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THE EFFECT OF UNILATERAL 6-HYDROXYDOPAMINE LESIONS IN THE SUBSTANTIA NIGRA ON HIPPOCAMPAL NORADRENALINE-INDUCED FEEDING AND OTHER BEHAVIOUR IN THE RAT

ROBERT D. OADES

Zoologisches Institut der Technischen Hochschule, 61 Darmstadt, Schnittspahnstrasse 3 (G.F.R.)

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SUMMARY

The latency, duration of feeding and number of feeding periods recorded from rats after noradrenaline injection to the hippocampus show little change after *unilateral* 6-hydroxydopamine injections to the substantia nigra. It is suggested that 6-hydroxydopamine-induced weight losses result from non-specific effects of injection because increased durations for grooming, decreased latencies for resting and short periods of feeding follow injection.

Intracerebral injection of noradrenaline (NA) into the hippocampus [2] or to the ventricles [1] can induce feeding in the rat. Bilateral injection of 6-hydroxydopamine (6-OHDA) to the substantia nigra (SN) will induce aphagia [10].

Injection of 6-OHDA into the SN induces a loss of hypothalamic innervation [6]. Lateral hypothalamic-lesion-induced aphagia may be a result of damage to the nearby nigrostriatal pathway [10]. To investigate further the effect of lesions of the SN, feeding was first induced by NA administration to the dorsal hippocampus (HpC). Then unilateral SN lesions were made with 6-OHDA to see if there was a lateralized effect on feeding behaviour. Several items of behaviour were recorded after injection so that the results of injection might be better understood.

Cannulae were implanted bilaterally into the dorsal HpC and SN of 20 albino rats (250—350 g). Results are reported from 25 HpC sites for animals with cannulae in the SN. Food and water were continually available.

The animals were anaesthetized with pentobarbital and stainless steel cannulae (0.7 mm outer, 0.4 mm inner diameter) were stereotaxically implanted into the HpC [4] and SN [5]. The cannulae were sealed in position

with dental cement continuous with three skull screws. Animals were allowed to recover for one week after surgery.

All animals were kept singly and tested in their perspex home cage (60 × 25 × 15 cm) containing sawdust litter. The cage was placed in a sound attenuating chamber (100 × 100 × 75 cm) illuminated by a 40 W bulb. The behaviour was observed through a double perspex window from under a hood. Foot-movement, shaking, grooming, rearing, resting (immobile with eyes closed) and feeding were recorded on a multi-channel Esterline Angus event recorder. Behavioural effects of the 6-OHDA lesion were recorded in a circular open field (840 cm diameter) marked into 12 sections.

Data were obtained during the light period of a 12 h light/dark cycle. Observations started 2 min after the start of injection from a Hamilton microsyringe (1 μl/min). One week after surgery NA-induced feeding (13 μg NA hydrochloride, 0.6 μl saline) was established following HpC injection. A criterion for feeding was taken as a minimum duration of 30 sec elicited by two injections on successive days. A maximum of two sites (6-h interval) were tested in one animal on the same day. On the day after establishment of feeding saline solution alone was injected to all cannulae. On the next day 6-OHDA (40 μg, 10 μl ascorbic/saline) was given unilaterally to the SN. NA-induced feeding from the HpC was investigated on days 1, 2, 3 and 5 after SN treatment with 6-OHDA.

On five occasions after 6-OHDA injection behavioural effects of the lesion were measured from 10-min periods in the open field. An effective lesion decreased locomotion and increased rotation producing a high coefficient $\left(\frac{\geqslant 10,\ \text{latency to 2nd square} \times \text{no. of revolutions}}{\text{no. of squares crossed}}\right)$. Median coefficients were as follows: 4—6 h, 460; 21 h, 138; 27 h, 281; 48 h, 109; 72 h, 112.

Observations lasted for 20 min after the start of injection or until 3 min had elapsed from the end of feeding. Behaviour was analyzed by 3-min time samples. Feeding periods were separated from each other by a minimum of 10 sec.

After testing rats were perfused with 10% formalin solution and cannula placement was verified by freezing and section of the brain. Unless otherwise stated all statistical comparisons were two-tailed and made by the Wilcoxon matched pairs test.

Feeding was elicited by NA injection to 25 out of 30 HpC sites. No feeding was elicited by saline administration to the same cannulae. More feeding behaviour was elicited from sites where no leakage to the ventricles was suspected (88% of tests) than other sites from which, after histological examination, leakage might be suspected (36% of tests). Feeding was not induced by spreading depression [4] which is usually associated with shaking behaviour, ($\geqslant$7 shakes on 3% of tests). After SN treatment with 6-OHDA, NA elicited feeding from all HpC sites on two or more occasions.

