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Apomorphine: Effects on the Timing and Sequencing of Pecking Behavior in Chicks

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MACHLIS, L. E. *Apomorphine: Effects on the timing and sequencing of pecking behavior in chicks.* PHARMAC. BIOCHEM. BEHAV. 13(3) 331–336, 1980.—Stereotyped behavior induced by apomorphine is thought to be "autistic", that is, impervious to environmental influence. This assumption is tested by analyzing the patterning of pecks at two differently colored stimuli in three-day old chicks treated with either 0.3 mg-kg^{-1} or 0.4 mg-kg^{-1} apomorphine. While normal chicks strongly prefer one stimulus over the other, apomorphine appears to render the choice behavior of chicks insensitive to differences between the stimuli. This result might suggest that apomorphine-treated chicks no longer perceive differences between the stimuli, but an analysis of the timing of pecks reveals that differences are still perceived since the two stimuli elicit different rates of pecking.

Apomorphine-induced pecking Stimulus preference Chicks Ethological analysis

APOMORPHINE (APO), a presumed dopamine agonist, when injected into a variety of animals causes striking changes in behavior (reviewed in [5,32]). Thse changes are thought by some to mimic abnormalities present in the mentally ill ([26] but see [17]). Despite the diversity of behavior patterns influenced by this drug (e.g., running in dogs [23], gnawing in rats [19], pecking in pigeons [11–14] and chicks [24] and biting in tortoises [1]), each is altered in a similar manner. This emergent property of the behavior has been vividly described as "compulsive" [12], "persistent" [12] and "stereotyped" [25].

The extent to which the neurochemical mechanisms underlying these stereotypies are related to those involved in schizophrenia and amphetamine psychosis is an area of intensive research [31], but no studies exist which quantify the precise changes in the organization of behavior in animals treated with apomorphine. (However, several studies do exist which describe alterations in behavioral organization induced by amphetamines (which also induce stereotypies in animals) e.g. [29,33].) Precision at the neurochemical and pharmacological level should be mirrored at the ethological level as well, since ultimately it is the behavior of animals including human beings which we wish to understand [20].

While "stereotyped" behavior most frequently refers to an increased rhythmicity in the timing of behavior, it has also been described as "autistic" [28]. Austistic is used to "designate behavior that is determined exclusively from within and not influenced by the environment" [27]. The extent to which this term applies to the "stereotyped" pecking behavior of APO-treated chicks is the subject of this report.

METHOD

The subjects were male (Dekalb Leghorn) chicks, aged between 50–60 hours. The original purpose of these experiments was to gather sufficient data to allow a quantitative analysis of the alterations in temporal patterning induced by apomorphine. Since the APO-treated chicks peck at such high rates, I decided to test twice as many controls as APO-treated chicks, to make the amount of data collected from the two groups more nearly equal. Thus, there were 52 chicks in the control group and 26 in each of the two APO-treated groups. The chicks were assigned at random to each group and the three groups did not differ significantly in mean weight.

The chicks were housed in a wire mesh cage (108×63×19 cm) containing a test compartment (8×8×19 cm). Through the floor of the test compartment protruded two hat-pins (5 mm in diameter, 4 mm apart), one colored red (Humbrol enamel paint no. 6) and the other pearl-white (colored as purchased). To enhance the contrast of these targets, a 12 W, high intensity bulb was placed 30 cm above the stimuli and black mulch covered the area underneath the test compartment. There was no control for possible differences in the intensity of these stimuli. (Thus it is for the sake of convenience only that I will use the term "color" preference in this report. In so doing, I do not mean to imply that the chicks are using only differences in wavelength (and not other cues such as intensity or saturation) to discriminate between stimuli.)

The floor of the cage was constructed with 0.64 cm^2 wire mesh and a patch (3.2×2.5 cm) of 0.25 cm^2 wire mesh surrounded the area through which the stimuli emerged and served to prevent the chicks from grabbing the pin-heads (a behavior which can create peck artifacts).

An automated recording system [9] was used to determine the timing and sequencing of pecks. The two stimuli were attached to separate gramophone pick-ups and when a peck

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occurred a pulse was produced which was then automatically converted into a frequency (tone) characteristic of the particular stimulus pecked. These pulses were recorded in real time on magnetic tape and then automatically decoded by computer, producing a record of which stimulus was pecked and the time at which each peck occurred. Full details concerning this event recording system and the accuracy of the apparatus are in [22].

