striatal slices

Quinpirole conc.		Evoked DA release (S2/S1 ratio)		
μM	*n*	without PEA	*n*	with PEA (0.5 μM)
0	12	1.08 ± 0.08	12	1.16 ± 0.04
0.1	6	1.04 ± 0.06	6	1.11 ± 0.04
0.3	6	0.66 ± 0.06[a]	6	0.84 ± 0.08[bc]
1	6	0.60 ± 0.04[a]	6	0.81 ± 0.05[ac]
3	6	0.63 ± 0.04[a]	6	0.79 ± 0.05[ad]

DA, dopamine; PEA, 2-phenylethylamine; conc., concentration. two-way ANOVA, treatment $F(1, 40) = 17.63$; $P = 0.00015$.
[a] $P < 0.01$.
[b] $P < 0.05$ compared to each control (quinpirole absent).
[c] $P < 0.01$.
[d] $P < 0.05$, compared to the same concentration of quinpirole without PEA.
Value is mean ratio ± S.E.M., *n* represents the number of slices from 3 to 6 rats.

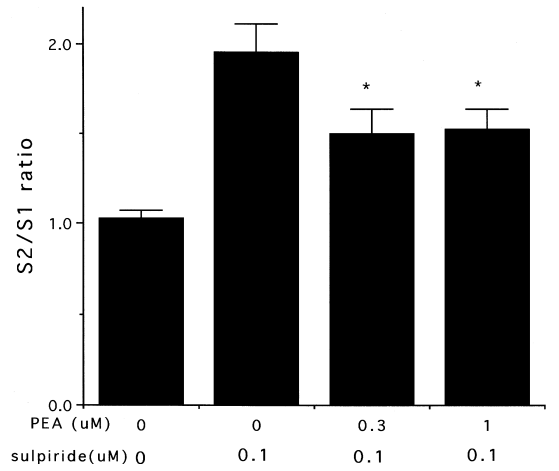

Fig. 2. Effect of β-phenylethylamine on the (−)-sulpiride-induced increase in evoked dopamine release from striatal slices in the rat. The (−)-sulpiride-induced increase in the evoked dopamine release was attenuated by superfusion with β-phenylethylamine (one way ANOVA $F(2, 21) = 6.58$, $P = 0.006$; * $P < 0.05$, compared to (−)-sulpiride group, Scheffe's *F*-test, $n = 8$ in each group, *n* represents number of slices taken from 4 animals). Values are mean ± S.E.M. of S2/S1 ratios.

3.2. Striatal level of β-phenylethylamine

Rats killed by microwave irradiation had striatal β-phenylethylamine levels of 46.1 ± 3.42 ng/g wet tissue (mean ± S.E.M., $n = 8$), a level seven-fold higher than that seen following decapitation (6.3 ± 0.41 ng/g wet tissue, mean ± S.E.M., $n = 5$, Student's t-test, $t = 3.2$, $P < 0.01$).

