

# **JOURNAL OF THE AMERICAN MANUAL MEDICINE ASSOCIATION**



*The Professional Journal of Advanced and Postgraduate  
Medical Massage and Medical Manual Therapy*

## **TOWARD A NEUROPHYSIOLOGICAL UNDERSTANDING OF MEDICAL MASSAGE THERAPY**

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# Journal of American Manual Medicine Association

The Journal of American Manual Medicine Association was created to serve as a rational scientific voice for the medical massage and medical manual therapy community. The AMMA Journal is peer reviewed scientific publication. Articles and papers that are published in the AMMA Journal are presented in three main subject groups, editorial opinion, and scientific research, and legal, regulatory, and political events that pertain the medical massage and medical manual therapy professions.

Articles and papers written by outside contributors to the AMMA Journal do not necessarily reflect the view or position of the American Manual Medicine Association.

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## ***From the editor...***



Dr. Gregory T. Lawton

**Dear AMMA Member:**

**In this issue you will find articles and research papers that have been submitted by the AMMA membership. The purpose of this issue is to provide our members with an “inclusionary” experience and the ability to contribute directly to their professional journal, JAMMA.**

**There is a noticeable lack of quality research and articles prepared and written by massage and manual therapists. One of the avowed purposes of JAMMA is to remedy this deficiency by giving our medical massage and medical manual therapy members a voice. This issue is dedicated to our members who have prepared papers related to the study and practice of medical massage and medical manual therapy.**

**This issue is also, in a sense, a celebration of our associations diversity of interests and expression of opinions. Through these articles and papers the contributing AMMA members demonstrate that we are indeed an organization of varied backgrounds and a broad membership base.**

**As a member of the AMMA you have completed a concentrated program of study in medical massage, passed the most difficult national board exam in the profession, and you stand at the highest pinnacle of the massage profession. To remain at the top you need to invest in your professional development on a daily basis. Since you are a medical massage therapist there is simply no limit to the knowledge that you need and can acquire that pertains to the conditions that you treat and the practice skills that you need to master. Your acquired knowledge and abilities pertain to being able to sort out the numerous false doctrines, pseudo scientific theories and fringe practices of your profession so that you do not commit the ethical errors of other massage therapists and so that you can select the most appropriate technique or treatment protocol for your patient.**

**One of the primary purposes of the American Medical Massage Association is to create a distinctive identity for our members through the actualization of the highest professional standards in the industry. Hopefully it is the members of the AMMA, through their professional conduct and high educational standards that will contribute to uplifting this noble profession.**

**Yours in good health,**

**Dr. Gregory T. Lawton**

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# Guest Editorials

## ABOUT BEING A MEDICAL MASSAGE THERAPIST

### A Massage Therapists Perspective

**Mason Garnett, CMT, RN**

When I tell people that I am a massage therapist I get a variety of responses from snickers and snide remarks of a suggestive nature, to comments about crystals and locker room rub downs. I am not infrequently called a masseuse. This is annoying to me because not only am I a registered nurse with a background in cardiac surgery, but I practice **medical massage** and not therapeutic or relaxation massage. You can't really blame the public for being confused about massage therapy; the profession itself is confused about its identity. As a nurse I know exactly what I am and what I represent, the public knows about nurse training and job performance, but as a massage therapist all the public has to go on is what they may have experienced getting a hotel or spa massage, or what they see on TV or in other media.

Even the massage therapists that I meet are confused about medical massage and its differences from therapeutic, cosmetic, or relaxation massage. When massage therapists that I work with notice the words medical massage and American Medical Massage Association on my business card I get a variety of responses from mild interest to outright hostility. I have been accused of "breaking the law" by even calling myself a medical massage therapist, and one school has even announced that medical massage therapy is "illegal" in the state that I practice, Michigan.

Admittedly, there is good cause for confusion since there is such a wide range of diversity among massage therapists. Many massage therapists have completely embraced the new age movement and use shamanistic practices involving crystals, hot rocks and other shamanistic tools. I have personally visited massage therapists whose offices were lit by candles and perfumed with the heavy, almost overpowering, smell of incense, which I like many others am allergic to.

Therapists who are actually trained in medical massage are a rare group and even among those therapists with related training in orthopedic or sports massage, finding a therapist with the education and clinical experience to actually provide competent musculoskeletal therapy and soft tissue rehabilitation, for the purpose of corrective and restorative care, is very rare. This is a sad state of affairs because there is a significant need for medical massage therapists. There is a void of massage therapists who can actually do therapy. When I am asked by my patients for a referral for a friend or a relative to a massage therapist who works like I do, I am usually at a loss as to where to send them, or what I might be referring them to!

Most massage therapists that I meet or visit just seem to have very general and superficial skills and most seem content to provide the most basic massages. I find this confusing since my desire is to help people who are in pain and who have physical problems. I entered this profession as a nurse and a helping professional. I don't do relaxation massage. I don't cover my patients in oil for an hour. Frankly, I fail to understand the concept of a "therapist" rubbing oil on a client to increase their relaxation and pleasure. I provide specific therapeutic applications to the patient's problem area

and as form or corrective and restorative manual therapy.

I don't mean to disparage non medical massage therapists, there are far more of them than medical massage therapists. Many of the massage therapists that I meet simply have no interest in medical massage or the education and training that it requires. I say more power to them and to each his or her own. The non medical massage therapists that I meet are nice people and they are sincere in their beliefs about the value of what they have to offer. One relaxation massage therapist that I met at a medical massage CEU seminar, was obviously bored and told me that this was just too much work and that she became a massage therapist so that she didn't have to work too hard or think about it.

Since medical massage therapists are so rare and non medical massage therapists are so common and since there is no legal distinction between the various levels of training and practice, like we have in nursing, an unfortunate side effect of this is that many in the professional health care community have little respect for massage therapists. Many mainstream health care professionals view all massage therapists as lacking in basic education and skills, poorly trained, and frequently on the outer fringe.

I think that it would be good if we could all come together to remedy the problems that we have in terms of education, recognition, and practice, but I do not see that happening. I can't see how a new age massage therapist who employs metaphysical or shamanistic practices can be reconciled with a medically trained massage therapist. With such a wide divergence in our training, skills, practices, and interests how can we sit in the same classes, belong to the same organization, take the same exams, or be represented by the same massage laws? I am not even certain that I understand why therapeutic, cosmetic, or relaxation massage is state licensed. A license is essentially an earned privilege, not a right, to perform an activity that is inherently dangerous so that the public is protected. What is inherently dangerous about a cosmetic or relaxation massage? Health insurance was established in the United States to cover critically needed essential medical expenses and care. Using medical health insurance coverage to pay for relaxation or cosmetic massage services is inappropriate in most cases.

In medical health care, medicine has adopted standard procedures for patient care; this is true in physical therapy, nursing, and in all aspects of medical care. Most of the massage therapy community has not done this yet. As a medical massage therapist many of my techniques, treatment protocols, and therapeutic applications are based on research and clinical outcome data. The general non medical massage therapist is not trained in these approaches and most massage therapists don't even know that they exist. What they do practice is what they learned in massage schools from other massage therapists and many of the dozens and dozens of popular techniques are just based on a therapist's idea or opinion about massage. Much of what is commonly accepted among massage therapists as advanced technique or as therapeutic simply is not supported by research or has already been shown not to be effective.

When I am asked just what medical massage therapy is I usually just tell the person what I was taught, "Medical Massage therapy is corrective restorative treatment that is addressed to the area or region of the patient's chief complaint. Medical massage therapy is based upon massage techniques and protocols that provide and facilitate therapeutic responses in all of the body's connective tissue, joints and body systems. Medical massage therapy produces a clinical response and positive clinical outcomes."

I will continue to work and celebrate the rewards of being a medical massage therapist. I will continue to educate my patients regarding medical massage and its value. I also hope that more massage therapists will be motivated to seek out good medical massage training and will begin using it in their practices. There are a lot of people who are hurting and suffering and who need competent medical massage care. Try it you may just like it, and you will be amazed at how many people you help!

About the author:

Mason Garnett CMT, RN is a registered nurse and medical massage therapist in private practice in Ann Arbor, Michigan and specializing in the treatment of patients recovering from cardiac surgery through the University of Michigan.



### **Conference on the Biology of Manual Therapies**

The National Center for Complimentary and Alternative Medicine, of the National Institutes of Health conducted a conference entitled, "Conference on the Biology of Manual Therapies in June of 2005. In part the following is an outline of what was covered at that conference.

### **Overview of Manual Therapy Use in Canada**

**Maria Verhoef, Ph.D., Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada**

Recent surveys conducted by Statistics Canada show that the most commonly used manual therapies in Canada are chiropractic and massage therapy. Much less common are Feldenkreis, Alexander therapy, rolfing, and reflexology. No data are available about osteopathic medicine, which is not very common in Canada. This presentation will, therefore, focus mostly on chiropractic and massage therapy. Manual therapy use varies by gender, age, income, education, province and health status.

While chiropractic is regulated in all Canadian provinces, massage therapy is only regulated in three provinces. Education requirements differ as well. After a minimum of

three years of university, a chiropractic student must complete another four years of professional education. The Canadian Massage Therapists Alliance (CMTA) has set a gold standard for massage therapy education of 2200 practice hours. While some provincial insurance plans cover chiropractic; massage therapy is not covered in any provincial plan. However, both may be covered by third party payers.

Demographic characteristics of practitioners will be presented as well as the most common reasons for chiropractic and massage therapy use. Both patients using chiropractic as well as massage therapy tend to be very satisfied with this type of care.

Physician surveys conducted in Canada indicate that while physicians know relatively little about chiropractic and massage therapy, they tend to find them useful and to refer patients to these modalities. Several initiatives are underway to integrate chiropractic and massage therapy with medicine. In addition, chiropractors as well as massage therapists, play a role in several initiatives, such as: 1) a Canadian initiative to develop CAM curriculum for Undergraduate Medical Education, and 2) an initiative to develop and promote interdisciplinary CAM research.

In conclusion, manual therapies are not only considered to be of clinical important by the Canadian population, these modalities are also included in strategic initiatives to develop interdisciplinary practice, research and education.

### **Overview of Manual Medicine Use in the U.S.**

#### **Janet R. Kahn, Ph.D., L.M.T., Integrative Consulting, Burlington, Vermont**

It seems a universal human impulse to put our hands to areas of pain or injury. Forms of manual medicine appear in every system of healing, with references found in ancient Indian and Chinese texts, as well as the writings of Hippocrates. In the U.S. today, there are many different types of manual medicine, but the primary disciplines are Osteopathic Manual Medicine (OMM), Chiropractic, and Therapeutic Massage and Bodywork.

Both osteopathy and chiropractic are relatively recent arrivals in the world of healing, being developed in the United States in the late 19th century. Contemporary U.S. massage, by contrast, is an amalgam of approaches, including both Eastern and Western, as well as ancient and relatively contemporary modalities. They differ also in the extent of training required for practice. Osteopaths and chiropractors complete 4 year programs beyond the undergraduate level, with osteopaths also having a required internship and an optional specialization residency. State licensure requirements for massage range from 500 to 1,000 hours--notably less than the Canadian requirements. A significant, though unspecified, proportion of massage therapists will substantially increase this training with post-graduate trainings in areas of specialization producing noteworthy inconsistency in the field.

Recent surveys estimate that Americans make 192 million visits per year to chiropractors and 114 million to massage therapists. The popularity of these disciplines alone warrants research into their safety and efficacy and the past 15 years has seen a dramatic increase in clinical trials. The past 5-7 years has seen an increase in their quality. While none of these disciplines has a long-standing tradition of research as part of their training, this is beginning to change, and both the osteopathic and chiropractic

disciplines have begun investigation of the presumed mechanisms of action--a welcome and commendable development.

This presentation will offer brief descriptions of the major techniques involved in manual medicine, their presumed intent, and where possible their presumed mechanism of effect. For purposes of generating a research agenda, attention will be paid to data on the conditions for which treatment is sought, conditions for which the disciplines believe they are effective and areas where the lines between the disciplines blur. For instance, craniosacral therapy, originally an aspect of osteopathy, is practiced by many massage therapists and chiropractors. Both massage therapists and osteopaths utilize muscle energy, counter strain, and myofascial release techniques; both chiropractors and osteopaths employ thrusting techniques of various force and velocity.