Apomorphine hydrochloride (Lilly) was prepared fresh on the morning of each test day from the salt, using 0.90% physiological saline and kept on ice throughout the experiment to prevent degradation. The volume injected was proportional to body weight: a 30 g chick received 0.30 ml. Two groups of chicks received intraperitoneal doses of apomorphine: 0.3 mg-kg^{-1} (APO-0.3 mg) or 0.4 mg-kg^{-1} (APO-0.4 mg) with an estimated dose error 8–10%. A third (control) group received injections of physiological saline.

(I arrived at the apomorphine doses through preliminary experiments with doses ranging between 0.25 mg-kg^{-1} and 1.0 mg-kg^{-1} (based on data from [12]). Subjective observations suggested that the stereotyped pecking behavior occurred most consistently with doses between 0.3 and 0.4 mg-kg^{-1}.)

The chicks in these experiments were deprived of food and water. They were tested in a sound-proof room, darkened from 2100–0700 whose temperature ranged between 21° and 24°C. To eliminate any systematic effects due to the time of day at which the chicks were tested (experiments ran from 0900–1800) the treatment given to each successive chick was determined by rotating through the sequence: control, APO-0.3 mg, control, APO-0.4 mg.

Immediately following injection a chick was placed in the test compartment. The test chick was physically and visually isolated from both his companions and me (although the data were recorded automatically, I was present during all trials). The time between the injection of APO and the onset of pecking was found to be quite variable (i.e., 0.5 to 15 min) and so a trial was defined as lasting for 10 minutes beginning with the first peck. APO treated chicks who did not peck within 15 minutes were rejected, as were control chicks who did not peck within 5 min. Rejections were rare.

In order to obtain enough data for this analysis, seven different batches of chicks were tested and the data from all batches within each treatment group were combined. No batch was disproportionately represented in any treatment group. The effect of any position preference was controlled for by appropriate alternations in the positions of the two stimuli.

The temporal patterning of pecking in chicks is complex [22] and the methods for estimating the variability in the statistics describing such a time series are not straightforward. Therefore, even though there are indications that subtle differences do exist between the effects of the APO-0.3 mg and APO-0.4 mg dosages, no direct statistical comparisons between these groups are made in this paper. Instead, I present those results which can be demonstrated by analyzing data within each group. Furthermore, since the distributions are highly skewed I have analyzed all the data using non-parametric statistics [30] and report medians (rather than means) as the measure of central tendency.

RESULTS

Apomorphine induces striking changes in many facets of a chick's behavior, the most obvious being an apparently

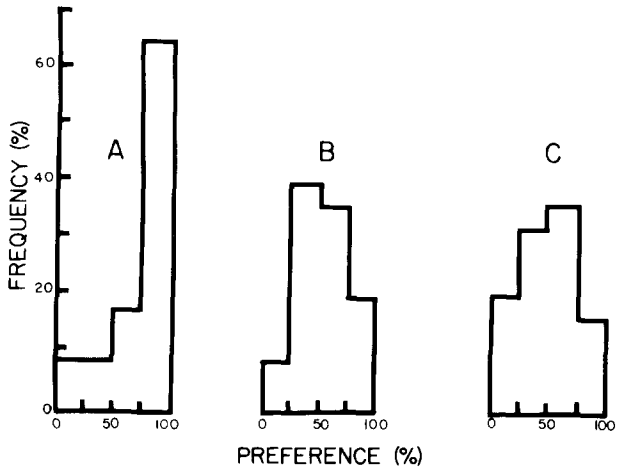

FIG. 1. The distribution of preferences for the white stimulus in control chicks (A) and chicks treated with 0.3 mg-kg^{-1} (B, APO-0.3 mg) and 0.4 mg-kg^{-1} (C, APO-0.4 mg) apomorphine. Pecks were elicited by both a red and a white stimulus. Within each treatment group, each chick was classified into one of four bins according to its preference (i.e. the proportion of pecks directed at the white stimulus). The control chicks pecked significantly more at the white target ($p<0.0001$, N=52, Wilcoxon Matched Pairs test) whereas there are no differences in response frequency towards the two stimuli in the APO-0.3 mg ($p<0.38$, N=26) or APO-0.4 mg ($p<0.93$, N=26) chicks.

radical restructuring in the temporal organization of pecking. In these experiments apomorphine increased median peck rates twelve-fold (from 2.7 pecks-min^{-1} in controls to 33 pecks-min^{-1} in both APO-treated groups). A detailed quantitative analysis of these temporal alterations in the pecking behavior is the subject of another report (Machlis, in prep.); the results presented here stem from an unexpected change in the sequential organization of APO-induced pecking.

