Comments and Discussion

Short-latency discriminative unit responses: One way to search for the engram

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A strategy for locating learning centers in mammalian brain was proposed by Olds, Disterhoft, Segal, Kornblith, and Hirsh (1972). An important aspect of it was to locate those regions showing short-latency changed responses after learning which were specific to the positive conditioned stimulus. It was pointed out that previous studies which recorded electrical activity in the nervous system before and after conditioning (e.g., reviews in John, 1972; Morrell, 1960) showed that changed responses, due to conditioning, were detectable throughout the brain. However, no method was available for differentiating changed responses which were locally mediated ("engrams"?) from those projected in a secondary fashion from some other brain region. It was reasoned that, on any one conditioning trial, the shortest latency conditioned responses detectable could not have been projected from some other brain region and "might thus be considered to be at the site of conditioning" (Olds et al., 1972, p. 202).

Gabriel (1976) has recently published a theoretical paper in which he argued that the search for short-latency discriminative unit responses that we proposed would select for neurophysiological evidence of "bias" operating within sensory systems rather than engram location. Gabriel's purpose was apparently to infer that we were unaware of, or chose to disregard, the potentially important factor of efferent feedback in sensory system operation.

I would like to briefly reply to Gabriel in two ways. First, to set the record straight, I will show that the late Professor Olds and the rest of our group were very much aware of the possible operation of "bias" in the production of short-latency responses, and that our research strategy was designed to detect it. Evidence for this may be found in our first paper (Olds et al. 1972) as well as in our later reports. Secondly, I would like to reemphasize that the search for short-latency changed responses is a useful

strategy for systematically analyzing the formation of the conditioned reflex arc, even if bias is operating.

As Gabriel (1976) pointed out, we stressed the advantages of searching for short-latency responses in our first paper reporting the results of our attempt to map learning in the rat brain (Olds et al., 1972). This was to be expected, since the short-latency responses portion of the data was reported in that paper. But we did discuss the possible effect of bias (Olds et al., 1972, p. 216). It was pointed out "that some of the new responses might be generated by tonic presynaptic influences (which would be 'dynamic engrams')." One potential presynaptic influence would be sensory system bias. But the short-latency changed response would be "the effective site of the dynamic engram." The operation of bias or a dynamic engram on a locus yielding a short-latency conditioned response could very well be reflected as an alteration in background firing rate at its effective site or at the site of the dynamic engram itself. Since background firing rates were monitored as well as responses to the CS, we were in a position to detect this evidence of bias.

Alterations in the background firing rates of cortical units were shown to precede the emergence of thalamic changed responses to the tone CS in the trial series in two subsequent reports (Disterhoft & Olds, 1972; Disterhoft & Stuart, 1976). In both papers, the potential dependence of posterior nucleus of thalamus responses on altered tonic input from reciprocally connected cortex was stressed. It was suggested that posterior cortex could have released a presynaptic inhibitory input operating, via interneurons, on cells in posterior nucleus. Posterior cortex neurons could have been the actual locus of the dynamic engram or bias resulting in the posterior nucleus responses.

Kornblith and Olds (1973, pp. 499-500) discussed the operation of dynamic traces which may have contributed to their short-latency responses in reticular formation at length. They noted that neurophysiological recording of background activity was a powerful technique for detecting their presence. They also pointed out that to account for short-latency learned responses, dynamic engrams should be associational in nature, i.e., a result of pairing tone and food, and be specific enough to cause increased responses to the CS+ and not the CS-. Their description of the operation of the dynamic trace is very similar to Gabriel's (1976) description of "bias."

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Segal and Olds (1972) reported interesting shifts in subiculum background firing rates. However, these shifts were not of the appropriate pattern to account for hippocampal CA3 learned responses.

Finally, Disterhoft and Stuart (1977) have reported differentiated short-latency response increases in inferior colliculus neurons. We pointed out that efferent control processes could account for, or contribute to, the inferior colliculus increases.

Work from other laboratories, in addition to the Gabriel's (1976) evidence for bias in medial geniculate, also supports the potential importance of background firing rate levels and of tonic efferent modulation during learning. Ben Ari and Le Gal La Salle (1972) recorded intertrial firing changes during sensory-sensory associations and postulated that such changes could reflect the effect of the US input on the neuron under study. O'Brien, Packham, and Brunnhoelzl (1973) reported changes in background interspike interval of single neurons in postcruciate cortex of paralyzed cats during classical conditioning. And Oleson, Ashe, and Weinberger (1975) have recorded differentiated multiple unit increases in anterior ventral cochlear nucleus of paralyzed cats during pupillary conditioning. They postulated that these cochlear nucleus responses could have been dependent on efferent control originating in auditory cortex.

In summary, it is obvious that Olds and his co-workers were and are aware of the potential importance of dynamic engrams or tonic modulation or "bias" in the production of short-latency learned responses. We gathered our data in a manner designed to detect the presence of dynamic engrams. And we specifically discussed this important problem in many of our reports. We did not give superficial consideration to the operation of tonic modulation as Gabriel (1976) inferred. And work from other laboratories has offered other examples of tonic modulating effects which may be important during learning.

