Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture

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ABSTRACT **The mechanism of action of acupuncture remains largely unknown. The reaction to acupuncture needling known as 'de qi', widely viewed as essential to the therapeutic effect of acupuncture, may be a key to understanding its mechanism of action. De qi includes a characteristic needling sensation, perceived by the patient, and 'needle grasp' perceived by the acupuncturist. During needle grasp, the acupuncturist feels pulling and increased resistance to further movement of the inserted needle. We hypothesize that *1)* needle grasp is due to mechanical coupling between the needle and connective tissue with winding of tissue around the needle during needle rotation and *2)* needle manipulation transmits a mechanical signal to connective tissue cells via mechanotransduction. Such a mechanism may explain local and remote, as well as long-term effects of acupuncture.—Langevin, H. M., Churchill, D. L., Cipolla, M. J. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. *FASEB J.* 15, 2275–2282 (2001)**

Key Words: collagen · mechanotransduction · meridian

ACUPUNCTURE, A COMPLEX therapeutic system used in China for more than 2000 years (1), has become increasingly popular in the West as a therapy for pain and a wide variety of mostly chronic disorders difficult to manage with conventional treatment (2). Although considerable research has been directed toward elucidating the mechanism underlying acupuncture, several fundamental aspects of acupuncture treatments remain poorly understood (3). Gaining knowledge of therapeutic mechanisms is essential to validating therapies such as acupuncture that are difficult to test under double-blind, placebo-controlled conditions (4, 5). Perhaps more important, understanding the mechanism of acupuncture may provide insight into unexplored physiological phenomena (3).

According to traditional Chinese theory, the needling of 'acupuncture points' has specific therapeutic effects believed to occur either locally or at a distance via the system of acupuncture 'meridians' (6). Mechanistic models of acupuncture based on laboratory experiments performed over the past 30 years have mostly abandoned these traditional concepts in favor of viewing the effects of acupuncture as taking place essentially through the nervous system (7). Rather than forming an integrated system, acupuncture points are thought to represent discrete locations on the body where manual or electrical stimulation can activate appropriate neural pathways (8, 9). A fundamental distinction therefore currently exists between traditional and scientific views of acupuncture. A mechanistic explanation incorporating both classic acupuncture theory and available scientific evidence would therefore be a major unifying step in the field.

An important key to such a mechanism may be the characteristic reaction to acupuncture needling known as 'de qi' (1, 6, 7, 10, 11). De qi is elicited by brief manual manipulation (e.g., rotation, up-and-down motion) of the inserted acupuncture needle. This method is used to elicit de qi whether or not electrical stimulation is subsequently applied (1, 7). De qi has a sensory component perceived by the patient as an ache or heaviness in the area surrounding the needle and a simultaneous biomechanical component, needle grasp, perceived by the acupuncturist. During needle grasp, the acupuncturist feels as though the tissue is grasping the needle, such that there is increased resistance to further motion of the manipulated needle (1, 7, 10). This 'tug' on the needle is classically described as "like a fish biting on a fishing line" (12). Needle grasp has been described in traditional acupuncture texts for more than 2000 years (13) and is still widely considered essential to acupuncture's therapeutic effect (1, 6, 7, 10, 11), yet its underlying mechanism is unknown.

We hypothesize that, during de qi, the needle is being grasped by connective tissue as a result of collagen and elastic fibers winding and tightening around the needle during needle rotation. In this manner, a mechanical coupling is developed between needle and tissue. We further hypothesize that needle manipulation transmits a mechanical signal into connective tissue via this needle/tissue coupling. The subsequent transduction of this mechanical signal to a cellular response may underlie some of the therapeutic effects of acupuncture both locally and at remote locations.

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PROPOSED MECHANISM OF NEEDLE GRASP

Role of connective tissue and winding of collagen

Needle grasp is unlikely to be due to a muscle contraction, as has been suggested (7, 14), since it can be observed even at locations where no skeletal muscle is present (such as at the wrist) as well as on the palms and soles where there are no arrector pili smooth muscles. Tenting of skin observed during needle grasp (**Fig. 1**) also suggests that tissues superficial to muscle are grasping the needle.