Chicks are well known for exhibiting strong "color" preferences [15] and the control chicks in this experiment are no exception; the white stimulus elicits over 75% of all pecks in 65% of the controls (Fig. 1). In contrast, the proportion of APO-treated chicks displaying such a strong preference for white is less than 20%. The more even distribution of preferences in the APO-treated chicks suggests that neither the white (W) nor the red (R) stimulus is particularly favored, and a statistical examination of absolute peck numbers (see caption, Fig. 1) provides no evidence that the APO-treated chicks are responding more frequently to one stimulus than the other.

Since these two measures of preference consider only relative frequencies, they give no indication as to "how" this change in preference is effected. For example, a strict alternation between stimuli (e.g., RWRWRWRWRW) yields a 50% preference as does the pattern RRRRRWWWWW, in which two "runs" of pecks, of equal length, are elicited by each stimulus. In Fig. 2 a comparison is made, for each group, between the distributions of the runs at the red and white stimuli. In the control chicks, white runs predominate over red and are twice as long (as measured by the medians), whereas in the APO-treated chicks the distributions tend to converge, and the median run lengths become identical (3.9 pecks per run) in the APO-0.4 mg group. A statistical inspection (see caption, Fig. 2), sensitive to any differences

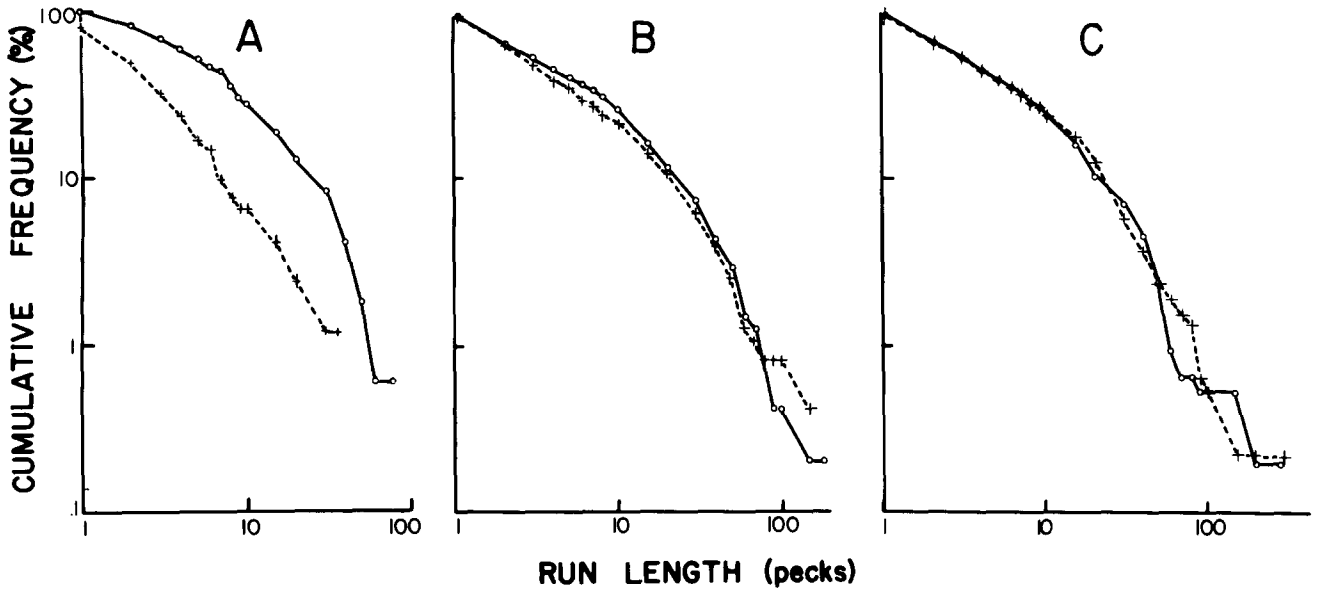

FIG. 2. The survivorship function of runs of pecks at the red (R, X--X--X) and white (W, 0–0–0) stimuli for control chicks (A) and chicks treated with 0.3 mg-kg^{-1} (B, APO-0.3 mg) or 0.4 mg-kg^{-1} (C, APO-0.4 mg) apomorphine. Chicks frequently direct several pecks in succession at the same stimulus (e.g., RRRRR) and these runs can vary in length. A survivorship function is derived by cumulating the frequency distribution of run lengths from right to left. To compare the two distributions within each group I have scaled each with the larger of the total number of runs at red (N_R) or at white (N_W). The two