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Stereotyped Behavior Affected by Peripheral and Intracerebroventricular Apomorphine Administration in Pigeons

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DEVICHE, P *Stereotyped behavior affected by peripheral and intracerebroventricular apomorphine administration in pigeons* PHARMACOL BIOCHEM BEHAV **18**(3) 323–326, 1983 —In pigeons, peripheral injection of apomorphine HCl (1 5 mg) produced a rapid pecking response while intracerebroventricular administration of the drug (60 μg) was ineffective in this respect Both peripheral and to a larger extent central treatment with apomorphine stimulated another activity, that is headshaking The frequency of other behavioral patterns was either decreased (preening) or unaffected (yawning, stretching) following both treatments Together with previous studies, these data suggest that (a) apomorphine stimulates pecking in pigeons by activating dopaminergic mechanisms lying in brain areas situated away from the ventricles, (b) dopaminergic mechanisms situated in periventricular regions may take part in the control of some patterns, e g headshaking, and (c) other activities do not appear to depend directly on these mechanisms

Apomorphine Pigeons Brain ventricles Pecking Headshaking Stereotypy

SEVERAL studies have demonstrated that the dopamine agonist apomorphine [12], when peripherally administered to birds, characteristically elicites a pecking fit, the duration and intensity of which are positively related to the doses of the drug which are given [3, 4, 6, 10, 14] In pigeons, apomorphine-induced pecking is accompanied by a variety of other stereotyped activities, such as mandibulating, swallowing and headshaking [6]

At the present time, the mechanisms and the site of action of the drug in the avian brain are not precisely known Experiments involving systemic or central treatment with pharmacological agents which can interfere in various ways with dopamine receptors have led to the conclusion that apomorphine alters behavior through the stimulation of these receptors in the meso-paleostriatal system [2, 7, 8, 13] This conclusion is consistent with the observation that in the avian brain highest concentrations of dopamine are found in the paleostriatum [13] It is still unknown, however, whether the various behavioral changes which occur following apomorphine treatment originate from an influence of the drug upon one single rather than upon several different brain regions This issue was investigated by comparing the effects of apomorphine administered either peripherally or directly into the central nervous system

METHOD

Animals

The subjects were 12 adult domestic pigeons (*Columba livia*) of undetermined sex, weighing 350–480 g and purchased from local breeders They were maintained on a 12 hr light 12 hr dark lighting schedule (lights on at 8 a m) and housed individually in wire mesh cages (40×45×35 cm) Food, grit, and tap water were provided ad lib except during testing sessions (see below) The pigeons had been previously used in a study on the effects of intraventricular ACTH(4–10) administration upon learned behavior They had not been used for at least one week before the start of the present experiment

Surgery

Operations were performed at least 6 weeks before starting this experiment Birds were anaesthetized with Equithesin and their heads were held in a stereotaxic apparatus modified for the pigeon after Karten and Hodos [9] A hole was drilled through the skull at coordinates A7, L3 [9] and a plastic cannula (length 13 5 mm, outer and inner diameters 0 96, 0 58 mm) was then slowly inserted obliquely into the brain until a small quantity of cerebrospinal fluid oozed out of the cannula when it reached a lateral ventricle The cannula was then anchored to the skull surface with dental cement Correct implantation was checked *post mortem* for all birds The median coordinates of the cannula tips were A6 5, L0 5, D10 5 [9]

Injections

In the first half of the experiment, all pigeons received an intraventricular injection of 60 μg of either apomorphine hydrochloride (6 μl, Woelm Pharma) and of control saline (6 μl NaCl 0 9%) For this, the cannula was connected to a 10 μl Hamilton syringe with a piece of flexible plastic tubing which

had been preloaded with the solution to be administered The liquid was then infused into the ventricles in the course of 30 seconds

In the second part of the experiment, all birds were injected with 1 5 mg apomorphine HCl (0 15 ml) and with an equivalent volume of saline, into the left or right pectoral muscles This quantity of apomorphine has been shown to induce a submaximal behavioral response [6]

Drug and control solutions were always given in a random order A delay of at least two days separated any injection from the next one Test sessions started within 3 min following the injection

Apparatus

At least 3 hours before starting a session, pigeons were individually placed into cages (40×45×35 cm), the bottom and 3 side walls of which were covered by black paper sheets with yellow dots on them (8 mm dia, 5 5 dots/dm^2) This environment was chosen on the basis of previous observations showing that the frequency of apomorphine-induced pecking is higher when the birds are tested using a background containing contrast rather than one which is uniformly colored [1] Light was provided by a 150W cool-light bulb suspended 60 cm over the cages Behavioral events were recorded through a one-way mirror by an observer situated in a separate room, minimizing disturbance of the birds Food, but not water, was withdrawn at the beginning of the session

Behavioral Patterns

The activity of the birds was recorded for 30 consecutive minutes following each injection At the end of each 30 sec period, the occurrence of 11 different behavioral patterns was noted The maximum possible score for each pattern was therefore 60 per session The patterns studied were pecking at the floor, side walls, their own plumage or toes, drinking, wing-flapping, stretching one or both wings, body shaking, headshaking and finally yawning These names are sufficiently descriptive as to make further comments unnecessary

