Deamination of Norepinephrine, Dopamine, and Serotonin by Type A Monoamine Oxidase in Discrete Regions of the Rat Brain and Inhibition by RS-8359

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ABSTRACT—Levels of monoamines and their metabolites were determined in the cortex, hippocampus, and striatum of rats killed by microwave irradiation. Moclobemide (20 mg/kg, p.o.) and clorgyline (10 mg/kg, p.o.), type A monoamine oxidase (MAO-A) inhibitors, increased the levels of normetanephrine (NM) and 3-methoxytyramine (3MT) and decreased those of 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), and 5-hydroxyindoleacetic acid (5HIAA) in almost all three regions. Deprenyl (10 mg/kg, p.o.), a type B monoamine oxidase inhibitor, however, little affected monoamine and metabolite levels in all regions. The maximum effects of RS-8359 (10 mg/kg, p.o.) were obtained at 2 to 6 hr after administration, when the levels of norepinephrine (NE), NM, 3MT, and serotonin (5HT) in all regions and dopamine (DA) in the striatum increased, while DOPAC and HVA levels decreased. The levels of monoamines and metabolites had returned to normal by 20 hr after administration. Dose-dependency of the effects of RS-8359 on monoamine metabolites was observed at doses up to 30 mg/kg (p.o.) at 1 and 6 hr after administration. In conclusion, NE, DA, and 5HT are exclusively or preferentially deaminated by MAO-A in the cortex, hippocampus, and striatum of rats, and RS-8359 exhibits a reversible MAO-A inhibitory action in all three regions tested in vivo.

Monoamine oxidase (MAO), which is responsible for deamination of norepinephrine (NE), dopamine (DA), and serotonin (5HT), is classified into two forms: MAO-A and MAO-B, each of which can be defined by its sensitivity to inhibition by clorgyline (an MAO-A inhibitor) or deprenyl (an MAO-B inhibitor) (1-3).

RS-8359 ((±)-4-(4-cyanoanilino)-7-hydroxy-cyclopenta(3,2-e)pyrimidine) is reported to be a highly selective and reversible MAO-A inhibitor from in vitro experiments (4, 5). The in vivo effectiveness of a reversible MAO-A inhibitor in the brain can be evaluated from the inhibitor-induced changes in the brain levels of monoamines and/or their metabolites (1); RS-8359 has already been shown to increase monoamine levels and to decrease deaminated metabolite levels in mouse whole brain (4). However, in order to estimate exactly the in vivo effect of RS-8359 on MAO-A, its effect on monoamine and metabolite levels must be determined in discrete regions of the brain, since monoamines are unevenly distributed in the brain (6, 7). Moreover, the degree to which MAO-A contributes to the deamination of monoamines in discrete brain regions in vivo remains obscure, since most
studies on the in vivo selectivity of MAO subtypes have used only the whole brain (8-10) or the striatum (9, 11-13). Therefore, the present study was designed first to clarify the subtype of MAO participating in the deamination of NE, DA, and 5HT in the striatum, cortex, and hippocampus and second, to estimate the MAO-A inhibitory action of RS-8359 in these discrete regions in vivo.

MATERIALS AND METHODS

Male Wistar rats (12-14 weeks) were used. Rats were sacrificed by head-focused microwave irradiation (3.5 kW, 2.3 sec; Metabostat, New Japan Radio, Tokyo, Japan). After each brain was removed, the cerebral cortex, hippocampus, and striatum were dissected out and stored at -80°C. The frozen tissues were first homogenized with 0.1N perchloric acid (PCA) containing 0.1% ethylenediaminetetraacetic acid disodium salt (EDTA2Na) and 0.1% sodium bisulfite (Na2S2O5), and then sonicated (30 sec, UR-20P, Tomy Seiko, Tokyo, Japan). The homogenates were centrifuged (10000 rpm) for 20 min. The monoamine concentrations in the supernatant were determined by high-performance liquid chromatography with electrochemical detection (HPLC-ECD). HPLC consisted of a pump (655 Liquid Chromatograph, Hitachi, Tokyo, Japan) and a column (EICOM PAK MA-ODS, 4.6 X 250 mm, Eicom, Kyoto, Japan). Citrate-sodium acetate buffer (0.1 M, pH 4.0) containing 3 mg/l EDTA2Na, 144 mg/l sodium octanesulfonate, and 17% methanol was used for the mobile phase, which was degassed (Model 545, Gasukuro Kogyo, Tokyo, Japan). The flow rate used was 0.8 ml/min. An electrochemical detector (EC-100, Eicom, Kyoto, Japan) was used, and 750 mV was applied vs. Ag/AgCl. Standard solutions of monoamines and their metabolites (NE, DA, 5HT, normetanephrine (NM), 3-methoxytyramine (3MT), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), and 5-hydroxyindoleacetic acid (5HIAA), all purchased from Sigma) were prepared every day in 0.1 N PCA containing 0.1% Na2S2O5 and 0.1% EDTA2Na. The concentrations of monoamines in the supernatant were calculated by comparing the peak heights of the samples with those of standards. Protein concentrations were determined by the method of Lowry et al. (14) after solubilization in 0.1 N NaOH.

