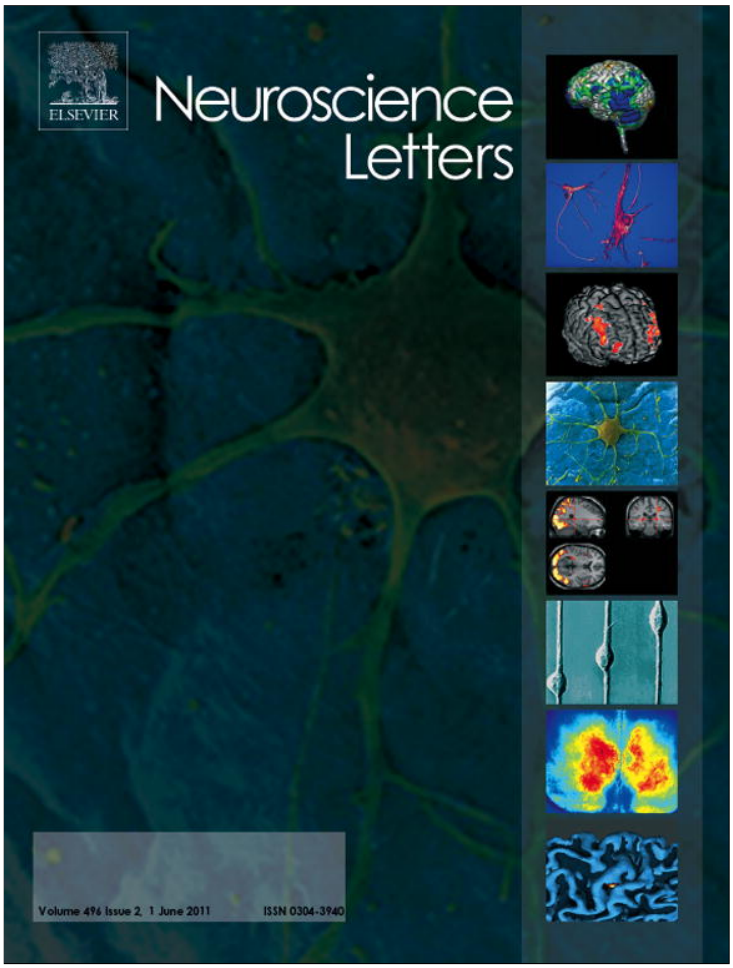

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Differential expression of FosB, c-Fos, and Zif268 in forebrain regions after acute or chronic L-DOPA treatment in a rat model of Parkinson's disease

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ABSTRACT

A study was carried out to examine the effects of acute and chronic L-DOPA treatment on the distribution of the immediate-early gene (IEG) proteins (FosB, c-Fos, and Zif268) in forebrain regions in a unilateral 6-hydroxydopamine (6-OHDA) rat model of Parkinson's disease. During a course of chronic L-DOPA treatment (15 mg/day, 15 days), rats with a 6-OHDA lesion developed abnormal involuntary movements. Compared with the rats in the acute L-DOPA treatment group, those in the chronic treatment group had significantly more FosB-immunopositive cells in the anterior cingulate (Cg) and the dorsolateral caudate-putamen ipsilateral to the lesion and significantly fewer c-Fos-immunopositive cells in the Cg, the nucleus accumbens shell, and the basolateral nucleus of amygdala ipsilateral to the lesion. No significant difference was observed in the number of Zif268-immunopositive cells between the acute and chronic L-DOPA groups. In summary, differential expression of three IEG proteins was observed in the forebrain regions during a course of chronic L-DOPA treatment of 6-OHDA-treated hemiparkinsonian rats.

Pharmacological dopamine (DA) replacement therapy using L-DOPA remains the most effective treatment for Parkinson's disease (PD). However, long-term L-DOPA treatment of patients with PD often induces not only motor complications such as fluctuation and dyskinesia but also psychotic conditions such as hallucinations, delusions, and impulse control problems [14,24]. The mechanisms underlying the L-DOPA-induced motor complications have been investigated in a number of neuropharmacological studies [7]. However, few studies have investigated the mechanisms underlying the L-DOPA-induced psychotic conditions.

