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Behavioral Correlates of Neural Readout

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In previous work (1), we reported that the waveshape of the response evoked by presentations of a neutral stimulus which resulted in behavioral generalization closely resembled the evoked response to the conditioned stimulus (CS) which was the usual signal for performance of the same conditioned behavior. When the same neutral stimulus failed to elicit generalization, the waveshape of the evoked response was markedly different, lacking a set of components. These components were identified as endogenous, and were suggested to reflect the readout of memory, released by the stimulus but having a form determined by prior experience.

By subtraction of the response evoked by a neutral stimulus when it failed to elicit generalization (afferent input alone) from the response when the same stimulus elicited generalization (input plus readout), it was possible to obtain an approximate picture of the process released in different anatomical regions under these conditions (2). This readout process displayed similar waveshapes but different latencies in a number of different regions, and apparently originated in a cortico-reticular system from which it propagated to other brain regions, appearing latest in the lateral geniculate body.

Since this phenomenon involved the difference between the waveshapes of responses evoked by a stimulus when a behavioral performance took place and when performance failed to occur, it was possible that the observed differences were due to unspecific factors. In order to control for such factors, we devised a procedure called "differential generalization". Cats were trained to perform one conditioned response (CR_1) to an intermittent stimulus consisting of flicker at frequency 1 (V_1) and a different conditioned response (CR_2) to flicker at frequency 2 (V_2). After substantial overtraining of this differential behavior, a third frequency (V_3) was presented which was midway between V_1 and V_2. When generalization occurred, V_3 elicited behavior which was sometimes appropriate to V_1 (V_3CR_1) and sometimes to V_2(V_3CR_2). It was found that the waveshape appearing in many brain regions during V_3CR_1 was markedly different from that evoked during V_3CR_2. Further, the waveshape during V_3CR_1 closely resembled that observed during V_1CR_1, while the waveshape during V_3CR_2 closely resembled that observed during V_2CR_2 (3).

These results showed that the waveshape of the response evoked by V_3 did not solely depend upon the physical stimulus or upon unspecific factors such as arousal, attention or drive level, but also depended upon the significance attributed to the stimulus by the animal. Further, the results showed that the brain could release a particular waveshape, closely resembling the usual response evoked by a differential conditioned stimulus, when a novel stimulus caused generalized performance of the usual behavioral response to that CS. This released waveshape was interpreted as the electrophysiological reflection of activation of a specific memory.

A number of further controls have been carried out to establish that these released waveshapes were not due to unspecific factors. Response-specific readout waveshapes have been obtained using auditory, as well as visual stimuli, showing that these processes are not restricted to stimuli in a particular sensory modality. They have been observed in appetitive-appetitive, aversive-aversive, and appetitive-aversive discriminations, showing that they are not restricted to tasks based only upon one kind of motivation, nor do they depend upon differences in motivation for the differential behaviors. They have been obtained using direct electrical stimulation of brain structures as the CS, showing that they are not due to changes in orientation or direction of gaze. They do not reflect pupillary dilation, since visually elicited readout waveshapes are not altered by homatropine. They have been observed

in lever-pressing and hurdle-jumping tasks and in observational as well as conventional instrumental learning situations, showing that they are not restricted to a particular kind of learning or behavioral task. They do not reflect performance of the instrumental movement since readout waveshapes elicited by stimuli in one sensory modality usually do not appear in the same brain regions when the same conditioned responses are performed for cues in other sensory modalities. Set and response bias have also been ruled out as responsible for the differences in waveshape evoked during trials resulting in different behavioral outcomes. No readout components were discerned in the waveshapes evoked by meaningless flicker stimuli yoked to differential auditory cues, whereas readout components appeared in evoked responses to those flicker stimuli after they acquired cue values by transfer of training (4).

