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SOUND THERAPY AND MUSIC MEDICINE: BIOLOGICAL MECHANISMS (Part 2)

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Abstract

This article provides clinicians and other medical professionals with an introduction to the related fields of Sound Therapy and Music Medicine, outlining some of the many biological mechanisms advantageously activated by these modern modalities. The umbrella term for audible sound therapies is often popularly referred to as «Vibrational Medicine», embracing the energetic (vibrational) interconnectedness of the mind-body system. The information provided is intended for physicians, psychologists, music therapists, nurses, integrative medicine practitioners, and wellness practitioners utilizing the therapeutic potential of Vibrational Medicine. Since the body is comprised of vibrational energy, a wide variety of energetic modalities are available to support the patient's physiology, and the article describes some of the many physiological mechanisms initiated by Sound Therapy and Music Medicine, perhaps most importantly, pain mediation, achieved by locally applied specific sound frequencies. Other mechanisms, such as vagal stimulation, are described and achieved by experiencing specific sound frequencies or music via headphones. The article is in two parts: **Part 1** was published in the past issue (3-2023) of the «Medicine and Art» journal (https://doi.org/10.60042/2949-2165-2023-1-3-60-93). It provides a short history of therapeutic sound, followed by definitions of Music Therapy, Music Medicine, and Sound Therapy, followed by sections on some of the many biological mechanisms activated by full body immersion in music or specific sound frequencies, including an introduction to pain mediation by sound. **Part 2** includes breaking the pain-spasm pain cycle in spinal injury by sound; pain relief and anxiety relief by acupressure and sonopuncture; oxygen-driven healing by sound; musical stimulation of the immune system; sonic stimulation of the vagus nerve via headphones and by vocalizations; and last, a look into the future of vibrational medicine.

Key words: Sound Therapy, Music Medicine, Vibrational Medicine, Ultrasonic

Speakers, Nitric Oxide, Chronic Pain Mediation, Gate Control Theory of Pain.

ЗВУКОВАЯ ТЕРАПИЯ И МУЗЫКАЛЬНАЯ МЕДИЦИНА: БИОЛОГИЧЕСКИЕ МЕХАНИЗМЫ (Часть 2)

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Аннотация

Эта статья знакомит читателей со смежными областями звуковой терапии и музыкальной медицины, очерчивая контуры некоторых из многочисленных биологических механизмов, которые были успешно выявлены этими современными направлениями. Для звуковой терапии часто используется общий термин «вибрационная медицина», отражающий энергетическую (вибрационную) взаимосвязь системы разум-тело. Предлагаемая информация предназначена для врачей, психологов, музыкальных терапевтов, медсестер, специалистов интегративной медицины и оздоровительных практик, использующих терапевтический потенциал вибрационной медицины. Поскольку организм утилизирует вибрационную энергию, для поддержки физиологических функций пациента доступен широкий спектр энергетических модальностей. В статье описываются отдельные физиологические механизмы, инициируемые звуковой терапией и музыкальной медициной. Возможно, одним из наиболее важных эффектов является нейтрализация боли, достигаемая с помощью локально применяемых особых звуковых частот. Описаны и другие механизмы, такие как стимуляция блуждающего нерва с помощью прослушивания определенных звуковых частот или музыки через наушники. Статья состоит из двух частей. **В первой части статьи** (https://doi.org/10.60042/2949-2165-2023-1-3-60-93), которая была опубликована в предыдущем номере (3-2023) журнала «Медицина и Искусство», представлена краткая история терапии звуком, за которой следуют определения музыкальной терапии, музыкальной медицины и звуковой терапии. Далее описываются некоторые из многих биологических механизмов, активируемых при полном погружении организма в музыку или при воздействиях конкретными звуковыми частотами, включая введение в обезболивание звуком. **Часть 2** описывает прерывание звуком болевого цикла «боль-спазм» при травме позвоночника; облегчение боли и тревожных состояний с помощью точечного массажа и сонопунктуры; кислородное исцеление звуком; музыкальную стимуляцию иммунной системы; звуковую стимуляцию блуждающего нерва через наушники и вокализацию; и наконец, взгляд в будущее вибрационной медицины.

Ключевые слова: звуковая терапия, музыкальная медицина, вибрационная медицина, ультразвуковые динамики, оксид азота, медиация хронической боли, теория контроля боли.

BREAKING THE «PAIN-SPASM-PAIN» CYCLE IN SPINAL INJURY, BY SOUND

The first suggestion of a pain-spasm-pain cycle is generally credited to Janet Travell who wrote in 1942, «If muscle spasm causes pain, and pain reflexly produces muscle spasm, a self-perpetuating cycle might be established…» [94]. Today, it is well known that spinal injuries typically create muscle spasm to «splint» the site of injury, providing protection while the healing process takes place.

In a round table discussion between four physicians, titled, *Diagnosis and Treatment of Low-Back Pain because of Paraspinous Muscle Spasm: A Physician Roundtable,* published in the journal Pain Medicine, Dr. McCarberg states:

«From an initial injury the patient develops pain. Motor neurons are activated as a reflex to splint that area causing muscle spasm. Muscle spasm clearly causes pain, but the exact cause of pain is poorly understood. Regardless, this pain will cause more muscle spasm…Hopefully, if this cycle is interrupted, a chronic problem will not occur» [95].

The trauma caused by a spinal injury, or other injury, causes pain, which leads to muscle tension. A cascade of effects then results in which the muscle tension decreases the blood circulation, which (hypothetically) causes hypoxia and further pain in the affected muscles. The spasm then intensifies, which causes the hypoxia to intensify and the pain to intensify, therefore causing far more pain than the injury (Fig.15).

The decrease in blood circulation is hypothesised to be a direct result of compression of intramuscular blood vessels, a concept that is supported by the fact that it is known that blood supply to a muscle is decreased during voluntary contraction and that pain following muscular exercise is very similar to pain induced by experimental reduction in the blood supply to a muscle [96].

Further support for hypoxia in muscles comes from a study of intramuscular blood flow in the supraspinatus muscle of six healthy subjects. A muscle contraction pressure of 5.6 kPa (42mm Hg), which is 16% of maximal voluntary contraction, reduced local muscle blood flow significantly. The authors concluded that high intramuscular pressures found in supraspinatus muscle during exercise, impeded local muscle blood flow [96].

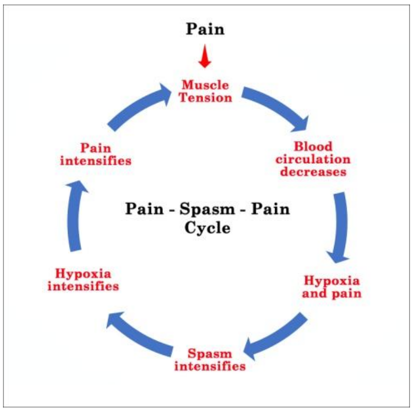

Fig. 15. *Pain Cycle*

Pain > Muscle tension > Blood circulation decreases > Hypoxia and pain > Spasm intensifies > Hypoxia intensifies > Pain intensifies

Рис. 15. *Болевой цикл*

Боль > Мышечное напряжение > Снижение кровообращения > Гипоксия и боль > Усиление спазма > Усиление гипоксии > Усиление боли

A potential solution to breaking the pain-spasm-pain cycle is by locally applied low frequency sound <50Hz. KKT International offer therapeutic support for spinal injuries by the application of very low frequency sound (primarily 16Hz), a non-invasive treatment to relieve pain by improving spinal alignment of the back, shoulders and pelvis, while enhancing the health of the spinal discs, ligaments and muscles (Fig. 16) [30].

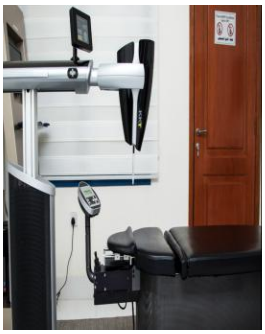

Fig. 16. *KKT Spine device (photo courtesy of KKTspine.com)*

Рис. 16. *Устройство ККТ терапии позвоночника (фото от KKTspine.com)*

During the author's in vitro experiments with whole human blood, conducted in 2021, significant increases in the level of pO_2 were measured with an Oxford Instruments 'Oxylite' system when the blood was immersed in low frequency sound for 20-minutes This research will be the subject of a forthcoming paper, however, the likely mechanism that underpins this phenomenon is the mechanical pressure generated by low frequency sound, similar to the low frequency pressure pulses from heart beats in the circulatory system, thus increasing oxygen-binding to haemoglobin molecules in red blood cells. Support for this potential method of increasing oxygen availability, comes from the earlier mentioned study on Whole Body Vibration in which the oxygen saturation level was found to increase significantly between the first and second minute, following application of low frequency vibrations to supine patients [80].

Further support for breaking the pain-spasm-pain cycle by sound arose from the author's acoustics experiments in Egypt's Great Pyramid, in 1997. An injury to the author's lower back, three weeks prior to the experiments, caused the muscles in the sacroiliac joint area to spasm, creating intense pain. Taking over-the-counter analgesic medications provided no noticeable mediation of the pain. However, within twenty minutes of generating low frequency sound in the King's Chamber, the pain completely subsided. It is assumed that the injury had been healed during the three-week prior period, but the splinting pain spasm had remained. Hypothetically, the low frequency sound environment in the King's Chamber was largely, or perhaps wholly, responsible for reversing the hypoxic environment in the muscles of the sacroiliac area, thus causing the spasm to release (Fig. 17).

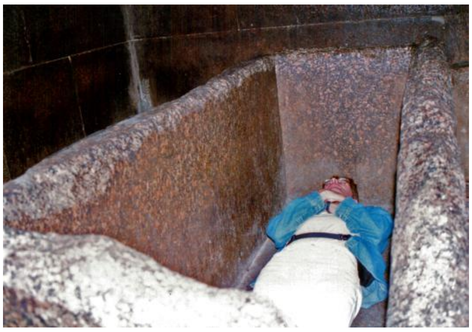

Fig.17. *John Stuart Reid in King's Chamber sarcophagus, 1997*

Рис. 17. *Джон Стюарт Рид в помещении Королевского саркофага, 1997*

In addition, as mentioned earlier in the section on Nitric Oxide, NO is generated by the alveoli in the lungs [56] and can be stimulated by both active and passive sonic stimulation. In the highly reverberant King's Chamber, the low frequency sounds passively excited the author's lungs, presumably leading to an increase in NO, with consequent vasodilatation effects, thus helping to break the pain-spasm-pain cycle.

PAIN RELIEF AND ANXIETY RELIEF BY ACUPRESSURE AND SONOPUNCTURE

Acupressure is an alternative medicine methodology that originated in ancient China. Treatment effects are achieved by stimulating acupuncture points using acute pressure.

