

114. Cheng N 1982 The effects of electric currents of ATP generation, protein synthesis, and membrane transport in rat skin. *Clinical Orthopaedics and Related Research* 171: 264-272
115. Reid B L 1986 Propagation of properties of chemical reactions over long distance in the atmosphere as seen by crystal growth pattern changes. *Australian Journal of Medical Laboratory Science* 7 (Feb): 30-35
116. Sydney University News 18(22), 1986
117. Reid B L 1985 The causation of cervical cancer (Parts 1 and 2). *Clinics in Obstetrics and Gynaecology* 12(1): 1-32
118. Taubes G 1986 An electrifying possibility. *Discoverer*, April: p22-37
119. Rein G 1985 Corona discharge photography of human breast tumour biopsies. *Acupuncture and Electrotherapeutics Research* 10: 305-308
120. Payne B 1984 A new device which detects and measures an energy field around the human body. *American Journal of Acupuncture* 11(4): 353-358
121. Prince J P 1983 Further experience with low strength magnets applied to EAV acupuncture points. *American Journal of Acupuncture* 11(3): 249-254
122. Schuldt H 1978 Body potential and electroacupuncture in amputation pains and internal organ functions. *American Journal of Acupuncture* 6(2): 103-106.
123. Hsu M, Fong C 1978 The biomagnetic effect: its application in acupuncture therapy. *American Journal of Acupuncture* 4(6): 289-296
124. Rose-Neil S 1979 *Acupuncture and the life energies*. ASI Publishers, New York
125. Kleinkort J A, Foley R A 1984 Laser acupuncture: its use in physical therapy. *American Journal of Acupuncture* 12(1): 51-56
126. Zalesskiy V N, Belousova I A, Frolov G V 1983 Laser acupuncture reduces cigarette smoking. *Acupuncture and Electrotherapeutics Research* 8: 297-302
127. Trelles M A, Rotinen S 1983 He/Ne laser treatment of haemorrhoids. *Acupuncture and Electrotherapeutics Research* 8: 289-295
128. Tang H, Fu Y D 1981 Helium-Neon laser irradiation of acupuncture points in treatment of 50 cases of acute appendicitis. *Journal of Traditional Chinese Medicine* 1(1): 43-44
129. Olson J E, Schimmerling W, Tobias C A 1981 Laser action spectrum of reduced excitability in nerve cells. *Brain Research* 204: 436-440
130. Uzdensky A B 1982 On selectivity and locality of the effects of laser microirradiation of cells. *Cytology* 24(10): 1110-1133
131. Simon J, Guiraud G, Esquerre J P, Lazorthes Y, Guiraud R 1988 Acupuncture meridians demystified. Contribution of radiotracer methodology. *Presse Medicale* 17(26): 1341-1344

FURTHER READING

- Hu X, Wu B, You Z et al 1986 Preliminary analysis of the mechanism underlying the phenomenon of channel blocking. *Journal of Traditional Chinese Medicine* 6(4): 289-296
- Baker D W 1984 An introduction to the theory and practice of German EA and accompanying medications. *American Journal of Acupuncture* 12(4): 327-332
- Brown M L, Ulett G A, Stern J A 1974 Acupuncture loci: techniques for location. *American Journal of Chinese Medicine* 2(1): 67-74
- Schuldt H 1981 The application of nosodes in EAV. *American Journal of Acupuncture* 9(2): 161-164

NB!

4. Paradigms of the biomedical action of acupuncture

If any distinctive theme pervades research on acupuncture it is the attempt to fit this elusive therapy into western biomedical paradigms. Acupuncture initially met with disbelief amidst cries of 'placebo' and 'hypnosis', but this response has been gradually superseded by the neurological paradigm. However, despite the scale of recent research, suggestions that placebo and hypnosis are the beginning and end of acupuncture still exist.¹

The neurological paradigm conceives of acupuncture working through mechanical nerve contact, with all influences transmitted via neural pathways. This view initially took form in Melzack and Wall's 'gate control theory' in 1965 (see Ch. 5). It subsequently prompted the attention of sympathetic researchers whose work aimed at confirming the hypothesis that acupuncture only operated within dermatomal regions, and thereby endorsed the principles of the gate control theory as originally presented. In 1973 Chinese investigators found that there existed a significant humoral component during acupuncture therapy.² This once again led to a wave of research in the West, with experiments on endocrine and blood changes. An appropriate paradigm shift followed to incorporate the concept that therapy was at least partly a result of humoral influences.

Another theme seems to be an attempt to remain as true as possible to the concept of 'Qi', however interpreted.³ This line of investigation explores the bioelectric phenomena of the channels and points, and even the possible ways in which the neural or humoral response might occur as a result of initial bioelectric influences. The thesis is still limited to certain scientific circles in Eastern Europe, Asia and some Scandinavian countries.

So many paradigm shifts in such a short span of investigation suggests a fertile approach to research. However, even a cursory look at the changes in direction indicates that these rapid shifts stem more from initial lack of knowledge, and better awareness later, of the nature and characteristics of acupuncture therapy. For example, Melzack's gate control theory was developed initially with only a spinal gate in mind. However, traditional teaching about acupuncture points includes far more than a segmental neural response. To the Chinese empiricist, the early gate control theory was incomplete. This also happened with research that confined acupuncture to dermatomal influences, or limited it to the concept of a double gate theory, and so on.

Information regarding the nature and characteristics of acupuncture therapy is not new to this decade, and has existed for hundreds of years, but research questions regularly fail to incorporate this knowledge.

The distinct neurological and humoral models mentioned above, rapidly blended to form a more generalised 'neurohumoral' paradigm, and researchers have emphasised either the humoral or neural aspects of this paradigm to suit their needs. The weight placed on the neurohumoral thesis by researchers is a reminder of the one-dimensional thinking predominant in the West. The acceptance of the neurohumoral theory can be accounted for if we examine history.

President Nixon's trip to China in 1972 brought to the West a glimpse of acupuncture in action—surgery carried out under acupuncture anaesthesia. That highly impressed Nixon's entourage of doctors. In the eyes of the West it represented the pinnacle of success for acupuncture. As surgical anaesthesia was the issue, no great conceptual leaps were required to see that it was the result of neural interference that was being observed. Investigators already had their sights directed—acupuncture must affect nerve pathways. These beginnings still influence most research.

Yet the neurohumoral paradigm falls short in its ability to explain some aspects of acupuncture. It has failed to address the importance of point specificity, a case that has been clearly represented by the work of Takeshige and others.^{4,5} There is no reason contained within the neurohumoral hypothesis as to why acupuncture works well at a particular locus or possesses specific therapeutic indications there, yet may induce a negligible change just one centimetre away, although the sham locus still is within the same area of nerve distribution. The sham locus may even be richer in blood vessels and nerve distribution.

Other than a handful of researchers exploring the concepts of neurohumoral mediators, few have tackled the relationship between 'Qi sensation' and the value of treatment. This is no small aspect of acupuncture therapy. Appropriate 'Qi sensation' is closely correlated to the success of acupuncture. This has also been verified experimentally.^{6,7} Differences in the skill of the practitioner also warrant attention, especially in the light of the large number of current studies that do not acknowledge the importance of needling experience.

Despite these drawbacks there is considerable sophistication in neurohumoral research into acupuncture (as will shortly become evident) but to suggest that we have arrived at an acceptable 'mechanism of action' is premature. The ultimate measure of the credibility of any scientific model lies in its ability to predict consequences of experimental or natural situations. The neurohumoral model lacks the ability to specify the use of any points for particular diseases. On the other hand the Chinese have had available a theory providing guidance on treatment for thousands of years (for example, 5 Phase (Element) theory defines the functions of the Antique-Shu points). The inability to correlate the needling of specific acupuncture loci with results is the most significant shortfall of the neurohumoral concept.

Current western medical research, it appears, has been more fruitful in accounting for the gamut of effects brought about by acupuncture therapy than predicting the result of its application. Many theories are on offer, and most explain the treatment of specific diseases.^{8,9} No one theory is capable of accounting for the broad effects of acupuncture and but few theoretical proposals can be discarded completely.

The success of acupuncture therapy has all too often been dismissed as the result of either placebo, hypnosis, stress analgesia, or ethnic differences. None account for the variety of success acupuncture has and it is worthwhile illustrating some of the relevant research which should have buried these theories.

Acupuncture therapy has an outstanding record of clinical effectiveness. It has succeeded in some cases where all other therapies have failed. This ancient medical procedure does require more thorough explanation, but this should not be a barrier to its adoption in the western health care system. Research, however, needs to be directed more clearly to define the limitations of acupuncture technique and produce guidelines that act more successfully as predictors of its efficacy. There is very little information to date on this.