Clorgyline and deprenyl were respectively used as irreversible MAO-A and MAO-B inhibitors each at a dose of 10 mg/kg (p.o.), which has been reported to inhibit each type of MAO selectively (inhibiting each respective type of MAO to less than 20%, while maintaining the other enzyme at more than 80%) (15). Since the ED50 values of moclobemide, a reversible MAO-A inhibitor (16), for MAO-A and MAO-B are reported to be 1.1 mg/kg, p.o. and over 100 mg/kg, p.o., respectively (17), a dose that would inhibit MAO-A to less than 20% was used (20 mg/kg, p.o.) (18). Moclobemide (synthesized in Chemical Labs., Sankyo Co., Ltd.), clorgyline (Sigma), and deprenyl (Research Biochem. Inc.) were suspended in 0.5% sodium carboxymethylcellulose (CMC) solution; they were administered orally to rats at 2, 4, and 4 hr, respectively, before the animals were sacrificed. RS-8359 was also suspended in 0.5% CMC solution; it was given orally (3, 10, and 30 mg/kg) to rats at the indicated times before they were sacrificed.

Data are expressed as means ± S.E.M. and were analyzed by the Mann-Whitney U-test.

RESULTS

Effects of moclobemide, clorgyline, and deprenyl on monoamines and their metabolites in the cortex, hippocampus, and striatum

As shown in Table 1, moclobemide and clorgyline induced similar changes on monoamine and metabolite levels. NM levels drastically increased in all three regions examined (9- to 37-fold), as did 3MT levels in the striatum (9- to 21-fold) following the administration of either moclobemide or clorgy-
Monoamine Oxidation by MAO-A In Vivo

