NEUROPHYSIOLOGY OF ACUPUNCTURE

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INTRODUCTION

Western scientists only began to take acupuncture seriously in 1972 after visits to China increased in frequency. In recent years in the west, acupuncture analgesia (AA) has been restricted mainly to the treatment of acute and chronic pain. However, even for the treatment of pain, many western physicians were sceptical at first, despite a vast body of anecdotal evidence from both China and Europe.

How could a needle in the hand possibly relieve a toothache? Because such phenomena did not fit into the existing knowledge of physiology, scientists were puzzled and sceptical. Many explained it by the well known placebo effect which works through suggestion, distraction or even hypnosis. However, there were several problems with this idea. How does one explain its use in vetenary medicine over the past 1000 years in China and approximately 100 years in Europe and its growing use in America? Similarly children also respond to AA.

In the past 13 years, scientists have been asking two important questions

1. Does AA really work (that is by a physiological rather than a placebo / psychological effect)?
2. If it does work, what is the mechanism?

The first question had to be approached by way of controlled experiments to factor out placebo effects, spontaneous remissions etc. These have been carried out in clinical practice on patients with chronic pain, in the laboratory on humans, studying acute laboratory induced pain and in animals. From numerous studies it can be concluded that AA works much better than placebo.

Hence, AA must have some physiological basis. But what are the possible mechanisms? Only the answer to the second question (how does AA work) could possibly dispel the deep scepticism toward acupuncture.

Neural Mechanisms of Acupuncture Analgesia

Ten years of research coupled with over a hundred papers from the western scientific literature have led to a compelling hypothesis. Figures 1 to 3 **summarize** various aspects of the hypothesis of the neural mechanism of AA. Figure 1 shows how pain messages are transmitted from the skin to the cerebral cortex.

On the left is skin with a muscle beneath it in the lower left corner. An acupuncture needle penetrates the muscle. The next rectangle is spinal cord, and to the right are rectangles depicting various brain structures: midbrain, thalamus, pituitary- hypothalamus and cerebral cortex.

An injury to the skin activates the sensory receptors of small afferent nerve fibres (labelled 1) of A delta and C axon size. Cell 1 synapses onto the STT (spinothalamic tract) cell in the spinal cord (labelled 2). The STT (cell 2) projects its axon to the thalamus to synapse onto cell 3, which sends impulses to the cortex to activate cell 4 (probably in the primary somatosensory cortex). This diagram is OVERSIMPLIFIED, since there are at least six possible pathways carrying painful messages from the spinal cord to the cortex, but for the sake of clarity only the STT is shown.

In figure 2 the acupuncture needle activates a sensory receptor inside the muscle, and this sends impulses to the spinal cord via the cell labelled 5, which represents type II and III muscle afferent nerves (small myelinated afferents). Cell number 5 synapses in the spinal cord onto an ALT (anterolateral tract) cell (labelled 6) which projects to one of three centres ; to the spinal cord, to the mid brain, and to the pituitary- hypothalamic complex. Within the spinal cord, cell 6 sends a short segmental branch to cell 7, which is an endorphinergic cell. This cell releases either enkephalin or dynorphin. There are three families of endorphins : enkephalin, beta endorphin and dynorphin and these are labelled E in Fig. 2. The spinal cord endorphins cause presynaptic inhibition of cell 1 (preventing transmission of the painful message from I to 2). There are also postsynaptic endorphin synapses acting directly onto cell 2 from cell 7, though these are not shown. The presynaptic inhibition probably works by reducing calcium current flow during the action potential in the terminals of cell 1, resulting in reduced release of the pain transmitter which has been suggested to be glutamate, substance P and ATP. There are numerous peptides present in the terminals of cell 1. So far only cholecystokinin (CCK) has been shown to play a role in AA, acting like naloxone, the opiate antagonist, to block endorphin-mediated AA (perhaps the ratio of CCK and endorphins is the important variable in producing analgesia). Cell 6 projects to the mid brain, ascending the spinal cord in the ALT. Here it excites cells in the periaqueductal grey (PAG; cells 8 and 9), which releases enkephalin to disinhibit cell 10 (which is thus excited) and in turn activates the

raphe nucleus causing it to send impulses down the DLT to release monoamines (serotonin and norepinephrine; labelled M) onto the spinal cord cells. Cell 2 is inhibited by postsynaptic inhibition, while cell 1 is presynaptically inhibited via cell 7 (cell 7 is excited while cell 2 is inhibited by the monoamines). Either of the two monoamine mechanisms can suppress the pain transmission. Some believe that serotonin and peptide neurotensin may be the excitatory transmitter between cells 10 and 11. More work is needed on the role of the monoamine system in AA.

