CROATICA CHEMICA ACTA CCACAA **75** (1) 235–245 (2002)

ISSN-0011-1643
CCA-2796 *Original Scientific Paper*

Binding of Dihydroergosine to 5-HT_{1A} Receptors of Human and Rat Brain

Dorotea Mück-Šeler and Danka Peričić*

Ruđer Bošković Institute, Division of Molecular Medicine, Laboratory for Molecular Neuropharmacology, P.O.B. 180, 10002 Zagreb, Croatia

Received July 24, 2000; revised July 27, 2001; accepted August 3, 2001

Interaction of the ergot alkaloid dihydroergosine with the binding of (^{3}H)8-hydroxy-2-(di-n-propylamino)tetralin (^{3}H8-OH-DPAT), a selective agonist for 5-HT_{1A} binding sites, to hippocampal membranes isolated from human and rat brain was studied. Competition binding experiments showed that dihydroergosine is a potent displacer of (^{3}H)8-OH-DPAT binding at brain 5-HT_{1A} receptors of both species. Scatchard analysis of (^{3}H)8-OH-DPAT binding to rat hippocampal membranes in the presence of dihydroergosine revealed that this ergot compound markedly decreases the number and the affinity of hippocampal (^{3}H)8-OH-DPAT labelled binding sites. Preincubation of rat hippocampal membranes for 180 min with dihydroergosine (2 nmol dm^{-3}) completely prevented the binding of (^{3}H)8-OH-DPAT (2 nmol dm^{-3}). The data suggest that dihydroergosine is approximately as potent a ligand as 8-OH-DPAT for the hippocampal 5-HT_{1A} receptors from human and rat brains, although their kinetics of association and dissociation are apparently different.

Key words: ergot alkaloid, 5-HT_{1A} receptors, (^{3}H)8-OH-DPAT binding, hippocampus, human brain, rat brain.

INTRODUCTION

Based on their structural, functional and pharmacological characteristics, 5-hydroxytryptamine (5-HT, serotonin) receptors have been classified into seven receptor families (5-$HT_{1–7}$).[1] 5-HT_{1A} receptor, a subtype of 5-HT_1

* Author to whom correspondence should be addressed. (E-mail: seler@rudjer.irb.hr)

receptor family, was identified almost 20 years ago[2,3] and 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) was soon recognised as its selective agonist.[4] 5-HT_{1A} receptor was also the first 5-HT receptor to be fully sequenced.[5,6] Electrophysiological studies have demonstrated that activation of 5-HT_{1A} receptors produces hyperpolarisation, *i.e.* inhibition of neuronal activity.[7] 5-HT_{1A} binding sites are mainly found in limbic areas (hippocampus, amygdala),[8,9,10] in cortex[11] and in the midbrain raphe nuclei.[10,12,13] The distribution of mRNA encoding the 5-HT_{1A} receptor corresponds to that of the 5-HT_{1A} binding sites.[14,15] This distribution is consistent with the involvement of 5-HT_{1A} receptors in mood control, as suggested by anxiolytic and antidepressant properties of many 5-HT_{1A} agonists.[16,17,18] Besides, hippocampus is the brain region supposed to be involved in learning and memory processes.[19,20]

Ergot alkaloids are drugs that have potent and various effects on the brain tissue and central nervous system functions.[21] One of these drugs, dihydroergosine, produces in different animal species behavioural changes that strongly suggest its antidepressant properties, as well as the involvement of the 5-HT system.[22,23,24] We have already demonstrated that dihydroergosine inhibited the binding of (^{3}H)5-HT to the whole population of rat hippocampal 5-HT_1 receptors with nanomolar affinity.[25] The aim of the present work was to determine the effect of dihydroergosine on the binding of (^{3}H)8-OH-DPAT to the rat and human hippocampal membranes in order to verify dihydroergosine's affinity for 5-HT_{1A} receptors. Our data demonstrate that dihydroergosine possesses a very high affinity for 5-HT_{1A} receptors of both species.