Table 1. Changes in monoamine levels by moclobemide, clorgyline, and deprenyl

|                | Control       | Moclobemide | Clorgyline | Deprenyl       | Clorgyline + Deprenyl |
|----------------|---------------|-------------|------------|----------------|-----------------------|
| Cortex         |               |             |            |                |                       |
| NE             | 20.6 ± 1.2    | 27.6 ± 1.3* | 26.1 ± 1.4*| 20.5 ± 0.6     | 27.7 ± 0.6            |
| NM             | 0.16 ± 0.03   | 1.77 ± 0.21*| 1.40 ± 0.09**| 0.18 ± 0.03 | 2.86 ± 0.47*       |
| DA             | 3.73 ± 0.70   | 3.79 ± 0.77 | 2.73 ± 0.30| 2.83 ± 0.37    | 3.20 ± 0.23           |
| DOPAC          | 0.48 ± 0.11   | 0.11 ± 0.06*| 0.04 ± 0.01**| 0.43 ± 0.08 | 0.04 ± 0.01       |
| HVA            | 0.32 ± 0.11   | 0.00 ± 0.00**| 0.22 ± 0.05| 0.54 ± 0.05*   | 0.08 ± 0.04*       |
| 5HT            | 26.7 ± 1.4    | 42.5 ± 2.1* | 33.9 ± 1.9*| 27.6 ± 0.7     | 36.0 ± 2.3           |
| 5HIAA          | 7.6 ± 0.3     | 5.5 ± 0.4*  | 5.7 ± 0.2**| 8.8 ± 0.3*     | 5.7 ± 0.6            |
| Hippocampus    |               |             |            |                |                       |
| NE             | 28.4 ± 1.3    | 36.2 ± 1.7**| 36.1 ± 1.8**| 31.6 ± 1.5    | 38.1 ± 1.8           |
| NM             | 0.08 ± 0.02   | 0.91 ± 0.02*| 0.73 ± 0.13*| 0.16 ± 0.04   | 1.87 ± 0.97          |
| DA             | 2.95 ± 0.60   | 2.74 ± 0.36 | 2.46 ± 0.19| 2.86 ± 0.18    | 3.28 ± 0.32          |
| DOPAC          | 0.26 ± 0.05   | 0.02 ± 0.01**| 0.11 ± 0.04*| 0.30 ± 0.03   | 0.10 ± 0.02          |
| HVA            | 0.26 ± 0.05   | 0.01 ± 0.01**| 0.05 ± 0.01**| 0.36 ± 0.03   | 0.15 ± 0.05*        |
| 5HT            | 39.7 ± 2.4    | 51.2 ± 3.5* | 48.8 ± 2.1*| 38.6 ± 1.1     | 52.7 ± 2.3           |
| 5HIAA          | 17.6 ± 0.7    | 13.4 ± 0.7**| 15.0 ± 0.9 | 19.2 ± 0.4     | 16.2 ± 0.9           |
| Striatum       |               |             |            |                |                       |
| NE             | 11.9 ± 1.3    | 13.3 ± 1.6  | 14.2 ± 0.8 | 12.9 ± 1.1     | 18.4 ± 1.5*          |
| NM             | 0.03 ± 0.01   | 1.10 ± 0.18**| 0.73 ± 0.09**| 0.06 ± 0.04   | 1.04 ± 0.22          |
| DA             | 750 ± 35      | 886 ± 46    | 895 ± 32*  | 818 ± 16       | 949 ± 38             |
| 3MT            | 1.9 ± 0.2     | 39.0 ± 7.6* | 18.0 ± 1.7**| 2.5 ± 0.6     | 21.1 ± 3.6           |
| DOPAC          | 46.7 ± 3.6    | 7.3 ± 1.1*  | 17.6 ± 1.6**| 45.7 ± 1.3    | 13.6 ± 2.0           |
| HVA            | 30.9 ± 1.9    | 6.5 ± 1.1*  | 14.0 ± 1.2**| 30.9 ± 0.8    | 14.1 ± 1.2           |
| 5HT            | 40.9 ± 2.4    | 64.7 ± 1.1* | 50.8 ± 2.2*| 39.3 ± 1.6    | 50.7 ± 2.0           |
| 5HIAA          | 23.5 ± 0.8    | 16.0 ± 1.1* | 18.4 ± 1.0**| 25.7 ± 0.6    | 18.8 ± 1.3           |

Means ± S.E.M. (N = 7–9). The data are expressed as pmol/mg protein. Rats were killed by microwave irradiation 2 hr after administration of moclobemide (20 mg/kg, p.o.) or 4 hr after administration of clorgyline (10 mg/kg, p.o.) or deprenyl (10 mg/kg, p.o.). NE, norepinephrine; NM, normetanephrine; DA, dopamine; 3MT, 3-methoxytyramine; DOPAC, 3,4-dihydroxyphenylacetic acid; HVA, homovanillic acid; 5HT, serotonin; and 5HIAA, 5-hydroxyindoleacetic acid. *P < 0.05, **P < 0.01, as compared with the control (Mann-Whitney U-test). *P < 0.05 as compared with rats treated with clorgyline alone (Mann-Whitney U-test).

line. NE and 5HT levels in the cortex and hippocampus increased significantly; and the levels of their metabolites, such as DOPAC, HVA, and 5HIAA, in all three regions tested clearly decreased following treatment with either of these MAO-A inhibitors (Table 1). The increase in the DA level in the striatum induced by clorgyline was statistically significant, while that induced by moclobemide was not statistically significant. These two MAO-A inhibitors did not alter DA levels in the cortex and hippocampus. Deprenyl, an MAO-B inhibitor, did not affect any monoamine or metabolite level in any region, except for increases in HVA and 5HIAA in the cortex. When deprenyl was administered simultaneously with clorgyline, deprenyl did not modify the effects of clorgyline, except those on NM in the cortex, NE in the striatum, and HVA in the cortex and hippocampus.