Less well understood is the action of cell 6 onto cells 12 and 13 (the pituitary hypothalamic complex), where cell 12 in the arcuate nucleus may activate the raphe via beta endorphin and cell 13 in the hypothalamus may release beta endorphin from the pituitary gland. While there is some agreement that AA is accompanied by elevated beta endorphin in the CSF (and blood) and that pituitary lesions suppress AA, there is no agreement on how the beta endorphin from the pituitary reaches the brain to cause analgesia. Too little reaches the blood to cross the blood-brain barrier in sufficient quantities to produce analgesia. Some evidence suggests that the pituitary-portal venous system can carry hormones in retrograde direction directly to the brain. Perhaps cell 14 can influence cell 9 as shown by the thin arrow, without having to cross the blood-brain barrier. If so , the role of circulating endorphins in the blood is unclear. However there is an important correlate of pituitary beta endorphin release : ACTH and beta endorphin are both coreleased on an equimolar basis into the circulation (they are both made from a common precursor). The ACTH travels to the adrenal cortex, where cortisol is released into the blood, which may explain why acupuncture is helpful in blocking the inflammation of arthritis and the bronchospasms of asthma (the doses of cortisol released by acupuncture are small and finely regulated, thus avoiding the side effects of cortisol drug therapy).

In summary, acupuncture activates nerve fibres in the muscle, which send impulses to the spinal cord and activate three centres (spinal cord, midbrain, and hypothalamus-pituitary) to cause analgesia. The *spinal* site uses enkephalin and dynorphin to block incoming messages with stimulation at low frequency, and other transmitters (perhaps GABA) with high frequency stimulation. The *midbrain* uses enkephalin to activate the raphe descending system, which inhibits spinal cord pain transmission by a synergistic effect of the monoamines, serotonin and norepinephrine. Finally, at the third centre, the *hypothalamus- pituitary*, the pituitary releases beta endorphin into the blood and CSF to cause analgesia at a distance (e.g. the midbrain). Also the hypothalamus sends long axons to the midbrain and via beta endorphin activates the descending analgesia system. This third centre is activated only at low frequency stimulation.

What is the practical significance of this three level system? When needles are placed close to the site of pain, or in the tender (trigger, or ah shi) points they are maximizing the segmental circuits operating at cell 7 within the spinal cord, while also bringing in cells 11 and 14 in the other two centres. When needles are placed in distal points far away from the painful region they activate the midbrain and hypothalamus-pituitary (cells 11 and 14) without the benefit of local segmental effects at cell 7. (Cells 11 and 14 produce analgesia throughout the body, while cell 7 produces analgesia locally.)

Local segmental needling usually gives a more intensive analgesia than distal non segmental needling, because it uses all three centres. Generally the two kinds of needling (local and distal) are used together, to enhance one another. Another important practical consequence of this system is the frequency/intensity effect. Low frequency (2 - 4 Hz), high intensity needling works through the endorphin system and acts in all three centres, while a high frequency (50 - 200 Hz) and low intensity only activates cells 7 and 11, bypassing the endorphin system. The low frequency produces the analgesia of slower onset, and more importantly, of long duration. Also, its effects are cumulative, becoming increasingly better after several treatments. The high frequency analgesia, in contrast, is rapid in onset but is very short lasting, with no cumulative effects.

Of course some patients will never respond to acupuncture for various reasons : nonresponders may be genetically deficient in opiate receptors. Others may be deficient in endorphin molecules. Hence in clinical practice a strategy must be developed to allow nonresponders to be recognised while not aborting therapy too soon for potential responders who might show delayed cumulative effects. One way is to decide after 5 treatments : if there is no benefit whatsoever, abort ; if mild to moderate effects occur continue and reassess after 10 to 15 treatments.

Because acupuncture is so controversial, and relatively new to western medicine, more data are needed to convince the student that the acupuncture mechanisms outlined are well established. Scrutinizing the huge amount of research literature available on the neurophysiology of acupuncture, it should become apparent that we know more about AA than about many chemical drugs in routine use.

