their pollen is not likely to be picked up by flower piercers.

Although our primary purpose was to test SEM analysis for effectiveness, we were able to make some preliminary observations. In all samples one pollen species was in great predominance (90 to 100 percent), possibly reflecting the floral species constancy already known in some hummingbirds' feeding patterns (*4*). Neotropical nectarivorous bats, however, are thought not to display much feeding constancy (*3*).

The advantage of the high resolution of SEM is obvious and was recently shown (*5*) to distinguish easily between the pollen of two species of the genus *Crescentia*, which were difficult to tell apart with a light microscope. Also, the technique previously used to study vector-borne pollen depended on staining the pollen grains. Difficulties in interpretation due to differential uptake of stain by different pollen types was a complicating factor (*1*). Since our SEM technique does not require staining, this variable is eliminated. Finally, the SEM is useful since it is simple to carry out statistical analyses of the bird's feeding behavior and pollination efficiency by scanning the samples even though the bird may carry seemingly invisible amounts of pollen. The double-stick tape loads consistently and completely with pollen, providing an even, rapidly analyzable sample of statistically useful size (1000 to 2000 grains) even when limited quantities of pollen are present. We hope that this technique will be useful in studies of other pollinators, especially those carrying relatively small amounts of pollen.

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Evoked Response Correlate of Symbol and Significate

Abstract. *Changing the source and intensity of the auditory signal to six trained cats responding to meaningful auditory stimuli permits exogenous and endogenous processes in the auditory evoked potential to be separated. For short-latency exogenous processes, latency and amplitude depend on the parameters of the physical stimulus. However, the amplitude and shape of longer-latency endogenous processes are essentially independent of the location and intensity of the signal source and seem to be invariant concomitants of the significance of the signal.*

In a series of papers (*1*), we have presented evidence that the evoked potential (EP) recorded from trained cats is a composite of exogenous processes reflecting afferent sensory input and endogenous processes reflecting central reactions to such input. The results of a wide variety of controls devised to rule out the possibility that the observed endogenous processes were of unspecific origin established that they (i) were not a function of type or level of motivation; (ii) were observed in a variety of different instrumental tasks; (iii) were elicited by visual, auditory, or direct electrical stimulation of brain structures; (iv) appeared in the absence of any visible changes in head or body position or orientation to the stimulus revealed by cinegraphic analyses; (v) were not a reflection of changes in receptor sensitivity or stimulus intensity; (vi) and were not related to response bias or the intention to perform a particular set of motor responses.

In view of this evidence that endogenous processes could not plausibly be attributed to unspecific factors, we concluded that they probably reflected the release of neuronal activity representing the activation of specific memories about the meaning of the afferent input. However, reports in the literature indicated that marked changes in EP waveshapes in untrained animals could result from changes in the spatial relationship between stimuli and exteroceptors (*2*). Reservations about our interpretation would not be eliminated merely by our failure to observe changes in stimulus-receptor geometry when changes in EP waveshape occurred, because our control methods for such effects might have been inadequately sensitive. A better answer to such reservations could be obtained by devising an experimental procedure in which changes in the spatial relationship between exteroceptors and conditioned stimuli with specified meaning were deliberately imposed while we sought invariant features of the endogenous processes. We now report the result of such an experiment.

Six cats, each having 34 electrodes permanently implanted into various brain regions, were differentially trained in a series of stages to obtain food in an L-shaped runway (*3*). Initially the animals were trained to make a free operant response, leave the elevated platform (start), descend to the runway, and proceed to the feeder (goal) at the far end of the L, where a morsel of raw meat was delivered from an automatic turntable if the cat stepped up and touched it with its paw. After learning the free operant response (oscillation, back and forth, from start to goal), the animals were given discrimination training in which food at the goal became contingent upon the presence of a positive conditioned stimulus (CS+)—a click train presented at the rate of two clicks per second (2 sec^{-1}), the "go" stimulus. After acquiring the discriminative performance, the animals were given differential training in which a negative conditioned stimulus (CS−), a 5 sec^{-1} click train, required the animal to "stay" on the starting platform. During both discrimination and differentiation, the animals were required to return to the starting platform and sit down before the next trial began.

