

Unit activity of anterior cingulate cortex in differential conditioning and reversal

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Neuronal activity of the anterior cingulate (AC) region of the rabbit cerebral cortex was recorded during differential conditioning and reversal of a behavioral avoidance response. Discriminative neuronal activity, in the form of a greater neuronal response to CS⁺ relative to CS⁻, occurred in the intermediate and final sessions of original conditioning. The latency of this effect was 85 msec. A large neuronal discrimination effect appropriate to original conditioning occurred in the first session of reversal training, at 85 msec, and at briefer latencies (e.g., 15 msec). Neuronal discrimination did not occur in pretraining with noncontingent presentations of the stimuli to be used for conditioning. No consistent discrimination appropriate to the reversal problem was observed.

Recent studies have demonstrated that multiple-unit activity of the rabbit limbic cortex exhibits associative properties characteristic of learned responses (Gabriel, Wheeler, & Thompson, 1973a, b). Specifically, activity of the anterior cingulate cortical area (AC) showed: (1) an increase over trials of single-session behavioral avoidance conditioning, and (2) stimulus control, revealed in a single-session generalization test given after conditioning. These results suggested that the activity of AC was involved in neural information processing relevant to conditioning. However, the associative unit activity did not covary directly with the learned behavioral response. It was not clear what functions of AC were reflected by the results.

More recently, we have employed a different behavioral paradigm (differential conditioning and reversal) from that used in our original studies, in order to provide a different context in which to observe neuron-task and neuron-behavior relationships in AC. The present report is a preliminary one of the data obtained with this approach.

METHOD

Subjects

The subjects were 15 adult male albino rabbits.

Apparatus and Procedure

Each rabbit was surgically implanted with stainless steel multiple-unit electrodes in AC. The tips of the electrodes ranged in length from 20 to 60 microns. Unit activity was monitored continuously during implantation as an aid to placement of the

electrodes. Each rabbit was allowed a minimum of 7 days to recover from surgery.

The subjects underwent differential avoidance conditioning and reversal in a wheel apparatus (Brogden & Culler, 1936) located within a shielding chamber, in a room adjacent to that containing apparatus for controlling the experiment. In conditioning, a tone signal (CS⁺, 8 kHz or 1 kHz) was followed after 5 sec by a shock UCS. The other tone (CS⁻, 1 kHz or 8 kHz) was interspersed with the CS⁺ but was never followed by shock. Sixty trials with each stimulus were given in each daily session. The order of the stimuli was randomized so that the subjects could not "predict" which would occur on a given trial. Locomotion during the tones terminated them and prevented delivery of the shock UCS on CS⁺ trials. Each rabbit was trained to a criterion of discrimination performance which had to be met on 2 consecutive days. Following original conditioning, 14 of the rabbits received reversal training to the same criterion. Eight of the rabbits received the 8-kHz CS⁺ and seven received the 1-kHz CS⁺ in original conditioning.

Prior to conditioning, each rabbit received a session of pretraining, in which the tone signals and the shock UCS were presented noncontingently, to control for possible nonassociative effects of the stimuli.

Data Analysis

Tapes of the unit activity recorded during conditioning and reversal were played into Schmidt triggers. The trigger levels were set independently for each record, in such a way that they were exceeded by only the largest three or four neuronal spikes. Each Schmidt trigger produced an output pulse each time a neuronal spike exceeded its level, and the output pulses were fed into a PDP-12 computer. The computer counted the number of pulses per 10-msec interval (bin), preceding and following CS onset, and the number of pulses in each bin was summed across trials to produce a peristimulus histogram. Separate histograms for the CS⁺ and the CS⁻ were constructed by combining all trials with each stimulus in each conditioning session. Thus, each histogram was based on a total of 60 trials. Standard scores (z scores), normalized with respect to the pre-CS baseline, were computed for each of the first 10 bins after CS onset. Further details of these methods are provided elsewhere (Gabriel, 1973; Gabriel, Miller, & Saltwick, 1976a, b).

Following completion of behavioral testing, each rabbit was given an overdose of barbiturate and perfused with saline, followed by 10% formalin. The brains were frozen and sectioned at 40 microns, and the sections containing the electrode tracks were photographed while still wet (Fox & Eichman, 1959).

