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Bromocriptine Enhances Feeding Behavior Without Changing Dopamine Metabolism

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INOUE, K., N. KIRIIKE, M. KURIOKA, Y. FUJISAKI, S. IWASAKI AND S. YAMAGAMI. *Bromocriptine enhances feeding behavior without changing dopamine metabolism.* PHARMACOL BIOCHEM BEHAV **58**(1) 183–188, 1997.—Bromocriptine is an ergot derivative and has been thought to act as a selective D_2 receptor agonist, but its effects on dopamine release in vivo have not been confirmed. We administered bromocriptine into the striatum of rats and studied the effects on feeding behavior and dopamine release. Bromocriptine was perfused via a microdialysis probe into the ventrolateral striatum of rats fasted for 22 h, and the rats were then allowed to feed freely for 6 h. Bromocriptine perfusion increased food intake in a dose-dependent manner, whereas the extracellular concentrations of dopamine, 3,4-dihydroxyphenylacetic acid (DOPAC), and homovanillic acid (HVA) did not change. Perfusion of (−)sulpiride, a selective D_2 receptor antagonist, decreased food intake, but increased dopamine release and the levels of DOPAC and HVA. Pretreatment with (−)sulpiride perfusion for 1 h prior to bromocriptine perfusion inhibited the increase of food intake induced by bromocriptine, and it increased dopamine release and the levels of DOPAC and HVA. These findings suggest that bromocriptine directly perfused into the ventrolateral striatum acts selectively on postsynaptic D_2 receptors and enhances feeding behavior. © 1997 Elsevier Science Inc.

Bromocriptine Feeding behavior Dopamine receptor Microdialysis Ventrolataral striatum Rat

BROMOCRIPTINE is an ergot derivative that has been shown to act as an agonist on D_2 receptors at micromolar concentrations and as an antagonist on striatal D_1 receptors at nanomolar concentrations (21,25). However, a 33,000-fold higher concentration of bromocriptine is required to cause an accumulation of cyclic adenosine monophosphate (AMP) than to inhibit prolactin release (26). In addition, the IC50 of bromocriptine for D_1 and D_2 receptors has been demonstrated by using autoradiography to be 133 μM and 8.5 mM, respectively (29). For these reasons, bromocriptine has recently been thought to act as a selective D_2 receptor agonist and has been widely used for treatment of psychiatric and neurological diseases such as Parkinson's disease.

Bromocriptine, as well as other ergot derivatives such as lisuride and lergotrile, has been shown to reduce the consumption of standard laboratory diets during periods of restricted access to food (2). Treatment with bromocriptine, the recently developed specific D_2 agonist quinpirole, or the specific D_1 agonist SKF 38393 induced dose-dependent anorexia in rats; the anorectic effect of bromocriptine was antagonized by pretreatment with pimozide (a D_2 antagonist) (30). In other studies, however, intraperitoneal injections of *l*-dopa or bromocriptine did not change food intake (10), and intracerebroventricular administrations of bromocriptine and amphetamine increased food intake (7). These findings concerning food intake following intraperitoneal and intracerebroventricular injections of bromocriptine are clearly inconsistent. Furthermore, in none of these studies were the effects on dopamine metabolism assessed in vivo, except in that using bromocriptine as a D_2 receptor agonist. There is also no evidence that the behavioral effects induced by bromocriptine are related to dopamine metabolism.

The heterogeneity of organization in the striatum (9,16,23) and the different roles for various striatal subregions in the control of certain motor functions have been reported. In the

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rat, the medial striatum mainly receives projections from the medial frontal cortex and is selectively involved in the performance of spatial learning tasks (5,6,19). In contrast, the lateral striatum mainly receives projections from the dorsolateral frontoparietal cortex and is involved in the motor control of segmental movements such as tongue and forelimb movements (4,22). The ventrolateral striatum is closely involved in the motor control of oral activity (16,17,22,24). Perfusion of the ventrolateral striatum with the D_2 receptor agonist quinpirole at 10^{-5} and 10^{-4} M concentration (2.56×10^{-2} and 2.56×10^{-1} pg/μl) increased food intake by 41% relative to the control value, whereas perfusion with the D_2 receptor antagonist (−)sulpiride suppressed both food and water intake (13). Quinpirole perfusion decreased not only dopamine release but also the concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in a non-dose-dependent manner (13). Sulpiride perfusion increased the release of dopamine, DOPAC, and HVA at all concentrations (13). See et al. (27) also reported that administration of a D_2 receptor agonist and antagonist elicits the same changes in dopamine release. These findings suggested that D_2 receptors in the ventrolateral striatum are involved in the regulation of food intake in the rat.