To investigate the role of the skin and/or subcutaneous (s.c.) connective tissues in needle grasp, we used rat abdominal wall explants as an experimental model (**Fig. 2**). Using tissue explants allowed us to examine histological changes associated with acupuncture needle manipulation in large viable tissue samples that could be rapidly fixed after needle manipulation. Full-thickness 4 × 4 cm rat abdominal wall samples including dermis, subcutaneous (s.c.) muscle, s.c. tissue, and abdominal wall muscles were excised from normal male Wistar rats (250–275 g) immediately after death and placed in 37°C HEPES buffer, pH 7.4. Five minutes after excision, a stainless steel acupuncture needle (Seirin, Tokyo, Japan; 0.25 mm diameter) was inserted in the center of each sample and either rotated in one direction for 32 revolutions (Fig. 2*b*) or not rotated (Fig. 2*a*). After 1 min, tissues were immersion-fixed in formalin. Fixed samples were paraffin-embedded, sectioned parallel to the needle track, and processed for histology. We observed that needle rotation was accompanied by marked thickening of the s.c. connective tissue layer in the area surrounding the needle (Fig. 2*b*). There was no structural change in dermis, s.c. muscle, or abdominal wall muscles other than displacement by the thickened s.c. tissue layer. Masson trichrome staining showed collagen winding around the needle track with acupuncture needle rotation (Fig. 2*c*, *d*). Consistent with these findings is an electron microscopy study of debris found on acupuncture needles after insertion, manipulation, and removal in humans, revealing elastic and collagen fibers entwined around the needle (15). Together, these observations support the hypothesis that connective tissue winds around the needle during needle rotation.

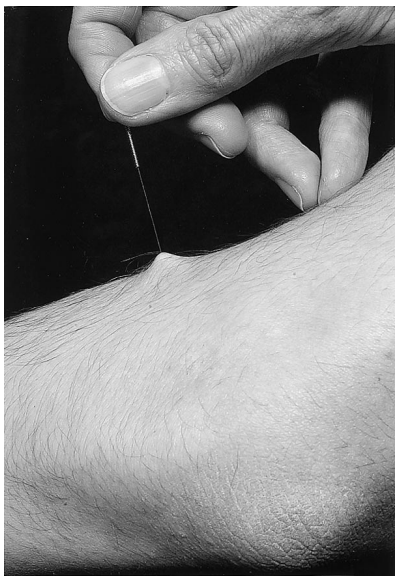

Figure 1. Tenting of skin observed during needle grasp. An acupuncture needle (Seirin; 0.25 mm diameter) was inserted into the forearm of a human volunteer. After insertion, the needle was rotated until needle grasp was observed. Pulling back on the needle resulted in visible tenting of the skin.

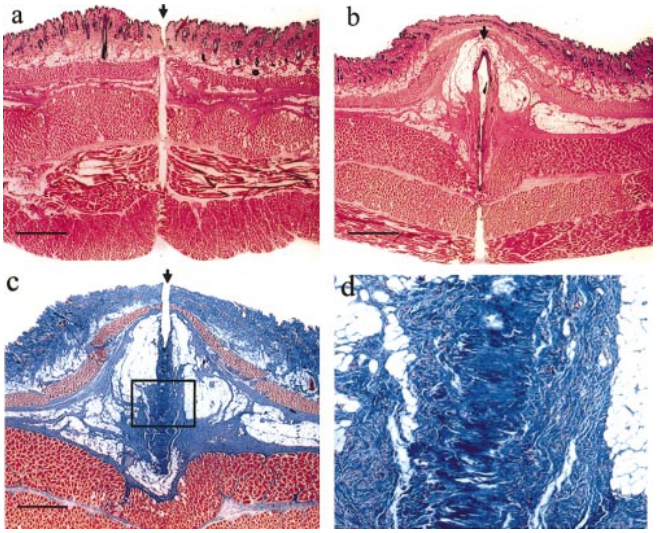

Figure 2. Winding of connective tissue with acupuncture needle rotation vs. needle insertion without rotation in rat tissue explants. Acupuncture needles were inserted into rat abdominal wall explants including dermis, s.c. muscle, s.c. tissue and abdominal wall muscle. The needle was either rotated in one direction for 32 revolutions (*b–d*) or not rotated (*a*). After 1 min, tissues were immersion-fixed in 10% formalin. The acupuncture needle track was labeled with India ink and tissue blocks were cut so that the sectioning plane ran through the needle track. Samples were embedded in paraffin, sectioned at 6 μm thickness, and stained with hematoxylin/eosin (*a, b*) or Masson trichrome counterstained with aniline blue, where collagen is stained blue and muscle is stained red (*c, d*). Arrows indicate needle track. Scale bar, 1 mm. *b, c)* Adjacent sections from the same tissue block; *d)* close-up of box area in panel *c*.

