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INVESTIGATION OF CONDITIONAL DIFFERENTIAL INHIBITION IN THE CEREBRAL CORTEX IN MIDDLE-AGED MALE PATIENTS WITH ESSENTIAL HYPERTENSION STAGE II DURING OPERATIVE ACTIVITY

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ABSTRACT

The study aimed to investigate the conditional differential inhibition in the cerebral cortex during operative activity and its influence on the cardiohemodynamics parameters in middle-aged male patients with essential hypertension stage II.

In total 60 male middle age patients with essential hypertension stage II, which were 6 months prior to enrollment in the study, did not receive antihypertensive therapy, were examined. Conventional differential inhibition in the cerebral cortex at operational activities was studied by means of Anfimov's test; blood pressure and heart rate data were collected at the initial state, immediately right after and in 3 minutes after Anfimov's test.

According to Anfimov's test, 3 types of mental task performance were revealed. Low mental task performance was determined at 45% (n=27), middle one – at 43.3% (n=26) and high level mental task performance was characteristic of 11.7% (n=7) patients. The general patterns of minute dynamics of mental task performance in each group were revealed. The study of the influence of conditional differential inhibition in the cerebral cortex during Anfimov's test allowed to reveal 2 main types of blood pressure and heart rate parameters changes – normotonic and hypertonic. There were no significant changes in blood pressure and heart rate in patients with normotonic type of response (n=13; 21.7% of the total number of patients). The second type of reaction, hypertonic, was detected in 47 patients (78.3%) and was characterized by a significant increase in blood pressure and heart rate by more than 5% of the initial values.

Obtained data indicate a decreased overall level of mental task performance in patients with essential hypertension of II stage, the imbalance of processes of excitation and inhibition in cerebral cortex, blood pressure regulation imbalance, stagnation of processes of excitation in cerebral cortex, the inertness of the system regulating blood pressure.

KEYWORDS: *essential hypertension, blood pressure, mental task performance, conditional differential inhibition.*

INTRODUCTION

Hypertension is a leading risk factor for mortality and disability [*Mancusi C et al., 2017; Barrera L, 2018*]. An estimated 874 million adults worldwide have a systolic blood pressure of 140 *mm Hg* or higher. With its association with cardiovascular diseases, stroke (cerebrovascular accident), heart failure, and chronic kidney disease, hypertension is the second only to cigarette smoking as a preventable cause of death in the United States. Given demographic trends and the increasing prevalence of hypertension with increasing age (79% of men and 85% of women >75 years old have hypertension), the consequences of hypertension are expected to increase [*Cifu A, Davis A, 2017*].

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The association between psychological symptoms such as anxiety and depression and cardiovascular diseases remains an intense subject of debate. Different mechanisms have been put forward to explain these associations. In a large population-based cohort of 57.953 Norwegians, followed for 11.4 years, self-reported symptoms of depression and anxiety were associated with an increased risk of an acute myocardial infarction. But further analyses suggest that this association partly reflects reverse causation and confounding by co-morbidities [*Gustland L et al., 2014*]. In a review by Hare D. an co-authors (2014), depression was also a major determinant of life quality in patients with cardiovascular diseases; in another systematic review of 53 studies on depression and adverse medical outcomes after an acute coronary syndrome consistent associations were found [*Lichtman J et al., 2014*]; so, it seems that the debate is not closed as of yet.

High neuropsychic stress, chronic stress and sleep disorders are considered as significant risk factors of essential hypertension. According to Lang's stress theory, the primary initial cause in the development of essential hypertension belongs to cerebral cortex and hypothalamus centers function disorders [*Lang G, 1950*]. Experiments have shown that stimulation of the dorsal nucleus of the hypothalamus caused systolic hypertension development, and stimulation of the central nucleus – of diastolic one. Irritation of the "emotional centers" of the brain also leads to a hypertensive reaction. Numerous detailed studies of this disease established that this pathology is not the result of primary damage of blood vessels and organs or the endocrine system, but the result of dysfunction of higher neurohumoral apparatus that regulates blood pressure [*Lang G, 1950; Kushakovsky M, 1995; Shulutko B, 2001*]. Brain tissue is especially sensitive to circulatory disorders; the slightest changes in hemodynamics inevitably affect brain tissue function and, in particular, influence such basic processes in the cerebral cortex as excitation and inhibition [*Kushakovsky M, 1995; ESH/ESC Guidelines, 2013*].