The presentation will also highlight some of the current controversies and challenges within the field of manual medicine including differing views on the type of patient for whom manual medicine may be most effective, multiple studies indicating inability to establish inter-rater reliability on palpation of the cranial rhythmic impulse, and the like.

### **Mechanical States Encoded by Mechanoreceptors and Mechanonociceptors**

**Partap S. Khalsa, D.C., Ph.D., D.A.B.C.O., Vice-Chair and Graduate Program Director, Department of Biomedical Engineering, Associate Professor of Biomedical Engineering, Neurobiology, and Orthopaedics, College of Engineering & Applied Sciences and School of Medicine, State University of New York at Stony Brook, Stony Brook, New York**

Sensory neurons that are mechanically sensitive innervate all of the paraspinal connective tissues including ligament, joint capsule, annulus fibrosus of the IVD, muscle, tendon, and skin. These afferents can be broadly classified into two subcategories based on whether they respond to non-noxious or noxious mechanical loads (mechanoreceptors or mechanonociceptors, respectively). By definition, a noxious mechanical load is such that it actually is or is close to damaging the tissue. Histologically, mechanonociceptors (MN) have small diameter axons (< ~ 1mm) with either no or minimal myelination (and hence conduct action potentials at < ~2 m/s) and their receptive endings are either "free" or non-capsule. In contrast, mechanoreceptors (MR) have larger diameter axons with myelination (conducting at > 20 m/s) and terminal endings with distinct corpusculature. During an externally applied mechanical load (e.g. compression and/or stretch), the terminal endings experience the internal locally developed stress (related to force) and/or strain (related to deformation). Using intact, ex-vivo nerve-tissue preparations, at the macroscopic level, both MR and MN have been shown to encode the local stress or a stress-related quantity, rather than the strain, deformation, or force. At the cellular level, the stress-field in the extracellular matrix (collagen, elastin, laminin, etc.) is coupled to the cytoskeleton by transmembrane proteins called integrins. Disrupting the integrin attachment with monoclonal antibodies or specific RGD peptides substantially reduces MR sensitivity to mechanical stimuli and MN inflammatory-induced hyperalgesia.

Recommendations for future research: 1) Determine local and systemic inter-relationships between microvasculature and MN peripheral sensitization. 2) Determine

effects of peripheral mechanical stimuli (e.g., spinal manipulation) on spinal cord gating mechanisms and synaptic plasticity.

### **Sensory Input Elicited by Manual Therapies**

**Joel G. Pickar, D.C., Ph.D., Professor, Palmer Center for Chiropractic Research, Palmer College of Chiropractic, Davenport, Iowa**

Manual therapies, like mobilization and manipulation, by their very nature impose mechanical inputs upon the body. A substantial body of literature identifies primary afferents capable of responding to mechanical inputs. Sensory input arrives at the spinal cord along Group I (A ), II (A $\beta$ ), III (A ), and IV (C-fiber), afferents from superficial and deep tissues. Muscle stretch is an adequate stimulus for the receptive endings of Group Ia and II muscle spindle afferents. It can also stimulate Group Ib Golgi tendon organ afferents although muscle contraction appears more effective. Subpopulations of Aa skin afferents and Group II, III and IV skin and deep tissue afferents respond to innocuous and/or noxious mechanical input. Some are sensitized to mechanical input by the presence of chemical mediators in the extracellular space. In an animal model, grade III mobilization of the normal knee joint reduces secondary hyperalgesia produced at the more distal ankle joint. Large diameter Group I muscle afferents as well as Group II and III muscle and joint afferents could contribute to the antihyperalgesia via central serotonergic or adrenergic receptors, but not opioidergic or GABAergic receptors. In humans, stimulation of muscle spindle afferents using vibration reduces pain thresholds in unexercised leg muscle, but in contrast, exacerbates the delayed onset muscle soreness of eccentrically exercised leg muscles. Spinal manipulation has been applied to the lumbar spine in an animal model. Impulse loading of the paraspinal tissues activates both muscle spindle and Golgi tendon organ afferents. The duration of the impulse load strongly affects the instantaneous discharge frequency of Group Ia and Group II muscle spindle afferents. The magnitude of their discharge increases non-linearly as the impulse duration becomes similar to that used clinically. Further work is necessary to determine whether the force-time profile of a particular manual therapy and the condition of the tissues to which the therapy is delivered has selective effects on primary afferents or the central neurons on which they synapse.

Recommendations: 1) Determine the discharge characteristics (i.e. the pattern or frequency of action potentials) of primary sensory neurons in response to the force-time profiles used in manual therapies. 2) Determine how the patterns of activity from neurons innervating superficial versus deep tissues affect the signaling properties of neurons in the central nervous system. 3) Determine if manual therapies produce long-lasting changes in tissue biomechanics which would presumably produce long-lasting changes in mechanosensory input.

### **Spinal Processing of Sensory Inputs: Lessons From Animal Models**

**James L. Henry, Michael G. DeGroote Institute for Pain Research and Care, McMaster University, Hamilton, Ontario, Canada**

The objective of this presentation is to present data that describe the effects of sensory inputs on spinal sensory mechanisms under normal conditions. Importantly, these effects are altered in animal models of chronic pain. Data will be presented that indicate

that sensory inputs, particularly nociceptive inputs, are exaggerated in these models. Further investigation indicates that the explosive nature of nociceptive inputs in these models is partially due to increased excitability to excitatory chemical mediators of synaptic transmission. In addition, however, there is also a change in effects of inhibitory transmitters, whereby these now express not only inhibitory effects, but also excitatory effects. It is concluded that under pathological conditions, the neural substrate of pain transmission and integration in the spinal cord undergoes a loss of the normal buffering capacity that governs the flow of sensory information. This loss of buffering capacity could account for at least some types of chronic pain, but would also suggest that extrasegmental sensory inputs could have greater inhibitory effects under conditions of pathology, and this warrants further investigation.

(Supported by the Canadian Institutes for Health Research, the University of Western Ontario and McMaster University)

### **Genetic and Synaptic Studies of Sensory-related Central Sensitization**

**Min Zhuo, Ph.D., Department of Physiology, Faculty of Medicine, University of Toronto Centre for the Study of Pain, University of Toronto, Toronto, Ontario, Canada**

Neuronal synapses in the central nervous systems are plastic and can undergo long-term changes throughout life. Studies of molecular and cellular mechanisms of such changes not only provide important insight into how we learn and store new knowledge in our brains, but also reveal the mechanisms of pathological changes occurring following a noxious stimulus. Using integrative approaches including genetic, pharmacological, electrophysiological, and behavioral studies, we demonstrated that neuronal mechanisms underlying physiological functions such as learning and memory may share some common signaling molecules with abnormal or injury-related changes in the brain. In the first sensory synapses of spinal cord dorsal horn, serotonin (5-HT), a key neuromodulatory transmitter, recruited silent glutamatergic synapses through the AMPA receptor-PDZ protein interaction. The recruitment of silent synapses provides a potential mechanism for long-term facilitation of sensory transmission in case of neuropathic pain. Activity-dependent potentiation also takes place in the higher brain structures that are critical for pain perception and pain-related unpleasantness. In the anterior cingulate cortex (ACC), N-methyl-D-aspartate (NMDA) receptor-dependent, calcium-calmodulin activated adenylyl cyclases (AC1 and AC8) are important for the induction of long-term potentiation, a potential cellular model for the expression of persistent inflammatory and neuropathic pain. Long-term plastic changes in glutamate receptors, including the upregulation NMDA NR2B receptors in the ACC, may contribute to behavioral allodynia. Finally, neuronal activity in the ACC can also influence nociceptive transmission in the spinal cord dorsal horn through activation of endogenous descending facilitatory system. Our results provide important synaptic and molecular insights into physiological responses to the injury including behavioral, emotional, and memory.

## Antistress Effects in Response to Non-noxious Sensory Stimulation

**Kerstin Uvnas Moberg, M.D., Ph.D., Professor, Department of Environment and Health, Swedish University of Agriculture, Sweden**

Somatosensory stimulation is normally associated with pain and stress reactions. It is however also possible to induce an anti-stress pattern including stimulation of social behavior, mental calm, and physical relaxation by non-noxious somatosensory stimulation. Thick myelinated fibers as well as thin C fiber afferents may be involved in these effects.

The peptide oxytocin is produced in the SON and PVN of the hypothalamus and released from neurons projecting not only to the neurohypophysis but also to the amygdala, PAG, hippocampus, striatum, raphe nuclei, NTS, DMX etc. OT stimulates milk ejection, maternal behavior, induces calm, increases pain threshold, and induces physical relaxation including lowering of blood pressure and cortisol levels when released by breastfeeding. In addition, the activity of the vagal nerve is increased to promote digestive processes and storing of nutrients.

The same effect pattern is induced if oxytocin is administered to male or female rats, suggesting that the effects are not restricted to lactating females. In addition, if oxytocin is given repeatedly, long-term effects are induced by secondary effects on other transmitter systems. The function of alfa 2 receptors is increased and opioidergic, serotonergic, and cholinergic function may be influenced. The function of the HPA axis is influenced in an anti-stress direction at the level of the hippocampus (MR, GR) hypothalamus (CRF), pituitary (ACTH) and adrenal (corticosterone production). If oxytocin is administered repeatedly during the neonatal period, life long effects may be induced.

Interestingly, oxytocin can be released and an oxytocin-like effect spectrum induced by non-noxious stimulation from several parts of the body in both sexes to e.g., by stroking, warmth, light pressure, low intensity nerve stimulation in anaesthetized animals. If a conscious rat (male or female) is stroked on the ventral side at a frequency of 40 strokes/ minute for 5 minutes, an anxiolytic-like and/or calming effect is induced, pain threshold is elevated, blood pressure, pulse rate and cortisol levels fall, and the levels of some gastrointestinal hormones rise. The effects are particularly strong when induced on the front side. This may be due the presence of a subpopulation of vagal nerve afferents originating in this area. Most of the effects are blocked by an oxytocinantagonist suggesting that oxytocin may be an important mediator of the anti-stress effects induced by non-noxious sensory stimulation. A similar response pattern is induced in humans of both sexes and all ages in response to close physical contact.

## **Manipulating Pain and Inflammation**

**Jon D. Levine, M.D., Ph.D., Professor of Medicine (Divisions of Rheumatology and Clinical Immunology, and Clinical Pharmacology and Experimental Therapeutics), Division of Neuroscience, Program in Biomedical Sciences, University of California, San Francisco, California**

There is a long and very extensive history of somatic manipulations for the treatment of signs and symptoms of disease from every corner of the world. While it is difficult to study these therapeutic modalities in double-blind placebo controlled studies, the universality of this type of therapy strongly suggests it has a role in the treatment of a variety of clinical conditions, and certainly its side-effect profile is outstanding. The two most common uses of these treatments have been in the treatment of pain, a symptom responsible for great morbidity in society, and inflammatory diseases, among the most common and disabling medical conditions. Discussion of mechanisms by which manipulative therapies may influence pain and inflammation will focus on: 1) visceral, 2) stressful, and 3) painful manipulations. These interventions will be discussed in terms of their use as complementary as well as alternative therapies

## **Biological Mechanisms Underlying the Inflammatory and Healing Phases in Trauma of the Muscle-tendon Unit: What Have We Learned Recently?**

**Claude H. Côté, Ph.D., CHUL Research Center and Laval University, Faculty of Medicine, Department of Rehabilitation, Québec, Canada**

Acute trauma of the muscle-tendon unit can result from a variety of mechanical, metabolic, histotoxic, or physiological insults, which can lead to chronic syndrome if not tightly managed. Aseptic tissue injury rapidly triggers a transient inflammatory reaction whose physiological significance is complex and still not completely understood. Normally, resolution of inflammation should set the ground for an efficient tissue repair. Inflammation is primarily a perturbation of the vascular homeostasis and it is widely believed that the nature of the inflammatory reaction induced by trauma does not vary with the type of insult and that inflammatory cells invade the injured tissue in a highly orderly sequence. Such dogma often constitutes the basis of the clinical approach for the management of inflammation. This presentation will review recent evidence obtained with various models of skeletal muscle and tendon injuries suggesting that this may not be the case. It will also make a case against the use of aggressive and prolonged anti-inflammatory modalities in acute trauma. The modulation of inflammatory cells trafficking in inflammation is under the control of complex signaling cascades, several originating from the vascular bed. Therefore any modality that can affect the physiology of vascular cells could theoretically influence inflammation and tissue healing. Further research aimed at identifying signals governing leukocyte migration in skeletal muscle, their specific role and endogenous anti-inflammatory molecules should undoubtedly help design therapeutic strategies accelerating muscle-tendon recovery following trauma and disease. This presentation should open avenues for discussion on the biological impact of complementary and manual therapies (CAM). It should also emphasize the need to select appropriate and significant outcome measures to measure the influence of CAM.