EXPERIMENTAL

Tissue Preparation

Human tissue was obtained at autopsy, 12 h after death, from two middle-aged subjects who had no history of neurological or psychiatric illness and were not known to be taking any psychoactive medication. Male Wistar rats (200 to 250 g) were killed with a guillotine, brains were removed, placed over ice and the hippocampus, was dissected. The tissue, pooled from ten animals or a piece (about 1 g) of human brain hippocampus was homogenised in 30 volumes of cold Tris buffer (50 mmol dm^{-3}, pH = 7.4 at 25 °C) and centrifuged at 20 000 × g for 10 min. The pellet was resuspended in 20 volumes of the same buffer and incubated in a water bath at 37 °C for 20 min to remove endogenous 5-HT.[26] The pellet was washed twice by resuspension and centrifugation. The final pellet was resuspended in the incubation buffer (50 mmol dm^{-3} Tris HCl containing 5.8 mmol dm^{-3} $CaCl_2$) to obtain about 15 mg of wet weight rat or human hippocampus (1.2 to 1.4 mg protein per mL of membrane preparation).

Binding Assay

Competition binding experiments were performed, with slight modifications, as described by Peroutka.[27] Briefly, 16 to 19 concentrations (10^{-12} to 10^{-4} mol dm^{-3}) of dihydroergosine were used. Each tube contained 0.5 mL of membrane preparation, 0.1 mL of dihydroergosine (dissolved in water) or water, 0.1 mL of (^{3}H)8-OH-DPAT (final concentration 1 nmol dm^{-3}) and incubation buffer (0.3 mL). Non-specific binding was determined using 0.01 mmol dm^{-3} of cold 5-HT, and accounted for 10 to 25% of total binding.

Saturation binding experiments were performed using different concentrations (from 0.063 to 8.00 nmol dm^{-3}) of (^{3}H)8-OH-DPAT in the absence (control) or presence of dihydroergosine (4 nmol dm^{-3}). Non-specific binding was determined using 0.01 mmol dm^{-3} of cold 5-HT, and accounted for 6% and 34% of the total binding at 0.063 and 8.00 nmol dm^{-3} of (^{3}H)8-OH-DPAT, respectively. Following preincubation with dihydroergosine for 15 min, the incubation at 25 °C for 30 min started with the addition of (^{3}H)8-OH-DPAT and was terminated by rapid filtration through Whatman GF/C filters (pre-soaked overnight in 1% polyethylenimine) to separate bound from free radioactivity. The filters were washed two times with 5 mL of cold Tris HCl buffer, transferred to the vials and dried for 1 h at 80 °C. Three mL of the scintillation cocktail (PPO, POPOP in toluene) was added and the vials were stored at 4 °C overnight to extract the radioactivity from the filters before liquid scintillation spectroscopy at 49% efficiency. All experiments were performed in triplicate and were repeated three times.

In one group of experiments, membranes were preincubated with dihydroergosine (2 nmol dm^{-3}) at 25 °C for different lenghts of time (10–180 min) before addition of (^{3}H)8-OH-DPAT (2 nmol dm^{-3}). Incubation was continued for a further 30 min, as described in competition experiments. The same data, *i.e.*, the decline of specific (^{3}H)8-OH-DPAT binding, were used to estimate the time course of dihydroergosine binding to rat brain membranes.

Protein in the membrane preparation was determined according to Lowry *et al.* [28]

Data Analysis

The data from saturation and displacement binding experiments were analysed using a computer-based equilibrium binding data (EBDA) program.[29] EBDA calculates the apparent dissociation constant (K_d) and the maximum density of the binding sites (B_{max}) by the Scatchard transformation of saturation binding data. For inhibition experiments, the iterative curve-fitting program was used to calculate the IC_{50} value (the drug concentration displacing 50% of specific radioligand binding) and the slope factor (analogous to the Hill coefficient). For the indirect estimation of the time course of dihydroergosine binding to rat brain membranes, the data were plotted as $\ln B_0 / (B_0 - B)$ *vs.* association time, where B_0 was the estimated specific binding of dihydroergosine in the steady state, and B was the estimated specific binding of dihydroergosine for the association time shown. Results are expressed as the mean ± standard error.

Compounds

Dihydroergosine methane sulphonate (Lek, Ljubljana, Slovenia), polyethylenimine (Sigma, St.Louis, USA), 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide (8-OH-DPAT HBr, Research Biochemicals Inc., Natick, USA), (^{3}H)8-OH-DPAT, specific activity 40.25 Ci/mmol (Amersham, Buckinghamshire, England).

