



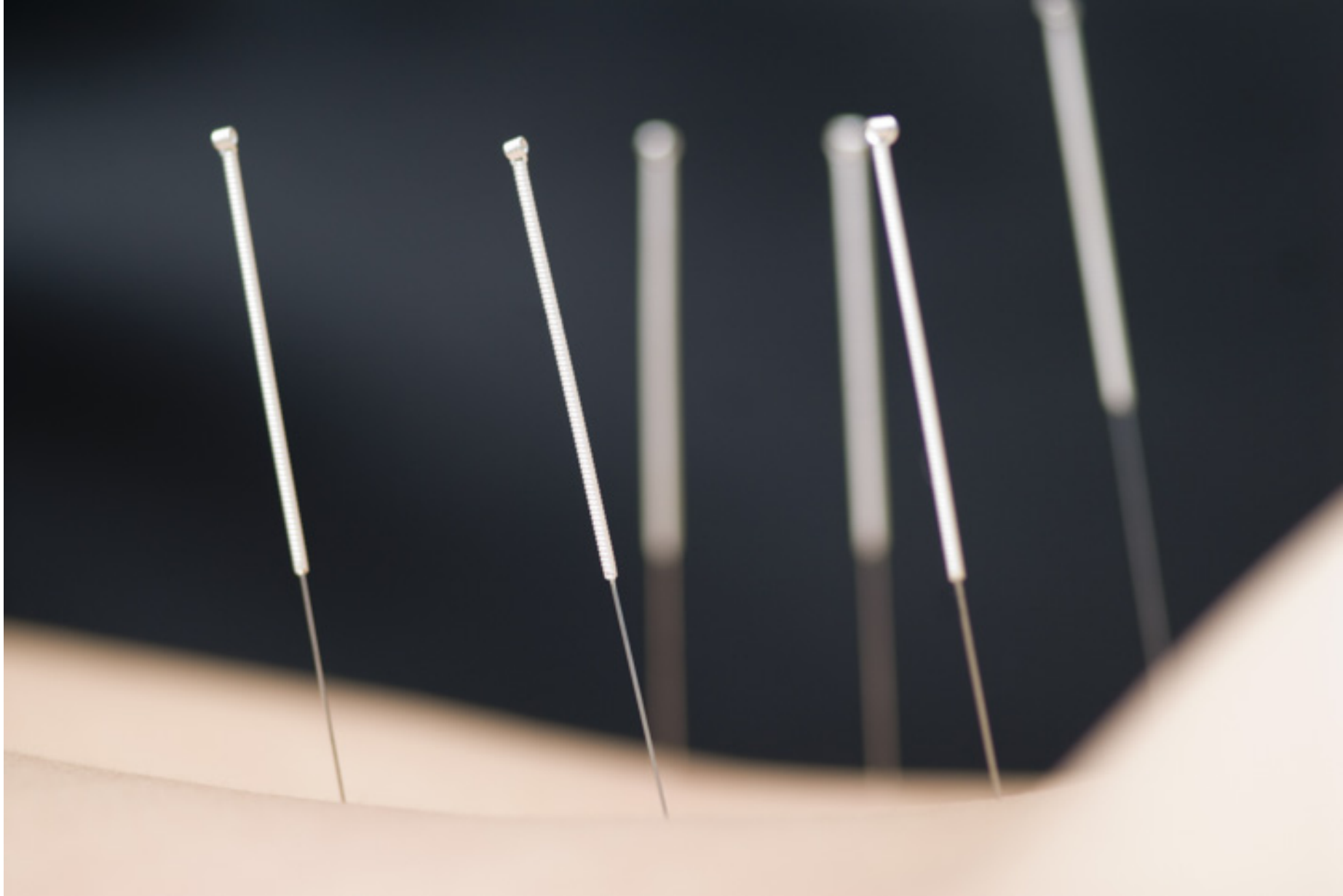
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Acupuncture Increases Bone Strength, Repairs Nerves

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Researchers find acupuncture effective for increasing bone strength and preventing bone loss. In a laboratory investigation, electroacupuncture significantly enhanced outcomes by increasing the efficacy of physical therapy procedures. The application of electroacupuncture significantly improved bone density and strength when engaging in load-bearing exercises and treadmill running exercises. Based on the results of the study, the researchers conclude that acupuncture significantly increases bone strength and density, stimulates peripheral nerve repair, and increases the effectiveness of physical therapy procedures.