Daily sessions of 25 to 50 trials of randomly intermixed CS+ and CS− were run on weekdays after 24 hours of food deprivation. Trials were presented at random intervals averaging 2 minutes. Animals were fed freely on Saturday.

Evoked potentials (EP's) were recorded on magnetic tape during each session, and videotape records were made of each trial. Cross-trial running average EP's were obtained by averaging the first through third, second through fourth, third through fifth (and so forth) responses on all CS+ trials resulting in correct performance.

During training, all stimuli (*4*) were delivered from loudspeaker 1, mounted behind the cat above the starting platform. The secondary component structure of the EP became dramatically altered as the CS+ acquired significance during three stages of training that preceded differential training (Fig. 1). All data are from the medial geniculate bodies because much of our previous data collected in response to visual rather than auditory stimuli showed that both exogenous and endogenous representational pro-

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cesses were particularly well manifested in lateral geniculate body EP's. These EP's can be compared with those in Fig. 2 for cat 4 (after differential training). The late components of the EP's are enhanced when the CS becomes meaningful (Fig. 1, column 2), and the secondary component structure changes further as this meaning becomes more specific (Fig. 1, column 3, and Fig. 2, cat 4, column 1).

After attaining 90 percent or better differentiation for three successive days, each animal was subjected to several days of testing in which 25 to 50 randomly intermixed CS+ and CS− trials were delivered randomly from either the usual loudspeaker 1 or an identical loudspeaker 2, mounted at the far end of the runway above the feeder. Running average EP sequences were computed separately for CS+ at each of the two loudspeaker positions; an average of 92 percent of CS+ trials at speaker 1 and 89 percent of CS+ trials at speaker 2 resulted in the appropriate behavior (Fig. 2). The latency of the primary response (short latency, sharp component) increased as the animals moved away from speaker 1 (column 1) and decreased as they approached speaker 2 (column 2). Videotape analyses showed this latency shift to correspond to the distance of the cat from the CS source. The mean latency shift for the primary response across the cats, from the start to goal positions, was 5.4 ± 0.3 msec, a close approximation to the 5.1 msec for the expected difference in transmission time through air (under our laboratory conditions) resulting from the cat's change in position with respect to the sound source. Further, the relative intensity of the CS was about 12:1 when the cats were near or far from the loudspeaker. If the average EP at the medial geniculate body passively reflected only the physical features of the CS, the size as well as shape of the average EP's when the cats were near the CS source (top of column 1 versus bottom of column 2) should be similar. Further, EP's when the cats were far from the CS source (bottom of column 1 versus top of column 2) should be similar to each other but quite different from the EP's obtained when the cats are near the CS source. In addition, the amplitude of the average EP's when the cats were at the start position should be much larger in column 1 than in column 2. This is not the case. Instead, both size and shape of the large positive late components are similar whether the animal is near or far from the CS source. This is especially true during the deci-

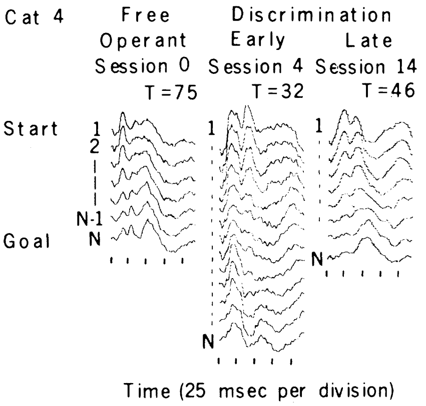

Fig. 1. Example of changes in cross-trial running average EP's to a 2 sec^{-1} click train during maze performance at three stages of training. Data were recorded from bipolar electrodes implanted in the right medial geniculate body. The animal was at the start position at the top of each column and at the goal position at the bottom of a column; column length corresponds to the animal's mean latency to traverse the maze. (Column 1) Irrelevant background click as the animal oscillates from start to goal during continuous free-operant performance. (Column 2) First discrimination session during which the animal reliably oriented to the loudspeaker at CS onset. Secondary EP components were enhanced even as the animal ran the maze and reached the goal. (Column 3) Well-established discriminative performance. The number of appropriate response trials (*T*) is given at the head of each column.