In this work, we found that the differences between V_3CR_1 and V_3CR_2 were obscured by whole trial averaging, and could be accentuated by experimenter selection of typical readout waveshapes from the later portions of behavioral trials (3). It was suggested that such selection made it possible for subjective bias to invalidate the apparent significance of these findings (5). Accordingly, a computer sorting program was devised to perform this analysis in an objective way. Essentially, this program constructs homogeneous subgroups of evoked potentials out of the heterogeneous population of waveshapes produced by the non-stationary processes which characterize behavioral situations (6).

Using this program, we demonstrated that the waveshapes objectively selected by the computer closely approximated the waveshapes subjectively selected on the basis of experimenter judgment (7).

It remained, however, to demonstrate that readout waveshapes thus selected in any animal were distributed throughout a large number of behavioral trials in which the same outcome occurred, and that different readout waveshapes were predictive of different behaviors. A film was made which enabled audiences to predict performance in differential generalization on the basis of the waveshapes recorded from the lateral geniculate body and displayed on an oscilloscope (8). Numerous audiences (9) have found it possible to predict performance accurately from examination of these waveshapes.

This film demonstrated the ease with which accurate prediction of behavioral outcome in differential generalization could be made by subjective evaluation of a set of trials performed by one cat. The purpose of this paper is to demonstrate the extremely reproducible content of different waveshaped modes identified by computer selection in a large number of behavioral trials with the same outcome, to establish the correlation of a

specific readout waveshape or evoked potential mode with a particular behavior, and to establish that such correlations have been found in a large number of animals.

Figure 1 shows the distribution of 3 different modes of evoked response in 6 groups of different types of behavioral trials from the same animal. The cat from which these 59 trials were recorded was trained to press the left bar on a work panel to avoid electric shock from a floor grid within 15 seconds after the onset of a 4.0 Hz flash (V_1), and to avoid shock by pressing the right bar after a 2.0 Hz flash V_2. After overtraining, a number of presentations of a 3.0 Hz neutral flash (V_3) were randomly interspersed among a sequence of V_1 and V_2 trials, sometimes eliciting left-bar and sometimes right-bar response. The three groups of trials in the left half of the figure all resulted in left-bar response. However, these similar behaviors were elicited by 3 different stimuli. The trials in Column 1 came from V_2 errors, in Column 2 from V_1 correct responses, and in Column 3 from V_3 left-bar generalization. The three groups of trials in the right half of the figure all resulted from right-bar response, also from three different stimuli: Column 4 from V_3 right-bar generalization, Column 5 from V_2 correct responses, and Column 6 from V_1 errors. The spot displays indicate the points in each trial at which the corresponding mode of evoked response occurred. Examination of the figure shows that all trials began with an evoked potential of Mode 1, progressed to a period dominated by potentials of Mode 2, and concluded with a period in which Mode 3 potentials were most probable.

Figure 2A presents the actual waveshapes which correspond to the 3 modes of response for the two types of behavior. The top waveshape shows 6 Mode 1 waveshapes superimposed, which correspond to the 6 types of trials in the previous figure. These waveshapes were essentially identical, indicating that the state of the nervous system of this animal was approximately the same at the onset of trials of each behavioral type. The Mode 2-Left waveshapes present superposition of the 3 Mode 2 waveshapes which dominated the early portion of trials resulting in left-bar responses to the three different stimuli, and show that these waveshapes were closely similar. Mode 2-Right waveshapes are superimposed in the 3rd row, and show not only that the early portion of trials resulting in right-bar responses were closely similar independent of the eliciting stimulus, but also illustrate the similarity between the early modes of left-bar and right-bar trials. Mode 3-Left waveshapes are superimposed in the 4th row, and are closely similar independent of the stimulus. Mode 3-Right waveshapes are shown in row 5 and are also very similar.

However, Mode 3-Left and Mode 3-Right waveshapes are significantly different. Figure 2B shows the results of sorting on V_3-Left and V_3-Right generalization trials, using the Mode 3-Left and Mode 3-Right waveshapes as classification criteria. These data show clearly that the probability of these 2 kinds of waveshapes occurred much more frequently in V_3-Right trials. This distribution deviated significantly from random, as assessed by computation of exact probability.

