Beyond Endorphins in Acupuncture Analgesia: The Science Behind the Art

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In the last 20 years much has been written about acupuncture and its efficiency in relieving pain. The ancient Chinese clinicians practised acupuncture based on Traditional Chinese Medicine (TCM) principles using well established guidelines. Their reasoning were based on empirical responses rather than scientific principles. This discussion hopes to bring to highlight some recent research findings. Acupuncture research however cannot stagnate as we move towards the next century in pursuit of a better understanding of its mechanics.

Since the discovery of enkephalins from pigs' brains (by Hughes, Kosterlitz at Aberdeen) in 1975, the scientific community has tried to explain scientifically how acupuncture's pain relieving mechanisms really works. When Beta-endorphin was discovered (by C.H. Li at Stanford University) in 1976 and dynorphin (by Goldstein) in 1979 it began to become clear that electro-acupuncture (EA) will increase the levels of B-endorphin at 2-4Hz and dynorphin at 100-200Hz. Enkephalins will be released at frequencies of 2-200Hz. Based on the tail flick latency response in rats, Professor Han (Beijing University) also found that naloxone will even block EA response to high frequency stimulation. This was previously unknown as the dose of naloxone used was 1-2mg/kg whereas Han used 10-20mg/kg. In his experiments on rats Professor Han also used Captopril (a commonly used ACE inhibitor in general practice). When injected into the peri-aqueductal grey (PAG) Captopril prolongs the analgesic effects of EA as it is also an enkephalinase inhibitor.

Anti-opioid substances (AOS) were also described. These are released due to excessive EA and are thought to account for acupuncture tolerance. Indeed GABA and CCK8 have also been found to be increased after excessive morphine usage. Morphine tolerance hence often equated to EA tolerance. Whether the biochemical interaction are similar needs clarification. Recent studies show that the two main morphine metabolites are morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G). M3G antagonises morphine analgesia while M6G is an agonist. This relationship needs to be translated to EA tolerance but much research needs to be done. It may also help us understand the difficulty in treating patients addicted to opiates with EA.

At the last IASP conference in 1993, researchers have mentioned the discovery of morphine within the human body. This endogenous morphine (not endorphins) was found in patients who were taking L-Dopa for Parkinson's disease. As these patients were not on morphine medication the plasma levels of morphine must have been produced by the body itself. However, so far no details are known of

the exact pathways involved. Perhaps in the future EA responses may have to be interpreted in a different manner in the light of this new knowledge.

The 1993 IASP Conference in Paris also produced evidence of a new pain pathway. The French team described this new pathway, called the spino-ponto-amygdaloid pathway. Noxious stimuli have been shown to project to the lateral parabrachial (PB) nucleus at the pontine level, and then directly to the central nucleus of the amygdala. Morphine needed to depress the noxious signals in the PB and amygdala are lower than that required at the spinal levels. This new pathway which have been implicated in the affective emotional aspects of pain. It seems to be highly sensitive to morphine. The amygdala has also been researched by Professor Han and has been found to involve serotonin and endorphins. When tested with cinanserin (a serotonin receptor blocker) and naloxone, EA analgesia was attenuated. This nucleus seem to play a big role in facilitating EA responses for pain relief. The discovery of this new pain pathway should add impetus for more research.

Serotonin (5HT) receptors sites have also been the subject of intense scrutiny over the last few years. There are now many subtypes of 5HT receptors namely 5HT, 5HT2, 5HT3, 5HT4 etc. 5HT1 is further subdivided into 5HT1A, 5HT1B, 5HT1C, 5HT1D. Research into the latter has given us sumatriptan which is a currently clinically used for migraine. The effect of EA on release of monoamines (down the descending inhibitory pathway) is well documented. Research using cinanserin (a 5HT receptor antagonist) and parachlorophenylalanine (PCPA - a 5HT synthesis antagonist) have shown EA to be decreased markedly. Conversely, Tryptophan (the precursor of 5HT) would enhance EA. However the many subtypes of 5HT receptors add a new challenge to acupuncture research. It is interesting to speculate if different frequencies will stimulate different 5HT receptors. If this is more clearly understood perhaps TCM may one day be explained along scientific paradigms.

Research into naloxone have shown that ultra-low doses (in nanograms) can have an analgesic effect. This seemingly paradoxical effect have mystified and at the same time excited scientists around the world. Various experiments performed in rat models of clinically induced arthritic pain have shown that extremely low doses of naloxone can have a paradoxical analgesic effect, while high doses induce hyperalgesia. It must be remembered that we often use naloxone for reversal of opiate toxicity.

Recent research into spinal receptor systems have revealed an important receptor which is currently the centre of great scientific interest. The NMDA (N-methyl-D-Aspartate) receptor reflects Aspartate and Glutamate activity in nociception. Ketamine (a NMDA antagonist) has been shown to produce analgesia when introduced to the dorsal horn. Glutamate and GABA seem to have opposing effects on neuronal cells. GABA anti-sera has been used to reverse acupuncture and morphine tolerance as well as non-responders to EA.

Quite clearly the NMDA receptor should be more thoroughly researched in relation to acupuncture induced analgesia.

It can be seen from the above discussion we may have to rethink how acupuncture works. More and more research have enabled us to understand the complexities of nociceptive afferent stimulation of the dorsal horn, especially laminae I & II. It is to be hoped that acupuncture researchers will keep up with the new knowledge and perhaps unravel the mechanics of how acupuncture works in pain relief.

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