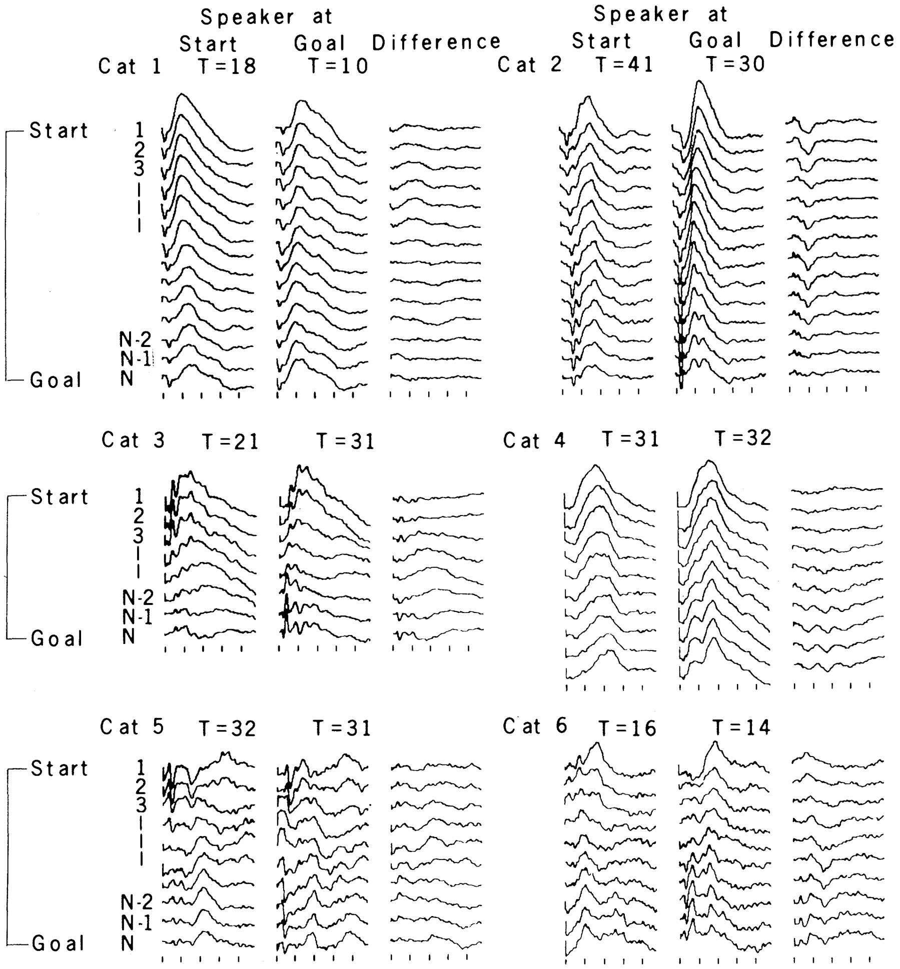

Fig. 2. Experimental data for six differentially trained cats. Data from cats 1 to 5 were recorded from bipolar electrodes implanted in the right medial geniculate bodies; in cat 6, monopolar electrodes recorded from the left medial geniculate body. For each cat, only the data for the CS+ are presented (column 1, for each cat). The CS+ was delivered from a loudspeaker behind the cat's starting position in the L-maze. The sequence of waves are the same as those in Fig. 1. The sequence of EP's from top to bottom spans the cats' cognitive-behavioral events from CS+ onset through appropriate CS+ interpretation and response execution. (Column 2). The CS+ was delivered from a loudspeaker near the goal position of the maze. The late component waveshape during CS+ interpretation, while the animal is on the starting platform, is similar (columns 1 and 2) despite the disparate locations of the loudspeakers with respect to the cat. The amplitude of the late component when the cat was at the start was larger in column 2 than in column 1 in some cases, even though the sound source was farther away. (Column 3) Difference waves obtained by subtracting the waves of the second column from those in the first, after compensating for EP latency differences resulting from the differences in CS+ transmission time in air as a function of the gross changes in the animal's location with respect to the source loudspeaker (6). Each epoch, 120 msec.

sion-making period (*5*), while the cats are still on the starting platform (waves 1 to 4), before they begin their long approach to the goal.