The World Health Authority, in their 1991 international acupuncture nomenclature report, lists 14 main meridians and 361 classical acupuncture points, in addition to 8 extra meridians and 48 extra points [99]. These same classical acupuncture points, which can be activated by acute local pressure, can also be activated by sound, since sound may be defined as: «Mechanical radiant energy that is transmitted by longitudinal pressure waves in a material...» [76].This is the basis of 'sonopuncture', a therapeutic modality that is a species of acupressure.

A comprehensive review paper of fifteen acupressure studies concluded that acupressure is shown to reduce dysmenorrhea pain, labor pain, low back pain, chronic headache, and other traumatic pains. The clinical trials showed that acupressure can be efficiently conducted by health care professionals as an adjuvant therapy in general practice for pain relief [100]. The authors also concluded that their systematic review paper begins to establish a credible evidence base for the use of acupressure in relieving pain and that an evidence-base of reliable and valid evaluation is crucial for clinicians. In terms of the implication for nursing education, practice, and research, the review provides important evidence that acupressure uses a noninvasive, timely, and effective way to support its effectiveness in relieving a variety of pains [100].

D. Carey, a licensed acupuncturist, developed a therapeutic method using tuning forks of specific frequency to activate acupuncture points while she was Clinical Dean at the Northwest Institute of Acupuncture and Oriental Medicine, in 1995. The intent was to seek a non-invasive therapy that could be taught to students and used in clinics with patient populations who were critically ill, including those suffering from HIV/AIDS, chronic pain, and trauma [101]. Today, this method of sonopuncture training is available in a certified course, providing an integrative medicine model that dovetails with many clinical specialities and can provide support for patients pursuing traditional Western medicine therapies [102].

Dr. E. Franklin, a colleague of D. Carey, who suffered from stress-related asthma, mild depression, and severe lower back pain, experienced immediate relief from one treatment with tuning forks applied to acupuncture points (Fig.18).

Fig.18. *Sonopuncture, self-applied or practitioner-applied, by tuning forks (Courtesy of Dr. E. Franklin)*

Рис.18. *Сонопунктура, применяемая самостоятельно или практикующим специалистом, с помощью камертонов*
(С разрешения доктора Э. Франклина)

Her pain level was reduced from an 8/10 to a 3/10 and her depression lifted. Dr. Franklin submitted her dissertation in 2014, a multiple case study of self-care with seven hospital nurses, using tuning forks as an intervention to ameliorate symptoms of severe stress and compassion fatigue. At the outset of the study, six of the participants reported pain that they attributed to the stress in their lives. At the conclusion of the study, four reported reduced pain. All participants identified some aspects of working with the tuning forks that had archetypal significance and expressed interest in continuing to use the tuning forks. An important finding of the study was the recognition of the potential for tuning fork therapy in supporting patients suffering from pain and those in palliative care or hospice [103].

Licensed acupuncturist, M.E. Wakefield, L.Ac., awarded 'Educator of the Year' by the American Association of Oriental Medicine in 2005, is co-author of V*ibrational Acupuncture: Integrating Tuning Forks with Needles [104]* with MichelAngelo, M.F.A., vibrational medicine advisor. Their book uniquely explores the synergy of tuning forks and acupuncture. For pain mediation, via sonopuncture, the authors recommend applying a tuning fork of 136.1Hz to specific acupuncture points. Although sonically activating acupressure points typically supports several interconnected bodily systems, the following examples focus mainly on pain mediation:

Lu-7 Lieque, 'Broken Sequence' alleviates headaches, sore throat, migraines, toothache, pain in the wrist.

SI-3 Houxi, ‘Back Stream’ alleviates neck pain, acute lumbar sprain, pain in the shoulder and elbow.

UB-62 Shenmai, ‘Extending Vessel’ alleviates headache, backache, leg ache, insomnia.

TH-5 Waiguan, ‘Outer Pass’ alleviates headache, facial pain, finger pain, hand tremors.

Bl-58 Feiyang ‘Taking Flight’ mediates sciatic pain, alleviates headache, back pain.

Another important therapeutic use of tuning forks was discovered by E.D. McKusick, M.A., author of the book, *Tuning the Human Biofield* [105]. Energy-information is constantly radiated from the body in the form of biofields, as mentioned in the introduction to part 1 of this article [1]. The biofields include bio-photonic energy, for example, modulated infrared electromagnetism that is a natural consequence of cellular metabolic processes, in addition to modulations in the electromagnetic fields emitted by the heart, brain and other organs.

Quoting from the book’s foreword by Dr. Karl H. Maret, who practices Complementary and Alternative Medicine, «when a holographic sound field such as that produced by a tuning fork, which contains complex data structures of pure frequencies with changing phase relationships interacts with the biofield of a person, the cellular memories of various tissues can be reawakened, potentially leading to a healing response. Quantum physical field theory predicts the occurrence of a number of coherent dynamic phenomena in liquid water inside cells and tissues that may be stimulated by sound. This process affects the free electron clouds existing within these coherent water domains, [thus modifying] cellular processes through their interaction with the hydration shells surrounding cell membrane receptors».

The biofield tuning method has been shown to consistently reduce anxiety, as well as relieve pain, and in a collaborative, grant funded, Institutional Review Board study, between the Biofield Tuning Institute and the Consciousness and Healing Initiative, fifteen participants with clinical anxiety received a one-hour session each week, for three weeks, followed by interviews (Fig.19).

The study implemented the State-Trait Anxiety Inventory (STAI) to measure anxiety level, and participants were screened for clinically significant levels of anxiety using the Generalized Anxiety Disorder (GAD) system. All participants met clinical thresholds for generalized anxiety disorder. The results of the study were significant, with the mean level of STAI moving from 52 to 33. Most participants reported that although their anxiety did not completely go away, they were able to separate themselves from the anxiety and had developed a new relationship to it. Participants also found that they were more in touch with their anxiety triggers and, therefore, these triggers did not have as much of an impact or influence on their behavior [106].

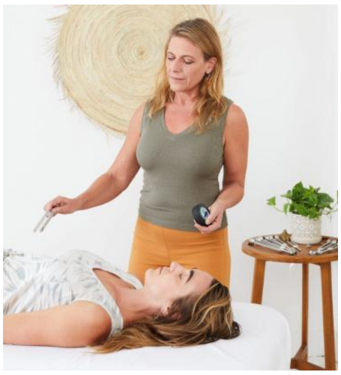

Fig.19. *A biofield therapeutic tuning session in progress (Courtesy of E.D. McKusick)*

Рис.19. *Сеанс терапевтической настройки биополя (С разрешения доктора МакКьюсика)*

PAIN RELIEF BY SONOPUNCTURE ADMINISTERED BY ELECTRONIC DEVICES

Although sonopuncture is typically applied by tuning forks, devices that emit low frequency vibration can also achieve sonic activation of acupressure points [107] in addition to devices that emit ultrasound [108]. The acupressure points on the soles of the feet can also stimulate the meridian system by applying audible sound frequencies [109]. Dr. M. Cromwell developed a therapeutic device that uses a vibro-tactile transducer, emitting a range of audible sound frequencies into acoustic gel-filled pads on which the soles of the feet rest, thus stimulating the meridian system (Fig.20). Together with her assistant, Kate Holland, CCP, they conducted a six-week investigative pain study in 2016, with three individuals, a female of 30-years, a male of 38-years and a male of 68-years [110].

The female participant entered the study with chronic headaches and sciatica and rated her neck pain at 6 on the VAS scale, which escalated to an 8 during headaches. She was unable to sleep due to her lower back pain and sciatica, which she remarked was constant and rated as a 6 on the VAS scale. She was taking over-the-counter medication for pain and insomnia. During the period of the study, the souls of her feet were sonically stimulated twice a week, for 30-minutes.

Fig.20. *Sonopuncture applied via vibro-tactile transducer and acoustic gel-filled pads (Courtesy of Dr. M. Cromwell)*

Рис.20. *Сонопунктура с помощью вибротактильного датчика и акустических гелевых подушечек. (С разрешения доктора М. Кромвеля)*

During the third week she reported that her back pain had diminished to 3 on the VAS scale. By the end of the study, her ability to sleep had improved significantly and she was no longer taking over-the-counter pain medications. She also reported a reduction in the number and severity of headaches and rated the headache pain as 4 on the VAS scale [110].

The 38-year old male entered the study with a rotator cuff injury of the right shoulder and was suffering chronic pain, registering 8 on the VAS pain scale, though not taking pain medication. His arm abduction was limited to 50 degrees. During the period of the study the souls of his feet were sonically stimulated once a week, for 30 minutes. During the sonic therapy he reported feeling warmth and movement of the muscles of his shoulders. At the end of the study, he reported minimal pain of 2 on the VAS scale and demonstrated that he had recovered a full range of motion of his right shoulder [110]. The 68-year old male military veteran entered the study with chronic neck pain, symptoms of PTSD and insomnia. He chose to participate in the study by utilizing a daily, at-home program, involving two thirty-minute daily sessions. He reported pain of 8 on the VAS scale and high levels of anxiety at varying times of the day or evening. He could only sleep two-three consecutive hours without waking and occasionally took over-the-counter sleep aids. After the first two weeks of daily sonic stimulation of the souls of his feet his sleep patterns improved and he decided to stop taking sleep medication. At the end of the six-week study he was able to sleep approximately 6 hours each night without interruption. At the end of the study the military veteran also reported a reduction of neck pain to 3 on the VAS scale and reported feeling less stress when going into public places [110].

In summary for this section on Acupressure/Sonopuncture, these studies show that there exists a significant potential for pain reduction, in addition to support for arrange of other chronic conditions, including depression, PTSD, insomnia and others.

OXYGEN-DRIVEN HEALING BY SOUND

Limitations in the ability of the vasculature to deliver O_2-rich blood to tissue leads to, among other consequences, systemic hypoxia. Cells confronting hypoxic challenges either induce an adaptive response that includes increasing the rates of glycolysis and conserving energy, or undergo cell death. [111] Conversely, cells utilize O_2 in the aerobic metabolism of glucose to generate Adenosine Triphosphate (ATP) which fuels most active cellular processes, including tissue repair [111]. Hypoxia sensing and response is activated upon exposure to a state of oxygenation that is lower than the pO_2 to which the cells or tissue is adjusted under normal conditions. This response cascade is centrally important in coping with the challenge of O_2 deficiency. Hypoxia is a hallmark of all ischemic diseases [111].

