A NEW, NON-INVASIVE METHOD FOR THE MONITORING OF ALTERATION OF PHYSIOLOGICAL PARAMETERS IN BRAIN

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The knowledge of the actual state of physiological parameters in the brain is very important for the selection of the correct and most efficient therapy for humans and for the study of pathophysiological processes in animal experiments.
Using barbiturate-anaesthetized male rats (Wistar-Munich), we tested a new non-invasive acoustic (ultrasound) measurement technique for estimating the actual parameters of the state of the brain. The method is based on quasi-continuous acoustic wave packets. It is therefore possible to perform real-object investigations by determining their material parameters: For example through the propagation of the velocity of acoustic wave or the localization of its inner structures. In our study we monitored rats under different physiological conditions (anaesthetized, dead, locally stimulated-stressed) using phase and time methods. Furthermore using this technique we observed in some cases the changes caused by hemorrhage processes in brain tissue. Moreover, the following data were collected using the appropriate laboratory equipment and taken into consideration during analysis: body temperature, cortex temperature, blood pressure, expiration CO_2 as well as the blood flow in the medial meningeal artery and cortex.
The new measurement method is well suited for the detection and analyzation of blood circulation changes in the encephalonial blood vessels of rats. Distinguishing between ischaemia and hemorrhage processes is also made possible by the new method.
The employment of this method provided valuable insight in the understanding and analyzation of correlations between the shape of recorded signal and some of physiological parameters recorded, which are relevant to experimental and medical diagnostic practice. Further questions regarding the characteristics of depth of anesthesia, effects of drugs, etc., could be probably answered using this method.
We conclude that the presented features make this method attractive for medical and experimental application. The obtained results show that the method can be applied in the monitoring of biological experiments and in medical diagnostics.

The animals used in all our experiments done were acquired and treated in accordance with guidelines of the Council of the German Physiological Society as well as regulations of State of Bavaria and the Federal Republic of Germany. Additionally our experiments were reviewed and consented to a local committee for animal care.

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INTRODUCTION

The knowledge of the actual state of physiological parameters in the brain is very important for the selection of the correct and most efficient therapy for humans and for the study of pathophysiological processes in animal experiments. One of the expressive parameters describing the changes in brain seems to be a tissue density.
In our study the first recordings on animals were aimed to assess the non-invasive diagnostic information of an ultrasound intracranial device that is capable to monitor the density fluctuation in the brain. This measurements were done using a new developed device for determining density variations of a solid, liquid or gaseous medium.

METHODS

Animals and preparation:
Using barbiturate-anaesthetized male rats with a weight of 430-500 g, we tested a new non-invasive acoustic measurement technique for estimating the actual parameters of the state of the brain. The animals were anaesthetized (Thiopental) and the depth of narcosis was monitored using different parameters such as blood pressure and reflexes. In order to continuously monitor the animal's blood pressure, an artery catheter was inserted into the A. femoralis. A vein catheter was inserted into the V. femoralis of the left leg to allow for the administering of small doses of glucose solutions and infusions of physiological saline solution.
The animals used in this study were acquired and treated in accordance with guidelines of the Fed. Rep. of Germany; the experiments were reviewed and consented to a local committee for animal care.

Experimental background and Experiment Set-up:
The new measurements method is based on quasi-continuous acoustic wave packets. The measurement technique in our experiments used the difference in phase of two signals. Using wave packets and analysis of the phase dependencies R = $\phi_1 - \phi_0$ between transmitted and received waves gives solution easy to performed in practice, and moreover it ensures higher resolution of time measurements.

The system consists of measurement vessel of the length L and transmitter and receiver of ultrasonic waves. As it is shown in [A] at the given transmitters frequency within a vessel length a certain utter number of the oscillation periods P and "a part of period" expressed as phase difference R = $\phi_1 - \phi_0$:

$$\Phi = 2pfTp = 2pP + (j_1 - j_0)$$

Depending on specific character of investigations (changes detection in a phase method or parameter determination in a time method) the problem is always reduced to determination of phase relations R = $\phi_1 - \phi_0$ with the lowest experimental error. For of the run time measurement Tp an additional determination of utter number of the wave length P within the probing distance L is necessary.
A correct and vibration free connection of the U/S sensor to the test object is very important for this extremely sensitive measurement set-up [B].