In a study of the biomechanical response to acupuncture needling in humans, we quantified needle grasp by measuring the force required to pull out an inserted acupuncture needle (pullout force). Pullout force was significantly greater with needle rotation compared with needle insertion without rotation (16). This result demonstrates that needle rotation enhances needle grasp. Pullout forces of 100–300 g were routinely observed after needle rotation, and occasionally pullout forces that saturated our 500 g load sensor were seen. These are substantial loads considering the small diameter (250 μ) of the needle.

The winding of strands of material around a rotating drum or shaft, resulting in progressive tightening, is a common phenomenon observed in many settings. Simple friction resists sliding of the material around the

shaft. Because the material is wrapped around the shaft, the compressive force between the shaft and the material augments as the tension in the strands increases. This in turn increases the friction force, allowing more tension to be developed in the strands. In simple systems, such as a cable wrapping around a winch drum, the maximum tension that can be developed in the free end of the cable before the cable slips on the drum increases exponentially with increased winding (17). The winding amplifies the inherent friction between the cable and drum. This exponential increase occurs when the cable does not wrap over itself. If the material is allowed to wrap over itself, as we believe happens in the case of connective tissue winding around an acupuncture needle, the material can become self-locking in several revolutions. That is, the friction force is amplified so much that the material cannot slip on the shaft no matter how much tension is applied. This self-locking winding of connective tissue is familiar to surgeons using rotating equipment such as drills or reamers.

Winding of connective tissue around the needle results in a marked amplification of the mechanical coupling between the needle and the local connective tissue. Some initial coupling must be present, however, for the tissue to begin wrapping around the rotating needle shaft. We believe that the initial mechanical coupling results from attractive forces between needle and tissue, such forces likely being surface tension and electrical attraction. Connective tissue is composed of cells embedded in extracellular matrix made of interwoven collagen and elastic fibers associated with glycoproteins and negatively charged proteoglycans (18). Electrical attraction may therefore occur between the metal needle and fixed tissue charges. Such attractive forces are likely to be relatively weak, but strong enough to cause initial winding of tissue around the rotating needle. This is made easier by the small diameter of the needle. Once some wrapping has occurred, frictional forces take over. The collagen and elastic fiber network is likely to have some initial laxity, allowing the initial wrapping to occur without having to overcome large tensile forces.

In our human experiments, we typically observed that the torque required to rotate the needle increases continuously as needle rotation proceeds (**Fig. 3**). This is consistent with our hypothesis of connective tissue winding around the needle. The torque reflects the tension developed in the tissue during winding. The torque curve was similar in most cases except for a variable duration between the start of needle rotation and the beginning of the steep torque increase. We believe that this represented a 'prewinding' period during which the tissue had not yet become 'caught' on the needle, allowing the needle to slip.

Once the acupuncture needle becomes coupled to tissue, movements of the needle (rotation or pistoning) may send a signal through connective tissue via deformation of the extracellular matrix. To investigate this hypothesis, we examined the orientation of collagen

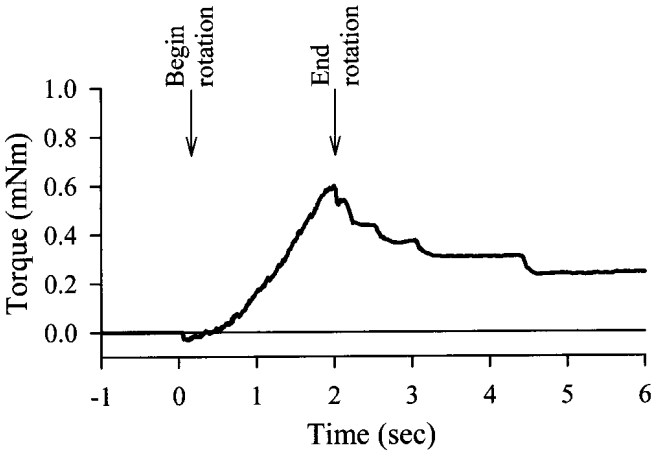

Figure 3. Torque developing during acupuncture needle grasp. A computer-controlled acupuncture needling instrument including a miniature servomotor was used to insert and rotate an acupuncture needle in a normal human volunteer. The needle was rotated at a constant speed for 16 revolutions over 2 s. At the end of rotation, the final position of the needle was held stationary. The amount of torque developed at the needle/tissue interface is shown graphically.