Statistical analyses were performed with the Wilcoxon and the Friedman analysis of variance tests [15] Two-tailed probabilities $\leq 0\ 05$ were considered significant

RESULTS

Several of the behavioral patterns (pecking at toes, drinking, wing-flapping and -stretching, body shaking, yawning) always occurred with very low frequencies, thus preventing any further analysis

Pecking at plumage was observed only in one bird (43 positive scores after intramuscular apomorphine), and will therefore also not be considered further Results obtained for the other patterns are summarized in Fig 1 These data were analysed after grouping into either 5 min (periods 1 to 6, pecking at floor+sidewalls) or 10 min (periods 1 to 3, preening and headshaking) periods of observation

Pecking at the floor and side walls occurred with a very low frequency following injections of saline as well as after intraventricular administration of apomorphine By contrast, peripheral injections of apomorphine strongly stimulated pecking This effect was rapid, as it was significant already during the second 5 min period of testing, it lasted until the end of the session

Shortly (first ten minutes of testing) after brain infusion of saline, headshaking was more frequent than later on in the observation period (Friedman test, $p \leq 0\ 003$) This was not observed in birds receiving intramuscular saline ($p > 0\ 30$) and should therefore be attributed to the manipulation of the pigeons associated with brain injections The frequency of headshaking was strongly enhanced following injection of apomorphine into the ventricles and to a lesser extent into the pectoral muscles The time course of these effects, however, differed strikingly in the two cases Indeed, when apomorphine was given centrally the frequency of headshaking increased immediately, decreasing later ($\leq 0\ 00006$), though it remained well above control levels to the end of the session By contrast, a time delay of about 10 min occurred before the frequency of headshaking was elevated above control level when the drug was delivered peripherally

The overall frequency of preening (total scores for 30 min of observations) was not different after injection of saline into the ventricles or into the muscles (Wilcoxon test, $p > 0\ 05$) It should, however, be pointed out that after the administration of the control solution into the ventricles, but not into the muscles, preening frequency progressively decreased in the course of the observation period (Friedman test $p \leq 0\ 001$ and $p > 0\ 90$ respectively) This decrease did not occur after intracerebral apomorphine ($p > 0\ 25$), which explains why preening was more frequent during the last 10 min of testing following this treatment than after saline injections Finally, preening was completely absent after peripheral treatment with apomorphine

DISCUSSION

Results of the present experiment are in agreement with previous studies, since they show that peripheral injection of apomorphine to pigeons can induce within a few minutes a significant burst of pecking even in the absence of food [1, 2, 3, 4, 6] Strikingly, pecking was completely absent after intraventricular infusion of apomorphine This lack of effect cannot be attributed solely to the fact that the dose of the drug which was given (60 μg) was too low or that the delay between the infusion and the appearance of the response was longer than the observation period (30 min) Indeed, when injected into some other regions of the pigeon brain, namely into the *nucleus basalis* (Delius and Audick, in preparation), or into the paleostriatum [7], smaller amounts of apomorphine elicit within a few minutes an intense pecking response

The pecking response observed here after intramuscular injection of apomorphine may have resulted from an action of the drug on some dopamine receptors situated peripherally, that is outside the central nervous system [5] It is more likely, though, that apomorphine stimulated pecking by activating brain areas situated away from the ventricles, such as the paleostriatum, which contains high amounts of dopamine in birds [13], or the *nucleus basalis*

It should also be stressed that although ineffective on the pecking response, intraventricular injection of apomorphine elicited other behavioral activity, it strongly stimulated headshaking Goodman [6] had observed a stimulation of this pattern, together with other activities, after peripheral apomorphine administration To our knowledge, however, this is the first report that headshaking is increased by intracerebroventricular administration of apomorphine There is a striking difference with respect to the time course and the extent of the stimulation of headshaking by apomorphine