It should be emphasized that despite the known achievements in the study of the pathogenesis of arterial hypertension and the existing methods of its treatment, the causes and mechanisms of essential hypertension formation are still not fully clear [*Shulutko B, 2001; Kapadia S, 2017; Mancusi C et al., 2017*]. Well-known conceptions of essential hypertension pathogenesis (G.F. Lang, A.L. Myasnikov, Y.V. Postnov, S.N. Orlov, B.I. Shulutko, etc.) elucidate individual pathogenesis links without appropriate consideration of the causal factor and without proper consideration of the neuro-regulatory mechanisms formation, causes and nature of the state changes of the cerebral neurophysiological systems.

The blood pressure regulation system consists of a number of hierarchical levels [*Sherstnev B, 2007; Sudakov K, 2011a*]. The highest level of blood pressure regulation is a system that includes the cerebral cortex [*Sudakov K, 2011b*]. It is through the cerebral cortex influences are mediated, including negative social factors on the human body [*Bahtereva N, Kambarova D, 1988; Danilova N, Krylatova A, 2005; Sudakov K, 2011a*]. As a result of such excitation and inhibition in the cerebral cortex disorders persistent negative dominants appear. This manifests in emotional stresses that lead to violations in regulation of the autonomic functions of the body and functions of the system regulating blood pressure – in particular [*Bekhtereva N, Kambarova D, 1988; Danilova N, Krylatova A, 2005; Shulutko B, 2001*].

The significance of the strain and overstrain of inhibition processes in the cerebral cortex, disorders of the interaction between the cerebral cortex and subcortical formations in the development of visceral systems pathology have not been sufficiently investigated. At the same time, I.P. Pavlov (1950) accentuated significance of overstrain of inhibition process in cerebral cortex in the occurrence of neuroses, which leads not only to phase disturbances of higher nervous activity, but also to violations of autonomic functions, and, in particular, to the development of arterial hypertension [*Vvedensky N, 1962; Kushakovsky M, 1995; Sudakov K, 2011a*]. In addition, the reduction of cognitive functions is one of the highly actual problems of modern medicine. Recent literature sources de-

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scribe the influence of hypertension as a modifiable risk factor in the development of cognitive impairment [*Gerasimenko L, 2017*].

In connection with the above-mentioned, taking into account the important role of disorders in the higher parts of the central nervous system in the development of pathology of the visceral systems of the body, the high prevalence of arterial hypertension [*Kapadia S, 2017; Katsi V et al., 2017*] and its medical and social importance it is relevant to study cardiohemodynamics in patients with essential hypertension of II stage in terms of the conditional differential inhibition in the cerebral cortex.

Present study aimed to investigate the conditional differential inhibition in the cerebral cortex during operative activity and its influence on the cardiohemodynamic parameters in middle-aged male patients with essential hypertension.

MATERIAL AND METHODS

Totally 60 male patients (volunteers) of middle age with essential hypertension (stage II) were examined. The clinical characteristics of the examined patients with hypertension are presented in the table.

The study was approved by the Ethics Committee of State Institution "Zaporozhye Medical Academy of Post-Graduate Education of Ministry of Health of Ukraine" 23.04.2013, Protocol No 4 and corresponds to the principles set out in the Helsinki Declaration (Br. Med. J. 1964; p. 177), with later amendments.

Patients with symptomatic hypertension were excluded from the study. Exclusion of symptomatic hypertension was based on the clinical examination, anamnesis of the disease, research of outpatients medical records, additional research methods (if it was necessary). The criteria for entry into the study group were: signed Informed Consent Form, verified essential hypertension of stage II with mild or moderate hypertension level, the absence of acute and exacerbation of chronic diseases; for at least 6 months prior to the study patients did not receive

TABLE

Clinical characteristics of patients with essential hypertension stage II

Parameters, the metric unit of measurement		
Number of the examined patients, abs.		60
Middle age (*years*)		45.6±3.49
Body mass index (*kg/m²*)		23.7±1.25
Essential hypertension duration (*years*)		5.38±2.57
Number of risk-factors		2.6±0.41
Systolic blood pressure (*mmHg*)		164.2±5.68
Diastolic blood pressure (*mmHg*)		105.3±2.39
Essential hypertension level, abs. (%)	Grade 1 hypertension (mild, mild, blood pressure ≥140-159/90/99 *mmHg*)	15 (25)
	Grade 2 hypertension moderate, blood pressure ≥160-179/100-109 *mmHg*)	36 (60)
	Isolated systolic hypertension (systolic blood pressure≥140 mmHg, diastolic blood pressure ≤90 *mmHg*)	9 (15)
Stratification of cardiovascular risk in hypertension, abs. (%)	Low	6 (10)
	Moderate	17 (28.3)
	High	37 (61.7)
	Very high	-

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antihypertensive medications or were not on stable antihypertensive therapy.