If we grant that tonic modulation exists and that it may actually cause some short-latency differentiated responses recorded after conditioning, can we still defend the search for short-latency responses as a useful strategy for finding local changes (engrams) after learning?

As Gabriel (1976) and Olds et al. (1972) pointed out, short-latency learned responses cannot be secondary reflections of changes occurring at more peripheral loci on that trial. They must be either primary sites of memory traces or the sites at which dynamic engrams are expressed. The localization of short-latency learned responses allows further analyses to determine their physical basis. Various methods may be used to determine whether they are primary or secondary. As mentioned above, back-

ground firing rate changes at the site may reflect increased or decreased modulating inputs. Changes occurring in a region which projects to the site and which precede the emergence of the changed responses appropriately in the trial series may be candidates for dynamic engrams (Disterhoft & Olds, 1972; Disterhoft & Stuart, 1976). Intracellular recording may be done at the site during learning to determine if subthreshold modulating inputs, which decrease the firing threshold of neurons at the site but do not increase their background firing rates, may be causing the learned responses. Or, efferents to the site may be determined by retrograde tracing after injections of substances such as horseradish peroxidase. Single neuron recording at the loci of efferent inputs could then determine whether any of them change in such a way as to cause the short-latency responses.

And it is certainly possible for short-latency learned responses to represent locally mediated changes, even in peripheral portions of the auditory input pathway such as the cochlear nucleus. As pointed out above, Oleson et al. (1975) found conditioned changes in anteroventral cochlear nucleus which they attributed to downstream modulation from auditory cortex. Those changes they recorded in posteroventral cochlear nucleus though, could not be attributed to auditory cortex as they preceded both the cortex and behavior in the trial sequence.

Anatomical analyses (Disterhoft & Perkins, 1976; Morest, Kiang, Kane, Guinan, & Godfrey, 1973) show that the cochlear nucleus, and particularly the dorsal cochlear nucleus, is a structurally complex region which would seem capable of mediating changes after learning. If local changes do occur in cochlear nucleus after conditioning, tone CS arrival must be associated with the US. Efferent inputs to the cochlear nucleus (Elverland, 1977; Harrison & Howe, 1974) which could relay information necessary for a cochlear nucleus association to be formed are well known. Evans (1974) has hypothesized, on the basis of anatomical and physiological data, that dorsal cochlear nucleus could be the origin of a portion of the auditory pathway specialized to subserve discrimination functions.

Buchwald and her associates (Brown & Buchwald, 1976; Buchwald & Humphrey, 1972) have demonstrated that cochlear nucleus is capable of mediating habituation. If it can be shown that locally mediated short-latency learned responses are present in cochlear nucleus after conditioning as well, they will be amenable to analysis by available anatomical and neurophysiological methods. With appropriate controls, these changes will be analyzable with confidence that they could not have been projected in a secondary fashion from a more peripheral locus.

Work on analyzing learned changes which may exist in cochlear nucleus is now in progress in this laboratory.

The cochlear nucleus is discussed as one hypothetical example of the utility of the short-latency strategy in analyzing an engram. It might be well to recall that Lashley was "trying to trace conditioned reflex *paths* through the brain or to find the locus of specific memory *traces*" (Lashley, 1950, *italics added*). At this point, we have no certain idea what form the "engram" might take. It does seem, though, that it could take different forms in different neural subsystems if multiple engrams are formed. The possibility of multiple engrams is justification for strategies designed to detect them at different portions of the reflex arc. The search for short-latency responses is particularly appropriate for detecting memory traces that may be found on the sensory input pathway of the conditioned stimulus. It seems premature to conclude that such traces most likely reflect tonic bias rather than locally mediated engrams (Gabriel, 1976).

The possibility that the auditory system can selectively increase or decrease its own gain on stimuli according to their significance has been of interest since the investigations of Hernández-Peón and his collaborators (Hernández-Peón, Scherrer, & Jouvét, 1956) more than 20 years ago. The possibility still exists that "engrams" may be formed in the auditory pathway, even as far peripherally as the cochlear nucleus.

Olds et al. (1972), when they described the search for short-latency changed responses to localize learning centers, discussed dynamic engrams or tonic bias as a potential cause for the existence of some short-latency changes after learning. In addition, they described some procedures for detecting the location of such dynamic engrams. Gabriel (1976) has correctly reemphasized that response changes which may be shown after learning in relatively peripheral sensory structures must be evaluated with care because of this important possibility. But the appeal of the short-latency method was, and still is, its directness: the shortest latency learned responses cannot be projected in secondary fashion from a more peripheral station on the incoming conditioned reflex pathway. And, if it is shown that they are not reflections of modulation by more central dynamic engrams, they must be at a site of learning.

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