Ontogenetic Development of Dopaminergic Regulation of Grooming Behavior in Rats

L. M. Lepekhina and E. A. Tsitsurina

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 148, No. 9, pp. 251-253, September, 2009
Original article submitted November 7, 2007

The effect of the developing *nucleus accumbens* and ventrolateral striatum on grooming behavior in rat pups (1st month of life) and adult rats (2-12 months of life) was studied during activation of D1 and D2 dopamine receptors with apomorphine. Over the 1st week of life, apomorphine treatment was followed by hypersensitivity of D1 receptors in the *nucleus accumbens*. It was manifested in the early appearance of scratching and washing movements during ontogeny. The effect of activation was reduced after neonatal gangliosympathectomy. D2 receptors in the *nucleus accumbens* are identified on day 22 of life. D2 receptors in the ventrolateral striatum become functionally active during this period. Under these conditions, apomorphine increased significantly the duration of licking and biting movements. The number of D2 receptors in the ventrolateral striatum increases sharply during sexual maturity (2nd month of life). These changes are accompanied by an increase in the duration of oral stereotyped behavior. The duration of grooming movements was significantly reduced by the end of stereotyped behavior. The effect of apomorphine was most pronounced in 9-month-old animals. We conclude that the immature ventrolateral striatum has a reciprocal stimulatory effect on licking and biting movements during ontogeny. By contrast, the mature striatum produces a subordinate reciprocal inhibitory influence on various types of grooming movements.

Key Words: *grooming behavior; apomorphine-dopaminergic regulation; neonatal gangliosympathectomy; ontogeny; rat*

Grooming behavior is a highly-specialized skin response (washing, scratching, licking, and biting) to tactile stimulation. Its regulation is realized via stimulation of D1 and D2 receptors in the *nucleus accumbens* [5,6]. The *nucleus accumbens* is responsible for the relationship between the limbic and motor systems that have a regulatory effect on integrative functions [7]. The maturation of D1 and D2 receptors occurs successively in the ontogeny [4].

Apomorphine stimulates D2 receptors and ventrolateral striatum, which is manifested in the appearance of oral stereotyped behavior [3]. This provides the possibility of studying whether the developing striatum can regulate grooming behavior in rats determined by the *nucleus accumbens*. The ontogenetic development of coordination relations in CNS is an urgent problem of evolutionary physiology.

This work was designed to study grooming behavior of rats during ontogeny of the *nucleus accumbens*.

MATERIALS AND METHODS

Experiments were performed on 47 rat pups (156 series), 15 male rats (20 series), and 4 rat pups with neonatal gangliosympathectomy (8 series). Bilateral removal of the upper cervical sympathetic ganglia in rat pups was conducted on days 1 and 2 of life.

I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Russian Academy of Sciences, St. Petersburg, Russia. ***Address for correspondence:*** ksv@iephb.ru. L. M. Lepekhina

0007-4888/09/1483-0363

Locomotor activity of freely moving rats in a highly sensitive actograph was recorded graphically using an electroencephalograph. The study was performed over 1 h before and 1 h after treatment with apomorphine. Apomorphine was injected intraperitoneally in a dose of 0.5 mg/kg. The number and duration of grooming movements were estimated on the actogram. The total duration of these movements was calculated. The results were analyzed statistically.

