With millions of people suffering from long-term pain, acupuncture is a popular, but mysterious, alternative to painkilling drugs. Research carried out by Dr Takahiro Takano, at the University of Rochester Medical Center, not only sheds light on how acupuncture works – and why it sometimes does not – but may lead to a whole new line of pain-relieving treatments.

**Chronic pain and acupuncture: from needles to analgesia**

Chronic (or persistent) pain, often defined as pain lasting for at least twelve weeks, affects huge numbers of people, including over one-third of the American population. Existing treatments for chronic pain heavily depend on opioid drugs, such as morphine, codeine and tramadol. However, these drugs have disadvantages including side effects, addiction and tolerance, which cause many pain sufferers to turn to alternative treatments, such as acupuncture.

While acupuncture has many devotees, its efficacy has proven hard to document and its success is often highly variable. However, ground-breaking research by Dr Takahiro Takano is beginning to shed light on the physiological basis of acupuncture, and opens up new possibilities for chronic pain treatment that may bridge the gap between conventional and alternative medicine.

**Peripheral Pain Relief**

Unlike mainstream painkillers, which target the central nervous system (the brain and spinal cord) where pain is perceived, acupuncture targets the peripheral nerves in the rest of the body. Developed in China over 4,000 years ago, it is perhaps the most widely-accepted of all the ‘alternative’ forms of medicine. Over ten million treatments are carried out each year in the US, with the World Health Organization endorsing it for over two dozen medical conditions. Acupuncture is now even available on the UK’s National Health Service.

Acupuncture claims to be a side effect-free form of pain relief – when it works. But so far there is no scientific explanation for its action, and its effects vary significantly from patient to patient, and even day to day. Some of acupuncture’s effects are thought to result from the release of opioid chemicals in the central nervous system, but this by no means explains its entire action, particularly at a more peripheral level. This is where Dr Takano’s research comes in. His work at the University of Rochester Medical Center has helped demonstrate not only how acupuncture works, but also why its effects are so unpredictable. His findings may ultimately help improve the efficacy of acupuncture itself, and enable us to exploit its underlying mechanisms in developing new treatments for chronic pain.

Chronic pain may be of two types: inflammatory pain associated with tissue damage, and neuropathic pain associated with nerve damage. Dr Takano’s team developed mouse models to characterise both these situations, and showed that acupuncture suppresses both types of pain in these animals. Simultaneously, they found that a small molecule, adenosine, was released at the site of the acupuncture treatment. They later confirmed that the same ‘neuromodulator’ is released during acupuncture treatment in human patients.

Adenosine was already known to have pain-relieving properties, mediated through receptor molecules called ‘adenosine A1 receptors’, which are found throughout the human body. Dr Takano’s research showed that these A1 receptors are essential for the adenosine released during acupuncture to cause pain relief. He also found that injecting mice with CCPA, a molecule that mimics
What are the problems with the current ‘medical’ approach to treating chronic pain?

In a nutshell, side effects and tolerance. Opioids mess up your brain. Steroids affect the reproductive system, growth and other systems. Over-the-counter pain medicines such as non-steroidal anti-inflammatory drugs (NSAIDs) are wonderful, but even they can cause problems in digestive and cardiovascular systems when taken continuously. Many of them are thus unsuitable for patients with multiple medical conditions or during pregnancy. The situation is worsened by the drug tolerance, requiring patients to take a higher dose or switch to another drug.

How did you hit upon adenosine as the key actor in pain relief brought about by acupuncture?

Our research focused on purinergic signalling, cell-to-cell communication via release of ATP and adenosine molecules. We knew that cellular injury or mechanical stress induces purine release, and adenosine is a suppressor of neuronal activity. So the only “jump” we made was to apply the knowledge to peripheral nerve tissue and pain suppression. The needle insertion causes minor injury, and the manual manipulation of the needle causes tissue stretch. It turned out that needle insertion itself was not enough, but manipulation of the needle induced adenosine increase, mediating the analgesic effect.

How important have animal models been to your research?

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