Table 1 shows similar results for 14 cats. For each animal, a mixed set of trials was constituted, containing iterated examples of trials resulting in two different behavioral outcomes to the same physical stimulus. The population of evoked potentials recorded from the lateral geniculate body or other brain regions during the whole set of trials was then subjected to sorting analysis. The data in the table show that each mixed population contained two different readout modes, one of which was highly correlated with each of the differential behaviors. The differential distribution of the two readout modes in the two kinds of behavioral trials was highly significant. The temporal distribution and actual waveshapes of these various readout processes will be presented in a forthcoming paper (10).

These results show that readout processes can be objectively defined and automatically identified, that they appear consistently in an extensive sample of behavioral trials from a given animal, that they can be found in most, if not all, animals in an experimental population, and that they are strongly correlated with a particular differential behavior. These findings, in conjunction with control data showing that readout processes are not attributable to unspecific factors such as arousal, attention, orientation, motivation, pupillary dilation, change in direction of gaze, movement, intention to move, or response bias, support the interpretation that readout processes reflect the activation of a specific memory.

LEGENDS

Fig. 1. Each column represents a set of trials in which the same behavioral response was performed to a particular stimulus, as indicated in the heading. V_1 (4.0 Hz flicker) was the CS for a left bar press, V_2 (2.0 Hz flicker) was the CS for a right bar press, and V_3 (3.0 Hz flicker) was a test stimulus used to elicit differential generalization. The 59 trials included 5 V_2 errors, 11 correct responses to V_1, and 12 generalization-L responses to V_3, all resulting in left bar responses, and 10 generalization-R responses to V_3, 16 correct responses to V_2, and 5 V_1 errors, all resulting in right bar responses. Both left and right bar responses were to avoid electric shock from a floor grid. The bars were mounted side by side on a work panel.

The top row of white dots in each black rectangle represents the occurrence of successive light flashes in the behavioral trials. Each row of dots corresponds to a separate trial, beginning at the left vertical bar and ending at the right bar. The occurrence of a dot indicates that the potential evoked for that light flash was classified as an example of the indicated mode. Three modes were identified within all 6 types of trials, and are represented by the three horizontal arrays of data.

Fig. 2A. Mode 1 consisted of the initial evoked potential in 46 of the 59 trials, plus a small number of additional evoked potentials all of which occurred early in the trials. The Mode 1 potentials from the 6 types of trials are superimposed in the top row of data. They were essentially identical.

Mode 2 consisted of the evoked potentials which dominated the early portions of all types of trials. The second row of data, Mode 2-L, shows the superimposed waveshapes of this mode for the three sets of trials which resulted in left bar responses, while the third row, Mode 2-R, illustrates the corresponding data for right bar responses.

Mode 3 consisted of the evoked potentials which dominated the final portions of all types of trials. The fourth row of data, Mode 3-L, shows the superimposed waveshapes of this mode for the different sets of left bar responses, while the corresponding data for right bar responses is illustrated in the bottom row.

Note that the 3 different Mode 3-L waveshapes are closely similar, independent of whether they were elicited by V_1, V_2 or V_3. Similarly, the 3 Mode 3-R waveshapes are essentially identical. However, Mode 3-L waveshapes are markedly different from Mode 3-R.

All data were recorded from the lateral geniculate nucleus, bipolar.

Fig. 2B. Correlation between evoked response modes and behavior. Each rectangle contains 8 V_3 trials which resulted in left bar generalization (trials 1-8) and 8 V_3 trials which resulted in right bar generalization (trials 9-16). The rectangle on the left shows the incidence of Mode 3-L waveshapes in 16 generalization trials, while the right rectangle shows the incidence of Mode 3-R waveshapes in the same trials. The trials were randomly selected from those shown in Fig. 1. and were truncated so that only the late portion dominated by Mode 3 waveshapes was subjected to this further analysis. These results showed a significant deviation from randomness in the probability that a particular waveshape mode would occur in a trial with a particular behavioral outcome. ($p = 0.00001$).

