International Journal of Advances in Life Science and Technology
2015 Vol.2, No.1, pp.1-15
ISSN(e): 2313-8335
ISSN(p): 2412-3803
DOI: 10.18488/journal.72/2015.2.1/72.1.1.15
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RHEOENCEPHALOGRAPHY: PAST POPULARITY, OBVILION AT PRESENT AND OPTIMISTIC FURURE

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ABSTRACT

The reoencephalographic method (REG) has been known for a number of decades. The history of this method includes loss of its popularity, years of oblivion and a second wave of recognition. Such a tumultuous history is common for methods based on physical principles, such as capacitance and resistance, when applied to physiology and medicine prior to serious preliminary investigations to establish indices for living tissues common to natural subjects. In this case because blood characterize by comparatively low electrical resistance it was concluded that the volume of blood and its circulatory processes could be monitored by this method. In reality this proved to be an over simplification. In particular, applying such methods to issues of cerebral circulation did not provide any significant understanding for medicine. Years passed before it was understood that CSF circulation played a significant role within the cranial cavity and that the REG signal reflected not only blood volume but also the volume of distribution between blood and CSF. Additionally it was found that the electrical conductivity of blood depends on its velocity of movement. These factors together with progress in electronics and application of computer techniques which allow for coupling of REG with other methods have given a "second birth" to the REG method which can become important to physiology and medicine. The new "face" of REG is introduced in the present paper.

Keywords: Intracranial liquids, Electrical properties, Correlations of blood and SCF volumes, Cerebrovascular reactivity.

Contribution/ Originality

This study uses new estimation of rheoencephalography (REG), which expanded its applications for the study of fundamental and practical problems of intracranial liquid volume fluctuations. Biophysical analysis shows that REG could reflect cerebrovascular compensatory capabilities and with in coupling with transcranialdopplerography permits to evaluate CSF-mobility and skull mechanical properties.

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1. INTRODUCTION

The method REG was created for cerebrovascular investigations on the base of the fundamental approach of electrical impedance as we have applied this methodology for our cerebrovascular investigations, is based on the fundamentals of electrical impedance plethysmography [1], but it use high frequency electrical voltage, applied to electrodes, because scull bone electrical conductivity become less with increase of frequency [2]. This allowed evaluation of the changes of the pattern of impedance periodic waves of the intracranial contents initiated by heart activity. The changes of electrical impedance between electrodes placed on the scalp of humans were shown to correlate with changes of the brain blood volume in the region of the cranial cavity involved. To apply REG methods to everyday medical practice it was to investigate a number of fundamental issues connected with cranial electrical impedance measurements.

2. FUNDAMENTAL APPROACH OF REG

Numerous reasons for the changes of electrical impedance responsible for the REG signal were established by special investigations [3]:

- The REG signal depends on the change of volume ratio between blood and cerebrospinal fluid (CSF) inside the investigated region of the cranial cavity. This statement is supported by the results of the study of electrical conductivity of different media between electrodes. The highest electrical conductivity is that of CSF, twice less is for blood, 10 times less for brain tissue; and the conductivity for living skull bone is 15 times less as compared to CSF,

- Pulsatile changes of electrical impedance between electrodes placed on the human head are strongly dependant on the frequency of alternating electrical current used for investigations. It is determined by the difference of conductivities of the liquid media (CSF, blood) and structured tissues (brain and its membranes, skull bone, tissues around the skull, including skin). The conductivities of both decrease with increase of frequency, but much more so for structured tissues. The second is polarization, which occurs on flat metal (electrodes) and electrolyte conductors (living tissues) and depends on current density.

- The frequency for REG recordings on one hand should be low as possible, taking into account the difference of electrical conductivities between liquid and structured tissues, but on the other hand it should be high enough from point of view of the influence of pre-electrode polarization. The selection of a frequency for REG is a process of optimization, which should take into account the mentioned frequency dependences. Additionally, the investigator should take into account the dependence of blood conductivity related to blood volume movement velocity [4]. The head tissue may also be affected by the electrode 'sending' or stimulating current, as it passes through the head. These dependencies are shown in Fig. 1:

