Mechanisms

Some of the effects of acupuncture in knee pain may be due to activation of the reward system

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**Abstract**

Acupuncture is an ancient therapy with a variety of different explanatory models. A cascade of physiological effects has been reported, both in the peripheral and central nervous systems, following the insertion of a needle. Clinical trials testing the specific claims of acupuncture have generally tried to focus on testing the efficacy of applying specific techniques and/or specified points. However, different conditions may respond differently to different modes of stimulation. Also, insertion of needles into the body can stimulate effects not dependent on the locations of stimulation. Recently, it was demonstrated that both superficial and deep needling (with *de qi/Hibiki*) resulted in amelioration of patellofemoral pain and an increased feeling of wellbeing. One area in the brain that is affected by acupuncture stimulation is the limbic system. The limbic system consists of a group of brain structures, including the hippocampus, amygdala, and their interconnections, and connections with the hypothalamus, septal area, and portions of the tegmentum. It contains many of the centres related to emotion and reward.

The pleasurable aspect of the acupuncture experience has largely been ignored as it has been considered to be part of its antinociceptive effects. It has previously been reported that physical exercise and electroacupuncture in animals result in modulation of the peptidergic content in limbic structures. These results are supported by recent animal studies in Japan that have clearly demonstrated that acupuncture results in the activation of the reward system. These findings are supported by positron emission tomography studies in patients, which showed that the insula ipsilateral to the site of needling was activated, as well as the dorsolateral prefrontal cortex, the anterior cingulate and the midbrain.

Taken together, these results suggest that acupuncture, as well as the patient’s expectation and belief regarding a potentially beneficial treatment, modulate activity in the reward system.

**Keywords**

Acupuncture, limbic system, reward system, placebo control.
Mechanisms

reported. An orthopaedic surgeon and a physical therapist consecutively examined 75 patients clinically diagnosed as having PFPS. Radiography revealed pathology in 15 patients, and scintigraphic examination revealed focal uptake of technetium in two patients indicating local pathology. Diffusely increased uptake was present in 29 patients. In the remaining 29 patients, radiographic and scintigraphic examinations were normal. Subjects with healthy knees differed significantly from the three patient groups in all clinical tests measuring pain in response to provocation: ie compression test, medial and lateral tenderness and passive gliding of the patella. Differences in clinical tests between the patient groups were not significant. The main finding was that, in patients with PFPS, peripheral pathology could not be detected with the tests used and it was suggested that the pain might be due to sympathetic hyperactivity.

Recently, a randomised controlled study was conducted to evaluate the effect of acupuncture treatment in PFPS. Fifty eight patients, clinically and radiologically examined, were randomly assigned to either deep or minimal superficial acupuncture treatment. The patients were treated twice weekly for a total of 15 treatments. The main outcome measurements were one leg vertical jump, functional score, daily visual analogue scale (VAS) recordings and skin temperature. Fifty seven patients completed the study. Pain measurements with VAS decreased significantly within both groups; in the deep acupuncture group from 25 minutes before treatments to 10 minutes afterwards, and in the superficial (‘control’) acupuncture group from 30 minutes before to 10 minutes after. There was no significant difference between the groups. The improvement on the VAS recordings remained significant even after three and six months. Even though the pain decreased after sensory stimulation, neither the ability to jump on one leg, the functional score, nor the skin temperature changed. This study showed that patients with PFPS benefit from both electroacupuncture treatment and subcutaneous needling. The pain relieving effect of acupuncture remained for at least six months and was attributed to central mechanisms.

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The pleasurable aspect of the acupuncture experience has been largely ignored as it has been considered to be part of its antinociceptive effects. Bucinskaite et al have previously reported on the effects of repeated electroacupuncture treatments on open-field behaviour and on hippocampal concentrations of neuropeptide Y (NPY), neurokinin A (NKA), substance P (SP), galanin (GAL) and vasoactive intestinal peptide (VIP)-like immunoreactivities (LI) in Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR). Significantly higher concentrations of SP-LI, NKA-LI and NPY-LI were found in the hippocampus immediately after three weeks of electroacupuncture treatment. Changes in neuropeptide concentrations were similar in the two rat strains. Open-field behaviour was significantly reduced during the treatment period in both strains. Also, rats receiving treatment had higher thresholds to nociceptive stimuli and were calmer than control rats. There were significant negative correlations between behaviour and neuropeptide concentrations in spontaneously hypertensive rats, suggesting interdependency with sympathetic activity. It was proposed that some of the effects of electroacupuncture in rats are related to increases in NPY-LI, NKA-LI and SP-LI in the hippocampus. Interestingly, it has been reported that basal NPY-LI is lower in the hippocampus of ‘depressed’ rats (Flinders Sensitive Line) as compared with controls, and that electroconvulsive stimuli (ECS) raise NPY-LI in the hippocampus. These findings suggest that NPY is involved in depressive disorder and that antidepressant effects of ECS may in part be mediated through NPY. Also, the hippocampus has been implicated in the regulation of anxiety and memory processes and low concentrations of SP-LI and NKA-LI has been seen in rats with chronic ‘pain’. Possibly, this is compensated for by repeated electroacupuncture treatments.