Induction of cellular immediate-early genes (IEGs) may be a critical signal transduction step in neuronal plasticity induced by neurotransmitters and drugs, with the protein products of the IEGs functioning to either activate or repress genes that encode the proteins involved in the differentiated functions of the target neurons. This study examined the distribution of the IEG proteins (FosB, c-Fos, and Zif268) after acute and after chronic L-DOPA treatment in the forebrain regions including the striatal and limbic structures (anterior cingulate (Cg), nucleus accumbens shell (AcbSh), caudate-putamen (CPu), and basolateral nucleus of amygdala (BLA)) in a unilateral 6-hydroxydopamine (6-OHDA) rat model of Parkinson's disease.

The 6-OHDA lesioned rat model of Parkinson's disease has been instrumental in studies using a variety of approaches to investigate L-DOPA-induced plasticity at multiple levels. Among the postsynaptic changes examined, the striatal expression of prodynorphin (preproenkephalin-B) mRNA and FosB/ΔFosB-like transcription factors has shown a particularly strong positive correlation with the severity of L-DOPA-induced dyskinesia [2,6,25]. Cenci found that acute injection of L-DOPA increased the levels of FosB and c-Fos in the 6-OHDA-lesioned striatum, whereas repeated administration of the drug caused downregulation of c-Fos and upregulation of FosB [5,8]. Carta et al. found that zif268 mRNA levels increased in the 6-OHDA-lesioned striatum after either acute or subchronic L-DOPA treatment [4]. However, there have been few investigations of the L-DOPA-induced IEG proteins in the brain structures other than the striatum [10].

The study reported here examined the effects of acute and chronic L-DOPA treatment on the distribution of the IEG proteins in forebrain regions in a unilateral 6-OHDA rat model of Parkinson's disease. The experimental protocols used were approved by the ethical committees of animal experimentation at the University of Miyazaki. Anesthetized male 120–130 g Wistar rats (Charles River, Japan) received stereotaxic injections of 8-μg 6-OHDA hydrobro-

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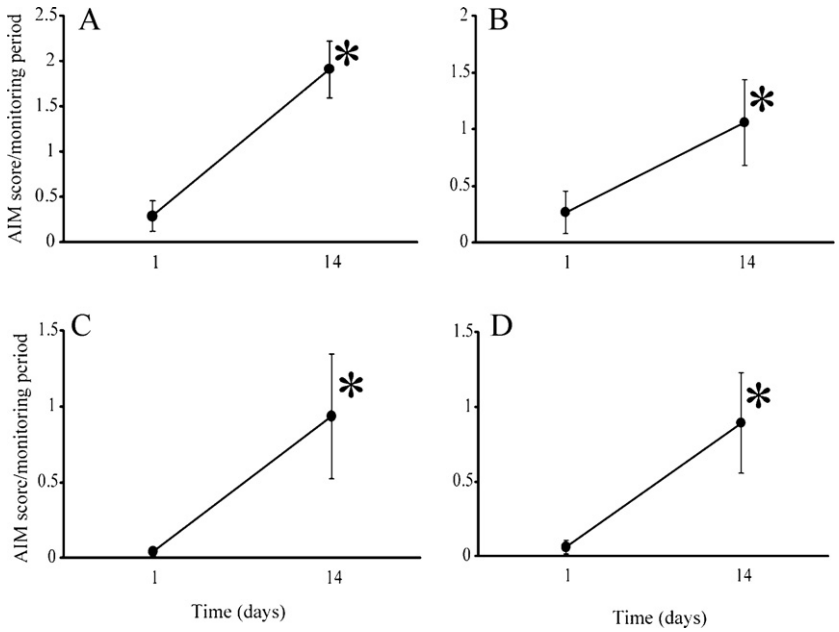

Fig. 1. Effect of chronic L-DOPA treatment on AIMs. Four subtypes of AIMs (locomotive (A), axial (B), forelimb (C), and orolingual (D)) were scored on the 1st and 14th days of L-DOPA administration for the chronic L-DOPA treated rats ($n = 8$). Data represent the mean (±SEM) AIM score for first 60 min after L-DOPA administration. Each score showed a significant increase on the 14th day compared to that on the 1st day of L-DOPA administration (*$P < 0.05$, Wilcoxon signed rank test).

mide (Sigma, MA, USA) in 4 μl of sterile saline containing 0.01% ascorbic acid. The stereotaxic coordinates for the lesion were 3.2 mm rostral to the interaural line, 1.3 mm left of the midline, and 6.7 mm ventral to the dural surface. The incisor bar was set 2.4 mm below the level of the ear bars [20]. The injections of 6-OHDA immediately and almost completely destroyed the DA neurons of the substantia nigra and of the ventral tegmental area, resulting in the near total depletion (2% of normal) of DA in the ipsilateral striatum [16].