fibers in rat s.c. tissue with and without needle rotation. Collagen bundles were straighter and more nearly parallel to each other after needle rotation (**Fig. 4*b***) than after needle insertion without rotation (Fig. 4*a*), clearly demonstrating local alignment of tissue with needle rotation. The importance of this effect is that pulling of collagen fibers during needle manipulation may transmit a mechanical signal, through deformation of the extracellular matrix, to cells such as fibroblasts that are abundant in connective tissue. The subsequent signal transduction events may contribute to the therapeutic effect of de qi.

Mechanical signal transduction

In many cell types such as fibroblasts, endothelial cells, and sensory neurons, focal adhesions form a mechanical link between extracellular collagen matrix and intracellular cytoskeleton (19, 20). The mechanism of mechanical load detection is thought to be a mechanosensory complex composed of extracellular matrix-integrin-cytoskeletal components linked to a kinase cascade (21). In this model, load deformation displaces matrix molecules tethered to clustered integrins at focal adhesions (22). The cell membrane displacement is transduced by an integrin to an integrin binding protein such as talin and then to associated proteins such as vinculin, tensin, paxillin, Src, and focal adhesion kinase (23). In addition, one or more of these proteins can undergo a conformation change in response to displacement and initiate a series of phosphorylation and binding reactions in the protein complex (24). Therefore, the result of mechanical load deformation of an integrin molecule via extracellular matrix attachment is activation of a signaling cascade leading to a wide range of cellular responses, including