The present study was performed to clarify whether bromocriptine acts as a D_2 receptor agonist in vivo and, furthermore, whether it acts as a full or partial D_2 receptor agonist. Bromocriptine was directly perfused via a microdialysis probe into the ventrolateral striatum of fasted rats, and the extracellular concentrations of dopamine, DOPAC, and HVA as well as the food intake (as an index of oral activity as behavioral changes) (14) were measured hourly. Effects of (−)sulpiride perfusion alone and pretreatment with (−)sulpiride perfusion prior to bromocriptine perfusion on behavioral changes are also examined.

METHODS

Animals and Drug Treatment

Female Wistar rats (Keari Co., Osaka, Japan) each weighing 180–210 g were used in the study. The rats were housed individually and were fed laboratory chow (24.8% crude protein, 4.4% crude fat, 3.5% crude fiber, 7.0% crude ash, 51.6% nitrogen-free extract, 8.7% water; 345.2 Cal/100 g) and water ad lib. They were kept in plastic cages (30 × 30 × 35 cm) with a 12 L:12 D cycle (lights on 2000–0800 h) and ambient temperature regulated to 22 ± 2°C. They were cared for in compliance with the Guidelines for Animal Experimentation of Osaka City University.

Bromocriptine (Sandoz Pharmaceutical Ltd., Basel, Switzerland) and (−)sulpiride (Sigma Chemical Co., St. Louis, MO, USA) were dissolved in water with $(CH_3)_2SO$ and H_2SO_4 and then diluted with Ringer's solution (149 mM NaCl, 1.3 mM KCl, and 1.5 mM $CaCl_2$).

Surgery and Microdialysis

Each rat was anesthetized with chloral hydrate (400 mg/kg intraperitoneally), and a dialysis guide cannula was implanted in the left ventrolateral striatum according to the following coordinates from the atlas of Paxinos and Watson (20): AP +0.5 mm, L +3.0 mm, and V −3.5 mm from the bregma and dural surface. The cannula was secured to the skull with a screw and dental cement, and a wire stylet was placed in the guide to keep it free of debris. A 10-day period was allowed for the rat to recover from surgery.

Experimental Procedures and Drug Perfusion

At least 12 h before the beginning of each experiment, a dialysis probe with a 3-mm-long cellulose tip was inserted into the guide cannula. Ringer's solution was continuously perfused through the probe at a flow rate of 1 μl/min.

In experiment 1, after the basal levels of extracellular dopamine, DOPAC, and HVA became stable, three 20-min baseline samples were collected during a 1-h period (1000–1100 h) following 21 h of food deprivation. Ringer's solution containing bromocriptine (25×10^{-4}, 0.25, or 25 μg/μl) was perfused into the ventrolateral striatum for 6 h (1100–1700 h) through a microdialysis probe ($n = 5$ rats in each group). The animals were allowed free access to food, and food intake was measured hourly. A known weight of food (about 50 g) was provided in a removable plastic food container designed to allow access to the food and minimize food spillage. When spillage did occur, the spilled food was collected and added to the unconsumed total. The unconsumed food was weighed at hourly intervals and the remaining food was replaced after measurement. These measurements were done carefully so as not to disturb the rat. The extracellular concentrations of dopamine, DOPAC, and HVA were measured every 20 min. Ringer's solution containing (−)sulpiride at 2.5 μg/μl, a dose selected based on the results of a previous study (13), was also perfused into the ventrolateral striatum for 6 h (1100–1700 h) through a microdialysis probe ($n = 7$). The food intake and concentrations of dopamine and its metabolites were measured as described. Perfusion of Ringer's solution alone was performed as a control ($n = 8$).

In experiment 2, after the basal levels of extracellular dopamine, DOPAC, and HVA became stable, three 20-min baseline samples were collected during a 1-h period (0900–1000 h) following 20 h of food deprivation. Ringer's solution containing (−)sulpiride at 2.5 μg/μl was perfused into the ventrolateral striatum for 1 h (1000–1100 h), and then Ringer's solution containing both (−)sulpiride at 2.5 μg/μl and bromocriptine at the most effective dose found in experiment 1 (25 μg/μl) was perfused into the region for 6 h (1100–1700 h). The animals ($n = 6$) were allowed free access to food for the 6-h period (1100–1700 h). Food intake and the concentrations of dopamine and its metabolites were measured as in experiment 1.