Time course of RS-8359-induced changes in monoamine and metabolite levels in the cortex, hippocampus, and striatum

After treatment with RS-8359 (10 mg/kg, p.o.), the maximum increase in NE was
observed at 2 hr in the cortex, 2–6 hr in the hippocampus, and 6 hr in the striatum. Increases in NM levels in all three regions reached their maximum values at 6 hr after treatment with RS-8359 (Fig. 1). RS-8359 induced a significant increase in the DA level in the striatum, but not in the cortex and hippocampus, at 3 hr after administration. DOPAC in the cortex and hippocampus and HVA in the hippocampus were significantly decreased at 9 hr, and HVA in the cortex was reduced at 6 hr after treatment with RS-8359. An increase in 3MT and decreases in DOPAC and HVA in the striatum attained their maximum values at 6 hr after the treatment. Significant increases in 5HT levels were induced by RS-8359 at 6–9 hr in the cortex, at 2–9 hr in the hippocampus, and at 6–9 hr in the striatum. RS-8359 did not, however, change 5HIAA levels in any region at any period after administration. The levels of monoamines and their metabolites had returned to normal by 20 hr after administration.

**Dose-dependent effects of RS-8359**

Monoamine and metabolite levels were determined at 1 and 6 hr after administration of the doses (up to 30 mg/kg, p.o.) of RS-8359, since the effects of 10 mg/kg of RS-8359 appeared at one hr after administration and reached a maximum at 2 to 6 hr after administration.

At 1 hr after administration of RS-8359, increases in NE and NM levels were observed in the cortex and hippocampus at a dose of 30 mg/kg (Fig. 2). RS-8359 caused increases in 5HT levels in all regions at a dose of 30 mg/kg, although the 5HIAA level was not affected in any region. For the dopaminergic system, RS-8359 induced a decrease in DOPAC in the cortex and a dose-dependent increase in the DA level in the hippocampus (Fig. 3). In the striatum, RS-8359 induced dose-dependent decreases in DOPAC and...
HVA levels and a dose-dependent increase in the 3MT level.

At 6 hr after administration, the effects on the metabolite levels were greatest at 30 mg/kg (NM: 6- to 32-fold, 3MT: 9-fold, DOPAC: 33–39%, HVA: 16–43%), except for the 5HIAA levels in all regions. However, the changes in NE at 30 mg/kg were smaller than those at 10 mg/kg. DA levels in the striatum increased to the greatest degree at 30 mg/kg. The levels of 5HT increased at 30 mg/kg as much as they did at 10 mg/kg.

DISCUSSION

In our study, the following were clearly shown: Moclobemide and clorgyline increased the substrates for MAO and decreased the deaminated metabolites in the cerebral cortex, hippocampus, and striatum. On the other hand, deprenyl, an MAO-B inhibitor, caused no changes in NE, DA, 5HT, and their metabolites in all three regions, except for increases in HVA and 5HIAA in the cortex. The reason for the changes observed in HVA and 5HIAA by deprenyl, which cannot be explained by MAO inhibition, are not known at present. Furthermore, when deprenyl was coadministered with clorgyline, NM in the cortex and NE in the striatum increased while HVA in the cortex decreased, although NM in the striatum was not affected and HVA in the hippocampus was reversed by coadministration with deprenyl. Since the changes in NM by MAO-A inhibitors were much greater than those in NE, the increases in NE with no change in NM in the striatum induced by coadministration with deprenyl appear not to be due to MAO inhibition. From these results, NE and DA in the hippocampus and striatum and 5HT in the cortex, hippocampus, and striatum are suggested to be exclusively deaminated by MAO-A. Further, the present results suggest that MAO-B participates,
results that DA and DOPAC levels were affected by treatment with deprenyl. Moreover, Green et al. (10) also have suggested that DA is deaminated by both forms of MAO. Although all these previous studies used decapitation to sacrifice the animals, there have been some discrepancies in their results. Moreover, the results of some studies (11, 13, 20) are consistent with those of the present study using microwave irradiation to sacrifice the animals. Hence the inconsistency between the results of the previous studies and those of the present study cannot be explained simply by the difference in the methods used to sacrifice animals. However, because decapitation has been reported to change the levels of monoamines and metabolites (21, 22), the levels of monoamines and metabolites could be affected by the time required for preparing the samples following decapitation. This artifact is eliminated in the present study because we used microwave irradiation to sacrifice the animals. Thus it is concluded from the present study that these three monoamines are exclusively or preferentially deaminated by MAO-A in the cortex, hippocampus, and striatum.