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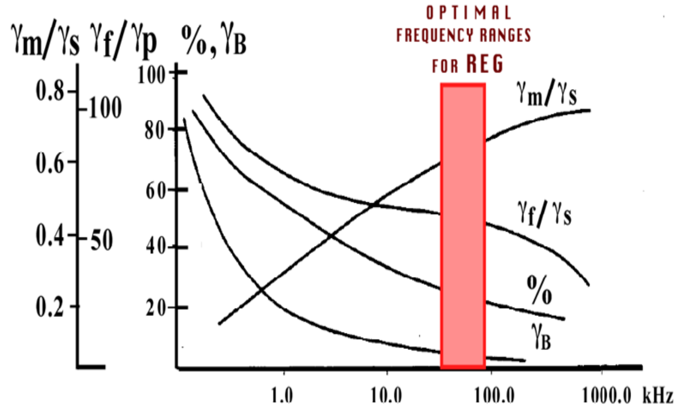

Fig-1 Selection of optimal frequency range for REG recordings. □□□□□□□□□ratio of electrical conductivity extracranial tissues (muscle and skin);□□□□□□□□□ratio of electrical conductivities of fluid and structural intracranial compounds;□□□ changes of electrical conductivity of moving blood (50cm/s), % - changes of electrical sensitivity of head skin.

It is possible to demonstrate that the optimal frequency range for REG in relation to skull mesurementsis 60 -100 kHz.. However, for some special purposes it is possibly to use a frequency as low as 20 kHz. The peculiarities of the electrical properties of living tissues have been carefully analysed from the viewpoint of modern physics [5], [6], [7]. The outcome of these investigations all support the selection of the optimal frequency ranges for REG recordings already established about 50 years ago.

-Although CFS and blood are the best electrical conductors inside the cranial cavity, the various tissues found inside and surrounding the skull also act as electrical conductors between the electrodes. However, most of these tissues exhibit only small changes in their electrical properties. These tissues around the skull, skull bones and brain membranes, have low blood circulatory patterns, and their functional activity doesn't change significantly during measurement as this group of tissues is a permanently influence on the base level of electrical impedance between the electrodes. However, in some cases of pathology, for example after head injury, the role of particular tissues in the level of electrical impedance between the electrodes may significantly change. Brain tissue in this situation plays a significant role in the level of electrical impedance between electrodes, because it is mainly responsible for the capacitance component between the electrodes and, therefore, for the overall base level. Under normal conditions the functional activity of the brain tissue itself continuously fluctuates and is directly related to local and regional blood supply. Electrical impedance conductivity of brain tissue may also change markedly under certain pathological conditions; for example brain edema, dehydration, or brain tumour. It is necessary to add that REG instruments are based on a "bridge circuit" which is characterized by a floating "0" and it has been difficult to determine a reason of its change – technical or physiological origin. Considering all the above mentioned, a time limit for continuous REG recording would at best be in the range of several minutes.

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- The area size and specific head placement positions of the electrodes play a significant role in the results obtained from REG investigations. The size of the electrode's surface area determines the current strength used as increases in surface area decrease the polarization effect. On the other hand, when increasing the distance between the electrodes, you must take into account the distribution of electrical current between both intracranial and extracranial tissues. Thus, it is necessary to carefully select the distance between the electrodes and also their size [8], [9]. From the viewpoint of biophysics, physiology and neurology that there are two optimal positions for REG electrodes: single or bi-hemispheric fronto-mastoidial and mastoidial-occipital positions. The first position is convenient for general hemispheric investigations, because the region of investigation basically includes the brain volume supplied by the middle cerebral artery. The second position of electrodes allows monitoring of the brain volume supplied by the vertebral arterial. The optimal size of electrodes is a circular configuration 15 mm in diameter. The surface of the electrodes should be covered by silver.

3. HISTORY OF DEVELOPMENT

Some inconclusive positions from early REG investigations connected with the fundamental significance of the REG signal remain unsolved up to the present day. The correlation between geometric indices of the REG pulse wave and the indices characterizing the functioning of the cerebrovascular system remain unclear. Nevertheless numerous investigations, primarily provided by clinicians, beginning in the late 1960's began to appear in publications on medical and physiological journals. The most likely indexes were provided by the REG waveform analyses of cerebral blood flow, cerebrovascular resistance and cerebrovascular reactivity. This data was significant in diagnosing neurological disease and cerebrovascular disorders connected with arterial hypertension. In these studies there was only data analysis in relative units; which cannot be interpreted as being specific quantitative analyses. However, it should be noted that only REG and EEG were effective as neurological measurement instrumentation for accurate data collection and analysis, associated with arterial hypertension. In these studies there was only data analysis in relative units; which cannot be interpreted as being specific quantitative analyses. However, it should be noted that only REG and EEG were effective as neurological measurement instrumentation for accurate data collection and analysis. From 1968 to 1980, REG was actively used in studying the effects From 1968 to 1980 REG was actively used to study the effects of weightlessness on the human body during space missions. In this period a number of recordings of REG at rest and during functional tests (veloergometry and negative pressure to the lower body) were made on the Russian space station, 'Salyut" [10]. A number of books, describing the clinical application of REG [11, 12]. By the middle of the 1970's the popularity of REG had reached its peak.

