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PRINCIPLES OF CARDIORESPIRATORY INTERACTION IN REALIZATION OF CHEMO- AND BAROREFLEXES

KUPRIYANOV S.V.*, SEMENOVA L.M., BOCHKAREV S.V.

Department of Normal and Pathological Physiology of FSBEI HPE

"Chuvash State University after I.N. Ulyanov", Cheboksary, Russia

"Adaptation of an organism to constantly changing environmental conditions requires a wide range of functional opportunities and a rapid change of the most important physiological systems to a new mode of vital functioning".

N.A. Agadzhanyan et al. [2]

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Abstract

Acute experiments on anesthetized cats showed that local acidification or blood pH increase in humorally isolated vertebral arteries form functionally unidirectional proper and conjugated reflexes on respiratory and cardiovascular systems. Vertebral arteries are independent vascular reflexogenic zones represented by a cluster of interoceptive structures, which should be classified as baro- and chemoreceptors. A particular status of vertebral arteries zone as a peripheral component of interoceptive analyzer, validated by physiological research methods, requires further morphological confirmation. Afferentation from vascular reflexogenous zones is a significant factor, which implements the principles of cardiorespiratory interaction. Physiological activation of baro- and chemoreceptors of vertebral and carotid artery zones generates a type of cardiorespiratory reactions with dominance of respiratory component over the cardiac and vascular ones.

It is revealed, that the receptive field of vascular reflexogenous zone of vertebral arteries is represented not only by baroreceptors but by chemoreceptors as well, characterized by highly-sensitivity to blood acidity changes. In response to blood pH changes, both to acidic and alkaline side, chemoreceptive zone of vertebral arteries causes reflex reactions, for which a short latent period is characteristical. Reflex reactions of external respiration stimulation and systemic blood pressure increase implemented as a response to perfusion of vertebral and carotid arteries zones with lactic acid solutions in physiological concentrations, as well as with venous blood injection were studied. Opposing reflexes of external respiration suppression and blood pressure decrease are observed at the insertion of alkaline buffered solution of trisamine/trisaminomethane (0.3 M) into vertebral arteries and/or carotid body zones.

An important conclusion is experimentally justified for practical medicine on inadmissibility of the use of alkaline hydrocarbonate solutions in the clinic, because their insertion in vascular reflexogenous zones results in reflexes of chemoreceptors which are identical to body reactions in blood acidification. Only alkaline buffer solutions similar to trisamine/trisaminomethane should be used to compensate acidosis in humans.

It was revealed that chemoreceptive activity of vertebral and carotid artery zones leads to the implementation of depressor reflexes on systemic blood pressure and suppression of external respiration at perfusion of an ozonized physiological solution in concentrations corresponding to those used in clinic (400-1600 μg/l). This demonstrates the reflexive component of hypotensive therapeutic effect of ozone infusion which was not previously described.

KEYWORDS: *cardiorespiratory system, vascular reflexogenous zone, vertebral arteries, interoreceptors, baroreflexes, chemoreflexes.*

INTRODUCTION

Joint activities of hemodynamic and respiratory systems in modern physiology are united in the concept of cardiorespiratory functional system, which is principally explained by its final result – correction of acid-base balance in tissues and gaseous exchange in them [*Aghajanyan N et al., 2003; Krivoshchekov S et al., 2006; Kupriyanov S, Aghajanyan N, 2008; Taylor E et al., 2014*]. Taking into account that all tissues are constantly under load,

ADDRESS FOR CORRESPONDENCE:
Chuvash State University after I.N. Ulyanov
Prospect Moscow 15, Cheboksary 428015, Russia
Tel.: +7(8352) 58-67-93, +7(917) 672-36-09
E-mail: Kuper-SV@yandex.ru

cardiorespiratory system should be determined as ever-present particular functional system [*Vanyushin Yu, Sitdikov F, 2003*]. As N.A. Aghajanyan notes (2005), cardiorespiratory functional system is "…a universal indicator of functional reserves and adaptive functions of the organism..." At the same time, I.G. Gerasimov and E.V. Samokhina (2003) note that the unifying factor of formation and activity regulation of cardiorespiratory system remains unknown for today.