If we hypothesize that the major difference between columns 1 and 2 of Fig. 2 will be in exogenous processes (short latency) reflecting location and intensity of the physical stimuli, while endogenous processes (longer latency) reflecting the meaning of the repetition rate of the click will be relatively independent of CS location and intensity, the difference waves (column 3) should consist primarily of early components. The later portions of the difference waves should be relatively flat, indicating that endogenous processes of similar size and shape were released regardless of the CS location and consequent intensity differences. As expected, the difference waveshapes consist largely of the early components with some indications of a phase reversal as the animals moved past the midpoint of the runway, results compatible with the interpretation that they reflect the relative intensities of clicks from speakers 1 and 2. However, the rather large differences in intensity of the CS as a function of distance from the loudspeakers and the gross differences in CS location imposed in the experimental design had surprisingly little effect on the average EP in the medial geniculate bodies as evidenced by the relatively low energy in the difference waves compared with the EP's. The later portions of the difference waves are approximately flat, indicating little difference in the endogenous processes under the two stimulus conditions. Similar phenomena were observed at other central sites, and latency measurements suggest that the later phenomena seen at the geniculate level result from propagation of centrifugal processes.

Further quantitative assessment of the differential sensitivity of primary (short latency) and secondary (longer latency) average EP components to exogenous and endogenous processes was obtained by correlating either the early (1- to 10-msec) or the late (11- to 120-msec) portions of the average EP's (Fig. 2) (*6*). Two sequences of correlation coefficients were computed for each latency band for each cat.

Sequence 1 was obtained by correlating EP 1 of the "speaker-at-start" trial with EP *N* of the "speaker-at-goal" trial, EP 2 of "speaker-at-start" with EP *N*-1 of "speaker-at-goal," and so forth. This sequence corresponds to an increasing distance between the cats and the cue source. Since the successive phases of the decision-making and response-execution process are systematically counterbalanced across these two sets of waves, this series of correlation coefficients reflects the degree to which similar exogenous processes were evoked during the two types of trials, independent of decision making and response execution (Fig. 3).

Sequence 2 was obtained by correlating average EP's from trials with the speaker at the start with those from trials with the speaker at the goal, for waves 1 through *N*. This sequence corresponds to successive phases of the decision-making and response-execution process. Since the cats' distance from the cue source was systematically counterbalanced across the two sets of waves, this series of correlation coefficients reflects the degree to which similar endogenous processes were released during the two different types of trials, independent of loudspeaker location.

Treatments by trials by subjects' analyses of variance with a repeated-measures design using z-transformed correlation coefficients showed the EP primary components to be significantly ($P < .05$) more highly correlated as a function of loudspeaker distance than with respect to phases of decision making and response execution. Conversely, the secondary components were significantly ($P < .05$) more highly correlated as a function of the phases of decision making and response execution than with respect to loudspeaker distance. Correlation coefficients for secondary components were higher during the decision-making process than during response execution ($P < .05$) and were also higher when the cats were near rather than far from the loudspeaker ($P < .05$).