We used commonly known research methods: a proof-reading test of mental task performance by the Anfimov's method, blood pressure and heart rate measurement.

Anfimov's proof reading test (PRAT) was used as it is a well-known simple five-minute test, which is essentially a discrete conditional differential inhibition. According to Anfimov's test the following parameters were determined: S – quantity of the seen letters for each of minutes and in the sum; S – quantity of correctly deleted letters for each of five minutes and in the sum; O – quantity of mistakes (quantity of the missed letters which subject should delete and quantity of wrongly deleted letters). On the basis of the received data we built individual diagrams (histograms) of work efficiency dynamics. Under the total data work accuracy index A, calculated according to the following formula:

$$A = \frac{\Sigma}{\Sigma + O}$$

accurate within 0,001 and net productivity index: E, calculated according to the following formula:

$$\mathbf{E = SxA},$$

accurate within 1 was determined.

Blood pressure and heart rate were measured by means of recently calibrated and passed metrology control electronic automatic blood pressure measuring device OMRON M6 Comfort (Japan). Blood pressure parameters and heart rate parameters were obtained at initial state, directly after and 3 minutes after PRAT. Obtained data were inserted in to investigation protocol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined. Pulse pressure (PP) and average flowing pressure (AFP) were calculated according to the appropriate formulae

$$\mathbf{PP = SBP - DBP}$$

and

$$\mathbf{AFP} = \mathbf{DBP} + \frac{1}{3} \text{x } \mathbf{PP}$$

respectivelly. Both values are measured in *mmHg*.

Statistical analysis of the study results was performed on a personal computer using the Microsoft Excel and "STATISTICA Version 6.0" software. To assess the significance of differences in sample populations the criteria of parametric and non-parametric statistics were used. The level of $p<0.05$ was considered as lower confidence limit.

RESULTS AND DISCUSSION

Individual by-the-minute and total results of task performance investigation by means of Anfimov's test in patients with essential hypertension stage II were inserted in the table. Average total seen by one investigated subject letters for 5 minutes made 1428.3±12.8 ($\bar{x}$±m). Average total number of correctly deleted letters one investigated for 5 minutes made 150.4±4.6 ($\bar{x}$±m). Mean quantity of errors for 5 minutes of deleting for one person made 0.8. Mean value of work accuracy (A) made 0.734. Mean value of net productivity (E) made 1394.5. Mean value of correctly deleted letters during the first minute made 27.4±0.57. On the second minute of letter deletion mean value of correctly deleted letters made 32.7±0.6 and significantly ($p<0.001$) exceeded those one of the first minute mean value by 19.3%. This is the so-called positive warming-up effect. On the third minute arithmetical mean value of correctly deleted letters for one person of all sample made 38.1±0.61 and by that even more exceeded such values for the first and second minutes ($p<0.001$).

On the fourth minute arithmetical mean value made 36.8±0.54, i.e. was slightly less comparing to those at 3rd minute, but was significantly higher than such at 1st minute. And, only on the fifth minute of PRAT the mean value of correctly deleted letters made 25.2±1.12, that indicated a significant decreasing, in comparison with the fourth minute and first minute ($p<0.05$). Thus, the general, typical for the whole sample (60 examined persons), is the pattern of significant increasing of task performance on the second and third minutes of maximal intensity work. There was still high productivity in the fourth minute – higher than in the first minute, but there is already a certain tendency of productivity decreasing in comparison with those of the third minute.

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On the fifth minute there was the tendency of work productivity decreasing that can reflect fatigue development and, possibly, developed the mechanism of protective inhibition [*Vvedensky N, 1962; Pavlov I, 1963*]. As to hypothesis of protective inhibition development, it can be verified in further studies by means of moral stimulation of the examined subject in the fifth minute of investigation.

As it follows from the obtained data, there is a significant interobserver variability of such parameters of mental task performance, as general quantity of viewed letters, general quantity of correctly deleted letters and of work accuracy parameters. This reflects that variational series are inhomogeneous. In this connection we generated ranged variational series by quantity of correctly deleted letters and define the range: 220-119=101. On the basis of quantity of correctly deleted letters we divided this range into 3 equal parts: 101:3≈33.6.