RESULTS

Increasing concentrations of dihydroergosine (10^{-12} to 10^{-4} mol dm^{-3}) displaced the specific (^{3}H)8-OH-DPAT binding to the human and rat hippocampal membranes (Figure 1). The IC_{50} values were 14.6 (±5.2) and 2.00 (±0.23) nmol dm^{-3} for human and rat hippocampal membranes, respectively. The log-logit transformation of the data yielded a slope of 1.09 ± 0.08 for human, and 1.21 ± 0.07 for rat brain membranes. In both species, computer assisted analysis of the data showed that dihydroergosine inhibition of (^{3}H)8-OH-DPAT binding may be adequately explained by a single site model ($P > 0.05$, one-site *versus* two-site model) with an apparent K_i value of 0.73 (±0.08) nmol dm^{-3} for the rat hippocampal membranes.

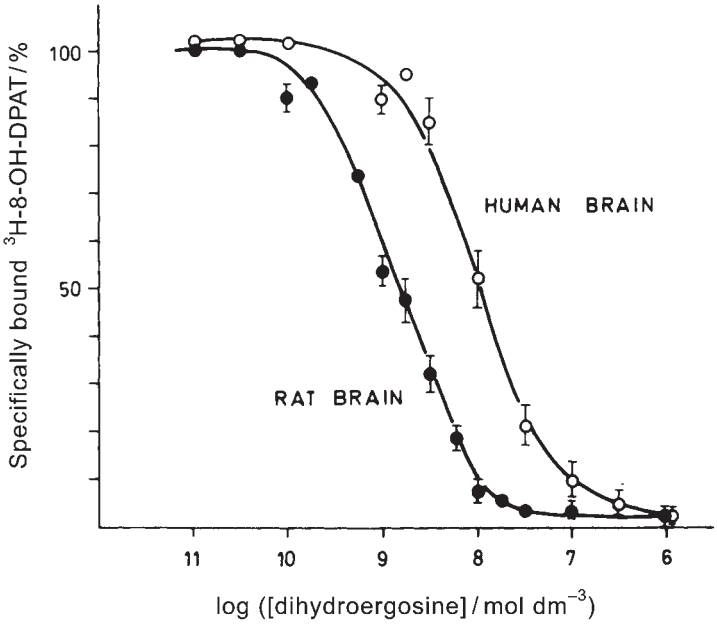

Figure 1. Inhibition of specific (^{3}H)8-OH-DPAT (1 nmol dm^{-3}) binding to hippocampal membranes, isolated from human (open circles) and rat (filled circles) brain, by dihydroergosine. The points are the mean ±SEM of three separate experiments, each performed in triplicate.

Saturation curves (Figure 2) indicated that (^{3}H)8-OH-DPAT labelled an apparently homogenous population of high affinity binding sites from the rat hippocampus. In the presence of dihydroergosine (4 nmol dm^{-3}), the binding of (^{3}H)8-OH-DPAT was drastically reduced (Figure 2). Both the maximum number (B_{max} = 0.043 (±0.017) pmol/mg protein) and the affinity (K_d = 1.85 (±0.15) nmol dm^{-3}) of hippocampal (^{3}H)8-OH-DPAT binding sites were significantly ($P < 0.05$, Student t-test) lower in the presence of dihydroergosine when compared with the density (B_{max} = 0.185 (±0.015) pmol/mg protein) and affinity (K_d = 0.58 (±0.10) nmol dm^{-3}) of the (^{3}H)8-OH-DPAT binding sites in the absence of dihydroergosine (controls).

