6. G. J. Everson, R. E. Shrader, T. C. Wang, *J. Nutr.* **93**, 533 (1967).
7. J. W. Wilkie, *Aust. Vet. J.* **35**, 209 (1959).
8. W. Carlton and W. A. Kelly, *J. Nutr.* **97**, 42 (1969).
9. R. L. Sidman, M. M. Dickie, S. R. Appel, *Science* **144**, 309 (1964); N. A. Baumann, C. A. Jacque, S. A. Pollet, M. L. Harpin, *Eur. J. Biochem.* **4**, 340 (1968).
10. Purina Laboratory Chow (Ralston Purina Co., St. Louis, Mo.).
11. L. S. Hurley and L. T. Bell, *J. Nutr.* **104**, 133 (1974).
12. Unicam SP-90 atomic absorption spectrophotometer.
13. G. L. Henderson and D. E. Woolley, *J. Pharmacol. Exp. Ther.* **175**, 113 (1970).
14. Grass Instruments, Quincy, Mass.
15. Supported in part by NIH grant HD-02355. We thank Dr. Dorothy Woolley for advice and use of equipment, Donna Dungan for technical assistance, Fred Hegge for performing a preliminary experiment, and Linda Theriault Bell for her overall contribution to the work.

6 April 1976

Neuroelectric Correlates of Conditioning

Gabriel *et al.* (*1*) reported changes in multiple-unit responses in the rabbit's medial geniculate body associated with the acquisition and reversal of a discriminative conditioned avoidance response. In both stages of the experiment the positive conditional stimulus (CS^+), which was followed by shock, purportedly evoked larger neural responses than the CS^-, which was not followed by shock. The conditioned discrimination and its reversal were regarded as adequate conditions for "producing unambiguous associative effects."

The controls employed by Gabriel *et al.* are appropriate for one kind of nonassociative effect, specifically, effects that are not correlated with conditioned changes in behavior. They are not adequate, however, for nonassociative effects that actually depend on conditioned changes in behavior. Suppose, for example, that an increase in level of arousal leads to an increase in neural activity evoked by a CS. Such an increase in arousal can result from the presentation of a noxious unconditional stimulus (UCS) like electric shock. A general increase in arousal might occur in an aversive conditioning situation and have little or no relationship to the conditioned changes in behavior. It might, nevertheless, enhance the neural activity evoked by the CS as long as the heightened arousal is maintained by the repeated presentation of shock in the conditioning procedure. Such a change in evoked activity would be revealed as nonassociative by the discrimination and reversal controls employed by Gabriel *et al.* If, on the other hand, the increase in arousal were itself conditioned together with, say, an instrumental avoidance response, one might expect the conditioned arousal to lead secondarily to a "conditioned" increase in the CS-evoked response. Is this an associative change in the evoked response? Only in a trivial sense, because it is not unique to the conditioning operation and throws little light on the conditioning process. It is, nevertheless, correlated with conditioned changes in behavior, and one would expect it to remain so throughout discrimination and reversal learning.

It is possible that the effects reported by Gabriel *et al.* are of this kind, although that is not the only possibility. Other behavioral changes, for example, in orientation toward conditional stimuli, may also be confounded with conditioned changes in behavior, and one needs assurances that adequate measures have been taken to eliminate such possibilities. Level of arousal seemed the most appropriate variable to illustrate the argument, however, for we (*2*) and others (*3*) have shown that changes in late components of evoked activity in primary afferent pathways during conditioning can reflect mainly conditioned arousal or fear responses. Such changes in the later components of evoked activity remain a strong possibility in the experiment by Gabriel *et al.* To show that modifications in evoked activity are in some way unique to a conditioning process or are primary changes not dependent upon behavioral modifications has become a demanding task. This is not to argue that such modifications cannot be found; there is some evidence for them (*4*), but very little considering the numerous claims. Ad hoc arguments that the data have not been compromised are encountered more often than adequate controls.