The placebo effect

A placebo factor does exist in acupuncture just as with all types of medical intervention. However acupuncture offers more than simply a placebo response. This is endorsed by many experiments which have attempted to measure the placebo effect by of stimulating nonpoints.^{4,5,10,11,12,13} Many investigators exploring analgesia or other physiological responses have used nonpoint acupuncture on control groups to calculate the effective placebo. Other experiments involved needling real points without giving electrostimulation,^{14,15} needling real points that were inappropriate to the treatment,¹⁶ attachment of inert surface electrodes,¹⁷ holding down experimental animals, or even carrying out double blind studies where the practitioner himself did not know the value of the chosen points.^{11,14,18} The majority of this research significantly endorses the value of true acupuncture over sham, with the real acupuncture groups responding markedly better.

Takeshige^{4,5} in 1983 and 1985 confirmed some earlier work¹⁰ to conclude that stimulation of correct acupuncture points is imperative to cause significant acupuncture analgesia, while nonpoint stimulation causes insignificant analgesia, which is also different in nature. He went on to illustrate that acupuncture analgesia differs from nonacupuncture analgesia, (that is, acupuncture stimulation but not at an actual acupuncture point), in several ways⁴:

Acupuncture analgesia:

1. lasts for a long time after cessation of stimulation (aftereffect),
2. exhibits individual variation in effectiveness, and
3. is completely blocked by naloxone, but not by dexamethasone (a glucocorticoid).

On the other hand...non-acupuncture analgesia:

1. decreases gradually after a definite time during stimulation,
2. has no individual variation in effectiveness, and
3. is blocked by dexamethasone but not by naloxone. (p 323)

As chemical nerve inhibitors are capable of distinguishing between acupuncture and nonacupuncture treatments, there must exist differing pharmacological, and therefore neurological, pathways. Although Takeshige found the descending pain inhibitory system to be the same for real and placebo treatment, the afferent pathways differed. The weight given to the placebo effect is certainly diminished in the light of experiments that indicate the importance of needling real loci. But there is other evidence to undermine the placebo claim (as the only effect of acupuncture).

With repeated use a placebo becomes less effective, in contrast to acupuncture therapy. It is generally observed in China and elsewhere that greater frequency of acupuncture treatment only improves the result. (Some experiments repeat treatment until a certain pattern of response has been obtained and the placebo effect thereby diminished. Data uncontaminated by the placebo effect is then collected).¹⁹ Furthermore a placebo is not likely to work when no relief has been obtained with many other forms of therapy, a stage most western patients have reached by the time they opt for acupuncture. This is especially so if morphine and other analogues have already been tried and proved unsuccessful. Natural opiates have been shown to be involved in placebo analgesic responses, however they are not likely to exhibit much potency during acupuncture if the morphine analogues were ineffective in earlier therapy.

There are other inconsistencies. Experimenters in Shanghai have shown that needling on a limb where circulation has been occluded results in the same pain threshold rise as needling without occlusion of circulation, a fact which does not fit the concept of placebo analgesia.² The whole field of veterinary acupuncture also sheds considerable doubt on the validity of the placebo, as animals are not likely to be aware of the positive purpose of needle insertion, although no doubt stress responses warrant consideration here.

Claims have been made that the exotic nature of acupuncture acts strongly in its favour to produce a placebo response, however, as Kaptchuk has already argued, this is hardly likely in the case of the Chinese where results using their home medicine are no less effective than other forms of therapy, and if anything only reflect a greater expertise than in the West due to the quality of experience and training.²⁰

Placebo acupuncture can at least in part induce a release of endogenous opiates and hence influence analgesia, drug withdrawal, and other disorders to some degree.^{21,22} It would appear sensible to incorporate as baseline in future clinical studies the placebo effect and distinguish it from pure acupuncture results, a suggestion already proposed by Joseph Needham.²³ (p 261) Individual differences in experimental subjects may prove this too complex

an option, in which case acupuncturing nonpoints or inappropriate acupuncture points would represent a satisfactory form of control.

Finally, many other characteristics peculiar to acupuncture need to be borne in mind. In placebo acupuncture it should not matter what point is needled on the surface of the body, all having a relatively equivalent influence. Yet the very fact that acupuncture loci are electrically definable, as mentioned in Chapter 3, emphasises the importance of meridian theory. As such it not be surprising that needling an identifiable point would achieve a more specific result than needling a random point on the skin. Similarly, different frequencies of stimulation or manual manipulation techniques produce different results, a fact not easily reconcilable with a placebo effect. Furthermore, over 20 neurotransmitters have been found to be involved in the acupuncture effect, including many hormone substances.

And so the evidence mounts. Clearly placebo has an influence but is far from the full picture. Clinical studies that still make such claims need to be scrutinised very closely as regards their definitions and techniques, and ultimately, whether true acupuncture was performed.

Hypnosis

Most of the issues raised with the placebo concept could be raised again in the context of hypnosis, although the majority of work here has focussed on comparing hypnotic analgesia to acupuncture analgesia. There is a multitude of observations that really do not lend much support to the hypnosis hypothesis. But one of the most powerful arguments is that whilst acupuncture analgesia is reversible by naloxone, hypnotic analgesia is not, indicating that a different mechanism is operating.²⁴ Different states of awareness of the patient are also exhibited.

Many mediators, (neurotransmitters in particular), are engaged more fully during acupuncture than hypnosis, and the efficacy of acupuncture shows a close correlation with the release of these mediators. Surgery under hypnotic analgesia is considered viable in 10% to 14% of the population, in contrast to acupuncture anaesthesia, which may be workable in as much as 80% to 90% of the population.²³ (p 239) The significance of this is that there is 70% of population for whom acupuncture analgesia works, yet hypnotic analgesia does not.

Animals, children and babies can be treated successfully with acupuncture but are not easily hypnotised.^{25,26,27} At the Beijing Children's Hospital acupuncture analgesia has been used on children from 4 months to 14 years old with good success. Although some operations were easier than others, the overall effectiveness was claimed to be approximately 80%.²⁸

On the other hand, work by Knox and Shum found that patients who are more susceptible to hypnotism are also more likely to be responsive to acupuncture, which suggests at least some common mechanisms.²⁴ In contrast

other researchers have found that the degree of susceptibility in different individuals had nothing to do with the effect of acupuncture analgesia.²⁹

Stress analgesia

It has long been established that the application of a variety of noxious and/or stressful manipulations result in the development of analgesia, both opiate and nonopiate.^{30,31,32} The whole domain of physiological pain relieving systems is vast. Multiple analgesic systems exist, including the opiates and nonopiates, and each system may be called into action dependent upon the variables of stimulation, such as region,⁴ duration, frequency^{33,34} and intensity.^{35,36}

Obviously the question arises as to how much of acupuncture therapy or, more specifically, analgesia, is a result of stressful intervention? Despite the amount of conflicting information in stress induced analgesia and acupuncture research, some specific and consistent observations may be selected and highlighted in order to illustrate the difference between the two.

Zhang Anzhong (1980)³⁷ and Bruce Pomeranz (1986)³⁸ are two of the only investigators who attempt to address this question thoroughly. In brief, Pomeranz points out that:

1. Sham acupuncture (needles placed in nonacupuncture points) fails to produce analgesia whereas true acupuncture (needles placed in true points designated by Chinese atlases) produces analgesia in awake animals³⁹ and human subjects.⁴⁰ Both sham and true acupuncture produce the same amount of stress. (Similar work was also performed by Takeshige.⁵)
2. Electroacupuncture given at three different frequencies in awake rodents produces different effects, yet all three should be equally stressful. At 0.2 Hz no analgesia was observed.⁴¹ At 4 Hz there is an analgesia mediated by endorphins.^{39,41} At 200 Hz there is an analgesia mediated by serotonin.⁴² Similar results have been observed in humans.³³
3. Acupuncture in awake horses releases cortisol. However sham acupuncture has no cortisol effect even though it should be equally stressful.⁴³
4. Finally, that acupuncture analgesia is targeted to specific painful sites. For example, stimulation of Hegu (Co 4) produces analgesia of the face and neck, but not of the lower extremities.⁴⁴ Stress induced analgesia should produce analgesia over the entire body equally in a fight or flight response. (p 444)

Zhang also mentions a plethora of observations that distinguish acupuncture analgesia from stress induced analgesia. For example, in one experiment assessing the effect of naloxone on acupuncture analgesia produced by different strengths of electrostimulation, it was observed in rabbits that under weak intensity stimulation the plasma cortisol and cAMP levels were normal or low, and that the analgesic response could be reversed by naloxone.⁴⁵ However, under stronger stimulation the animals struggled, the plasma cortisol and cAMP rose, and the analgesia was not reversed by naloxone. From this experiment it could be concluded that the mechanism of stress analgesia, that is, the stronger stimulation which causes the animals to struggle,

differs from moderate strength acupuncture, where the analgesia is partially a result of the activity of opiate receptors.