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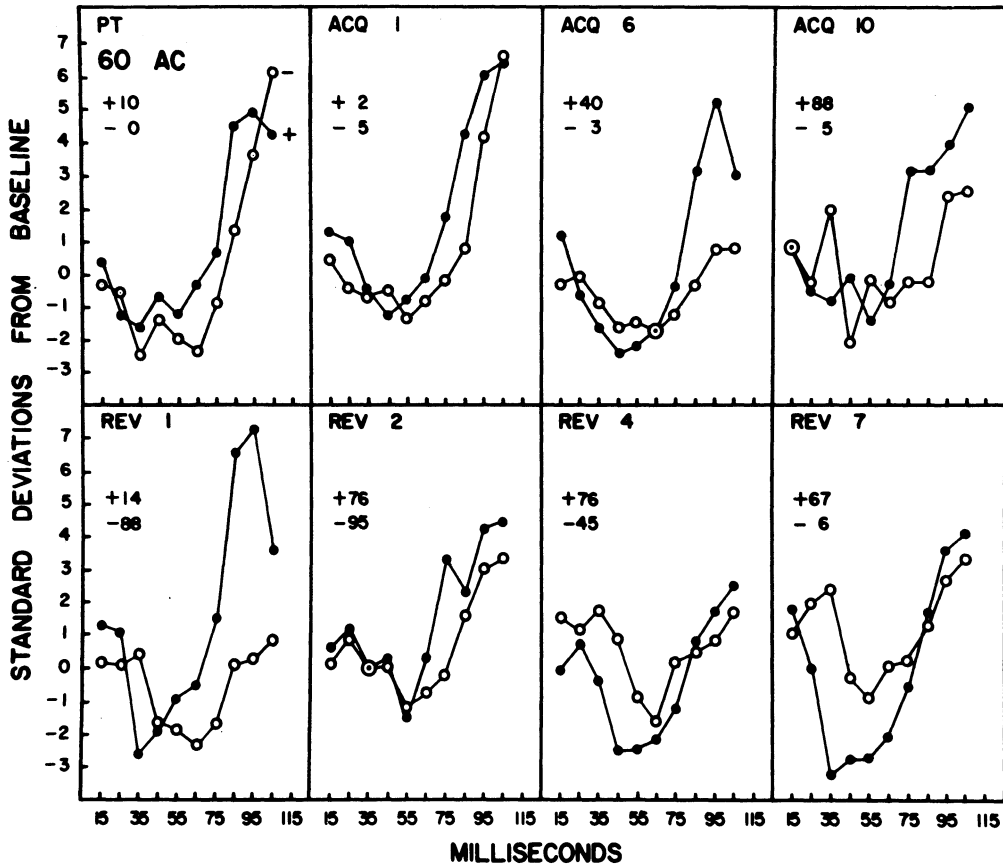


Figure 1A. This portion of the figure shows the neuronal response of AC from Rabbit 60 in pretraining (PT), the first session of conditioning (ACQ1), the middle session of conditioning (AC6), the final session of conditioning (ACQ10), the first two sessions of reversal (REV1, REV2), the middle session of reversal (REV4), and the final session of reversal (REV7). Open circles represent the 1-kHz tone CS and filled circles represent the 8-kHz tone. The CS⁺ and CS⁻ in original conditioning are designated with + and - in the upper left cell (PT cell) of the figure. The figure also shows in each cell the percentage of behavioral CRs to the CS⁺ and CS⁻ for the session. The rabbit attained behavioral criterion during the session portrayed in the rightmost cell of each row.

RESULTS

The mean number of sessions prior to the criterion of original conditioning was 5.3 and the mean for reversal was 8.9. A t test showed this difference to be significant ($p < .001$), indicating a greater difficulty of behavioral reversal relative to original conditioning.

The neuronal data considered in this report were those obtained in pretraining, the first, middle, and final sessions of conditioning, and the first, second, middle, and final sessions of reversal training. Representative data obtained in these sessions are shown in Figure 1 for two subjects (45 and 60).

All of the rabbits showed triphasic neuronal responses to the CSs, as in Figure 1. The effect consisted of increased activity, relative to the pretone baseline, in the first three bins (15-35 msec) following tone onset, decreased activity in Bins 4 through 7 (45 to 75 msec), and increased activity beginning in Bin 8

(85 msec) and continuing to the end of the analysis period.

The individual records showed discriminative neuronal activity, that is, a greater neuronal response to the CS⁺ than to the CS⁻. This effect was present during the middle session of original conditioning in seven of the subjects (e.g., Figure 1A). It occurred in the third (85-msec) component of the triphasic response. Twelve subjects showed a large-magnitude discrimination in the first two sessions of reversal training, in the third component of the triphasic response. Five of these subjects also showed the effect in the first (15- to 35-msec) component of the response (e.g., Figure 1B, Reversals 1, 2, and 4).

There was no clear reversal of the neuronal response concomitant with reversal of the behavioral response. Four of the subjects showed a negative (inhibitory) response to the original CS⁺ and no response to the current CS⁺ in the final session of