## **A Hassle a Day May Keep The Doctor Away: Enhancing Versus Suppressive Effects of Stress on Immune Function**

**Firdaus S. Dhabhar, Ph.D., Associate Professor, College of Dentistry & College of Medicine, The Ohio State University, Columbus, Ohio**

It would be extremely beneficial if one could harness an individual's natural, endogenous, health-promoting survival mechanisms to fight disease and restore or maintain health. Interestingly, the psycho-physiological stress response is the most under-appreciated of nature's survival mechanisms. We initially hypothesized that just as an acute stress response prepares the cardiovascular and musculoskeletal systems for fight or flight, it may also prepare the immune system for challenges (e.g. wounding and antigen entry) that may be imposed by a stressor (e.g. predator or surgical procedure).<sup>1</sup> We have defined stress as a constellation of events, comprised of a stimulus (stressor), that precipitates a reaction in the brain (stress perception), that activates physiologic fight/flight systems in the body (stress response).<sup>2</sup> Chronic stress (lasting for weeks, months or years) is known to suppress or dysregulate immune responses. In contrast, acute stress (lasting for minutes to hours) has been shown to augment in vivo immune function.<sup>3</sup>

Our studies examine neuro-endocrine-immune interactions during primary and secondary immune responses using in vivo models of leukocyte trafficking and cell-mediated immunity (CMI).<sup>3-5</sup> CMI responses are crucial for conferring immunoprotection during vaccination, or infection, but may also mediate immunopathology during inflammatory (e.g. cardiovascular disease, gingivitis, hypersensitivity) or autoimmune (e.g. psoriasis, arthritis, multiple sclerosis) diseases. Studies showed that acute stress experienced before either primary (innate immune response) or secondary (adaptive immune response) antigen exposure induces a large and long-lasting enhancement of CMI.<sup>3,5</sup> This acute stress induced immunoenhancement is mediated systemically by physiological levels of the stress hormones, corticosterone and epinephrine,<sup>6</sup> and locally by gamma-interferon.<sup>7</sup> Compared with controls, sites of immune activation from acutely stressed mice show significantly greater erythema and induration, numbers of infiltrating leukocytes, and levels of cytokine gene and protein expression.<sup>5</sup> In contrast to acute stress and acute exposure to stress hormones, chronic stress is immunosuppressive and chronic exposure to corticosterone, or acute exposure to synthetic glucocorticoids like dexamethasone, significantly suppresses skin immunity.<sup>2,6</sup> Our results suggest that during acute stress, endogenous stress hormones enhance skin immunity by increasing leukocyte trafficking and cytokine and chemokine gene expression at the site of wounding or antigen entry. Basic mechanistic experiments as well as clinical studies examining the immunological effects of acute versus chronic stress will be discussed. An attempt will be made to place these findings in the context of manual therapies and their effects on endocrine and immune function. (Supported by: NIH RO1 AI48995, AR 46299, CA107498, & The Dana Foundation Clinical Hypotheses Program in Brain-Body Interaction.)

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### **How Biomechanics and Medical Imaging Have Helped To Unravel the Biological Effects of Manual Therapies: An Historical Perspective**

**Linda Woodhouse, Ph.D. (Candidate), B.Sc. (P.T.), Assistant Professor, School of Rehabilitation Science, McMaster University, Hamilton, Ontario Canada**

A myriad of different manual therapy treatments are used worldwide to ameliorate pain, reduce impairment, and restore physical function. Included under the rubric of manual therapies are acupuncture, deep friction and massage, mobilization, passive movements, neuromuscular facilitation techniques, percussion, and mobilization therapies to name but a few. Common to all of these therapies is that the therapist or caregiver performs the work, while the patient or client is the passive recipient.

As biological tissues are by and large extremely adaptable, the aim of these therapies is to apply the appropriate stimuli (mode, dose, and duration) to induce biological change at the cellular, tissue and whole body systems levels. These changes may include local responses of underlying bone, joints, and soft tissues (muscle and connective tissues) through to whole body neural, immune, endocrine, circulatory, and lymphatic system responses.

In many areas of manual therapy, clinical practice appears to be a decade or so ahead of the science. Although some clinical evidence (including systematic reviews) for the effectiveness of manual therapies exists, few studies have systematically explored the biological effects of these therapies to elucidate their underlying mechanisms of action. In part, the limitation has been a lack of available instrumentation to objectively quantify in vivo responses to manual therapy stimuli in humans. This session will provide an overview of the contributions that biomechanics and medical imaging have made to our current understanding and highlight some of the limitations and challenges faced in trying to unravel the biological effects of manual therapies.

## Manual Therapies: A Biomechanical Continuum

**John J. Triano, D.C., Ph.D., F.C.C.S., Research Professor, Department of Engineering, University of Texas, Arlington, Co-director for Research, Texas Back Institute, Texas**

Over 200 differently named systems of manual treatments exist worldwide. Systems are often clustered under headings of massage, neuromuscular therapy, mobilization and high velocity, low amplitude manipulation procedures. Common to all of them is the application of forces and moments to patient body segments, expecting to influence soft-tissue condition or joint behavior, physiologic responses, and associated symptoms. These loads may serve both in efforts to diagnose and to treat. Successful transfer of mechanical energy into positive clinical change is likely to rely on the match of procedure characteristics common to all treatments (threshold, dose and duration) and biomechanical properties of the affected tissues. In theory, transduction mechanisms may include the altering of local tissue constitutive properties and fluid content, cellular or reflex reactions.

Manual therapies have multiple parameters that can be independently controlled for each administration including relative body segment orientation, static or dynamic initial conditions, application area concentration, frequency, pre-load amplitudes, direction, load rise-time, peak amplitudes, and sustained load duration. Little information currently exists on the association of changes in these parameters with threshold-dose relationships.

During this session, the several types of studies used to quantify some of the more common procedures will be reviewed. Thus far, only a small number of diagnostic and therapeutic procedures have received attention. Efforts have been made to quantify in vitro intradiscal pressures, point loads at select landmarks of the motion segment, ligamentous and arterial strains. Acoustic and acceleration sensors have triangulated joint cavitation with respect to targeted joint structures. Kinematics has been monitored in vitro with bone pins and in vivo by optoelectronic sensors and MRI in some diagnostic and therapeutic maneuvers. Uniaxial or triaxial loads at the applied site for the cervical, thoracic and lumbar regions have been reported. Force and moment components transmitted through the targeted body segment slice for the low back and neck are available. Analytic methods have explored kinetoelastostatic, direct and inverse dynamic, as well as vibrational and energy models.

Understandably, the descriptive biomechanical data has grown most quickly over the past two decades, forming the basis for future work. Efforts to understand the transduction of input energy to physiologic processes has lagged behind. Early efforts sought threshold relationships with circulating biological markers and recent evidence has begun to map load intensity and direction to neural response. The role of skill in performance is just beginning to be investigated. Variability between operators is evident in cross-sectional studies. Within an operator's performance, early evidence suggests a systematic variation and reproducibility in response to patient characteristics.

Future work must build an understanding of the differences in procedures and identify markers for mechanical transduction, carrying studies more expansively into mapping

the relationship of the controllable biomechanical parameters of the various manual methods to physiologic and, ultimately, clinical effects

### **Timing is Everything in a Column and Segment that Can Buckle**

**David G. Wilder, Ph.D., P.E., C.P.E., Director, Jolt/Vibration/Seating Lab, Senior Research Scientist, Iowa Spine Research Center, Associate Professor, Biomedical & Mechanical Engineering, University of Iowa, Iowa City, Iowa**

The health of the spine, a complex mechanism, depends on the successful interaction of a network of active and passive components. Active parts of the network, the muscles, are located on opposite sides of the spine and need to operate in a coordinated fashion to stabilize or move the spine safely. One limitation of our neuromuscular control system is that it takes time to sense the need for muscle action and then call for it. Injury can occur due to rapid uncoordinated muscle action when the spine is exposed to conditions that occur faster than the control system can cope with such as buckling of the spinal motion segment, whole-body vibration, and surprise loads. Understanding these limitations can help in optimizing back treatments and the interaction between people and their environments. Using hands-on demonstrations, the audience will explore a simple six-degree-of-freedom system (a mechanical metaphor for the spinal motion segment) and observe damage to a biological system produced due to a slow and poorly trained control system.

### **Connective Tissue Mechanotransduction Responses To Stretch and Acupuncture: From Ex Vivo Fibroblast Cytoskeletal Morphology to In Vivo Ultrasound Elasticity Imaging**

**Helene Langevin, M.D., L.Ac., Research Assistant Professor, University of Vermont, Department of Neurology, Burlington, Vermont**

A common feature of manual therapies is the therapeutic application of mechanical forces (e.g. stretching, pressure) on either "dense" (tendons, ligaments, joint capsules) or "loose" (fasciae, subcutaneous, interstitial) connective tissues. Tissue viscoelastic responses to mechanical forces are determined by their connective tissue matrix composition (collagen, glycosaminoglycans (GAGs), water content) and architecture. Connective tissue fibroblasts play a pivotal role in both immediate and long term connective tissue responses to mechanical forces by 1) secreting matrix components and thus regulating matrix composition and 2) actively responding to mechanical forces via mechanotransduction or mechanisms that directly link mechanical forces to active changes in cell shape, intracellular signaling mechanisms and/or expression of specific mechanosensitive genes (including collagen, GAGs, metalloproteinases and growth factors).

Thus, mechanical forces actively participate (via cellular responses) in remodeling of connective tissue's extracellular matrix. The effect of mechanical forces on connective tissue fibroblasts may be key to the therapeutic mechanism of manual therapies by causing important cellular effects both immediate (activation of signaling mechanisms) and delayed (gene expression, modification of extracellular matrix composition) which may affect future biomechanical tissue behavior during movement.

**Ex vivo and in vivo animal models can be used to study the effect of mechanical forces on fibroblasts in whole tissue.** Using histochemistry and confocal microscopy, we found that both tissue stretch and acupuncture induced a dynamic, reversible change in fibroblast morphology within 30 minutes. During acupuncture, connective tissue mechanical stimulation is caused by winding and pulling of collagen during needle manipulation. With both types of mechanical stimulation, fibroblasts cell bodies became large, flat and "sheet-like" in contrast to the small cell bodies and long branching processes seen without stretch. These changes in cell shape required the presence of both intact microtubules and microfilaments, implying an active, cytoskeletal-dependent mechanism. Results obtained with these cell imaging techniques therefore suggest that acupuncture may share common cellular mechanotransduction mechanisms with a range of manual therapies. Further studies will be needed to examine the effects of varying force amplitude, frequency and duration on these mechanisms, and how these effects may differ across treatment modalities.

**In vivo ultrasound elasticity imaging techniques can be used to study the effect of applied mechanical forces on tissues in humans.** Using a combination of ultrasound elasticity imaging and robotic acupuncture needling, we quantified spatial and temporal tissue displacement and strain patterns during acupuncture needling in humans. We found that rotation of the acupuncture needle preconditioned the tissue and modified its biomechanical behavior during subsequent axial needle motion. Ultrasound elasticity imaging is emerging as a powerful non-invasive technique to quantify biomechanical tissue behavior that may be applied to investigating the mechanism of manual therapies as well as acupuncture.

**Combined approaches using these ex vivo and in vivo techniques** may ultimately allow translation of findings from animal models leading to mechanistic studies of therapeutic mechanisms in humans.