Feeding behaviour often occurred in short periods when elicited by NA to the HpC (Fig. 1B). The number of periods did not change after 6-OHDA treatment. There was no change in the latency or duration of feeding elicited from the contralateral HpC. After NA injection to the ipsilateral HpC there was a longer interval before feeding 24 h after 6-OHDA treatment ($0.02 < P < 0.05$) but this was not maintained on subsequent tests (Fig. 1A). The duration of feeding elicited from the ipsilateral HpC showed a non-significant tendency to decrease. Although the mean food intake per test was equivalent before and after 6-OHDA treatment (1.57 g : 1.55 g), there was a temporary decrease of body weight until the third day after 6-OHDA treatment (25%, $P \ll 0.01$, Fig. 2B).

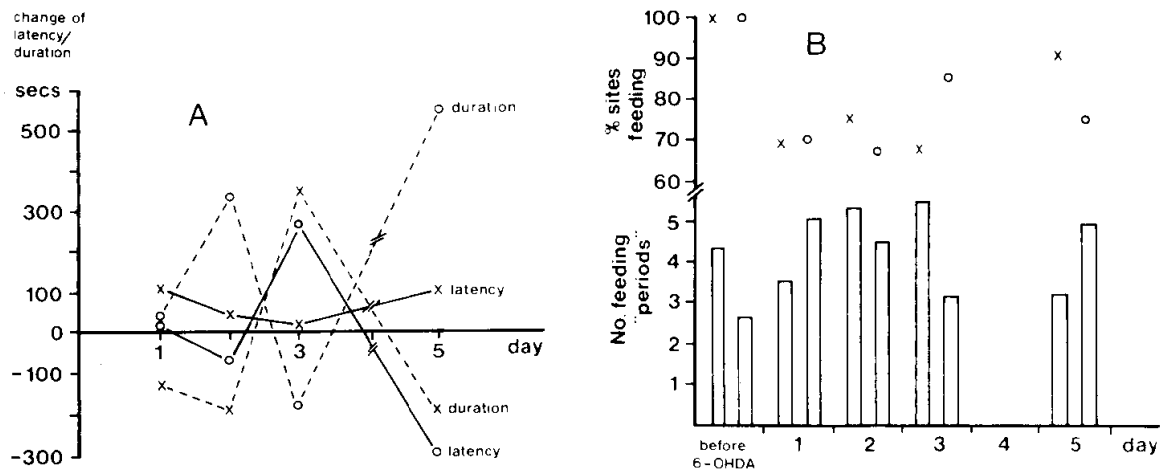

Fig. 1. A: the median changes of latency (——) and duration (- - - -) of feeding on successive days are shown for ipsi- (×) and contralateral (○) sites of NA injection with respect to pre-6-OHDA levels. B: the percentage of sites (upper) from which NA elicited feeding are shown for 13 ipsilateral (×) and 12 contralateral (○) HpC injection sites on successive days. The histogram shows the mean number of feeding periods for the same animals on each day (see text for details).

There were no significant locomotor changes after NA or saline treatment before or after 6-OHDA treatment. The first injections caused a slight increase (12.4, NA-pre-6-OHDA; 8.7, saline; 8.8, NA-post-6-OHDA, mean foot-moves/min). Saline injected rats showed a decreased latency to rest compared with latencies after NA injections (saline 15.2 min; NA 21.3 min, $P < 0.01$). Rats groomed longer after saline injection than after NA injection following 6-OHDA ($P < 0.01$). More grooming followed NA injection after than before 6-OHDA treatment ($0.02 < P < 0.05$, Fig. 2A). The amount of rearing was similar after all three treatments.

Unilateral treatment of the SN with 6-OHDA did not clearly interfere with four measures of feeding elicited by NA injection to the ipsi- or contralateral HpC. Similar treatment of the SN does affect feeding elicited by cortical spreading depression (Huston and Siegfried, unpublished data). These results suggest that there are central sites for eliciting feeding that are affected differ-