Two weeks later, motor disturbance was assessed by counting the full rotations per min in a cylindrical container (30-cm diameter) at 10-min intervals for the first 60 min after methamphetamine (3 mg/kg, i.p.) administration. The animals that turned no less than seven times/min were included in the study.

The rats that were included were allocated into three well-matched groups (in accordance with the methamphetamine-induced rotation): (1) chronic L-DOPA treatment ($n = 9$), (2) acute L-DOPA treatment ($n = 7$), and (3) saline treatment ($n = 8$). Those in the first group received a daily injection of L-DOPA methyl ester hydrochloride (15 mg/kg, i.p.; Sigma, MA, USA) plus an injection of benserazide hydrochloride (15 mg/kg, i.p.; Sigma) for 15 days. Those in the second group received a daily injection of an equivalent volume of saline (i.p.) for 14 days and then an injection of L-DOPA plus benserazide on the 15th day. Those in the third received a daily injection of an equivalent volume of saline for 15 days. This pattern of L-DOPA administration was based on previous findings that circling is significantly enhanced after 7 or 8 daily injections of L-DOPA (13 mg/kg, i.p.) and that this potentiated behavioral response reaches a plateau by day 14 [15]. This enhanced response is thought to be a useful model for the L-DOPA-induced dyskinesia seen in human patients with PD [15].

The L-DOPA-induced abnormal involuntary movements (AIMs) of the rats in the chronic treatment group were scored on the 1st and 14th days in accordance with a rat dyskinesia scale [6] with modification. The rats were observed at 10-min intervals for the first 60 min after L-DOPA administration (6 monitoring periods of 1 min each). The AIMs were classified into four subtypes: locomotive (increased locomotion towards the side contralateral to the lesion), axial (dystonic posturing or choreiform twisting of the neck and upper body towards the contralateral side), forelimb (abnormal, purposeless movements of the forelimbs and digits contralateral to the lesion), and orolingual (empty jaw movements and contralateral tongue protrusion). A score from 0 to 4 was assigned to each rat for each of the four subtypes on the basis of the proportion of the monitoring period during which the given behavior was observed.

The animals in all three groups were perfused on the 15th day. Two hours after the final injection, they were deeply anesthetized with an overdose of pentobarbital and perfused transcardially with saline followed by 4% paraformaldehyde in 0.1-M phosphate buffer (PB; pH 7.4). Their brains were removed immediately and postfixed at 4 °C for 1 h in the above fixative. After fixation, the samples were immersed at 4 °C for 1 h in 0.1-M PB with 10% sucrose and then cryoprotected at 4 °C overnight in the same buffer with 30% sucrose. The samples were subsequently cut on a freezing microtome into 50-μm coronal sections for immunohistochemistry. An immunohistochemical examination of FosB, c-Fos, or Zif268 expression was performed, as described elsewhere [17]. The antibodies for FosB (diluted 1:5000), c-Fos (1:5000), and Zif268 (1:3000) were rabbit polyclonal antisera (sc-48, sc-52, and sc-110, respectively; Santa Cruz Biotechnology, CA, USA). The anti-pan-FosB antibody was raised to the N-terminus of FosB and recognizes both ΔFosB and full-length FosB. ΔFosB is a member of the Fos family of transcription factors, which dimerize with a member of the Jun family and form activator protein-1 (AP-1) transcription factor complexes. These complexes bind to AP-1 sites in the regulatory regions of many genes [21]. ΔFosB is induced in the brain in response to chronic perturbations and lives much longer than other Fos-like proteins (for example, c-Fos, FosB, Fra-1, Fra-2) induced acutely [9].