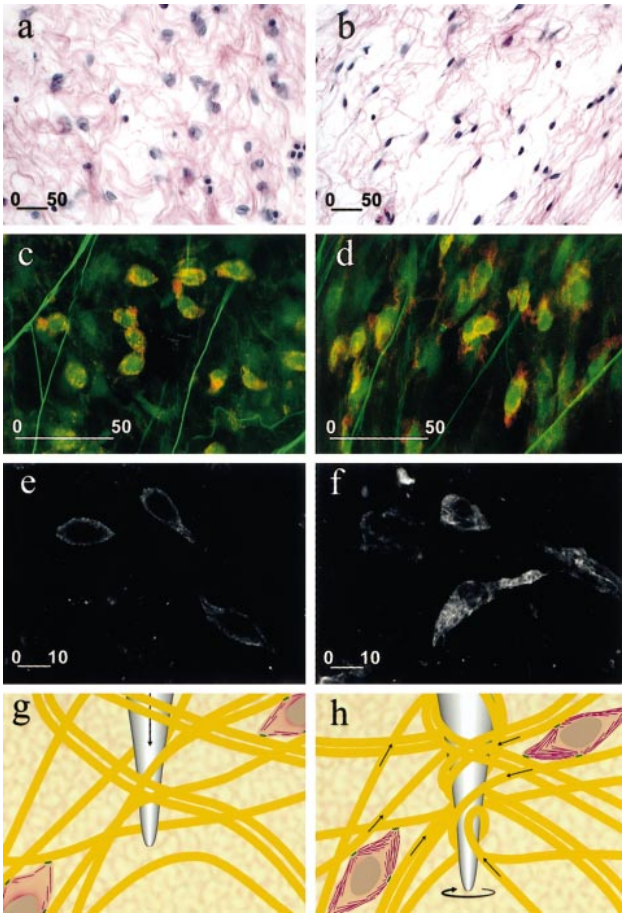

Figure 4. Extracellular and intracellular effects of acupuncture needle rotation compared with needle insertion without rotation in rat tissue explants. Rat abdominal wall explants were obtained and needled as described in Fig. 2. The needle was either rotated (*b, d, f*) or not rotated (*a, c, e*). After 1 min, tissues were immersion-fixed in 10% formalin (*a, b*) or 3.5%formalin (*c–f*). s.c. connective tissue was dissected apart from adjacent muscles. Samples *a* and *b* were processed for histology, sectioned (6 μm thickness) parallel to the s.c. connective tissue plane, and stained with hematoxylin and eosin. In samples *c–f,* whole tissue mounts (~200 μm thick) were examined with confocal microscopy. Samples *c* and *d* were stained with Texas red-phalloidin (a specific stain for polymerized F-actin), and Oregon green-DNase1 (a specific stain for soluble G-actin). Samples *e* and *f* were stained with phalloidin only. Scale bars are labeled in microns. *g)* Illustrated insertion of an acupuncture needle into connective tissue. *h)* Rotation of the needle pulls on collagen fibers (arrows); the mechanical signal generated by needle rotation is transduced into local fibroblasts. Yellow lines represent collagen bundles; pink lines inside fibroblasts represent actin cytoskeleton; green dots represent focal adhesion complexes.

changes in the actin cytoskeleton with formation of stress fibers (24–26).

Using rat s.c. tissue explants, we have found that acupuncture needle rotation caused fibroblasts to become aligned with collagen fibers and change shape from a rounded appearance (Fig. 4*a, c, e*) to a more spindle-like shape (Fig. 4*b, d, f*). Increased cytoplasmic staining for polymerized filamentous (F-) actin can be seen in fibroblasts 1 min after needle rotation (Fig. 4*d, f*) compared with needle insertion only (Fig. 4*c, e*). Redistribution of polymerized actin is known to occur in cultured fibroblasts and endothelial cells within minutes of applying a force to the cell surface using magnets or mechanical traction (27–29). The pulling of collagen fibers induced by acupuncture needle manipulation appears to have a similar effect on connective tissue fibroblasts via their attachment to collagen fibers at focal adhesion complexes.

These observations suggest that the mechanical signal created by acupuncture needle manipulation can induce intracellular cytoskeletal rearrangements in fibroblasts and possibly in other cells present within connective tissue, such as capillary endothelial cells. Cytoskeletal reorganization in response to mechanical load signals has been shown to induce cell contraction, migration, and protein synthesis (26, 30). Potentially powerful effects may derive from this mechanical signal transduction, including autocrine and paracrine cellular effects, with modification of the surrounding extracellular matrix (31).

Figure 4*g, h* illustrates our proposed mechanism for needle grasp involving mechanical signaling through connective tissue: *1)* winding of connective tissue around the acupuncture needle, *2)* pulling of collagen fibers and matrix deformation, *3)* transduction of the mechanical signal into fibroblasts and/or other cells attached to collagen fibers at focal adhesions, and *4)* cellular response, including cytoskeletal rearrangement, with potentially therapeutic downstream effects.

POSSIBLE DOWNSTREAM EFFECTS OF NEEDLE GRASP

Autocrine and paracrine effects

Cells are thought to exist in a dynamic state of balance that is a function of the polymerization state of the cytoskeleton, the amount of extrinsic applied deformation, and the number and quality of focal adhesions (24, 32). This state of balance is itself linked to complex cascades of events, including activation of intracellular signaling pathways with phosphorylation of focal adhesion kinase and extracellularly regulated kinase (ERK). Cell deformation may also lead to autocrine release of growth factors, binding to extracellular membrane receptors, and activation of ERK (24). ERK phosphorylation can lead to activation of ribosomal S6 kinase, which can initiate protein synthesis (33). Activated ERKs can also enter the nucleus and up-regulate the expression of gene transcription factors or activate nuclear binding proteins such as NF-κB, which may promote the transcription of specific 'stress-responsive' genes such as collagen XII, tenascin-C, and platelet-derived growth factor (24, 34).