distributions differ significantly (Kolmogorov-Smirnov two-sample test, where D is the maximum difference between the two functions), in the controls ($p<0.001$, D=34%, $N_R=137$, $N_W=165$) but no significant differences between the distributions can be demonstrated in the APO-0.3 mg ($p>0.05$, D=8%, $N_R=470$, $N_W=468$) or APO-0.4 mg ($p>0.10$, D=1%, $N_R=438$, $N_W=441$) chicks. The median run lengths at the red (M_r) and white (M_w) stimuli are: controls ($M_r=2.5$, $M_w=5.8$), APO-0.3 mg ($M_r=3.0$, $M_w=3.9$), and APO-0.4 mg ($M_r=3.9$, $M_w=3.9$).

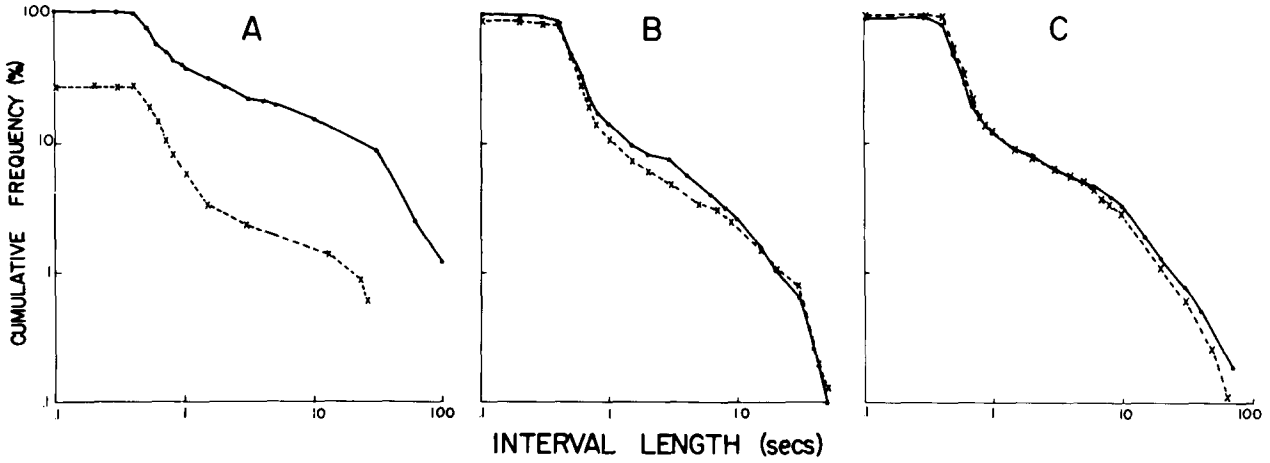

FIG. 3. The survivorship function of the intervals between pecks at the red (R-R intervals) and white (W-W intervals) stimuli for control chicks (A) and chicks treated with 0.3 mg-kg^{-1} (B, APO-0.3 mg) and 0.4 mg-kg^{-1} (C, APO-0.4 mg) apomorphine. These functions show the distributions of intervals generated between pecks occurring at the red and white stimuli. The survivorship curve is derived by cumulating the frequency distribution from right to left; within each group both survivorship curves are scaled using the same constant, either the total number of W-W intervals (N_w) or R-R intervals (N_r) depending upon which is greater. For each group, the two distributions differ significantly (where D is the maximum deviation between the two functions) controls ($p<0.001$, D=16%, $N_r=395$, $N_w=1421$); APO-0.3 mg ($p<0.001$, D=5.6%, $N_r=3382$, $N_w=3821$); APO-0.4 mg ($p<0.001$, D=11%, $N_r=3725$, $N_w=3645$, Kolmogorov-Smirnov two-sample test).

between the distributions (e.g. skewness, dispersion, central tendency) can detect no difference between the two distributions in either of the groups treated with apomorphine, whereas the distributions differ significantly ($p<0.001$) in the controls.

One interpretation of these data might be that the chicks are no longer discriminating between the stimuli, an inference consistent with the notion that "stereotyped" behavior is rendered impervious to environmental influence. However, such a conclusion would be premature in light of the results presented in Fig. 3.