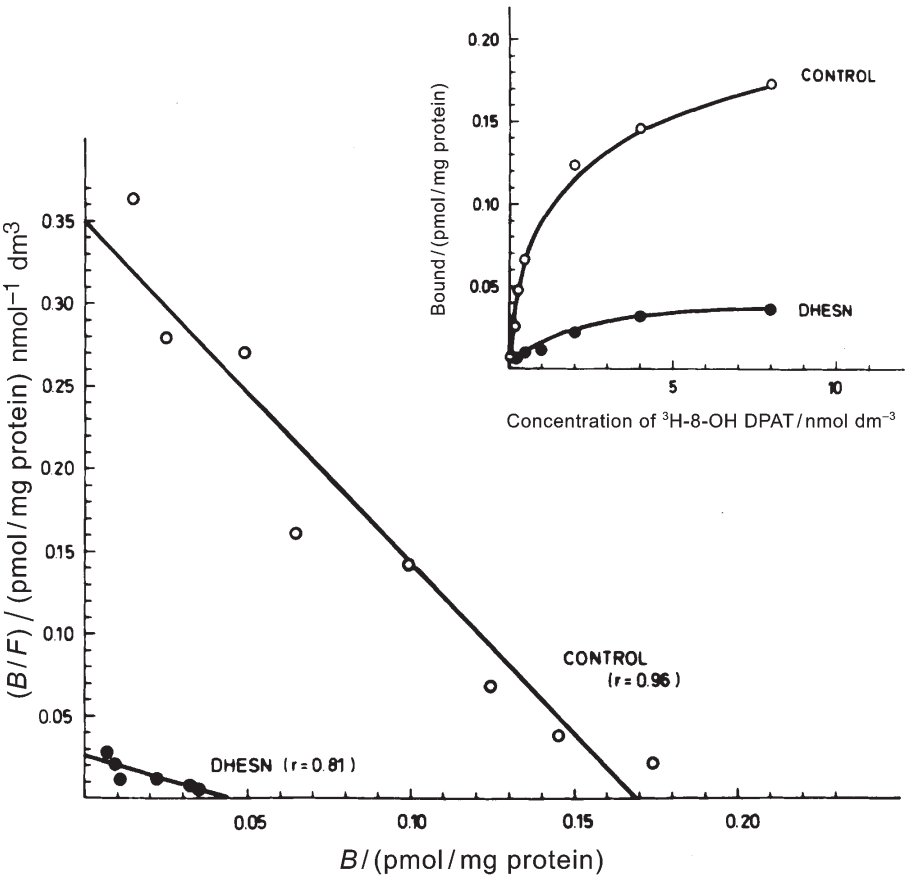

Figure 2. Representative Scatchard plots and saturation isotherms (inset) of the specific (^{3}H)8-OH-DPAT binding to the rat hippocampal membranes in the absence (control) and in the presence of dihydroergosine (4 nmol dm^{-3}). The points are the means of triplicate determinations from a typical experiment.

The binding of (^{3}H)8-OH-DPAT (2 nmol dm^{-3}) to the rat hippocampal membranes was diminished or completely abolished when the membranes were preincubated with 2 nmol dm^{-3} of dihydroergosine (Figure 3). The specific binding of (^{3}H)8-OH-DPAT in the presence of dihydroergosine was 17 200 dpm at time »zero« (*i.e.*, when the 30-min incubation started with addition of membranes). This is 54.7% lower than the specific binding of (^{3}H)8-OH-DPAT obtained in the absence of dihydroergosine (37 969 dpm), indicating that the latter drug inhibits the same percent of specific (^{3}H)8-OH-DPAT (2 nmol dm^{-3}) binding. From the data presented in Figure 3 it was calculated that fifty percent of this initially observed (^{3}H)8-OH-DPAT binding in the presence of dihydroergosine had declined when the membranes were preincubated for 23.9 min with 2 nmol dm^{-3} of dihydroergosine. Three hours preincubation with dihydroergosine induced a complete inhibition of (^{3}H)8-OH-DPAT binding. If we estimate the binding of dihydroergosine from the decline of specifically bound (^{3}H)8-OH-DPAT, we can obtain a curve showing the association time course of specific dihydroergosine binding to rat brain membranes, although in the presence of (^{3}H)8-OH-DPAT for