From 1975 to 1980 interest in REG began to decrease. There were two reasons for this. Firstly, the informational meaning of the data received by REG investigations was relatively clear if it was received during investigations of healthy subjects, but even in this case the data was not

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quantitative. REG data received in clinical situations, especially from subjects with complicated pathologies, often confused physicians more than it clarified the patient's situation. Secondly, non-invasive methods of cerebrovascular investigations based on the Doppler effect were being rapidly developed from the beginning of 80-ties and become real "concurrent" to REG.

This situation required serious revision of the informational meaning of REG and shortly publications appeared [9], presenting a detailed analysis as to the nature of REG in a scheme format using up to date data as shown in Fig.2, which shows the direct relationships of the factors responsible for the REG signal. There are indices of cerebrovascular activities: vascular tone and pulse changes related to brain blood volume. Brain blood volume was correlated with CSF volume in the skull. CSF volume is determined by Intracranial Pressure (ICP) levels, in turn affected by blood flow into the skull and the biomechanical properties of the skull bones or cranial compliance. The REG signal consist of intracranial pressure changes, blood and CSF volume movements, and cranial compliance.

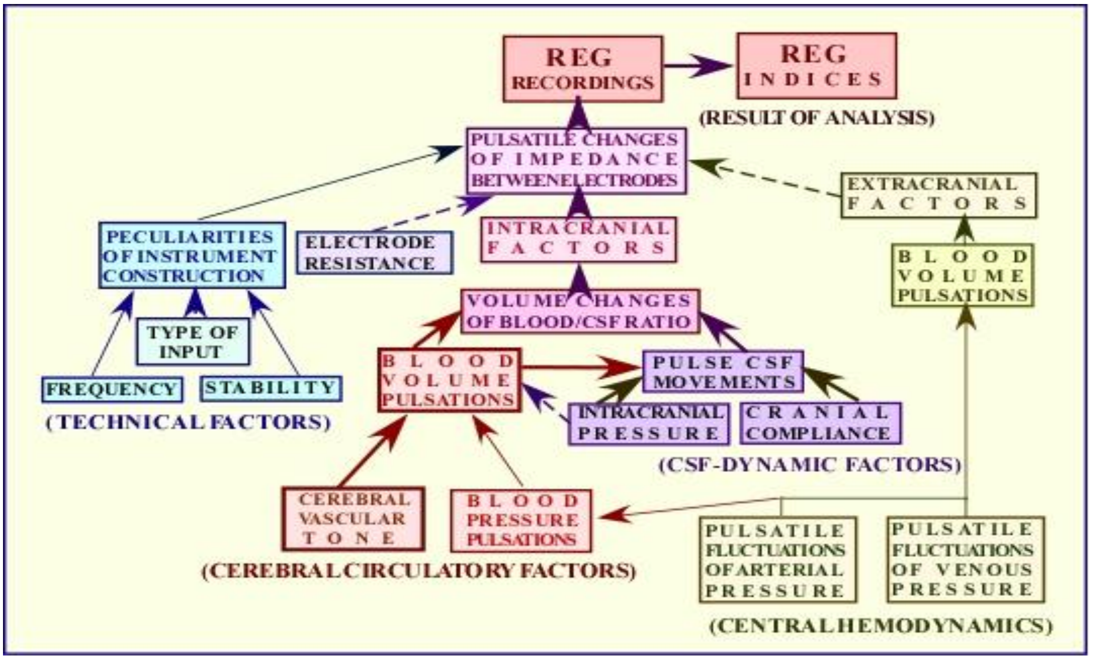

Fig-2. Block-diagram showing factors, which determine REG signal, include a group of technical factors (blue), cerebrovascular circulatory factors(brown), CSF-Dynamic factors (violet) and central hemodynamic factors (dark green). Bold arrows show dependences, which form the REG signal, broken line – dependences, which may interfere with REG signal. Usual arrow show intermediate connections.