As mentioned earlier, in the section, ‘Breaking the pain-spasm-pain cycle in spinal injury, by sound’, pO_2 was shown to significantly increase during experiments with in vitro blood immersed in a low frequency sound environment, thus increasing oxygen binding to hemoglobin molecules in red blood cells. Support for this sonic method of increasing oxygen in blood, comes from the earlier mentioned study on Whole Body Vibration in which the oxygen saturation level was found to increase significantly between the first and second minute, following application of low frequency vibrations to supine patients [80]. Also, in the author’s forthcoming paper on this subject, the optimal range of sonic frequencies, found during in vitro experiments to power the increase in pO_2 in blood, was 20Hz to 120Hz, which is similar to sounds created by human hearts [112] when auscultated by electronic stethoscope. This suggests that immersing patients in low frequency sounds is mimicking the heart’s low frequency pressure pulses, thus supporting their pO_2 level.

MUSICAL STIMULATION OF THE IMMUNE SYSTEM (VIA HEADPHONES OR FULL BODY IMMERSION)

Illness in any form can cause emotional distress and emotions can play a significant role in a patient’s recovery from illness or from an operating procedure.

Stress and fear cause the release of cortisol [and adrenalin/ epinephrine] from the adrenal glands [113] helping prepare the body for 'fight or flight' by providing extra glucose, tapping into protein stores via gluconeogenesis in the liver [114].

However, cortisol also suppresses the immune system [115] and other bodily systems considered by Nature to be 'non-essential' in the short term, making the patient more vulnerable to contracting pathogens. While pharmaceutical sedatives are routinely prescribed to mediate a patient's stress and fear, music can produce a similar outcome without medication. Music can evoke happy memories of times, places, or life events that can quickly transform a patient's mood into a sense of joy, in which state the brain and enteric nervous system in the digestive tract produces dopamine, which boosts the immune system [116, 117]. In parallel with the increase in dopamine, a patient's favorite music causes a reduction in cortisol levels [118]. Joy also triggers the pituitary gland in the brain to release beta-endorphins into the bloodstream, which produce analgesia by binding to mu-opioid receptors that are present throughout peripheral nerves. Mu-opioid receptors have been identified in the central terminals of primary afferent neurons, peripheral sensory nerve fibres and dorsal root ganglia [119].

The pituitary gland also stores of the neuropeptide, oxytocin, colloquially known as the 'love hormone'. Oxytocin is made in the hypothalamus and transported to large, dense-core vesicles of the posterior lobe of the pituitary gland [120] where it is released into the blood stream in response during sexual activity and orgasm in addition to childbirth. In a broader context there appears to be a general consensus among studies that music listening enhances oxytocin synthesis [121] and postoperative patients listening to music through headphones demonstrated an increase in serum oxytocin and reported higher levels of relaxation, compared to a control group with no music [122].

Oxytocin and its receptors appear to hold the leading position among the candidates for the substance of 'happiness', [123] and in a study focused on autistic children, significantly lower levels of oxytocin was found in their blood plasma, suggesting a ray of hope in finding a role for oxytocin in treatment of autism [123] that is, in both of these cases, (evoking happiness and supporting the treatment of autism) there is an obvious link in the form of music, whether applied via headphones or full body immersion.

A further important connection between music and the immune system was reported in a 2019 study by Augusta University, USA. The researchers found that when mice were subjected to low frequency sound vibrations, macrophages in their bloodstream proliferated significantly [124]. This effect has not yet been demonstrated in humans, however, it seems likely that human blood will respond in a similar way to that of murine blood. The possible mechanism that powers the proliferation of macrophages in blood that is immersed in low frequency sound, is an increase in the pO_2 level, as discovered in the Whole Body Vibration study on supine humans, mentioned in the above section, 'Oxygen-driven healing by sound'. In that study the level of pO_2 was found to increase significantly between the first and second minute, following application of low frequency vibrations to supine patients [80]. It is important to mention that this aspect of the connection between music and the immune system would occur only during full body immersion, since the full circulatory system would require stimulation by low sonic frequencies.

BINAURAL BEATS (VIA HEADPHONES) TO CREATE CHANGES IN BRAIN STATE, WITH PHYSIOLOGICAL BENEFITS

Binaural beats were discovered accidentally in 1839 by the Prussian scientist, Heinrich Wilhelm Dove, during experiments with two tuning forks of dissimilar frequency. He has been referred to as 'The Father of meteorology' [125] for his work in that field; however, as late as 1915 his discovery of binaural beats was considered a trivial special case of monaural beats [126]. Monaural beats occur when two sounds of slightly different frequency sound simultaneously, resulting in a pulsating effect caused by the mixing of the two sounds, which are reinforced during moments when their phases align, and diminished when their phases oppose each other (Fig.21).

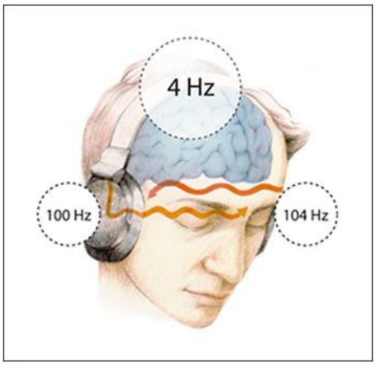

Fig.21. *Depiction of binaural beats (Courtesy of Hemi-Sync® hemi-sync.com)*
Рис.21. *Изображение бинауральных ритмов (с разрешения Hemi-Sync® hemi-sync.com)*

But during headphone listening, when two slightly different frequencies are experienced, the composite difference frequency is known as a binaural beat and it provides a mechanism for stimulating the auditory system at very low frequencies, below the frequency range of hearing [127]. Listening to binaural beats produces the illusion that the sounds are located somewhere within the head.

The lower auditory centers of the brain are in the medulla oblongata, and impulses from the right and the left ears first meet in the left or right superior olivary nucleus. These structures are part of the olive, an organ that in this view lies behind the brain stem. It is probable that binaural beats are detected here [126]. The difference frequency between sounds presented to the left and right ears entrains the brain rhythms to that frequency.

In a carefully designed, double-blind, binaural beats crossover study, titled: *Binaural Auditory Beats Affect Vigilance, Performance and Mood. Physiology and Behavior,* 29 volunteers were tested. The recordings used in the study contained a background sound of pink noise and a carrier tone, within which was embedded an entraining difference frequency between left and right channels. (The purpose of the pink noise was to mask the sound of the carrier tone).

The participants were kept blind to the true purpose of the study and were unaware of the presence of binaural beats in the headphones. The results of the study provided evidence that presentation of simple binaural auditory beat stimuli during a 30-minute vigilance task can affect both the task performance and changes in mood associated with the task.

The effects on behavior and mood were observed in the absence of participant expectations, and experimental control ruled out placebo effects. The authors concluded that simple binaural-beat auditory stimulation can influence psychomotor and affective processes, even when people are unaware that such signals are being presented, and that this technology may have applications for the control of attention and arousal and the enhancement of human performance [127].

In another double-blind crossover study, titled: *Reduced pain and analgesic use after acoustic binaural beats therapy in chronic pain - A double-blind randomized control cross-over trial*, the authors concluded that theta rhythm binaural beats reduced pain intensity, stress and analgesic use, compared to sham stimulation, in chronic pain patients. A further conclusion was that the subsequent significant reduction in analgesic medication consumption in chronic pain patients' daily living could offer a valuable tool, augmenting the effect of existing pain therapies [128].

Robert Monroe of The Monroe Institute, created a system of binaural beats in which individuals listen to a combination of audio binaural beats mixed with music, pink noise and/or the natural sound of the ocean waves that has been named the ‘Hemi-Sync’ process. Studies with this system have shown improvements in sensory integration [129] relaxation, meditation, stress reduction, sleep and pain management [130] enriched learning environments and enhanced memory [131].

SONIC STIMULATION OF THE VAGUS NERVE (VIA HEADPHONES) AND BY VOCALISATIONS

The vagus nerve represents the main component of the parasympathetic nervous system, which oversees a vast array of crucial bodily functions, including control of mood, immune response, digestion and heart rate and carries an extensive range of signals from the digestive system and organs and vice versa [132]. Upon exiting the jugular foramen, an auricular branch is given off, giving innervation to the auditory canal and external ear. This is the only branch of the vagus nerve given to the head. As the vagus nerve descends the neck via the medulla oblongata, branches leave to the pharynx and larynx before continuing into the thorax where it connects with the heart and other major organs (Fig.22). The laryngeal and auricular connections are of special interest in the context of sound therapy and music medicine, discussed later in this section, following an overview of the vagus nerve and methods of its therapeutic stimulation.

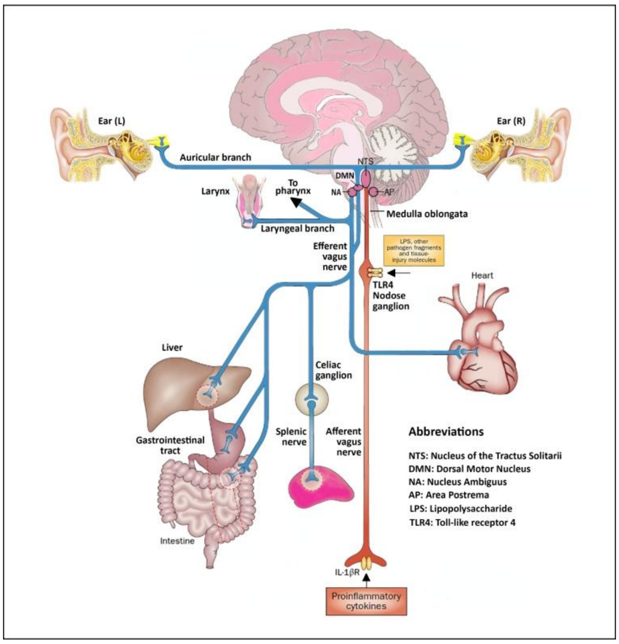

Fig.22. *Vagus nerve branches and functional anatomy of the inflammatory reflex (Adapted with permission, Pavlov and Tracey [133])*

Рис.22. *Ветви блуждающего нерва и функциональная анатомия* *воспалительного рефлекса (Адаптация с разрешения Павлова и Трейси [133])*

Schematic description:

Inflammatory mediators, such as cytokines, are released by activated macrophages and other immune cells upon immune challenge. These mediators are detected by sensory components of the afferent arm of the inflammatory reflex. Neural interconnections between the NTS, AP, DMN, NA and higher forebrain regions integrate afferent (red) and efferent (blue) vagus output, thus, regulating immune activation, suppressing pro-inflammatory cytokines [132] and reducing inflammation. Vagus efferent output can be supported by auricular and laryngeal input.