Here the distributions of intervals between pecks at red (R-R intervals) and at white (W-W intervals) are compared, and again, as was found for the distributions of run lengths,

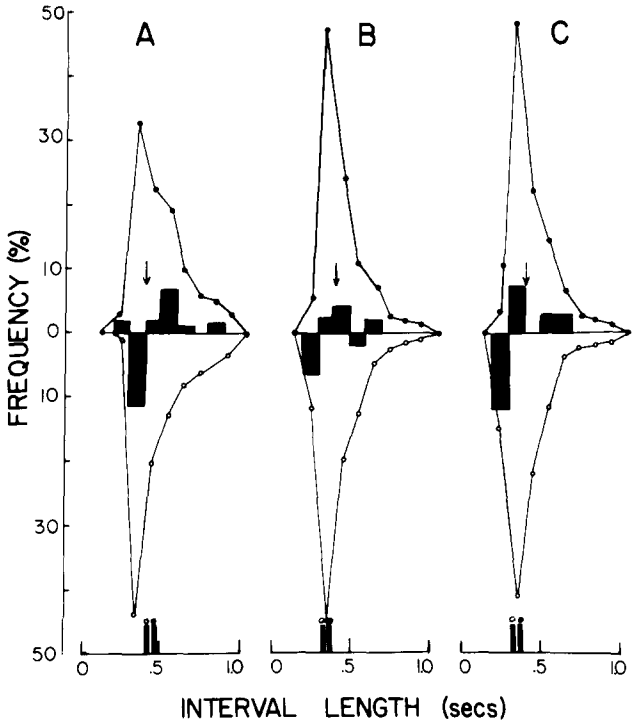

FIG.4. A comparison of the effect of apomorphine on the distribution of intervals between pecks at the red stimulus (R-R intervals) and white stimulus (W-W intervals) for control chicks (A) and chicks treated with 0.3 mg-kg^{-1} (B, APO-0.3 mg) and 0.4 mg-kg^{-1} (C, APO-0.4 mg) apomorphine. For each treatment group the R-R (●—●—●) and W-W (○—○—○) interval distributions were each truncated at 1 sec, normalized to 1.0 and graphed as polygons. Those regions of the black histogram falling above the abscissa indicate where R-R intervals occur with a greater probability than W-W intervals; regions below indicate the reverse. The arrow is fixed at 0.4 seconds in each graph to highlight the shift in the peaks of the histogram in the APO-treated chicks. The heavy lines on the (graduated) abscissa show the median interval lengths (●=red, M_R; ○=white, M_W) for the truncated distributions. These medians (secs) are: M_R=0.47, M_W=0.42 (controls); M_R=0.39, M_W=0.38 (APO-0.3 mg); M_R=0.40, M_W=0.38 (APO-0.4 mg).

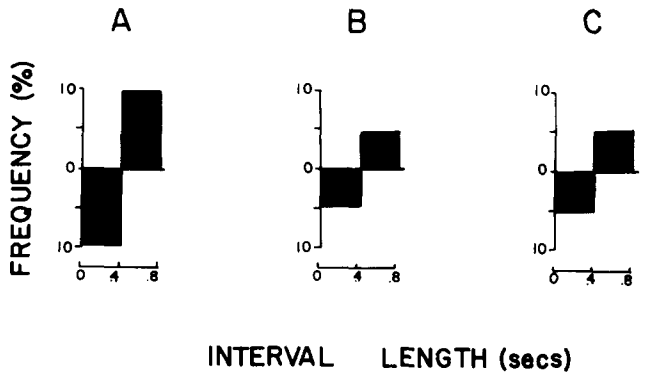

FIG. 5. A comparison of the effect of apomorphine on the distribution of intervals between pecks at the red stimulus (R-R intervals) and the white stimulus (W-W intervals) for control chicks (A) and chicks treated with 0.3 mg-kg^{-1} (B) and 0.4 mg-kg^{-1} (C) apomorphine. These distributions were calculated by regrouping the data in Fig. 4 into two class intervals of 0.1–0.4 sec and 0.5–0.8 sec, and then determining the algebraic difference between the R-R and W-W interval distributions over these two intervals. Those regions of the histogram falling above the abscissa indicate where R-R intervals predominate over W-W intervals; regions below indicate the reverse.

there is an apparent convergence of the distributions in the two apomorphine groups. However, a statistical examination of the two distributions shows them to be quite different (see caption, Fig. 3) in all three treatment groups.

(In the two APO-treated groups the sample sizes are so large that even a comparatively small difference becomes significant. However, the fact that this deviation is actually quite substantial, 6% (APO-0.3 mg) and 11% (APO-0.4 mg), is somewhat obscured by the logarithmic scale which is used on the ordinate.)