4. Discussion

The striatal level of β-phenylethylamine in rats killed by decapitation was comparable to the levels reported in previous studies (Lauber and Waldmeier, 1984; Juorio, 1988; Boulton et al., 1990). However, when rats were killed by microwave irradiation, the striatal level of β-phenylethylamine was seven-fold higher than that associated with decapitation. It has been reported previously that the level of β-phenylethylamine in the whole rat brain after killing with microwave irradiation is twice that seen after decapitation (Lauber and Waldmeier, 1984). Our results indicate that β-phenylethylamine has an extremely rapid turnover rate in the brain, which is compatible with a previous report that the half-life of the endogenous pool of β-phenylethylamine is 0.4 min (Durden and Philips, 1980). Since it takes less than 1.3 s to stop the oxidative deamination of β-phenylethylamine, the physiological concentration of β-phenylethylamine in the striatum would be approximately 0.3 μmol/l. In our study, low concentrations of β-phenylethylamine up to 1 μmol/l had no effect on the spontaneous dopamine release from striatal slices, but 10 μmol/l β-phenylethylamine caused a 32% increase in spontaneous dopamine release (Table 1). Substantial evidence suggests that β-phenylethylamine stimulates the release of dopamine from synaptosomes (Raiteri et al., 1977), striatal slices (Dyck, 1983) and in the perfusate from a cannula in vivo (Philips and Robson, 1983). This dopamine release is thought to be from the cytoplasmic dopamine pool and carrier-mediated and Ca^{2+} independent (Liang and Rutledge, 1982; McMillen, 1983). As the tissue was superfused with nomifensine in the present experiment, β-phenylethylamine may enter the cell membrane by simple diffusion. β-Phenylethylamine (10 μmol/l) caused a reduction of the dopamine release induced by electrical stimulation (Table 1). High concentrations of β-phenylethylamine may reduce the amount of dopamine in the synaptic vesicles, resulting in the reduction of depolarization-induced dopamine release from synaptic vesicles as reported by Kamal et al. (1983) who studied the effect of amphetamine on evoked dopamine release, or the β-phenylethylamine-induced increase in basal release of dopamine may activate dopamine autoreceptors to reduce the evoked dopamine release from the slices. However, all these effects were observed at higher concentrations of β-phenylethylamine (more than 5 μmol/l; Raiteri et al., 1977; Dyck, 1983; Philips and Robson, 1983). In electrophysiological studies, iontophoretic application of β-phenylethylamine potentiates caudate neuron responses to the iontophoretic application of dopamine and to electrical stimulation of the substantia nigra (Paterson et al., 1991). Partial agonistic properties of β-phenylethylamine at α_1-adrenoceptors in rat aortic strips and cerebral cortex have been reported when high concentrations (> 26 μmol/l) of β-phenylethylamine was applied (Hausen et al., 1980; Dyck and Boulton, 1989). However, no one has been able to show a direct interaction of submicromolar concentrations of β-phenylethylamine at any site other than monoamine oxidase type B (EC1.4.3.4, Li et al., 1992) and dopamine-induced change in membrane fluidity (Harris et al., 1988). In our study, a low concentration (0.3 μmol/l) of β-phenylethylamine alone had little effect on spontaneous or evoked dopamine release, but had an inhibitory effect on the quinpirole-induced reduction or (−)-sulpiride-induced enhancement of evoked dopamine release. This is the first report of a significant effect of submicromolar concentrations of β-phenylethylamine on dopamine neurotransmission. Dopamine D2 receptor agonists reduce and D2 receptor antagonists enhance the evoked dopamine release either by activation or blockade of release-modulating dopamine autoreceptors at dopamine nerve terminals (Farnebo and Hamberger, 1971; Arbilla and Langer, 1981; Starke et al., 1983; Parker and Cubeddu, 1985; Lane and Blaha, 1986; Yamada et al., 1993, 1994b). The present results indicate that β-phenylethylamine interacted with dopamine autoreceptor-mediated changes in the evoked dopamine release. The mechanism underlying the partial agonist-like properties of β-phenylethylamine for dopamine autoreceptors remains unknown. Chronic administration of a low dose of β-phenylethylamine (10 mg/kg for 28 days) caused a down-regulation of dopamine D2 receptors in rats (Paetsch and Greenshow, 1993), indicating that β-phenylethylamine could affect the function of dopamine D2 receptors. High-affinity binding sites for [^{3}H]β-phenylethylamine have been reported (Hauger et al., 1982) but which were mainly to monoamine oxidase type B and specific binding sites for [^{3}H]β-phenylethylamine have not been reported (Li et al., 1992). This latter report showed that specific binding of [^{3}H]β-phenylethylamine at more than 0.3 μmol/l was found even in the presence of monoamine oxidase inhibitors (Li et al., 1992). The data indicate that a low-affinity binding site for β-phenylethylamine should not be ruled out. β-phenylethylamine is catabolized by monoamine oxidase type B (Philips and Boulton, 1979). Monoamine oxidase inhibitors, including phenelzine, which is catabolized to β-phenylethylamine in vivo (Paetsch and Greenshow, 1993), (−)-deprenyl and pargyline which have a structure similar to that of β-phenylethylamine, inhibit [^{3}H]quinpirole binding in rat striatal membranes (Levant et al., 1993). β-Phenylethylamine may inhibit the quinpirole-induced reduction of evoked dopamine release by inhibiting the binding of

quinpirole. Further study would be necessary to determine whether β-phenylethylamine displaces quinpirole and sulpiride from their binding to dopamine D_2 receptors. The presence of nomifensine, a dopamine uptake inhibitor, in the Krebs solution that increased dopamine levels in the synaptic cleft, may have resulted in tonic activation of the dopamine autoreceptors. This may have modified the effects of β-phenylethylamine in our experimental set up.

In conclusion, the present results suggest that β-phenylethylamine at physiologically relevant concentrations could affect the biochemical mechanisms interposed between presynaptic autoreceptors and dopamine release, which could be responsible for the neuromodulatory effect of β-phenylethylamine.