For each animal and each IEG protein, three sections through the Cg, AcbSh, and dorsolateral CPu approximately 1.2 mm rostral to the bregma and three sections through the BLA approximately 2.3 mm caudal to the bregma were selected for quantitative analysis [23]. FosB, c-Fos, or Zif268 immunoreactivity in the Cg, AcbSh, CPu, and BLA was quantified by counting the number of cells immunopositive for FosB, c-Fos, or Zif268, respectively, in 0.25 mm × 0.25 mm (0.0625 mm^2) squares using a 20× microscope

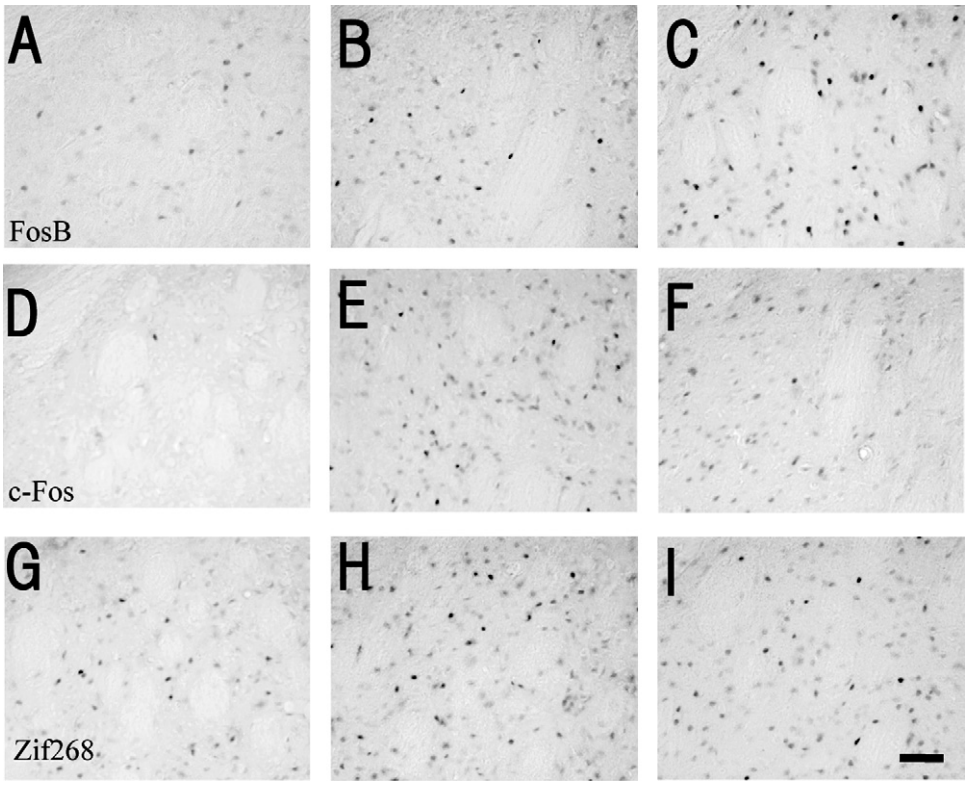

Fig. 2. Photomicrographs of FosB (A–C), c-Fos (D–F), and Zif268 (G–I) expression in dorsolateral CPu ipsilateral to the 6-OHDA lesion for rats in saline (A, D, and G), acute L-DOPA (B, E, and H), and chronic L-DOPA (C, F, and I) treatment groups. Scale bar = 100 μm.

objective. The numbers obtained for the three sections in each area (Cg, AcbSh, CPu, and BLA) were averaged to give the results for each animal and each IEG protein. The data are therefore presented as the number of cells immunopositive for FosB, c-Fos, or Zif268 per 0.0625 mm^2 of striatal or amygdalar tissue.

The behavioral data for the AIMs were analyzed nonparametrically using the Wilcoxon signed rank test. Two-way ANOVA with repeated measures was used to statistically analyze the histological data followed by Bonferroni post hoc tests. P values < 0.05 were regarded as being statistically significant.