The bi-directional communication between the brain and the gastrointestinal tract, sometimes called the 'brain-gut axis', is a complex system that includes the vagus nerve, and is becoming increasingly important as a therapeutic target for gastrointestinal and psychiatric disorders, such as inflammatory bowel disease, depression and posttraumatic stress disorder [132]. The gut is an important control centre of the immune system and the vagus nerve has immunomodulatory properties. As a result, this nerve plays important roles in the relationship between the gut, the brain, and inflammation [132].

There is a 'hard-wired' connection between the nervous system and immune system as an anti-inflammatory mechanism. Counter regulatory mechanisms, such as immunologically competent cells and anti-inflammatory cytokines normally limit the acute inflammatory response and prevent the spread of inflammatory mediators into the bloodstream. The dorsal vagal complex, responds to increased circulating amounts of tumor necrosis factor (TNF-α) by altering motor activity in the vagus nerve [132] therefore, stimulation of the vagus nerve can help restore cytokine balance, leading to a reduction in chronic inflammation. The vagus nerve is a major component of the neuroendocrine-immune axis which is involved in coordinated neural, behavioral, and endocrine responses that provide an important first-line innate defense against infection and inflammation and helps restore homeostasis in the body [134]. Inflammatory diseases in which tumor necrosis factor (TNFα) is a key cytokine are good candidates for treatment targeting cholinergic anti-inflammatory pathway (CAP) [134].

In essence, the inflammatory reflex is a physiological mechanism through which the vagus nerve regulates immune function and inhibits pro-inflammatory cytokine production [133] thus, preventing excessive inflammation by alerting the brain to the presence of cytokines, which triggers the release of anti-inflammatory molecules that reduce the inflammation and maintain a healthy balance [135].

One of the most important potentials for vagus nerve stimulation concerns its role in cancer prognosis. In a review paper titled, *The Role of the Vagus Nerve in Cancer Prognosis: A Systematic and Comprehensive Review,* the authors highlight the fact that cancer remains the second leading cause of mortality worldwide, with prostate cancer being the most prevalent cancer type in men and breast cancer in women. Cancer is a complex condition since it includes several hundreds of different types and because it involves and is affected by multiple body systems. Studies have shown that three basic biological factors contribute to the onset and progression of tumor genesis: (1) oxidative stress, leading to DNA damage, (2) inflammation that contributes to escape from apoptosis, angiogenesis and metastasis, and (3) excessive sympathetic activity, which affects where cancer cells will metastasize. One factor common to these three factors, which inhibits all three and influences cancer prognosis, is vagus nerve stimulation because it reduces oxidative stress, informs the brain about inflammation and profoundly inhibits inflammation, and inhibits sympathetic activity since it is a major branch of the parasympathetic nervous system [136]. An interesting and potentially crucial aspect of vagus nerve activity concerns the link to Heart Rate Variability (HRV), the variability of interbeat cardiac intervals that is strongly correlated with vagal nerve activity and cardiac autonomic regulation (Fig.23).

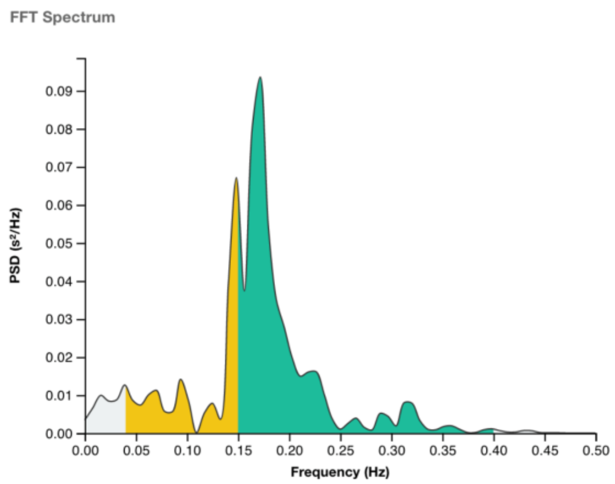

Fig.23. *Power Spectral Density of HRV is typically expressed in milliseconds squared (ms^2), plotted against frequency (Courtesy of EliteHRV.com)*

Рис.23. *Мощность спектральной плотности вариабельности сердечного ритма (ВСР) обычно выражающаяся в миллисекундах в квадрате (мс2), отображена в зависимости от частоты (с разрешения EliteHRV.com).*

The Power Spectral Density (PSD) of high frequency heart rate variability, (HF-HRV is cardiac frequency activity in the range, 0.15 to 0.40 Hz) is strongly associated with cardiovagal activity [137]. (By comparison, low frequency cardiac activity (LF) is in the range 0.04 to 0.15Hz). LF and HF frequency bands are widely used to quantify parasympathetic and sympathetic regulation [137].

The vagus nerve plays a major homeostatic role, indicated by people with high HRV who have shown improved recovery rates to physiological stress in cardiac, hormonal and immune systems, compared to those with lower HRV.

In twelve studies that investigated the association between vagal tone activity and prediction of prognosis in cancer, which included 1822 patients, the emerging evidence was consistent in demonstrating a prognostic role of vagal activity and a significant correlation between survival time and high frequency heart rate variability.

Using the vagal nerve index of HF-HRV, when data was analyzed from a cohort of women with metastatic and recurrent breast cancer it was found that in a sample of 87 women, higher HF-HRV significantly predicted long term survival. It was also found that the predictive validity of HF-HRV improved when dividing it by the patients' heart rate, thus reflecting a more vagal/sympathetic ratio. The authors of the review study call for seriously considering adding HRV to the clinical estimation of prognosis in oncology [136].

In the next section, methods of vagus nerve stimulation are discussed including electrical, sonic, auricular and laryngeal, all of which improve vagal tone with many potential health benefits. The vagus nerve can also be stimulated by acupuncture, which is discussed in Dr. Solar's chapter.

Electrical stimulation of the vagus nerve (VNS) was first studied in the 1930s and 1940s with animals, which laid the groundwork for studies in humans. Following successful clinical trials, the FDA approved the use of an implanted electrical vagus nerve stimulator for the treatment of certain types of epilepsy in 1997. The procedure involves implanting electrodes near the vagus nerve in the neck, along with a control device and battery implanted into the chest.

The same mode of treatment was later also approved by the FDA for use in chronic, drug resistant depression [135].

Transcutaneous (through the skin) vagus nerve (tVNS) is currently emerging as an alternative and seeks to administer electrical stimulation to the vagus nerve without the need for implant surgery, thus avoiding the associated risks. Stimulation is typically applied via the auricular branch of the vagus nerve via the tragus of the pinna (Fig.24). The European Union certified tVNS as an alternative treatment for epilepsy and pain in 2010 and 2012 respectively [135].

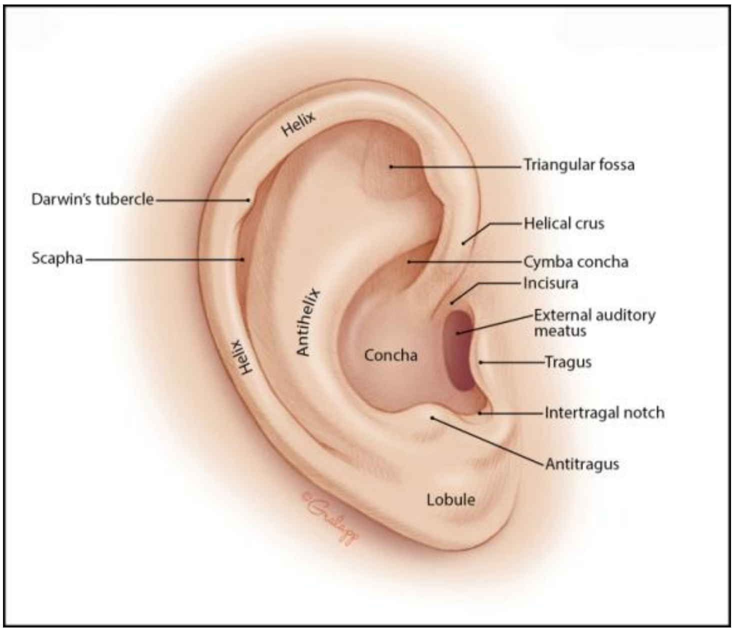

Fig.24. *The pinna, showing the location of the tragus, where the vagus nerve terminates (Courtesy of Tori Lewis Fibonacci Web Studio)*

Рис.24. *Ушная раковина, с изображением козелка, где заканчивается блуждающий нерв (с разрешения веб-студии Тори Льюис Фибоначчи)*

As early as 2001, researchers showed that electrical stimulation of the vagus nerve via the tragus, using a form of electro acupuncture reduced the dependence of patients with coronary arterial disease on vasodilator medication [138]. In their study, titled, *Vagal neurostimulation in patients with coronary artery disease*, the authors stimulated the area of the ear near the auditory passage that contains endings of the auricularis nerve, by means of electrodes attached to short acupuncture needles, inserted to a depth of 0.1 to 0.3 mm. The authors concluded that electrical stimulation of the auricularis nerve results in tonic activation of the central vagus nerve structures and that an increase in vagal tone improves cardiac blood supply in patients with severe angina via dilation of spastic cardiac micro vessels [138]. Referred pain to the ear from myocardial infarction has also been reported, due to the connectivity of ear and the heart, via the vagus nerve [139].

A carefully designed study concerning speech category learning in adults revealed that a simple, earbud-like device, developed at University of California San Francisco (UCSF), significantly improves the ability to learn the sounds of a new language (Fig.25). Mandarin Chinese is a particularly challenging language to learn due to its distinctive changes in pitch, which change the meaning of words. In their study, titled, *Non-invasive peripheral nerve stimulation selectively enhances speech category learning in adults* [140] the authors moulded the shape of a participant's left ear using silicon putty. The resulting silicon form was embedded with two-disc electrodes, 4mm diameter, contacting the cymba concha and cyma cavum of the outer ear, regions shown to be innervated by the auricular branch of the vagus nerve [141]. Electrical stimulation of the electrodes was provided by a commercial constant current device, deploying amplitudes below perceptual thresholds to allow participant blinding, resulting in stimulation intensities several milliamps lower than those used in previous non-invasive tVNS work [140].

Fig.25. *Experimental tVNS device, University of California San Francisco, Department of Neurological Surgery (Courtesy of Dr. M.K. Leonard)*
Рис.25. *Экспериментальное устройство tVNS, Калифорнийский университет Сан-Франциско, кафедра нейрохирургии (С разрешения доктора М.К. Леонард)*

An earphone was inserted in the participant's right ear and fed with specific tones, to train the participant in tonal recognition and Mandarin speech training. The authors' primary focus was to investigate the extent to which pairing non-invasive, sub-perceptual threshold tVNS with behavioral training enhances the ability to categorize non-native speech categories in adults. Their results showed that when tVNS was paired with speech categories that were easier to learn, participants performed significantly better that those who did not receive tVNS stimulation [140].