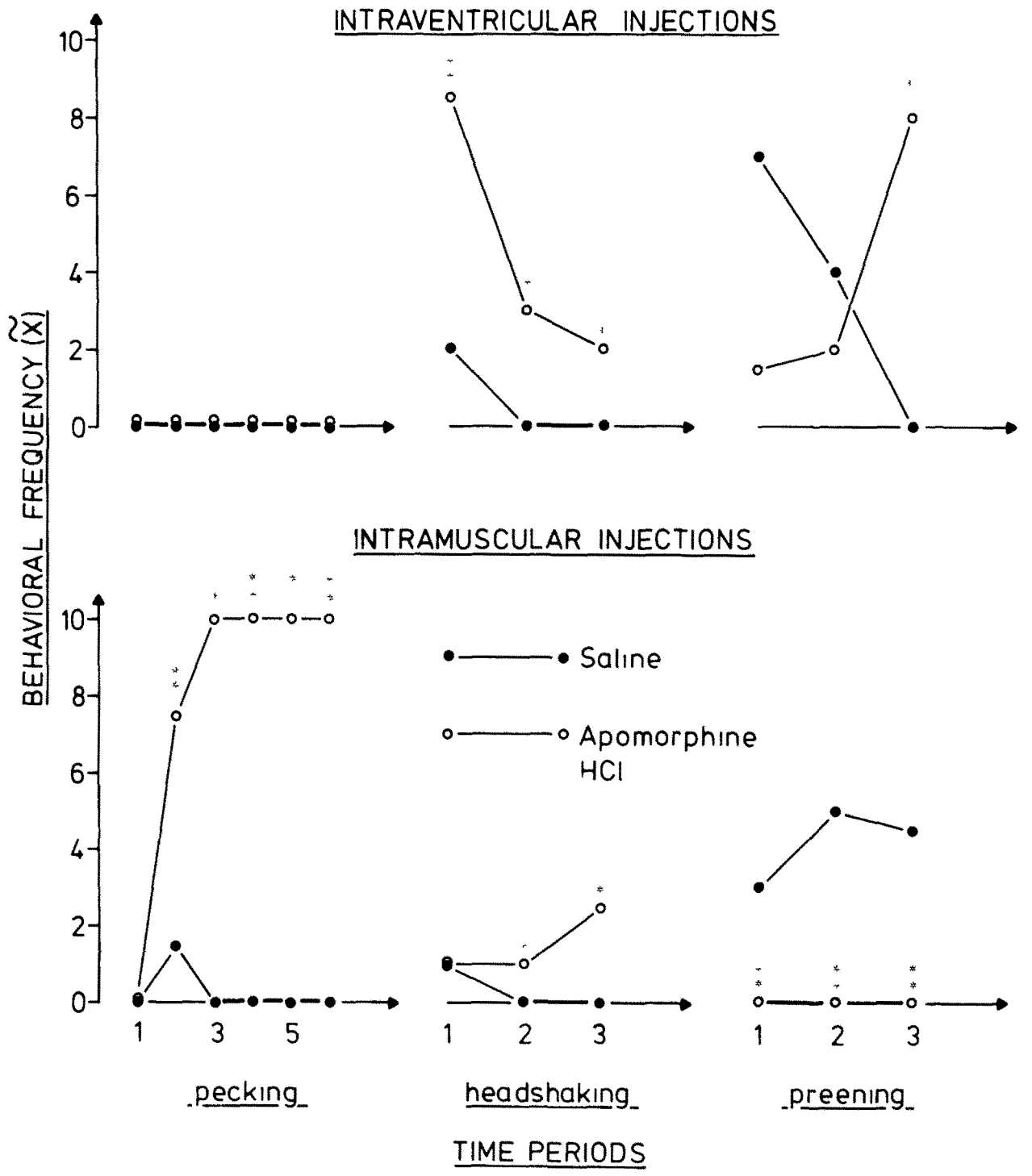

FIG 1 Effect of apomorphine HCl injection into the brain ventricles (60 μg, 6 μl) or into the pectoral muscles (1 5 mg, 0 15 ml) of pigeons (n=12) on the frequency of pecking, preening and headshaking Control injections consisted of an equivalent volume of saline given to the same birds Immediately after an injection, the activity of the pigeon was recorded for 30 min divided into either 6 five-min (pecking) or 3 ten-min (preening, headshaking) periods Differences from the control injections were determined using the Wilcoxon test Only two-tailed significant probabilities are reported *=$p \leq 0$ 05, **=$p \leq 0$ 001

following the two modes of administration of this drug On the one hand, headshaking was more frequent after central than after peripheral treatment with apomorphine though the dose in the latter case was 25 times higher than that in the former case On the other hand, the frequency of headshaking was increased immediately after the intracerebroventricular injection of apomorphine, but only after a delay when the drug was given into the muscles This delay may correspond to the time necessary for apomorphine to reach the brain and activate headshaking after peripheral treatment Altogether, these results suggest that in pigeons, headshaking is under the influence of dopaminergic mechanisms They also show that the brain areas which are involved in the apomorphine-induced pecking response and headshaking are anatomically different The exact location of the areas involved in the control of the latter pattern remain, however, to be determined at the present time

Our results also show an inhibition of preening by apomorphine treatment to pigeons When the drug was given peripherally, preening was completely suppressed during the whole session After the infusion of apomorphine into the ventricles, preening was also depressed, though this effect did not reach significance and occurred only at the beginning of the session Later on, it may be supposed that apomorphine was progressively eliminated, so that preening could be released and eventually became more frequent than after control injection toward the end of the observation period

It should finally be pointed out that several activities which were studied here (yawning, stretching, body shaking) were not influenced by apomorphine injected either peripherally or centrally It is therefore possible that in the pigeon, only some behavioral patterns (e g pecking, headshaking, preening, also circling, swallowing, and mandibulating, see [6,7]) are under dopaminergic control, while others depend on other mechanisms In the rat, for example, yawning is controlled by both dopaminergic and cholinergic mechanisms [11,16] Whether the same is true for birds has, however, not been determined so far

In conclusion, our study suggests that in the pigeon, some activities are under activating (pecking, headshaking) or inhibiting (preening) control of dopaminergic mechanisms located in different areas of the central nervous system, while other activities depend at least partially on other mechanisms This investigation also stresses the usefulness of birds as models for studying the neurochemical bases of behavior

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