This diagram demonstrates that it is impossible use REG for CBF and vascular tone measurements. Only one index can be used for REG in the comparative monitoring of cerebrovascular reactivity (CVR). This is a functional measurement index due to physiological challenges measured during space missions. Recently informational meaning of CVR it

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wasconfirmed by animal investigations [10]. However, this diagram show, that REG contents related to important physiologicalconfirmed by animal investigations of CVRconfirmed by animal investigations of CVR information about pulsating CSF movements and skull biomechanics. This may also be measurable by other instrumentation. For this purpose, we coupled REG recordings with another methodology to provide additional information for evaluating indices of CSF mobility and Cranial Compliance.

Progress in microelectronics together with the development of computer techniques has given a "second breath" to the development of REG. Construction of a simple to use and time - stable instrumentation using modern "analog-digital' transformers as a base allows coupling of REG with other methods, most importantly to transcranial Doppler, which makes it possible to significantly increase the informational meaning of these methods. For example it is possible to calculate CSF mobility and Cranial Compliance which are included in Fig.2, as internal components, but which could not be obtained from REG signals alone. Therefore, it looks worthwhile to combine the REG method with the TCDG method, because REG indices generally reflect changes of intracranial liquid volume, and TCDG reflect pulsation in the arteries at the skull basement corresponding to pulsation of CSF pulse pressure in the skull basement [13, 14].

Taking all this into account: *Theaim of the present paper is to show new informational possibilities of REG based on modern instrumentation, new computer-aided methods of data analysis and the coupling of REG with other methods, in particular with TCDG as a way of increasing its informational meaning.*

4. INSTRUMENTATION

Further development of REG instrumentation depends on progress in electronics. The first REG models used two electrode inputs, a balancing "Bridge" circuit and an amplifier based on vacuum tubes. For simplicity of data recording, EEG or ECG could be used. Technical construction was complex and was not simple to use, as it was characterized by high sensitivity to various interferences. While REG usage increased, there was scepticism due to the quality of data received and subsequent analysis. Comparatively stable REG instrumentation, using semiconductor circuits, made it possible to record the impedance pulse signal and its first derivative. This in turn improved the resultant analaysis. The input circuit was also upgraded, so instead of two electrodes a four electrode circuit was introduced with two voltages and two current electrodes. Such an input decreases the influence of the skull component in the impedance data collection. A more complicated 4-electrode circuit, a "screen electrode" was developed; where two small round electrodes were surrounded by two annular electrodes. Analysis of different electrode inputs determined that the use of bi-polar electrodes constitute the best system [15, 16].

The electronic circuitries of REG instruments were modernized over the period of development with the intention of increasing the stability, especially at low frequency outputs and to increase the number of independent channels up to reasonable limits, which now has reached 4 to 6. Recently models of impedance tomography instruments have appeared [17], but analysis of

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this modification of tomography shows it has very low resolution and thus the perspectives for cerebral investigations with impedance tomography do not look optimistic. Much more favorable results can be achieved from the modernization of the electrical circuit of the REG instrument based on microelectronic units combined with computer processing. A good example of a modern version of REG instrument has been recently introduced by the Mitsar Company (St. Petersburg, Russia). The modernization of this REG instrument is based on bi-polar automatically balanced input which has some advantages compared with other REG instruments. The most important advancement of this instrument is that it provides bi-hemispheric measurements, using three frequencies (16-20kHz, 100kHz, 200kHz) simultaneously from the same electrodes. This allows for calculation of different components of impedance on the base of two electrical circuits, simulating distribution of resistances and capacitances between electrodes [18].

The Mitsar version of the REG instrument has three types of outputs: Pulsatile signals recorded from both hemispheres and using three frequencies, in total 6 channels. Signal inputs are presented in two forms, digital for direct connection with a computer and analog to use with an external analog-digital transformer. The ADI PowerLab for example offers software possibilities for analyzing the recordings in a number of ways such as comparison in Decartes coordinates of two recorded processes, spectral analysis in a wide range of frequencies from very low 0.005Hz up to 100 Hz., and to present a selected fragment of two recordings in the square area of their interaction with changeable scales. Technical features of the Mitsar 6 channel REG unit include generating alternate current in wide ranges of frequencies from 20 to300 kHz, (any three can be selected for all channels and are composed of bi-polar current sources). The frequencies and the order of switching of current sources are regulated by a special generator based on a microcontroller. Consequently electrical current switching to each pair of electrodes is accomplished by a multiplexor, regulated by a microcontroller. The voltage, which is appearing between the electrodes is captured by a differential amplifier. Its value is measured by a synchronized detector. The voltage received in this way, which is proportional to the cross-electrode resistance, is saved on the capacitances of the multiplexor. Electrical current between the electrodes is presented as a number of impulses, each one being particular to the frequency of that channel. For every pair of electrodes there are three channels of analog analysis of the signal – uneven for the first pair and even for the second pair of electrodes. The signal to noise ratio during change of polarity of the measured current is improved by eliminating voltage measurements when there is a time interval in the synchronized detector. The multiplexor, connected with a buffer amplifier with single unit amplification, provides a direct current, which corresponds to the electrical resistance of the object under investigation. Then, after amplification, the signal passes through a high frequency filter with time constant 0.8 s. After amplification and filtration the signal passes through low frequencies (27 Hz) on the output of the channel which corresponds to the current changes of the object under investigation. These signals could be taken from the analog outputs of the REG-unit or to the multiplexor ADT, where these signals are imitated and are passed to the PC via a galvanic circuit [19, 20]. Special circuits have been