At the end of the experiment, the rats were killed and their brains were removed and frozen. Examination of the cannula track was carried out using thin sections cut with a razor blade. The ventrolateral striatum was defined through reference to the atlas of Paxinos and Watson (20). The track, at least 3 mm from the tip, was found to be correctly located and to terminate within the ventrolateral striatum in all rats.

High-Performance Liquid Chromatography (HPLC)

For quantification of the levels of dopamine, DOPAC, and HVA in the dialysate, samples were collected every 20 min and injected through an automatic injector (AS-10, Eicom, Kyoto, Japan) into an HPLC apparatus with an electrochemical detector (EP-10 and ECD-100, Eicom) and an ODS reverse-phase column (Eicompac MA-5ODS, Eicom). The mobile phase consisted of 80% (vol/vol) 0.1 M KH_2PO_4, 20% (vol/vol) methanol, 150 mg/liter sodium octane sulphonate, and 10 μM EDTA2Na. Detection was with a graphite working electrode coupled to the electrochemical detector.

Statistical Analysis

Data for each group of five to eight rats each are reported. For the analysis of food intake, a repeated-measures analysis

TABLE 1

EFFECTS OF DRUGS ON FOOD INTAKE OF FASTED RATS

Treatment	*n*	Food intake (g)					
		1 h	2 h	3 h	4 h	5 h	6 h
Ringer's solution	8	3.8 ± 0.9	4.7 ± 1.1	5.2 ± 1.1	7.5 ± 1.5	8.7 ± 1.1	10.3 ± 1.3
BC 25 × 10^{-4}	5	4.2 ± 0.2	5.8 ± 0.7	6.6 ± 0.6	8.3 ± 0.5	9.5 ± 1.0	11.3 ± 1.5
BC 0.25	5	5.9 ± 0.7	6.8 ± 0.6	7.7 ± 0.8	10.5 ± 1.1	11.8 ± 0.9	12.1 ± 0.9
BC 25	5	8.2 ± 1.6	8.7 ± 1.4	11.5 ± 0.8	12.4 ± 1.2	13.8 ± 1.9	14.9 ± 1.5
SUL 2.5	7	3.5 ± 0.6*	4.2 ± 1.0*	4.6 ± 0.8*	4.8 ± 1.0*	5.5 ± 0.9*	6.0 ± 1.1*
BC 25 + SUL 2.5	6	2.2 ± 0.8*	2.5 ± 0.6*	3.9 ± 1.1*	4.2 ± 1.0*	6.1 ± 1.6*	6.3 ± 1.5*

Cumulative food intake during perfusion of Ringer's solution (control), bromocriptine (BC), sulpiride (SUL), and BC + SUL into the ventrolateral striatum for 6 h is reported. Drug doses are expressed as μg/μl/min. Values are mean ± SEM. *$p < 0.05$ compared with BC 25 μg/μl/min group (Scheffé's *F*-test).

of variance (ANOVA) with factors of pretreatment and time was performed. Then, if appropriate, comparisons between the control group and each drug-treated group were carried out using Scheffé's *F*-test.

Due to the large variations among individual rats for the basal extracellular concentrations of dopamine, DOPAC, and HVA, the data for each parameter were normalized as a percentage of the mean value in the three samples taken for basal release. Then, a repeated-measures ANOVA with factors of pretreatment and time was performed for group comparisons. To compare the basal level and experimental values obtained at any specific time point in each group, a two-sample *t*-test with Welch's correction (11,18) was used because variances were unknown and not necessarily equal.

RESULTS

Experiment 1

Perfusion with bromocriptine increased food intake [factor drug effect, $F(3, 19) = 3.82$, $p < 0.05$; pretreatment × time interaction, $F(15, 95) = 0.50$, $p = 0.93$] in a dose-dependent manner. Bromocriptine at 25 μg/μl/min increased food intake to 210% during the first hour of the free feeding period compared with the control group (8.2 ± 1.6 g vs. 3.8 ± 0.9 g; Table 1). The extracellular concentrations of dopamine, DOPAC, and HVA at each concentration of bromocriptine are shown in Fig. 1. Perfusion with bromocriptine did not change the extracellular concentration of dopamine [factor drug effect, $F(3, 11) = 0.32$], DOPAC [$F(3, 11) = 0.90$], or HVA [$F(3, 11) = 0.13$]. Bromocriptine perfusion at all doses tested did not change the dopamine, DOPAC, or HVA concentration significantly at any time during the 6-h perfusion period compared with the basal level, although DOPAC and HVA concentrations in the control group and bromocriptine-treated groups increased to maximally 120% of basal levels during perfusion. Sulpiride perfusion at 2.5 μg/μl/min tended to decrease food intake during the 6-h perfusion period compared with the control group [$F(1, 13) = 3.78$, $p = 0.7$]. The dopamine, DOPAC, and HVA concentrations were significantly increased by sulpiride perfusion, with the maximal changes being about 60%, 80%, and 100% compared with their basal levels, respectively (Fig. 2).