Afterwards, we formed three types of mental task performance: the class of relatively low mental task performance: 120–(120+33.6)≈120–154; the class of middle mental task performance: 155–(155+33.6)≈155–189; the class of relatively high mental task performance: 190–(190+33.6)≈190–224. Thereafter, using the "class – frequency" principle we draw up the table of distribution of 60 investigated patients with essential hypertension stage II on classes of mental task performance. There were 45% (n=27) of subjects with low mental task performance, 43.3% (n=26) subjects with middle mental task performance and 11.7% (n=7) of subjects with high mental task performance. On the basis of the abovementioned data we formatted the curve of distribution of class rates of mental task performance according to the quantity of correctly deleted letters for 5 minutes. At the same time task performance distribution polygon of investigated patients was relative to normal curve. Using data of the table we created individual, statistically analyzed, comparison table of the data: with low mental task performance, middle mental task performance and high mental task performance. Difference was considered as significant at $p<0.05$.

Mean quantity of correctly deleted letters for 5 minutes in group of low mental task performance made 141.3±4.2 ($\bar{x}\pm m$) and were less than appropriate general mean values of whole sample (167.7±2.9). By-the-minute mean values of mental task performance in this group were also significantly lower than appropriate all-mean data in sample 60n. However, the General pattern of significant increasing of the average arithmetic indices of mental task performance from the 1st to the 3rd minutes of work was clearly observed in the subjects with a relatively low level of mental task performance. There was also a tendency to decreasing of productivity in the fourth minute compared to the third minute. In the fifth minute the result of productivity did not differ from that of the first minute. Thus, it can be concluded that in this group of low mental task performance, also in the fifth minute of the PRAT shows a tendency of fatigue on the mechanism, possibly, of protective inhibition.

In group of middle mental task performance arithmetic mean value of correctly deleted letter for 5 minutes was 166.4±1.53 ($\bar{x}\pm m$) and was some higher than appropriate (167.7±2.9) general mean values of whole sample (60n). By-the-minute mean values were close to the general by-the-minute values. Patterns of mental task performance increasing significantly developed on the second and third minutes of PRAT. There was tendency to decreasing of mental task performance on the fourth minute. On the fifth minute there was no significant difference comparing with 1st minute.

In group with high level of mental task performance mean value of correctly deleted letters for 5 minutes (195.3±2.85 ($\bar{x}\pm m$) was significantly higher than appropriate general mean value of whole sample (167.7±2.9). By-the-minute mean values of mental task performance were also higher than appropriate all-mean values. Significantly higher levels of task performance at third, fourth and fifth minute, comparing with those of the first minute were the characteristic features of this group. Possibly, this fact suggests about greater excitation force at brain cortex at patients of this group.

The study of the influence of conditional differential inhibition in the cerebral cortex during Anfimov's test allowed to reveal 2 main types of

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blood pressure and heart rate parameters changes – normotonic and hypertonic.

To the group with the normotonic type of response were assigned to those examined patients, in which the PRAT did not cause significant (less than 5% of the initial value) changes in SBP, i.e. deviations from the SBP did not go beyond the error of the method of measuring of BP. If the changes in blood pressure were more expressed (more than 5% of the initial value), they were considered as a significant increase in blood pressure – as a reaction to the hypertensive type, hypertonic type of response.

First type of reaction – normotonic, was revealed at 21.7% (n=13) of the examined patients with essential hypertension stage II. This group included those subjects, at which PRAT does not caused significant BP and heart rate changes (systolic and diastolic blood pressure variation was no more than ±6 *mmHg*, $p>0.05$) and characterizes certain stability of blood pressure regulating system in such patients.

Second type of reaction – hypertonic, was revealed at 78.3% (n=47) of the examined patients with essential hypertension stage II. This group included those subjects, at which PRAT caused significant ($p<0.05$) increasing of SBP, DBP, PP and AVP for more than 5% from basic ones levels. Significant SBP elevation took place right after completion of PRAT (up to 16±3.5) *mmHg*. DBP also increased by an average of (11±2.1) *mmHg*. Against the background of a significant increase in blood pressure also heart rate increased by (9±3.6) *beats/min*. 3 minutes after the PRAT, the parameters of SBP, DBP, AFP and HR were also significantly higher than the baseline values on (14±2.1) *mmHg*, (12±2.4) *mmHg*, and (8±2.9) *beats/min*, appropriately.