My main intention in this note has been to call attention to conceptual difficulties in the study by Gabriel *et al.* which are not, however, peculiar to this study. There are, however, several technical shortcomings in their report. Consider, for example, the data in the left-hand column of their figure 1, which presumably support the conclusion that in the final stage of acquisition the geniculate responses to the CS^+ were larger during the first 40 msec than the responses to the CS^-. This appears to be the case for subject 44; but the opposite relationship is seen in the data from subject 42, and it is difficult to distinguish any systematic differences between the curves for the other three subjects. There is no statistical evaluation of this difference. Moreover, the arbitrary selection of different points on the curves of individual subjects as illustrative of significant differences is at variance with accepted statistical practices; and the standard deviations used as the measure of those differences have no relevance to statistical decisions about the differences between the curves for the CS^+ and CS^- conditions. The reversal data in the right-hand column are only a little less disturbing, especially in view of a confounding difference between the initial (preconditioning) amplitudes of the responses to the two CS's (which Gabriel *et al.* were preparing to explain in a later publication) and a statistical evaluation based on not just the early (5 to 40 msec) activity, but on the complete response.

ROBERT D. HALL
Neurosciences Research Program,
165 Allandale Street,
Boston, Massachusetts 02130

References

1. M. Gabriel, S. E. Saltwick, J. D. Miller, *Science* **189**, 1108 (1975).
2. R. D. Hall and R. G. Mark, *J. Neurophysiol.* **30**, 893 (1967).
3. Z. S. Khachaturian and H. Gluck, *Brain Res.* **14**, 589 (1969); G. F. Ricci, F. Valassi, L. Zamparo, *Arch. Ital. Biol.* **105**, 413 (1967).
4. Z. S. Khachaturian, T. M. Shih, J. L. Kerr, K. L. Reisler, *Brain Res.* **91**, 299 (1975).

28 October 1975; revised 6 February 1976

Hall agrees that differential conditioning and reversal of short-latency medial geniculate nucleus (MGN) neuronal activity (*1*) is an associative neuronal effect. However, he argues that the effect may be associative "only in a trivial sense." Hall's judgment of triviality seems to us to be based on his belief that our effect "depend[s] on conditioned changes in behavior." We presume Hall expects a trivial neuronal effect to be "correlated with conditioned changes in behavior . . . and to remain so [correlated] throughout discrimination and reversal learning."

We interpreted Hall's phrase, "depend[s] on conditioned changes in behavior," to mean either (or both) of the following: (i) the associative neuronal responses were mediated by prior conditioned behavioral activity; (ii) the effects were positively correlated with conditioned behavioral activity in all stages of conditioning and reversal. Neither assertion is descriptive of the data. The latencies of the differential neuronal responses (5 to 40 msec) were too brief for those responses to have been mediated by prior conditioned stimulus (CS) related behavioral responses. In fact, it is unlikely that the briefest latencies of neu-

ronal discrimination and reversal (5 to 15 msec) in our study were mediated by any prior CS-related activity except transmission from the auditory periphery (*2*). Moreover, the random sequence of CS^+ and CS^- controlled for differential behavioral predispositions (for example, receptor orientation) prior to CS onset. Our study was designed with these problems in mind (*3*). We did not make "ad hoc arguments that the data have not been compromised."

The differential neuronal responses showed positive covariation with differential behavioral responses at the end of conditioning and at the end of reversal training. However, MGN activity showed abrupt shifts between the conditioning pattern and the reversal pattern of the differential response in the early and intermediate sessions of reversal training. Behaviorally, the subjects responded nondifferentially (that is, equally to CS^+ and CS^-) in these sessions. In short, there was absence of positive covariation of neuronal and behavioral responses in these sessions (*4*). These results are at odds with interpretation (ii) above. The neuronal responses clearly were not "correlated" with conditioned behavior in all stages of conditioning and reversal. Unfortunately, Hall did not ask to see our detailed report which, in (*1*), we cited as "in preparation." [This report has subsequently been accepted for publication (*4*).] Had he requested it, we would have sent it to him.

Suppose, hypothetically, that short-latency neuronal responses *were* correlated with behavioral responses in all stages of conditioning and reversal. This outcome would not be a trivial one. Instead, it would suggest an important neuronal precursor of conditioned behavior whose specific behavioral function should be explored in subsequent experiments. Hall's assertion that such an outcome would not be "unique to the conditioning operation" seems uninterpretable to us. In fact, this result would be a specific *product* of the conditioning operation, just as learned behavior. Moreover, the associative character of the effect would not be negated, nor would understanding of the effect be promoted, by arbitrary application of a label such as "conditioned arousal" (*5*).