Urgent adequate blood redistribution in the organism is provided by permanent functioning of vascular reflexogenic zones. They launch mechanisms of operative supporting of the optimal intensity of O_2 delivery to organism tissues and removal of metabolites from them. Vascular reflexogenic zones form both proper reflexes to the cardiovascular system and conjugated ones to other organism systems [*Stemper B et al., 2004; Johansson M et al., 2005; Ruiz J et al., 2005; Fu Q et al., 2006*]. Unfortunately, there are very few new works directed to the search and study of previously unknown vascular reflexogenic zones in recent years. Wherein, there is a large amount of clinical data, indirectly confirming the significant receptive activity of vertebral arteries, which are known to be of great importance in nutrition of brain's base [*Vereschagin N, 1980; Yamasoba T et al., 1993; Popelyanskiy Ya et al., 2003*].

Historical background. Within the limited scope of the present article, it is impossible to cover completely a large number of studies of vascular zone's chemoreceptors regulatory importance that have been carried out for many decades. For the first time the stimulation of vascular chemoreceptors was carried out in 1867 [*Bezold A, Hirt L, 1867*]. However, the priority in irrefutable physiological evidence of special functional entities existence – chemoreceptors of carotid sinus capable to regulate blood circulation and breathing in response to their stimulation with endogenous factors (CO_2, O_2, pH), belongs to the C. Heymans and co-authors, who were the first to obtain such data in experiments on isolated carotid sinus [*Heymans C et al., 1930*]. A Belgian physiologist Cornelius Heymans was awarded the Nobel Prize for his studies of the aortic arch zone role in regulation of blood pressure and respiration [*Heymans C, 1938*].

It should be mentioned, that arterial baroreflexes prevent orthostatic hypotension from arterial bed during the transition to a vertical position by their simultaneous influence on arterial pressure, heart rate, respiration and sympathetic nervous activity [*Schwartz C, Stewart J, 2012*]. Alternatively, the reactions from classic vascular reflexogenic zones are able to move into their new pathological quality in certain circumstances [*Kindig A et al., 2007*]. However, even such threshold issue as a specific chemical carotid body stimulant, remains open. Some authors determine it as a change of CO_2 partial pressure [*Fitzerald R, 2000*], while others consider it to be a significant reduction of O_2 blood content [*Timmers H et al., 2003*]. There is a theory, that the intensity of afferent drive increases during hypercapnia (as well as at $[H^+]$ increase), and, vice versa, decreases at hyperoxia [*Breslav I, Nozdrachev A, 2007*]. Thus, the problem of baro- and chemoreflexes interaction with vascular reflexogenic zones is difficult to recognize as completely solved [*Stewart J et al., 2011*].

Special attention should be paid to several distinctive features of modern study of cardiorespiratory system activity. First, the presence of not multiple data obtained as a result of experiments on laboratory animals. Whereas, maximum standardization can be achieved only in conditions of acute or chronic experiments that can be carried out only on animals. Second, the studies of baro- and chemoreceptors of vascular reflexogenic zones, basically, were conducted either with their role in regulation of only blood circulation or external breathing, separately. For example, a separate registration of various indices in external respiration, hemodynamics and cardiac activity was performed in an extensive research of studying impacts on cardiorespiratory system of muscle activity and increasing physical load [*Vanyushin Yu, Sitdikov F, 2003*]. But in similar works, there are a great number of significant factors which are practically impossible to be taken into account even with standardization of loading conditions. Endocrine status, which can be changed, for example, depending on the time of day or the season [*Aghajanyan N et al., 2005*], constantly changing excitability of central and peripheral nerve structures, activity of the digestive system, affecting gross and standard metabolism and,

consequently, the parameters of respiratory and cardiovascular systems and many other factors are among them. Such deficiencies can be prevented by the fixation of respiration and blood circulation intensity simultaneously on the same object. Unfortunately, the number of works derived of the above-mentioned deficiencies, is critically low, and most of them belong to rather early studies. Thus, the insufficiency of perceptions about reflectory mechanisms, providing various expressions of respiratory and cardiovascular components of cardiorespiratory system in provision of the common final adaptive result, should be admitted [*Oikawa S et al., 2005*].

