

# Stereotyped Behavior in the Ontogeny of Rats

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The ontogenetic development of stereotyped behavior induced by activation of dopamine D1 and D2 receptors with apomorphine was studied in rat pups (1st month of life) and adult rats (2nd-12th months of life). Stereotyped sniffing and licking movements developed not simultaneously under the influence of apomorphine. Apomorphine-induced sniffing hyperactivity was observed in newborn animals, but disappeared after eye opening (day 18 of life). Stereotyped licking movements (long-term intense licking of the wall of the actograph) induced by activation of dopamine D2 receptors with apomorphine were revealed in rat pups on the 4th week of life. The duration of these movements in rats was maximum by the 9th month of life. The dynamics of stereotyped behavior probably reflects the non-simultaneous formation and development of dopamine D1 and D2 receptors in the ventrolateral striatum during the ontogeny of rats.

**Key Words:** *stereotyped behavior; apomorphine; ontogeny; rat*

Published data show that apomorphine causes stereotyped behavior as a result of stimulation of dopamine D1 and D2 receptors [8] in the ventrolateral (VL) striatum [5]. Stimulation of dopamine D1 receptors induces sniffing movements, while stimulation of dopamine D2 receptors induces stereotyped licking behavior [3]. During the ontogeny, D1 receptors in the VL striatum develop earlier than D2 receptors [9].

Here we studied ontogenetic development of stereotyped sniffing and licking behavior.

## MATERIALS AND METHODS

Experiments were performed on 36 adult male freely moving rats (2-12 months) and 79 rat pups (1st month of life).

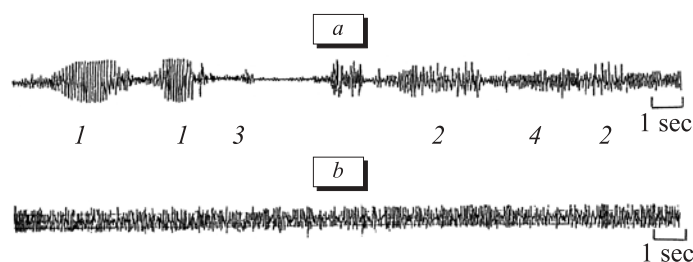
Stereotyped behavior in rats was induced by administration of apomorphine. Locomotor activity of intact and treated rats was recorded simultaneously using individual highly sensitive actographs

with a piezoelectric sensor [1] and ink-writing electroencephalograph. Apomorphine in a dose of 0.5 mg/kg was injected subcutaneously after recording of basal locomotor activity for 1 h. The response to apomorphine was monitored for at least 1 h. The data were processed statistically.

## RESULTS

The actogram of adult rats contains numerous grooming movements, including scratching, licking, washing, and sniffing (Fig. 1, *a*). For example, 12-month-old rats exhibited  $188.2 \pm 11.5$  grooming movements over 1 h ( $43.1 \pm 8.1$  licking,  $44.0 \pm 8.3$  washing,  $26.5 \pm 11.0$  scratching, and  $74.6 \pm 12.4$  nibbling). Stereotyped licking movements in adult rats were observed 5-6 min after administration of apomorphine. The rats exhibited a long-term intense licking of the wall of the actograph while standing on hindlimbs. The duration of one licking episode does not exceed 6 sec. Apomorphine-induced licking movements continued for 1 h ( $52.0 \pm 2.7$ ) and were accompanied by intense sniffing (Fig. 1, *b*). These movements are essential for the maintenance of stereotyped licking behavior at a high level [11].

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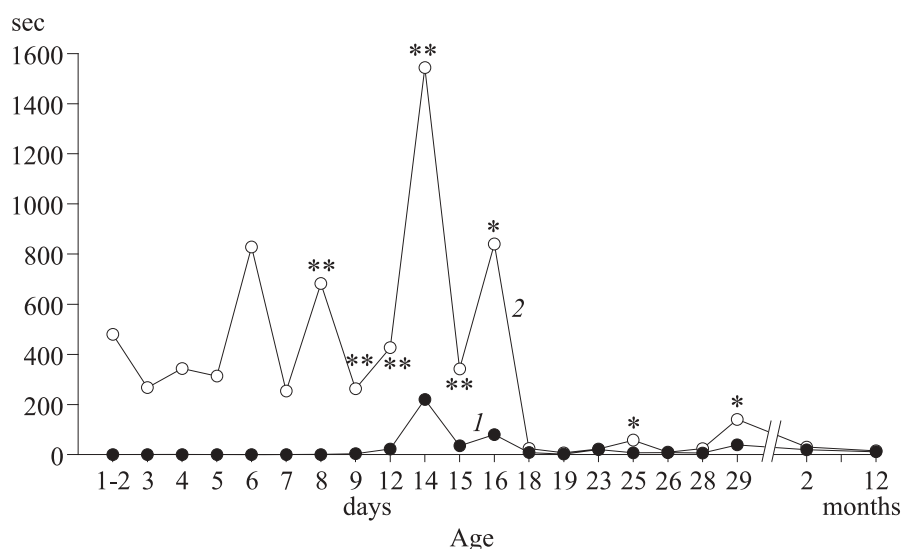
**Fig. 1.** Effect of apomorphine on stereotyped licking movements. *a*: grooming behavior of an intact rat: scratching (1), licking (2), sniffing (3), and nibbling (4); *b*: long-term intense licking and sniffing.