Summing up the results of our study of the influence of the Anfimov's proof reading test, i.e. the effect of differential inhibition in the cerebral cortex on the parameters of cardiohemodynamics, it can be noted that the results of the proof reading Anfimov's test allowed us to identify different classes of mental task performance in the examined patients with essential hypertension of stage II. Three groups were identified among the examined patients: a group with low level of mental task performance (45% of the surveyed, 120-154 correctly deleted letters for 5 minutes), a group with middle level of mental task performance (43.3% of the examined subjects, 155-189 correctly deleted letters for 5 minutes) and a group with relatively high level of mental task performance (11.7% of the examined subjects, 190-224 correctly crossed out letters for 5 minutes).

Obtained data have theoretical significance and can be used in the professional selection of people for a specific job that requires sustained attention, significant mobility and strength of the main, basic nervous processes (excitation and inhibition in the cortex), advanced information analysis system, significant energy reserves of the nervous system (scientists, analysts, translators, managers, etc.). Also, we found out a certain per-minute dynamics of intensive mental work efficacy: task performance increasing was noted at the 2nd and 3rd minute of test and there was also still high task performance on the 4th minute of Anfimov's test. It was determined, that on the 5th minute of proof reading test there was decreasing of mental task performance up to the 1st minute productivity level. This work productivity plot should be taken into account by economists, product managers and in occupational medicine. It is clear that exceeding of a certain limit of internal inhibition in the cerebral cortex, as it was demonstratively shown by I.P. Pavlov [*Pavlov S, 1963*], may lead to the neurosis development and as a result, to mental, somatic and visceral functions disorders.

It should be taken into account that at stress and overexertion of basic nervous processes in the cerebral cortex disorders of body functions, primarily, manifested in a certain regulation system - the so-called "weak point" – individually. Thus, some people have disorders in heart regulating system: cardiac arrhythmias, myocardial ischemia, myocardial infarction. The other category of people have circulatory disorders of the brain – headache, migraine, stroke; in some cases the function of the digestive system is impaired; at that disturbances of the secretory function and dysfunction of local blood circulation can lead to the development of

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gastric ulcer and duodenal ulcer [*Sudakov K, 2011a*]. Very sensitive to stress and overexertion of basic nervous processes in the cerebral cortex is the system of regulation of circulation and blood pressure regulating system – in particular. As a result of blood pressure regulating system dysfunction may develop arterial hypotension, dystonia, hypertension [*Vvedensky N, 1962; Kushakovsky M, 1995; Shulutko B, 2001; Danilova N, 2005*].

In this connection, obtained data of blood pressure and pulse rate changes at conditional differential inhibition (Anfimov's test) have certain theoretical and practical significance. Special importance, in our opinion, have our data revealing multidirectional influence of Anfimov's test on different subjects and individual reactions of cardio-vascular system at conditional differential inhibition in the cerebral cortex. These data, together with family history and oculocardiac reflex may have a certain diagnostical and preventive importance. The obtained data indicate a decrease in the overall mental task performance in patients with stage II hypertension, an imbalance in the processes of excitation and inhibition in the cerebral cortex according to the study of conditional differential inhibition, an imbalance in the regulation of blood pressure in the direction of the tendency to react to the hypertensive type, stagnation of excitation processes in the cerebral cortex, the inertia of the regulation process of blood pressure.

CONCLUSION

Anfimov's proof reading test in patients with essential hypertension stage II makes it possible to determine the type of individual task performance: low, medium or high, which has a certain theoretical and practical significance. Also, by means of investigation of conditional differential inhibition in the cerebral cortex during operative activity, performed together with blood pressure and pulse rate measurement we revealed two possible types of influence of conditional differential inhibition in the cerebral cortex on blood pressure regulating system functional state: normotonic and hypertonic.

Obtained data indicate a decreased overall level of mental task performance in patients with essential hypertension of II stage, the imbalance of processes of excitation and inhibition in cerebral cortex (according to the study of conditional differential inhibition), blood pressure regulation imbalance (in the direction of predisposition to response to hypertonic type), stagnation of processes of excitation in cerebral cortex, the inertness of the system regulating blood pressure.

Anfimov's proof reading test allows to identify the tendency to certain disturbances of the functional state of the system of regulation of blood pressure, which together with the data of family history, may have a preventive significance.

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