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FOCUSED ULTRASOUND AS A STIMULATOR OF THE NERVE STRUCTURES

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Pulsed focused ultrasound can stimulate the receptor and conductive nerve structures of man and animals, as well as neurons of the central nervous system of the invertebrates. The possibility of a wide practical use of this method in medicine and physiology is considered. For example, the stimulating ability of focused ultrasound is applied for neurological disease diagnosis, to study skin and tissue sensitivity of man, to diagnose hearing disorders and to introduce auditory information to the deaf with certain forms of hearing pathology. The effecting factors of focused ultrasound as a stimulus for nerve structures irritation are discussed.

1. Introduction

It was shown in our previous investigation [1-4] that pulses of focused ultrasound with the duration of the order of parts and units of milliseconds could stimulate various human peripheral receptor structures. The main advantages of the ultrasonic method for stimulation of nerve structures are as follows. The use of this method makes it possible not only to avoid operative intervention for effect on deep structures, but also ensures precise control of stimulus characteristics: intensity, duration of action, as well as change of area to be stimulated, if necessary. All this holds much promise for application of focused ultrasound as a stimulus of nerve structures.

2. Stimulation of skin and tissue receptors and neurons

Using pulses of focused ultrasound directed towards sensitive points of man's arm, it is possible to evoke sensations, the character of which depends on the parameters of ultrasonic action and localisation of the focal region [1 –4]. By applying different ultrasonic intensities and action durations it is possible to evoke all the sensations that a man can perceive through his skin: tactile, tickling, temperature (warmth and cold), pain, etc. Pain sensations can be evoked by focused ultrasound stimulation not only of surface nerve structures, but also of deep ones.

Experiments on the invertebrates (edible snail) showed the possibility of using focused ultrasound for stimulation not only of receptor structures but also of central nerve structures. The thresholds for stimulation of the latter proved to be much higher than those for stimulation of receptors. For instance, the thresholds of the oscillation displacement amplitude that corresponded to the stimulation of receptor and central nerve structures of the snail were 0.1 and 0.25 μm, respectively. The results of these studies form the basis for promotion of similar investigations on the vertebrates including mammals.

3. Diagnosis of neurological diseases

The ultrasonic method was employed to diagnose a number of neurological diseases relating to changes of skin sensitivity [4]. The frequency of ultrasound was 1.95 MHz. A comparison was made between tactile sensations on the skin of the fingers in a control group of healthy people (21 subjects) and 30 patients with 8 forms of neurological diseases. All the patients showed deviation of tactile sensitivity from normal: ranging from considerable increase of tactile thresholds up to the entire absence of tactile sensitivity.

For example, Fig. 1 presents the results of examination of the tactile

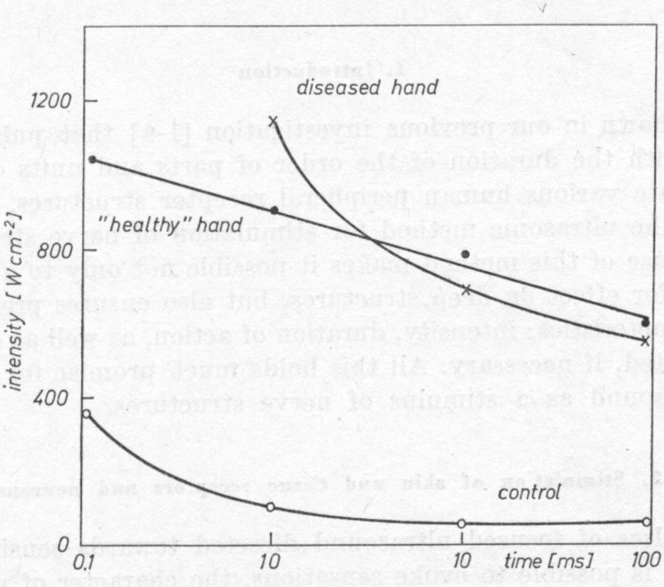

Fig. 1. Tactile sensitivity thresholds in the patient with syringomyelia: ○ — thresholds in normal people (control group); × — thresholds in the right (affected) hand; ● — thresholds in the left hand, where clinico-neurological examination showed no sensitivity disorders

sensitivity in one of the patients with syringomyelia. The y-axis is the intensity of ultrasound in the focal region, the x-axis is the stimulus duration. One can see that with the stimulus duration 0.1 ms the tactile sensitivity on the right (affected) hand was absent even at maximum intensities. On the left hand, where standard clinical examination showed no sensitivity disorders, there was a considerable deviation from normal.