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devised to diminish the time transient process to reduce the artifacts which could appear during the process of electrode replacement due to extreme changes of resistance between electrodes when signal amplifiers may receive too much voltage and temporarily close. Power is supplied to the REG unit by alkaline batteries. The REG unit is controlling by a PC, running the dedicated software program, "ReoLead"This brief overview of the modern REG unit clearly shows how it is different from REG instruments of the past that utilized alternating frequencies (80-100), a stabilized generator, and a bridge circuit, one **"shoulder"** of which is subject under investigation, then a narrow frequency amplifier, a detector and finally a DC amplifier.

5. CLASSICAL METHODOLOGY OF REG INVESTIGATION

During the many years of REG analysis and the numerous special papers directed to the subject the focus was to defined and describe some correlations between the geometric indices of the REG pulse as presented in Fig.3 and the physiological indices that reflect cerebral circulation. It was shown that the wave forms and indices do significantly change during application of cerebrovascular physiological tests (Fig.4). Although the efforts to find correlations were generally unsuccessful some variable relations were found. Correlations were established that were acceptable for normal physiological conditions. For example, angle "□" was often proportional to cerebral blood flow under normal conditions, but not for most pathological cases. Some additional dichotic waves, which appeared during diastolic decrease of REG pulse, indirectly indicated cerebrovascular changes connected with arterial hypertension. In 1974 the REG method was used during the space missions of "Salyut" and the changes in cerebrovascular reactivity under microgravity conditions were established by this method [10]. Serious clinical investigations continued after this [11]. But this was the high point of REG popularity. And shortly afterward the collected data contributed by different investigators made increasingly confusing results of the REG investigations. By 1983 analytical investigations began to disappear. There were significant reasons for this. The main reason was it was difficult to establish correlations between cerebrovascular physiology indices and the pattern of geometrical indices of the REG pulse wave.

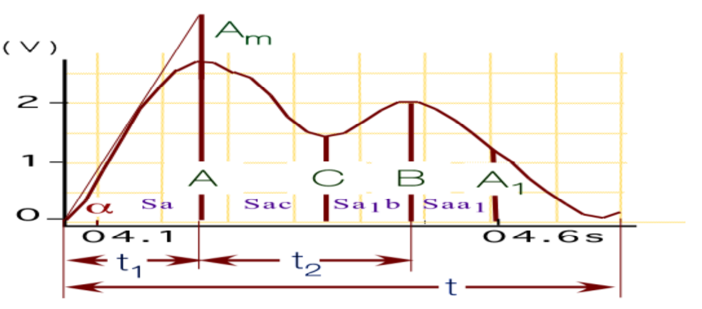

Fig-3. Typical REG pulse wave and amplitude (A,C,B,A_1), squaire (Sa,Sac,Sa_1b,Saa_1) and time (t_1, t_2, t) indices using for REG analysis.

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Even though deformation of the REG pulse, in response to functional tests, would suggest the presence of a geometric index responding to change of cerebrovascular reactivity and that it was sometimes possible to observe changes between the angle “□” and the level of CBF, if venous pressure did not change, still no significant correlations between REG pulse wave and indices of the cerebrovascular system could be found. The reason for this is based on the fact that there is a quite different origin to the geometric pattern of the REG pulse wave and the physiological background of REG. Nevertheless some geometric indices, for example amplitude of the pulse wave may correlate in some situations because the initiating forces responsible for changes in REG amplitude have some common roots with its geometric equivalent. This was the reason that REG was found to be so attractive in the early years of investigations. However, geometric indices have no causal connections with brain circulatory processes. This single physiological index, which is reflected by REG but could be evaluated only in some particular situations by its pattern analysis was in fact not valid for cases of pathological dependences. This have been noticed by specialists, who did not belong to the group of “REG enthusiasts”. The single index which REG data can provide in most situations is cerebrovascular reactivity, because cerebrovascular changes, resulting from the application of a definite functional test, will evoke wide changes in REG form, and each type of functional test evokes its special change in REG wave pattern.