Crucially, this group-specific learning improvement also generalized to new speech exemplars presented without accompanying stimulation and corrective feedback, thus demonstrating that tVNS can be used to accelerate speech perceptual learning in humans in a highly specific manner.

The authors posit that sub-threshold tVNS engages the ascending brainstem network, and that some aspect of these neuromodulatory pathways causes a learning enhancement [140].

In the study titled, *Anti-inflammatory properties of the vagus nerve: potential therapeutic implications of vagus nerve stimulation* [134] electrical tVNS frequencies used to activate vagal afferents to mediate depression and epilepsy are quoted as 20-30Hz and activation of the cholinergic anti-inflammatory pathway (CAP) as 1-10Hz. The authors mention anti-inflammatory properties of the vagus nerve both through its afferent (activation of the HPA axis) and efferent (activation of the CAP) fibres and that it is a good therapeutic target in inflammatory conditions of the digestive tract, for example, irritable bowel syndrome, and rheumatoid arthritis.

Sonopuncture tVNS

Several commercial manufacturers are now producing devices that provide electrical transcutaneous vagus nerve stimulation [142,143,144] and others that utilize infrasonic sound [145].

Returning to the subject of sonopuncture and to the research by the Niels Bohr Institute, discussed earlier in this chapter, it was shown that nerves conduct sound (soliton impulses), which in turn generate electrical pulses, due to the piezo-electric effect [72].

Therefore, although a corpus of research shows that the vagus nerve can be electrically stimulated via the tragus and other acupressure points of the ears, it is clear that this can also be achieved sonically, and that such sonic stimulation will, automatically, lead to electrical stimulation of the auricular branch of the vagus nerve, due to the piezo-electric effect. In this scenario full ear headphones should be worn, enabling the full pinna of the ear to receive sound frequencies (Fig.26).

Fig.26. *Very low frequencies for tVNS can be delivered sonically, via headphones*

Рис.26. *Очень низкие частоты для tVNS можно передавать звуковым путем через наушники*

The very low frequencies commonly deployed in tVNS therapies can be created sonically via high specification headphones, and several manufacturers now produce headphones that can deliver sounds as low as 5Hz. [146,147,148] Although no studies of this type have yet been conducted, this form of sonopuncture may hold great therapeutic potential in support of a wide variety of illnesses, some of which have been mentioned in this section, including chronic inflammation. Sonic stimulation of the vagus nerve would be achieved by sinusoidal tones, generated by an audio signal generator and fed to headphones via a suitable audio amplifier with the ability to handle very low frequencies. However, specially prepared music could also be deployed therapeutically, that is, music to which the very low frequencies identified in tVNS studies could be added to the music, either embedded in the recording or added separately to the amplifier input feed from an electronic signal generator. In such a scenario the patient would be able to enjoy the many health marker benefits of listening to music, mentioned earlier in this chapter, while the vagus nerve would be vibrationally stimulated by sonopuncture frequencies below the range of hearing, adding further health benefits, for example, reducing chronic inflammation.

Before discussing vocal stimulation of the vagus nerve we make a special mention of the work of French otolaryngologist, Alfred A. Tomatis (b.1920, d. 2001). Dr. Tomatis received his Doctorate in Medicine from the Paris School of Medicine and formulated a theory that many vocal problems are actually hearing problems, based on the concept that *the voice cannot produce what the ear cannot not hear*, today referred to as ‘The Tomatis Effect’.

Tomatis developed the ‘Electronic Ear’, a device that utilizes bone conduction and sound filters to improve the tone of the muscles in the middle ear, to sensitize the listener to the missing frequencies, particularly in the high registers. The ear starts forming a few days after conception and is fully developed by the fourth month of pregnancy. Tomatis theorized that information coming from the fetal ear stimulates and guides the development of the brain. He believed that a number of auditory communication problems begin in pregnancy, with the fetus not properly responding to the voice of the mother. In children with ASD, he believed that his electronic ear device simulated the sound of the mother's voice as heard in the uterus, leading the child to gradually accept and respond to her real unfiltered voice. He reported that this method often brought startling results, with children crying with joy as they recognized their mother's voice for the first time. He wrote: «It is this [vagus] nerve that helps the singer to consciously rediscover the correct respiration rhythm as well as cardiac and visceral rhythms so that a synergy is created between this internal network and the larynx…It is equally important in mastering a fluid and correct verbal flow of speech…Without doubt singing is one of the best ways to free ourselves from the burden of parasympathetic or neurological imbalances» [149].

Vocal stimulation of the vagus nerve

Last in this section, the laryngeal connection to the vagus nerve expresses and directly influences internal visceral states through the voice. In the article, *Stalking the calm buzz: how the polyvagal theory links stage presence, mammalian evolution, and the root of the vocal nerve* [150] Joanna Cazden discusses Stephen W. Porges 'polyvagal theory' which emphasises phonation, respiration and hearing. Porge's research proposes that the voice is strongly influenced by neuro-regulation that underlies our ability to communicate, and because the vagus nerve mediates our emotional state and our laryngeal muscle activity, our visceral states directly influence and are expressed through the voice.

Full appreciation of the autonomic vagus nerve, its influence on behavior and its implications for vocal performance, requires a distinction between the neurophysiologic aspects of the autonomic system's two main sub-branches, the sympathetic and parasympathetic [150]. These two aspects of the autonomic nervous system can be thought of as a sympathetic accelerator and a parasympathetic break, providing bidirectional neural communication between our organs and brainstem [151].

Several nerve tracts in the brain can send sympathetic signals to stimulate a faster heart beat but only the vagus nerve sends a slowing signal, achieved during exhalation: the heart beats slightly faster as we inhale and slower as we exhale [152]. This effect is termed, Respiratory Sinus Arrhythmia (RSA), which is a measure of vagal tone.

The auditory nerve (CN VIII) that carries sound signals from the ears to the brain receives close crosstalk from the myelinated vagus nerve. Porge mentions that the voice is a potent trigger of the physiological states of others and that emotional prosody is an audible sign of autonomic status, recognized in the brain of the listener. Because the laryngeal nerves branch directly from the vagus, the voice transmits our inner resilience and expressive visceral state to others through sound [150].

In the study, *Music Structure Determines Heart Rate Variability of Singers*

[153] it is suggested that singing can be viewed as initiating the work of a vagal pump: Singing produces slow, regular and deep respiration which in turn triggers RSA, causing a pulsating vagal activity. In addition, as discussed in the section *Active and passive sonic stimulation of the nasal cavities and lungs,* singing, chanting and humming stimulates nitric oxide production in the nasal cavities and lungs, with many associated health benefits.

Playwright, John Guare, said, «the purpose of art is to exercise the muscles of the soul, so that when the challenges of life come, we are prepared». Porge's polyvagal theory suggests that these «muscles of the soul» may be found in the tiny area of the brainstem where a single myelinated pathway influences the remarkable vagus nerve [150].

VIBRATIONAL MEDICINE: THE FUTURE

The depiction of a therapeutic bed of the future, as fictionalized in the television series 'Star Trek', inspired the imagination of millions of viewers into what may be possible in the twenty-third century. Yet even now, medical physics of the twenty-first century is beginning to develop a non-invasive diagnostic bed capable of indicating asthma, sepsis, and even several types of cancer by monitoring exhaled gases and compounds from patients.

The technology that makes this possible is a mass spectrometer, the same type of instrument on board NASA's Perseverance rover on Mars, searching for signs of life. Other instruments that can be integrated into this future bed include **thermal and hyper-spectral imagers** that will track temperature and skin color to monitor a patient's metabolism, while ultrasound sensors will non-invasively measure **blood flow and oxygenation** to analyze the heart's activity and blood circulation in real-time [154].

Brain activity can also now be measured without attaching electrodes to a patient's scalp, by superconducting quantum interference device (SQUID) magnetometer, making it possible to monitor neurological conditions remotely. The distance between the skull and the magnetometer is typically 2cm at present but future improvements in sensitivity may make it possible to build the magnetometer into the structure of the bed, providing EEG readouts in bed-head displays. Such powerful diagnostic aids seem like science fiction, yet are becoming a reality.

Also mirroring Star Trek, active healing technology could be built into hospital beds of the future. For example, as this chapter has highlighted, chronic pain mediation without use of analgesics is already possible by means of sound vibrations applied to specific body parts, which can be achieved while a patient is supine. Commercial vibro-acoustic beds have been developed by several manufacturers [155,156,157] and their use in clinical environments is likely to play an increasingly important role in hospitals of the future.

In addition to pain mediation, whole body vibration to supine patients could greatly enhance a patient's blood oxygen levels, as the author's preliminary studies have shown, thereby supporting the healing of many illnesses. Sonic stimulation of a patient's lungs and nasal cavities would also increase their nitric oxide levels, thereby encouraging vasodilatation, lowering blood pressure and providing many other health benefits.

Music delivered to every patient, via ultrasonic speakers, would help elevate their mood and therefore, dopamine levels, providing a helpful boost to their immune system, crucial to healing processes.

One of the greatest challenges facing medicine in the twenty-first century is in eradication of cancer, yet a discovery made by Professor James Gimzewski of UCLA, in 2002, offers an intriguing potential for eradicating not only cancer cells but perhaps any pathogen. Using an Atomic Force Microscope, he and his colleague, Dr. Andrew Pelling and team, were able to listen to the sounds of cells for the first time. Surprisingly, they found that the respiration sounds of cells lie in the audible range when amplified, naming their new approach to cell biology, 'sonocytology', referring to the 'songs' of cells [158,159].

Raman spectroscopy offers an accessible alternative method of recording the songs of cancer cells, which differ significantly from that of healthy cells. In a study by the author, in collaboration with Professor Sungchul Ji of Rutgers University, sounds from cancer cells and healthy cells, derived by Raman spectroscopy, were made visible with the aid of a cymascope instrument, imprinting the sound vibrations onto medical grade water, rather like a fingerprint on glass, thus leaving a visual signature of the cell sounds.

A typical cymaglyph (sound image) of a healthy cell sound is symmetrical, while that of a cancer cell is skewed by comparison (Fig.27).

The study, titled, *Imaging Cancer and Healthy Cell Sounds in Water by Cymascope, Followed by Quantitative Analysis by Planck-Shannon Classifier* was published in the Water Journal (waterjournal.org), as the revealing medium of sonic vibrations in the cymascope instrument is water.

This collaborative study was a first step toward creating visual imagery for a surgeon who would wear specially adapted eyewear, to see, in real time, changing sound patterns as the Raman laser probe is scanned across the tissues during an operating procedure.