In addition, it is important to determine the fractional role of respiratory and cardiovascular components of cardiorespiratory system in the provision of adaptational effects under different conditions for successful mathematical modeling of cardiorespiratory interaction, attempts of which are intensively implemented today [*Lin J et al., 2012*].

Regulatory importance of vertebral artery receptors. Clusters of nerve endings similar to baroreceptors of carotid glomerulus and aortic body were revealed using histological methods in vertebral arteries during one of the studies [*Myamlina G, 1953*]. The priority of evidence of vertebral arteries reflexogenous zones' existence in pure physiological experiment (with an obligatory hemodynamic isolation of vascular receptive field under study) belongs to the founder of the normal physiology department of the Chuvash State University, professor V.S. Kupriyanov, who together with Yu.G. Aleksandrov observed the reflectory increase of systemic arterial pressure in cats upon clipping the vertebral artery in its initial part; and in final part – its decrease [*Kupriyanov V, Aleksandrov Yu, 1977*]. Subsequently, similar data were obtained by other laboratories including foreign ones. Particularly, in laboratory of A.Y. Popelyanskiy it was revealed, that spinal nerve stimulation with electrical impulses (100*Hz*; 2-5 *V*) causes arterial pressure increase, and systemic arterial pressure decrease, while supplying to one vertebral artery (but without its obligative hemodynamic isolation) under hypertension of defibrinated blood [*Bogdanov E, Popelyanskiy A, 1980*].

Discirculation in vertebral arteries leading to ischemia of the brain base is one of the main reasons for the development of well-known vertebral artery syndrome in neurology. Clinically some authors associate causes of hemodynamics change in vertebrobasilar system with irritation of sympathetic nerve formations of vertebral arteries, while the others – with extra- and intravasal mechanical stimuli on this vascular zone. However, it should be mentioned, that all the experiments on the baro- and chemoreceptors activation of vertebral artery zones [*Tudorache* C *et al., 2010*] were carried out without its hemodynamic isolation. In the absence of such isolation the study results of the activity of any vascular reflexogenic zone receptor apparatus are hard to be recognized as absolutely significant.

Earlier, baroreflexes with vertebral artery zones were demonstrated upon hemodynamic and respiration systems in normal status and in pathologies under hemodynamic isolation conditions. For example, the importance of this zone's baroreceptors in the regulation of external respiration, arterial pressure, spleen volume, heart functioning, the tonus of coronary vessels, and vessels of inner ear, brain, pelvic limbs, eye conjunctiva, retina arteries as well as in the development of vertebral artery syndrome, in treatment of Meniere disease and Arnold-Chiari syndrome was shown. However, data about regulatory role of vertebral artery zone chemoreceptors under the conditions of methodically pristine experiment on animals were absent. It was also failed to reveal confusing data on the importance of afferentation from various vascular reflexogenic zones (baro- or chemo-) in the formation and regulation of cardiorespiratory system.

Following questions were raised: if chemoafferentation of classical vascular reflexogenous zones caused by natural acidic or alkaline solutions is one of the important adaptation mechanisms launchers, do vertebral artery zone chemoreceptors described by us take part in this process? If they do, then what is the directionality of reflexes upon external respiration and systemic arterial pressure? What is the role of respiratory and cardiovascular components of cardiovascular system in their fractional provision of the common adaptive result in the realization of chemoreflexes with vertebral artery zone and carotid?