The major point of our study was the empirical demonstration of short-latency associative change of neuronal activity in MGN. This had not clearly been shown before. However, we also attempted to develop testable ideas about the function of the associative activity based on its relations to the learning task, learned behavior, the neuroanatomical context, and so forth (*4*). Given the role of MGN in auditory processing, corticofugal projections to MGN, and the unique neuron-behavior relations observed in our study, we proposed acquired sensory filtering as the adaptive function reflected by our data. Studies are under way to test this idea. This approach seems preferable to any based on a priori assumptions about the relevance (for example, triviality) of the data.

On the technical side, Hall points out that not every subject showed conditioning and reversal in every bin from 5 to 40 msec. However, we did not claim that differences occurred in every bin, and our conclusions did not depend on such invariant differences.

We demonstrated a significant "crossover" effect from conditioning to reversal in each subject in the first 100 msec, using a standard statistical test. Given that the effect was significant in the first 100 msec, and given the conceptual importance of latency, we sought to determine the "earliest" 10-msec bin in each subject to show a significant differential effect both in conditioning and in reversal. The claims of significance of the differences between CS^+ and CS^- effects in these earliest bins were questioned by Hall. Although not stated explicitly in our report, the claims were based on the distribution of *differences* between pre-CS^+ and pre-CS^- (baseline) bin values. A difference of 2.8 or greater in our units represents a significant ($P \leq .05$) normal deviate in that distribution. A significant difference in conditioning alone, or in reversal alone, could by this criterion be attributed to "prewired" effects of the tones. However, significant superiority of the response to CS^+, relative to CS^-, both in conditioning and in reversal, cannot be attributed to prewired effects of the tones. Rather, this outcome indicates associative modification of neuronal activity. Moreover, if prewired effects accounted for the differential responses in conditioning, or in reversal, then differential responses should also have been present during pretraining with tones and noncontingent shock. Although small differences did exist in pretraining, significant short-latency (single-bin) differential responses occurred both in conditioning and in reversal when the pretraining responses to the tones were subtracted from the data (*4*). Based on these outcomes, our claims of significance of differences at the earliest bins stand as reported. Again, we would have sent the analyses involving corrections for pretraining differences to Hall, had he requested them.

MICHAEL GABRIEL
STEVEN E. SALTWICK
JOSEPH D. MILLER
Department of Psychology, University of Texas at Austin, Austin 78712

References and Notes

1. M. Gabriel, S. E. Saltwick, J. D. Miller, *Science* **189**, 1108 (1975).
2. It is because of the minimal possibility of mediation that study of short-latency associative reactions is an important facet of the electrophysiological approach. This view is elaborated by J. Olds, J. H. Disterhoft, M. Segal, D. L. Kornblith, and R. Hirsh [*J. Neurophysiol.* **35**, 202 (1972)].
3. We were especially concerned with these problems in designing our study because confounding of neural activity by feedback from CS-related behavior (for example, muscle tension) existed in several previous studies of the neural correlates of conditioning [see (*6*)].
4. M. Gabriel, J. D. Miller, S. E. Saltwick, *Physiol. Psychol.*, in press.
5. Hall and Mark have criticized the concept of arousal on grounds of vagueness [(*6*), p. 908]. In its original usage, the term denoted nonspecific activation. It is surprising to us that Hall has contributed to a broadening of the concept by invoking associative, stimulus-specific arousal. Moreover, Hall seemed to us to be acting inconsistently in applying the label "arousal" to our results, while citing the study of Z. S. Khachaturian, T. M. Shih, J. L. Kerr, and K. L. Reisler [*Brain Res.* **91**, 299 (1975)] as providing evidence for neural modifications "unique to a conditioning process." Our study and the study of Khachaturian *et al.* both reported the same basic finding, that is, neural change which was specific to a conditioned stimulus, and which did not occur in response to an interspersed irrelevant stimulus. Both studies provided controls to rule out behavioral mediation of the neural effect.
6. R. D. Hall and R. G. Mark, *J. Neurophysiol.* **30**, 893 (1967).

21 May 1976