Experiment 2

When an ANOVA was done comparing groups treated with sulpiride perfusion for 1 h prior to bromocriptine perfu-

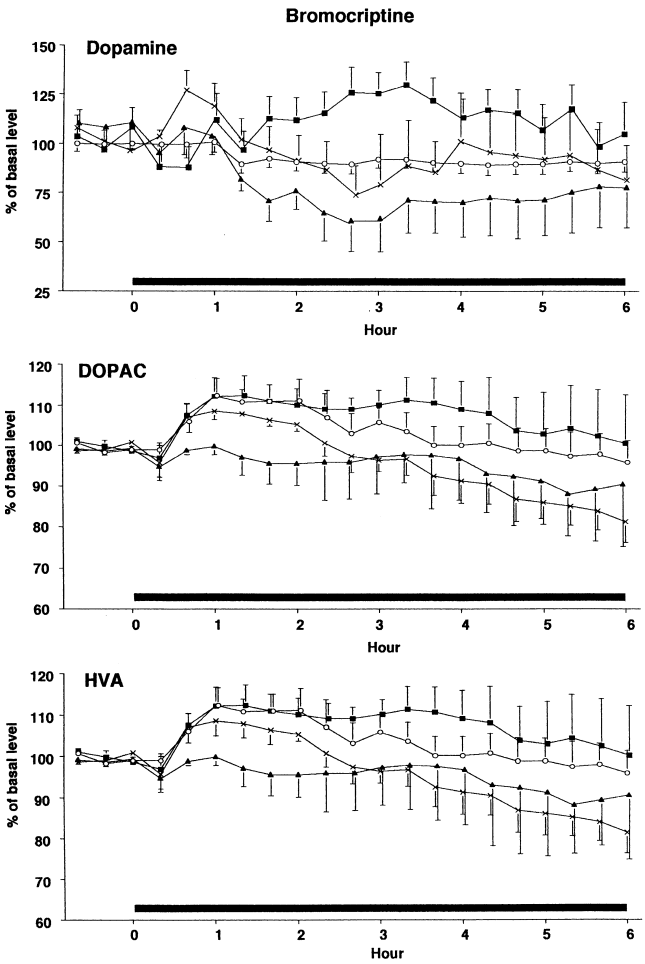

FIG. 1. Changes of the striatal extracellular concentrations of dopamine, DOPAC, and HVA during perfusion of bromocriptine (■) into the ventrolateral striatum for 6 h. Circles, triangles, crosses, and squares represent the data for the control group ($n = 8$), the 25 × 10^{-4} μg/μl/min group ($n = 5$), the 0.25 μg/μl/min group ($n = 5$), and the 25 μg/μl/min group ($n = 5$), respectively. Values are mean ± SEM.