Zhang, summarising some of the recent Chinese literature makes the following claims³⁷:

1. Acupuncture analgesia (AA) is naloxone reversible, but stress analgesia (SA) is not. Some authors have reported that SA could be partially antagonised by large doses of naloxone, twenty times higher than that for reversing AA, thus suggesting that even if there are endorphin factors involved in SA, they might act on different opiate binding sites.
2. During AA, plasma cAMP level decreases and plasma cortisol level remains normal both in human beings and rabbits; but these two biochemical indices markedly increase during SA.
3. The central grey is essential for the AA effect, but not for SA.
4. Using radioimmunoassay, it was found that changes of enkephalins content during AA are quite different from that during SA.
5. Dorsolateral spinal cord lesions eliminated AA but not SA, which could be abolished by spinal transverse dissection, suggesting that the descending pathway essential for AA is different from that for SA. (p 143)

There seems little doubt that acupuncture treatment adds up to much more than a stress response.

Medical anthropologists have explored cultural components related to pain and have gone so far as to measure the response between some ethnic groups. Zborowski⁴⁶, and Josey and Miller⁴⁷ all found that cultural origin was significant in any individual's tolerance to pain.^{23(p236),48} Other fascinating research is reported in textbooks of medical anthropology, where it is illustrated that culture determines the very nature of complaints and symptoms that are expressed by a patient.⁴⁹ For example, Jenyi Wang details the somatization of symptoms in Chinese culture as a means of circumventing cultural inhibitions of presenting with emotional or psychological disorders.⁵⁰ In the context of pain sensitivity and acupuncture, these findings are further endorsed by studies on genetic variations in animals. Peets and Pomeranz observed that a specific breed of mice, deficient in opiate receptors, were not as responsive to acupuncture analgesia, and concluded that 'presumably some patients might be genetically more susceptible to acupuncture than others.'⁵¹ Interestingly enough such genetic variations were also noticeable in the context of stress induced analgesia.⁵²

Hence it may prove fruitful for medical anthropologists and researchers to explore further the ethnic and cultural complexities of acupuncture.

THE NEUROHUMORAL PARADIGM

Research into what mediates the acupuncture effect has directed our attention into three broad areas:

1. *Neural mediation* which incorporates the concept that nerve fibres carry and transmit the acupuncture and is confirmed largely by experiments which test the acupuncture influence after denervation in the region of

needling, nerve section, or interference with neural transmission of the acupuncture impulse:

2. *Humoral mediation* which includes communication of the acupuncture effect via the circulation of neurotransmitters and other hormones in the blood stream and cerebrospinal fluid; and
3. *Bioelectric mediation* which is a theory that maintains that the meridians are electrically distinct and that changes in them act as precursors to neurological and humoral responses.

In this section I will address the research relating to the first two areas only. A preference for adopting the concept of either neural or humoral mediation depends largely on the physiological context being explored. For example, if investigating the acupuncture treatment of an endocrine disorder, it would be sensible to begin with measurements of blood hormone changes subsequent to treatment. On the other hand, when exploring the analgesic responses to acupuncture, it is a logical step to consider the role of nerve distribution and interaction of neural impulses. However, the predominance of either neurological or humoral influences is difficult to gauge and their perceived relevance to any disease is largely dependent upon the medical models of the time. Richard Bergland explores this cogently in his recent publication *The Fabric of Mind*.⁵³ He presents a strong case for discarding the antiquated paradigm of the brain as a dry electrical organ operating like a computer. Instead Bergland proposes that the brain behaves more like a gland in the way it releases, and is influenced by, hormones. Hormonal codes may travel to and from the brain, and the brain, therefore, shares influence with all parts of the body. The process of thinking, which in the past has been considered strictly neurological, is a consequence of hormonal action not only in the brain but all over the body.

If we relate Bergland's concept back to the range of influences produced by acupuncture, it is not difficult to conceptualise acupuncture as a technique which orchestrates hormonal symphonies. Despite the significant overlap between the domains of neurological and hormonal influences, the concept of a harmonious 'symphony' may be a helpful tool in understanding how acupuncture works. But first we should turn our attention more to research that defines the neurological mechanisms behind acupuncture.

Neural mediation

Modern neuroanatomical knowledge relates in distinct ways to the acupuncture system. The existence of referred pain, trigger points, and somatovisceral reflexes, all linked into the theory of dermatomes, is significant as evidence of the connection of cutaneous areas of the body with the viscera. It also suggests the possible neural pathways of the acupuncture model, as somatic stimulation, at least at a segmental level, may be able to treat visceral disorders. That

the Chinese were aware of these possibilities early in their investigations is substantiated by the many experiments that monitor visceral responses to the acupuncture stimulation of cutaneous areas of the body.^{23(p 209)54,55}

However, comparative studies by various researchers on the role of Lissauer's tract and intersegmental reflexes provide evidence that dermatomes are flexible in their boundaries and associated segmental spinal levels^{56,113} Furthermore, actual clinical experience of acupuncture therapy indicates that treatment responses, analgesic or otherwise, are not restricted to operating within segmental, or neighbouring segmental, levels, contrary to the conclusion propounded by many researchers including Needham and Lu²³ and MacDonald.⁵⁶

In acupuncture analgesia it has become more and more evident that the needles must be placed in the same dermatome as the surgical intervention. (Needham and Lu, p 207)

The insertion of the acupuncture needles in the region (painful area) or others sharing the same segmental supply is more likely to produce a beneficial effect with less stimulation than inserting them elsewhere. (McDonald, p 278)

The use of Hegu (Co 4) for dental analgesia could be forced into this restricted segmental concept. The use of other points, however, such as Guangming (GB 37) for eye diseases, or Houxi (SI 3) for low back pain, and the ear points Lung and Shenmen as the most successful for chest analgesia⁵⁷ are some of the evidence that does not support the segmental spinal concept as the principal neuroanatomical pathway involved in the acupuncture response.

Acupuncture analgesia is effective on the head and the face and areas which are not supplied by any segmental spinal nerve, hence the inhibitory effect of acupuncture must be possible at different levels of the central nervous system, such as the spinal cord, brainstem, and limbic system. This helps explain anomalies regarding point selection that are puzzling in the light of dermatome theory.

There appears little doubt that an intact functioning nervous system is required at all times for acupuncture to induce analgesia, or, for that matter, any physiological changes in the subject. Specifically, section of the principal nerve innervating a region will result in placement of the acupuncture stimulus there having no effect whatsoever.

Studies in Nanjing found that if rabbit limbs were denervated by removal of the femoral and sciatic nerves prior to needling, no analgesic effect would be observed.⁵⁸ Similar results were also obtained in Pennsylvania.^{25,59} Nerve sections are also responsible for obstructing the more general physiological effects of acupuncture. For example, Needham reports on some interesting personal observations of experiments in Shanghai.²³ In these studies, which concerned experimental appendicitis in dogs, he states:

The tip of the caecum was tied off and a mixed culture of staphylococci and streptococci injected into it; then acupuncture treatment was given, and the tissues of both treated and control animals removed for histological analysis on the fourth day. Inflammation was very heavy in the latter and light to medium in the former. Particularly interesting

was the fact that if the dorsal sympathetic ganglia and the trunk with its roots was cut on both sides between the 5th and 12th segments the protective function of the acupuncture was completely inhibited. (p 202)

Approaching from a different perspective, it is apparent that interference with circulation does not prevent the analgesic effect of acupuncture. Shanghai physiologists Chiang and colleagues illustrated that vascular occlusion of the upper limb in a group of volunteers did not stop acupuncture induced analgesia.² Needling an acupuncture locus on the hand below the level of the vascular occlusion (with a tourniquet) still induced the same analgesic response (as measured by rise in pain threshold) at a distant target site.

After introducing local anaesthetic both deeply and cutaneously, these physiologists also concluded that the deep, as opposed to superficial, nerve receptors were responsible for transmission of the acupuncture stimulus. It appeared that the afferent impulses for acupuncture analgesia are transmitted mainly via the deep nerves. It is also worthwhile noting that the superficial nerve block did not inhibit the Qi sensation either, whilst the deep block did.

Certain experiments performed on cats in Nanjing Medical College involved the bilateral transection of the dorsal and lateral funiculi to observe the role of these nerve tracts in transmission of the analgesic effect of acupuncture.⁵⁸ Transection below the spinal level of incoming acupuncture impulses brought no change, whilst transection above did. It was found that the central afferent pathway in acupuncture analgesia follows the lateral funiculus of the spinal cord, particularly the anterolateral part, (otherwise commonly known as the spinothalamic tract, although also includes the spinoreticular tract).⁶⁰ Transection of the dorsal funiculus (lemniscal pathway), on the other hand, appeared to have no significant effect on acupuncture analgesia. This was also confirmed by Levy and Matsumoto who claimed that the lemniscal system is not strongly involved, if only because the animal's proprioceptive function seems unaltered with acupuncture analgesia.²⁵

We are already beginning to touch on the general concepts of afferent and efferent inhibition of pain signals by acupuncture. Afferent inhibition of pain refers to the modulation of pain information as a consequence of the interaction of ascending impulses from the site of pain with those due to stimulation from the acupuncture point. This afferent interaction may occur at various levels of the central nervous system with the result of diminution of the pain sensation. Efferent inhibition, on the other hand, refers to acupuncture analgesia brought about as a direct consequence of the influence of descending neural pathways on the ascending (afferent) pain impulses. Both afferent and efferent inhibition have a role to play in the management of pain, and therefore it is likely that they are also involved in other physiological responses to acupuncture.