In order to better contrast the dif-

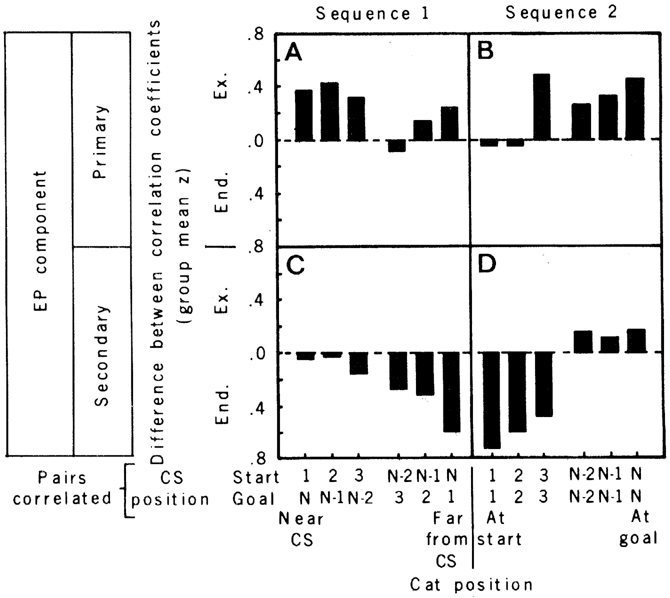

Fig. 3. Differential reflection of exogenous and endogenous neural activity in the primary and secondary EP components, computed from medial geniculate recordings (Fig. 2) obtained by correlating either the early (1 to 10 msec) or the late (11 to 120 msec) portions (*6*). Two sequences of correlation coefficients were computed for each component. The first sequence counterbalanced the phases of decision-making and response execution. The second counterbalanced the cat's position with respect to the cue source. The waveforms correlated are indicated on the abscissa where the numbers 1 to *N* are identical to those on the ordinate of Fig. 2. Thus, four sequential sets of correlation coefficients were obtained for each cat: early exogenous (*Ex.*), early endogenous (*End.*), late exogenous, and late endogenous. All coefficients were transformed to z values, averaged across cats to provide four group mean sequences, then averaged within each sequence to provide four sequence means. The differential, exogenous versus endogenous, assessment was obtained by subtracting the appropriate sequence mean from each value of the indicated mean sequence. If the estimate of exogenous activity was the greater, then the difference was plotted upward (*Ex.*) on the ordinate. If the estimate of endogenous activity was the greater, then the difference was plotted downward (*End.*) on the ordinate. (A) The early 'endogenous' sequence mean was subtracted from the values of the early exogenous mean sequence yoked to the cat's position relative to the loudspeaker. Note the differential sensitivity to exogenous activity of the primary component, particularly when the cats were near the loudspeaker. (B) The early exogenous sequence mean was subtracted from the early endogenous mean sequence yoked to the cognitive-behavioral performance. Note that during response execution the estimate of released neural activity reflecting this phase in the primary component was small relative to the degree of representation of the cat's distance from the loudspeaker. (C) Subtraction as in (A). Note that even when the cats were next to the loudspeaker, the magnitude of secondary component activity reflecting that fact was slightly less than the average of activity reflecting the phases of cognito-behavioral performance; this difference became pronounced as the distance between the cats and the loudspeaker increased. (D) Subtraction as in (B). Note that during the decision-making phase, the estimate of neural activity representing this phase was substantially greater than the estimate of activity reflecting the cat's location relative to the loudspeaker. The dominance of endogenous representation in the secondary components substantially disappeared with the onset of response execution.

ferential sensitivity of primary and secondary EP components to exogenous and endogenous processes, respectively, these data are presented as four sequences of differences between estimates of the magnitudes of exogenous and endogenous representations (Fig. 3). If the influences of these two classes of process on the average EP components were not differential, the difference between coefficients should vary randomly about zero. However, if the influences are differential, the particular sensitivity of a component would be manifested in a systematic and nonzero difference; the magnitude of the difference reflects how selectively the average EP components reflect exogenous and endogenous influence, and the sign corresponds to the particular sensitivity.

The primary component of the EP appears particularly sensitive to exogenous representational processes (Fig. 3, A and B), whereas the secondary components tend to reflect endogenous processes (Fig. 3, C and D). Dynamic changes in the manifestation of these representations with the cat's movement relative to the cue source and with phases of cognitive-behavioral performance are apparent.

Thus, in trained cats responding to meaningful auditory stimuli, deliberate change in the location of the auditory signal permits some separation of exogenous and endogenous processes in the auditory EP. Short-latency exogenous processes show a dependence of latency and amplitude upon parameters of the physical stimulus, in agreement with the results of other workers who studied responses of untrained animals (*2*). However, the size and shape of longer-latency endogenous processes are relatively independent of the location or intensity of the signal source, and they seem to reflect the significance of the signal (*7*). Further, the evidence suggests that this reflection is dynamic, being most apparent during the decision-making process and relatively less apparent during response execution, once the animal begins to traverse the runway. Since in this paradigm, stimulus significance can be evaluated only by reference to past experience with the experimental cues, we suggest that these endogenous processes reflect the operation of neural mechanisms involved in memory reconstruction.