### **Rehabilitation Robotics and Movement Therapy: Implications for Manual Therapy**

**Hermano Igo Krebs, Ph.D., Principal Research Scientist & Lecturer, Massachusetts Institute of Technology, Mechanical Engineering Department, Adjunct Assistant Research Professor of Neuroscience, The Winifred Masterson Burke Medical Research Institute, Weill Medical College of Cornell University, New York**

In "Why Michael Couldn't Hit," Harold Klawans (Freeman Press, 1996) raises an interesting question about brain plasticity: why can a superstar professional athlete in a sport, say basketball, only achieve mediocre competence in another sport, say baseball? It appears that the motor control system gets hardwired to perform one task seamlessly, but not another, and that there are particular periods of massive organization of the motor control system. Outside these windows of opportunity, plasticity still occurs, albeit of a much smaller and subtle proportion. But what about an adult broken brain following a stroke? There may be a window of opportunity that might allow us to maximize motor neuro-recovery. Our efforts have been concentrated on applying robotics and information technology to determine how to augment therapy; harness plasticity so that this window (if it exists) might be fully exploited.

In this presentation, I will review results using rehabilitation robots developed at MIT during clinical trials with 96 stroke inpatients at the Burke Rehabilitation Hospital (White Plains, NY) and 110 persons with chronic impairment after stroke at the Burke Rehabilitation Hospital (White Plains, NY), Spaulding Rehabilitation Hospital (Boston, MA), and the Baltimore VA Medical Center (Baltimore, MD). Results suggest that robot-aided training enhances recovery; and that this effect is not due to a general physiological improvement--in fact, it appears to be limb- and muscle-group specific. Results also suggest the reduction in the incidence of shoulder and hand pain as well as tone. We will review existing technology and new technology under development, including algorithms for evaluating patients' performance and different modalities of robot-aided therapy being investigated. We will also discuss how rehabilitation robotics afforded new insights into the process of neuro-recovery and how the same evidence-based tools, which were applied to movement therapy, might allow a natural segue into manual therapy.

### **Functional Neuroimaging Techniques in Manual Therapy Research: Current Status and Future Directions**

**Norman W. Kettner, D.C., Chair, Department of Radiology, Logan College of Chiropractic, Chesterfield, Missouri**

Manual therapy research has made little use of modern multi-planar (3D) imaging techniques. One barrier to their use has been the problem of motion artifacts. There are imaging designs however, which may circumvent these and other technical constraints. Imaging of the clinical response rather than the technique, for example. In this design, interventions are done outside of the scanner with baseline and follow up imaging providing the opportunity to monitor results. Examples of these imaging techniques include structural magnetic resonance imaging (MRI) and its more recent advance, functional, or fMRI. Magnetoencephalography (MEG) and positron emission tomography (PET) are techniques also capable of catalyzing the progress of manual therapy research by virtue of their unique imaging capabilities particularly in the brain. The relatively high spatial and temporal resolution of these in vivo imaging techniques provides a structural (anatomical) display, which is co-registered in 3D space with functional (physiological i.e. synaptic activity, vascular perfusion) information. Such techniques offer the possibility of exciting new advances especially in the exploration of interactions of manual therapy with the central nervous system (CNS). Sensory, cognitive, and motor functions are displayed in response to a controlled series of stimuli in normal and disordered sample populations. The investigation of manual therapy interactions with clinically important CNS networks such as the pain neuromatrix, attentional or affective allocation in pain perception, or the potential for beneficial neuroplastic and autonomic modulation are a few promising areas for investigation.

This session will briefly highlight the technical principles, assumptions, and constraints of these imaging techniques with respect to exploration of the biological actions of manual therapy. Emphasis will be on the underlying biomechanical and CNS mechanisms. An overview of current work and some proposed areas for research in manual therapy utilizing these techniques is to be presented.

Both manual therapy and another CAM technique from Traditional Chinese Medicine, acupuncture, may share some mechanisms of action with respect to mechanoreceptor

signaling and CNS modulation. These parallels will be used as a guide to stimulate future research directions in manual therapy.

### **Biomechanics and Medical Imaging: Applying New Strategies To Answer Elusive Questions**

**Linda Woodhouse, Ph.D. (Candidate), B.Sc. (P.T.), Assistant Professor, School of Rehabilitation Science, McMaster University, Hamilton, Ontario Canada**

The last decade or so has seen an explosion of non-invasive biomechanical instruments and medical imaging techniques that can be used for reliable and precise measurement of in vivo biological responses (central and peripheral) in humans. In a quest to bridge the existing gap between clinical experience and science, this session will explore how advances in biomechanics and medical imaging (presented by the invited speakers) might be used to investigate the underlying biological effects of manual therapies in both animal and human models.

Our goal is to identify and prioritize key research questions in manual therapy that should benefit from the application of these new technologies. Some approaches and strategies will be presented for consideration when setting these priorities.

### **Manipulative and Body-Based Practices: An Overview**

**The following article was prepared by the National Center for Complimentary and Alternative Medicine of the National Institutes of Health. TheNCCAM provides information on CAM, including publications and searches of Federal databases of scientific and medical literature.**

#### **Introduction**

Under the umbrella of manipulative and body-based practices is a heterogeneous group of CAM interventions and therapies. These include chiropractic and osteopathic manipulation, massage therapy, Tui Na, reflexology, rolfing, Bowen technique, Trager bodywork, Alexander technique, Feldenkrais method, and a host of others (a list of definitions is given at the end of this report). Surveys of the U.S. population suggest that between 3 percent and 16 percent of adults receive chiropractic manipulation in a given year, while between 2 percent and 14 percent receive some form of massage therapy.<sup>1-5</sup> In 1997, U.S. adults made an estimated 192 million visits to chiropractors and 114 million visits to massage therapists. Visits to chiropractors and massage therapists combined represented 50 percent of all visits to CAM practitioners.<sup>2</sup> Data on the remaining manipulative and body-based practices are sparser, but it can be estimated that they are collectively used by less than 7 percent of the adult population.

Manipulative and body-based practices focus primarily on the structures and systems of the body, including the bones and joints, the soft tissues, and the circulatory and lymphatic systems. Some practices were derived from traditional systems of medicine, such as those from China, India, or Egypt, while others were developed within the last 150 years (e.g., chiropractic and osteopathic manipulation). Although many providers have formal training in the anatomy and physiology of humans, there is considerable variation in the training and the approaches of these providers both across and within

modalities. For example, osteopathic and chiropractic practitioners, who use primarily manipulations that involve rapid movements, may have a very different treatment approach than massage therapists, whose techniques involve slower applications of force, or than craniosacral therapists. Despite this heterogeneity, manipulative and body-based practices share some common characteristics, such as the principles that the human body is self-regulating and has the ability to heal itself and that the parts of the human body are interdependent. Practitioners in all these therapies also tend to tailor their treatments to the specific needs of each patient.

## **Scope of the Research**

### **Range of Studies**

The majority of research on manipulative and body-based practices has been clinical in nature, encompassing case reports, mechanistic studies, biomechanical studies, and clinical trials. A cursory search in PubMed for research published in the last 10 years identified 537 clinical trials, of which 422 were randomized and controlled. Similarly, 526 trials were identified in the Cochrane database of clinical trials. PubMed also contains 314 case reports or series, 122 biomechanical studies, 26 health services studies, and 248 listings for all other types of clinical research published in the last 10 years. On the other hand, for this same time period, there have been only 33 published articles of research involving in vitro assays or employing animal models.

### **Primary Challenges**

Different challenges face investigators studying mechanisms of action than those studying efficacy and safety. The primary challenges that have impeded research on the underlying biology of manual therapies include the following:

- Lack of appropriate animal models

- Lack of cross-disciplinary collaborations

- Lack of research tradition and infrastructure at schools that teach manual therapies

- Inadequate use of state-of-the-art scientific technologies

Clinical trials of CAM manual therapies face the same general challenges as trials of procedure-based interventions such as surgery, psychotherapy, or more conventional physical manipulative techniques (e.g., physical therapy). These include:

- Identifying an appropriate, reproducible intervention, including dose and frequency. This may be more difficult than in standard drug trials, given the variability in practice patterns and training of practitioners.

- Identifying an appropriate control group(s). In this regard, the development of valid sham manipulation techniques has proven difficult.

- Randomizing subjects to treatment groups in an unbiased manner. Randomization may prove more difficult than in a drug trial, because manual therapies are already available to the public; thus, it is more likely that participants will have a preexisting preference for a given therapy.

Maintaining investigator and subject compliance to the protocol. Group contamination (which occurs when patients in a clinical study seek additional treatments outside the study, usually without telling the investigators; this will affect the accuracy of the study results) may be more problematic than in standard drug trials, because subjects have easy access to manual therapy providers.

Reducing bias by blinding subjects and investigators to group assignment. Blinding of subjects and investigators may prove difficult or impossible for certain types of manual therapies. However, the person collecting the outcome data should always be blinded.

Identifying and employing appropriate validated, standardized outcome measures.

Employing appropriate analyses, including the intent-to-treat paradigm.

## **Summary of the Major Threads of Evidence**

### **Preclinical Studies**

The most abundant data regarding the possible mechanisms underlying chiropractic manipulation have been derived from studies in animals, especially studies on the ways in which manipulation may affect the nervous system.<sup>6</sup> For example, it has been shown, by means of standard neurophysiological techniques, that spinal manipulation evokes changes in the activity of proprioceptive primary afferent neurons in paraspinal tissues. Sensory input from these tissues has the capacity to reflexively alter the neural outflow to the autonomic nervous system. Studies are under way to determine whether input from the paraspinal tissue also modulates pain processing in the spinal cord.

Animal models have also been used to study the mechanisms of massage-like stimulation.<sup>7</sup> It has been found that antinociceptive and cardiovascular effects of massage may be mediated by endogenous opioids and oxytocin at the level of the midbrain. However, it is not clear that the massage-like stimulation is equivalent to massage therapy.

Although animal models of chiropractic manipulation and massage have been established, no such models exist for other body-based practices. Such models could be critical if researchers are to evaluate the underlying anatomical and physiological changes accompanying these therapies.

### **Clinical Studies: Mechanisms**

Biomechanical studies have characterized the force applied by a practitioner during chiropractic manipulation, as well as the force transferred to the vertebral column, both in cadavers and in normal volunteers.<sup>8</sup> In most cases, however, a single practitioner provided the manipulation, limiting generalizability. Additional work is required to examine interpractitioner variability, patient characteristics, and their relation to clinical outcomes.

Studies using magnetic resonance imaging (MRI) have suggested that spinal manipulation has a direct effect on the structure of spinal joints; it remains to be seen if this structural change relates to clinical efficacy.

Clinical studies of selected physiological parameters suggest that massage therapy can alter various neurochemical, hormonal, and immune markers, such as substance P in patients who have chronic pain, serotonin levels in women who have breast cancer, cortisol levels in patients who have rheumatoid arthritis, and natural killer (NK) cell numbers and CD4+ T-cell counts in patients who are HIV-positive.<sup>9</sup> However, most of these studies have come from one research group, so replication at independent sites is necessary. It is also important to determine the mechanisms by which these changes are elicited.

Despite these many interesting experimental observations, the underlying mechanisms of manipulative and body-based practices are poorly understood. Little is known from a quantitative perspective. Important gaps in the field, as revealed by a review of the relevant scientific literature, include the following:

- Lack of biomechanical characterization from both practitioner and participant perspectives
- Little use of state-of-the-art imaging techniques
- Few data on the physiological, anatomical, and biomechanical changes that occur with treatment
- Inadequate data on the effects of these therapies at the biochemical and cellular levels
- Only preliminary data on the physiological mediators involved with the clinical outcomes

### **Clinical Studies: Trials**

Forty-three clinical trials have been conducted on the use of spinal manipulation for low-back pain, and there are numerous systematic reviews and meta-analyses of the efficacy of spinal manipulation for both acute and chronic low-back pain.<sup>10-14</sup> These trials employed a variety of manipulative techniques. Overall, manipulation studies of varying quality show minimal to moderate evidence of short-term relief of back pain. Information on cost-effectiveness, dosing, and long-term benefit is scant. Although clinical trials have found no evidence that spinal manipulation is an effective treatment for asthma,<sup>15</sup> hypertension,<sup>16</sup> or dysmenorrhea,<sup>17</sup> spinal manipulation may be as effective as some medications for both migraine and tension headaches<sup>18</sup> and may offer short-term benefits to those suffering from neck pain.<sup>19</sup> Studies have not compared the relative effectiveness of different manipulative techniques.