RESULTS

The effect of apomorphine on grooming behavior of rats was detected on day 2 of life, which coincides with the appearance of D1 receptors in the *nucleus accumbens* [4]. Injection of apomorphine over the 1st week of life was followed by early appearance of washing and scratching movements during ontogeny. Activation of these movements was related to stimulation of D1 receptors [5]. Spontaneous and apomorphine-induced washing movements in rats were observed on days 6 and 3 of life, respectively. Spontaneous scratching movements were revealed in rat pups at the age of 7 days. After treatment with apomorphine, these movements were found on day 3 of life. Previous studies showed that the destruction of brain D2 receptors in adult animals is followed by hypersensitivity of D1 receptors in the *nucleus accumbens* [2]. It can be hypothesized that hypersensitivity of D1 receptors in the *nucleus accumbens* of rat pups on the 1st week of life is associated with the absence of D2 receptors [4]. As differentiated from D2 receptors, stimulation of D1 receptors increases activity of adenylate cyclase. Activation of grooming behavior upon stimulation of D1 receptors is mediated by the noradrenergic mechanisms [8]. The ontogenetic development of scratching and washing movements in rat pups was delayed after neonatal gangliosympathectomy. Apomorphine had a weak stimulatory effect under these conditions, which is consistent with published data [1]. The stimulatory effect of apomorphine was much less pronounced on the 2nd week of life. The total duration of apomorphine-induced grooming increased by 780 and 91% during the 1st and 2nd weeks of life, respectively. The duration of scratching movements was reduced (Fig. 1). D2 receptors in the *nucleus accumbens* are identified on day 22 of life [4]. However, injection of apomorphine was followed by oral stereotyped behavior (licking of the actograph wall and intense sniffing) of short duration (1 min). The observed changes reflect the appearance of D2 receptors in the ventrolateral striatum [2]. It is probably related to innervation of the ventrolateral striatum from the *substantia nigra*, which occurs on days 22-24 of life. Grooming movements of licking and biting are observed in the earlier period (days 14 and 18, respectively). The stereotyped response of rat pups to apomorphine is not found on day 22 of life. The total duration of licking and biting movements increased significantly during this period (by 631 and 331%, respectively; Fig. 1). The appearance of grooming behavior (*e.g.*, licking and biting) is associated with activation of not only D1 receptors, but also of D2 receptors. The reciprocal stimulatory effect of the ventrolateral striatum is probably realized via activation of D2 receptors in the *nucleus accumbens* [4]. The number of D2 receptors in the ventrolateral striatum of rats increases sharply during sexual maturity (2nd month of life). These changes are accompanied by a significant increase in the duration of apomorphine-induced stereotyped behavior (Fig. 2). The duration of grooming movements was significantly reduced in the follow-up period (termination of

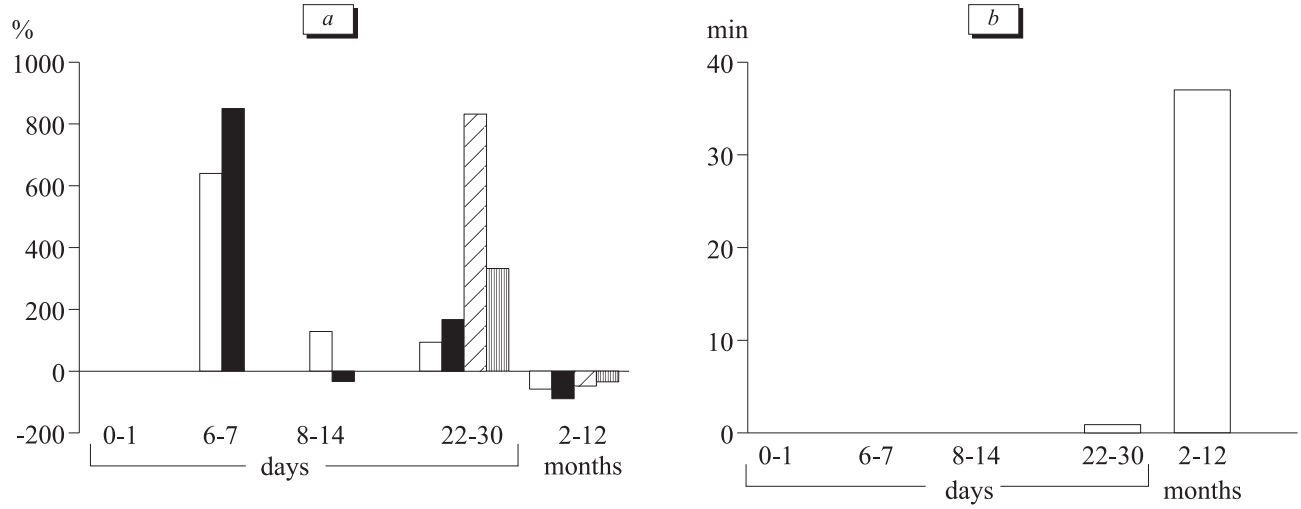

Fig. 1. Ontogenetic changes in the total duration of grooming movements (*a*) and duration of stereotyped behavior (*b*) after treatment with apomorphine. Light bars: washing; dark bars: scratching; slant shading: licking; vertical shading: biting.