The application of this method made it possible not only to characterize quantitatively the extent of sensitivity disorders for every form of pathology, but also to identify "subclinical" disorders, which the traditional methods failed to record.

4. Introduction of auditory information to the deaf

It is know that 3-5 per cent of the population in developed countries suffer from deafness and hearing disorders. In combatting this affliction much success has been achieved. New methods of operative and medicamental treatment appear, more and more improved models of hearing aids are designed. However, there is a large group of practically deaf people for whom the existing means are ineffective or of little effectiveness. It has just been with this aim at assisting such people that an attempt has been undertaken to use the ultrasonic method for hearing prosthesis.

In the initial experiments on frogs it was shown [2, 4] that under the action of focused ultrasound stimuli on the internal ear the auricular centers of the brain responded with electrical reactions similar to the responses to auditory stimuli.

In the course of further investigations a new method for introduction of auditory information to man was suggested [4]. The essence of the method resides in the fact that amplitude-modulated ultrasonic oscillations are directed to the labyrinth; the carrier frequency in this case is far above the upper limit of frequency perceived by man (for instance, from 0.5 to 3 MHz) and modulation frequency corresponds to the transmitted auditory information. In essence, this method has no limitations in the frequency of modulating (audio) signals. Under the action of focused ultrasound modulated in amplitude by oscillations of a complex form (for example, signals from a microphone, tape recorder, etc.) on the internal ear, normal people hear the transmitted undistorted acoustic information (speech, music).

The most substantial result is that by means of focused ultrasound it is possible to stimulate not only the receptors (hair cells) of the internal ear, as in the event of ordinary sound stimulation, but also auditory nerve fibers, which could be stimulated until recently only by implanted electrodes. This significant result was supported by experiments on animals with preliminary destroyed receptor system of the labyrinth. In the midbrain auditory centers in animals, responses to ultrasonic stimulation were recorded, which were comparable with responses from the opposite, normally functioning receptor system, but with higher thresholds.

Finally, the possibility of direct stimulation of auditory nerve fibers by ultrasound is supported by the fact that the deaf whose receptor system is diagnosed to have been destroyed, may perceive auditory informtion delivered by means of amplitude-modulated ultrasound, whereas the standard hearing aids cannot help them.

5. Diagnosis of aural diseases

The possibility of using ultrasound not only for stimulation of receptors, but also the nerve fibers of the auditory system is very important for clinical diagnosis in order to determine hearing disorders at different levels.

A comparison was made between frequency-threshold curves obtained by means of amplitude-modulated ultrasound and the curves of audibility thresholds obtained by sound stimulation of the labyrinth [4]. For normally hearing subjects these curves are quite comparable, despite some differences. It should be noted that for subjects with various forms of hardness of hearing these curves differ greatly.

For instance, Fig. 2 shows the audiogram and ultrasonic frequency-threshold curve of a patient with otosclerose. The y-axis presents loss of hearing relative to the level of normal hearing, the x-axis gives the frequency of tone

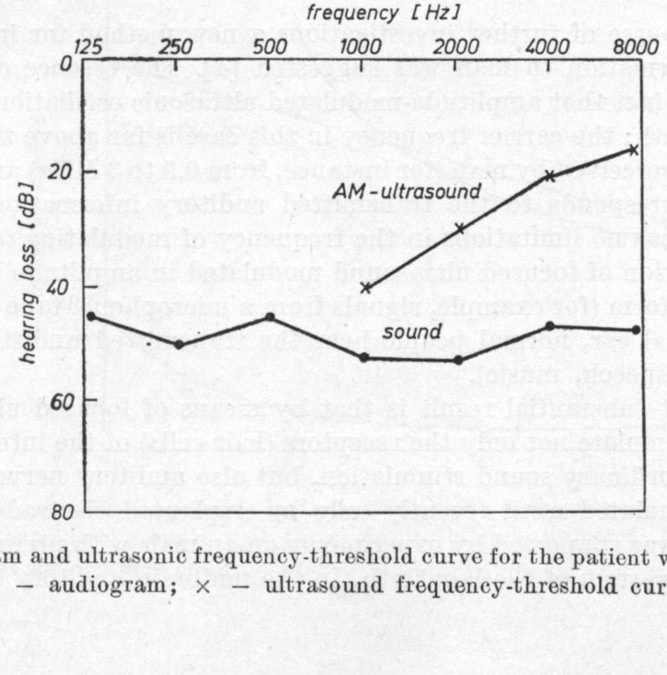

Fig. 2. Audiogram and ultrasonic frequency-threshold curve for the patient with otosclerose: ● – audiogram; × – ultrasound frequency-threshold curve