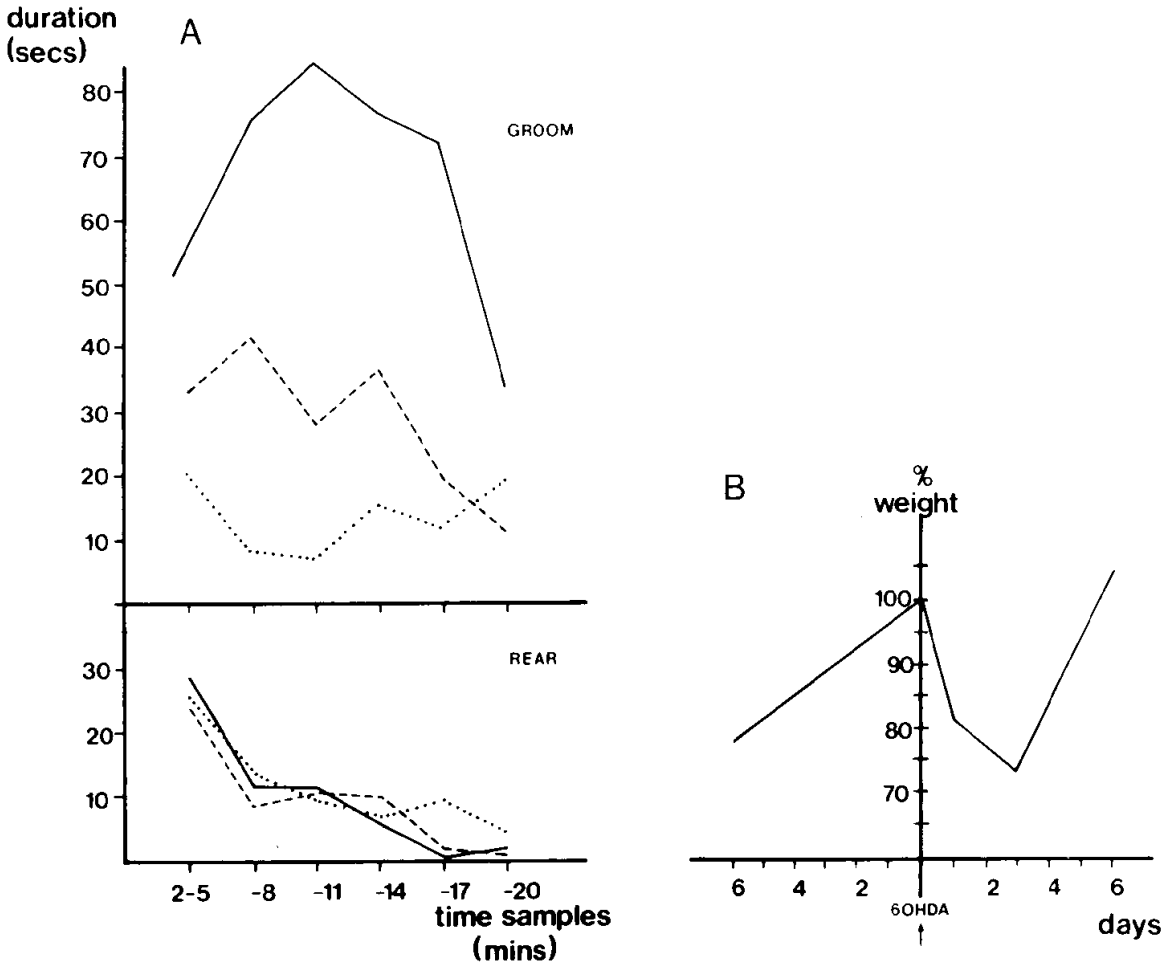

Fig. 2. A: the length of time spent grooming (upper) and rearing (lower) in successive 3-min time samples for animals after saline (———), HpC-NA before SN-6-OHDA (. . . . .) and HpC-NA after SN-6-OHDA (— — — —) injections (25 sites, see text for details). B: the percentage change of weight over 6 days before and 6 days after 6-OHDA injection (13 animals).

ently by unilateral 6-OHDA lesions of the SN. Although feeding was less reliably obtained from animals where NA leakage to the ventricles was suspected, one cannot be certain whether feeding was elicited from NA in the HpC or the ventricles.

An influence of 6-OHDA in the SN was shown by an increased latency to move, increased rotation in the open field and a temporary loss of weight. Transient weight losses have been reported before [9] and been attributed to regulatory deficits rather than hypophagia [3].

After injection of saline and NA after 6-OHDA treatment the latency to rest decreased and the duration of grooming increased. These changes contrast with reports [7] of no spontaneous behavioural changes in cats after NA treatment. The lack of locomotor changes do not support contentions that such behaviour is influenced by NA administration in the rat [8]. These differences may result from tests in the home cage rather than in novel areas.

These behavioural changes may reflect the stress induced by injection. If such changes occur after unilateral intracerebral injection and the body weight is not maintained, it must also be suggested that the loss of weight after bilateral lesion of the SN with 6-OHDA may also in part be due to non-specific effects of the injection.

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