Material and methods

The study of vertebral artery zone and carotid sinus chemoreceptive activity was conducted on 183 mature cats of both sexes weighing 1.9-4.5 *kg* under intravenous urethane anesthesia (1 *g/kg* of animal mass) at initial arterial pressure of 110-130 *mm Hg*. Totally 741 observations were performed including control ones. In all experiments, hemodynamic isolation of vertebral artery zones was carried out. Earlier publications describe its technique developed in our laboratory [*Kupriyanov S et al., 1996*]. In all cases the carotid sinus was pre-isolated, and in a number of experiments the aortic arch zone was pharmacologically denervated. External respiration registration was carried out by tracheostomy pneumography using Marey capsule in our modification. At the same time, arterial blood pressure was recorded in the femoral artery with the help of mercurial manometer or electromanometer by occlusion method (Fig. 1). The example of registered results is given in figure 2.

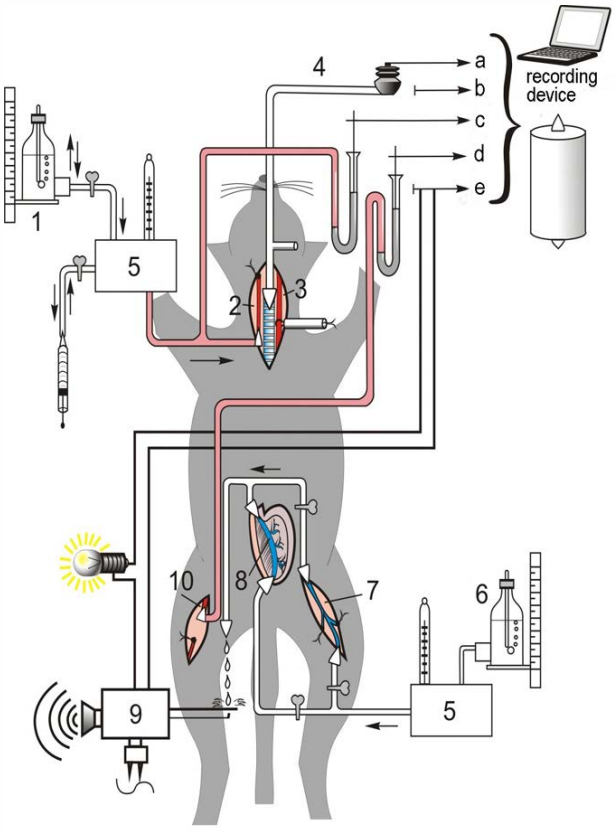

Figure 1. *Total principal scheme of experiments*

Notes: ***1, 2, c*** *– system for perfusion of vertebral artery zone, pressure changes and their registration in it;* ***3*** *– special ligature for artery (vertebral or carotid) clipping;* ***4, a*** *– external respiration registration;* ***5*** *– calorstat;* ***1, 6*** *– "injector-monometer" system, Mariotte vessel;* ***7*** *– femoral vein;* ***8*** *– colic vein;* ***9, e*** *– light- and audio-registration of perfusion volume velocity;* ***b*** *– time marker;* ***10, d*** *– systemic arterial pressure registration.*

Acid stimulation of vertebral reflexogenous zones was performed with solutions (in physiological solution base) of D, L (2-oxy-propionic, $C_3H_6O_3$) lactic acid, having pH 7.34-7.08, which corresponds to the normal and elevated lactate content in blood plasma under natural conditions [*Berezov T, Korovkin B, 2004*]. Experimental alkalosis simulation was carried out by introduction of a standard trisamine (tris-aminomethane, tris buffer), used in the clinic, 0.3 *M* solution to vertebral or carotid arteries zones. As stimuli we also used a $NaHCO_3$ solution (310, 620 and 700 *mmol/l*, pH 8.1-8.15) or a standard clinical ozone solution (with O_3 content from 400 to 1600 μg/l) [*Maslennikov O, Kontorschikova K, 2003*], or venous blood. In all the cases in these zones chemoreceptors stimulation was performed under perfusion pressure 110±20 *mm Hg*, i.e. their baroreceptors activation did not occur. Control observations took place after vascular zones pharmacological blockade with 2% novocaine solution. In addition, perfusion of indicated parts of arteries with physiological solution alone (pH 7.84-7.86) was another way of control.