or amplitude modulation of ultrasound. Otosclerose is characterized by absence of auditory sensation at one or several ultrasound modulation frequencies (Fig. 2 – 125, 250 and 500 Hz), while the sounds of the same frequencies are distinctly heard by subjects with otosclerose. In the cases of other diseases the form of ultrasonic frequency-threshold curves is rather individual. This is already being employed in clinical practice to diagnose not only otosclerose, but also neurosensory hearing disorders, auditory nerve neurinoma, etc.

6. Possible mechanisms of focused ultrasound stimulation

A study was made on the factors of focused ultrasound responsible for stimulation of skin receptors and emergence of tactile, temperature, pain and other sensations.

Fig. 3 [4] displays relative changes in some characteristics of focused ultrasound with frequency changing from 0.5 up to 3 MHz for tactile and thermal sensations on human hand. The characteristics for a frequency of 0.5 MHz are assumed to be unitary. From the graph, it is obvious that only one characteristic – displacement amplitude – remains unchanged for every form of sensations with frequency changing over a wide range. The rest of the characteristics (intensity, ultrasonic pressure, increment of tissue temperature, particle velocity, acceleration, radiation pressure, etc.) greatly change, sometimes over a range of several orders of magnitude.

There are some of the experimental data below concerning the threshold values of the displacement amplitude necessary to realize stimulation of peripheral nerve structures by means of focused ultrasound [4]:

Receptors of labyrinth (frog)	0.004 – 0.01 μm
Pacinian corpuscles (cat)	0.03 – 0.05 μm
Tactile sensations on the skin of human fingers	0.08 – 0.11 μm
The same on palm	0.13 – 0.18 μm
The same on forearm	0.2 – 0.58 μm
Warmth and cold sensations on the skin of palm	0.43 – 0.6 μm
Pain sensation on the skin of palm	0.38 – 0.64 μm

However, the actual mechanism of stimulation of the nerve structures is most probably related to a certain unidirectional, "rectified" action rather than sign-alternating oscillation displacement of the medium per se. Indeed, the subjects could not differentiate tactile sensations in response to a long stimulus or two short stimuli. A change of the carrier frequency at the same displacement amplitude exerted no effect on the character of sensations. However, the mechanism that transforms sign-alternating displacement into a unidirectionally acting factor is still unknown.

Under the action of amplitude-modulated ultrasound on the internal ear, other acting factors are added. First of all, one should bear in mind that the organ of hearing is an extremely sensitive instrument reacting to the action of adequate sound information. Therefore, it is necessary to take into account the possible effect of the sound component on it, resulting from the radiation pressure of amplitude-modulated ultrasound. In this case, adequate, that