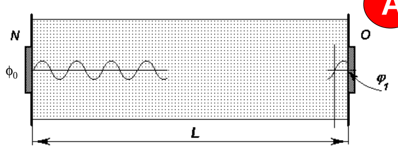
CONCLUSIONS

The employment of quasi-continuous acoustic wave packets ultrasound method provided valuable insight in the relations between the shape of recorded signal and some of physiological parameters recorded.

The presented features make this method attractive for medical and experimental application. The obtained results show that the method can be applied in the monitoring of biological experiments and in medical diagnostics.

EXPERIMENTAL SET UP

A



The general idea of measuring method is presented for the simplest case, i.e., for homogenous and isotropic media. In this case phase velocity of an acoustic wave depends on both the medium elasticity K and the density r in accordance with equation:

$$c = \sqrt{\frac{K}{r}}$$

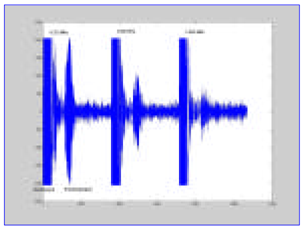
From the relation between acoustic and structural properties of a limited medium we obtain the run time Tp of an acoustic wave

$$T_p = \frac{L}{c}$$

The time measurements (delays) are at present the base foranalysis of object properties due to their simplicity, high measuring accuracy and the numerous system solutions. A change of one of the parameters (L, c) results in a change of run time of the acoustic wave D Tp.

B

The transducer (red) is positioned perpendicular to the skull at the point at which both sides of the skull are parallel to one another.



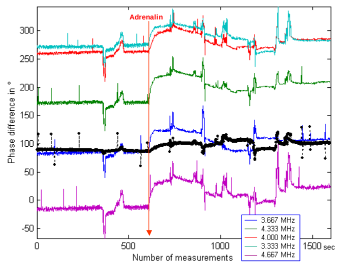
Example of a trace recorded by the receiver. It consists of the three transmission impulses (4.33 MHz, 4.66 MHz and 5.0 MHz) and the respective echoes. The amplitude of the echo is reduced due to the minimal bandwidth of the U/S sensor and the decrease in signal strength due to the tissue when using higher frequencies.

RESULTS

1

The employment of this method provided valuable insight in the understanding and analyzation of correlations between the shape of recorded signal and some of physiological parameters recorded, which are relevant to experimental and medical diagnostic practice.

The new measurement of quasi-continous acoustic wave packets ultrasound method is well suited for the detection and analyzation of blood circulation changes in the brain blood vessels of rats [1] .

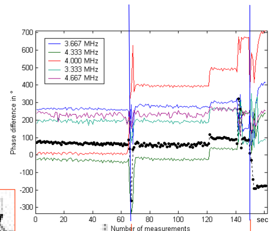


Injection of suprarenine at sample point 600. The pressure changes as well as changes in consistency and density of the cell substances could be measured directly.

2

It is anticipated that the proposed system would be capable to monitor brain density variations that are considered to be of very high value for accurate diagnosis and assessment of:

- head injuries (hemorrhage)
- monitoring of blood flow in the skull
- monitoring of blood pressure variations in the brain
- stress and pain monitoring [2]
- recognition of cranial vessel disorders
- estimation of the degree of pathological changes in the brain



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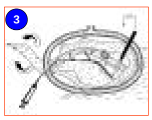

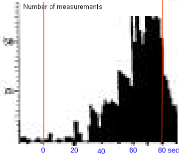

The right femur was fixed in supinated position by a special grip [3]. In a pool formed by skin flaps and filled with warm paraffin oil, afferent single units were dissected free from the nerve and subsequently placed over a platinum electrode to enable single unit extracellular recording. Afferent activity was then recorded electrophysiologically in response to non-noxious (the normal working range of the knee) and noxious (extreme movements of the joint against tissue resistance) inward and outward rotations of the knee joint.
An increase of the recorded spikes correlate with a rising of the curve (green dotted lines).