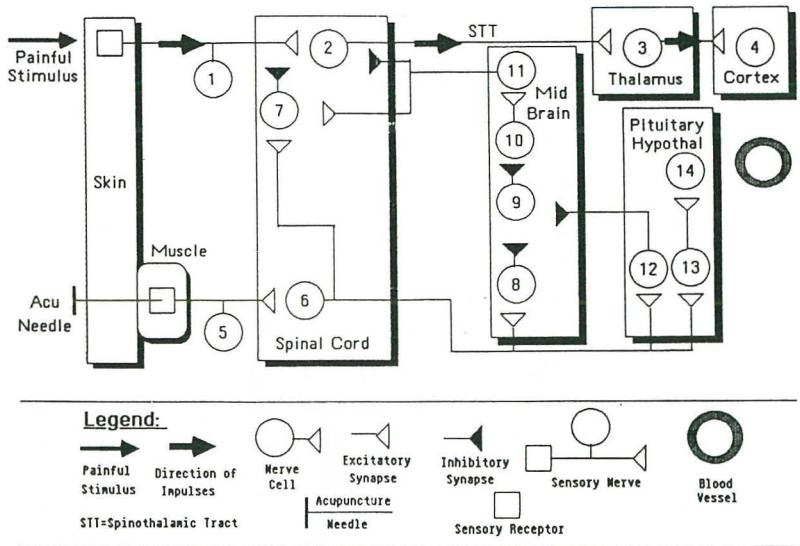

Fig. 1. Pain Transmission

4 Scientific Basis of Acupuncture

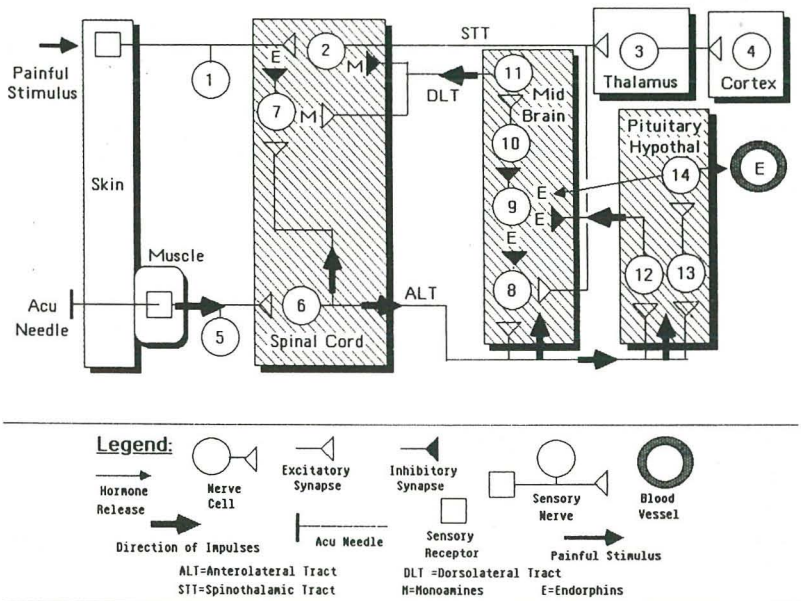

Fig. 2. Acupuncture (Low Frequency High Intensity)

6 Scientific Basis of Acupuncture

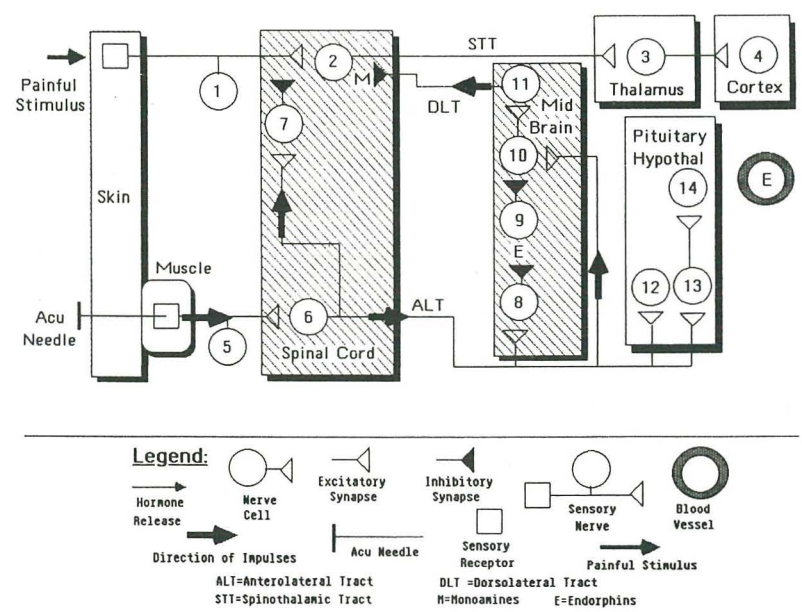

Fig. 3. Acupuncture (High Frequency, Low Intensity)