Afferent impulses arising from the site of pain may interact at various levels of the central nervous system with those impulses derived from the point of acupuncture. That is, inhibitory gates are possible at different levels of the neuroaxis, resulting in the modulation of pain information. Chang Hsiangtung illustrated that this inhibition may occur in the thalamus, specifically in the nucleus parafascicularis and the nucleus centralis lateralis⁶¹:

Experiments performed in albino rats and rabbits showed that certain neurons in nucleus parafascicularis (Pf) and also nucleus centralis lateralis (CL) of thalamus could give rise to characteristic unit discharges in response to nocuous stimuli, and these discharges...were concerned with pain. Pain responses of the Pf and CL neurons could be inhibited by electrical needling of certain acupuncture points, squeezing the Achilles tendon or weak electrical stimulation of a sensory nerve. Too strong stimulation, however, tended to exaggerate the response to pain. (p 25)

Chang's experimentation further suggested that the efficacy of acupuncture for analgesia is determined mainly by the state of brain excitability. Similar work by Shen, Tshai and Lan illustrated that inhibitory gating actions are present in the brainstem.⁶² (see Ch. 5).

Acupuncture analgesia is also strengthened by descending or efferent inhibition. The pathway of descending inhibition appears to be located in the dorsolateral (corticospinal) portion of the spinal cord, transection of which may result in elimination or attenuation of the analgesic effect of acupuncture below the transected level.⁵⁸ As early as 1973, Anderson had concluded that the gradual onset and decline of the pain threshold implied the existence of a descending control system in electroacupuncture analgesia.⁶³

So far we have mainly discussed the mechanical severing of nerve pathways in order to test the subsequent potency of acupuncture. There are other tools which have been used to map the neurological action of needling. Chemical blockers may be introduced, for example, in the form of antagonists to particular neurotransmitters, and consequently obstruct neural pathways. As an example, naloxone, a morphine antagonist which takes up receptor sites to the natural opiate neurotransmitter substances in the body, when introduced subcutaneously or intrathecally, will suppress the analgesic effect caused by needling. This provides important evidence that the naturally occurring opiate like substances in the body, (neuropeptides such as endorphins and enkephalins), act as neurotransmitters in nerve pathways at least in the context of acupuncture analgesia.^{4,39,64}

At this stage it is worth clarifying the role of neurotransmitter substances and their receptor sites. Neurotransmitters act to communicate one neurone with another, to carry a signal on in a sequential fashion to its targeted region (see Fig. 4.1). Responding to the catalyst of a nerve signal impulse, neurotransmitters are released from the synaptic vesicles (contained in the pre-synaptic knob of Neurone 1), and travel across the synaptic cleft to take up receptor sites on the post-synaptic membranes, thereby exciting or inhibiting Neurone 2.

Each neurone produces and releases only one single type of neurotransmitter substance. These neurotransmitters will have a positive or negative modulating influence on the nerve impulse depending on the nature of the uptaking receptors. Note that Figure 4.1 illustrates a more complex involvement where Neurone 3 has a presynaptic influence on the normal Neurone 1 to 2 pathway. In this case an impulse travelling along Neurone 3 will cause a release of enkephalins which will in turn inhibit the release of acetylcholine (Ach) and thereby suppress the impulse travelling along from Neurone 1 to 2.

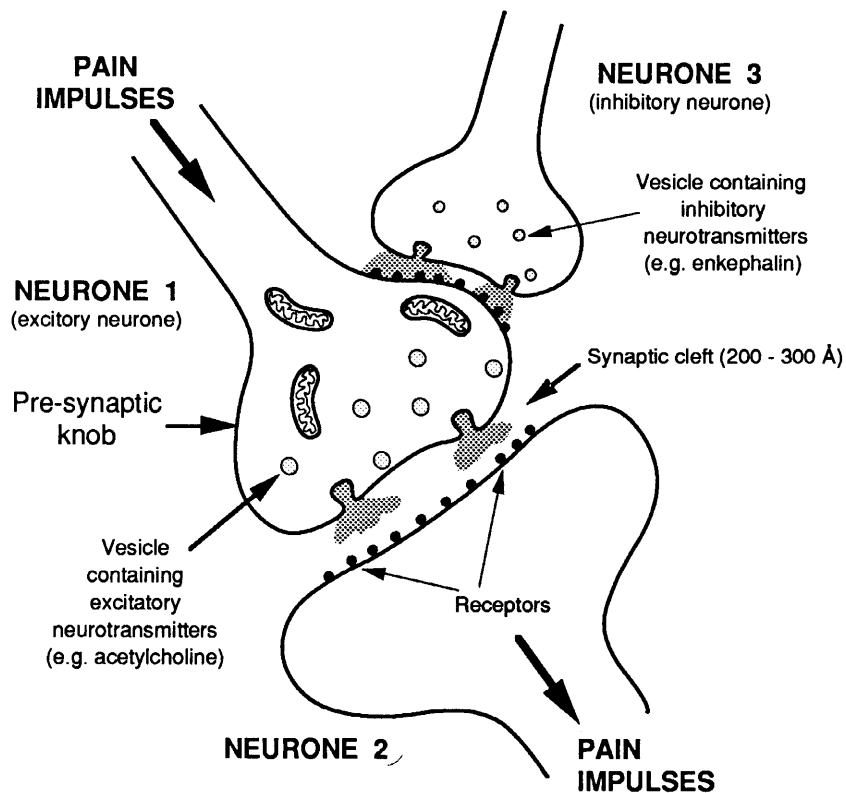


Fig 4.1 Schematic representation of pre-synaptic inhibition. Neurone 3, the inhibitory neurone, releases inhibitory neurotransmitters, such as enkephalin, which act to suppress the release of the excitatory transmitter from Neurone 1. This results in attenuation of the transmission of the pain impulse from Neurone 1 to Neurone 2.

Much work has also been done on the nature of opiate receptors with the resultant identification of multiple opiate receptors, some of which are specific to particular (groups of) neurotransmitters whilst others are influenced by a broader group of neuropeptides.^{65,66} Furthermore, these receptors are differentially distributed throughout the brain and central nervous system yet are ubiquitous in their influence.^{67,68}

There are approximately 50 different neurotransmitters which have been identified to date in humans.^{53 (p 104)} A large number of these have been determined to be involved in the mediation of the acupuncture effect. The box on page 90 contains a list of the majority of transmitter substances for which research data has positively established some role in acupuncture. The roles of many of these substances will become more explicit in Chapter 5.

It is apparent from the boxed information that many neuronal pathways are affected aside from those that adopt opiate like substances as their transmitters.

For example, in the case of allergic shock reaction, Mu Jian has shown, via the use of chemical antagonists, that the alpha and beta-2 adrenergic receptors are important sites of transmission of the acupuncture influence, an influence which significantly controls the death rate of the experimental animals.^{69,70} This suggests there may be a difference between mechanisms underlying the analgesic effect and those permitting a diminished allergic shock reaction.

In the latter case, adrenergic neurones, representing in principle the sympathetic nervous system, are called into action. However, at different times, yet quite significantly, the serotonergic, cholinergic and other pathways are also influenced. Many of these neurotransmitters also behave as hormones. Besides their role in the neurological context, they move about in the cerebrospinal fluid (CSF), and in some cases the bloodstream.

The fact that so many chemical substances have a role to play in maintaining communication between one neurone and another results in a drug vulnerability specifically at the synaptic sites. Introducing drugs that influence these sites is the experimental technique used to assess the importance of specific neurotransmitters during acupuncture. Our earlier example with naloxone illustrates its adoption as an antagonist to opiate neurotransmitters by preferentially taking up receptor sites usually reserved for endorphins and the like. Therefore communications along the original endorphinergic pathways are restricted.

Pomeranz and Mayer were amongst the first to implicate the involvement of endorphins in acupuncture by injection of naloxone.^{39,71} Pomeranz's work on mice was soon followed and confirmed by similar experiments in humans^{64,72,73}, cats⁷⁴, rats^{75,76}, rabbits^{73,77}, pigs and monkeys⁷⁸ and mice.³⁹

This produced a windfall of experiments in China and overseas during the late 1970s and early 1980s exploring precisely the role of endorphin and nonendorphin systems in acupuncture anaesthesia and the stereospecificity of the receptors involved. The result of much of this work confirmed the variability and complexity of neurotransmitters and receptors that participate not only in acupuncture anaesthesia, but also acupuncture therapy with any physiological outcome.⁷⁹ For example, Pomeranz, at the vanguard in much of this field, illustrated that the neurotransmitter predominantly involved is dependent upon the frequency of stimulation in the case of electroacupuncture.⁸⁰ These findings validated earlier work performed in various countries throughout the world,^{39,64,74,80} including the studies by Meg Patterson on the treatment of drug addiction.⁸¹ Pomeranz showed that acupuncture anaesthesia due to low frequency stimulation (4Hz) could be completely blocked by naloxone, however naloxone would have no inhibitory effect on acupuncture anaesthesia due to high frequency stimulation (200Hz). Conversely, parachlorophenylalanine, which is a serotonin synthesis inhibitor, reduces high frequency analgesia but produces no effect on low frequency electroacupuncture analgesia. Hence, it seems that electroacupuncture analgesia induced by low frequency stimulation is mediated by endorphins while high frequency stimulation is not endorphinergic but at least partly serotonergic.