TABLE I. Distribution of CR_1 and CR_2 waveshape modes in sets of trials resulting in either CR_1 or CR_2 behavioral performance to the same flicker signal. Number of trials and evoked potentials in each set is indicated for each animal, as is the structure from which the data were recorded. The exact probability of obtaining the observed distributions from a randomly distributed population was calculated and is shown in the rightmost column.

LG - lateral geniculate body, VIS - visual cortex, MRF - mesencephalic reticular formation, M - monopolar derivation, B - bipolar derivation, + + = approach-approach discrimination, - - = avoidance-avoidance discrimination, + - = approach-avoidance discrimination, 0 + = no response versus generalization of approach discrimination.

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9) This teaching film has been shown at symposia, congresses and 23 universities here and abroad. Interested readers may make arrangements to view our film by contacting us.

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DISTRIBUTION OF EVOKED POTENTIAL MODES

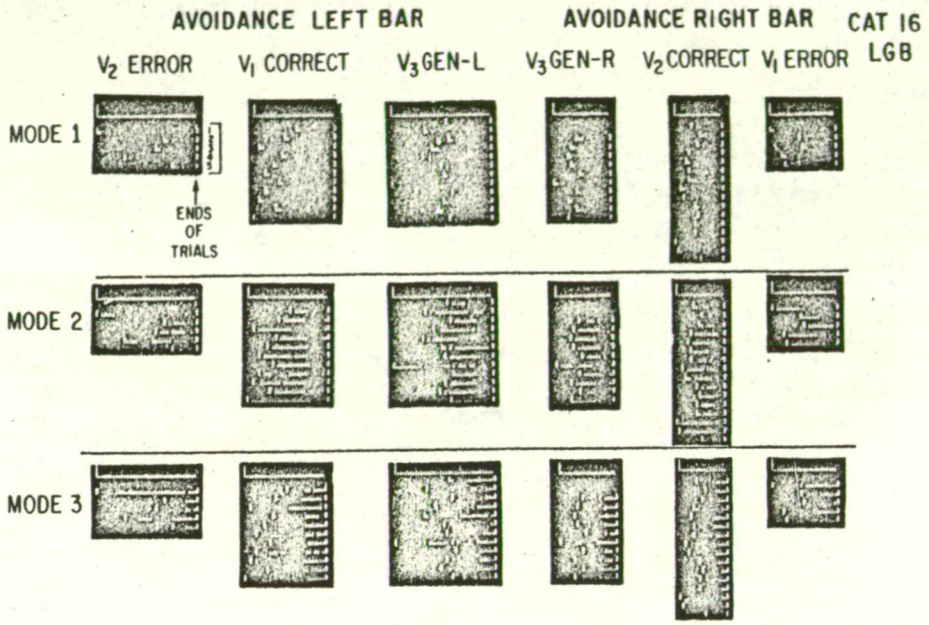

Fig. 1

DISTRIBUTION OF EVOKED POTENTIALS INTO DIFFERENT MODES

Cat	Structure	N trials CR_1	N trials CR_2	EP's CR_1	EP's CR_2	%CR_1 in CR_1	%CR_1 in CR_2	%CR_2 in CR_1	%CR_2 in CR_2	$p <$
2	LG_B + -	7	10	95	159	.48	.16	.22	.54	10^{-8}
3	VIS_B + -	9	10	118	137	.37	.17	.27	.45	10^{-4}
4	LG_M 0 +	5	5	131	125	.87	.10	.13	.90	10^{-37}
5	LG_B + -	9	4	174	81	.58	.21	.03	.41	10^{-14}
7	LG_B + -	7	8	97	120	.55	.30	.45	.69	10^{-3}
8	VIS_B + -	3	5	56	104	.45	.14	.27	.62	10^{-5}
9	LG_B + +	5	5	128	128	.58	.34	.27	.50	10^{-4}
10	LG_B + -	7	7	128	128	.47	.14	.00	.41	10^{-20}
11	VIS_M + -	4	3	154	102	.37	.15	.23	.36	10^{-3}
12	MRF_M + -	9	9	101	149	.77	.50	.23	.50	10^{-4}
13	LG_M + -	5	5	104	150	.57	.04	.10	.31	10^{-16}
14	LG_M + -	3	4	79	177	.73	.24	.27	.76	10^{-12}
16	LG_B - -	11	11	63	55	.70	.31	.13	.53	10^{-5}
21	LG_B - -	6	6	128	128	.79	.46	.18	.48	10^{-7}

Table 1

EVOKED POTENTIAL MODES

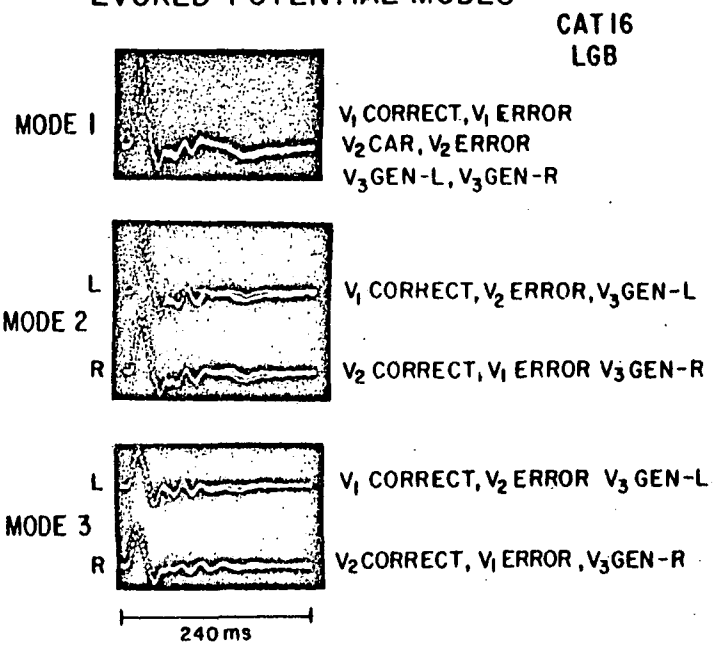

Fig. 2A

CORRELATION BETWEEN
EVOKED RESPONSE MODES
AND BEHAVIOR

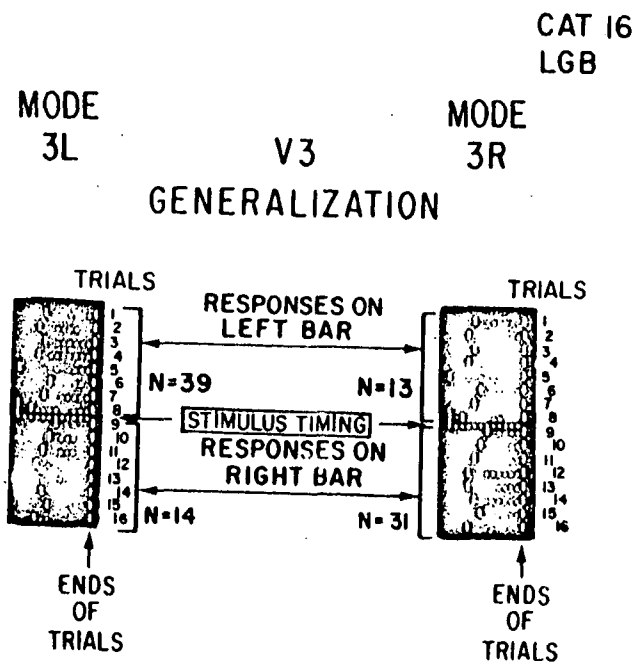

Fig. 2B