Although there have been numerous published reports of clinical trials evaluating the effects of various types of massage for a variety of medical conditions (most with positive results), these trials were almost all small, poorly designed, inadequately controlled, or lacking adequate statistical analyses.<sup>20</sup> For example, many trials included co-interventions that made it impossible to evaluate the specific effects of massage, while others evaluated massage delivered by individuals who were not fully trained massage therapists or followed treatment protocols that did not reflect common (or adequate) massage practice.

There have been very few well-designed controlled clinical trials evaluating the effectiveness of massage for any condition, and only three randomized controlled trials have specifically evaluated massage for the condition most frequently treated with

massage--back pain.<sup>21</sup> All three trials found massage to be effective, but two of these trials were very small. More evidence is needed.

### **Risks**

There are some risks associated with manipulation of the spine, but most reported side effects have been mild and of short duration. Although rare, incidents of stroke and vertebral artery dissection have been reported following manipulation of the cervical spine.<sup>22</sup> Despite the fact that some forms of massage involve substantial force, massage is generally considered to have few adverse effects. Contraindications for massage include deep vein thrombosis, burns, skin infections, eczema, open wounds, bone fractures, and advanced osteoporosis.<sup>21,23</sup>

### **Utilization/Integration**

In the United States, manipulative therapy is practiced primarily by doctors of chiropractic, some osteopathic physicians, physical therapists, and physiatrists. Doctors of chiropractic perform more than 90 percent of the spinal manipulations in the United States, and the vast majority of the studies that have examined the cost and utilization of spinal manipulation have focused on chiropractic.

Individual provider experience, traditional use, or arbitrary payer capitation decisions--rather than the results of controlled clinical trials--determine many patient care decisions involving spinal manipulation. More than 75 percent of private payers and 50 percent of managed care organizations provide at least some reimbursement for chiropractic care.<sup>24</sup> Congress has mandated that the Department of Defense (DOD) and the Department of Veterans Affairs provide chiropractic services to their beneficiaries, and there are DOD medical clinics offering manipulative services by osteopathic physicians and physical therapists. The State of Washington has mandated coverage of CAM services for medical conditions normally covered by insurance. The integration of manipulative services into health care has reached this level despite a dearth of evidence about long-term effects, appropriate dosing, and cost-effectiveness.

Although the numbers of Americans using chiropractic and massage are similar,<sup>1-5</sup> massage therapists are licensed in fewer than 40 states, and massage is much less likely than chiropractic to be covered by health insurance.<sup>2</sup> Like spinal manipulation, massage is most commonly used for musculoskeletal problems. However, a significant fraction of patients seek massage care for relaxation and stress relief.<sup>25</sup>

### **Cost**

A number of observational studies have looked at the costs associated with chiropractic spinal manipulation in comparison with the costs of conventional medical care, with conflicting results. Smith and Stano found that overall health care expenditures were lower for patients who received chiropractic treatment than for those who received medical care in a fee-for-service environment.<sup>26</sup> Carey and colleagues found chiropractic spinal manipulation to be more expensive than primary medical care, but less expensive than specialty medical care.<sup>27</sup> Two randomized trials comparing the costs of chiropractic care with the costs of physical therapy failed to find evidence of cost savings through chiropractic treatment.<sup>28,29</sup> The only study of massage that measured costs found that the costs for subsequent back care following massage were 40 percent lower than those following acupuncture or self care, but these differences were not statistically significant.<sup>30</sup>

## **Patient Satisfaction**

Although there are no studies of patient satisfaction with manipulation in general, numerous investigators have looked at patient satisfaction with chiropractic care. Patients report very high levels of satisfaction with chiropractic care.<sup>27,28,31</sup> Satisfaction with massage treatment has also been found to be very high.<sup>30</sup>

## **Definitions**

**Alexander technique:** Patient education/guidance in ways to improve posture and movement, and to use muscles efficiently.

**Bowen technique:** Gentle massage of muscles and tendons over acupuncture and reflex points.

**Chiropractic manipulation:** Adjustments of the joints of the spine, as well as other joints and muscles.

**Craniosacral therapy:** Form of massage using gentle pressure on the plates of the patient's skull.

**Feldenkrais method:** Group classes and hands-on lessons designed to improve the coordination of the whole person in comfortable, effective, and intelligent movement.

**Massage therapy:** Assortment of techniques involving manipulation of the soft tissues of the body through pressure and movement.

**Osteopathic manipulation:** Manipulation of the joints combined with physical therapy and instruction in proper posture.

**Reflexology:** Method of foot (and sometimes hand) massage in which pressure is applied to "reflex" zones mapped out on the feet (or hands).

**Rolfing:** Deep tissue massage (also called structural integration).

**Trager bodywork:** Slight rocking and shaking of the patient's trunk and limbs in a rhythmic fashion.

**Tui Na:** Application of pressure with the fingers and thumb, and manipulation of specific points on the body (acupoints).

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## Research articles

### **The effectiveness of extra corporeal shock wave therapy for plantar heel pain: a systematic review and meta-analysis**

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## Background

There is considerable controversy regarding the effectiveness of extracorporeal shock wave therapy in the management of plantar heel pain. Our aim was to conduct a systematic review of randomized controlled trials to investigate the effectiveness of extracorporeal shock wave therapy and to produce a precise estimate of the likely benefits of this therapy.

## **Methods**

We conducted a systematic review of all randomized controlled trials (RCTs) identified from the Cochrane Controlled trials register, MEDLINE, EMBASE and CINAHL from 1966 until September 2004. We included randomized trials which evaluated extracorporeal shock wave therapy used to treat plantar heel pain. Trials comparing extra corporeal shock wave therapy with placebo or different doses of extra corporeal shock wave therapy were considered for inclusion in the review. We independently applied the inclusion and exclusion criteria to each identified randomized controlled trial, extracted data and assessed the methodological quality of each trial.

## **Results**

Six RCTs (n = 897) permitted a pooled estimate of effectiveness based on pain scores collected using 10 cm visual analogue scales for morning pain. The estimated weighted mean difference was 0.42 (95% confidence interval 0.02 to 0.83) representing less than 0.5 cm on a visual analogue scale. There was no evidence of heterogeneity and a fixed effects model was used.

## **Conclusion**

A meta-analysis of data from six randomized-controlled trials that included a total of 897 patients was statistically significant in favor of extracorporeal shock wave therapy for the treatment of plantar heel pain but the effect size was very small. A sensitivity analysis including only high quality trials did not detect a statistically significant effect.

## **Background**

Plantar heel pain (plantar fasciitis) can be debilitating, often with severe limitations on activity. Typically, patients present with pain in the plantar aspect of the heel whilst walking, particularly after rest. Pain on first weight-bearing in the morning is a prominent diagnostic feature. The precise nature of the condition is poorly understood but literature suggests it is an enthesitis at the attachment of the plantar fascia to the plantar medial tubercle of the calcaneum.

A systematic review of the management of heel pain has highlighted the paucity of evidence for managing the condition. The review concluded that treatments used to reduce heel pain, including steroid injections, NSAIDs, night splints, orthoses and stretching regimes, seem to bring only marginal gains [1]. Extracorporeal shock wave therapy (ESWT) was originally used for lithotripsy, but within the last 10 years has become increasingly used to treat musculoskeletal injuries including calcific tendinitis of the shoulder [2], lateral epicondylitis (tennis elbow) [3-5], non-union or delayed osseous union [6] and plantar heel pain [1,7].

Non-systematic review articles, specific to the effectiveness of ESWT in the treatment of plantar heel pain, produce conflicting conclusions. One 'biometric' review [7] suggested that there is insufficient evidence on which to draw conclusions on the effectiveness of ESWT and that more trials are required to detect any benefits from the intervention. Bodekker et al [7] incorporated all levels of evidence, including 4 randomized trials, that did not permit pooling of data or statistical synthesis. Study characteristics and quality assessments were provided in the form of lists. Ogden et al's review of ESWT [8] used a "vote counting" method to conclude that ESWT was a useful treatment for plantar heel pain. No quality assessment of the included trials was presented, but a quantitative data synthesis claims success rates ranging from 34% to 88%. Unfortunately, these estimates are not clearly attributed to any specific outcome. Heller and Niethard [9] identified poor trial methodological quality as a barrier to an assessment of the effectiveness of ESWT and were unable to demonstrate any benefit from the treatment in this narrative review article.

There is considerable controversy emerging regarding the use of ESWT for plantar heel pain. Three recent randomized controlled trials have failed to demonstrate a beneficial effect from the use of ESWT [10-12] and it has been suggested that no more clinical trials should be conducted to evaluate this therapy as a treatment for the painful heel [11]. A narrative review article [13] concluded that the available data do not provide substantive support for its use but this prompted correspondence which illustrates the defense for this electrophysical modality in the management of heel pain [14,15]

The purpose of this systematic review was to conduct a rigorous evaluation using a quantitative synthesis of evidence from randomized controlled trials to make a precise estimate of the effectiveness of ESWT. Our aim was to determine if ESWT is effective in the treatment of patients with plantar heel pain when compared with a control group.

### **Search strategy**

Randomized controlled trials were identified by searching the following data sources: The Cochrane Musculoskeletal Injuries Group specialized register of trials (August 2003), the Cochrane Central Register of Controlled Trials (The Cochrane Library issue 3, 2003), MEDLINE (from 1966 to September 2004), EMBASE (from 1982 to September 2004), CINAHL (from 1982 to September 2004) and reference lists of articles and dissertations. In Medline (SilverPlatter), the first two levels of the optimum search strategy [16] were combined with the following subject-specific search terms:

1. HEEL\* and SYNDROME\*
2. (JOG\* or TENNIS\* or POLICE\* or GONORREAL) near HEEL\*
3. PLANTAR near FASCI\*
4. explode "FASCIITIS"/ all subheadings
5. (PLANTAR or HEEL\* or CALCAN\* or FOOT\*) near PAIN\*
6. HEEL near SPUR
7. "CALCANEUS"/ all subheadings

8. #1 or #2 or #3 or#4 or #5 or #6 or #7

Further details of the search strategy and details of the hand search have been previously published.

### **Study selection**

We considered all randomized controlled trials of plantar heel pain treatments for inclusion in the review. Trials comparing ESWT with placebo or different doses of ESWT were considered. Participants with a clinically confirmed diagnosis of plantar heel pain were included. Adult participants in any trial whether they were part of the general population, athletes, or individuals with seronegative arthropathies and enthesopathies were also considered for inclusion. Any age group was admissible. It was our intention that trials involving children alone, or dealing specifically with young athletes, would be analysed separately. We excluded trials evaluating treatments for plantar heel pain arising from calcaneal fractures, calcaneal tumours, previous surgery for plantar heel pain, or posterior heel pain.

### **Outcome measures**

We chose morning pain as our a priori primary outcome measure for this systematic review. We consider it to be the most important outcome as it is the single most consistent feature of plantar heel pain. Morning pain (pain on first rising, first step pain or start up pain) is universally reported by patients complaining of plantar heel pain and it is also strongly diagnostic for the condition[17]. The secondary outcome measures were walking pain, pressure pain, any measure of disability, quality of life measures and adverse events.

### **Data abstraction**

Two of the authors (CT,FC) independently applied the inclusion and exclusion criteria to each trial and then extracted data regarding details of the patients (number, mean age and age range, inclusion and exclusion criteria), details of the interventions, nature and timing of outcome measures. Disagreements were resolved by discussion of the articles by the reviewers. We wrote to trialists for additional information on trial methodology (method of randomization) and results (usually requests for data not presented in the original reports such as standard deviations or some other measure of variance).

### **Validity assessment**

A quality assessment tool[18] adapted for use in a related systematic review of interventions for the treatment of plantar heel pain for the Cochrane Library [1] was applied to each of the included trials. This addressed the following questions:

1. Was the generation of randomization sequence described?
2. Was the method of allocation concealment described?
3. Was an intention to treat analysis used?

We assessed intention to treat on the basis of whether patients were analyzed according to the allocated treatment irrespective of whether this treatment was delivered or not.

4. What number of patients were lost to follow-up?

In assessing loss to follow-up we considered whether authors had presented numbers lost and timing, and the reasons for the loss. We presented the numbers lost to follow up as percentages.

5. Was the outcome assessment blind?

6. Was the patient blind to treatment allocation?

This led to each trial being attributed a quality score out of a maximum of 6 points.

