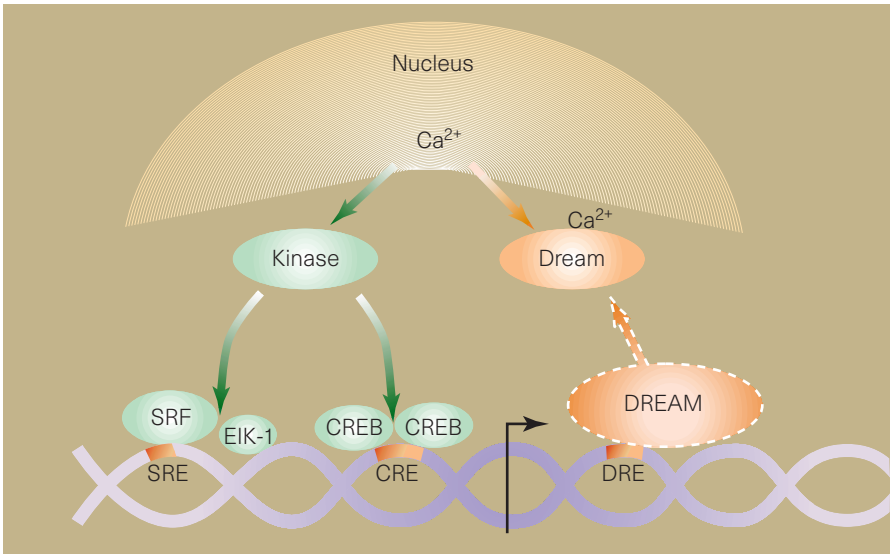

Figure 1 **The transcriptional repressor DREAM is regulated by direct binding to calcium. In the basal state, DREAM is bound to DRE located downstream from the transcriptional start site (black arrow). When the intracellular Ca^{2+} concentration rises, DREAM binds to Ca^{2+} and comes off the DRE, permitting a higher level of promoter activity. In contrast to DREAM, the transcriptional activators CREB and SRF/Elk-1 sense Ca^{2+} through the action of intermediary kinases, and remain bound to the Ca/CRE and SRE sites, respectively, in the presence of Ca^{2+}.**

cortical neurons after treatment with the neurotransmitter glutamate[6]. The magnitude of these changes might be sufficient to affect DREAM structure and DNA binding. For other proteins, such as the neuronal calcium-binding proteins VILIP and NCS-1, binding of Ca^{2+} or Mg^{2+} has very different effects: NCS-1 structure is altered by binding of either Ca^{2+} or Mg^{2+}, whereas binding of Mg^{2+} to VILIP does not cause any structural change[7].

Indeed, the finding that DREAM binds Ca^{2+} at all comes as a surprise, because the DRE was first characterized by its ability to mediate PKA-dependent de-repression of prodynorphin gene expression[8]. Carrión *et al.* had previously shown that PKA decreases binding of DREAM to the DRE[8]. In their latest report, forskolin had no effect on DREAM function; also, the DREAM complementary DNA sequence does not predict a consensus PKA-recognition site. It is possible that PKA might phosphorylate DREAM through another kinase pathway. Alternatively, the 110-kilodalton protein regulated by PKA might contain DREAM as a subunit; or the PKA effects they observed in their earlier study could be a result of an alteration in the function of Ca^{2+} channels.

Now that the DREAM complementary DNA has been isolated, it should be possible to generate antibodies to determine the properties of the endogenous DREAM protein in neuronal cells. This is important because regulation by DREAM is not likely to be restricted to the prodynorphin gene. The DRE sequence is found in at least one other gene regulated by Ca^{2+}, the immediate-early gene c-*fos*. Carrión *et al.*[1] have shown that disruption of the EF-hands in DREAM, or mutation of the DRE, blocks the de-repression of c-*fos* reporter genes that normally occurs in response to treatment with caffeine, which raises the intracellular Ca^{2+} concentration.

However, the relative contribution of the DRE in the context of other regulatory elements is not assessed in the new study[1]. This is an important point, because two other well characterized calcium-responsive elements, the CARE/CRE and the serum-response element (SRE), contribute to the regulation of the c-*fos* gene[9]. Thus, the physiological function of DREAM is still uncertain. Perhaps J. A. Hadfield[10] had it right when he answered his own question: "Would we say that the function of the dream is to express something or to hide something? It is both at once." But he was probably not thinking of prodynorphin. □

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Daedalus

Bugging the brain

Last week Daedalus outlined his new 'microdermic needle' injection technology. A giant multilayered carbon nanotube, a micrometre across and coated with slippery graphite fluoride, is drawn into the body by ultrasonic pulses sent down it. It noses its way harmlessly between the cells, even those of bone, and is steered under imaging control to the injection site.

Daedalus now muses that, thanks to its insulating coating of graphite fluoride, his new needle is an ideal biological electrode. It could sense an electrical potential at its tip, and relay electrical signals back down again.

The obvious target organ is the brain. Unlike electroconvulsive therapy, microdermic therapy would allow precise intervention. Far too fine to hurt or even be noticed, a microdermic needle could be inserted into the skull of the conscious patient, and steered around his brain. Like a precision electroencephalograph, it would detect the electrical activity of the cells it encountered. Pulses could then be sent down it to reinforce or modify their action. Sudden memories, ideas, or motives might grip the patient, revealing their exact site in the brain. His mentality could be mapped in detail and its troubles precisely located.

The same needle could then be used for therapy. A drug — say a neurotransmitter or an antipsychotic — could be passed down it to normalize the local brain cells. Alternatively, a pattern of electrical pulses might be devised for the same purpose. Inert, painless, undetectable, the needle could be left in place indefinitely, for future (or even maintained 'depot') corrective action. Manias, obsessions and delusions could be erased, tics and seizures switched off. Psychiatry would become an exact science at last.

The technology might even be developed into quite a general man–machine interface. Inserted into a nerve, a microdermic needle could read the traffic in that nerve, and launch impulses into it. A computer attached to the needle could learn to command that nerve. The first applications would be prosthetic — restoring sensation and action to victims of paralysis, or sensory and functional disorders. But a mass of needles densely distributed through the nervous system, all connected to a true back-pack 'personal computer', would create the very first cyborg robot: a computer seeing through human eyes and controlling a human body.

David Jones