Common neurotransmitters involved in acupuncture

Neurotransmitter	Major area of Influence
<i>Neuropeptides (opiate-like substances)</i>	
Endorphins	Each a different fraction of the lipoprotein/lipotropin substrate. Are found principally in the spinal cord and brain although are also present in the bloodstream. Alpha & beta-endorphins are found particularly in the pituitary. ⁶⁷ Beta-endorphins are found in the hypothalamus (especially) and rostral brain stem. ⁹⁷ Endorphins are 4 times more prevalent in the thalamus and hypothalamus than enkephalins and hence may have a more significant role to play in pain management with acupuncture. ⁶⁸ They are released after stress or painful stimuli. ⁹⁸ and are closely involved with emotional states.
Enkephalins (leu-enkephalin met-enkephalin)	Also responsible for presynaptic inhibition in brain. Highest concentrations in the globus pallidus, midbrain, PAG, hypothalamus and limbic areas. Are also found in the dorsal horns in small interneurons. Widely spread in low concentration in the central nervous system, but are rapidly inactivated by endorphins. ⁶⁷
Dynorphin A Dynorphin B	Dynorphin A and dynorphin B both operate as opioid peptides in the spinal cord. ^{27,110} Dynorphin B in the spinal cord of the rat may be important in mediating electroacupuncture analgesia. ¹⁰⁷
Substance P	Is present in substantia gelatinosa in spinal cord, and in brain. Its presence appears to inhibit acupuncture analgesia, however under other conditions it appears to have dual action. ⁹⁹ Experiments indicate that it many have an analgesic effect in the brain whilst promoting the pain stimulus in the spinal cord. ^{100,23(p 262),101,102}
Serotonin (5HT)	Is an inhibitory neurotransmitter which acts particularly in the raphe nuclei and thalamus. ¹⁰⁴ Concerned with functions such as pain, sleep, mood-elevation, aggression, appetite. Diminished serotonin levels have been associated with chronic depression and suicidal tendencies. ^{81 (p 264, p 146)}

Neurotransmitter	Major area of Influence
<i>Simple amino acids</i>	
Histamine	Content of histamine is highest in skin, lung and peripheral nervous tissue, but also exists in the brain. Its presence in the periphery appears to encourage the pain stimulus whilst in the brain it may play a role similar to morphine. ¹⁰³
<i>Bradykinin</i>	
Cholecystokinin (CCK)	Exists in brain and gut, and in substantia gelatinosa of spinal cord. Behaves as an endogenous anti-opiate, and acts to suppress acupuncture analgesia.
<i>Catecholamines</i>	
Adrenalin (epinephrine) noradrenalin (nor-epin)	Both are secreted by the medullary part of the adrenal gland and found throughout the brain and spinal cord. ^{67,81 (p 262)} Noradrenalin is also found in the N, habenula and the PAG. Noradrenalin in the brain is antagonistic to acupuncture analgesia, whilst in the spinal cord it mediates acupuncture analgesia. ^{69,70} Central noradrenalin exerts an antagonistic effect on AA via alpha-receptors and an augmentary effect via beta-receptors. ¹¹⁶
Dopamine	It is found in significant concentration in the basal nuclei of the brain. In inhibits the extrapyramidal system and inhibits acupuncture analgesia. ^{81 (p 259),116}
<i>Acetylcholine</i> (ACh)	Predominantly in the parasympathetic nervous system and behaves as an excitatory neurotransmitter. Acetylcholine is an important mediator of AA. ^{111,116}
<i>Other non-opiates</i>	
Somatostatin	Is released from the hypothalamus and prevents growth hormone release from the pituitary.
Luteinising hormone releasing hormone (LHRH)	
Thyrotropin-releasing hormone	
Gamma-amino-butyric acid (GABA)	Exists in many areas especially the spinal cord, cerebellum and cortex, with highest concentrations in the midbrain and thalamus. ^{23 (p 242)} It functions as an inhibitory neurotransmitter in all regions of the brain and spinal cord. It may

Neurotransmitter	Major area of Influence
	be related to anxiety states, and is deficient in several neuromuscular diseases. ⁸¹ (p 260) It is interesting that it appears to operate antagonistically to acupuncture analgesia. ^{108,112}
Adrenocorticotrophic hormone (ACTH)	Secreted by the pituitary gland to maintain homeostasis in many body functions. Triggers increased release of cortisol when under stress. Increased plasma levels noted under acupuncture. ^{15,14,115}
Glycine	Inhibits at the spinal cord level.
Glutamic acid	Causes excitation in many regions including the thalamus, limbic system (hippocampus) and cortex.
Prostaglandins	Prostaglandins and enkephalins are mutually antagonistic in context of pain perception. ⁸⁵
Cyclic AMP	Intraventricular injections antagonise acupuncture analgesia in rats. ¹⁰⁵ Plasma cAMP increases during strong intensity electroacupuncture. ³⁷
Cyclic GMP	Observed to rise in rat diencephalon and lower brainstem in acupuncture analgesia. ¹⁰⁶ In some clinical situations. cGMP is markedly elevated after acupuncture. ¹⁰⁹

This has important implications for treatment with electroacupuncture, in particular choosing which frequency of stimulation to use. For example, serotonin has many physiological properties other than pain relief, including inhibition of gastric secretion (important in the management of stomach ulcers), stimulation of smooth muscles, and the production of vasoconstriction (useful in the management of migraines). Therefore high frequency electroacupuncture may be preferred in illnesses where such factors are important.

Conversely, stimulation frequencies to release endorphins may be more appropriate in acute pain and opiate drug dependencies. The widespread distribution of opiate receptors in the nervous system implies that opiate peptides are involved in a broad range of functions other than analgesia. The endogenous opiates act on prolactin and growth hormone release⁸² and are also involved in the inhibition of gastrointestinal motility.⁶⁵ Morphine itself is known to cause sleepiness, mood changes and alterations of activity levels.

This kind of data is important to bear in mind when reviewing the work of prominent physicians and authors on acupuncture, such as Dr Julian Kenyon.⁸³ Contrary to an enormous wealth of information in this area, his trial on naloxone intervention in the acupuncture treatment of chronic pain

concludes that the hypothesis that acupuncture therapy is mediated even in part by endorphins cannot be supported. Although Kenyon does not use electroacupuncture, in his report he makes no mention of the needle technique adopted or the points needled (Yet both factors have been well established as important criteria affecting the outcome of acupuncture, reported by the Chinese from the earliest texts, and confirmed scientifically more recently—see Ch. 3.)

Other suggestions have been made that, whilst low frequency stimulation is mediated by endorphins, high frequency stimulation is strictly segmental and interferes with the transmission in the pain pathway in the central nervous system at the segmental level.⁸⁴

Antagonist drugs which block the nerve impulse are not the only chemical substances which are introduced experimentally to assess the significance of particular neurotransmitters. Drugs which increase the synthesis or degradation of neurotransmitters may also be employed during acupuncture to witness amelioration or deterioration of response, and thereby determine the importance of any particular neurotransmitter.

Prevention of the degradation of endorphins will prolong and promote electroacupuncture anaesthesia. This has been demonstrated by Pomeranz with the application of D-amino acids (DAA).⁷⁴ DAA blocks the peptidases, e.g., carboxypeptidase A, which normally breaks down peptides such as endorphins. Introduction of DAA will increase the electroacupuncture analgesia effect by increasing available endorphin, a consequence of its decreased rate of destruction. Naloxone, of course, may still be used to block this rise in analgesia.^{85,86}

The drug reserpine, on the other hand, releases serotonin from the pre-synaptic terminals of the descending monoaminergic tracts, and by doing so enhances the analgesic effect of acupuncture at least in rabbits, despite the fact that it blocks morphine analgesia. The monoaminergic tracts terminate in the dorsal horns, but serotonin may also transfuse through the cerebrospinal fluid to various spinal levels and in this fashion also exert a blocking influence on ascending pain impulses. Of course, diffusion through the cerebrospinal fluid would be considerably slower than any direct neural transmission. Accumulation of these research results detailing responses to nerve sections and chemical nerve agonists and antagonists strongly underscores the importance of the neural mediation of the acupuncture effect. However, caution is needed here not to make too much of a quantum leap by assuming that nerves mark the beginning and end of acupuncture therapy.

It is worthwhile at this stage to contrast our neural paradigm with the sort of research which highlights the humoral responses to acupuncture.