### **Quantitative data synthesis**

When measures of variance were not available from the original report, it was our intention to derive these from p-values. When data were available for a pooled estimate of the impact of intervention it was intended that meta-analyses would be conducted for direct comparisons. We intended to present weighted mean differences and 95% confidence intervals for outcomes for each randomized controlled trial and group them in relevant sub-groups according to the specific question they addressed. We intended to use a fixed effects model to estimate the pooled effect as our primary analysis where no evidence of heterogeneity was detected [19]. However, if evidence of heterogeneity was found to be present we intended to use a random effects model [20]. Meta-analyses were generated using RevMan software. We planned to perform subgroup analyses and sensitivity analyses, regarding any anomalies with the included trials, methodological scores and industry sponsorship. We proposed to perform a funnel plot to detect publication bias.

### **Selection of trials**

The search strategy identified a total of 205 studies, of which 15 were identified as RCTs that evaluated ESWT for plantar heel pain. Two of these were translated from German into English [21,22]. Four trials [23-26] were excluded from the review: in one, the intervention and control groups were treated at different time points making valid comparisons of patient outcomes in both groups impossible [24]. The second trial contained five year follow-up data from an RCT published in 1996 [23]. These trial data were confounded by placebo patients receiving additional therapies after 12 weeks. The third [25] and fourth [26] excluded trials were duplicated data previously reported by Buch [27] and by Ogden [28] respectively. The flow diagram in Figure 1 provides details of the included and excluded trials and those included in the final meta-analysis[29].

### **Description of included studies**

Eleven RCTs were included in this review and they reported data published between 1996–2003 from trials involving 1290 patients [10-12,21,22,27,28,30-33]. Table 1 shows the quality assessment scores and Table 2 and Table 3 the baseline data. The trials evaluated different doses of ESWT against either a placebo dose or a control dose so low as to be considered therapeutically ineffective [10] (Table 4). Only five of the trial

reports contained summary statistics to permit pooling of data collected at 12 weeks in a forest plot [10-12,27,28]. Standard deviations were derived from the p value reported in one manuscript in order to incorporate a sixth trial in the meta-analysis, the timing of the outcomes varied between 17 and 20 weeks for this trial [21].

Table 2 and table 3 present details of the baseline pain scores, and demographic variables for participants from all eleven included trials. All included adult patients only. The duration of pain was greater than 6 months in ten trials [11,12,21,22,27,28,30-33]. In one trial [10] the duration of pain was shorter than six months for some patients but no patient had a duration of pain less than 8 weeks. The duration of pain ranged from 8–600 weeks and 8–980 weeks for the ESWT and placebo groups respectively. The median values for duration of pain were 36 weeks and 43 weeks. The demography of the patients in this systematic review of ESWT for plantar heel pain was similar to those patients who have participated in evaluations of other interventions for heel pain [1]. The effects of ESWT in people who had a calcaneal spur on x-ray [4,32], were running athletes [31], were being considered for surgical intervention [30,32,32], had failed to respond to conservative treatments [27,28,30,32], or were defined as recalcitrant cases [22], were all included in this systematic review.

There was diversity in the types of primary and secondary outcomes collected from patients in the 11 RCTs. summarizes the most commonly reported outcomes measures indicating, where available, the outcomes provided. With the exception of three trials [22,30,32] all presented data for visual analogue scale scores of morning pain. Walking pain is a relevant outcome measure and was reported by eight trials [10,11,21,22,30,32,33]. Only two of these trials contained compatible data [30,32] and insufficient data are provided to permit pooling. The remaining trials described a wide variety of walking ability using incongruous scoring systems. Six of the trials [11,21,22,30,32,33], show a favorable outcome for walking pain after ESWT. Resting and night pain are not common symptoms of heel pain, in our experience, but data for these outcomes were collected in four trials [12,21,30,32]. Five trials reported the collection of pressure pain outcomes from the application of pressure from either a manual application or an electronic device [21,27,28,30,32]. Other outcomes reported were Roles and Maudsley scores [11,21,27], Maryland Foot score [10], SF12 [27], SF36 [10], problem elicitation technique [10] and The Ankle Hindfoot Scale [31].

Of the 11 RCTs that met our inclusion criteria, eight were placebo controlled trials [11,12,21,27,28,31-33]. Three trials used a low, sub-therapeutic dose as control [10,22,30]. The doses for the intervention groups and methods used to disable the equipment for the placebo group and the sub-therapeutic groups are provided in Table 2 and Table 3. The dose of ESWT varied between trials in both energy levels and the number of impulses administered. With the exception of two trials, [10,12], all excluded patients had the condition for less than six months. Only one trial [10] did not require patients to have exhausted conservative therapies for recalcitrant plantar heel pain before embarking on treatment with ESWT but information presented reveals that the majority of patients did receive a number of conservative therapies. Krischek et al [22] and Rompe et al [31] included only patients whose next management option was surgery.

## Quantitative data synthesis

Figure 2. shows the pooled analysis of data from 6 trials which produce a weighted mean difference of 0.42 in favor of ESWT. This treatment effect is statistically significant ( $p = 0.04$ ), but the effect is small (95% confidence interval of 0.02 to 0.83) with respect to morning pain (first step pain). All outcomes were taken at 12 weeks, except for one trial [21] which reported the first outcome measured at (on average) 19 weeks. There was no evidence of heterogeneity ( $p = 0.11$ ) and a fixed effects model was used.

We repeated the meta-analysis excluding the data from the trial by Abt et al [21], the only trial for which we had to impute measures of variance. The resultant weighted mean difference was 0.30 in favor of ESWT, with a 95% confidence interval of -0.12 to 0.72. This effect is no longer statistically significant.

We performed a sensitivity analysis for the quality of trial reports by dividing the six trials into two groups; those that received a quality assessment score of four or more [10-12,27] and those receiving a score of less than four [21,28] to perform meta-analyses using fixed effects models. The four better quality trials produced a non significant result (weighted mean difference 0.21, 95% confidence interval -0.29 to 0.70 cm,  $p = 0.41$ ) whereas the two trials scoring less than three produced a significant result in favor of active treatment (weighted mean difference -0.90, 95% confidence interval -1.62 to -0.19,  $p = 0.01$ ).

## Adverse events

Two trials did not report adverse events [12,30]. Buchbinder et al [10] reported pain for one week by one patient in each arm of the trial; one patient in the active arm of the trial reported a sensation of heat and numbness, whilst another complained of bruising. One patient in the placebo arm complained of a burning sensation in the heel and ankle. Ogden et al [28] reported 38 procedure related complications, 18 of which occurred in the active treatment arm. The most common procedure related complications were mild neurological symptoms (numbness, tingling). One patient who suffered a plantar fascial rupture 4 weeks after active treatment had undergone multiple cortisone injections prior to embarking upon treatment with ESWT.

Haake et al [11] reported a statistically significant difference in the number of side effects in the active and placebo groups; OR 2.26 (95% confidence interval 1.02 to 5.18) [11]. These were; skin reddening, pain and local swelling. The same authors [11] also describe less frequent complaints of dizziness, sleep disturbance haematoma, nausea and hair loss as non-serious effects and discounted one report of a deep vein thrombosis in a placebo participant as a co-incidental event. In two trials, [31,32] the unpleasant nature of ESWT experienced by patients during treatment was reported. These sensations were regarded as less unpleasant than local cortisone infiltration. Krischek et al [22] reported that there were no adverse events noted in trial participants.

## Industry sponsorship

Companies who produce ESWT equipment provided some sponsorship in three trials [11,27,28] (Table 6). One trial [28] was the basis for the first Food and Drug Administration (FDA) approval for ESWT. A financial interest with HealthTronics was declared in correspondence following the publication of the trial [34,35]. The trial by

Buch et al [27] was sponsored by Dornier Med tech Inc and the data were also used to gain approval for the use of ESWT in the management of plantar heel pain from the FDA. Haake et al [11] stated no competing interests but did declare that a manufacturer of ESWT equipment had provided the machine used in the trial. Two trials [10,12] declared funding from sources other than industry. In the remaining trials there was no explicit declaration of competing interests [21,22,30-33] (Table 6).

## Discussion

The lack of convergence of findings from randomized evaluations of ESWT for plantar heel pain has resulted in clinical uncertainty about its effectiveness. Within this systematic review, we have been able to evaluate the effectiveness of ESWT in a meta-analysis and used the pooled data to arrive at more precise conclusions about its usefulness in clinical practice.

The meta-analysis shows a statistically significant benefit with ESWT on plantar heel pain from outcomes of 897 patients' VAS scores of morning (first-step) pain assessed at or around 12 weeks but we do not consider this clinically significant since the observed benefit equates to less than one half centimeter on a 10 cm VAS. The 95% confidence interval is compatible with a mean treatment benefit of at most 0.83 cm. A sensitivity analysis including only those higher quality trials did not produce evidence of a statistically significant benefit. Only one trial included in the review discussed what might constitute a clinically meaningful reduction in plantar heel pain: Buchbinder et al [10], suggest that 0.7 cm reduction of heel pain may not be clinically relevant.

We included one trial in the meta-analysis which used sub-clinical doses as controls [10] and combined these patient outcomes with those from trials which used sham treatments as controls [11,12,21,27,28]. All six trials [10-12,21,27,28] also used different doses of ESWT but, despite the differences in the use of control interventions and doses, no evidence of heterogeneity in the patient outcomes was detected in the pooled estimate (figure 2). Nor does there appear to be a dose-response relationship for ESWT; trials using both high and low doses have reported similar effects as is evident from the estimates from the trials by Haake et al [11] and Abt et al [21] (Table 6, figure 2).

We were grateful to the authors of trials included in this review who provided supplementary data in response to our correspondence [10,11] but disappointed that data from all 11 trials were not available to us. Five trials were not included in the meta-analysis either because adequate data were not provided [22,33] the timing of the outcomes differed greatly from the other trials [31] or the outcomes were clinically irrelevant [30,32]. Consequently, information about the effects of ESWT in 310 patients with heel pain was effectively lost to re-analysis. Any future reporting of patient outcomes should include means of pain scores with measures of variance in order that new trials can be included in meta-analyses and weighted mean differences and confidence intervals calculated [36].

Rompe et al conducted a small trial (n = 40) which evaluated the benefits of ESWT in running athletes [31] and reported a mean difference of 2.60 (95% confidence interval 1.37 to 3.83) for morning pain at 6 months. This effect size is statistically significantly different from the combined outcomes presented in Figure 2 but not statistically different from the mean difference in outcomes reported in the small trial by Abt et al [21] 2.00 (95%confidence interval 0.47 to 3.53) at 19 weeks (n = 37). That the two smallest trials

included in the review should produce between-group comparisons of pain in the morning that reach statistical significance when estimates from larger studies do not is surprising. Sample size is an important factor in experimental bias in clinical trials as effect size estimates from small studies can be highly variable [37]. The effect sizes from these small studies may be due to ESWT being beneficial in certain sub groups within the population (e.g. runners), or may be as a result of a failure to blind the participants successfully to their treatment allocation, as previously reported by one of the authors [30]. Alternatively, these data may be aberrant values that are more likely to occur by chance in small studies than larger ones [38].

ESWT was not considered a suitable therapy for the first-line management of heel pain by the majority of the investigators. This may be because of limited access to this relatively new and expensive equipment or, more likely, because of the favorable natural history of this condition.

In the absence of a validated heel pain specific outcome measure, our a priori choice of morning pain as the primary outcome measure was vindicated by eight of the eleven included trials collecting morning pain or first step/start up pain outcomes. One trialist [10] used a problem elicitation technique which confirmed "walking after getting out of bed in the morning" as the most frequently reported problem by patients with heel pain. We had planned to pool additional secondary outcome measures, such as walking pain, but this was not possible because of the diversity of the outcome measures used and differences in the data collected. Some of the outcomes that have been used to assess the effects of treatments were clinically irrelevant in our opinion [30-33]. Night pain and resting pain are not symptoms that we commonly encounter in patients seeking treatment for plantar heel pain. Three trials [11,21,27] incorporated the Roles Maudsley scale and one trial [10] used the Maryland Foot Score as measures of disability. It is commendable that two of the investigators [10,27] used generic health outcomes, SF36 and SF 12 respectively. Future trials should include outcomes of disability as well as the impact on health related quality of life and not just pain when assessing the effect of interventions for heel pain.

