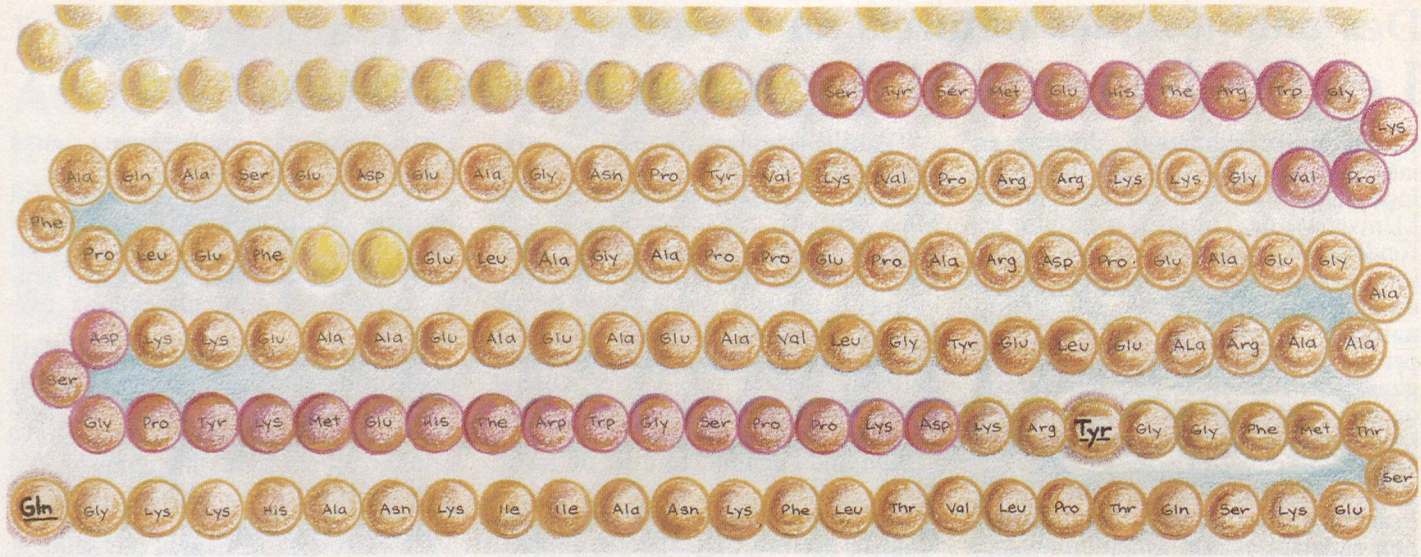

(Aili Kurtis)

The amino acid sequence of pro-opiomelanocortin, a protein synthesized by the hypothalmus region of the brain and the pituitary gland; this molecule contains as many as 10 peptide messengers in its structure, which exhibit hormonal or other kinds of activities in the body. The amino acid sequence of beta-endorphin, the analgesic released by acupuncture, is one of these peptides, stretching from glutamine (Gln) at bottom left to tyrosine (Tyr) 31 units along the chain. The last five amino acids in endorphin (methionine (Met) to tyrosine) are the sequence for enkephalin, a smaller peptide which also exhibits strong analgesic properties.

Séquence d'acides aminés de la protéine pro-opiomélanocortine, synthétisée au niveau de l'hypothalamus et de l'hypophyse, dans le cerveau. Cette molécule contient dix peptides messagers qui remplissent plusieurs fonctions dans l'organisme. La bêta-endorphine, analgésique sécrété sous l'effet de l'acupuncture, est l'un de ces peptides; elle correspond à la séquence de 31 acides aminés allant de la glutamine (Gln), dans la partie inférieure gauche du dessin, à la tyrosine (Tyr). Ses cinq derniers acides aminés (de la méthionine (Met) à la tyrosine) constituent la séquence de l'enképhaline, peptide plus petit et possédant également d'importantes propriétés analgésiques.

The gate theory did not apply because acupuncture took 20 min to take effect; pain reduction should have happened with lightning speed and faded fast — in milliseconds, not hours.

"Our data were so original and perplexing," continues Pomeranz, "that we held back from publishing. The acupuncture was too slow in starting and took too long to shut off, a contradiction to all ideas about neural events. We couldn't make sense of our findings; so, we just kept gathering results, looking for clues."

Jointly with his colleague Dr. Daryl Chiu, Pomeranz then devised new animal models to study pain in awake mice by noting how long it took for them to pull back from a heat lamp. "Since it didn't harm the skin," says Pomeranz, "it was less stressful to the animals, controlling and avoiding the complicating factor of stress on the body. Again we ran countless controls. Again the results were the same — a slow onset of relief due to acupuncture, which then persisted for an hour or more."

After recording pain thresholds before acupuncture on each animal, electroacupuncture was applied via tiny needles in the forepaw. Pain was reduced, and sham acupuncture at incorrect sites did not relieve pain. These studies, together with the previous single cell work, were the first rigorous scientific proof showing that acupuncture induces physical changes in nerves and slows down the firing rate of pain cells.

Although the time course was perplexing it resembled clinical practice in China where needling of patients was habitually done for 20–30 min prior to surgery. It was also supported by other work on humans by Sven Anderson, in Sweden, and Richard Chapman at Washington University, in the United States, on tooth pain in volunteer dental students who had experienced a gradual build-up of analgesia (pain relief) due to acupuncture. Laboratory-induced tooth pain was considerably lessened by electroacupuncture correctly given at the Hoku point at the back of the hand, but not relieved by sham acupuncture at other sites.

Despite accumulating evidence that acupuncture has real physiological effects on nerve cells, acupuncture's mechanism remained a mystery until the discovery of a class of brain peptides discovered about a decade ago which affected cells in the same manner as opiates like morphine. Called endorphins (a contraction of *endo*genous mo*rphine*) the peptides (31 amino acids in length) are located in the brain at the base of the hypothalmus and in the anterior lobe of the pituitary gland (see box). Smaller molecules with similar opiate-like characteristics called enkephalins (about 5 amino acids long) have also been detected and identified as breakdown products of the longer endorphins. More interesting, particularly for Pomeranz, is the knowledge that certain brain cells have receptors (molecular structures on the surface) which specifically bind opiates, and some of these are located in areas involved in the perception of pain.

"These chemicals act like morphine," explains Dr. Pomeranz, "and cause pain relief or happiness depending on which receptors (at nerve endings) they activate and where they come from. When the endorphins were first discovered, scientists hoped they would lead to the production of more effective narcotics (painkilling drugs). But this has been disappointing because, as Pomeranz points out, "anything taken in exogenously — from outside the body — is addictive and acts as a poison." In fact Pomeranz adds that painkilling endorphin-like drugs have been synthesized which are 20 000 times more potent painkillers than morphine, but unfortunately also 20 000 times more addictive. He suggests that a far better route is to try turning on the body's own endorphin production which is nonaddictive. Acupuncture does just that.

The discovery of endorphins gave Pomeranz and co-workers the clue to the mechanism of acupuncture. "As soon as we heard about endorphins," relates Pomeranz, "we gave naloxone — a drug that blocks endorphins — to anesthetized animals and found that it abolished the pain relief provided by acupuncture. This proved endorphins