The values of registered hemodynamic and respiratory systems indices taken in every experi-

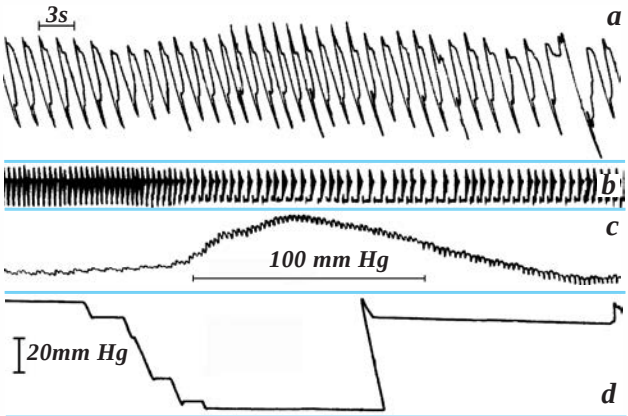

Figure 2. *Unidirectional reflex reactions of external respiration stimulation (pneumogram; time calibration 3 sec.) (a), v. colicae perfusion intensity decrease (b) and systemic arterial pressure elevation (isoline – 100 mm Hg) (c) induced by local decrease of pressure in the isolated zone of vertebral arteries (pressure decrease, calibration – 20 mm Hg) (d)*

ment at the peak of their reactions pronouncement were used for statistical analysis. Data were numerically evaluated either in absolute units or in percentage; in the latter case they were compared with the initial level (prior to invasion moment) or with control observations values when their intensity was taken as 0. Statistical processing was performed with MS ® Excel ® 2003 ™ and Statistica ® 7.0 (StatSoft Inc., USA) programs software. Differences in continuous variables between cases and controls were analyzed using the unpaired Student's *t*-test and/or by sign test [*Kaminskiy L, 1964*]. The differences were considered significant at $p<0.01$ or $p<0.05$ in some cases.

The used techniques are fully compatible with conventional procedures of studying baro- and hemoreceptive activity of vascular reflexogenous zones [*Chernigovskiy V, 1960; Sergievskiy M et al., 1975*]. All the experiments were conducted with regard to ethical norms of animals' treatment; they were approved by the University Committee on bioethics, and were in line with the principles of the Guide for the care and use of laboratory animals.

Results

The impact on chemoreceptors of vertebral artery zones and carotid sinus with lactic acid solution in concentrations corresponding to hypoxic condition led to reflex increase of systemic arterial pressure and stimulation of external respiration (Table 1). After novocaine blockade 34 observations in different series were made. In all 34 cases, the studied reactions didn't occur, which conclusively testifies their reflectory nature.

Opposite reflexes of cardiorespiratory activity decrease are observed in response to trisamine infusion to indicated zones (Table 2).

The indicated reactivity of the respiratory and cardiovascular systems disappeared after 20 minutes of exposure in isolated vascular areas with 2% novocaine solution. Loss of the reactions after novocaine blockade is a convincing proof of their reflex nature. The results of table 1 show that the direction of reflexes on respiratory and cardiovascular systems did not depend on concentration of the lactic acid solution being perfused, whereas the reflexes intensity was directly proportional to the concentration of solutions. In this, the power relationship is manifested as a characteristic of the central nervous system nuclei functioning, when the strength of responses is greater in case of stronger stimuli.

What is the possible worthwhileness of above-described reflexes?