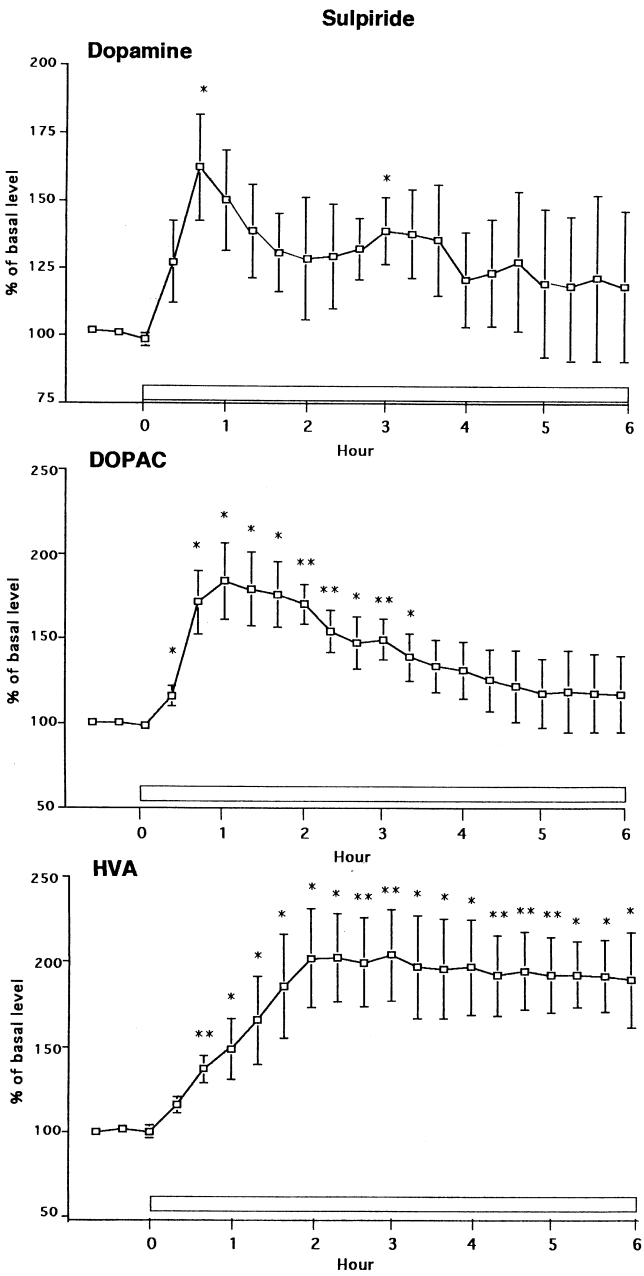

FIG. 2. Changes of the striatal extracellular concentrations of dopamine, DOPAC, and HVA during perfusion of sulpiride (□) at 2.5 μg/μl/min into the ventrolateral striatum for 6 h. Values are mean ± SEM ($n = 7$). *$p < 0.05$ and **$p < 0.01$ compared with the basal level (two-sample t-test with Welch's correction).

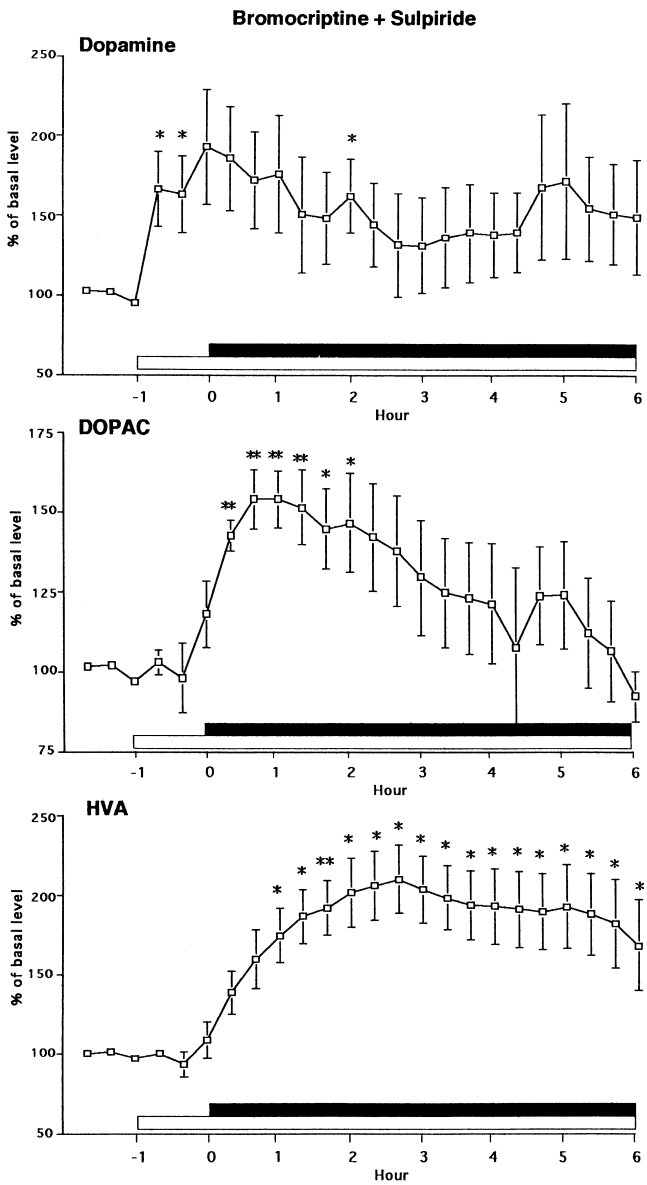

FIG. 3. Changes of the striatal extracellular concentrations of dopamine, DOPAC, and HVA during perfusion of sulpiride at 2.5 μg/μl/min (□) and bromocriptine at 25 μg/μl/min (■) into the ventrolateral striatum for 6 h ($n = 6$). Values are mean ± SEM. *$p < 0.05$ and **$p < 0.01$ compared with the basal level (two-sample t-test with Welch's correction).