References

Antelman, S.M., Edwards, D.L., Lin, M., 1977. Phenylethylamine: Evidence for a direct, postsynaptic dopamine-receptor stimulating action. Brain Res. 127, 317–322.

Arbilla, S., Langer, S.Z., 1981. Stereoselectivity of presynaptic autoreceptors modulating dopamine release. Eur. J. Pharmacol. 76, 345–351.

Bailey, B.A., Philips, S.R., Boulton, A.A., 1987. In vivo release of endogenous dopamine, 5-hydroxytryptamine and some of their metabolites from rat caudate nucleus by phenylethylamine. Neurochem. Res. 12, 173–178.

Barroso, N., Rodrigez, M., 1996. Action of β-phenylethylamine and related amines on nigrostriatal dopamine neurotransmission. Eur. J. Pharmacol. 297, 195–203.

Boulton, A.A., Juorio, A.V., Paterson, I.A., 1990. Phenylethylamine in the CNS: Effects of monoamine oxidase inhibiting drugs, deuterium substitution and lesions and its role in the neuromodulation of catecholeaminergic neurotransmission. J. Neural. Transm. 29, 119–129.

Dourish, C.T., Cooper, S.J., 1984. Environmental experience produces quantitative changes in the stimulant effect of β-phenylethylamine in rats. Psychopharmacology 84, 132–135.

Durden, D.A., Philips, S.R., 1980. Kinetic measurements of the turnover rates of phenylethylamine and tyramine in vivo in the rat brain. J. Neurochem. 34, 1725–1732.

Durden, D.A., Philips, S.R., Boulton, A.A., 1973. Identification and distribution of β-phenylethylamine in the rat. Can. J. Biochem. 51, 995–1002.

Dyck, L.E., 1983. Release of monoamines from striatal slices by phenelzine and β-phenylethylamine. Prog. Neuropsychopharmacol. Biol. Psychiatry 7, 797–800.

Dyck, L.E., Boulton, A.A., 1989. Effects of β-phenylethylamine on polyphosphoinositide turnover in rat cerebral cortex. Neurochem. Res. 14, 63–67.

Farnebo, L.O., Hamberger, A.B., 1971. Drug-induced changes in the release of ^{3}H-monoamines from field stimulated rat brain slices. Act. Physiol. Scand. 371, 35–37.

Greenshaw, A.J., Juorio, A.V., Nguyen, T.V., 1986. Depletion of striatal β-phenylethylamine following dopamine but not 5-HT denervation. Brain Res. Bull. 17, 477–484.

Harris, J., Trivedi, S., Ramakrishna, B.L., 1988. A contribution to the neuromodulatory/neurotransmitter role of trace amines. In: Boulton, A.A., Juorio, A.V., Downer, R.G.H. (Eds.), Trace Amines Comparative and Clinical Neurobiology. Humana Press, Clifton, New Jersey, pp. 213–221.

Hauger, R.L., Skolnik, P., Paul, S.M., 1982. Specific [^{3}H] β-phenyl-ethylamine binding sites in rat brain. Eur. J. Pharmacol. 83, 147–148.

Hausen, T.R., Greenberg, J., Mosnaim, A.D., 1980. Direct effect of phenylethylamine upon isolated rat aortic strip. Eur. J. Pharmacol. 63, 95–101.

Huebert, N.D., Schwach, V., Richter, G., Zreika, M., Hinze, C., Haegele, D., 1994. The measurement of β-phenylethylamine in human plasma and rat brain. Anal. Biochem. 221, 42–47.

Juorio, A.V., 1988. Brain β-phenylethylamine: Localization, pathways and interrelation with catecholamines. In: Sandler, M., Dahlstrom, A., Belmaker, R.H. (Eds.), Progress in Catecholamine Research, vol. 42B: Central Aspects. Neurology and Neurobiology. Alan R. Liss, New York, pp. 433–437.

Juorio, A.V., Paterson, I.A., Zhu, M.Y., Matte, G., 1991. Electrical stimulation of the substantia nigra and changes of 2-phenylethylamine synthesis in the rat striatum. J. Neurochem. 56, 213–220.

Kamal, L.A., Arbilla, S., Galzin, A.M., Langer, S.X., 1983. Amphetamine inhibits the electrically evoked release of 3H-dopamine from slices of the rabbit caudate. J. Pharm. Exp. Ther. 227, 446–458.

Konig, J.F.R., Klippel, R.A., 1963. In: The Rat Brain: A Stereotaxic Atlas of the Forebrain and Lower Parts of the Brain Stem. Williams and Wilkins, Baltimore.