RS-8359 clearly elevated the substrates for MAO and reduced almost all of the deaminated metabolites in all three regions tested. These changes in monoamine and metabolite levels induced by RS-8359 were almost identical to those induced by moclobemide and clorgyline. Significant changes were observed at doses over 10 mg/kg, and the maximum effects appeared at 2 to 6 hr after administration. These results show that RS-8359 exhibits its reversible MAO-A inhibitory action in the cerebral cortex, hippocampus, and striatum in vivo. A previous report (4) from our laboratory has also shown that RS-8359 caused increases in NE, DA, and 5HT and decreases in DOPAC and HVA in mouse whole brain. The maximum effects of RS-8359 on the mouse brain were obtained 1 hr after administration. There probably are some differences in the absorption and/or metabolism of RS-8359 between the mouse and rat.
RS-8359 did not affect 5HIAA levels at any dose or in any region tested, while it clearly increased 5HT levels. Since clorgyline, which increased 5HT levels as much as RS-8359, decreased 5HIAA levels, RS-8359 probably has other effects on the serotonergic system, such as the activation of synthesis and/or release. Further studies are required to clarify these possibilities.

The dose of RS-8359 responsible for the maximum effects on NE levels was different from that on NM (30 mg/kg for NE vs. 10 mg/kg for NM) in all three regions tested, although DA and its metabolites were affected to the greatest degree at a dose of 30 mg/kg of RS-8359. These findings imply that the regulation mechanisms of the levels of NE and DA are different. The noradrenergic system appears to be more sensitively regulated by feedback inhibition (e.g., tryptophan hydroxylase inhibition by NE) than the dopaminergic system.

In conclusion, NE, DA, and 5HT are exclusively or preferentially deaminated by MAO-A in the cortex, hippocampus, and striatum of rats, and RS-8359 exhibits a reversible MAO-A inhibitory action in all three regions in vivo.