Of the eight rats that received chronic L-DOPA treatment, six reached maximal dyskinesia severity (grade 4) in at least one of the four AIM subtypes, and the other two reached grade 3 severity in at least one subtype by the end of the treatment. As shown in Fig. 1, the score for each subtype (locomotive, axial, forelimb, and orolingual) showed a significant increase (about 7-, 4-, 22-, and 14-fold, respectively) on the 14th day compared to on the 1st day of L-DOPA administration.

In the saline-treated control animals, the number of FosB-immunopositive cells was significantly greater in the dorsolateral CPu on the lesion side than on the intact side (Table 1), and the number of c-Fos- and Zif268-immunopositive cells was significantly smaller in the Cg on the lesion side than on the intact side (Tables 2 and 3). In the acute L-DOPA treated animals, the number of FosB-immunopositive cells was significantly greater in the AcbSh and CPu (Table 1), the number of c-Fos-immunopositive cells was significantly greater in the Cg, AcbSh, CPu, and BLA (Table 2), and the number of Zif268-immunopositive cells was significantly greater in the AcbSh and CPu on the lesion side than in the corresponding regions on the lesion side of the control animals (Table 3). In the chronic L-DOPA treated animals, the number of FosB-immunopositive cells was significantly greater in the Cg and CPu on the lesion side than in the corresponding regions on the lesion side of the acute L-DOPA treated animals (Table 1 and Fig. 2), and the number of c-Fos-immunopositive cells was significantly smaller in the Cg, AcbSh, and BLA on the lesion side

Table 1
Mean ± SEM of number of FosB-immunopositive cells/0.0625 mm^2.

Structure	Saline		Acute L-DOPA		Chronic L-DOPA	
	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)
Cg	7.6 ± 1.2(8)	9.8 ± 1.8(8)	6.4 ± 0.4(7)	6.1 ± 0.6(7)	13.5 ± 1.0(8)**,‡	6.8 ± 1.4(8)$^{\$\$}$
AcbSh	37.3 ± 3.4(8)	30.8 ± 3.0(8)	62.5 ± 6.3(5)*	36.4 ± 6.0(5)$^{\$}$	78.2 ± 7.6(7)**	34.4 ± 5.3(7)$^{\$\$}$
CPu	33 ± 6.2(8)	3.9 ± 0.6(8)$^{\$\$}$	76.9 ± 7.4(5)**	3.8 ± 0.8(5)$^{\$\$}$	102.1 ± 4.4(7)**,†	4.2 ± 1.0(7)$^{\$\$}$
BLA	6.0 ± 1.0(8)	7.7 ± 0.8(8)	5.9 ± 1.1(5)	2.1 ± 0.9(5)	17.2 ± 7.0(5)	10.6 ± 2.5(5)

* $P < 0.05$ vs. corresponding side of saline group.
** $P < 0.01$ vs. corresponding side of saline group.
† $P < 0.05$ vs. corresponding side of acute L-DOPA group.
‡ $P < 0.01$ vs. corresponding side of acute L-DOPA group.
$^{\$}$ $P < 0.05$ vs. lesion side of each structure/group.
$^{\$\$}$ $P < 0.01$ vs. lesion side of each structure/group.

Table 2
Mean ± SEM of number of c-Fos-immunopositive cells/0.0625 mm^2.

Structure	Saline		Acute L-DOPA		Chronic L-DOPA	
	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)
Cg	8.7 ± 0.7(8)	16.2 ± 2.5(8)$^{\$\$}$	28.1 ± 2.8(7)**	20.8 ± 2.4(7)$^{\$\$}$	16.3 ± 2.3(8)*,‡	11.5 ± 1.3(8)$^{\$,\dagger}$
AcbSh	18.1 ± 2.6(8)	20 ± 2.1(8)	102.3 ± 22.3(6)**	17.5 ± 3.6(6)$^{\$\$}$	50.8 ± 5.1(9)**,†	15.8 ± 2.2(9)$^{\$\$}$
CPu	2.9 ± 0.9(8)	3.5 ± 1.3(8)	86.2 ± 12.5(6)**	8.4 ± 4.4(6)$^{\$\$}$	59.6 ± 9.3(9)**	5.6 ± 0.8(9)$^{\$\$}$
BLA	5.4 ± 1.2(8)	5.7 ± 0.9(8)	24.7 ± 1.8(5)**	14.6 ± 5.2(5)$^{\$\$}$	12.8 ± 1.3(7)*,‡	10.7 ± 1.5(7)

* $P < 0.05$ vs. corresponding side of saline group.
** $P < 0.01$ vs. corresponding side of saline group.
† $P < 0.05$ vs. corresponding side of acute L-DOPA group.
‡ $P < 0.01$ vs. corresponding side of acute L-DOPA group.
$^{\$}$ $P < 0.05$ vs. lesion side of each structure/group.
$^{\$\$}$ $P < 0.01$ vs. lesion side of each structure/group.