Researchers at Washington University (St. Louis, Missouri), in association Heilongjiang University (Harbin, China), find electroacupuncture with load-bearing exercise is effective for increasing bone mass density (BMD) and bone strength after sciatic nerve injury. Their laboratory tests, conducted on rabbits, also show that levels of the neuropeptide Substance P (SP) were increased in correlation with bone health by application of electroacupuncture. This study shows that damage to the peripheral nervous system (PNS) can have a detrimental effect on bone health, and that electroacupuncture at Huatuoji (Jiaji) points enhance the effects of load-bearing exercise for the improvement of bone health and peripheral innervation.

Bones appear static, but they are under constant remodeling; osteoclasts break down bone and osteoblasts build it back up again. This process maintains the crystalline structure of the bone to preserve its density and strength. When bones are under stress, such as during load-bearing exercise, osteoclasts and osteoblasts become more active, repairing micro-damage. Bones under higher levels of stress are generally better reinforced by the remodeling process, which seems counter-intuitive,

but it increases their strength. Thus, load-bearing exercise is known to increase bone mass after damage. The researchers therefore investigated the effect of electroacupuncture in conjunction with load-bearing exercise to determine whether electroacupuncture had a complementary effect for the treatment of bone loss after peripheral nerve damage.

They used four indices to measure the effects of electroacupuncture and exercise on peripheral innervation and bone health. The toe-spreading index (TSI) is used to measure the reflex of rabbits to spread their toes as they are lowered onto a surface; “the toe-spreading reflex is a reliability, sensitivity and non-invasive method for assessing recovery of peroneal nerve function after injury,” [1] and the test is employed because it is thought to assess the endpoint of regeneration of the peroneal nerve, a nerve distal to, and innervated by, the sciatic nerve. [2] The results of this study show that, “TSI, BMD, bone strength, and SP expression can be partially restored by intervening with treadmill running alone. However, TSI, BMD, bone strength, and SP expression levels were further improved by added Jiaji-electroacupuncture to the treadmill therapy. In the current study, the better TSI, BMD and bone strength found in the ET group are associated with increased expression of SP. SP-immunoreactive nerve fibers innervate the bone and adjacent tissues. SP-immunoreactive axons have been localized in bone, and SP receptors are widely distributed in osteoclasts and osteoblasts.” [3]

The study compared four test groups so that the researchers could assess the scale of the effect of electroacupuncture. The control group was given surgery to expose the sciatic nerve --- but was not subject to the sciatic nerve crush injury — in order to keep the conditions as similar as possible. The other three groups all underwent the sciatic nerve crush (SNCr). The SNCr group was used as a nerve damage control for the two test groups, one which was exposed only to load-bearing exercise on a treadmill, and the other which received electroacupuncture at six Jiaji points (bilateral to lumbar vertebrae L4, L5 and L6) in addition to the treadmill exercise. “The motor function of the left hind limb was assessed before the crush injury and 4 weeks post injury using the toe-spreading reflex.” [4] After live tests were conducted, the rabbits were euthanized so that BMD, bone strength and SP density could be measured.

The test groups were chosen so that the researchers could determine not only the effects of the treatment protocols on bone health, but also the effect of denervation on bone health. “Sciatic neurectomy has been used by many as a standard model of disuse osteopenia, as loss of musculature from denervation effectively stops active motion in the limb. So recent is the prevalence of the thought that nerves may

interact with bone metabolism directly, that most of the papers do not even recognize that neurectomy may have direct effects on bone cells from lost bone innervation, above and beyond denervation of muscle and disuse of the limb.” [5] Here, however, the researchers recognized the need to investigate the negative effect of nerve injury on bone health as well as the positive effects of the treatment protocols. They found that SNCr group scored below both treatment groups and the control on all four indices of nerve and bone health.