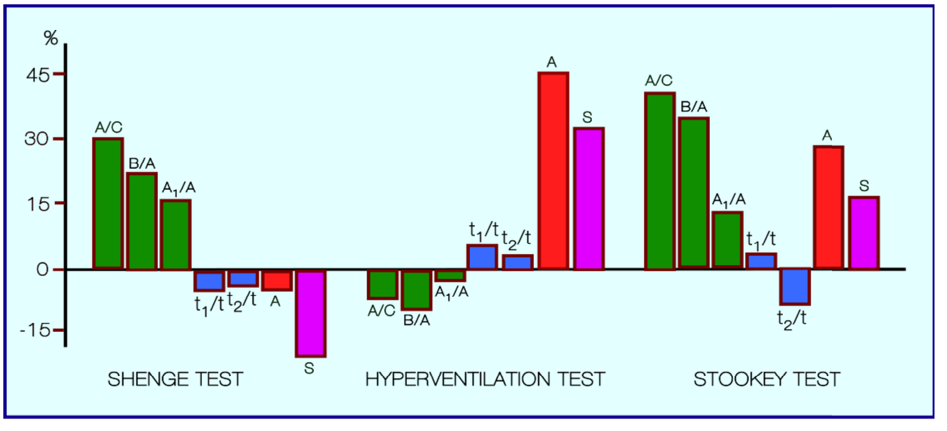

Fig-4. Changes of main indices of pattern of REG wave as response to cerebrovascular functional tests.

In additional, during all the years of REG application to medicine the question remained unclear concerning the comparative distribution of electrical current between intracranial and extracranial tissues between the electrodes placed on the human head. In other words, it was never clear if classical REG methodology reflected intracranial circulatory processes or the circulation of fluids in the scalp and soft tissues covering the skull. This question was a focus of attention during all the years of REG investigations and significantly inhibited REG investigations and their application. All of these are the reasons why the popularity of such a simple method and a method convenient for wide use has dramatically disappeared. After 1980 the

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number of publications connected with this method diminished and today publications describing the use of REG technologies rarely appear. Only a few companies continue to manufacture REG instrumentation. The single application of REG which continues to this day is monitoring cerebrovascular reactivity.

6. MODERN METHODOLOGY OF REG INVESTIGATIONS

During the most recent years the situation connected with REG application to physiology and medicine has significantly changed. REG instruments like the model described earlier are recent arrivals. REG recordings on three frequencies simultaneously and the consequent calculations, based on two different electrical circuits, composed of three variables, representing the composition of the head contents [21], have shown that at comparatively low frequency (15 – 25 kHz) the electrical current between electrodes passes mainly through extracranial tissues and the high frequency current (100 kHz and above) passes mainly through the intracranial tissues and reflects the intracranial fluctuations of electrical conductivity determined by change of the volume composition between blood and CSF inside the cranial cavity between the electrodes. This conclusion follows from data, shown in Fig.1, which only recently was confirmed by direct facts. This conclusion unlocks the gates for clinical application of REG. But the gates are not held open yet, it is necessary to find new methods for analysis and 'extraction' of significant information.

When searching for new ways of understanding the informational meaning of REG signals it is important to recognize that the information inclusive in the REG recording is complex. Therefore it is necessary to find ways of clarifying the physiological meaning and significance of its various components. There are two ways of extracting the physiological information. One is based on the advantages of the newly developed multi frequency REG. The other consists in finding new computer aidmethods for REG recording analysis. To further increase the informational meaning of the recorded results it is reasonable to couple REG with some other method, which is dynamic and reflects different physiological indices of cerebral circulation than the REG itself. Among the numerous methods available the most attractive is transcranial Dopplerography. It too is non-invasive, dynamic, portable and relatively inexpensive. Simultaneous recording of TCD and REG began at the beginning of this century [20, 22]. Since then significant new perspectives have been received by this combined method [14, 23, 24]. These investigations were based on using a single frequency REG (100 kHz) applied to the brain region supplied by the Middle Cerebral Artery. The Doppler probe was focused to measure pulse changes of linear blood velocity at the M1 segment of the MCA, and the REG electrodes were placed in the fronto-mastoidal positions on the human head. It was shown that this method, recorded onto a PC, using an analog-digital transformer "PowerLab-8" with supporting Chart 5 and Canvas 11 software, can be applied to the evaluation of a number of important indices which reflect the functional activity of the mechanism responsible for circulatory-metabolic supply of the brain. Only this instrument combination was successful in the investigation of this problem because the Doppler, in this probe position, gives data demonstrating intracranial pressure