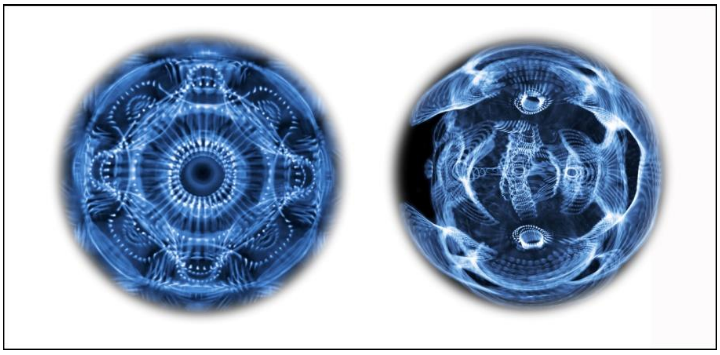

Fig.27. *Healthy cell cymaglyph (left), cancer cell cymaglyph (right)*
Рис.27. *Звуковые образы здоровой клетки (слева) и раковой клетки (справа)*

However, the most exciting aspect of this new technology lies in its potential for early cancer detection and ultimately to destroy cancer cells. By taking a biopsy of a cancer, its sonic signature could be detected and amplified, then used to modulate an ultrasound beam directed at a tumor. In such a scenario the tumor cells would absorb sufficient acoustic energy (of the cancer cell's own sonic signature) to be destroyed. Such a therapeutic procedure would likely be given during a series of outpatient visits, in which a percentage of the tumor's mass would undergo a controlled shrink on each visit, to minimize the toxic waste of dead cancer cell material. For leukemia sufferers, this principle holds the potential for sonic irradiation the patient's blood via a specially adapted intraoperative recirculating system.

Another area of future sound-based medical physics concerns the G0 phase of the cell cycle in which a system of cells becomes quiescent due to environmental changes, for example, glucose depletion, heat shock, free radicals, pathogen invasion, or toxicity. When a system of cells is in the G0 phase this creates imbalance in the body, resulting in physiological symptoms, yet, hypothetically, cells in this 'sleeping' state can be stimulated to return to the normal cell cycle by immersion in specific sound frequencies or in music. (Recall that Professor James Gimzewski's research [158, 159] indicated that the sounds emitted by cells are in audible frequency ranges, typically centered around 1kHz.) The quasi-holographic nature of sound, and the spherical space-form of audible sounds, mentioned in the introduction to this chapter, is why Faraday Wave patterns manifest on the surface membranes of cells, organs, visceral fascia and in visceral fluids. Although not within the scope of this chapter, it is also why all of the energy information within a specific sound frequency, or within music, is conveyed to the cell's interior.

Also popularly known as 'cymatic patterns' after Dr. Hans Jenny, who coined the term to mean 'visible sound', the importance of this natural phenomenon is vital in relation to the future of vibrational medicine. The integral membrane proteins and primary cilia of cells are, in a very real sense, massaged by the anti-nodal pressure points of such microscopic sound patterns, stimulating cells in ways that have yet to be discovered.

Sound organizes matter, a fact that can be seen in simple Chladni Plate experiments with particulate matter, and in more sophisticated experiments with the CymaScope instrument, in which liquid water is used as the imprinting medium to transpose sonic periodicities to water wavelet periodicities [7]. Life as we know it cannot exist without liquid water; 'structured water', or 'exclusion zone' (EZ) water is discussed in depth by Professor Gerald H. Pollack, in his ground-breaking book, *The Fourth Phase of Water* [161]. He proposes that EZ water (H_3O_2), literally generates the electricity that helps power all living creatures. Here then is a connection waiting to be explored between sound frequencies that organize water molecules, and EZ water that powers life. Professor Pollack has discovered that EZ water is built by light, particularly infrared light, yielding a potentially fascinating connection between sound and our physiology: *inelastic sonic collisions create sonically-modulated infrared light that powers the EZ water-building mechanism in cells, which in turn powers our biology*. The organizational aspect of sound and its EZ water-building mechanism is already beginning to provide insights into what might come to be termed 'sono-biology', a field in which the role of structured water and sound is likely to become increasingly important in medicine.

These are just some of the many advances in medical science that hold the potential to support humankind in the quest to reverse disease, extend life and improve quality of life. The role of sound in medical modalities is growing each year for drug-free therapies and for diagnostic applications, and is finding welcome support among many physicians, and in hospitals worldwide. I predict that Sound Therapy and Music Medicine will have an important role in the future of medicine, one that deserves to be developed and nurtured.

ADDITIONAL

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References/ Список литературы

1. Rubik B. The Biofield Hypothesis: Its Biophysical Basis and Role in Medicine. *The Journal of Alternative and Complementary Medicine*, Vol 8, No 6. DOI; 10.1089/10755530260511711
2. When Microbial Conversations Get Physical, Gemma Reguera, Trends in Microbiology, DOI: 10.1016/j.tim.2010.12.007
3. Das Wesen der Materie [The Nature of Matter] speech at Florence, Italy (1944) (from Archiv zur Geschichte der Max-Planck-Gesellschaft, Abt. Va, Rep. 11 Planck, Nr. 1797).
4. The Institute for Functional Medicine. Available at: https://www.ifm.org/functional-medicine/
5. Sound Intensity and Sound Level // Available at: https://courses.lumenlearning.com/physics/chapter/17-3-sound-intensity-and-sound-level/
6. Vatansever F. and Hamblin M.R. Far Infrared radiation (FIR): its biological effects and medical applications. *Photonics and Lasers in Medicine.* 2012 Nov 1;4: 255-266. DOI: 10.1515/plm-2012-0034

7. The Mereon Matrix, editors, McNair J.B., Dennis L., and Kauffman, L. p783-809: Reid J.S., The Emergent Science of Cymatics. World Scientific, ISSN 0219-9769. ISBN: 978-981-3233-55-3.
8. Life of Pythagoras, Iamblichus, Taylor T. Translated from the Greek, p. 7. Inner Traditions. (Iamblichus was a Syrian philosopher who lived circa 325 to circa 245 BC; therefore, a period of 170 years separates Pythagoras' death from Iamblichus' birth.)
9. The Athenian, Isocrates (436–338 BC), in his book Busiris, mentioned Pythagoras' travels in Egypt: Measuring Heaven: Pythagoras and his influence on thought and art in antiquity and the Middle Ages, Christiane L. Joost-Gaugier.
10. The Life of Pythagoras, Professor Moritz Cantor, Heidelberg, Germany. Open Court Magazine, Volume 6, Number 493, June 1897.
11. Pythagoras: His Life and Teaching, a Compendium of Classical Sources, Thomas Stanley, Ibis Press.
12. Thaut M.H. Music as therapy in early history. Progress in Brain Research, Vol 217, DOI: 10.1016/bs.pbr.2014.11.025
13. Nunn J.F. Ancient Egyptian Medicine, British Museum Press, 1997. p111 and p122. ISBN: 0-7141-1906-7
14. Lipton B. The Biology of Belief. Elite Books, 2005. ISBN: 0-9759914-7-7
15. Schwaller de Lubicz R.A. Sacred Science. Inner Traditions, Bear & Co, 1989. ISBN: 10:0892812222
16. Aristotle. Poetics. Loeb Classical Library. p395. ISBN: 0-674-99563-5
17. The Corpus Hermeticum, p74. Translated by Salaman C,. Oyen D., & Wharton, W.D. Gerald Duckworth & Co. Ltd, 1999. ISBN: 0-7156-2939-5
18. Imhotep. Available at: https://www.worldhistory.org/imhotep/
19. Manniche, L. Music and Musicians in Ancient Egypt. p72. British Museum Press, 1991. ISBN: 0-7141-0949-5
20. Therapeutic ultrasound: some historical background and development in knowledge of its effect on healing: https://www.ncbi.nlm.nih.gov/pubmed/25026107
21. Mason T.J. Therapeutic ultrasound, an overview. *Journal of Ultrasonics Sonichemistry,* 2011; 18 (4): 847-852. DOI: 10.1016/j.ultsonch.2011.01.004
22. Therapeutic Modalities for Allied Health Professionals. William E. Prentice. P271. McGraw-Hill publishing, p. 270.
23. Marberger, M, et al. Late Sequelae of Ultrasonic Lithotripsy of Renal Calculi.

The Journal of Urology. DOI: 10.1002/jum.15191

24. Dubinsky J.D, at al. Histotripsy: The Next Generation of High-Intensity Focused Ultrasound for Focal Prostate Cancer Therapy. DOI: 10.1002/jum.15191
25. Tian Y. at al. New Aspects of Ultrasound-Mediated Targeted Delivery and Therapy for Cancer. *Dove Press Open Access Journal.* https://doi.org/10.2147/IJN.S201208
26. Nicodemus N.E. et al. Focused transcranial ultrasound for treatment of neurodegenerative dementia. Alzheimer's & Dementia: Translational Research & Clinical Interventions, Volume 5, 2019, p374-381. DOI: 10.1016/j.trci.2019.06.007
27. Therapeutic Ultrasound // Available at: http://www.electrotherapy.org/ modality/ultrasound-therapy? highlight=over vieww#Therapeutic%2 0Ultrasound%20Thermal% 20and% 20 Non %20Thermal%20Effects %20Overview
28. Novasonic. // Available at: https://novafon.com/de/historie
29. Medsonix. // Available at: http://www.medsonix.com
30. KKT International. // Available at: http://www.kktspine.com
31. Cyma Technologies Inc. Available at: http://cymatechnologies.com
32. American Music Therapy Association. Available at: https://www.musictherapy. org/about/
33. Brad J, et al. The impact of music therapy versus music medicine on psychological outcomes and pain in cancer patients: a mixed methods study. Support Care Cancer. DOI: 10.1007/s00520-014-2478-7
34. International Sound Therapy Association. Available at: http://istasounds.org/ about-us/about/
35. Cochrane Library // Available at: https://www.cochranelibrary.com/cdsr/ doi/10.1002/14651858. CD006577.pub3
36. Music as Medicine // Available at: https://www.acc.org/about-acc/press-releases/2020/03/18/09/02/music-as-medicine-30-minutes-a-day-shows-benefits-after-heart-attack
37. Johns Hopkins Medicine // Available at: https://www.hopkinsmedicine.org/ center-for-music-and-medicine/ music-as-medicine.html
38. McGill // Available at: https://www.mcgill.ca/newsroom/channels/news/ major-health-benefits -music-uncovered-225589
39. Therapeutic effect: Musical medic plays to cancer patient, 10, during surgery //

