of frontal cortex[7] and the lateral portions of the medial forebrain bundle[8]. In these specific regions, but not in surrounding locations, brain stimulation during learning disrupted retention. Using the same paradigm we have found no effect of locus coeruleus stimulation[7]. The results cast doubts on the essentiality of the locus coeruleus to the learning and memory of movements.

Related to the issue of the involvement of the locus coeruleus in learning is the point made by Gilbert[1] that "the locus coeruleus... will support intracranial self-stimulation". Though it is not to be denied that intracranial self-stimulation (ICSS) can be obtained when electrodes are in the region of the locus coeruleus[9], it is by no means proven that the locus coeruleus or its axonal system is responsible for that behaviour. Our evidence argues against a role for the locus coeruleus in intracranial self-stimulation. Intracranial self-stimulation in the region of the dorsal bundle, the efferent ascending pathway of the locus coeruleus, is unaffected by the bilateral destruction of the locus coeruleus[10]: and intracranial self-stimulation has not always been obtained when electrodes are in the locus coeruleus[11,12]. Given the uncertainty of the locus coeruleus involvement in brain stimulation reward it seems premature to invoke a role for it in memorising learned movements.

The second point concerns the mechanism of storage proposed by Gilbert[1]: the phosphorylation of membrane protein. We have studied the endogenous phosphorylation of four protein components of brain membranes[13], and have found that one component, which we term band F, is altered by a training experience[14]. This effect is most noticeable in the caudate nucleus, but alterations (admittedly of a less dramatic nature) have also been observed in the cerebal cortex. An analysis of the vermis of the cerebellum, however, has yielded negative results; that is, there is no change in cerebellar membrane phosphorylation as a consequence of training such as was observed with membranes of the caudate nucleus. Although this represents an initial finding in two replicated experiments, the results gathered to date lend no support to Gilbert's views[1] on the location of the mechanism of storage. Actually, the phosphorylation mechanism itself may be appropriate, but its location may be elsewhere, for example, in the caudate nucleus, rather than in the cerebellum.

Though I am in sympathy with the approach offered by Gilbert, I question the detailed mechanism proposed, both with respect to the involvement of the locus coeruleus in learning and reinforcement and with respect to alterations in phosphorylation within the cerebellum. Our data, though negative on both specific points, point to particular brain locations potentially involved in memory, and to related regions where chemical storage mechanisms could be engaged following a learning experience.

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DR GILBERT REPLIES—To support my proposal about motor learning in the cerebellum[1], I cited a study[2] which showed that locus coeruleus lesions markedly impaired, or abolished, the ability to learn to run with increased speed in an L-shaped runway for a food reward. Routtenberg questions the result of my study (see refs 1 and 2) because there seems to be no learning deficit in a T-maze discrimination task for animals with locus ceoruleus lesions[3]. The types of learning being tested in those studies are, however, quite different, and the results are not necessarily contradictory. I have described[1,4] how the cerebellum could store information required for the production of coordinated muscular activity in a learned movement. I have not suggested that the cerebellum is involved in other types of learning such as T-maze discrimination, and the fact that there is no learning deficit for this task with locus coeruleus lesions is irrelevant to my proposal.

Stimulation of the locus coeruleus probably leads to an increased release of noradrenaline at Purkyne cells[5] and could therefore lead to enhanced retention. The enhancement of retention by central administration of noradrenaline only occurs after depletion of central noradrenaline stores[6], however, and the stimulation of the locus coeruleus could be expected to enhance retention only in similar conditions. Therefore, the negative results of locus coeruleus stimulation[7] do not conflict with its proposed role[1] in long term memory consolidation.

Two independent studies[8,9] have shown that the locus coeruleus will support intracranial self-stimulation (ICSS), though with different experimental conditions no ICSS is obtained[10,11]. There seems to be no doubt that the locus coeruleus is closely involved with the positive reinforcement system of the brain, although I agree that the details of this involvement have not been determined. My theory does not require that the locus coeruleus cells directly contracting Purkyne cells support ICSS, but only that the locus coeruleus cells receive an input from the positive reinforcement system.

My suggestions about learning in the cerebellum were made on the basis of the large amount known about cerebellar anatomy and physiology. I would expect a similar memory mechanism to operate in other parts of the brain, however, especially in view of the widespread distribution of noradrenaline nerve terminals[12]. It is therefore very encouraging that a change in membrane phosphorylation as a consequence of training has been demonstrated[13] for certain regions of the brain. The possibility that this mechanism operates in the cerebellum has certainly not been excluded by preliminary experiments on a small number of protein components of membranes from a restricted region of the cerebellum.

In conclusion I am pleased that experiments are being carried out which test my proposed memory mechanism. I would add that there is increasing support[14,15] for the idea that the cerebellum is involved in motor learning.

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