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fluctuations in the skull basement, while the REG shows volume changes in the ratio of blood and CSF inside the skull. Due to this, it became possible to calculate dynamic changes of cranial compliance, pulse CSF mobility and intracranial pulse blood volume under different physiological and pathological conditions. The principle of these calculations consists in the transformation of coordinates of the recorded indices on the "amplitude-time" scale to a scale reflecting intracranial puls "volume-pressure" as shown in Fig. 5, along with some detailed analysis described earlier [14]. The application of REG in combination with TCD allows data to be received noninvasively. It demonstrates dynamic pulse cranial compliance and CSF mobility which are important indices for neurology and neurosurgery and which were impossible to receive previously. Such data which is most valuable for neurologists and neurosurgeons during post surgical rehabilitation is also valuable in the specialties of gerontology and geriatrics for evaluation of the role of CSF mobility and cranial compliance as indicators of the brain circulatory metabolic supply which are on the decline during the development of aging dementia.

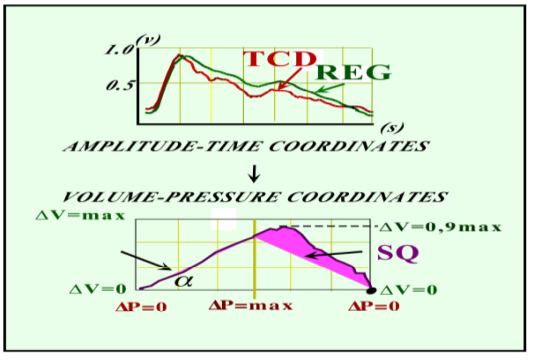

Fig-5. Principle of evaluation of data from simultaneous REG and TDC recordings, which correspond to pulse dynamic Cranial Compliance, mobility of CSF and actual comparative volume of pulse brain blood volume.

One more original application of the REG-TCD combination is based on spectral analysis of slow-wave fluctuations (0.01-0.3 Hz) of the volumes inside the skull by a module within the "Chart-5" software using the analog-digital transformer "PowerLab-8". The origin of slow fluctuations is complex [25] as is shown in Fig.6:

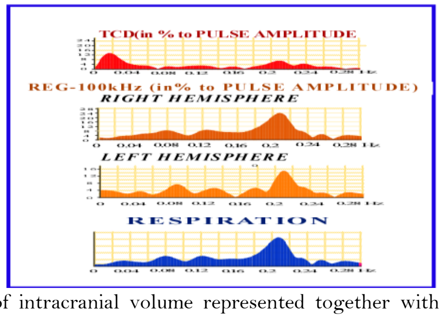

Fig-6. Spectrum of slow fluctuation of intracranial volume represented together with similar fluctuations of central arterial pressure and respiratory movements of chest. TCD and REG data normalized and showed in (%) to compare maximal amplitude of heart beats.

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In fig.6 it is possibly to see that spectrums on all diagrams have similar groups of spectral lines in the left and right parts. The group to the left represent control processes of arterial pressure and those to the right are chest respiratory movements. Between them there are groups of spectral lines, which occur only in the intracranial volume changes. In is difficult just now to provide identification of their spectral peaks, but it is reasonable to predict that they have connection with control processes in the cerebrovascular system and their identification may give significant information for practice in different branches of medicine, including neurology and neurosurgery as well as for the study of animal physiology, including agriculture animals.

It is necessary to mention another direction for application of TCD and REG recordings .Although REG alone can be used to monitor cerebrovascular reactivity as in the case for studying human reaction to micrograving [10] and for the study of cerebrovascular autoregulation [26] the combined use of TCD and REG allows monitoring of cerebrovascular reactivity much more exactly, because the combination.