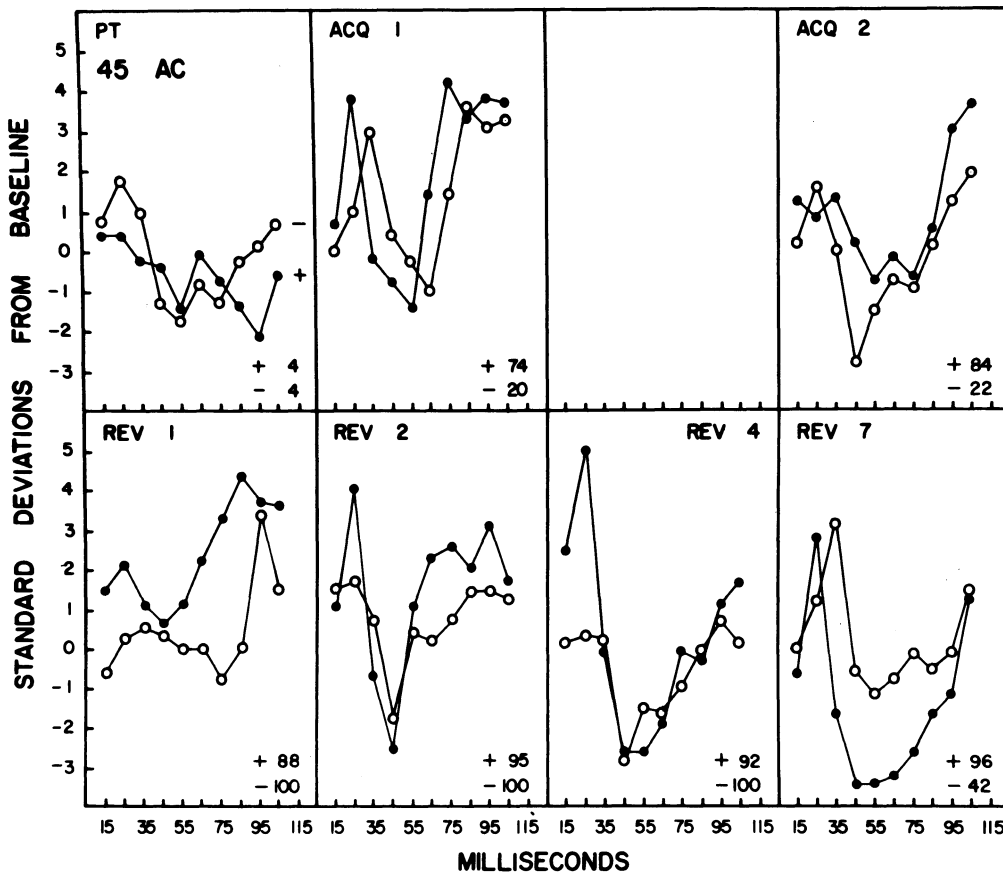


Figure 1B. This part of the figure shows data of a different subject (45). All aspects of the format for this part are identical to those of Part A except that no middle conditioning session is portrayed, because the subject made criterion in only two sessions.

reversal training. This effect occurred in the intermediate-latency inhibitory component of the triphasic response (e.g., Figure 1B, Reversal 7). The remaining subjects showed no consistent pattern of differences between responses to the CS⁺ compared with responses to the CS⁻ in the final session of reversal training. There were no discriminative neuronal effects in pretraining.

To summarize, neuronal activity of AC showed a differential conditioning effect in the first 100 msec after CS onset during original conditioning. The most pronounced conditioning effect occurred in the first two sessions of reversal training. There was no reversal of the cortical neuronal response in the final sessions of reversal training. These conclusions are supported by statistical analysis, to be presented in a forthcoming detailed report (Gabriel, Miller, & Saltwick, 1976b).

DISCUSSION

The present findings corroborated our previous studies (Gabriel, Wheeler, & Thompson, 1973a, b) in demonstrating associative neuronal activity in AC, in conjunction with behavioral avoidance conditioning. The attribution of associative properties to the

activity of AC is based, in the present study, on the observation of significant neuronal discrimination, that is, a greater neuronal response to the CS⁺ than to the CS⁻.

It is important to note the cue-specific nature of the associative activity of AC. The differential neuronal response depended on the acquired signal value of the tones. A differential state (arousal, receptor orientation, body orientation) existing prior to CS onset could not account for the effect. This is true because the tones always occurred in a random sequence; there was no basis for subjects to "predict" which would occur on a given trial. Moreover, the latency of the differential neuronal effect was sufficiently brief (< 100 msec) to shed serious doubt on a possible contribution by artifactual or neural feedback from CS-elicited behavioral activity. Thus, it seems clear that associative neuronal response originated within the CNS.

The first appearance of neuronal discrimination occurred in the intermediate sessions of conditioning, when behavioral learning was incipient. This suggests that the activity of AC may have been an important substrate of the learned behavioral response. This conclusion is supported by the abundant results, reviewed by McCleary (1966), demonstrating impairment of avoidance acquisition following induced damage in AC and related structures.

The largest neuronal discrimination appropriate to original conditioning occurred in the first two sessions of reversal training, when shock UCSs were delivered following nonresponse to the new CS⁺. This suggests that the magnitude of the neuronal discrimination was enhanced by the UCS occurrences in the first sessions of reversal. Thus, neuronal discrimination was a function of the CS-UCS contingencies and the number of aversive UCSs.

The discriminative neuronal activity in AC was appropriate to the

original learning task, but it did not reverse. The only neuronal discrimination that occurred during reversal training was the original discrimination, in the early sessions of reversal. Nevertheless, the subjects did achieve reversal behaviorally. Thus, discriminative activity of AC would not appear to be a necessary neural substrate of behavioral reversal.

Participation of AC in conditioning but not in reversal highlights an important potential outcome of studies such as the present one. It is that different brain regions may be implicated in control of different aspects of a learned behavior. The involvement of AC during original conditioning may account for the relatively rapid learning of original discrimination, whereas the conflicting involvement of AC during reversal training may account in part for the relative retardation of behavioral reversal.

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