sion, bromocriptine (25 μg/μl/min) alone, and sulpiride alone, there was a significant difference among groups [factor drug effect, $F(2, 15) = 19.47$, $p < 0.01$; pretreatment × time interaction, $F(10, 75) = 3.67$, $p < 0.01$]. Pretreatment with sulpiride perfusion for 1 h prior to bromocriptine perfusion decreased food intake to 27% compared with that of bromocriptine perfusion alone during the first hour (2.2 ± 0.8 g vs. 8.2 ± 1.6 g). The increase of food intake induced by bromocriptine perfusion at 25 μg/μl/min was significantly inhibited by the pretreatment with sulpiride perfusion throughout the feeding period [$F(1, 9) = 19.87$, $p < 0.01$; pretreatment × time interaction, $F(5, 45) = 2.03$, $p = 0.09$]. The food intake of the rats pretreated with sulpiride perfusion prior to bromocriptine perfusion was not different from that of the rats undergoing sulpiride perfusion alone [$F(1, 11) = 0.50$]. The extracellular concentrations of dopamine, DOPAC, and HVA in the ventrolateral striatum were significantly increased by the combined perfusion of sulpiride and bromocriptine, with maximal changes being about 90%, 60%, and 110% compared with their basal levels, respectively (Fig. 3). The extracellular concentrations of dopamine, DOPAC, and HVA in the rats pretreated with sulpiride perfusion prior to bromocriptine perfusion were

not different from those of the rats undergoing sulpiride perfusion alone [dopamine, $F(1, 11) = 1.09$; DOPAC, $F(1, 11) = 0.66$; and HVA, $F(1, 11) = 0.36$].

DISCUSSION

In this study, bromocriptine perfusion into the ventrolateral striatum increased food intake in a dose-dependent manner in rats fasted for 22 h. Bromocriptine perfusion did not change the extracellular concentrations of dopamine, DOPAC, or HVA. Although slight increases of DOPAC and HVA concentrations were observed, the increase might have been caused by feeding behavior itself, because it occurred in both the control and the bromocriptine-treated groups. Sulpiride perfusion at 2.5 μg/μl/min tended to decrease food intake and significantly increased the extracellular concentrations of dopamine, DOPAC, and HVA; these results are consistent with our previous report (13). Pretreatment with sulpiride perfusion for 1 h prior to bromocriptine perfusion completely inhibited the increase of food intake induced by bromocriptine perfusion.

The effect of bromocriptine perfusion into the ventrolateral striatum of increasing food intake in a dose-related manner is similar to that induced by quinpirole [see introduction; (13)]. However, perfusion of bromocriptine into the ventrolateral striatum at all concentrations did not change the concentrations of dopamine and its metabolites. This suggests that bromocriptine enhanced feeding behavior without changing dopamine metabolism in the ventrolateral striatum. Bromocriptine has been used as a dopamine D_2 receptor agonist in a variety of experiments. Recently, quinpirole has been used as a more specific D_2 agonist. There is a discrepancy between the effects of bromocriptine and quinpirole on the release of dopamine. Using a microdialysis technique, the effects of various dopamine receptor agonists (injected subcutaneously) on the release and metabolism of dopamine in the nucleus accumbens and the dorsal caudate have been examined (12). In these studies, with brain dialysis in freely mobile rats it was possible to distinguish the effects of full dopamine agonists on pre- and postsynaptic D_2 receptors [apomorphine, quinpirole, pergolide, and (+)-3PPP] from the effects of agonists preferentially acting on dopamine autoreceptors (BHT 920) and from the effects of partial D_2 agonists that behave in vivo as dopamine antagonists [(−)-3PPP]. Dopamine release is regulated primarily by the presynaptic autoreceptor, mainly of the D_2 subtype (3). Bromocriptine as applied in this study might act selectively on the postsynaptic D_2 receptor without release of dopamine but enhancing feeding behavior.