Lane, R.F., Blaha, C.D., 1986. Electrochemistry in vitro: Application to CNS pharmacology. Ann. N. Y. Acad. Sci. 473, 50–69.

Lauber, J., Waldmeier, P.C., 1984. Determination of 2-phenylethylamine in rat brain after MAO inhibitors and in human CSF and urine by capillary GC and chemical inonization MS. J. Neural. Transm. 60, 247–264.

Levant, B., Grigoriadis, D.E., DeSouze, E.B., 1993. Monoamine oxidase inhibitors inhibit [^{3}H]quinpirole binding in rat striatal membranes. Eur. J. Pharmacol. 246, 171–178.

Li, X.M., Juorio, A.V., Paterson, I.A., Boulton, A.A., 1992. Absence of 2-phenylethylamine binding after monoamine oxidase inhibition in rat brain. Eur. J. Pharmacol. 210, 189–193.

Liang, N.Y., Rutledge, C.D., 1982. Evidence for carrier-mediated efflux of dopamine from corpus striatum. Biochem. Pharmacol. 31, 2479–2484.

McMillen, B.A., 1983. CNS stimulants: Two distinct mechanisms of action for amphetamine-like drugs. Trends Pharmacol. Sci. 4, 429–430.

Paetsch, P.R., Greenshow, A.J., 1993. Down-regulation of β-adrenergic receptors induced by 2-phenylethylamine. Cell Mol. Neurobiol. 13, 203–215.

Parker, E.M., Cubeddu, L.X., 1985. Evidence for autoreceptor modulation of endogenous dopamine release from rabbit caudate nucleus in vitro. J. Pharmacol. Exp. Ther. 232, 492–500.

Paterson, I.A., Juorio, A.V., Boulton, A.A., 1990. 2-Phenylethylamine: A modulator of catecholamine transmission in the mammalian central nervous system?. J. Neurochem. 55, 1827–1837.

Paterson, I.A., Juorio, A.V., Berry, M.D., Zhu, M.Y., 1991. Inhibition of monoamine oxidase-B by (−)-deprenyl potentiates neuronal responses to dopamine agonists but dose not inhibit dopamine catabolism in the striatum. J. Pharmacol. Exp. Ther. 258, 1019–1026.

Philips, S.R., 1986. In vivo release of endogenous dopamine from rat caudate nucleus by β-phenylethylamine and α,α-dideutero-β-phenyl-ethylamine. Life Sci. 39, 2359–2400.

Philips, S.R., Boulton, A.A., 1979. The effect of monoamine oxidase inhibitors on some arylalkylamines in rat striatum. J. Neurochem. 33, 159–167.

Philips, S.R., Robson, A.M., 1983. In vivo release of endogenous dopamine from rat caudate nucleus by phenylethylamine. Neuropharmacol. 22, 1297–1301.

Raiteri, M., Del Carmine, R., Bertollini, A., Levi, G., 1977. Effect of sympathomimetic amines on the synaptosomal transport of noradrenaline,dopamine and 5-hydroxytryptamine. Eur. J. Pharmacol. 41, 133–143.

Reynolds, G.P., Sandler, M., Hardy, L., Bradford, H., 1980. The determination and distribution of 2-phenylethylamine in sheep brain. J. Neurochem. 34, 1123–1125.

Saavedra, J.M., 1974. Enzymatic isotopic assay for and presence of β-phenylethylamine in brain. J. Neurochem. 22, 211–216.

Starke, K., Spath, I., Lang, J.D., Adlung, C., 1983. Further functional in vitro comparison of pre- and post-synaptic dopamine receptors in the rabbit caudate nucleus. Naunyn-Schmiedebergs Arch. Pharmacol. 323, 289–306–791.

Wolf, M.E., Mosnaim, A.D., 1983. Phenylethylamine in neuropsychiatric disorders. Gen. Pharm. 14, 385–390.

Yamada, S., Yokoo, H., Nishi, S., 1993. Modulation of (−)-sulpiride-induced increase in electrically evoked release of dopamine from striatal slices of rats. J. Pharm. Pharmacol. 45, 479–481.

Yamada, S., Hirano, M., Nishi, S., Inokuchi, T., Uchimura, H., 1994a. Temperament traits associated with platelet monoamine oxidase activity and plasma 2-phenylethylamine in healthy volunteers. Biogenic Amines 10, 295–302.

Yamada, S., Yokoo, H., Nishi, S., 1994b. Differential effects of dopamine agonists on evoked dopamine release from slices of striatum and nucleus accumbens in rats. Brain Res. 648, 176–179.