A variety of mechanical stimuli (mechanical stretch, shear stress, pulsatile stress) has been shown to alter the expression of proto-oncogenes [c-fos (35–38), c-jun (38), Fra-1 (38)], as well as genes coding for extracellular matrix components [tenascin-C (34), collagen XII

(34)], enzymes [cyclooxygenase 2 (39), nitric oxide synthetase (40)], membrane proteins (connexin 43; ref 35), peptides (parathyroid hormone-related peptide; ref 41), and cytokines [PDGF (42), TGF-β1 (43, 44), and tissue plasminogen activator (45)]. The increase in cyclooxygenase 2 mRNA expression in response to fluid shear was blocked by cytochalasin D (39), demonstrating that this response involves actin cytoskeleton reorganization. Most of these studies were carried out in cultured fibroblasts, endothelial, and smooth muscle cells using either cyclical stretch or prolonged shear stress over several hours. Although less information is available on the effect of brief mechanical stimuli, several reports indicate that mechanical stimuli lasting 3 s (impulse flow, endothelial cells; ref 35), 1 min (mechanical stretch of intestinal smooth muscle cells; 43) and 15 min (mechanical stretch of vascular smooth muscle cells; ref 38) induced significant increases in cFos (35, 38), Cx43 (35), and TGF-β1 (43) mRNAs at 30 min, 90 min, and 4 h, respectively. Increased gene expression in response to mechanical stress has also been demonstrated in tissue explants (36, 46) and in vivo (41).

Downstream effects of the mechanical signal generated by acupuncture needle manipulation therefore potentially include synthesis and local release of growth factors, cytokines, vasoactive substances, degradative enzymes, and structural matrix elements. Release of these substances may influence the extracellular milieu surrounding connective tissue cells. Changes in matrix composition, in turn, can further modulate signal transduction to and within the cell (47).

Interstitial connective tissue network

The effect of mechanical forces on mesenchymal tissues has been studied extensively in tendon, ligaments, joint capsules, dermis, cartilage, and bone (48–51). Interstitial connective tissues, on the other hand, have so far received relatively little attention. These connective tissues constitute a network throughout the body, including intermuscular and s.c. tissue planes, and are continuous with more specialized connective tissues such as perimysium, periosteum, pleura, and peritoneum. Interstitial connective tissues also constitute the milieu surrounding nerves, blood vessels, and lymphatics. Modification of interstitial connective tissue therefore may have important biomechanical, vasomotor and neuromodulatory effects.

Contraction of interstitial connective tissue has been documented during wound healing, tissue remodeling, and fibrotic processes. During these types of contractions, fibroblasts undergo phenotypic changes occurring over days to years involving the expression of different actin isoforms and formation of 'myofibroblasts' (52). Rapid reversible contraction of fibroblasts, accompanied by phenotypic changes occurring over minutes, is well documented in vitro and involves polymerization of soluble actin and formation of actin stress fibers (53). These cytoskeletal changes are also thought to occur in vivo, as a step toward the formation of myofibroblasts (54), or in a reversible manner in response to temporary changes in tissue strain (55). During acupuncture needle manipulation, pulling of collagen may cause reversible contraction of large numbers of fibroblasts near the acupuncture needle. This is supported by the phenotypic change in connective tissue fibroblasts after needle rotation shown in Fig. 4. Local tissue contraction may contribute to the phenomenon of needle grasp and to the tugging sensation felt by the acupuncturist. Furthermore, the contraction of fibroblasts itself would cause further pulling of collagen fibers, resulting in a 'wave' of matrix deformation and cell contraction spreading away from the needle through interstitial connective tissue (**Fig. 5**). Patients frequently report a slow spreading of de qi sensation along acupuncture meridians (6). Acupuncture points and meridians typically are located between muscles or between a muscle and a tendon or bone (1, 56). The ancient maps of acupuncture points and