Of the eight outcomes listed in Table 5, only "pain at rest" is distinct with four of the five trials [11,21,30,32,33] favoring ESWT compared with placebo or reduced dose. As previously discussed, this outcome measure is not a key feature of plantar heel pain. All other outcome measures are equivocal.

Minimal side effects were reported by Abt et al [21] and Buchbinder et al [10]. The most frequently reported adverse event from the use of ESWT is pain [11,27,32,33] which appeared to affect some patients both during and after the procedure.

The quality of reporting varied amongst trials. The three most recent trials [10,11,31] all received above average quality scores for trial reporting. This is an encouraging development for those interested in improving the outcomes for patients who have heel pain and may reflect both the use of checklists such as the CONSORT statement [36] for trial reports now demanded by many journal editors as well as a greater awareness of good trial reporting practice by trialists themselves. There was however, a contrast in the results obtained from the four better quality trials, scoring three or above, when meta-analyzed separately from the two poorer quality trials. Better quality trials did not favor ESWT whilst the poorer quality ones did.

## **Industry sponsorship**

At least two of the trials included in our meta-analysis, received some form of sponsorship from a company manufacturing ESWT [27,28] although this has not been made explicit within the published papers. Both these trials reported significant benefit from ESWT. One further trial Haake et al [11] declared being supplied with the ESWT equipment and reported no statistically significant effects between the two groups. Six of the trials [21,22,30-33] have not made it clear whether there is any conflict of interest or not. In a systematic review to investigate whether the funding of drug studies by the pharmaceutical industry is associated with bias, Lexchin et al [39] concluded that industry sponsorship was more likely to produce results favoring the sponsors' product than studies funded from other sources.

## **Publication bias**

In view of concerns about publication bias, it is encouraging that three large, negative trials have been published in high impact journals. We were unable to recognize the existence of small, unpublished studies showing no statistically significant benefits. However, the existence of any such trials would only serve to endorse the findings of the meta-analysis in this systematic review.

## **Conclusion**

It has been suggested that the poor outcomes reported by recent randomized controlled trials evaluating ESWT for plantar heel pain means no further trials should be conducted [11]. A meta-analysis of data from six randomized controlled trials that included a total of 897 patients was statistically significant in favor of extracorporeal shock wave therapy for the treatment of plantar heel pain but the effect size was very small. When the two poorest quality trials, and therefore the greatest source of bias, are removed from the meta-analysis, the result is not statistically significant. This systematic review does not support the use of ESWT for plantar heel pain in clinical practice.

## **Abbreviations**

ESWT: Extracorporeal shock wave therapy

## **Competing interests**

The author(s) declare that they have no competing interests.

## **Authors' contributions**

FC and CT performed the literature search, extracted data, performed data analyses and compiled the manuscript. GM performed data analyses and compiled the manuscript. We can confirm that all authors have access to all data in the study and that they held final responsibility for the decision to submit for publication.

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**Psychosocial factors and their role in chronic pain: A brief review of development and current status** Stanley I Innes\*

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(Original source of article Biomedcentral. This version of the article cited above has been abbreviated from the original. Tables and illustrations are omitted)

**Abstract**

The belief that pain is a direct result of tissue damage has dominated medical thinking since the mid 20th Century. Several schools of psychological thought proffered linear causal models to explain non-physical pain observations such as phantom limb pain and the effects of placebo interventions. Psychological research has focused on identifying those people with acute pain who are at risk of transitioning into chronic and disabling pain, in the hope of producing better outcomes.

Several multicausal Cognitive Behavioral models dominate the research landscape in this area. They are gaining wider acceptance and some aspects are being integrated and implemented into a number of health care systems. The most notable of these is the concept of Yellow Flags. The research to validate the veracity of such programs has not yet been established.

In this paper I seek to briefly summarize the development of psychological thought, both past and present, then review current cognitive-behavioral models and the available supporting evidence. I conclude by discussing these factors and identifying those that have been shown to be reliable predictors of chronicity and those that may hold promise for the future.

**Introduction**

There is an increasing interest and acceptance in psycho-social factors and their correlations to the onset and outcomes of acute pain episodes. This review will briefly review its evolution and summarize the past and present theoretical models in relation to low back pain (LBP). Psychlit, MEDLINE and medindex searches were conducted to

identify relevant articles with the search words 'psychological factors, chronic/persistent pain'.

### Historical development

The psychological and psychiatric aspects of pain had been infrequently noted by modern writers as early as 1768. For a comprehensive historical review see Merksy & Spear [1]. By the second half of the 19th Century, however, pain was considered sensorial and organic causes were offered to explain all pains, even those without an obvious basis in tissue damage or organic disease. The belief that all pain was a direct result of tissue damage was firmly entrenched by the early 20th Century [2].

By the late 1950's it became increasingly evident that sensory explanations failed to account for certain puzzling pain phenomena (e.g., relief from pain with placebo interventions, phantom limb pain). Around the mid-20th Century several different theories were developed from differing theoretical backgrounds to explain the observation that sensory input did not always correlate with pain. I have summarized these differing schools of thought by précising a comprehensive review by Gamsa [3,4].

### Psychoanalytic Formulations

Here intractable pain, which defies organic explanations, was seen as a defense against unconscious conflict. Emotional pain is displaced onto the body where it is more bearable. For example, conscious or unconscious guilt with pain serving as a form of atonement, or the development of pain to replace feelings of loss. Critics have raised serious methodological and conceptual concerns [5,6]. For example; the ability to quantify and research the constructs of Id, ego and superego. Psychoanalytic thinking no longer forms a significant basis for research or source of current interventions.

### Behaviorist Models

Following the work of Skinner [7], behaviorists tried to show that all behavior could be shaped, altered, weakened or strengthened as a direct of environmental manipulations. Fordyce et al. [8] were the first to apply the behavior model to pain. It was thought that there was a simple causal connection between pain and its reinforcers. Respondent (acute) pain was seen as a reflexive response to antecedent stimulus (tissue damage). The respondent pain may eventually evolve into operant and persisting pain if the environment offers pain contingent reinforcement. Pain behavior may also be learned by observing "pain models" i.e., individuals who exhibit such behavior. More complex factors such as personal dynamics, emotional state, physical vulnerability, and numerous psychosocial variables were not addressed. It proposed that operant pain persists because the behavior of others (family, friends and health care providers) during the acute pain stage reinforced that pain returned secondary gains, such as permission to avoid chores, or obtain otherwise unobtainable attention and care. Behavior models have however contributed to the study of pain by the introduction of carefully designed control procedures and laboratory methods [4].

### Cognitive Approaches

Cognitive approaches were inspired in part by Melzack and Wall's [9] gate control theory, which established a role for the cognitive-evaluative process in the modulation of

pain. Since the mid 1970's proponents of cognitive theory studied the influence of the meaning of pain to patients, and examined the effect of coping styles on pain, for further review see Weisenberg [10]. Cognitive theory examines intervening variables such as attributions, expectations, beliefs, self-efficacy, personal control, attention to pain stimuli, problem solving, coping self-statements and imagery. Pain studies investigated the effects of these thought processes on the experience of pain and related problems. Cognitive theory has added an important dimension to psychological research into pain, but cognitive theorists themselves emphasize that they do not provide the solution, in isolation from other aspects of the multidimensional problem of pain [4,19]. The combination of cognitive and behavioral approaches has been employed extensively in pain programs during the last 15–20 years with some reported success [11].

### Psychophysiological Approaches

Examines the influence of mental events (thoughts memories and emotions) on physical changes which produce pain, for a comprehensive review see Flor and Turk [12]. For example, general arousal models propose that frequent or prolonged arousal of the Autonomic Nervous System (ANS) including prolonged muscular contractions, generate and perpetuate pain. Treatment, such as EMG, biofeedback, and relaxation techniques are designed to decrease the levels of muscular tension and ANS arousal and thereby decrease the pain. Studies have shown positive results from these interventions, but not necessarily more than other psychological techniques [3, 4].

In sum, psychological thought during the past half century has shifted from linear to multicausal models of pain. Methods of investigation have also improved.

### Current theoretical models

A substantial number of acute painful musculoskeletal injuries do not resolve quickly and account for the majority of the associated costs [13]. Early intervention appears to result in improved outcomes [14]. Consequently, it is not surprising that the on-going evolution of the understanding of the non-physical aspects of pain has been applied to the areas of screening for, intervening in and predicting those at risk of developing into a chronic and disabling situation [15,16,33]. The recent New Zealand Government review into LBP, its subsequent published guidelines, and resultant growing acceptance of the "Yellow Flags" concept is a pertinent example [17-19]. Variables such as attitudes, beliefs, mood state, social factors and work appear to interact with pain behavior, and are cumulatively referred to as psychosocial factors. However, to date there has not been developed a comprehensive, multivariate and empirically supported Integrated Biopsychosocial Risk-for-Disability Model. During a plenary session at the Forth International Forum on LBP Research in 2000 [20] Pincus et al amalgamated the Cognitive and behavioral thinking and proffered the closest structure yet to such a model. It has sought to incorporate many of these factors, and as such offers a structure from which to review these psychosocial factors.

The cognitive-behavioral researchers in the late 20th century noted that acute pain was associated with a pattern of physiologic responses seen in anxiety attacks, whilst chronic back pain was characterized more effectively by habituation of autonomic responses and by a pattern of vegetative signs similar to those seen in depressive disorders. One of the prominent researchers, Waddell, noted that one of the striking findings was that "fear of pain was more disabling than the pain itself" [21]. As a result

the notion that reduced ability to carry out daily tasks was merely a consequence of pain severity had to be reconsidered. Several studies have indicated that pain-related fear is one of the most potent predictors of observable performance and is highly correlated to self-reported disability levels in subacute and chronic pain [22, 23].

In the acute pain situation, "avoidance" behaviors, such as resting, are effective in allowing the healing process to occur [24]. In chronic pain patients, the pain and disability appear to persist beyond the expected healing time for such a complaint. The danger is that a protracted period of inactivity, as a strategy for coping with the persistent pain may lead to a disuse syndrome (see Figure 1). This is a detrimental condition. It is associated with physical deconditioning such as loss of mobility, muscle strength and lowered pain thresholds (allodynia). Consequently, the and will be less able to shift attention away from pain related information at the expense of other tasks, including actively coping with problems of daily life [34].

Although these and other factors such as coping strategies [35], sense of control [36], personality type [37], faith and religious beliefs [38], have been reported in literature (for a comprehensive review see Keefe et al.[44], the most significant and reproducible factors have been mood / depression and to a lesser extent somatization / anxiety [16,39]. Depression has been associated with decreased pain thresholds and tolerance levels, reduced ability, general withdrawal and mood disturbance such as irritability, anhedonia (loss of enjoyment of good things in life), frustration and reduced cognitive capacity.

Somatization disorder is a chronic condition in which there are numerous physical complaints. It is perceived as very similar in nature to, and difficult to differentiate from an anxiety disorder [40]. The most common characteristic of a somatoform disorder is the appearance of physical symptoms or complaints for which there is no organic basis. Such dysfunctional symptoms tend to range from sensory or motor disability, and hypersensitivity to pain. This is a difficult and complex syndrome and is more fully dealt with elsewhere [41].

A mention should be made of occupational factors. Job dissatisfaction has repeatedly demonstrated itself to be a significant factor in disability / persistent pain studies. The most recent literature has implicated such factors as support from supervisors at work and low job control (i.e., inadequate power to make decisions and utilize one's skills) which can create distress, and, when perpetual, may result in ill health [42].

## Conclusion

In sum, while this cognitive-behavioral model focused on fear / avoidance shows much promise; it has yet not been validated by the research to date [15]. There are studies in progress that may further our knowledge of identifying those at risk of progressing from acute to chronic [13]. Until the veracity of this model becomes further elucidated, depression and somatization / anxiety should be regarded as the central and dominant influencing psycho- logical factors in the assessment for identification and intervention strategies.

## Competing interests

The author(s) declare that they have no competing interests.

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## JAMMA ABSTRACT REVIEW

Journal of Bone and Joint Surgery

Senavongse W, Amis AA.

The effects of articular, retinacular, or muscular deficiencies on patellofemoral joint stability: A BIOMECHANICAL STUDY IN VITRO

JBJS B, 2005; 87(4):577-82.