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REFERENCES

1 Fowler, C.J. and Ross, S.B.: Selective inhibitors of monoamine oxidase A and B: Biochemical, pharmacological, and clinical properties. Med. Res. Rev. 4, 323–358 (1984)
2 Johnston, J.P.: Some observations upon a new inhibitor of monoamine oxidase in brain tissue. Biochem. Pharmacol. 17, 1285–1297 (1968)
3 Knoll, J. and Magyar, K.: Some puzzling pharmacological effects of monoamine oxidase inhibitors. In Advances in Biochemical Psychopharmacology, Edited by Costa, E. and Sandler, M., Vol. 5, Monoamine Oxidases–New Vistas, p. 393–408, Raven Press, New York (1972)
4 Yokoyama, T., Karube, T. and IWata, N.: Comparative studies of the effects of RS-8359 and safrazine on monoamine oxidase in-vitro and in-vivo in mouse brain. J. Pharm. Pharmacol. 41, 32–36 (1989)
5 IWata, N., Kobayashi, K., Kozuka, M., Tomohiro, T., Yoshimi, K. and Kubo, Y.: RS-8359, a reversible and selective inhibitor of MAO-A, ameliorates ischemia-induced brain damage. Soc. Neurosci. Abstr. 15, 44 (1989)
6 Brownstein, M., Saavedra, J.M. and Palkovits, M.: Norepinephrine and dopamine in the limbic system of the rat. Brain Res. 79, 431–436 (1974)
7 Saavedra, J.M., Brownstein, M. and Palkovits, M.: Serotonin distribution in the limbic system of the rat. Brain Res. 79, 437–441 (1974)
8 Strolin Benedetti, M., Dostert, P., Boucher, T., and Guiffroy, C.: A new reversible selective type B monoamine oxidase inhibitor: MD780236. In Monoamine Oxidase – Basic and Clinical Frontiers, Edited by Kamijo, K., Usdin, E. and Nagatsu, T., p. 209–220, Exerpta Medica, Amsterdam (1981)
9 Yang, H.-Y.T. and Neff, N.H.: The monoamine oxidases of brain: Selective inhibition with drugs and the consequences for the metabolism of the biogenic amines. J. Pharmacol. Exp. Ther. 189, 733–740 (1974)
10 Green, A.R., Mitchell, B.D., Tordoff, A.F.C. and Youdim, M.B.H.: Evidence for dopamine deamination by both type A and type B monoamine oxidase in rat brain in vivo and for the degree of inhibition of enzyme necessary for increased functional activity of dopamine and 5-hydroxytryptamine. Br. J. Pharmacol. 60, 343–349 (1977)
11 Waldmeier, P.C., Delini-Stula, A. and Maître, L.: Preferential deamination of dopamine by an A type monoamine oxidase in rat brain. Naunyn Schmiedebergs Arch. Pharmacol. 292, 9–14 (1976)
12 Fuller, R.W., Herrick-Luecke, S.K. and Perry, K.W.: Influence of harmaline on the ability of pergylene to alter catecholamine metabolism in rats. Biochem. Pharmacol. 30, 1295–1296 (1981)
13 Youdim, M.B.H.: In vivo, noradrenaline is a substrate for rat brain monoamine oxidase A and B. Br. J. Pharmacol. 79, 477–480 (1983)
14 Lowry, O.H., Rosebrough, N.J., Farr, A.L. and Randall, R.L.: Protein measurement with the Folin phenol reagent. J. Biol. Chem. 193, 265–275 (1951)
15 Strolin Benedetti, M., Dostert, P., Guiffroy, C. and Tipton, K.F.: Partial or total protection from long-acting monoamine oxidase inhibitors (MAOIs) by new short-acting MAOIs of type A MD780515 and type B MD780236. In Monoamine Oxidase and Its Selective Inhibitors, Edited by
Beckmann, H. and Riederer, P., Vol. 19, Modern Problems of Pharmacopsychiatry, p. 82–104, Karger, Basel (1983)

16 Da Prada, M., Kettler, R., Keller, H.H. and Haefely, W.E.: Neurochemical effects in vitro and in vivo of the antidepressant Ro 11-1163, a specific and short-acting MAO-A inhibitor. In Monoamine Oxidase and Its Selective Inhibitors, Edited by Beckmann, H. and Riederer, P., Vol. 19, Modern Problems of Pharmacopsychiatry, p. 231–245, Karger, Basel (1983)

17 Kan, J.-P., Steinberg, R., Mouget-Goniot, C., Worms, P. and Bizière, K.: SR 95191, a selective inhibitor of type A monoamine oxidase with dopaminergic properties. II. Biochemical characterization of monoamine oxidase inhibition. J. Pharmacol. Exp. Ther. 240, 251–258 (1987)

18 Waldmeier, P.C., Felner, A.E. and Lauber, J.: Reversible monoamine oxidase inhibitors: Relation between effects on enzymatic activity measured ex vivo and on amine metabolism. In Monoamine Oxidase and Disease, Edited by Tipton, K.F., Dostert, P. and Benedetti, S.M., p. 107–116, Academic Press, New York (1984)

19 Wolf, W.A., Youdim, M.B.H. and Kuhn, D.M.: Does brain 5-HIAA indicate serotonin release or monoamine oxidase activity? Eur. J. Pharmacol. 169, 381–387 (1985)

20 Ask, A.-L., Hellström, W., Normman, S., Ögren, S.-O. and Ross, S.B.: Selective inhibition of the A form of monoamine oxidase by 4-dimethylamino-α-methylphenylalkylamine derivatives in the rat. Neuropharmacology 21, 299–308 (1982)

21 Ishikawa, K., Shibanoki, S., Saito, S. and McGaugh, J.L.: Effect of microwave irradiation on monoamine metabolism in dissected rat brain. Brain Res. 240, 158–161 (1982)

22 Blank, C.L., Sasa, S., Isernhagen, R., Meyerson, L.R., Wassil, D., Wong, P., Modak, A.T. and Stavinoha, W.B.: Levels of norepinephrine and dopamine in mouse brain regions following microwave inactivation–Rapid post-mortem degradation of striatal dopamine in decapitated animals. J. Neurochem. 33, 213–219 (1979)