In each group of chicks a large proportion of the intervals fal in the region between 0.1 and 1 second (controls, 60%; both APO groups, 84%) and it is this portion of the distribution which is weighted most heavily by the statistical test. Thus, this region was scrutinized to more precisely delineate the nature of these differences in the timing of pecks.

Figure 4 shows these truncated interval distributions and in all groups they are skewed to the right with modal intervals of 0.4 sec. Despite the fact that the R-R and W-W interval distributions look quite similar, an examination of the algebraic difference (the black histograms) between the two distributions shows that a disproportionate number of pecks separated by intervals between 0.1 and 0.4 sec occur at the white stimulus whereas pecks separated by intervals between 0.5 and 0.8 sec occur more frequently at the red stimulus. This result is best illustrated in Fig. 5. Thus it is likely that this systematic difference in "pecking rates" accounts for at least some of the differences found in the distributions shown in Fig. 3.

Lastly, pecking in chicks does not occur randomly in time. Chicks peck in bursts (i.e., pecks separated by relatively short intervals, e.g., 0.1–1 sec) and these bursts, or "bouts", tend to cluster together into "super bouts" [22]. Because of this structure it would be possible for apomorphine to significantly increase the number of pecks generated over a ten minute period, without necessarily increasing the peck rates within the bout units. However, there is some suggestion (Fig. 4) that there has been a change in pecking rates within these bursts in the APO-treated chicks. The basis for this hypothesis is the substantial shifts in the medians of both the R-R and W-W interval distributions (as shown on the abscissas) between the controls and the APO-treated groups.

DISCUSSION

A helpful framework for examining the apparent differential effects of apomorphine on the timing and sequencing of pecks is one which assumes that two mechanisms are involved in generating a peck: a timing mechanism, which determines when a peck will occur, and a choice mechanism which determines which stimulus is pecked. (Evidence for such a model is presented by Dawkins [7,8] (but see [21]).) If one stimulus receives a larger proportion of pecks than another it is assumed that some properties (or property) of the stimulus (e.g., hue, saturation, intensity) has biased the choice mechanism. Similarly, if pecks occur more quickly at one stimulus than another, it is assumed that properties of the stimuli are differentially biasing the timing mechanism.

In the introduction the question was raised as to what extent the stereotyped pecking induced by apomorphine in chicks could be termed 'autistic' (i.e., behavior not affected by the environment). The results presented here suggest that this term be used with caution, since although the choice behavior of the APO-treated chicks appears no longer affected by the stimuli (as evidenced by their loss of "color" preference), the timing of pecks does seem to depend upon which stimulus is pecked. If we assume that the timing and choice mechanisms are biased by the same properties of the stimuli, we must conclude that the chicks are still perceiving these differences between the stimuli but that these properties are no longer affecting the choice behavior. However, if we assume, for example, that the choice mechanism is sensitive only to differences in hue and the timing mechanism only responds to differences in intensity, it could be inferred that apomorphine has altered the chicks' perception so that they are no longer perceiving differences in hue.

With these experiments it is not possible to distinguish between an hypothesis that the chick's perception is altered by apomorphine and one which proposes that the expression of a "color" preference has simply been suppressed. In a recent study of vocalizations in APO-treated chicks, De Lanerolle [10] suggests that apomorphine may be acting on both sensory-perceptual and motor mechanisms. Similarly, Saxena [28] argues for the involvement of the retina (in addition to generally accepted central sites) in APO-induced pecking in the pigeon. He bases this argument on qualitative behavioral observations (including the intriguing finding of Brunelli [3], that rates of pecking in APO-treated pigeons can be modulated by light intensity) and the existence of a dopamine-sensitive adenylate cyclase in the calf's retina that is also stimulated by apomorphine [2]. Stimulation of this retinal system with dopamine produces activity which is blocked by drugs known to inhibit APO-induced pecking in pigeons [4].

It is tempting to speculate that the apparent differential effect of the two stimuli on the timing and choice behavior of pecking in chicks results from apomorphine acting at both central and retinal sites. However, such speculation in either chicks or pigeons must take into account that in each species, centrifugal fibers exist [6,16], originating in the isthmo-optic nucleus and terminating on amacrine cells, which provide a mechanism for central modulation of input at the level of the retina.

The experiments I have described cannot determine where apomorphine is acting in the chick, nor by what mechanism, but this is not their purpose. Careful descriptions of the changes in behavior induced by apomorphine are needed so that we will know what it is that eventually must be explained at the neurochemical level.

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