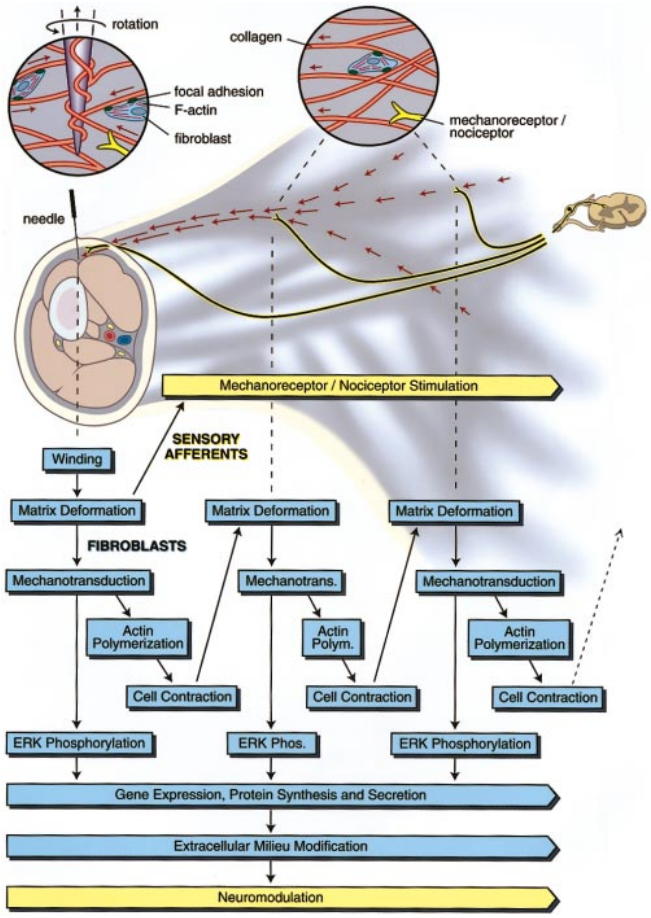

Figure 5. Hypothesis summary. Proposed mechanical signal transduction and downstream effects of acupuncture needle manipulation at gross and microscopic levels. Gray shaded areas represent deep connective tissue planes of the upper arm. The acupuncture needle is inserted on the lateral border of the biceps. Red arrows represent pulling of connective tissue and matrix deformation during acupuncture needle manipulation. The 'Lung' acupuncture meridian is located along the lateral border of the biceps and may coincide with some of the outlined connective tissue planes.

meridians may essentially be a guide to insert the needle into connective tissue. Spreading of matrix deformation and cell activation along connective tissue planes thus may mediate acupuncture effects remote from the acupuncture needle site (Fig. 5).

Sensory afferent stimulation

Different types of sensory receptors may be stimulated directly as a result of the matrix deformation generated by acupuncture needle manipulation. A study by Wang et al. (57) reported an association between stimulation of group III muscle afferents and sensations of heaviness, distention, and aching typically associated with de qi. This study has been quoted as evidence that the sensation perceived during de qi is due to a contraction of muscle (7). However, group III muscle afferents are found in perimuscular fascia and the adventitia of muscle blood vessels and respond to a variety of stimuli including pressure, stretch, and mechanical stimulation of the muscle surface (58), which could occur as a result of mechanical connective tissue matrix deformation. Group III muscle afferents, along with various other types of sensory receptors present within connective tissue, may therefore be activated directly as a result of the mechanical signal generated by needle manipulation. In addition to group III muscle afferents, other types of sensory receptors and primary afferent nerve fibers are known to transmit mechanosensory information in s.c. and deep connective tissues, and may be stimulated by connective tissue matrix deformation. Both slow-adapting (SA II) and fast-adapting (FA II) mechanoreceptive afferents have been described in dermis, s.c. tissue, and interstitial connective tissue planes. SA II receptors respond to both pressure and stretch and consist of bundles of collagen fibers with sensory axons branching between collagen fibrils (Ruffini endings). FA II receptors are associated with Pacinian corpuscles and most effectively transmit a sensation of vibration. Two main types of nociceptors can also transmit mechanosensory information in skin and deep connective tissues. Aδ mechanical nociceptors give rise to small myelinated fibers and are thought to respond to damaging mechanical stimuli, though the threshold for these receptors vary, many being in the innocuous range (59). Finally, C polymodal nociceptors give rise to small unmyelinated fibers and respond to noxious mechanical, thermal, and chemical stimuli.

Acupuncture needle manipulation therefore may (via connective tissue matrix deformation) cause stimulation of a wide variety of sensory mechanoreceptors and/or nociceptors.

The importance of this effect is that *1)* connective tissue matrix deformation may not be restricted to the area of the needle, but may spread along interstitial connective tissue planes; *2)* a wave of sensory receptor activation occurring over seconds to minutes may simultaneously follow the mechanical signal away from the needle site; *3)* a second wave of cellular activation, followed by altered gene expression, protein synthesis, and extracellular matrix modification, may ensue after a certain time delay and last hours to days; and *4)* subsequent stimulation of these connective tissue sensory receptors by body movement may be modulated by this sequence of events.