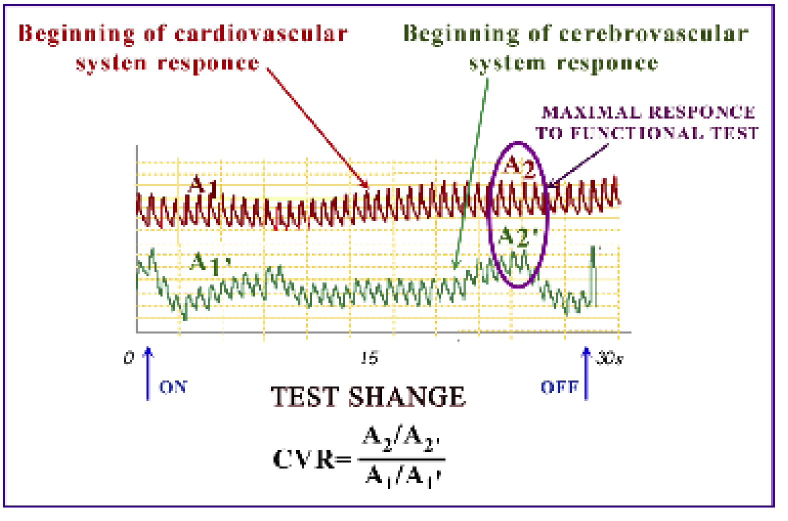

Fig-7. Changes of TCD and REG simultaneous records during "Shange" functional test (respiratory arrest during phase of expiration) A_1, $A_{1'}$ pulse amplitudes in the beginning and the maximal changes of CBF A_2, $A_{2'}$. Also, as is mentioned the: beginning of general cardiovascular and cerebrovascular reactions.

Allows selection of extracranial and intracranial vascular reactions in globally applied functional tests which are possible to study in human research as shown in Fig.7. In a similar manner it is possible to select general cardiovascular and special cerebrovascular reactions during others functional tests, used for determination of peculiarities of cerebrovascular reactivity in cases, when cardiovascular functional test systems are also involved such as in exercise physiology.

With the use of the three frequency REG, which measures the basic level of impedance between electrodes, it is possible to monitor changes of brain tissue hydration, in particular

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during the post surgical period. The ratio of basic impedance between electrodes, measured on 20,100 and 200 kHz depends on the size of extracellular spaces inside the brain tissue. Therefore, during the development of brain oedema, depending on whether its origin is intracellular or extracellular, the ratio of R(20kHz)/R(100khz) may change significantly, even by as much as 30% during the post surgical period [25]. This is important when monitoring patients after lateral brain surgery when one hemisphere remains intact. Using the multi-frequency REG it has been possible to observe oedema in the intact hemisphere which would have gone unnoticed because of absence of neurological symptoms and which did not correspond in time with edema of the operated hemisphere. The possibility to receive such data is critical during post surgery care.

7. CONCLUSIONS

More than 60 years have passed since the REG method was first applied to medicine. This method has a complicated story of development, from great popularity at first to nearly complete oblivion. There are two reasons for it. The first is based on the focus of data analysis. Numerous investigations were narrowed to receive a method for non-invasive CBF measurements: some relations were derived, but were not generally useful, because it was not recognized that the recorded pulsations do not reflect pure brain blood volume changes, but actually reflect the RATIO between blood and CSF volumes within the investigated skull region. Another widely held viewpoint contributing to the rejection of REG data was the notion that the REG recording reflects mainly the extracranial circulation. Although untrue, this notion added momentum to the declining popularity of REG investigations

The resurrection of the REG methodology is due, in part, to the biophysical analysis of REG, partly to a new generation of stable instrumentation and the coupling of REG with the transcranial Doppler, as well as the innovative multifrequency REG. All these advances established that REG wave signals generally represent intracranial volume changes of liquid media. They significantly increased the arena for REG application to physiology and clinical investigations. Spectral analysis of intracranial slow wave volume fluctuations, which may be very informative for the study of the control processes of circulatory-metabolic support of the brain blood supply, is in its earliest stages and the wide perspectives to use the multifrequency REG for non-invasive monitoring of brain oedema is likewise a new field for investigation.It is important to emphasize, that by combination of TCD and REG it is possible to receive data, concerning CSF mobility and Dynamic Cranial Compliance. This is important for a number of branches of medicine including gerontology. Thus, a new wave of interest in the multi-frequency REG may open some frontiers not only for general physiological investigations, including large agriculture animals, but also for a number of applied branches of human medicine, most importantly neurology, neurosurgery and preventive care for the world's aging population.

Supported by Grant RFFI 13-04-00612

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