Table 3
Mean ± SEM of number of Zif268-immunopositive cells/0.0625 mm^2.

Structure	Saline		Acute L-DOPA		Chronic L-DOPA	
	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)	Lesion side (n)	Intact side (n)
Cg	36.5 ± 7.1(8)	50.1 ± 10.1(8)$^{\$}$	53.2 ± 6.2(5)	43.6 ± 4.5(5)	28.6 ± 3.4(5)	30.0 ± 3.3(5)
AcbSh	44.7 ± 5.7(8)	40.5 ± 4.9(8)	109.3 ± 13.3(5)**	39.4 ± 6.9(5)$^{\$\$}$	79.8 ± 10.1(6)	46.3 ± 9.7(6)$^{\$\$}$
CPu	54.2 ± 7.4(8)	55.4 ± 3.7(8)	131 ± 10.6(5)**	80.5 ± 13.4(5)$^{\$\$}$	103.9 ± 5.5(7)**	78.2 ± 7.4(7)$^{\$}$
BLA	21.6 ± 3.9(8)	18.4 ± 2.7(8)	17.5 ± 3.6(5)	11.9 ± 4.8(5)	16.0 ± 3.4(6)	23.8 ± 8.6(6)

** $P < 0.01$ vs. corresponding side of saline group.
$^{\$}$ $P < 0.05$ vs. lesion side of each structure/group.
$^{\$\$}$ $P < 0.01$ vs. lesion side of each structure/group.

than in the corresponding regions on the lesion side of the acute L-DOPA treated animals (Table 2). Statistical analysis of the number of FosB-immunopositive cells in the AcbSh showed that the main effects of group (saline, acute L-DOPA, chronic L-DOPA), of laterality (lesion side, intact side), and of group × laterality were significant [group: $F(2,19) = 35.0$, $P < 0.01$; laterality: $F(1,19) = 31.2$, $P < 0.01$; group × laterality: $F(2,19) = 7.8$, $P < 0.01$]. However, subsequent post-hoc Bonferroni tests showed no significant difference between the acute and chronic L-DOPA groups ($P = 0.28$) (Table 1). A significant difference was not found for the number of FosB-immunopositive cells in the BLA among the three groups and between the two sides [group: $F(2,15) = 3.8$, $P = 0.05$; laterality: $F(1,15) = 3.3$, $P = 0.09$; group × laterality: $F(2,15) = 2.6$, $P = 0.11$].

In summary, comparison of the results of the acute and chronic L-DOPA treatment revealed that the chronic treatment resulted in a significant upregulation of FosB in the Cg and CPu and in a significant downregulation of c-Fos in the Cg, AcbSh, and BLA on the lesion side.

The results of this study show that chronic L-DOPA treatment of 6-OHDA rats causes an increase in the number of FosB-immunopositive cells not only in the dorsolateral CPu but also in the Cg on the lesion side. It also causes a decrease in the number of c-Fos-immunopositive cells in the Cg, AcbSh, and BLA on the lesion side. These results are the first to demonstrate that chronic L-DOPA treatment of 6-OHDA-lesioned rats can alter the FosB and c-Fos expressions in forebrain regions other than the CPu or nucleus accumbens (Acb).

The FosB/ΔFosB-like transcription factors in the striatum of dyskinetic animals account for a pronounced increase in protein-DNA binding activities at both AP-1 enhancers and cyclic AMP response elements [3]. These transcription factors have been implicated in the dyskinesia priming process by a study using antisense oligonucleotides against fosB/ΔfosB mRNA [2]. Similar to the findings of a previous study [11], this study found enhanced FosB expression in the dorsolateral CPu on the lesion side of 6-OHDA rats without L-DOPA treatment. This enhanced expression was also found in the CPu and AcbSh of both acute- and chronic-treated L-DOPA rats and in the Cg of the chronic L-DOPA treated rats.