As another possible explanation for the discrepancy of bromocriptine perfusion increasing food intake in a dose-dependent manner without changing dopamine metabolism, bromocriptine might influence behaviors through hormonal changes as it acts on prolactin suppression, or through changes of other neurotransmitters (15). In this study, pretreatment with sulpiride perfusion for 1 h prior to bromocriptine perfusion completely inhibited the increase of food intake elicited by bromocriptine perfusion. These results indicate that that D_2 receptor plays a major role in behavioral changes induced by bromocriptine.

Bromocriptine is also suggested to have antagonist actions in nanomolar concentrations on striatal D_1 receptors (21,25). However, other D_1 agonists (CY 208-243) and antagonists (SCH 23390) at all concentrations did not affect feeding behavior or the concentrations of dopamine and its metabolites (13). These findings suggest that the enhanced effect of bromocriptine on feeding behavior is not mediated by such antagonistic effects of the D_1 receptor.

Dopamine receptors can be classified into five or more subtypes (8,28). However, these can be broadly classified into two types. Receptors of the D_1 type stimulate the enzyme adenylate cyclase. Receptors of the D_2 type are not linked in a facilitative manner to adenylate cyclase (28). The D_1 type includes D_1 and D_5 receptors, and the D_2 type includes D_2, D_3, and D_4 receptors. In this study, dopamine receptors have been referred to as either D_1 or D_2.

Bromocriptine at 25×10^{-4}, 0.25, or 25 μg/μl/min was perfused into the ventrolateral striatum for 6 h in this study. The probes used had an average in vitro recovery for dopamine of 27%. However, the in vivo recovery for dopamine at the end of the study might be different from that at the beginning of the study, because chemical microenvironmental changes around probes during dialysis for 6 h might easily modify diffusion characteristics of dopamine (1). However, perfusion with three different concentrations of bromocriptine disclosed a consistent increase of food intake in a dose-dependent manner, but no change of dopamine release or the levels of DOPAC and HVA. Therefore, our results do not indicate a difference in recovery rate.

In summary, perfusion with bromocriptine into the ventrolateral striatum increased food intake in a dose-dependent manner without changing the extracellular concentrations of dopamine, DOPAC, and HVA. Pretreatment with (−)sulpiride perfusion for 1 h prior to bromocriptine perfusion completely inhibited the increase of food intake induced by bromocriptine perfusion. These findings suggest that direct perfusion of bromocriptine into the ventrolateral striatum acts selectively on postsynaptic D_2 receptors and enhances feeding behavior.

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REFERENCES

1. Benveniste, H.; Hansen, A. J.; Ottosen, N. S.: Determination of brain interstitial concentrations by microdialysis. J. Neurochem. 52:1741–1750; 1989.
2. Carruba, M. O.; Ricciardi, S.; Muller, R. E.; Montegazza, P.: Anorectic effect of lisuride and other ergot derivatives in the rat. Eur. J. Pharmacol. 64:133–141; 1980.
3. Carter, A. J.; Muller, R. E.: Pramipexole, a dopamine D_2 auto receptor agonist, decreases the extracellular concentration of dopamine in vivo. Eur. J. Pharmacol. 200:65–72; 1991.
4. Castro, A. J.: The effect of cortical ablations on tongue usage in the rat. Brain Res. 37:251–253; 1972.
5. Divac, I.; Markowitch, H. J.; Pritzel, M.: Behavioral and anatomical consequences of small intrastriatal injections of kainic acid in the rat. Brain Res. 151:523–532; 1978.
6. Dunnett, S. B.; Iversen, S. D.: Learning impairments selective kainic acid-induced lesions within the neostriatum of rats. Behav. Brain Res. 2:189–209; 1981.
7. Evans, K. R.; Eikelboon, R.: Feeding induced by ventricular bromocriptine and amphetamine: A possible excitatory role for dopamine in eating behavior. Behav. Neurosci. 101:591–593; 1987.
8. Gingrich, J. A.; Caron, M. G.: Recent advantages in the molecular biology of dopamine receptors. Annu. Rev. Neurosci. 16:299–321; 1993.
9. Groves, P. M.: A theory of the functional organization of the neo-