Humoral mediation

Many biochemical substances which behave as neurotransmitters exhibit an humoral nature. All do at least in the context of the cerebrospinal fluid, but some others pass through the blood-brain barrier and hence circulate in the bloodstream.²³ (p 213),⁵⁵

That humoral factors are active in acupuncture is shown by many of the characteristics of therapy. In acupuncture analgesia, for example, it takes approximately 20 minutes for the analgesia to be established, and then diminished pain sensation may last for up to an hour after the needles are removed.^{63,74}

The treatment of some diseases such as psoriasis and other skin disorders, menstrual disorders, and viral or bacterial infections would be more easily explained if humoral factors were taken into consideration. I have already shown that blood cell, hormone and immune factors change with treatment, but this does not necessarily mean they are primary mechanisms of acupuncture. However, there are some experiments designed to assess the importance of these humoral factors as mediators of the physiological changes due to needling. For example, in China and elsewhere, many experiments have been performed on rabbits,⁸⁷ dogs, cats, oxen and rats,⁸⁸ where blood is circulated between an acupunctured animal and an unneeded partner. The same, albeit diminished, acupuncture effect is observed in the unneeded partner.

Similarly, exchange of cerebrospinal fluid (CSF) between experimental animals by aspiration from the lateral ventricles, results in the same acupuncture analgesic effect in the unneeded partner, thereby also lending support to the argument that humoral factors operate as an integral part of acupuncture. In 1974 Chinese workers in Beijing transferred CSF from acupunctured mice to observe raised analgesia levels in the recipient, unacupunctured mice.⁸⁹ This result was more clearly understood after Sjölund and fellow workers in Sweden identified the increased presence of endorphins in the CSF of human patients after electroacupuncture.⁹⁰ Zhang Anzhong³⁷ also describes related Chinese experimental findings where cerebrospinal fluid was removed from the lateral ventricles after acupuncture in humans and increased endorphin activity observed,⁹¹ and from rabbits, with higher enkephalin contents noted.⁹² Further, in 1980 Clement-Jones and colleagues found increased beta-endorphins, but not met-enkephalins in human CSF after acupuncture.⁹³

Increased serotonin content in the cerebrospinal fluid could also explain the effects of these CSF exchanges. However, whilst the endorphins and enkephalins pass the bloodbrain barrier to some extent^{23 (p 243),72} serotonin does not normally permeate it, and its increased presence in the bloodstream after acupuncture may be the result of some precursor, such as tryptophan, initially entering the bloodstream or the direct release of serotonin by the pituitary.

Many experiments have measured increases in neurohumoral factors in the bloodstream.⁷² For example, Nappi and colleagues state that the plasma level of beta-endorphin, beta-lipotropin and ACTH are all increased under acupuncture.¹⁵ These substances may in turn exert an influence on other tissues and glands. Raised ACTH plasma levels as a consequence of stimulation of the pituitary by acupuncture could be responsible for an increase of corticosteroids from the adrenal cortex, and result in the inhibition of inflammatory reactions observed in, say, the treatment of acute or chronic arthritis.^{94,95}

Finally, opiates are also released directly from the pituitary into the bloodstream and give added credibility to the raised generalised analgesia levels, however opiates do not explain the specific localised effects so frequently seen in acupuncture analgesia. These localised effects point us once again to the existence of a central biasing system that controls impulse transmission in a selective fashion.⁹⁶ And our argument reverts to the simultaneous existence at least of neural transmission in acupuncture.

REFERENCES

1. Mendelson G, Selwood T S, Kranz H, Loh T S, Kidson M A, Scott D S 1983 Acupuncture treatment of chronic back pain: a double-blind placebo-controlled trial. *American Journal of Medicine* 74: 49-55
2. Chiang C Y, Chang C T, Chu H, Yang L 1973 Peripheral afferent pathway for acupuncture analgesia. *Scientia Sinica* 16(2): 210-217
3. Eisenberg D 1986 Encounters with Qi. Jonathan Cape, London
4. Takeshige C 1983 The central mechanism of analgesia in acupuncture anaesthesia—differentiation of acupuncture point and non-point by the central analgesia producing system. *Acupuncture and Electrotherapeutics Research* 8(3/4): 323-324
5. Takeshige C 1985 Differentiation between acupuncture and non-acupuncture points by association with analgesia inhibitory system. *Acupuncture and Electrotherapeutics Research* 10: 195-203
6. Zhang R, Zhao H 1984 Effect of AQSD resulted from Neiguan needling in cardiovascular disease; analysis of 112 cases. *Journal of Traditional Chinese Medicine* 4(4): 269-272
7. Meng Z, Zhu Z, Hu X 1984 New development in the researches of meridian phenomena in China during the past five years. *Acupuncture Research* 9(3): 207-222
8. Lee T N 1978 Thalamic neurone theory and classical acupuncture. *American Journal of Acupuncture* 6: 273-282
9. Jayasuriya A, Fernando F 1978 The motor gate theory: neurophysiological model to explain the phenomenon of late motor recovery following use of acupuncture in paralytic conditions. *American Journal of Acupuncture* 6: 197-204
10. Shen A C, Whitehouse M J, Powers T R, Young R C, Engleman E P 1973 A pilot study of the effects of acupuncture in rheumatoid arthritis. *Arthritis and Rheumatism* 16: 569-570
11. Wientraub M, Petursson S, Schwartz M et al 1975 Acupuncture in musculoskeletal pain: methodology and results in a double-blind controlled clinical trial. *Clinical Pharmacology and Therapeutics* 17: 248
12. Man S C, Baragar F D 1973 Preliminary clinical study of acupuncture in rheumatoid arthritis with painful knees. *Arthritis and Rheumatism* 16(4): 558-559
13. Knox V J, Handfield-Jones C E, Shum K 1979 Subject expectancy and the reduction of cold pressor pain with acupuncture and placebo acupuncture. *Psychosomatic Medicine* 41(6): 477-486
14. Meyer F P, Nebrensky A 1983 A double-blind comparative study of micro-stimulation and placebo effect in short term treatment of the chronic back pain patient. *California Health Review* 2(1) Aug/Sept
15. Nappi G, Facchinetti F, Legnante G et al 1982 Different releasing effects of traditional manual acupuncture and electroacupuncture on propiocortin-related peptides. *Acupuncture and Electrotherapeutics Research* 7: 93-103
16. Fung K P, Chow O K W, So S Y 1986 Attenuation of exercise induced asthma by acupuncture. *Lancet* Dec. 20/27: 1419-1421
17. MacDonald A J R, Macrae K D, Master B R, Rubin A P 1983 Superficial acupuncture in the relief of chronic low back pain: a placebo controlled randomised trial. *Annals of the Royal College of Surgeons England* 65: 44-46