M.V. Sergievskiy emphasized a close functional link of "two major physiological functions – breathing and blood circulation". He considered that their reflexes have a joint regulatory importance [*Sergievskiy M et al., 1975*]. It should also be taken into account, that the ventral parts of medulla oblongata are critically involved in reflex regulation of respiratory and vasomotor activity [*Breslav I, Nozdrachev A, 2007*], where the central respiratory regulator and a cardiovascular center are located. Moreover, it is shown that there are neurons in the respiratory center of medulla oblongata which activity results in arterial pressure changes. Neurons in area A5 of the pons are chemo- and baroafferent convergent inputs (from vascular reflexogenous zones) simultaneously receiving impulses from the respiratory center as well [*Pyatin V et al., 2007*]. That is, neurons of respiratory and cardiovascular centers besides morphologically close location in the brain stem are also functionally very closely connected. These two systems achieve one common adaptive result – they maintain tissue gaseous metabolic rate and regulation of acid-base balance in them [*Glass L, 2001; Gerasimov I, Samokhina E, 2003; Donina Zh et al., 2006*].

Based on the theory of P.K. Anokhin (1975), considering the commonality of external breathing and blood circulating purposes, it is appropriate to review these two systems as integral elements of cardiorespiratory functional system [*Kupriyanov S, Aghajanyan N, 2005; 2008*]. The above-described chemoreflexes are one of the mechanisms of this functional system regulation, where afferentation from zones of vertebral artery and carotid sinus acts as a systemically important factor in the formation of functionally-systemic cardiorespiratory reactions.

The results of the experiments with perfusion of hemodynamically isolated vascular reflexogenous zones of carotid and vertebral arteries with Na hydrocarbonate solution ("antagonist" of acids in an organism) are worth special attention. In this case, reflex reactions similar to the perfusion of lactic acid solutions (which however were less pronounced and sta-

Table 1.

Reflectory changes of external respiration and systemic arterial pressure in perfusion of vertebral artery zones with lactic acid solutions

Concentrations of solutions (*mmol/l*)		0.5-1.0	1.0-2.0	2.5-3.0	Total
Total number of experiments, (excluding control ones)		26	46	9	81
Initial level of systemic arterial pressure, (*mm Hg*), (M+m)		117.26±3.32 v*=0.011			
Number of experiments, *n*	with stimulation reactions	19	35	8	62
	with another direction of reactions	7	11	1	19
Increase of systemic arterial pressure., (*mm Hg*), (M+m)		11.73±1.21**	19.0±2.84**	35.49±6.2**	
External respiration stimulation (in % to initial level) (M+m)		120.63±24.71**	174.43±6.05**	248.44±56.58**	

Notes: 1. *Initial intensity of external respiration parameters is taken as 100%.* ***2.*** ** – relative standard deviation; ** – p<0.01.*

Table 2.

Reflexes upon external respiration and systemic arterial pressure in stimulation of chemoreceptors of vertebral artery zones with trisamine (prior and after their novocaine blockade)

Number of animals	Number of obsevations	Registered parameter	Direction of reactions	Number of single-valued observations	Mean value (M+m)	p	δ; v; sign test
10	40	*Systemic arterial pressure* level (*mm Hg*)	Decrease	39	15.27±5.62	<0.01	0.74; 0.048; <0.01
		External respiration	Decrease	33	38.52±1.95% *	<0.01	1.91; 0.049; <0.01
Novocaine blockade of chemoreceptors							
3	10	External respiration and *Systemic arterial pressure*	Absence of reflexes				-

Note: ** – relative to the initial level (prior to trisamine solution infusion).*

ble at their reproduction) occurred. Similar data referring to vascular reflexogenous zones are found in the works of other researchers [*Chernigovskiy V, 1960*]. Thus, it should be concluded, that compensation of metabolic acidosis development should only be carried out with medications, such as trisamine/tris buffer, which directly bind hydrogen ions. The use of Na^+, K^+, Ca^{2+} hydrocarbonate solutions for these purposes should be recognized as not only ineffective but even dangerous. In the conditions of (clinically significant) acidosis their infusion will undoubtedly result in increase of protons concentration and can be perceived as an extremely excessive overacidifying factor by the organism.