Available at: https://www.reuters.com/article/us-italy-hospital-piano-idUSKBN27X2HU

40. Audio Spotlight by Holosonics // Available at: https://www.holosonics.com/
41. Available at: https://ultrasonic-audio.com/
42. Cockroft J. Exploring vascular benefits of endothelium-derived nitric oxide Medicine. *American Journal of Hypertension.* DOI:10.1016/J.AMJHYPER.2005.09.001
43. Majida R. et al. Nitric Oxide and Wound Healing. World Journal of Surgery. DOI: 10.1007/s00268-003-7396-7
44. Moilanen E. and Vapaatalo, H. Nitric oxide in inflammation and immune response. Annals of Medicine. DOI: 10.3109/07853899509002589
45. Noboru T, et al. Cerebral Blood Flow Regulation by Nitric Oxide: Recent Advances. *Pharmacological Reviews.* DOI: 10.1124/pr.108.000547
46. Loscalzo J. Nitric Oxide Insufficiency, Platelet Activation, and Arterial Thrombosis. Circulation Research. DOI: 10.1161/hh0801.089861
47. Ashutosh K, et al. Use of nitric oxide inhalation in chronic obstructive pulmonary disease. *Thorax Journal*. DOI: 10.1136/thorax.55.2.109
48. Jones A, et al. Dietary Nitrate and Nitric Oxide Metabolism: Mouth, Circulation, Skeletal Muscle, and Exercise Performance. *Medicine and Science in Sports and Exercise*. DOI: 10.1249/MSS.0000000000002470
49. Majorana A, et al. Exercise and the Nitric Oxide Vasodilator System. Sports Medicine. DOI: 10.2165/00007256-200333140-00001
50. Weitzberg E. and Lundberg J.O. Humming Greatly Increases Nasal Nitric Oxide.
51. Goldman J. and Goldman A. The Humming Effect. https://www.goodreads.com/book/show/32071037-the-humming-effect
52. Lundberg J.O. and Weitzberg E. Nasal nitric oxide in man. *Thorax Journal.* dx.doi.org/10.1136/thx.54.10.947
53. World History Encyclopedia // Available at: https://www.worldhistory.org/timeline/Bhagavad_Gita/
54. Maniscalco M. et al. Assessment of nasal and sinus nitric oxide output using single-breath humming exhalations. *European Respiratory Journal.* 2003; 22:323-329. DOI: 10.1183/09031936.03.00017903
55. Masuda S., Role of the maxillary sinus as a resonant cavity. DOI: 10.3950/jibiinkoka.95.71
56. Pietropaoli A.P., et al., Simultaneous Measurement of Nitric Oxide Production

by Conducting and Alveolar Airways of Humans. American Physiological Society.

57. Henry B. and Royston J. T., A Multiscale Analytical Model of Bronchial Airway Acoustics, Department of Bioengineering, University of Illinois. DOI: 10.1121/1.5005497
58. Bogomolov A.V., et al. Mathematical Model of Sound Absorption by Lungs with Acoustic Stimulation of the Respiratory System. *Doklady Biochemistry and Biophysics*.2019; 487(1):247-250. DOI: 10.1134/S160767291904001X
59. White Noise definition: https://www.britannica.com/art/white-noise-music
60. Parametric Equaliser: https://www.presonus.com/learn/technical-articles/What-Is-a-Parametric-Eq
61. Sethi S., et al., Lung Flute Improves Symptoms and Health Status in COPD with Chronic Bronchitis: A 26 week randomized controlled trial. *Clinical and Translational Medicine*. DOI: 10.1186/s40169-014-0029-y
62. Reddi, D. et al. An introduction to pain pathways and mechanisms. *British Journal of Hospital Medicine*. DOI: 10.12968/hmed.2013.74.Sup12.C188
63. Wang X-M et al. Up-Regulation of IL-6, IL-8 and CCL2 Gene Expression After Acute Inflammation: Correlation to Clinical Pain. *Pain Journal*. 2009 Apr; 142(3): 275-283. DOI: 10.1016/j-pain.2009.02.001
64. Mills E.E.S. et al. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *British Journal of Anaesthesia*. DOI: 10.1016/j.bja.2019.03.023
65. Diatchenko L. et al. The phenotypic and genetic signatures of common musculoskeletal pain conditions. *Nature Reviews Rheumatology.* 2013; 9(6). DOI: 10.1038/nrrheum.2013.43
66. Raja N., et al. The revised International Association for Study of Pain definition of pain: concepts, challenges, and compromises. *Pain Journal*. DOI: 10.1097/j.pain.0000000000001939
67. Bonica J.J. The management of pain. Philadelphia: Lea & Febiger, 1953.
68. Merskey H., Bogduk N. Classification of chronic pain. 2nd ed. Seattle: IASP Press, 1994. p. 1.
69. Rodriguez-Raecke R., et al. Brain gray matter decrease in chronic pain is the consequence and not the cause of pain. *J Neurosci*. 2009;29:13746–13750. DOI: 10.1523/JNEUROSCI.3687-09.2009
70. Baldini A. et al. A Review of Potential Adverse Effects of Long-Term Opioid Therapy: A Practitioner’s Guide. The Primary Care Companion for CNS

Disorders. DOI: 10.4088/PCC.11m01326.

71. Schwiening C.J. A brief historical perspective: Hodgkin and Huxley. *The Journal of Physiology.* DOI: 10.1113/jphysiol.2012.230458
72. Heimburg T. and Jackson A.D. On soliton propagation in biomembranes and nerves. Proceedings of the National Academy of Sciences of the United States of America. DOI: 10.1073/pnas.0503823102
73. Kaufmann K. (1989). Action Potentials and Electrochemical Coupling in the Macroscopic Chiral Phospholipid Membrane. Caruaru, Brazil.
74. Shrivastava S. and Schneider M. F. Evidence for two-dimensional solitary sound waves in a lipid controlled interface and its implications for biological signalling. The Royal Society Publishing Interface. DOI: 10.1098/rsif.2014.0098
75. Shrivastava S. et al. Collision and annihilation of nonlinear sound waves and action potentials in interfaces. The Royal Society Publishing Interface. DOI: 10.1098/rsif.2017.0803
76. Merriam-Webster Logo // Available at: https://www.merriam-webster.com/dictionary/sound
77. Melzack R. and Wall P. Pain Mechanisms: A New Theory. *Science*, Volume 150, Number 3699.
78. Bartel L. and Mosabbir A. Possible Mechanisms for the Effects of Sound Vibration on Human Health. Healthcare, 2021, 9, 597. DOI: 10.3390/healthcare9050597
79. Wang W. et al. Efficacy of whole-body vibration therapy on pain and functional ability in people with non-specific low back pain: a systematic review. *BMC Complementary Medicine and Therapies.* (2020) 20:158 DOI: 10.1186/s12906-020-02948-x
80. Boeselt T. et al. Whole-body vibration therapy in intensive care patients: A feasibility and safety study. *Journal of Rehabilitation Medicine.* Vol 48, Issue 3.
81. Mosabbir A., et al. The Effects of Long-Term 40Hz Physioacoustic Vibrations on Motor Impairments in Parkinson’s Disease: A Double-Blinded Randomized Control Trial. Healthcare, 2020. DOI: 10.3390/healthcare8020113
82. Hollins M. et al. How does vibration reduce pain? *Perception* 2014; 43:70-84.
83. Naghdi L. et al. The effect of low-frequency sound stimulation on patients with fibromyalgia: A clinical study. *Pain Res. Manag.* 2015; 20: E21-e27.
84. Staud R. et al. Attenuation of Experimental Pain by Vibro-Tactile Stimulation in Patients with Chronic Local or Widespread Musculoskeletal Pain. European

Journal of Pain. 2011; 15(8): 836–842. DOI:10.1016/j.ejpain.2011.01.011.
85. Urien L. and Wang J. Top-Down Cortical Control of Acute and Chronic Pain. *Psychosomatic Medicine.* 2019;81(9):851-858. DOI:10.1097/PSY.0000000000000744
86. Pertovaara A. and Almedia A. Endogenous Pain Modulation. Chapter 13. Descending Inhibitory Systems. Handbook of Clinical Neurology, Vol. 81 (3rd series. Vol 3.) Pain. F. Cervero and T.S. Jenson, Editors. 2006, Elsevier.
87. Dobek C. et al. Music Modulation of Pain Perception and Pain-Related Activity in the Brain, Brain Stem, and Spinal Cord: A Functional Magnetic Resonance Imaging Study. *The Journal of Pain*. 2014; 15(10):1057-1068. DOI: 10.1016/j.jpain.2014.07.006.
88. Goldstein A. Thrills in response to music and other stimuli. *Physiological Psychology.* 1980; 8 (1):126-129. DOI: 10.3758/BF03326460
89. Beecher H.K. Pain in men wounded in battle. Annals of Surgery. 1946; 123(1): 96–105.
90. Susuki R. et al. Bad news from the brain: Descending 5-HT pathways that control pain processing. *TRENDS in Pharmacological Sciences.* 2004; 25(12). DOI: 10.1016/j.tips.2004.10.002
91. Gardner W.J. et al. Suppression of Pain by Sound. *Science* **132** (3418), 32-33. DOI: 10.1126/science.132.3418.32
92. Robson J.G. and Davenport H.T. The Effects of White Sound and Music upon the Superficial Pain Threshold. *Canadian Anaesthetists' Society journal*.1962;9:105-8. DOI: 10.1007/BF03021250
93. Fink D.J. What is a Safe Noise Level for the Public. *American Journal of Public Health.* 2017; 107(1): 44–45. DOI: 10.2105/AJPH.2016.303527
94. Travell J. et al. Pain and disability of the shoulder and arm. JAMA; 120: 417-422. DOI: 10.1001/jama.1942.02830410005002
95. McCarberg B.H. et al. Diagnosis and Treatment of Low-Back Pain because of Paraspinous Muscle Spasm: A Physician Roundtable. Pain Medicine, Volume 12, Issue suppl_4, November 2011, Pages S119-S127. DOI: 10.1111/j.526-4637.2011.01253.x
96. Roland M.O. A critical review of the evidence for a pain-spasm-pain cycle in spinal disorders. Clinical Biomechanics 1986; 1: 102-109 DOI: 10.1016/0268-0033(86)90085-9
97. Järvholm U. et al. Intramuscular pressure and muscle blood flow in supraspinatus. *European Journal of Applied Physiology and Occupational*