18. Peng A T C, Behar S, Yue S J 1987 Long term therapeutic effects of EA for chronic neck and shoulder pain: a double blind study. *Acupuncture and Electrotherapeutics Research* 12(1): 37-44
19. Shibutani K, Kubal K 1979 Similarities of prolonged pain relief produced by nerve block and acupuncture in patients with chronic pain. *Acupuncture and Electrotherapeutics Research* 4: 9-16
20. Kaptchuk T 1983 *The web that has no weaver: understanding Chinese medicine*. Rider, London
21. Karczyn A D 1978 Mechanism of placebo analgesia. *Lancet* 2: 1304-1305
22. Levine J D, Gordon N C, Fields H L 1978 The mechanism of placebo analgesia. *Lancet* 2: 654-657
23. Needham J, Lu G D 1980 *Celestial lancets: a history and rationale of acupuncture and moxibustion*. Cambridge University Press, Cambridge
24. Knox V J, Shum K 1977 Reduction of cold pressor pain with acupuncture analgesia in high and low hypnotic subjects. *Journal of Abnormal Psychology* 86: 639-643
25. Levy B, Matsumoto T 1975 Pathophysiology of acupuncture: nervous system transmission. *American Journal of Surgery* June p378-384
26. PLA Veterinary Diseases Prevention Research Institute 1979 The application of acupuncture anaesthesia in operations of domestic animals. National Symposium of Acupuncture and Moxibustion and Acupuncture Anaesthesia, Beijing Paper No 200
27. Han J 1984 On the mechanisms of acupuncture analgesia. *Acupuncture Research* 9(3): 237-245
28. Beijing Childrens' Hospital 1975 A clinical analysis of 1474 operations under AA among children. *Chinese Medical Journal* 1(5): 369-374
29. Xu L, Fu Z, Xiang M et al 1979 The effect of acupuncture analgesia and its relation to blood endorphin, blood histamine and suggestibility. National Symposium of Acupuncture and Moxibustion and Acupuncture Anaesthesia, Beijing Paper No 510
30. Vidal C, Jacob J 1986 Hyperalgesia induced by emotional stress in the rat: an experimental model of human anxiety hyperalgesia. *Annals of the New York Academy of Science* 467: 73-81
31. Kelly D D, Bodnar R J 1979 Intrinsic non-opiate mechanisms of analgesia. Letter to *Acupuncture and Electrotherapeutics Research* 4: 159-161
32. Kelly D D (ed) 1986 *Stress-induced analgesia*. Annals of the New York Academy of Sciences vol 467
33. Eriksson M B E, Sjolund B H, Nielzen S 1979 Long term results of peripheral conditioning stimulation as an analgesic measure of chronic pain. *Pain* 6: 335-347
34. Sjolund B H, Eriksson M 1979 The influence of naloxone on analgesia produced by peripheral conditioning stimulation. *Brain Research* 173: 295-301
35. Watkins L R, Mayer D J 1986 Multiple endogenous opiate and non-opiate analgesia systems: evidence of their existence and clinical implications. *Annals of the New York Academy of Science* 467: 273-299
36. Curzon G, Hutson P H, Kennet G A, Marcou M, Gower A, Tricklebank M D 1986 Characteristics of analgesias induced by brief or prolonged stress. *Annals of the New York Academy of Science* 467: 93-103
37. Zhang A Z 1980 Endorphin and acupuncture analgesia research in the People's Republic of China (1975-1979). *Acupuncture and Electrotherapeutics Research* 5: 131-146
38. Pomeranz B 1986 Relation of stress-induced analgesia to acupuncture analgesia. *Annals of the New York Academy of Science* 467: 444-447
39. Pomeranz B H, Chiu D 1976 Naloxone blockade of acupuncture analgesia: endorphin implicated. *Life Sciences* 19: 1757-1762
40. Chapman C R, Wilson M E, Gehrig J D 1976 Comparative effects of acupuncture and transcutaneous stimulation on the perception of painful dental stimuli. *Pain* 2: 265-283
41. Peets J M, Pomeranz B 1985 Acupuncture-like transcutaneous electrical wave stimulation analgesia is influenced by spinal cord endorphins but not serotonin: an intrathecal pharmacological study. In: *Advances in Pain Research and Therapy*. 9: Raven Press, New York 519-52
42. Cheng R, Pomeranz B 1981 Monoaminergic mechanism of electroacupuncture analgesia. *Brain Research* 215: 77-92
43. Cheng R, McKibbin L, Roy B, Pomeranz B 1980 *International Journal of Neuroscience* 10: 95-97
44. Shanghai College of Traditional Chinese Medicine 1981 *Acupuncture; a comprehensive text* O'Connor J, Bensky D (trans) Eastland Press, Seattle
45. Zhang A, Xu S, Zeng D, Zhang L 1979 The effects of naloxone on acupuncture analgesia produced by different strength of electric stimulation. National Symposium of Acupuncture and Moxibustion and Acupuncture Anaesthesia, Beijing Paper No 496
46. Zborowski M 1952 Cultural components in response to pain. *Journal of Social Issues* 8: 16
47. Josey C, Miller C 1932 Race, sex and class differences in the ability to endure pain. *Journal of Social Psychology* 3: 364
48. Kaptchuk T, Croucher M 1986 *The healing arts*. British Broadcasting Corporation, London
49. Kleinman A 1980 *Patients and healers in the context of culture*. University of California Press, Berkeley
50. Wang J Y 1983 Psychosomatic illness in the Chinese cultural context. In Romanucci-Ross L, *The anthropology of medicine; from culture to method*. Bergin & Garvey Massachusetts
51. Peets J M, Pomeranz B 1978 CXBK mice deficient in opiate receptors show poor electro-acupuncture analgesia. *Nature* 273: 675-676
52. Jacob J J, Nicola M A, Michaud G, Vidal C, Prudhomme N 1986 Genetic modulations of stress-induced analgesia in mice. *Annals of the New York Academy of Sciences* 467: 104-115
53. Bergland R 1985 *The fabric of mind*. Penguin, Melbourne
54. Lee D C 1974 Cardiovascular effects of acupuncture in anesthetized dogs. *American Journal of Chinese Medicine* 2(3): 271-282
55. Omura Y 1975 Pathophysiology of acupuncture treatment: effects of acupuncture on cardiovascular and nervous systems. *Acupuncture and Electrotherapeutics Research* 1: 51-140
56. MacDonald A J R 1983 Segmental acupuncture therapy. *Acupuncture and Electrotherapeutics Research*. 8: 267-282
57. Mu J 1985 Nanjing College of Traditional Chinese Medicine, Personal communication
58. Mu J 1984 Paper presented at the Fourth Advanced Acupuncture Studies Course, Nanjing
59. Bossy J 1984 Morphological data concerning the acupuncture points and channel network. *Acupuncture and Electrotherapeutics Research* 9: 79-106
60. Chiang C Y, Liu J I, Chu T H, Pai Y H, Chang S C 1975 Studies on the spinal ascending pathway for the effect of acupuncture analgesia in rabbits. *Scientia Sinica* 18(5): 651
61. Chang H T 1973 Integrative action of the thalamus in the process of acupuncture for analgesia. *Scientia Sinica* 16(1): 25
62. Shen E, Tshai T T, Lan C 1975 Supraspinal participation in the inhibitory effect of acupuncture on viscerosomatic reflex discharges. *Chinese Medical Journal* 1: 431
63. Anderson S A, Ericson T, Holmgren E, Lindqvist G 1973 Electroacupuncture effect on pain threshold measured with electrical stimulation of teeth. *Brain Research* 63: 393-396
64. Mayer D J, Price D D, Rafii A 1977 Antagonism of acupuncture analgesia in man by the narcotic naloxone. *Brain Research* 121: 368-372
65. Pasternak G W 1986 Multiple morphine and enkephalin receptors: biochemical and pharmacological aspects. *Annals of the New York Academy of Science* 467: 130-139
66. Cheng R, Pomeranz B 1980 Electroacupuncture analgesia is mediated by stereospecific opiate receptors and is reversed by antagonists of type 1 receptors. *Life Sciences* 26: 631-638
67. Lord J A H, Waterfield A A, Hughes J, Kosterlitz H W 1977 Endogenous opioid peptides: multiple agonists and receptors. *Nature* 267: 495-497
68. Chang K J, Cooper B R, Hazum E, Cuatrecasas P 1979 Multiple opiate receptors: different regional distribution in the brain and differential binding of opiates and opioid peptides. *Molecular Pharmacology* 16: 91-104
69. Mu J 1985 Influence of adrenergic antagonist and naloxone on the anti-allergic effect of electroacupuncture in mice. *Acupuncture and Electrotherapeutics Research* 10: 163-167
70. Mu J 1982 Effect of acupuncture on allergic shock of experimental mice. *Shanghai Journal of Acupuncture and Moxibustion* 3: 195-197
71. Mayer D J, 1975 Pain inhibition by electrical brain stimulation: comparison to morphine. *Neurosciences Research Program Bulletin* 13: 94-100
72. Malizia E, Andreucci G, Paolucci D, Crescenzi F, Fabbri A, Fraioli F 1979 Electroacupuncture and peripheral beta-endorphin and ACTH levels. *Lancet* 2: 535-536