The BLA has been implicated in the response to affective stimuli and in the process of conditioned reinforcement [12]. Furthermore, the BLA has a substantial projection directly to the Acb [1] and indirectly via the dorsal prefrontal cortex including the Cg [19]. The Acb area is thought to be integral to the reinforcing actions of drugs of abuse and to drug-induced psychosis. Thus, the BLA may be, at least in part, involved functionally in the mechanisms underlying L-DOPA-induced psychotic conditions. In agreement with a previous study [10], c-Fos expression was found to be induced by L-DOPA administration in the BLA ipsilateral to the lesion, especially for the rats in the acute L-DOPA treatment group. Additional findings, especially for FosB expression, were not observed in the immunohistochemical study.

Numerous studies of patients with schizophrenia or drug-induced psychosis have demonstrated functional or morphological alterations in the forebrain regions, including the Cg and Acb [13,18]. The Cg area is crucial for integrating cognitive and emotional processes in support of goal-directed behavior [13,22]. Therefore, the results of this study's immunohistochemical examination may be related to the pathogenesis of not only motor complications but also psychotic conditions induced by chronic L-DOPA treatment, implicated in schizophrenia and methamphetamine- or other drug-induced psychosis. Clearly, further work is needed to define the causal mechanisms of L-DOPA-related adverse events.

In conclusion, differential expression of FosB, c-Fos, and Zif268 was observed in four forebrain regions (Cg, AcbSh, CPu, and BLA) during a course of chronic L-DOPA treatment of 6-OHDA-treated hemiparkinsonian rats.

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References

[1] G.F. Alheid, L. Heimer, New perspectives in basal forebrain organization of special relevance for neuropsychiatric disorders: the striatopallidal, amyg-