That acupuncture activates the reward system is also strongly supported by recent animal studies in Japan. In animal experiments, the existence of a reward system was originally established with a self stimulation procedure. Electrodes were implanted into different brain areas and if the rats continued to
press a lever it was taken as a sign that that area of the brain reflected the presence of subjective pleasure and reward. Among the classical neurotransmitters with a suggested role in the reward system are serotonin (5-HT) and dopamine. The mesolimbic and mesocortical dopamine systems originate from the ventral tegmental area and project widely to different limbic and other brain structures involved in reward, including the nucleus accumbens and frontal cortex. Close concordances between the brain serotonin and the dopamine system exist. In the Japanese studies, the effects of electroacupuncture on serotonin and dopamine contents and their metabolites in the brain rewarding system were examined in restrained conscious rats. The results showed that electroacupuncture increased the serotonin and dopamine contents of the nucleus accumbens, caudate, putamen and lateral hypothalamus, and decreased the content of these monoamines in the dorsal raphe nucleus and amygdala. Differences in frequency effects (1Hz or 100Hz) on dopamine and serotonin were also reported. It was suggested that the effects of electroacupuncture compensated for the changes elicited by the restraint stress.

The results of the above studies are supported by studies of the human brain following acupuncture. Recently, Pariente and collaborators explored the cerebral consequences of needling and expectation with 'real' acupuncture, 'placebo control' acupuncture (Streitberger needle – non-penetrating, blunt telescopic needle) and skin prick (blunt needle), using a single blind, randomised crossover design with 14 patients suffering from painful osteoarthritis, who were scanned with positron emission tomography (PET). The three interventions, all of which were considered by the authors to be sub-optimal acupuncture treatment, did not modify the patients' pain. The insula ipsilateral to the site of stimulus was activated to a greater extent during real acupuncture than during the 'placebo control' intervention. Both 'real' and 'placebo control' acupuncture with the same expectation of effect caused greater activation than skin prick (which had no expectation of a therapeutic effect) in the right dorsolateral prefrontal cortex, anterior cingulate cortex, and midbrain. These results suggest that 'real' acupuncture and 'placebo control' acupuncture have specific physiological effects and that patients' expectation and belief regarding a potentially beneficial treatment modulate activity in component areas of the reward system. That 'placebo control' acupuncture may have a physiological effect is supported by recent studies showing that stimulation of skin mechanoreceptors coupled to C unmyelinated afferents result in activity in the insular region. Activity in these C tactile afferents has been implicated in a limbic reward response. It is likely that control procedures used in many acupuncture studies (superficial or minimal needling) aimed at being inert are in fact activating these C tactile afferents and consequently are not inert. These 'control procedures' probably activate the reward system and induce feelings of wellbeing.

Further studies are needed to explore the basis of acupuncture treatment reward or reinforcement (that may be delayed or uncertain), in implicit or procedural (stimulus-response) representational systems and in explicit or declarative (action-outcome-value) representational systems. Individual differences in sensitivity to delays and uncertainty may contribute to the variable responses to acupuncture. Learning (attributing a meaning) and choice (preference) with delayed and uncertain reinforcement (in this case pain alleviation) are related but in some cases dissociable processes. The contributions to 'delay discounting' and 'uncertainty discounting' of neuromodulators including serotonin, dopamine, and noradrenaline, and of specific neural structures including the nucleus accumbens, orbitofrontal cortex, amygdala, cingulate cortex, prefrontal cortex, insula, subthalamic nucleus, and hippocampus have recently been reviewed.

In conclusion, the results of current research suggest that acupuncture techniques as well as non-penetrating 'placebo controls' activate the patients' expectation and belief regarding a potentially beneficial treatment thereby modulating activity in the reward system. These mechanisms are in addition to the well known analgesic effects of acupuncture.

Summary points

- Acupuncture is known to produce a cascade of physiological effects in the body
- Some of its effects may be due to its effects on the limbic system
- These effects are pleasurable and involve the body’s reward system
Mechanisms

Reference list