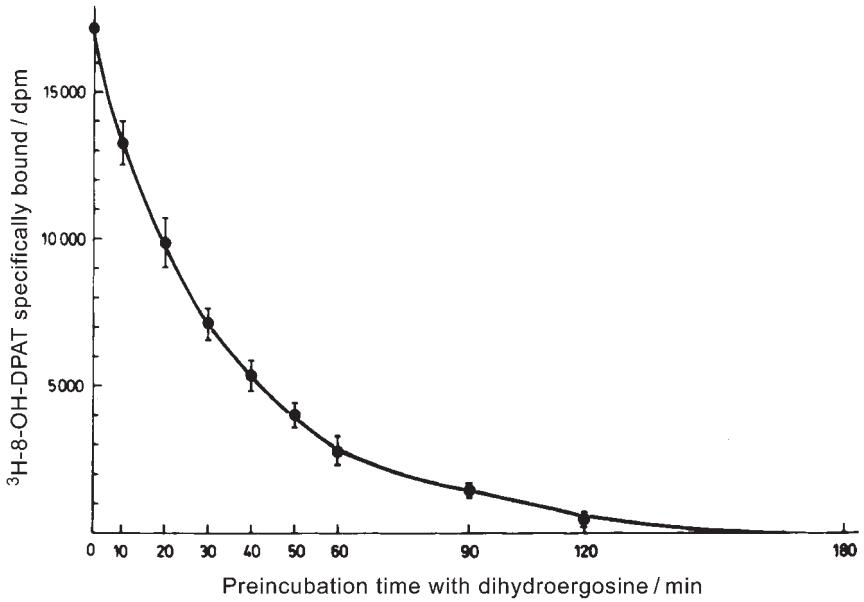

Figure 3. The binding of (^{3}H)8-OH-DPAT to the rat hippocampal membranes preincubated with dihydroergosine for different lenghts of time (10–180 min) before addition of the radiolabelled ligand. Time »zero« denotes the time when the incubation started with addition of membranes, so that both (^{3}H)8-OH-DPAT and dihydroergosine were incubated with the membranes for a further 30 min. Each point is the mean ± SEM of three independent experiments performed in triplicate.

the last 30 min (Figure 4A). Since the preincubation time »zero« (Figure 3) equals 30 min of incubation with (^{3}H)8-OH-DPAT, but also with dihydroergosine, our data suggest that, at 25 °C, the binding of dihydroergosine reached a steady state within 150 to 210 min. Thus, we could not have results showing the association of dihydroergosine to rat brain membranes during the initial half hour. However, semilogarithmic transformations of our estimated data yielded linear plots (r = 0.998) consistent with the association to a homogenous class of specific binding sites (Figure 4B).

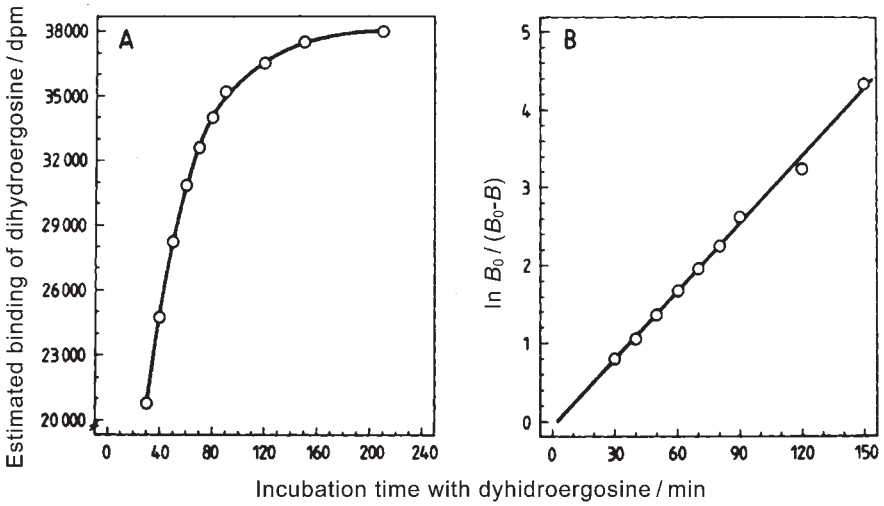

Figure 4. A. Association of dihydroergosine to rat hippocampal membranes estimated indirectly from the decline of specifically bound (^{3}H)8-OH-DPAT (see Figure 3). Inability of radioligand (2 nmol dm^{-3}) to label the membranes at 180 min (Figure 3) was taken as the point when the specific binding of dihydroergosine (2 nmol dm^{-3}) reached a steady state.

B. Semilogarithmic plot of the estimated association data. B_0 is the estimated binding of dihydroergosine in the steady state, and B is the evaluated binding of dihydroergosine for the association time if we take »zero« binding of (^{3}H)8-OH-DPAT, observed when dihydroergosine was preincubated with the membranes for 180 min, as the point when the specific binding of dihydroergosine reached the steady state.