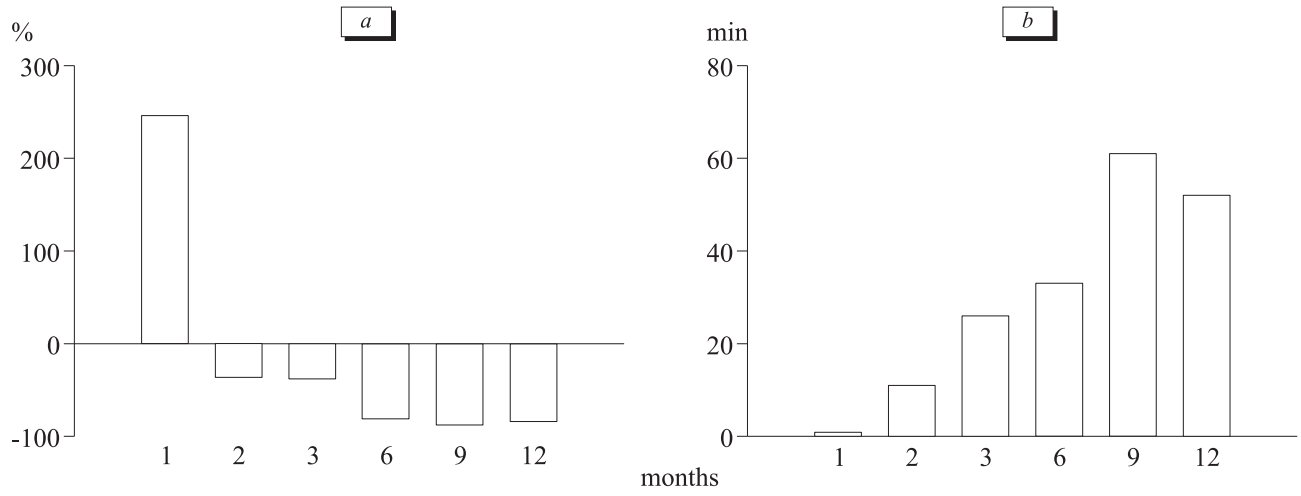

Fig. 2. Ontogenetic changes in the total duration of grooming movements after injection of apomorphine (*a*) and duration of stereotyped behavior (*b*).

stereotyped behavior). The degree of these changes increased progressively and reached maximum in 9-month-old rats (Fig. 2). Deep sleep was observed by the end of grooming.

The striatum has an important role in the regulation of behavior. Due to subordinate inhibition of grooming behavior, the striatum probably facilitates the transition of rats from wakefulness to sleep. Our results indicate that the ontogenetic development of dopaminergic regulation of grooming behavior is associated with progressive maturation of D1 and D2 receptors in the *nucleus accumbens* and D2 receptors in the ventrolateral striatum. The interaction between dopamine activity of the *nucleus accumbens* and ventrolateral striatum occurs in the ventral tegmental area.

REFERENCES

1. L. M. Lepekhina, *Adaptive and Graphic Influence of the Cervical Sympathetic Ganglia during Ontogeny* [in Russian], Leningrad (1984).
2. R. Brus, A. Plech, and R. M. Kostrzena, *Pharmacol. Biochem. Behav*., **50**, No. 4, 649-653 (1995).
3. J. M. Delfs and A. E. Kelley, *Neuroscience*, **39**, No. 1, 59-67 (1990).
4. G. Flores, G. K. Wood, and J. J. Liang, *J. Neurosci*., **16**, No. 22, 7366-7375 (1996).
5. Z. Merali and H. Piggins, *Eur. J. Pharmacol*., **191**, No. 3, 281-293 (1990).
6. A. Murray and J. L. Waddington, *Pharmacol. Biochem. Behav*., **35**, No. 1, 105-110 (1990).
7. S. R. Sesack and V. M. Pickel, *Brain Res*., **527**, No. 2, 266-279 (1990).
8. M. R. Zarrindast, M. Sharifzadeh, and A. I. Sadeghi, *Eur. J. Pharmacol*., **306**, Nos. 1-3, 1-4 (1996).