striatum and the neostriatal control of voluntary movement. Brain Res. Rev. 5:109–132; 1983.
10. Hawkins, M. F.: Synergistic effects of dopamine agonists and centrally administered neurotensin on feeding. Pharmacol. Biochem. Behav. 24:1195–1201; 1986.
11. Ichihara, K.: Statistics for bioscience—Practical technique and theory. Tokyo: Nankodo; 1990.
12. Imperato, A.; Tanda, G.; Frau, R.; DiChiara, G.: Pharmacological profile of dopamine receptor agonists as studied by brain dialysis in behaving rats. J. Pharmacol. Exp. Ther. 245:257–264; 1988.
13. Inoue, K.; Kiriike, N.; Fujisaki, Y.; Okuno, M.; Ito, H.; Yamagami, S.: D_2 receptors in the ventrolateral striatum are involved in feeding behavior in rats. Pharmacol. Biochem. Behav. 50:399–407; 1995.
14. Inoue, K.; Kiriike, N.; Okuno, M.; Ito, H.; Fujisaki, Y.; Matsui, T.; Kawakita, Y.: Scheduled feeding caused activation of dopamine metabolism in the striatum of rats. Physiol. Behav. 53:177–181; 1993.
15. Johnson, A. M.; Loew, D. M.; Vigouret, J. M.: Stimulant properties of bromocriptine on central dopamine receptors in comparison to apomorphine, (+)-amphetamine and L-DOPA. Br. J. Pharmacol. 56:59–68; 1976.
16. Kelley, A. E.; Gauthier, A. M.; Lang, C. G.: Amphetamine microinjections into distinct striatal subregions cause dissociable effects on motor and ingestive behavior. Behav. Brain Res. 35:27–39; 1989.
17. Kelly, P. H.; Seviour, P. W.; Iversen, S. D.: Amphetamine and apomorphine responses in the rat following 6-OHDA lesions of the nucleus accumbens septi and corpus striatum. Brain Res. 94:507–522; 1975.
18. Marascuilo, L. A.: Statistical methods for behavioral science research. New York: McGraw-Hill Book Company; 1971.
19. Oberg, R. G.; Divac, I.: Dissociative effects of selective lesions in the caudate nucleus of cats and rats. Acta Neurobiol. Exp. (Warsz.) 35:647–659; 1975.
20. Paxinos, G.; Watson, C.: The rat brain in stereotaxic coordinates, 2nd ed. San Diego, CA: Academic Press; 1986.
21. Pieri, L.; Keller, H. H.; Burkard, W.; DaPrada, M.: Effects of lisuride and LSD on cerebral monoamine systems and hallucinosis. Nature 272:278–280; 1978.
22. Pisa, M.: Motor functions of the striatum in the rats: Critical role of the lateral region in tongue and forelimb reaching. Neuroscience 24:453–463; 1988.
23. Roth, R. H.; Wolf, M. E.; Deutch, A. Y.: Neurochemistry of midbrain dopamine systems. In: Meltzer, H. Y., ed. Psychopharmacology: The third generation of progress. New York: Raven Press; 1987:81–94.
24. Salamone, J. D.; Mahan, K.; Rogers, S.: Ventrolateral striatal dopamine depletions impair feeding and food handling in rats. Pharmacol. Biochem. Behav. 44:605–610; 1993.
25. Schmidt, M. J.; Hill, L. E.: Effects of ergots on adenylate cyclase activity in the corpus striatum and pituitary. Life Sci. 20:789–794; 1977.
26. Schorderet, M.: Direct evidence for the stimulation of rabbit retina dopamine receptors by ergot alkaloids. Neurosci. Lett. 2:87–91; 1976.
27. See, R. E.; Sorg, B. A.; Chapman, M. A.; Kalivas, P. W.: In vivo assessment of release and metabolism of dopamine in the ventrolateral striatum of awake rats following administration of dopamine D_1 and D_2 receptor agonists and antagonists. Neuropharmacology 30:1269–1274; 1991.
28. Sibley, D. R.; Monsma, F. J.: Molecular biology of dopamine receptors. Trends Pharmacol. Sci. 13:61–69; 1992.
29. Trugman, J. M.; Arnold, W. S.; Wooten, F. W.; Charlottesville, V. A.: The D_1/D_2 dopamine receptor profile of bromocriptine, pergolide, and (+)-PHNO. Neurology 38:122; 1988.
30. Zarrindast, M. R.; Owji, A. A.; Hosseini-Nia, T.: Evaluation of dopamine receptor involvement in rat feeding behaviour. Gen. Pharmacol. 22:1011–1016; 1991.