DISCUSSION

In the present work, we extended and confirmed our previous data suggesting that the potential antidepressant[22,23,24] and anxiolytic[30] drug, dihydroergosine, binds with high affinity to the hippocampal 5-HT$_{1A}$ binding sites. Moreover, we have demonstrated for the first time, using (^{3}H)8-OH-DPAT as

a selective and specific radioligand for 5-HT_{1A} receptors, that dihydroergosine has a high affinity for this subtype of 5-HT_1 binding sites, in both rat and human hippocampus. This result is in good agreement with nanomolar affinity obtained for the same binding site in the rat brain using the non-selective ligand (^{3}H)5-HT in the presence of CGS 12066B and ritanserin to mask (^{3}H)5-HT binding to 5-HT_{1B} and 5-HT_{1C} receptor subtypes, respectively.[25] Although the concentration of dihydroergosine inhibiting 50% of specific (^{3}H)8-OH-DPAT binding (IC_{50}) appeared to be slightly higher for the human than for the rat brain membranes, the competition curves and the slope factors were very similar, indicating that dihydroergosine was bound to a single population of receptors. The findings of nanomolar affinity of dihydroergosine to 5-HT_{1A} (present work) and 5-HT_2 receptors[31] are in agreement with the reports of other authors,[32,33] showing that some other ergot derivatives have also a high affinity to these 5-HT receptors.

Our experiments indicate that dihydroergosine is approximately as potent a ligand as 8-OH-DPAT[34,35] for the hippocampal 5-HT_{1A} receptors, though the two drugs appear to have completely different kinetic properties. When the 30-min incubation started simultaneously with equimolar concentrations of both compounds, the specific binding of (^{3}H)8-OH-DPAT was about 50% lower than in the absence of dihydroergosine. These results suggest indirectly that half of the available binding sites were occupied by dihydroergosine. The association and dissociation of dihydroergosine are rather slow. Namely, our results demonstrated that the binding of dihydroergosine reached a steady state within 2.5 and 3.5 hours. This time is even longer than that observed by Hamblin *et al.*[33] for the association of (^{3}H)dihydroergotamine to rat brain membranes. However, we had no labelled dihydroergosine, so (^{3}H)8-OH-DPAT had to be present in the incubation medium for the last 30 min. We could not therefore have results showing the association of dihydroergosine to rat brain membranes during the initial half hour of incubation. It has been shown that another ergopeptine, (^{3}H)dihydroergotamine, is a high-affinity, slowly dissociating radioligand for 5-HT_{1B} binding sites in rat brain membranes.[33] The data on the association of this radioligand to rat brain membranes have shown that, at 37 °C, its specific binding reached a steady state within 1 h. Unlike dihydroergosine and (^{3}H)dihydroergotamine, the association and dissociation of (^{3}H)8-OH- DPAT, as reported by Hall *et al.*,[34] were rapid. At 37 °C, the binding of this ligand to hippocampal and striatal membranes reached equilibrium already within 5 to 7 min. The observed kinetic properties of dihydroergotamine[33] and dihydroergosine (this study) are in accord with our behavioural studies showing a very prolonged central serotonergic effect of this drug after a single i.p. injection.[23,36]

The present study demonstrates a high affinity of dihydroergosine for the hippocampal postsynaptic 5-HT_{1A} receptors. However, it may be expected

that this drug is also a high affinity ligand for the presynaptic, *i.e.*, somatodendritic, 5-HT_{1A} receptors. Indirect evidence for this presumption is the finding that dihydroergosine reduces the 5-HT turnover rate,[22] which is supposedly regulated by somatodendritic autoreceptors of the 5-HT_{1A} subtype located on the 5-HT cell bodies in the dorsal and median raphe nuclei of the brain stem.[13,17] Behavioural data indicating that dihydroergosine stimulates, in a (–)-propranolol sensitive manner, the 5-HT syndrome in rats,[31] shortens the immobility in the forced swim-test,[24] possesses antiaggressive properties,[37] produces hypolocomotion[22] and hypothermia,[41] might additionally suggest that dihydroergosine is a 5-HT_{1A} receptor agonist. Namely, the mentioned behavioural changes are believed to be mainly produced by the stimulation of 5-HT_{1A} receptors.[31,38,39,40] At present, however, it remains unclear whether this drug exhibits partial or full agonist properties at this receptor subtype. Our comparative studies [31] imply that the behavioural profile of this drug differs from the other known partial or full agonists of 5-HT_{1A} or 5-HT_{1B}/5-HT_{1A} receptor sites. This might be due to the fact that dihydroergosine possesses two components – one stimulating 5-HT_1, presumably 5-HT_{1A}, and the other inhibiting 5-HT_2 receptors.[31] Our studies *in vitro*, including this study, have shown a high affinity of this drug for both types of 5-HT receptors.[25,31]

In conclusion, this study has demonstrated that the ergot alkaloid dihydroergosine has a high nanomolar affinity for the 5-HT_{1A} receptors from the hippocampus of human and rat brains, additionally suggesting its potential as an antidepressive and anxiolytic drug.