Load-bearing exercise, which forces the body to work against gravity, is an effective form of exercise to increase bone strength; the US National Institutes of Health (NIH) recommends it for the prevention of bone fractures. [6] Tests conducted under conditions of reduced gravity show that “an exposure to prolonged microgravity may enhance sympathetic neural traffic not only to muscle but also to bone. This sympathetic enhancement increases plasma NE level, inhibits osteogenesis, and facilitates bone resorption through β -ARs signaling which in combination leads to reduced bone mass.” [7] On the other hand, “exercise training (treadmill running) increased cortical thickness in growing bone.” [8] Knowing this, the researchers in this study included treadmill running to compare the effects of load-bearing exercise with and without electroacupuncture, as well as to investigate the nerve involvement in bone loss. The researchers in this study propose that, “the main effects of treadmill running may be due to the suppression of bone mass reduction. BMD and bone strength of tibia in the treadmill group were significantly higher compared to the SNCr group but still significantly lower than the sham control, indicating decreases in load bearing play a part but are not solely responsible for bone loss.” [9]

The peripheral nervous system (PNS) controls sensory and motor innervation of the limbs. Nerve damage has a direct effect on sensation and motor function, but it can also have a myriad of other effects. Neurotransmitters such as neuropeptides send chemical messages by way of the nervous system. The researchers found that “several neuropeptides may be local modulators of bone metabolism, influencing periosteal and medullary blood flow, angiogenesis, and nociception, in addition to having direct effects on osteoblasts and osteoclasts. Furthermore, a recent study showed that bone and periosteum are innervated by sympathetic and sensory nerve fibers, implicating the peripheral nervous system in bone metabolism and indicating sensory and sympathetic neurotransmitters have crucial trophic effects essential for proper bone formation.” [10] Thus, it follows that damage to the peripheral nervous system may also have a direct effect on bone health. The peripheral nervous system can regenerate muscle, bone, and skin, but the healing is slow and often incomplete; experiments have shown the importance of peripheral nerve fibers to bone

homeostasis as well as fracture repair. [11] This pertains to human studies as well; it is becoming more widely recognized that strokes increase the incidence of hip fractures [12] and, “in patients with spinal cord injuries, a profound decrease of sublesional bone mineral density was measured in comparison with controls.” [13] Based on the evidence, it is reasonable to assert that restoring nerve supply is essential to proper healing after bone fracture. [14]

“The sciatic nerve crush model is a well-characterized model of peripheral nerve regeneration. After a crush lesion, nerve fibres in the distal stump degenerate and the expression of regeneration associated genes takes place. Presently, very few drugs are available that reliably enhance the rate and completeness of nerve regeneration.” [15] The researchers therefore chose electroacupuncture (EA) to stimulate nerve growth. Jiaji points are located lateral to the spine, around the area of the transverse processes; each thoracic, lumbar, and sacral vertebra has a bilateral pair. The three acupoints the researchers chose for this study were lateral to the L4, L5, and L6 lumbar vertebrae. “Neurons of the sciatic nerve and lumbosacral plexus are beneath these acupoints. Since adequate connectivity in spinal circuits and peripheral nervous system integration are also important factors in nerve regrow, Jiaji-EA may help to facilitate sciatic nerve regeneration after the nerve injury via stimulation of the sciatic nerve and lumbosacral plexus.” [16] Since electroacupuncture at Jiaji points has been successfully used to treat spinal cord injuries in both humans and animals, the researchers theorized that these points may also help stimulate the neurons of the sciatic nerve. [17] Additionally, a previous study conducted by the same researchers demonstrated that “secondary degeneration of neurons is reduced and axon regeneration is facilitated by Jiaji-EA after peripheral nerve injury.” [18] The rate of success for the treatment of nerve regeneration in this study was measured by the toe-spreading index (TSI), just as reflexes are measured in humans to test innervation.