In addition, the results of present studies confirm the priority of H^+ concentration as one of the major factors of chemoreceptors' stimulation. The existence of specific receptors on HCO_3^- is being questioned or denied by many researchers and by us, too.

The insertion of blood from the femoral vein to these isolated vascular zones was also done during present study. Venous blood is an endogenic, multi-component solution, unable to damage its own organism structures and having an increased acidity in relation to arterial blood. The direction of cardiorespiratory response, similar to reactions on infusion of lactic acid low concentrations (p<0.01) was obtained in these experiments.

Reflex reactions of external respiration inhibition and systemic arterial pressure level decrease were also observed while perfusing the vertebral and carotid artery zones with standard ozone-containing solution.

Discussion

Conducted own studies demonstrate that chemo- and baroreceptive vertebral artery zone, similar to other vertebral reflexogenous zones, is involved in reflex control of systemic arterial pressure level and external respiration intensity, i.e. with simultaneous participation of cardiovascular and respiratory centers. It can be reasonably supposed that the activity of vascular reflexogenous zone chemoreceptors is firstly stimulated in a holistic organism, for example, in condition of hypoxia development, which is directed to the increase of lungs ventilation and blood oxygenation. Simultaneously systemic arterial pressure elevation enhances blood delivery to the lungs. The activity of baroreceptors increases, when the gaseous exchange in body tissues is normalized, which ensures the decrease of previously elevated systemic arterial pressure level to norm. It is obvious that the given reflex reactions have a systematically functional character. One of the main methods of proving the functional-systemic reactions integration is to demonstrate their correlation dependence. A statistical processing (by Pearson product-moment correlation coefficient) of 50 observations taken from different series of experiments was performed to identify the correlation between above-described external respiration and systemic arterial pressure level simultaneous changes. Samples were randomized and distribution of studied values was under the law of Gauss.

Results of correlation analysis are presented in figure 3 as an influential curve between values of respiratory minute volume changes (DRMV) and systemic arterial pressure changes (Dp). The given curve proves the existence of quadratic dependence of parameters (R^2=0.56; q=+0.65). In present experiments, a greater respiratory reflex intensity correlated with a greater evidence of reflexes on systemic arterial pressure. This confirms the existence of coordination mechanism of respiratory and cardio-vascular centers' reactions under the influence of studied vascular reflexogenous zones' afferentation. That is, the given reflex reactions are the result of cardiorespiratory system activity actualization.

This conclusion was confirmed by us with the help of another mathematical method based on calculating the coefficient of Hildebrant. As it is known, this coefficient characterizing cross-system relationships in the activity of hemodynamics and respiration in norm in a human being is equal to 2.8-4.9 [*Pokrovskiy V, 2007*]. In our experiments the value of this index at rest, i.e. prior to the carotid arteries and vertebral zones receptors activation was 3.25-5.6 (δ=0.14). It is evident that a similar difference in actual values is associated with species difference. While realizing reflexes of studied vascular reflexogenous zones, this index (coefficient) virtually did not change, remaining at its initial (prior the intervention) value. Consequently, despite deviations in respiratory system and the heart functioning characteristics observed in our experiments, there was no disagreement in cardiorespiratory interaction. Similar results obtained in human being are provided in current physiological studies [*Trubachev V et al., 2008; Donina Zh, 2011; Taylor E et al., 2014; Sapozhnikov S et al., 2014*].

Comparison of reflexes with zones of vertebral artery and carotid sinus showed its functional unidirectionality, but the expressiveness of cardiorespiratory system reactions, occurring with vertebral arteries baro- and chemoreceptors was lower.