Acknowledgement. – We thank Mrs I. Fresl and Mrs Z. Tonšetić for their skilful technical assistance.

REFERENCES

1. N. M. Barnes and T. Sharp, *Neuropharmacology* **38** (1999) 1083–1152.
2. N. W. Pedigo, H. I. Yamamura, and D. L. Nelson, *J. Neurochem*. **36** (1981) 205–230.
3. D. N. Middlemiss and J. R. Fozard, *Eur. J. Pharmacol*. **90** (1983) 151–153.
4. S. Hjorth, A. Carlsson, P. Lindberg, D. Sanchez, H. Wikström, L-E. Arvidsson, U. Hacksell, and J. L. G. Nilsson, *J. Neural Transm*. **55** (1982) 169–188.
5. B. K. Kobilka, T. Frielle, S. Collins, T. Yang-Feng, T. S. Kobilka, U. Francke, R. J. Lefkowitz, and M. G. Caron, *Nature* **329** (1987) 75–77.
6. A. Fargin, J. R. Raymond, M. J. Lohse, B. K. Kobilka, M. G. Caron, and R. J. Lefkowitz, *Nature* **335** (1988) 358–360.
7. R. A. Nicoll, R. C. Malenka, and J. A. Kauer, *Phys. Rev*. **70** (1990) 5123–565.
8. A. Pazos and J. M. Palacios, *Brain Res*. **346** (1985) 205–230.
9. P. A Blurton and M. D. Wood, *J. Neurochem*. **46** (1986) 1392–1398.

10. C. Del Arco, I. Galende, and A. Pazos, *Naunyn-Schmiedeberg's Arch. Pharmacol.* **347** (1993) 248–256.
11. P. B. Crino, A. B. Vogt, L. Volicer, and R. G. Wiley, *J. Pharmacol. Exp. Ther.* **252** (1990) 651–656.
12. D. Verge, G. Daval, M. Marcinkiewicz, A. Patey, S. El Mestikawy, H. Gozlan, and M. Hamon, *J. Neurosci.* **6** (1986) 3474–3482.
13. C. Sotelo, B. Cgolley, S. El Mestikawy, H. Gozlan, and M. Hamon, *Eur. J. Neurosci.* **2** (1990) 1144–1154.
14. D. T. Chalmers and S. J. Watson, *Brain Res*. **561** (1991) 51–60.
15. P. J. W. Burnet, S. L. Eastwood, K. Lacey, and P. J. Harrison, *Brain Res*. **676** (1995) 157–168.
16. J. Traber and T. Glaser, *Trends Pharmacol. Sci.* **8** (1987) 432–437.
17. R. Schreiber and J. De Vry, *Prog. Neuro-Psychopharmacol. Biol. Psychiat*. **17** (1993) 87–104.
18. S. L. Handley, *Pharmacol. Ther.* **66** (1995) 103–148.
19. G. Rieder, J. Micheau, A. G. M. Lam, E. V. Roloff, S. J. Martin, H. Bridge, L. de Hoz, B. Poeschel, J. McCulloch, and R. G. M. Morris, *Nature Neurosci.* **2** (1999) 898–905.
20. S. J. Martin, P. D. Grimwood, and R. G. M. Morris, *Annu. Rev. Neurosci.* **23** (2000) 649–711.
21. A. Agnoli, G. Crepaldi, P. F. Spano, and M. Trabucchi, *Aging Brain and Ergot Alkaloids,* Raven Press, New York, 1983.
22. D. Peričić, H. Manev, S. Levanat, B. Jernej, D. Vujić, and N. Đorđević, *Psychopharmacology* **90** (1986) 112–118.
23. D. Peričić and H. Manev, *Eur. J. Pharmacol.* **137**(1987) 123–125.
24. H. Manev and D. Peričić, *Psychoneuroendocrinology* **13** (1988) 465–469.
25. D. Mück-Šeler and D. Peričić, *J. Neural. Transm.* **92** (1993) 1–9.
26. D. L. Nelson, A. Herbert, S. Bourgoin, J. Glowinski, and M. Hamon, *Mol. Pharmacol.* **14** (1978) 983–995.
27. S. J. Peroutka, *J. Neurochem.* **47** (1986) 529–570.
28. O. H. Lowry, N. J. Rosebrough, A. L. Farr, and R. J. Randall, *J. Biol. Chem*. **193** (1951) 265–275.
29. G. A. McPherson, *Computer Programs in Biomedicine* **17** (1983) 107–114.
30. D. Peričić and A. Tvrdeić, *Eur. J. Pharmacol.* **235** (1993) 267–274.
31. D. Peričić and D. Mück-Šeler, *Life Sci.* **46** (1990) 1331–1342.
32. P. M. Beart, D. McDonald, M. Cincotta, D. J. De Vries, and A. L. Gundlach, *Gen. Pharmacol.* **17** (1986) 57–62.
33. M. W. Hamblin, K. Ariani, P. I. Adriaenssens, and R. D. Ciaranello, *J. Pharmacol. Exp. Ther.* **243** (1987) 989–1001.
34. M. D. Hall, S. El Mestikawy, M. B. Emerit, L. Pichat, M. Hamon, and H. Gozlan, *J. Neurochem*. **44** (1985) 1685–1696.
35. M. Titeler, R. A. Lyon, K. H. Davis, and R. A. Glennon, *Biochem. Pharmacol.* **36** (1987) 3265–3271.
36. D. Peričić and H. Manev, *Life Sci.* **42** (1988) 2593–2601
37. H. Manev, D. Peričić, and D. Mück-Šeler, *Pharmacol. Biochem. Behav.* **32** (1989) 111–115.
38. M. D. Tricklebank, C. Forler, and R. J. Fozard, *Eur. J. Pharmacol.* **106** (1984) 271–282.