SP levels were also measured in relation to PNS and bone health. “Classically, tachykinin substance P (SP) is known as a mediator of nociception and of inflammation.” [19] However, SP-immunoreactive fibers, frequently co-localized with calcitonin-related peptides in the peripheral sensory axons of the bones, innervate the bone and adjacent tissues; their density depends on the location, development stage, and pathological conditions, suggesting a close relationship between SP neuropeptides and bone health. [20] “Bone fractures accompanied by peripheral nerve injuries heal slower and sensory denervation negatively affects long-term prognosis. Substance P (SP), a neuropeptide belonging to the tachykinin family, is widely distributed in the body, particularly in the central and peripheral nervous

systems where it acts as a neurotransmitter or neuromodulator. Studies suggest that the absence of SP reduces bone formation rate associated with fracture healing.” [21] Thus, the ability of electroacupuncture to promote an increase in SP — in conjunction with the correlation between SP levels and bone health — suggest one mechanism by which electroacupuncture is promoting bone strength and BMD.

Altogether, the evidence demonstrates that electroacupuncture, in conjunction with treadmill running, prevents bone deterioration after peripheral nerve damage. “This may occur in two ways: indirectly in association with axon regeneration and directly via loading on the bone mediated through increased SP expression.” [22] Nerve regeneration is crucial to improving bone mass after injury, and detrimental changes to the spinal cord may contribute to chronic deficits following peripheral nerve injury; thus, modulating nerve plasticity for regrowth is important for functional recovery. [23] “Evidence now suggests roles for neural control in fracture healing, bone development, bone mass control, and osteoporosis. These and other clinical scenarios of altered bone growth and metabolism require orthopaedic scientists to re-think underlying basic orthopaedic pathophysiology in light of recent insight of a neuro-osseous axis.” [24] The laboratory research indicates that electroacupuncture, used in conjunction with physical therapy, may be implemented to significantly improve bone health outcomes for patients with nerve injury.

Notes

1 Wang, Yan et al., “Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass,” pg 3.

2 Wang, Yan, Qiang Tang, Luwen Zhu, Ruyi Huang, Lei Huang, Melanie Koleini, and Dequan Zou. "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass and Substance P Expression of Rabbits with Sciatic Nerve Injury." Plos One 11, no. 11 (2016). Pg 8. doi:10.1371/journal.pone.0164652.

3 Wang, Yan et al, “Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass,” pg 6.

4 Wang, Yan et al, “Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass,” pg 3.

5 Bone and brain: a review of neural, hormonal, and musculoskeletal connections. The Iowa orthopaedic journal. Accessed March 14, 2017. Pg 126. <https://www.ncbi.nlm.nih.gov/pubmed/15296219>.

6 niams.nih.gov/health_info/bone/Bone_Health/Exercise/default.asp

- 7 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." *Arthritis Research & Therapy* 16, no. 6 (2014). Pg 9. doi:10.1186/s13075-014-0485-1.
- 8 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 7.
- 9 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 7.
- 10 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 7.
- 11 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." Pg 7.
- 12 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." Pg 1.
- 13 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." Pg 1.
- 14 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." Pg 7.
- 15 Hoang, Ngoc Son, Chamroeun Sar, Jean Valmier, Victor Sieso, and Frédérique Scamps. "Electro-acupuncture on functional peripheral nerve regeneration in mice: a behavioural study." *BMC Complementary and Alternative Medicine* 12, no. 1 (2012). doi:10.1186/1472-6882-12-141. Pg 1.
- 16 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 2.
- 17 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 8.
- 18 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 8.
- 19 Grässel, Susanne. "The role of peripheral nerve fibers and their neurotransmitters in cartilage and bone physiology and pathophysiology." Pg 2.
- 20 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 8.
- 21 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 2.
- 22 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-Acupuncture on Tibia Bone Mass," pg 1.
- 23 Wang, Yan et al, "Effects of Treatment of Treadmill Combined with Electro-

Acupuncture on Tibia Bone Mass," pg 8.

24 Bone and brain: a review of neural, hormonal, and musculoskeletal connections.

The Iowa orthopaedic journal. Pg 127.

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