The authors have performed an in vitro biomechanical study to compare the relative contributions of various patellar stabilizers. Eight cadaver knees were prepared and patellar stability tested in an intact knee and in various simulated deficiency conditions.

In an intact knee, lateral patellar displacement required least force at 200 of flexion. Contrary to popular belief, loss of VMO tension gave rise to increase of lateral patellar instability throughout the range of motion. Lateral trochlear dysplasia appeared to result in more instability compared to loss of VMO tension. Loss of medial retinacular constraint had little effect on instability on a flexed knee but became more important with increased knee flexion.

One has to be cautious in interpreting the results of an in vitro study. But an equivalent test would be difficult to perform in vivo for ethical reasons. The results would call into question the wisdom of exercising VMO in the last 150 of extension.

Clinical Biomechanics

Hortobagyi T et al.

Altered hamstring-quadiceps muscle balance in patients with knee osteoarthritis. Clin Biomech 20:97-104.

This article would be of interest to surgeons interested in physiotherapy as a mode of management in osteoarthritis. Various studies have shown that physiotherapy is a useful tool for treating early osteoarthritis of the knees. Physio mainly concentrates on quads build up exercise. In a non-randomised case control study, the authors show that quads-hamstrings muscle recruitment is altered in knee OA. Quad-hamstrings activity was tested with surface electrodes during level walking and stair climbing and descent. Hamstring muscle coactivity was found to be greater during ADL in OA subjects. That patients with knee OA have weak quads is well documented. However, studies in the past have not addressed the question of quads/hamstrings balance in OA. More importantly, the study also found that altered muscle response was more widespread than quads/hamstrings coupling and suggests that therapeutic interventions should not be limited to strengthening quadriceps muscles but also target other lower limb muscles.

Acta Orthopaedica Scandinavica

Rowe SM et al.

Why does outer joint motion predominate in bipolar hip prosthesis? Acta Orthop Scand 2004; 75(6):701-7.

Bipolar hip replacement has been advanced as a viable option in young patients with displaced subcapital fracture of neck of femur. The theoretical premise is that a bipolar head, in contrast to a unipolar one, would allow movement at the inner joint and preserve the acetabulum to some extent. Further studies have yet to prove this assertion. However, this has not distracted surgeons from offering bipolar hip prosthesis to their patients. Latest refutation of their practice comes from Korea. The authors examined the motion distribution of bipolar cup by inserting bipolar prosthesis in fresh frozen cadaver pelvis and observing the motions under video. They also did a fluoroscopic study of 50 bipolar hips done at their centre in different movements with or without weight bearing. They found that although both inner and outer motion coexisted in most of the patients, outer motion was predominant in all directions of leg movement. The authors feel that this could possibly be due to two reasons: early impingement of femoral neck on the liner and increased lubrication of the outer joint. The authors feel that variable degree of valgus positioning of the human acetabular cup results in early impingement of the prosthetic neck on the liner and induce outer cup motion. The other explanation offered is that on weight bearing synovial fluid is pressed out of the inner joint and lodges inside the less congruent outer joint. The more lubricated outer joint encourages more movement.

Journal of Bone and Joint Surgery (A)

Rodeo SA et al.

What's new in orthopaedic research? JBJS A 86 A Sept 2004 pp. 2085-97.

Authors have described recent advances in orthopaedic research in specialty update section in the recent issue of JBJS A.

Cartilage degradation and repair:

Our understanding of cartilage degradation and repair is still limited. Recent studies have indicated that extracellular matrix proteins, when fragmented, may have deleterious effect on chondrocyte metabolism. Many of the pathways involved in this interaction are being identified.

Using drugs to manipulate fracture healing:

It appears that our experience of treating osteoporosis could lead to increasing understanding of ways to use drugs to manipulate fracture healing. Bisphosphonate is used to treat osteoporosis. It prevents bone resorption by inhibiting osteoclasts. This mechanism also delays bone remodelling. Conversely, use of parathyroid hormone enhances bone formation and may help in treating disuse osteoporosis following trauma.

Use of NSAID following trauma:

There is concern that NSAIDs can impair fracture healing by inhibiting inflammation. Animal studies showed reversible impairment of fracture healing when COX 2 inhibitors were used. It is recommended that their short term use is safe in healthy patients but

NSAIDs should be avoided in patients with risk factors-diabetics, those on steroids, smokers etc.

Alternate implants:

To date implants used in orthopaedic practice are designed to transfer load to host bone. New hydrogel implants are being developed which intend to act as load sharing device. Hydrogel is hydrophilic polymer. Candidates for use would be meniscus replacement, IV disc replacement etc. Animal studies have shown promising results.

Tissue engineering:

One of the challenges of tissue engineering is to manufacture a tissue scaffold that can withstand in-vivo mechanical load and also allow biologic integration. The authors discuss studies that have explored nanotechnology to build better scaffolds.

Journal of Bone and Joint Surgery

V. Pinskerova; P. Johal; S. Nakagawa; A. Sosna; A. Williams; W. Gedroyc; M.A.R. Freeman

Does the femur roll-back with flexion? Volume 86-B Number 6 August 2004, 925-32.

The answer is, yes, but not as we know, or we like to think we know it does. In this multi-centre study, Pinskerova et al sets out to challenge this axiom of orthopaedic biomechanics. We are interested in the kinematics of the normal knee. That is what we would like to replicate in the prosthetic knee.

Femoral roll-back is a conceptual cornerstone around which controversy centres regarding modern design of total knee replacement. Proponents of PCL retaining prosthesis argue that keeping PCL helps to create nearer normal movement in the prosthetic knee. With increasing flexion, PCL tightens due to the four-bar rigid linkage mechanism which results in posterior roll-back of the femoral condyles and helps to give more ROM. However, studies comparing PCL retaining and sacrificing prostheses have not found this to be a significant factor.

The authors performed MRI scan on six cadaver knees and five living subjects during weight bearing squat and non weight bearing state to identify the relative position of the flexion facet centre of the two condyles and contact points at varying degrees of knee flexion. ( If you want to know what the flexion facet centre is you need to read another paper by the authors, which I have not yet read). Contact point was defined as the point at which medial and lateral subchondral plates of femur and tibia most closely approximated each other.

The study found posterior shift of contact points of both condyles in both living and cadaver knees, nullifying any possible role of muscular action. The PCL was never taut and could not have contributed towards a rigid linkage mechanism. The FFCs, on the other hand, moved differently. Lateral condyle moved backwards, but medial moved very little. The authors attribute this difference to the difference between the condylar articular shapes.

They conclude that femoral roll-back is a misnomer. There is posterior shift of the point of contact but the condyles essentially rotate externally with increasing flexion without any contribution from the PCL.

Journal of Bone and Joint Surgery

Noyes FR, Barber-Westin SD, Rankin M.

Meniscal Transplantation in Symptomatic Patients Less Than Fifty Years Old. J Bone Joint Surg Am 2004 86: 1392-1404.

A prospective review from Cincinnati on the results of meniscal transplantation in symptomatic young patients.

That menisci are important for shock absorption and load dissipation is now well known. Unfortunately, due to its poor vascularity very few menisci are amenable to repair. Partial or total meniscectomy results in early OA. A successful transplantation would be a great boon for many of these patients.

Noyes et al prospectively reviewed 40 allograft transplants in 38 knees. These were the result of sporting injuries. There was no control group. Patients with gross OA were excluded. Grafts were analysed pre and post transplantation by an independent observer with MRI. Most of the patients had single meniscal graft. Quite a few also had osteochondral graft and/or soft tissue procedures. The reported success rate is modest (more than 50% had abnormal allograft signal, 76% returned to light sports), the follow up is short (mean 40 months). Lateral meniscal graft is known to have better survival rate. They do not mention the side.

It can be argued that improvement in knee score could be due to the other procedures. Authors agree that the study shows the results of short term symptomatic beneficial effects only. They also recommend early than late transplantation. This is on the presumption that early transplantation would have some chondroprotective effect. Biomechanically, this makes sense.

Sadly, there are many unresolved issues with allograft. We do not know how meniscal allograft would respond to a different environment. Is there a long term chondroprotective effect? Future long term studies can answer that question. For now immediate short term effects seem to be encouraging.

Muschler GF, Nakamoto C, Griffith LG.

Engineering Principles of Clinical Cell-Based Tissue Engineering. J Bone Joint Surg Am 2004 86: 1541-1558.

A review article from USA on the principles of tissue engineering, including current position and future promises for the musculoskeletal system. The public perception of tissue engineering is limited to ex-vivo growth of new tissue and viable transplant in-vivo. Although we have not reached that stage as yet, research and development in this specialty has witnessed great strides. We learn about stem cell cycle, their broad phenotypic potential, and present efforts to utilize them. We learn of present strategies to target stem cells and future promises. Technology has advanced to the stage where it is

possible to harvest few stem cells and culture them to sufficient numbers to allow in vivo transplant. A major obstacle still is visible scaffolding that would protect transplanted cells and allow them intended function. Optimum type of scaffolding remains unresolved. A major emphasis in future is likely to be on modulation of local cellular environment. This could be a possibility with the use of viral vectors.

### **Journal of Biomechanics**

Lin TW, Cardenas L, Soslowky LJ.

Biomechanics of tendon injury and repair. J Biomech. 2004 Jun;37(6):865-77.

Type: review article

Setting: University of Pennsylvania, USA

Aims: To discuss tendon repair mechanisms, experimental animal models and current and future treatment modalities.

Tendons serve important functions. They transmit large tensile forces between bone and muscle. They are also prone to injury. Commonly, they are injured at the musculotendinous or osteotendinous junction due to overuse or tensile overload. Healing is difficult due to poor vascularity and cellular paucity. We know that functional outcome after tendon injury depends on many factors. There are proponents of both intrinsic and extrinsic tendon healing. Intrinsic theory demands that tendon can heal on it's own from local blood supply without scarring. Extrinsic theory proposes local inflammation, scarring and external blood supply to be important for healing. The truth, probably, is somewhere in the middle.

Natural history of tendon healing is with scar formation. This scar is biomechanically inferior to normal tissue. The gap has poor tensile strength and, if greater than 3 mm, does not improve over time.

Repair strength of tendon is directly proportional to the no. of strands crossing a repair site. Additional epitendon suture gives better strength over core suture alone.

Animal studies with activity have shown generally positive effect of exercise on tendon. Disuse has resulted in adhesion and poor functional property. Both active and passive motion of flexor tendons post-injury resulted in improved tensile property.

Finally, the paper discusses future treatment options. Biocomposite materials have been tested to serve as replacement tissue or to enhance healing. They have not been found to fulfill the biomechanical requirement of original in vivo function. Cytokines have also been proposed, but the delivery system is not still developed.

A new approach is functional tissue engineering (FTE). It intends to identify in-vivo functional requirement to design safer and more effective composite.

New developments in molecular biology are likely to make cell therapy a possibility. Mesenchymal stem cells are likely candidates for tendon healing therapy. They can be isolated from bone marrow. Delivery system is again a problem and to date, studies

have not showed marked difference in outcome. If the delivery system can be resolved, gene therapy could also become viable.

Chiropractic & Osteopathy 2005, 13:6 doi:10.1186/1746-1340-13-6

Stanley I Innes

Psychosocial factors and their role in chronic pain: A brief review of development and current status

Setting: Private Practice 35 Maroondah Highway, Lilydale, 3140, Australia

Published 27 April 2005

Abstract

The belief that pain is a direct result of tissue damage has dominated medical thinking since the mid 20th Century. Several schools of psychological thought proffered linear causal models to explain non-physical pain observations such as phantom limb pain and the effects of placebo interventions. Psychological research has focused on identifying those people with acute pain who are at risk of transitioning into chronic and disabling pain, in the hope of producing better outcomes.

Several multi-causal Cognitive Behavioral models dominate the research landscape in this area. They are gaining wider acceptance and some aspects are being integrated and implemented into a number of health care systems. The most notable of these is the concept of Yellow Flags. The research to validate the veracity of such programs has not yet been established.

In this paper I seek to briefly summarize the development of psychological thought, both past and present, then review current cognitive-behavioral models and the available supporting evidence. I conclude by discussing these factors and identifying those that have been shown to be reliable predictors of chronicity and those that may hold promise for the future.