Introduction

The 'magic' of acupuncture is that it can be used to treat many different symptoms of different aetiologies. Although there is robust evidence supporting acupuncture in comparison with other treatment strategies for some symptoms, its critics have attributed the reported and claimed effects to the patient's fantasy, i.e. placebo. Also, the state of induced placebo has been shown to be effective in many different conditions and to activate different areas in the brain depending on the expected effects. Expectation and conditioning are supposed to be the two main psychological mechanisms for inducing a placebo response. It has been demonstrated that prior positive experience plays a key role in maximising both behavioural and neurophysiological placebo responses, emphasising that the placebo effect is a learning phenomenon, which also affects the early central nociceptive processing. Clearly, expectancy as a part of the placebo effect has been reported to be one of the main factors accounting for a positive outcome in studies evaluating the effect of acupuncture treatment for pain relief. Furthermore, it has been shown that expectancy of pain relief may activate similar areas of the brain to acupuncture induced pain relief itself.

So is the clinical effect of acupuncture then merely an effect of placebo, i.e. expectancy and/or conditioning?

Observations from clinical trials

Eight patients referred to and included in a combined tinnitus and pain management programme were, for practical reasons (i.e. availability of acupuncturists during holidays, interfering with the treatment time schedule), given a course of acupuncture treatment before they started the programme, whereas 12 patients were given the acupuncture treatments during
the actual tinnitus and pain management programme. When assessing the outcome of the programme three months later, the patients who had received the acupuncture treatments first reported that their tinnitus and pain interfered less with their rated quality of life.

Furthermore, 16 patients with fibromyalgia syndrome were asked to rate their five worst symptoms associated with their pain intensity before starting a pain management programme. The patients complaining of pain and disturbed sleep (as one of their associated symptoms) were treated with a course of acupuncture and told that the last needle inserted was specifically aimed for the management of their sleep disturbance. After the end of the treatment sessions the patients were again asked to rate their pain and the five associated symptoms. From their reports it was obvious that acupuncture alleviated their pain intensity and sleep disturbance but not the other four associated problems. Also, the improvement in sleep was even more marked than the reported reduction in perceived pain intensity.

Taken together, these results suggest that acupuncture potentiates the expectancy of an effect although this is probably only a part of the total treatment effect.\textsuperscript{9-11} In the first case all patients expected the tinnitus and pain management program would result in amelioration of perceived pain and tinnitus. When acupuncture was administered before the treatment programme there was a better effect than if the acupuncture treatment was given within the management programme. The patients suffering from fibromyalgia and treated with acupuncture reported that they expected that the acupuncture treatment would alleviate their pain as well as their sleeping problems (due to the ‘specific needle’) but not the other associated problems.

Expectations in general, as well as effects of acupuncture (with or without expectancy), are probably partly based on self relevant phenomena and self referential introspection and are furthermore dependent on two integrated networks: a ventral medial prefrontal cortex-paralimbic-limbic ‘affective’ pathway and a dorsal medial prefrontal cortex-cortical-hippocampal ‘cognitive’ pathway.\textsuperscript{12-15} Limbic structures are implicated in the reward system, and the activation or deactivation of limbic structures and/or modulation of the default mode may partly explain the effects of acupuncture.\textsuperscript{16} Also, long term effects may be attributed to changes in the cerebellar system related to the expectancy.\textsuperscript{16,17} Interestingly, the proximity to reward over successive trials is associated with increased activity of the medial frontal cortex regardless of the modality. This part of the brain has been shown to be involved in regulations of emotions,\textsuperscript{17-19} and to physicians (experts) who practise acupuncture, interpreted as a sign of empathy.

However, another interesting question is: is this effect of acupuncture true only for the treatment of tinnitus and pain?

In a series of studies on the effect of acupuncture in xerostomia it was found that the experience of dry mouth decreased significantly after acupuncture,\textsuperscript{20-21} an effect expected or ‘hoped for’ by most of the patients. Interestingly, some patients had no change in salivary flow but still reported a reduction in the perception of dry mouth. On the other hand, some patients who had an increased salivary flow, but no expectancy of an effect, still reported no change in the perception of their dry mouth problems.\textsuperscript{22}

These clinical observations also suggest that acupuncture may ‘condition’ an expected effect of amelioration of symptoms. Also, ‘merely’ a modulation of the physiological response (in this case increased salivary flow) does not have to be associated with the perception of being relieved of suffering. However, the patients who had the best effect were the ones that both had an increased salivary flow and reported a reduction in the perception of their dry mouth problem.\textsuperscript{22}