daloid, and corticopetal components of substantia innominata, Neuroscience 27 (1988) 1–39.
[2] M. Andersson, A. Hilbertson, M.A. Cenci, Striatal *fos*B expression is causally linked with L-DOPA-induced abnormal involuntary movements and the associated upregulation of striatal prodynorphin mRNA in a rat model of Parkinson's disease, Neurobiol. Dis. 6 (1999) 461–474.
[3] M. Andersson, C. Konradi, M.A. Cenci, cAMP response element-binding protein is required for dopamine-dependent gene expression in the intact but not the dopamine-denervated striatum, J. Neurosci. 21 (2001) 9930–9943.
[4] A.R. Carta, E. Tronci, A. Pinna, M. Morelli, Different responsiveness of striatonigral and striatopallidal neurons to L-DOPA after a subchronic intermittent L-DOPA treatment, Eur. J. Neurosci. 21 (2005) 1196–1204.
[5] M.A. Cenci, Transcription factors involved in the pathogenesis of L-DOPA-induced dyskinesia in a rat model of Parkinson's disease, Amino Acids 23 (2002) 105–109.
[6] M.A. Cenci, C.S. Lee, A. Björklund, L-DOPA-induced dyskinesia in the rat is associated with striatal overexpression of prodynorphin- and glutamic acid decarboxylase mRNA, Eur. J. Neurosci. 10 (1998) 2694–2706.
[7] M.A. Cenci, H.S. Lindgren, Advances in understanding L-DOPA-induced dyskinesia, Curr. Opin. Neurobiol. 17 (2007) 665–671.
[8] M.A. Cenci, A. Tranberg, M. Andersson, A. Hilbertson, Changes in the regional and compartmental distribution of FosB- and JunB-like immunoreactivity induced in the dopamine-denervated rat striatum by acute or chronic L-DOPA treatment, Neuroscience 94 (1999) 515–527.
[9] J. Chen, M.B. Kelz, B.T. Hope, Y. Nakabeppu, E.J. Nestler, Chronic Fos-related antigens: stable variants of deltaFosB induced in brain by chronic treatments, J. Neurosci. 17 (1997) 4933–4941.
[10] D.G. Cole, J.H. Growdon, M. DiFiglia, Levodopa induction of Fos immunoreactivity in rat brain following partial and complete lesions of the substantia nigra, Exp. Neurol. 120 (1993) 223–232.
[11] J.P. Doucet, Y. Nakabeppu, P.J. Bedard, B.T. Hope, E.J. Nestler, B.J. Jasmin, J.S. Chen, M.J. Iadarola, M. St-Jean, N. Wigle, P. Blanchet, R. Grondin, G.S. Robertson, Chronic alterations in dopaminergic neurotransmission produce a persistent elevation of deltaFosB-like protein(s) in both the rodent and primate striatum, Eur. J. Neurosci. 8 (1996) 365–381.
[12] B.J. Everitt, J.A. Parkinson, M.C. Olmstead, M. Arroyo, P. Robledo, T.W. Robbins, Associative processes in addiction and reward. The role of amygdala-ventral striatal subsystems, Ann. N. Y. Acad. Sci. 877 (1999) 412–438.
[13] A. Fornito, M. Yücel, B. Dean, S.J. Wood, C. Pantelis, Anatomical abnormalities of the anterior cingulate cortex in schizophrenia: bridging the gap between neuroimaging and neuropathology, Schizophr. Bull. 35 (2009) 973–993.
[14] A. Friedman, J. Sienkiewicz, Psychotic complications of long-term levodopa treatment of Parkinson's disease, Acta Neurol. Scand. 84 (1991) 111–113.
[15] B. Henry, A.R. Crossman, J.M. Brotchie, Effect of repeated L-DOPA, bromocriptine, or lisuride administration on preproenkephalin-A and preproenkephalin-B mRNA levels in the striatum of the 6-hydroxydopamine-lesioned rat, Exp. Neurol. 155 (1999) 204–220.
[16] Y. Ishida, H. Hashiguchi, K. Todaka, I. Kuwahara, Y. Ishizuka, H. Nakane, D. Uchimura, T. Nishimori, Y.Y. Mitsuyama, Serotonergic activity in the rat striatum after intrastriatal transplantation of fetal nigra as measured by microdialysis, Brain Res. 788 (1998) 207–214.
[17] Y. Ishida, K. Kawai, Y. Magata, K. Ebihara, R. Takeda, H. Abe, M. Yoshimoto, H. Hashiguchi, K. Odagiri, H. Matsuo, T. Nishimori, Differential expression of Fos and Zif268 in the nigrostriatal system after methamphetamine administration in a rat model of Parkinson's disease, Synapse 62 (2008) 920–926.
[18] M. Iyo, Y. Sekine, N. Mori, Neuromechanism of developing methamphetamine psychosis: a neuroimaging study, Ann. N. Y. Acad. Sci. 1025 (2004) 288–295.
[19] P.W. Kalivas, K. McFarland, Brain circuitry and the reinstatement of cocaine-seeking behavior, Psychopharmacology (Berl.). 168 (2003) 44–56.
[20] J.F.R. König, R.A. Klippel, The Rat Brain. A Stereotaxic Atlas of the Forebrain and Lower Parts of the Brain Stem, Williams and Wilkins, Baltimore, 1963.
[21] J.I. Morgan, T. Curran, Immediate-early genes: ten years on, Trends Neurosci. 18 (1995) 66–67.
[22] T. Paus, Primate anterior cingulate cortex: where motor control, drive and cognition interface, Nat. Rev. Neurosci. 2 (2001) 417–424.
[23] G. Paxinos, C. Watson, The Rat Brain in Stereotaxic Coordinates, Academic Press, San Diego, 1997.
[24] V. Voon, P.O. Fernagut, J. Wickens, C. Baunez, M. Rodriguez, N. Pavon, J.L. Juncos, J.A. Obeso, E. Bezard, Chronic dopaminergic stimulation in Parkinson's disease: from dyskinesias to impulse control disorders, Lancet Neurol. 8 (2009) 1140–1149.
[25] C. Winkler, D. Kirik, A. Björklund, M.A. Cenci, L-DOPA-induced dyskinesia in the intrastriatal 6-hydroxydopamine model of Parkinson's disease: relation to motor and cellular parameters of nigrostriatal function, Neurobiol. Dis. 10 (2002) 165–186.