In the experiments, the mean extent of external

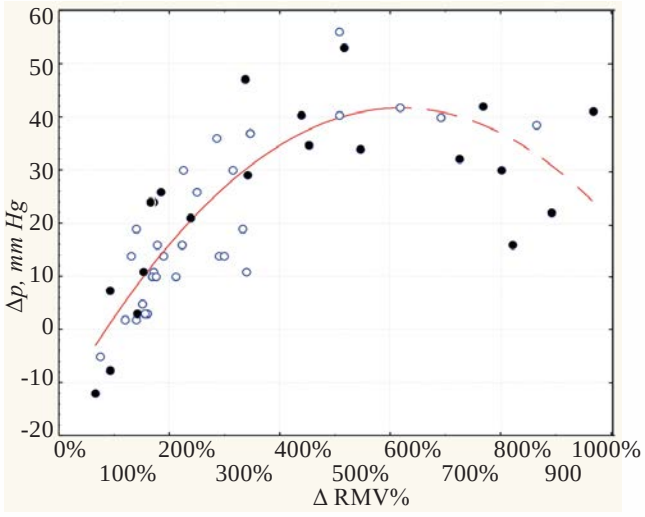

FIGURE 3. *Dependency of external respiratory changes (DRMV, %) relative to systemic arterial pressure changes (Dp, mm Hg). ○ – at activation of vertebral arteries zone chemoreceptors; ● – chemoreactions from the carotid sinus.*

respiration reactions increased almost threefold as regard to initial (prior to intervention) level. Moreover, systemic arterial pressure elevation was about 10% from the initial level of systolic pressure. So, while delivering chemical stimulation of physiological values cardiorespiratory interaction reaches an adaptive result due to higher intensity of external respiration reactions and, to a lesser extent, to changes in cardiovascular system functioning.

It was noticed that the most rigid homeostasis constants are related to blood system. Obviously, afferentation of the peripheral blood state is critical for the central nervous system and is formed by both neuronic nuclei central receptors and by peripheral ones located, particularly, in vertebral reflexogenous zones. It was established, that animals with denervated carotid sinuses and safe function of the cortex have less sensitivity to CO_2 threshold concentrations in comparison with animals with intact carotids and cortex which were on partial suppression condition. Thus, the significance of vascular reflexogenous zones in regulation of such body functions, as breathing and blood circulation is extraordinary. Receptive activity of vascular reflexogenous zones is one of the most convenient mechanisms for rapid adaptation of an organism as it is able to carry out reflex responses having a short latent period. From this point of view, a particular importance of baro- and chemoafferentation from vertebral and carotid arteries (and possibly from others) of vascular reflexogenous zones in formation of functional-systemic interaction of breathing and blood circulation becomes obvious.

Conclusion

The obtained results show, that afferentation from vertebral and carotid arteries vascular reflexogenous zone of vertebral and carotid arteries under the action of adequate chemical stimuli (corresponding to normal ones) is one of the significant factors in formation of functionally associated reactions of respiratory and cardiovascular systems. Impulsation from vascular reflexogenous zones participates in the determination of dominance within cardiorespiratory system breathing component. To a lesser extent, the adaptive reaction of tissue gaseous exchange and its acidity regulation is ensured by reflexes on tonic activity of the resistance vasculature. The least significant changes occur in the frequency of cardiac performance which often turns out not to be interested in this process. It is quite possible that more intensive reflex responses of hemodynamic component will occur with more powerful stimulation of vascular-reflexogenous zones receptors. In this case, cardiac function will be the "last frontier" in the implementation of cardiorespiratory system adaptation mechanisms. However, the role of vascular reflexogenous zones in the regulation of cardiorespiratory activity at strong mechanical and chemical interactions was not studied in present research.

The main factor of stimulation of vascular reflexogenous zone chemoreceptors is $[H^+]$, not $[HCO_3^-]$. Compensation of clinically relevant acidosis must be carried out with trisamine/tris buffer solution and their analogues. The use of alkaline solutions for this purpose is unacceptable.

The achievement of common adaptive result of gaseous exchange and acidity correction in tissues at moderate loads is implemented principally due to greater reactivity of external respiration and to a lesser degree – due to changes in tonic activity of resistive vessels and is less dependent on cardiac performance.

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