**Classical conditioning**

These clinical observations show similarities to the findings of the physiologist Ivan Petrovitch Pavlov,\textsuperscript{21,22} While investigating the causes of salivary secretions in the dog, he discovered a class of causes that he called psychic, since they were linked with perceiving food that normally created salivation. A temporary relationship was thereby recognised, between the secretory command and the cerebral site linked with an initially neutral stimulus that had become a signal of food. Pavlov dexterously created a coherent conceptual system that served as the basis for what he termed ‘conditional reflexes’. In 23 ‘lectures’ he summarised his views and retraced the fundamental issues explaining the main features of the purely
physiological cerebral command of behaviour. The Pavlovian system necessarily became, in the particular environment of its time, a kind of credo on physical-mental relationships based upon a generalised reflexology, not allowing any deviation, or any dissidence, or any concession to subjectivity. The notion of conditional reflex has persisted through time and possibly part of the objective effects of acupuncture (increased salivary flow) may be viewed in this perspective, whereas the subjective relief (decreased suffering from dry mouth) has been suggested to represent more complex affective and cognitive mechanisms of self appraisal, reward and learning.

**Extinction**

Through association, a large variety of stimuli acquire the property of signalling pleasant or aversive events. Pictures of a birthday party or of a terrorist attack may serve as cues to recall these events and/or others of a similar nature or emotional tone. Presentation of the cues disassociated with the events, particularly if repeated, reduces the tendency to retrieve the original learning based on that association. This attenuation of the expression of a learned response was termed ‘extinction’ by Pavlov. It has been shown that extinction is a new learning based on a new link formed by the cues and the absence of the original event(s) which originated the first association. Extinction does not consist of the erasure of the original memory, but of an inhibition of its retrieval; the original response reappears readily if the former association is reiterated, or if enough time is allowed to pass (spontaneous recovery). Extinction requires neural activity, in the ventromedial prefrontal cortex and/or basolateral amygdala, hippocampus, entorhinal cortex and eventually other areas. The site or sites of extinction vary with the task. Furthermore, extinction was advocated by Freud in the 1920s for the treatment of phobias, and is still used in cognitive therapy to treat diseases that rely on conditioned fear (phobias, panic, and particularly posttraumatic stress disorder). The treatment of learned fear disorders with medications is still unsatisfactory although some have been shown useful when used as adjuncts to behavioural therapy. Interestingly, in a pilot study, acupuncture has been shown to be effective in posttraumatic stress disorder. This would suggest that acupuncture can be used to induce a ‘neural’ activity resulting in Pavlovian extinction.

Remote ischaemic preconditioning (RIPC) represents a strategy for harnessing the body’s endogenous protective capabilities against the injury incurred by ischaemia and reperfusion. It describes a phenomenon in which non-lethal transient ischaemia and reperfusion of one organ or tissue confers resistance to a subsequent episode of lethal ischaemia reperfusion injury in a remote organ or tissue. In its original conception, it described intramyocardial protection, which could be relayed from the myocardium served by one coronary artery to another. It soon became apparent that myocardial infarct size could be dramatically reduced by applying brief ischaemia and reperfusion to an organ or tissue remote from the heart before the onset of myocardial infarction. The concept of remote organ protection has now been extended beyond that of solely protecting the heart to providing a general form of inter-organ protection against ischaemia-reperfusion injury. Interestingly, preconditioning stimuli tested to date also include a number of mildly noxious factors applied either locally to the myocardium or systemically. Possibly, acupuncture, inducing *de qi*, may be one such factor.

**Conclusions**

We suggest that acupuncture treatments may partly be regarded and used as an intervention that preconditions expectancy, resulting in both ‘conditional reflexes’ and conditioning of expected ‘reward’ and ‘self appraisal’. Conditioning and expectancy are the two mechanisms most associated with the placebo response. However, they are not the only psychological mechanisms involved in non-active therapeutic interactions. For example, there are therapist effects and also effects of motivation. The motivation effects are particularly germane to our arguments concerning the effects of acupuncture on the reward systems, ie satisfaction of motivation is rewarding. Possibly acupuncture may be used to precondition motivation as well as functions relating to well being and *allostasis* (restoration of equilibrium after a challenge) including immune functions. Acupuncture may also be used as a neural stimulus that triggers Pavlovian extinction. If so, acupuncture should preferably be applied before the start of (not during) any or possibly all specific
treatment (ie which has an intention of being specific) to enhance the specific and non-specific effects, as well as a tool for extinction of unpleasant associations like pain or anxiety.\textsuperscript{5,6,15}

**Conflict of interest**

TL chairs the not-for-profit charity ‘The Foundation of Acupuncture and Alternative Biological Treatment Methods’ which has received grants from AKAB Utbildning AB to support acupuncture research. IL has declared no conflict of interest.

**Reference list**

1. An Introduction to Acupuncture. Website for National Center has declared no conflict of interest. www.acupunctureinmedicine.org.uk/volindex.php


Acupuncture for preconditioning of expectancy and/or Pavlovian extinction

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