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3. The runway length was 140 cm from the step-down platform (start) to the center of the L-corner and 170 cm from the center of the L-corner to the step-up food delivery mechanism (goal). The runway was 38 cm wide. Loudspeaker 1 was located at the start end and loudspeaker 2 at the goal end of the L-runway.
4. All click stimuli were delivered from two speakers (Calectro S2-231). Stimuli were produced by delivering a 50-volt pulse for 0.3 msec from a single source, switched to one or the other speaker.
5. Behaviorally, the decision-making period appears to coincide with the orienting response of the cat to the signal. This orienting response to the signal is itself learned and modified during the course of training and overtraining [E. Grastyán and L. Vereczkei, *Behav. Biol.* **10**, 121 (1974)]. At this stage of learning, the orientation of the animals was facing away from speaker 1 and toward the runway. At click onset, the animals would alert (as indicated by a barely discernible head movement), hold that posture for as long as a few seconds, then initiate a slowly accelerating extension toward the alley; the extension would be abruptly transformed into a rapid leap from the platform and crossing of the L-maze. Video analyses indicated that this sequence of behavior was similar whether the CS's were presented at speakers 1 or 2. Although the decision-making period coincides with the motionless phase of the animal's orientation to the signal, the large late component (especially when CS is at the novel 2 position) can remain relatively stable throughout all phases of the animal's behavior (Fig. 1). Therefore, this component is not a consequence of the animal's maintaining a particular posture per se, but, rather, appears to reflect the operation of cognitive processes that normally occur during the motionless orientation phase, but that can continue throughout a variety of postural changes.
6. Compensation was performed by dropping initial time points (sample rate, 1000 per second), essentially shifting the average EP to the left, such that the primary peak appeared at 4 msec for all waves. No compensation was made for the differences in effective stimulus intensity resulting from distance.
7. V. L. Schwent and S. A. Hillyard [*Electroencephalogr. Clin. Neurophysiol.* **38**, 131 (1975)] have observed an early "late" component, 80 to 130 msec to peak (N_1), in the human vertex auditory EP associated with a "finely tuned" selective attention. The most prominent late component associated with stimulus significance in our data on the medial geniculate body of the cat has a substantially shorter latency, 30 to 50 msec to peak, with remarkable consistency in waveshape from animal to animal. Both of these bodies of data indicate that stimulus significance, as opposed to only physical characteristics or position relative to the source, can be reflected in the auditory evoked potential.
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Long-Term Treatment with Lithium Prevents the Development of Dopamine Receptor Supersensitivity

Abstract. *Long-term treatment of rats with haloperidol produced an increased sensitivity to the locomotor and stereotypic effects of apomorphine. This behavioral dopaminergic supersensitivity was accompanied by increased binding of [^{3}H]spiroperidol in the striatum. Rats treated concurrently with lithium and haloperidol failed to develop both behavioral sensitivity to apomorphine and increased striatal dopamine receptor binding. The ability of lithium to prevent recurrent manic-depressive episodes may be related, in part, to its ability to stabilize dopaminergic receptor sensitivity.*

An increased sensitivity to the behavioral effects of drugs that stimulate dopamine receptors is observed after long-term treatment with neuroleptics (*1*), tyrosine hydroxylase inhibitors (*2*), or reserpine (*2, 3*), or after interruption of dopaminergic transmission by lesions of the nigrostriatal dopamine pathway (*4*). Both the supersensitivity induced by chronically administered neuroleptics (*5*) and the nigrostriatal lesions (*6*) are accompanied by an increase in striatal dopamine receptor sites. This apparent proliferation of receptors after blockade of dopaminergic transmission may be causally related to behavioral supersensitivity (*5, 6*).

Changes in catecholamine receptor sensitivity may contribute to a number of human pathological states. Tardive dyskinesia may follow or be intensified by termination of long-term treatment with antipsychotic neuroleptic drugs, and may be related to increased dopamine receptor sensitivity (*7*). Klawans has proposed that lithium may be efficacious in preventing the development of tardive dyskinesia after phenothiazine therapy, since it blocked the increased stereotypy induced by apomorphine after chlorpromazine treatment (*8*). Oscillations in catecholamine receptor sensitivity have also been proposed to be a factor in the etiology of affective disorders (*9*), especially manic-depressive illness (*10*). Since lithium therapy is effective in alle-

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