Physiology. 58, pages 219–224 (1988). DOI: 10.1007/BF00417252
98. Luo D. et al. A comparison between acute pressure block of the sciatic nerve and acupressure; methodology, analgesia, and mechanisms involved. *Journal of Pain Research.* 2013:6 589–593. DOI: 10.2147/JPR.S47693
99. World Health Organization Geneva 1991, A proposed standard international acupuncture nomenclature. ISBN 92 4 154417 **1**
100. Chen Y-W and Wang H-H. The effectiveness of acupressure on relieving pain: a systematic review. *Pain Management Nursing.* 2014 Jun;15(2):539-50. DOI: 10.1016/j.pmn.2012.12.005
101. Franklin, E.F. Practitioner Self Care: A Study in the Applied Use of Sound-vibrations with Acutonics Sound-Based Therapeutics. *Oriental Medicine Journal.* Vol. 27, No.3 2019.
102. Franklin, E.F. and Carey, D. Acutonics at Twenty: Recollections and Reflections. *Oriental Medicine Journal*, Spring 2017, Vol 25, No. 3.
103. Franklin E.F. Dissertation: Acutonics Self Care Program and Stress: Multiple Case Study Exploration of an Intervention to Ameliorate Symptoms of Severe Stress and Compassion Fatigue in Nurses. Faculty of Saybrook University. San Francisco, 2014.
104. Acutonics // Available at: https://acutonics.com/news/vibrational-acupuncture-integrating-tuning-forks-with-needles
105. *Tuning the Human Biofield*, ISBN 10 1620552469
106. Biofield tuning study. Jain S, McKusick E, Ciccone L, Sprengel M, Ritenbaugh C. Sound healing reduces generalized anxiety during the pandemic: A feasibility study. *Complement Ther Med.* 2023 Jun;74:102947. DOI: 10.1016/j.ctim.2023.102947. Epub 2023 Apr 5. PMID: 37023932.
107. Novafon // Available at: https://novafon.com/en/magnetic-attachment?number=7001
108. Sonopuncture // Available at: https://www.acupuncturechicagoillinois.com/sonopuncture.html
109. Cyma Technologies // Available at: https://www.cymatechnologies.com
110. Green Medinfo // Available at: http://istasounds.org/pain-free-campaign/ International Sound Therapy Association.
111. Chandan K.S. Wound Healing Essentials: Let There Be Oxygen. *Wound Repair and Regeneration Journal.* 2009; 17(1): 1-18. DOI: 10.1111/j.1524-475X.2008.00436.x
112. Reznekov L. Understanding Heart Sounds and Murmurs, with an

introduction to Lung Sounds. *JAMA*.1985;254(1):124–125. DOI:10.1001/jama.1985.03360010134047

113. The Effects of Chronic Fear on a Person's Health // Available at: https://www.ajmc.com/view/the-effects-of-chronic-fear-on-a-persons-health
114. Thau L. et al. Physiology, Cortisol. StatPearls Publishing LLC. https://www.ncbi.nlm.nih.gov/books/NBK538239/
115. Segerstrom S.C. and Miller, G.E. Psychological Stress and the Human Immune System: A Meta-Analytic Study of 30 Years of Inquiry. *Psychological Bulletin*, 2004 Jul; 130(4):601-630 DOI: 10.1037/0033-2909.130.4.601
116. Salimpoor, V.N. et al. Anatomically distinct dopamine release during anticipation and experience of peak experience to music. *Nature Neuroscience.* 14, 257-262 (2011). DOI: 10.1038/nn.2726
117. Dopamine rewards immune cells through immunological synapse // Available at: https://www.kennedy.ox.ac.uk/news/dopamine-rewards-immune-cells-through-immunological-synapse
118. Bartlett D. et al. The Effects of Music Listening and Perceived Sensory Experiences on the Immune System Measured by Interleukin-1 and Cortisol. *Journal of Music Therapy*, Vol. 30, Issue 4, 1993, p 194-209. DOI: 10.1093/jmt/30.4.194
119. Sprouse-Blum A.S. et al. Understanding Endorphins and their Importance in Pain Management. *Hawai'i Medical Journal*, Vol. 69, 2010, Mar; 69(3): 70-71. PMC3104618
120. Ohytocin // Available at:https://www.bionity.com/en/encyclopedia/Oxytocin.html
121. Keeler J.R. et al. The neurochemistry and social flow of singing: bonding and oxytocin. Frontiers in Human Neuroscience. DOI: 1.3389/fnhum.2015.00518
122. Nilsson U. Soothing music can increase oxytocin levels during bed rest after open heart surgery: a randomised control trial. *Journal of Clinical Nursing*. 18, 2153-2161. DOI: 10.1111/j.1365-2702.2008.02718.x
123. Magon N. and Kalra S. The orgasmic history of oxytocin: Love, lust, and labor. *Indian Journal of Endocrinology and Metabolism.* 2011 Sep; 15 (Suppl3): S156-S161. DOI: 10.4103/2230-8210.84851
124. Yu J.C. et al. Whole Body Vibration-Induced Omental Macrophage Polarization and Fecal Microbiome Modification in a Murine Model. *International Journal of Molecular Sciences*, 2019, 20(13), 3125; DOI:

10.3390/ijms20133125

125. Scientific reports // Available at: https://www.nature.com/articles/019529d0.pdf
126. Oster G. Auditory beats in the brain. Scientific American, 229(4), 94-102. DOI: 10.1038/scientificamerican1073-94
127. Lane J.D. et al. Binaural Auditory Beats Affect Vigilance, Performance and Mood. *Physiology and Behavior*. Vol. 63, No 2, pp. 249-252, 1998. DOI: 10.1016/S0031-9384(97)00436-8
128. Gkolias V. et al. Reduced pain and analgesic use after acoustic binaural beats therapy in chronic pain - A double-blind randomized control cross-over trial. *European Journal of Pain*. DOI: 10.1002/ejp.1615
129. Morris, S.E. (1990). Hemi-Sync and the facilitation of sensory integration. *Hemi-Sync Journal*, VIII(4), pp. 5-6.
130. Wilson, E.S. (1990). Preliminary study of the Hemi-Sync sleep processor. Colorado Association for Psychophysiologic Research.
131. Kennerly, R. C. (1994). Available at: https://hemi-sync.com/research-papers/an-empirical-investigation-into-the-effect-of-beta-frequency-binaural-beat-audio-signals-on-four-measures-of-human-memory/
132. Breit S. et al. Vagus Nerve as Modulator of the Brain-Gut Axis in Psychiatric and Inflammatory Disorders. *Frontiers in Psychiatry*. DOI: 10.3389/fpsyt.2018.00044
133. Pavlov A., and Tracey J.T. The vagus nerve and the inflammatory reflex—linking immunity and metabolism. *Nature Reviews Endocrinology*, 2012; 8(12): 743-754. DOI: 10.1038/nrendo.2012.189
134. Bonaz B. eta al. Anti-inflammatory properties of the vagus nerve: potential therapeutic implications of vagus nerve stimulation. The Journal of Physiology. 594.20 (2016) pp 5781-5790. DOI: 10.1113/JP271539
135. https://vagus.net/what-is-tvns/
136. Marijke D.C. et al. The Role of the vagus Nerve in Cancer Prognosis: A Systematic and a Comprehensive Review. *Hindawi Journal of Oncology*, Volume 2018. DOI: 10.1155/2018/1236787
137. Heathers J.A.J. Everything Hertz: methodological issues in short-term frequency-domain HRV. *Frontiers in Physiology.* DOI: 10.3389/fphys.2014.00177

138. Zamotrinsky A.V. et al. Vagal neurostimulation in patients with coronary artery disease. *Autonomic Neuroscience: Basic and Clinical* 88 (2001) 109-116. DOI: 10.1016/S1566-0702(01)00227-2

139. Amirhaeri, S., Spencer, D. 2010. Myocardial infarction with unusual presentation of otalgia: a case report. *International Journal of Emergency Medicine* 3, 459-460. DOI: 10.1007/s12245-010-0222-8

140. Llanos F. et al. Non-invasive peripheral nerve stimulation selectively enhances speech category learning in adults. Npj Science of Learning. DOI: 10.1038/s41539-020-0070-0

141. Llanos F. et al. Hidden Markov modelling of frequency-following responses to Mandarin lexical tones. *Journal of Neuroscience Methods* 291, 101-112 (2017). DOI: 10.1016/j.neumeth.2017.08.010

142. Parasym // Available at: https://www.parasym.co/parasym-device-transcutaneous-vagus- nerve-stimulation.html (electrical stimulation)

143. Neuvana // Available at: https://neuvanalife.com/pages/using-xen (electrical stimulation)

144. Electrocore // Available at: https://www.electrocore.com/product/ (electrical stimulation)

145. Sensate // Available at: https://www.getsensate.com/pages/how-it-works

146. Senhheiser, model HD 820. 6Hz – 48,000Hz.

147. Focal, model Utopia. 5Hz – 50,000Hz.

148. Beyer Dynamic, model DT770 Pro. 5Hz – 35,000Hz.

149. Tomatis A.A. The ear and the voice. Scarecrow press Inc., 2005. ISBN: 0-8108-5137-7

150. Cazden J. Stalking the calm buzz: how the polyvagal theory links stage presence, mammalian evolution, and the root of the vocal nerve. *Voice and Speech Review.* Oct 6. 2017, vol11. DOI: 10.1080/23268263.2017.1374082

151. Siegel D. Pocket Guide to Interpersonal Neurobiology: An Integrative Handbook of the Mind. (2012). W.W. Norton & Co. New York. ISBN:-10-039370713X

152. Porges S.W. The Pocket Guide to the Polyvagal Theory. (2017). W.W. Norton & Co. New York. ISBN-10-9780393707878

153. Vickhoff B., et al. Music structure determines heart rate variability of singers. Frontiers in Psychology, 2013. DOI: 10.3389/fpsyg.2013.00334

154. Leicester scientists deploy space-age technologies at science-fiction style ‘sick bay’. University of Leicester. https://www.eurekalert.org/news-releases/674876
155. HealBed: Vibroacoustic Therapy Devices // Available at: www.healbed.com
156. Vibrobed // Available at: www.vibrobed.eu
157. Aquavibe // Available at: www.aquavibe.org
158. Pelling E.P et al. Local nanomechanical motion of the cell wall of Saccharomyces. Science, 2004. DOI: 10.1126/science.1097640
159. The dark side of the cell // Available at: http://www.darksideofcell.info/bg.html
160. Reid J.S., Park J.P., and Sungchul J. Imaging Cancer and Healthy Cell Sounds in Water by CymaScope, followed by Quantitative Analysis by Planck-Shannon Classifier. Available at: https://waterjournal.org/current-volume/reid/
161. Pollack G.H. The Fourth Phase of Water. Ebner & Sons Publishers, ISBN: 978-0-9626895-3-6 and ISBN: 978-0-9626895-4-3