39. I. Lucki and A. Frazer, *Changes in Behavior Associated with Serotonin Receptors Following Repeated Treatment with Antidepressant Drugs*, in: L. S. Seiden and R. L. Balster (Eds), *Behavioural Parmacology: The Current Status,* Alan R. Liss, New York, 1985, pp. 339–357.
40. L. O. Wilkinson and C. T. Dourish, *Serotonin and Animal Behavior*, in: S. J. Peroutka (Ed), *Serotonin Receptor Subtypes: Basic and Clinical Aspects*, Wiley-Liss, New York, 1991, pp. 147–210.
41. D. Peričić, unpublished work.

SAŽETAK

Vezanje dihidroergozina za 5-HT$_{1A}$ receptore humanog i štakorskog mozga

Dorotea Mück-Šeler i Danka Peričić

Istražen je utjecaj dihidroergozina (alkaloida ražene snijeti) na vezanje (^{3}H)8-hidroksi-2-(di-n-propilamino)tetralina (^{3}H8-OH-DPAT), liganda selektivnog za vezna mjesta tipa 5-HT$_{1A}$, za hipokampalne membrane izolirane iz mozga čovjeka i štakora. Pokusi kompeticije vezanja pokazali su da dihidroergozin snažno potiskuje vezanje (^{3}H)8-OH-DPAT za receptore 5-HT$_{1A}$ iz mozga obiju vrsta. Scatchardova analiza vezanja (^{3}H)8-OH-DPAT za membrane štakorskog hipokampusa u prisutnosti dihidroergozina pokazala je da taj spoj značajno smanjuje broj i afinitet hipokampalnih veznih mjesta obilježenih s (^{3}H)8-OH-DPAT. Preinkubacija membrana štakorskog hipokampusa s dihidroergozinom (2 nmol dm^{-3}) tijekom 180 min inhibirala je vezanje (^{3}H)8-OH-DPAT (2 nmol dm^{-3}). Rezultati upućuju da je dihidroergozin približno podjednako snažan ligand za hipokampalne 5-HT$_{1A}$ receptore iz mozga čovjeka i štakora kao i 8-OH-DPAT, iako se kinetika njihove asocijacije i disocijacije očito razlikuje.