100 YEARS AGO

The old view that insects, with all the lower animals, were created for man's benefit cannot reasonably be held at the present time, but it must, nevertheless, not be forgotten that there are very many beneficial as well as injurious insects. Dr L. O. Howard has recently summed up the good and bad qualities of insects so far as it is possible to do, and he finds that the insects of 116 families are beneficial, and the insects of 113 families are injurious, while those of 71 families are both beneficial and harmful or their functions have not been determined. The injurious insects are made up of 112 families which feed upon cultivated or useful plants, and one family the members of which are parasitic upon warm-blooded animals. Of the beneficial insects, those of 79 families are valuable as preying upon other insects, 32 families are of service as scavengers, two families as pollenisers, and three families as forming food for food fishes.

From *Nature* 4 May 1899.

50 YEARS AGO

In his monograph "Scientific Management" ... Mr. G. Chelioti urges that the essence of management is the art of getting things done through the agency of other human beings, and that management itself is incapable of becoming a science. He regards science as the foundation and the provider of the tools of industry, and the technician as the primary servant of science in industry; but he points out that the technician cannot manage human beings by means of his technology and that the manager dealing with a technical problem becomes a technologist for the time being. In urging this clear separation of the two functions of dealing with human beings and with technical problems or machines, Mr. Chelioti maintains that the undue domination of industry in the nineteenth century by the new element of modern technology, and failure to regard industry as the servant of humanity and to consider sufficiently the human beings employed, was responsible for the revolt of the human spirit against subordination to the machine which we are still experiencing in spite of a more enlightened managerial outlook.

From *Nature* 7 May 1949.

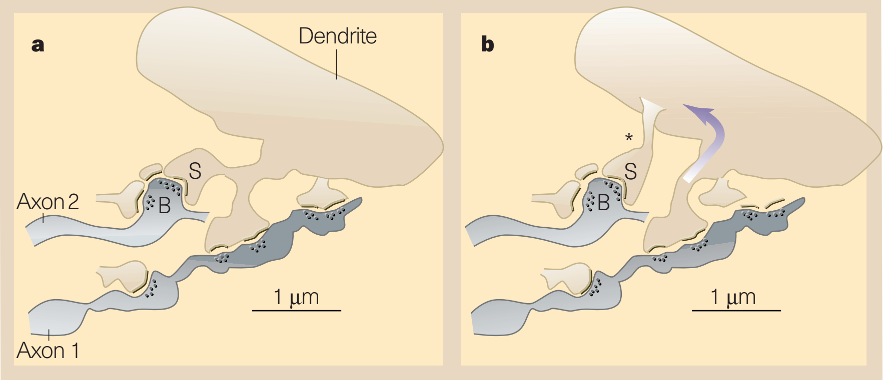

Figure 1 **Generation of new dendritic spines in response to long-term potentiation.** a, **A double-headed spine (S) could theoretically arise by a simple split in an existing spine. In all reconstructed cases, however, such double-headed spines are contacted by two different axons with boutons (B).** b, **Suggested scheme for the emergence of a new spine (asterisk), according to the results of Engert and Bonhoeffer[1]. The new spine grows towards, and eventually makes contact with, one of the existing boutons of axon 2, an interaction that is triggered, in part, by a signal from the activated spine (curved arrow), connected to axon 1.**

and, as expected, LTP was seen in most experiments. Using two-photon microscopy of the impaled and marked cells, the authors observed that new spines emerged about 30 minutes after the LTP was induced. But addition of AP5 (D(–)-2-amino-5-phosphonovalerate), which blocks NMDA (*N*-methyl-D-aspartate) receptors, prevented the appearance of new spines, indicating that calcium entry is important for this process.

The results are similar to those reported by Maletic-Savatic *et al.*[7], although these authors used younger organotypic cultures, and a high-frequency stimulation mode which, although not monitored, should elicit LTP in the same neurons. In this case, the changes appeared as filopodia (thin, thread-like protrusions), which are longer and more irregular, but may turn into dendritic spines. Again, appearance of the new projections was highly localized owing to the restricted stimulation, and the filopodia appeared after 20 minutes then continued to grow for another 40 minutes. But, as seen by Engert and Bonhoeffer, they did not appear when AP5 was added, and weak stimulation had no effect on them.

In both reports, the strength of the evidence comes from the highly localized nature of the structural changes — down to a handful of synapses on a small stretch of a dendrite. The thousands of surrounding, naive synapses are left unchanged. Synaptic changes have previously been seen in large networks of cells and synapses, although it is not known how many neurons are involved in these changes. And in the mollusc *Aplysia*, dramatic increases in the number of synapses have been reported after these creatures have learned a conditioned-reflex task[8]. Other examples where new spines have been induced in nerve cells thought to be specifically involved in learning include the lasting avoidance that chicks show after pecking once at a bead doped with a foul taste[9], spatial training in rats[10], and the response seen after the induction of LTP in anaesthetized rats[11].

Exciting (quite literally) as these new findings are, several questions remain. The most pressing is whether the new spines can explain the key element of LTP — the increased postsynaptic current. Are these new spines innervated, and, if so, by which fibres? A convincing answer requires the demonstration, by electron microscopy, that the presynaptic boutons of the stimulated nerve fibres are attached to the new spines, as well as proof that these spines are functionally competent. This could be done by looking at the levels of calcium in the new spine heads in response to synaptic activation.

Another question is this. How similar is the spine growth seen by Engert and Bonhoeffer to relevant data from whole animals? In organotypic cultures, full physiological maturation of synapses is either delayed or absent while considerable synaptic reorganization takes place[12]. The observed spine density is, for example, only one-fifth of that seen in the same cells in normal rats[11]. We cannot be sure about the function of the new filopodia until their relationship to normal dendritic spines is determined. New filopodia have also been seen after nerve fibres synapsing onto cells have been cut, so they could be a response to an unspecific signal associated with high-frequency synaptic activation

Finally, the mechanisms that underlie the emergence of new spines raise another set of questions. Which signals trigger and guide the new spines? How important is synaptic activation, given that miniature synaptic potentials are necessary to maintain the spines[13]? Does the activity-related increase in the concentration of calcium within the spines[14] — which is important for rapid changes in the shape of the spines[15]