Conditioning and Reversal of Short-Latency Multiple-Unit Responses in the Rabbit Medial Geniculate Nucleus

Abstract. *Rabbits were conditioned to avoid shock signaled by a tone. A second tone was randomly interspersed but did not signal shock. Neuronal activity 5 to 40 milliseconds after tone onset was greater to the shock-signaling tone than to the other tone. This difference reversed when the signal value of the tones was reversed.*

There has been great interest in the question of whether neural activity in the primary sensory pathways varies with the learned (associative) significance of incoming stimuli. The classical view has been that primary sensory activity serves merely to "represent" stimuli within the brain. This idea is supported by the relative invariance of sensory-evoked activity across stages of sleep (*1*), whether the stimuli evoking it were novel or familiar (*2*), and whether or not anesthetics were used (*3*).

On the other hand, there is considerable evidence suggesting that primary sensory activity varies with the associative properties of stimuli. Demonstrations of centrifugal pathways mediating modulatory effects at peripheral levels of some sensory systems (*4*) suggest a basis for central control of incoming activity, and hence a possible influence upon stimulus input by past learning. Unfortunately, the functional role of centrifugal pathways has not been established. Learning-related centrifugal modulation of sensory input has never been shown directly, during learning in a behaving animal.

Electrophysiological studies of behaving animals *have* demonstrated changes in the activity of primary sensory pathways during behavioral conditioning (*5*). However, the changes reported in these studies were not unambiguously associative in nature. Instead, they may have been produced by change in arousal which accompanied conditioning, or they may have reflected properties of the nervous system which existed prior to conditioning (*6*). The present experiment was designed to circumvent these problems by using behavioral procedures (differential conditioning and reversal) which produce unambiguous associative effects.

Five albino rabbits with multiple unit electrodes chronically implanted in the medial geniculate nucleus (MGN) were given differential avoidance conditioning to a behavioral criterion, followed by reversal to criterion. In differential conditioning, a pure tone (CS+) signaled shock which occurred 5 seconds after tone-onset. Locomotion within a wheel apparatus (*7*), during the tone, prevented the shock. A second tone (CS−) was randomly interspersed with the CS+ but did not signal shock. The tones were 80 db relative to 0.0002 dyne/cm^2, and had a rise-time of 3 msec. The CS+ was 1 khz for three rabbits and 8 khz for two rabbits. The CS− for each rabbit was the other (8-khz or 1-khz) tone. After learning to respond behaviorally to the CS+ and not to the CS−, each rabbit was given reversal training with the CS+ and the CS− frequencies interchanged. The tones were given in a random sequence so that the subjects could not predict which would occur, and orient differentially. Further details of these procedures are provided elsewhere (*6, 8*).

All of the rabbits showed significant acquisition and reversal of differential behavioral avoidance responding. This report is a preliminary one which focuses on short-latency MGN neuronal response to the tone stimuli in the final session of differential conditioning and in the final session of reversal, that is, times when the rabbits showed maximal behavioral discrimination on each problem. Other aspects of the data are in preparation (*6*).

The primary finding was the greater frequency of short-latency (< 40 msec) neuronal firing to the CS+ versus CS− both at terminal acquisition and at terminal reversal (see Fig. 1). In other words, MGN neurons showed a differential response favoring the CS+ at the end of acquisition. Like the behavior, the MGN neuronal response "crossed over" when CS+ and CS− were interchanged.

Two of the subjects (rabbits Nos. 41 and 44) showed this effect at a very short latency (the 15-msec bin). The amount of crossover from acquisition to reversal was defined as the difference between the CS+ score and the CS− score in acquisition, plus the difference between the *new* CS+ and CS− in reversal. Crossover of the