73. He L F, Dong W Q 1983 Activity of opioid peptidergic system in acupuncture analgesia. *Acupuncture and Electrotherapeutics Research* 8: 257-266
74. Pomeranz B, Cheng R 1979 Suppression of noxious responses in single neurons of cat spinal cord by electroacupuncture and its reversal by the opiate antagonist naloxone. *Experimental Neurology* 64(2): 327-341
75. Takeshige C, Luo P C, Kamada Y, Oka K, Murai M, Hisamitsu T 1978 Relationship between midbrain neurones (periaqueductal grey and midbrain reticular formation) and acupuncture analgesia, animal hypnosis. In: Bonica JJ (ed) *Advances in Pain Research and Therapy* 3: 615-621. Raven Press, New York
76. Takeshige C, Sato K, Komugi H 1980 Role of periaqueductal central grey in AA. *Acupuncture and Electrotherapeutics Research* 5: 323-337
77. Zhou G Z, Xu S F, Zhang A Z 1980 The effect of naloxone on electroacupuncture analgesia in rabbits. *Acupuncture and Electrotherapeutics Research* 5(2): 197-199
78. Huang Y, Wang Q W, Zheng J Z, Li D R, Xie G Y 1986 Analgesic effects of several modes of electroacupuncture in monkeys and their reversal by naloxone. In: Zhang X T (ed) *Research on acupuncture, moxibustion and acupuncture anaesthesia*. Science Press, Beijing
79. Pasternak G W 1981 Central mechanisms of opioid analgesia. *Acupuncture and Electrotherapeutics Research* 6: 135-149
80. Pomeranz B, Cheng R S S 1979 Electroacupuncture analgesia could be mediated by at least two pain-relieving mechanisms; endorphin and non-endorphin systems. *Life Sciences* 25: 1957-1962
81. Patterson M 1986 Hooked? NET: the new approach to drug cure. Faber and Faber, London
82. Bloom F, Segal D, Ling N, Guillemin R 1976 Endorphins: profound behavioural effects in rats suggest new etiological factors in mental illness. *Science* 194: 630-632
83. Kenyon J N, Knight C J, Wells C 1983 Randomised double-blind trial on the immediate effects of naloxone on classical Chinese acupuncture therapy for chronic pain. *Acupuncture and Electrotherapeutics Research* 8:17-24
84. Cheng R S S, Pomeranz B 1980 A combined treatment with d-amino acids and electroacupuncture produces a greater analgesia than either treatment alone; naloxone reverses these effects. *Pain* 8: 231-236
85. Ehrenpreis S, Balagot R C, Comaty J E, Myles S B 1978 Naloxone-reversible analgesia in mice produced by D-phenylalanine and hydrocinnamic acid inhibitors of carboxypeptidase-A. In: Bonica JJ (ed) *Advances in Pain Research and Therapy* 3: 479-486. Raven Press, New York
86. Ehrenpreis S 1983 Potentiation of AA by inhibitors of endorphin degradation. *Acupuncture and Electrotherapeutics Research* 8: 319-345
87. Yang M M P, Kok S H 1979 Further study of the neurohumoral factor endorphin in the mechanism of AA. *American Journal of Chinese Medicine* 7(2): 143-148
88. Lung C H, Sun A C, Tsao C J, Chang Y L, Fan L 1974 An observation of the humoral factor in AA in rats. *American Journal of Chinese Medicine* 2: 203-205
89. Beijing Research Group of Acupuncture Anaesthesia 1974 The role of some neurotransmitters of brain in finger acupuncture analgesia. *Scientia Sinica* 17: 112-130
90. Sjolund B, Terenius L, Eriksson M 1977 Increased CSF levels of endorphins after electroacupuncture. *Acta Physiologica Scandinavia* 100: 382-384
91. Pan X P, Lou X H, Yao S Y et al 1979 The relationship between the human CSF levels of endorphins and acupuncture analgesia. *National Symposium of Acupuncture and Moxibustion and Acupuncture Anaesthesia*, Beijing Paper No 494
92. Zou G, Wu S X, Wang F S et al 1979 Increased levels of endorphins in the cisternal cerebrospinal fluid of rabbits in acupuncture analgesia. *National Symposium of Acupuncture and Moxibustion and Acupuncture Anaesthesia*, Beijing Paper No 491
93. Clement-Jones V, Tomlin S, Rees L H, McLoughlin L, Besser G M, Wen H L 1980 Increased beta-endorphin but not met-enkephalin levels in human CSF after acupuncture for recurrent pain. *Lancet* 2: 946-948
94. Wen W L, Ho W K K, Wong H K, Mehal Z D, Ng Y H, Ma L 1978 Reductions of adrenocorticotrophic hormone (ACTH) and cortisol in drug addicts treated by acupuncture and electrical stimulation (AES). *Chinese Medicine: East & West* 6(1): 61-66
95. Wen W L, Ho W K K, Wong H K, Mehal Z D, Ng Y H, Ma L 1978 Changes in adrenocorticotrophic hormone (ACTH) and cortisol levels in drug addicts treated by a new and rapid detoxification procedure using acupuncture and naloxone. *Chinese Medicine: East & West* 6(3): 241-246
96. Oliveras J L, Besson J M, Guilbaud G, Liebeskind J C 1974 Behavioural and electrophysiological evidence of pain inhibition from midbrain stimulation in the cat. *Experimental Brain Research* 20: 32-44
97. Abrams G M, Recht L 1982 Neuropeptides and their role in pain and analgesia. *Acupuncture and Electrotherapeutics Research* 7: 105-121
98. Guillemin R, Vargo T, Rossier J et al 1977 Beta-endorphin and adrenocorticotrophin are secreted concomitantly by the pituitary gland. *Science* 197: 1367-1368
99. Zhang C L, Sun G D, Yan H J et al 1986 Substance P: its analgesic effect and influence on caudate neuronal activity in conscious rabbits. In: Zhang X T (ed) 1986 *Research on acupuncture, moxibustion, and acupuncture anaesthesia*. Science Press, Beijing, p388-396
100. Frederickson R C A, Burgis V, Harrell C E, Edwards J D 1978 Dual actions of substance P on nociception: possible role of endogenous opioids. *Science* 199: 1359-1362
101. Oehme P, Hilde H, Morgenstern E, Gores E 1980 Substance P: does it produce analgesia or hyperalgesia? *Science* 208: 305-307
102. Randic M, Miletic V 1977 Effect of substance P in cat dorsal horn neurones activated by noxious stimuli. *Brain Research* 128: 164
103. Lu Z S, Cheng J 1986 Role of histamine in acupuncture analgesia. In Zhang X T (ed) 1986 *Research on acupuncture, moxibustion, and acupuncture anaesthesia*. Science Press, Beijing
104. Wang Y J, Wang S K 1987 The role of alpha and beta receptors and their regulation of 5-HT metabolism of rat brain in electroacupuncture analgesia. *Journal of Traditional Chinese Medicine* 7(1): 57-62
105. Qiu X C, Gia G L, Han C S 1979 Effect of intraventricular injection of cAMP on acupuncture analgesia and morphine analgesia in rats. *Journal of the Peking Medical College*, 1: 4-6
106. Lu Z S 1983 The relationship between cAMP and cGMP in regions of rat brain and acupuncture analgesia. *Journal of Traditional Chinese Medicine* 3(1): 3-6
107. Xie G X, Han J S 1984 Dynorphin-B (Rimorphin) mediates electroacupuncture analgesia in the spinal cord of the rat. *Second National Symposium on Acupuncture and Moxibustion and Acupuncture Anaesthesia*, Beijing Paper No 446
108. Fan S G, Qu Z C, Zhai Q Z, Han J S 1984 Cerebral GABA: antagonistic effects on electroacupuncture analgesia and morphine analgesia in rats. *Second National Symposium on Acupuncture and Moxibustion and Acupuncture Anaesthesia*, Beijing Paper No. 491
109. Li C J, Bi L G, Zhu B J et al 1986 Effects of acupuncture on left ventricular function, microcirculation, cAMP and cGMP of acute myocardial infarction patients. *Journal of Traditional Chinese Medicine* 6(3): 157-161
110. Han J S, Xie G X, Xie C W 1984 Dynorphin has a potent analgesic action and mediates electroacupuncture analgesia in the spinal cord of the rabbit. *Second National Symposium on Acupuncture and Moxibustion and Acupuncture Anaesthesia*, Beijing Paper No. 445
111. Guan X M, Yu B, Wang C Y, Liu X C, 1986 The role of cholinergic nerves in electroacupuncture analgesia - influence of acetylcholine, eserine, neostigmine, and hemicholinium on electroacupuncture analgesia. In: Zhang X T (ed) *Research on acupuncture, moxibustion, and acupuncture anaesthesia*. Science Press, Beijing
112. Meng J B, Fu W X, Cai J H, Qi Y Z Yao S Z 1986 Effect of electroacupuncture on the oxygen metabolism of myocardium during myocardial ischaemic injury. *Journal of Traditional Chinese Medicine* 6(2): 201-206
113. Mann F 1983 *Scientific aspects of acupuncture*. Heinemann, London
114. Omura Y 1976 Pathophysiology of acupuncture effects, ACTH, morphine-like substances, pain, phantom pain and itch, brain microcirculation, and memory. *Acupuncture and Electrotherapeutics Research* 2: 1-32
115. Omura Y 1978 Pain threshold measurement before and after acupuncture: controversial results of radiant heat method and electrical method, and the roles of ACTH-like substances and endorphins. *Acupuncture and Electrotherapeutics Research* 3: 1-21
116. Han J S, Tang J, Ren M F, Zhou Z F, Fan S G, Qui X S 1980 Central neurotransmitters and acupuncture analgesia. *American Journal of Chinese Medicine* 8(4): 331-348

FURTHER READING

- Akil H 1975 Opiates; biological mechanisms. In: Barcas J D (ed) *Psychopharmacology; from theory to practice*. Oxford University Press, New York p 292–305
- Basbaum A I, Fields H L 1984 Endogenous pain control systems: brainstem spinal pathways and endorphin circuitry. *Annual Review of Neuroscience* 7: 309–338
- Goldstein A, Hilgard E R 1975 Failure of the opiate antagonist naloxone to modify hypnotic analgesia. *Proceedings National Academy of Science* 72: 2041–2045
- Kroner WS 1960 Hypnoanaesthesia in surgery and obstetrics. *Western Journal of Surgery Obstetrics and Gynecology* 68: 72–75
- Lee D C 1975 Cardiovascular effects of moxibustion at Renzhong (Du 26) during halothane anesthesia in dogs. *American Journal of Chinese Medicine* (3): 245–260.
- Romanucci-Ross L et al 1983 *The anthropology of medicine; from culture to method*. Bergin and Garvey Publ., Massachusetts
- Small T J 1974 The neurophysiological basis for acupuncture. *American Journal of Acupuncture* 2(2): 77–87
- Steiner R P 1983 Acupuncture—cultural perspectives. *Postgraduate Medicine* 74(4): 60–66
- Watkins L R, Mayer D J 1982 Organisation of endogenous opiate and non-opiate pain control system. *Science* 216: 1185–1192