Head-up sniffing movements are observed in intact rat pups at the age of 9 days. Under conditions of apomorphine administration, the rat pup demonstrated these movements immediately after birth (Fig. 2). On days 9-16 of life, the mean duration of sniffing movements in intact rats was  $72.6 \pm 12.3$  sec per 1 h. This parameter increased by 9.4 times after apomorphine administration ( $683.0 \pm 120.1$  sec,  $p < 0.001$ ). The mean duration of sniffing movements in intact rat pups and, particularly, in treated animals sharply decreased eye opening (day 18 of life). The mean duration of sniffing movements in intact rat pups decreased from  $72.6 \pm 12.3$  to  $15.2 \pm 2.4$  sec. The mean duration of sniffing movements in apomorphine-treated animals decreased from  $683.0 \pm 120.1$  to  $46.2 \pm 24.0$  sec. Differences in the duration of sniffing movements in intact and treated rat pups became less significant ( $p < 0.05$ ). No significant differences between intact and apomorphine-treated rats were revealed from the 2nd (beginning of sexual maturation) to the 12th month of life ( $15.09 \pm 2.9$  and  $22.5 \pm 4.6$  sec, respectively). Hence, the ontogenetic development of sniffing movements in apomorphine-treated rat pups is observed on day 1 and persists until the 16th day of life.

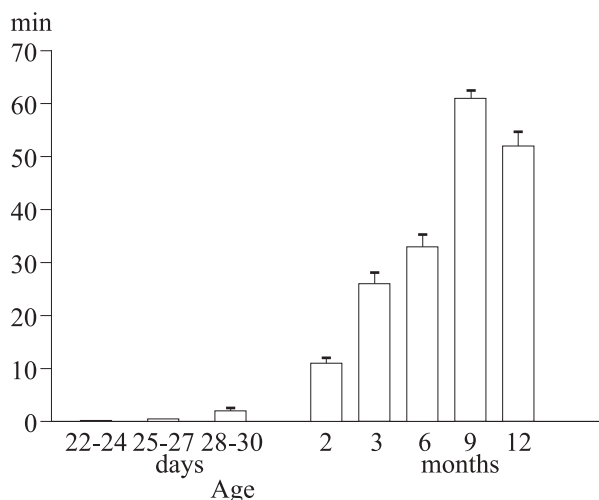
Apomorphine administration was followed by the appearance of stereotyped licking behavior in

22-23-day-old rat pups with low sniffing activity. As differentiated from adult animals, these first stereotyped movements were short-lasting ( $6.3 \pm 0.3$  sec). They were found in 33% animals receiving apomorphine. The duration and frequency of stereotyped licking movements increased with age. After apomorphine administration, stereotyped movements were revealed in 50-60% rat pups aging 28-30 days. The duration of these movements increased to  $2.0 \pm 0.6$  min. The duration of stereotyped licking significantly increased at the age of 2 months (period of puberty) and reached maximum in 9-month-old animals ( $61.1 \pm 1.5$  min, Fig. 3). Starting from the 2nd month life, stereotyped licking movements were observed in 100% animals receiving apomorphine.

Hyperactivity of stereotyped licking movements is probably associated with hypersensitivity of developing dopamine D1 receptors in the VL striatum [4]. They are formed and develop in rat pups from the 1st day of life. The number of these receptors peaked on day 16, which coincides with mature innervation pattern of dopamine D1 receptors [10]. As distinct from D2 receptors, activation of D1 receptors is associated with activation of adenylate cyclase [7] and occurs against the background of increased activity of the sympathetic nervous system [2] realizing its effects via the adenylate cyclase mechanism.



**Fig. 2.** Total duration of sniffing movements in rats during ontogeny before (1) and after apomorphine administration (2). \* $p < 0.05$  and \*\* $p < 0.01$  compared to 1.



**Fig. 3.** Development and duration of stereotyped licking movements in rats during ontogeny.

The appearance of stereotyped licking movements in rat pups on the 4th week of life corresponds to the development of dopamine D2 receptors in the VL striatum. The duration of stereotyped licking movements in 2-month-old rat pups increased by 5.5 times compared to 1-month-old animals ( $11.0 \pm 0.9$  and  $2.0 \pm 0.6$  min, respectively,  $p < 0.001$ ). These changes are accompanied by a sharp increase in the number of dopamine D2 receptors in the VL striatum. These data suggest that the progressive ontogenetic development of stereotyped behavior in rats is associated with the appearance

of dopamine D1 and D2 receptors and maturation of innervation.

Activation of stereotyped behavior due to stimulation of striatal dopamine D1 and D2 receptors is of particular biological significance in the ontogeny. Activation of sniffing movements in blind rat pups is the only distant reception to find out the mother's nipple and, therefore, to survive. Stereotyped licking movements probably underlie the development of drinking behavior (lapping).

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