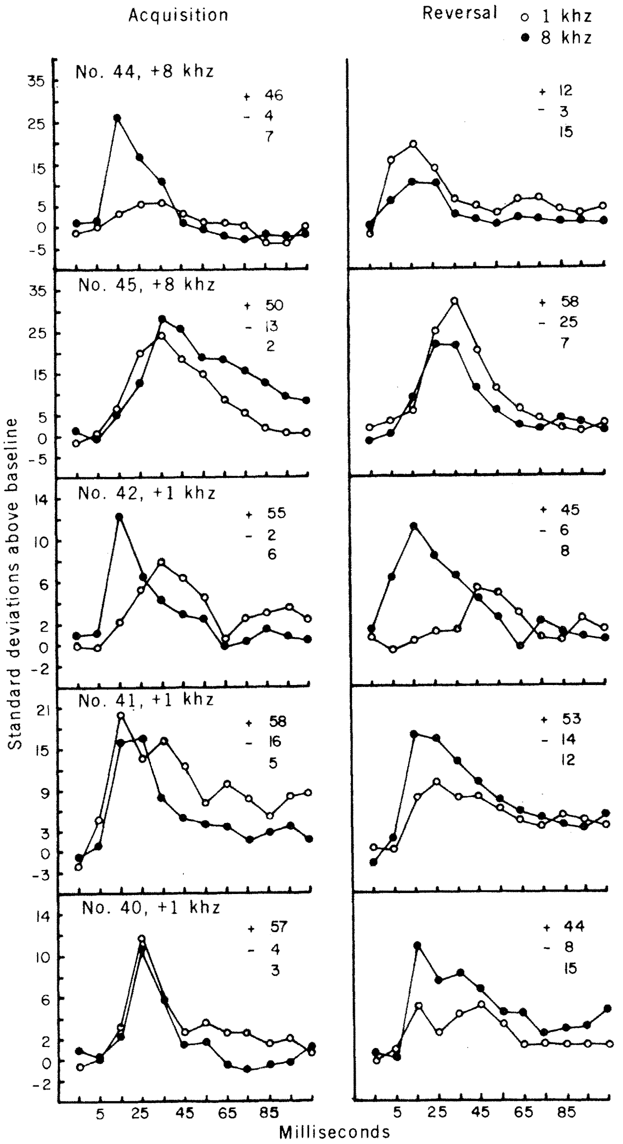

Fig. 1. The neuronal response is graphed for each of the rabbits over 120 msec (12 bins) beginning 10 msec prior to tone onset and including 110 msec (11 bins) following tone onset. The two plots in each cell show the response separately to CS+ and CS−. Terminal acquisition data are shown in the left column, and terminal reversal in the right column. The rows show data of different rabbits. Tone onset occurs in all cases at the onset of bin 2 (second of the plotted points). The abscissa values represent time in milliseconds from tone onset to the midpoint of each 10-msec bin. The number of behavioral responses out of 60 possible are shown for both CS+ and CS−, along with the number of days to the behavioral criterion in the upper right of each cell. The details of the procedures used to obtain the neuronal scores are in preparation (*6*).

MGN response at 15 msec equaled 27.6 standard deviations in No. 44 and 12.0 standard deviations in No. 41. Two other subjects (Nos. 42 and 45) showed crossover (12.4 and 12.7 standard deviations, respectively) at a longer latency (the 35-msec bin). Later bins showed crossover for all five subjects.

There was not a significant short-latency effect in acquisition for No. 40. Significant discrimination at terminal acquisition did not occur until the 55-msec bin in this subject. However, reversal showed a significant effect at the 15-msec bin equaling 9.4 standard deviations.

The overall reversal effect for each rabbit was tested with the Wilcoxon test (*9*). Specifically, the difference in the MGN response [R (1 khz) − R (8 khz)] at each of 11 acquisition bins was subtracted from the same quantity at each of 11 corresponding reversal bins. An average of zero would be expected if the MGN response were purely tone-specific, but reversal of the scores, or sufficient change approximating reversal, would produce a nonzero (statistically significant) outcome. The results showed a significant effect for each of the five rabbits (No. 40, $P < .005$; No. 41, $P < .005$; No. 42, $P < .045$; No. 44, $P < .020$; No. 45, $P < .005$).

Note that four of the electrode placements (in Nos. 40, 41, 42, and 45) showed relatively long-latency differential responses at terminal acquisition, whereas a short-latency differential response occurred in terminal reversal for these subjects. This effect may have resulted from the fact that the stimulus evoking the larger preconditioning response was acquisition CS– in all four cases. Further discussion of this point is in preparation (*6*).

Examination of the electrode placements revealed that all were in the anteromedial half of MGN, a region showing distinctive neuroanatomical and physiological properties in other studies (*10*).

The present data support the idea that neural activity of the MGN is involved in information processing above and beyond the function of stimulus representation traditionally assumed for structures of the primary sensory systems. The data show that even the very short latency components of the MGN response reflect associative significance acquired through discriminative conditioning. Unlike previous results with chronically implanted behaving animals, the present data cannot be accounted for by invoking a nonassociative factor such as arousal, or by preexisting properties of the central nervous system. Neither hypothesis is compatible with the observation of reversal of a stimulus-specific acquired response. Our effects cannot be explained in terms of differential orientation of the subjects to the two tones. Because the tones were always presented in a randomized sequence, there was no basis for the subject to "predict" which tone would occur and to orient differentially. Thus, our study has avoided basic problems that have beset other studies with similar intent [for example, (*11*)].

It is highly unlikely that conditioning and reversal could have been mediated by the middle ear muscle (MEM) mechanism. First, the short-latency (< 10 msec) associative response in some placements (in Nos. 41, 44, and 42) was too rapid to have been produced by the slower phasic MEM response (*12*). Second, the notion of a tonic MEM set is hardly tenable, since available data show MEM suppression of frequencies only below 2 khz, in a variety of mammalian species (*12*), and no studies have shown modification of MEM suppression, as required by our data.

Finally, unpublished data from another laboratory have partially corroborated our findings by showing differential conditioning, without reversal, of primary auditory neuronal activity (*13*).

Of particular interest was the acquired selectivity of sensory transmission shown by differential conditioning, and the *modification* of the selectivity shown by reversal. Both in acquisition and in reversal, the selectivity reflected the adaptive requirements of the behavioral task. To our knowledge, these effects have not unequivocally been shown before.

It seems reasonable to assume that the modifiable selectivity results from "tuning" of cells in the afferent pathway during conditioning (*12*). Once acquired, the tuning acts tonically to selectively facilitate or depress (or both) neural activity evoked by significant and nonsignificant stimuli, respectively. It is likely that the tuning effect does not originate within the MGN but rather is transmitted to the MGN over a centrifugal pathway. Viewed in this way, the present findings provide a functional counterpart to previous demonstrations of centrifugally mediated modulatory effects within the sensory systems (*4*).

Michael Gabriel
Steven E. Saltwick
Joseph D. Miller
Department of Psychology,
University of Texas, Austin 78712

References and Notes

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