Neuromodulation

Whether the sensation evoked by stimulation of various types of sensory receptors is experienced as pain (or not) depends not only on the type of receptor, but also on the status of the tissue and of synaptically related spinal cord neurons. Peripheral sensitization of primary afferents or changes in central synapses can contribute to an increased pain sensation (60). It is now widely accepted that target organs can influence the neurons that innervate them. Peripheral tissue factors known to influence sensory input include tissue perfusion and inflammatory mediators (61). Tissue perfusion is itself regulated by a complex interplay of autonomic, hormonal, and local controls (62, 63). In connective tissue, fibroblasts and collagen matrix are the underlying milieu in which these regulatory events take place. This connective tissue milieu has the property of responding to mechanical signals such as those produced by acupuncture needle manipulation. The effect of acupuncture needle manipulation on blood flow, cytokines, and/or growth factors may result in long-term modulation of sensory information. This may influence whether or not sensations generated by stretching of connective tissue during body movements are perceived as pain. The delayed cellular and molecular events triggered in connective tissue by acupuncture needle manipulation may therefore modulate processing of mechanical sensory stimuli that occur hours to days later.

Link to measurable clinical effects

Pain is a subjective symptom that is notoriously difficult to quantify, and the therapeutic effect of acupuncture in general has been difficult to study under placebo-controlled conditions (3, 5). Changes in tissue perfusion, pH, cytokines, or growth factors, however, can be studied objectively using techniques such as laser Doppler fluxmetry, isotope washout methods and microdialysis. These techniques may provide objective evidence of prolonged connective tissue changes after acupuncture treatments both near and distant from the needle along connective tissue planes. The connective tissue environment surrounding nerves, blood vessels, and lymphatics may play an important and largely unexplored role in various types of chronic pain. The effects of acupuncture on connective tissue may therefore be important from the point of view of *1)* establishing a mechanism linking acupuncture needle manipulation to a therapeutic effect, *2)* providing biological markers of the effect of acupuncture that can be used in clinical trials, and *3)* understanding the role played by connec-

tive tissue in the pathogenesis of chronic pain syndromes.

In summary, the insertion and manipulation of acupuncture needles may have both local and remote therapeutic effects based on the same underlying mechanism: mechanical coupling of needle to connective tissue, winding of tissue around the needle, generation of a mechanical signal by pulling of collagen fibers during needle manipulation, and mechanotransduction of the signal into cells. Downstream effects of this mechanical signal may include cell secretion, modification of extracellular matrix, amplification and propagation of the signal along connective tissue planes, and modulation of afferent sensory input via changes in the connective tissue milieu (Fig. 5).

We propose that mechanical signal transduction is a common mechanism underlying the effects of a variety of acupuncture needling methods. Modern acupuncture techniques using electrical stimulation may have additional effects through prolonged stimulation of nerves or muscle. However, de qi is a common denominator to both traditional and modern acupuncture treatments. Indeed, documentation of de qi is used as a criterion for evaluating the adequacy of both manual and electrical acupuncture treatments in clinical trials (64, 65). Acupuncture needle rotation (either uni- or bidirectional) may be important to initiate needle grasp, but other types of needle manipulation such as pistoning may also effectively transmit a mechanical signal to cells once needle grasp has been initiated. Transduction of the mechanical signal into cells with subsequent cellular response and downstream effects may explain the perplexing claim that acupuncture treatments have long term effects lasting for days to weeks and even permanently.

Traditional acupuncture theory is based on empirical observations first made over 2000 years ago that so far have remained without solid scientific validity. The field of mechanotransduction may now provide scientific grounding for this ancient form of therapy. In return, acupuncture may provide an important clinical application for the current explosion in basic knowledge of the powerful and diverse biological effects of mechanical signaling. FJ

This work was funded in part by the NIH Center for Complementary and Alternative Medicine Grant #R21 AT00300. We thank Jason A. Yandow and Marilyn Wadsworth for technical assistance as well as Gary J. Nelson for help with illustrations. We also thank Drs. James L. Oschman, Deborah A. Cook and Douglas J. Taatjes for their expert advice.

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Received for publication March 13, 2001.
Revised for publication June 20, 2001.

THE FASEB JOURNAL
The Journal of the Federation of American Societies for Experimental Biology

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FASEB J 2001 15: 2275-2282
Access the most recent version at doi:10.1096/fj.01-0015hyp