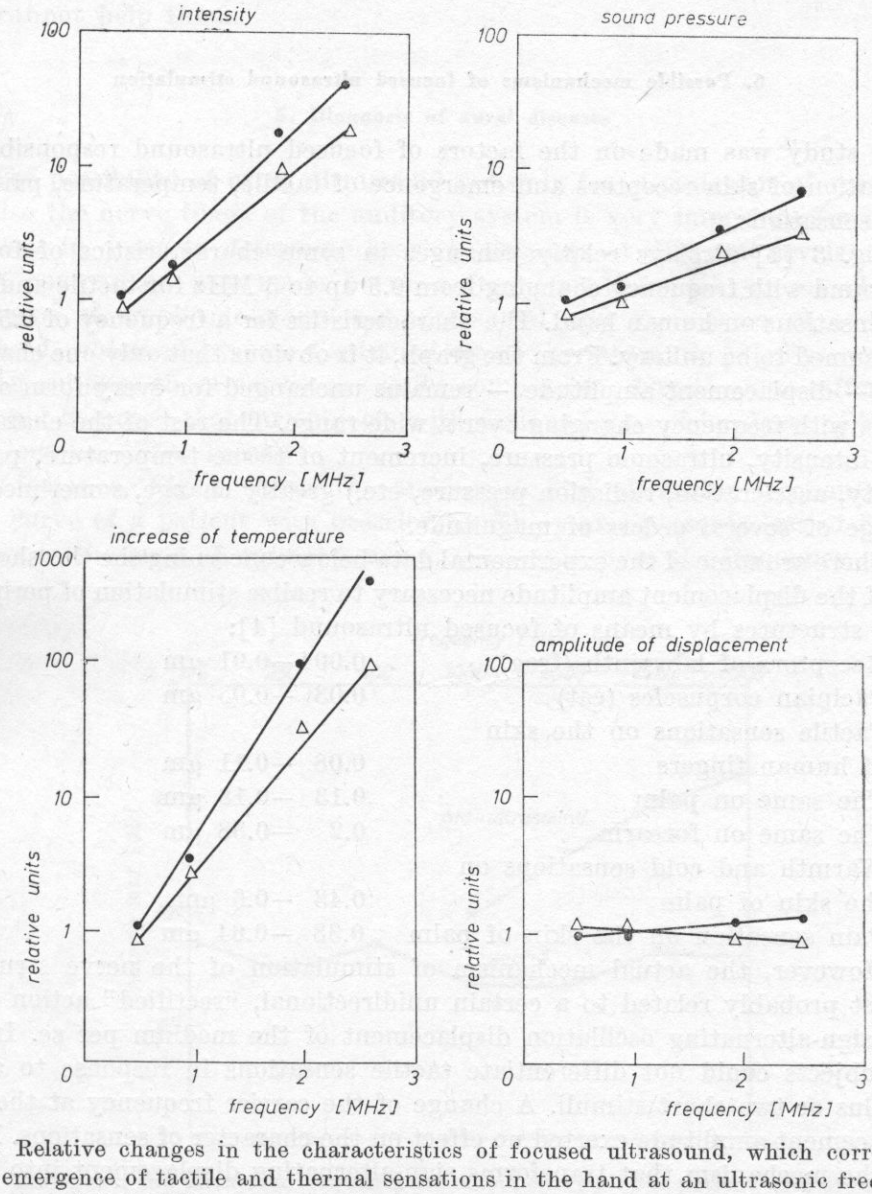

Fig. 3. Relative changes in the characteristics of focused ultrasound, which correspond to the emergence of tactile and thermal sensations in the hand at an ultrasonic frequency of 0.5-3 MHz: △ – tactile sensations; ● – thermal sensations

is sonic, information is channelled into the labyrinth, whereas ultrasound serves as a means of its delivery.

As has been mentioned above, amplitude-modulated ultrasound exerts a direct stimulating effect on the fibers of the auditory nerve. The basic acting factor of focused ultrasound in this event still remains to be discovered. This may be the mechanical action of ultrasound which has been discussed above. However, a certain role of transformation of ultrasonic oscilations into the electrical stimulus in this process cannot be ruled out. The physical character of this effect may be related to well known piezoelectric, and to be more precise, electromechanical properties of bone tissues.

7. Conclusion

The investigations carried out have shown that focused ultrasound is a useful and promising mean enabling the stimulation of both surface and deep nerve structures. It is not improbable that in the nearest future one can see the emergence of a new broad field of ultrasonic medical diagnosis, based on comparison of thresholds for various sensations in a normal man and in one or another pathological case. Great social importance is attached to the possibility of using ultrasonic methods for diagnosis of aural diseases and hearing prosthesis in patients with disorders of the receptor system.

This method holds much promise for physiological studies. It is of interest to elucidate the possibilities for stimulation of visual, olfactory, taste receptors, nerve fibers and central nerve structures, as well as to investigate the mechanisms of thermal reception, thermal production and thermal regulation in man and animals. Certain practical advantages may be gained from the use of focused ultrasound for acting on acupunctural points, for controlling the efficiency of anesthetics by measuring the threshold of pain sensations prior to administration of drugs and after it. At present it is difficult to circumscribe even approximately the medical and physiological problems, in tackling of which stimulating focused ultrasound may prove to be beneficial.

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