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# FUNCTIONAL CHARACTERISTICS OF BRAIN HEMODYNAMICS UNDER HYPOXIC STRESS IN THE ELDERLY

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**Abstract.** The brain's hemodynamic response to hypoxic stress in the elderly is determined by age-related physiological changes. This article analyzes scientific data on the influence of basal cerebral blood flow, cerebrovascular reactivity, brain tissue oxygenation, and intermittent hypoxia. The results demonstrate a decrease in basal cerebral blood flow and vascular reactivity in the elderly, as well as a limited vasodilator response under hypoxic conditions. When assessing hypoxic stress, it is important to consider cerebral perfusion and brain tissue oxygenation, along with peripheral oxygen saturation.
**Keywords:** aging, hypoxia, cerebral hemodynamics, cerebral blood flow, cerebrovascular reactivity, cerebral oxygenation, intermittent hypoxia.

**Аннотация.** Гемодинамический ответ головного мозга на гипоксический стресс в пожилом возрасте определяется возрастными физиологическими изменениями. В статье анализируются научные данные о влиянии базального мозгового кровотока, цереброваскулярной реактивности, оксигенации мозговой ткани и интермиттирующей гипоксии. Результаты показывают снижение базального мозгового кровотока и сосудистой реактивности у пожилых людей, а также ограничение вазодилаторного ответа в условиях гипоксии. При оценке гипоксического стресса важно учитывать церебральную перфузию и оксигенацию мозговой ткани наряду с периферической сатурацией кислорода.
**Ключевые слова:** старение, гипоксия, гемодинамика головного мозга, мозговой кровоток, цереброваскулярная реактивность, оксигенация головного мозга, интермиттирующая гипоксия.

## INTRODUCTION

The energy demand of brain tissue is high, and the functional activity of neurons depends on a continuous supply of oxygen and glucose through the cerebral blood flow. The control of cerebral blood flow is carried out with the participation of arterial perfusion pressure, $PaCO_2$ and $PaO_2$ levels, neurovascular coupling, endothelial mechanisms, and local metabolic signals [1, 2]. During hypoxemia, a decrease in arterial oxygen content causes vasodilation in cerebral resistance blood vessels. Increased blood flow partially compensates for the decrease in oxygen delivery to the brain. Hypoxic cerebral vasodilation is formed by the interaction of NO-synthase-dependent signals, erythrocyte-associated vasoactive mechanisms, prostaglandins, potassium channels, and reactive oxygen species [3].

The functional state of cerebral vessels changes during aging. Increased arterial wall stiffness, decreased endothelial function, and altered cerebral autoregulation and $CO_2$ reactivity may limit cerebral blood flow reserve [4–7]. Therefore, the same degree of arterial hypoxemia in the elderly may be accompanied by a different hemodynamic response than in young individuals. There is a methodological problem in studying age-related changes in cerebral hemodynamics under hypoxia. Some studies have assessed only cerebral blood flow, while others have assessed tissue saturation

or $CO_2$ reactivity using BOLD reactivity, transcranial Doppler, NIRS. Although these parameters are related, they do not represent the same physiological process.

**The aim of the study** is to analyze the functional changes observed in cerebral blood flow, cerebrovascular reactivity and brain tissue oxygenation under the influence of hypoxic stress in old age based on the scientific literature.

**MATERIALS AND METHODS**

The article was carried out in the form of an analytical literature review. Sources on the physiology of aging, cerebral hemodynamics and hypoxia were selected from the PubMed database. Studies conducted in humans, with an elderly age group or a comparative analysis with respect to age, were primarily included in the analysis. Large physiological reviews explaining the mechanisms of basal cerebral blood flow and aging were accepted as an additional theoretical source. Works performed in animals were not included in the analysis of the main results.

The selected sources were analyzed for the following physiological parameters: basal cerebral blood flow; cerebrovascular reactivity to $CO_2$ and hypoxia; blood flow velocity in the middle cerebral artery; oxygen saturation of brain tissue; cerebral oxygen consumption; recovery after hypoxic exposure; functional changes after intermittent hypoxia.

**RESULTS**

Comparative literature analysis has shown that not all parameters of cerebral hemodynamics change to the same extent with aging. The most consistent differences were observed in basal cerebral blood flow and vasodilator reactivity [4–7]. Studies performed using magnetic resonance imaging and arterial spin labeling methods have shown lower gray matter and whole brain blood flow in elderly groups compared to young groups. In one study, whole brain blood flow was 49±14 ml/100 g/min in young individuals and 40±9 ml/100 g/min in older individuals [4]. In another ASL study, gray matter cerebral blood flow was 57±8 and 46±9 ml/100 g/min, respectively [5]. In this study, cerebrovascular reactivity to $CO_2$, calculated based on ASL and BOLD, was also lower in the elderly group.

Long-term observational data have shown that age-related changes in cerebrovascular reactivity are not uniform across brain regions. In a four-year follow-up study of 116 healthy individuals, the rate of decline in reactivity differed across temporal, parietal, and frontal regions; changes in reactivity were associated with changes in information processing speed and episodic memory dynamics [6].

Studies investigating the effects of hypoxia have shown that age-related differences in basal hemodynamics persist during functional exercise. In healthy participants aged 18–62 years, cerebral blood flow reactivity decreased with age ($p=0.029$), oxygen consumption decreased ($p=0.036$), and brain lactate concentrations increased ($p=0.009$) during hypoxic air breathing [7].

Hypoxic studies directly comparing older and younger groups have also shown similar changes. Older participants had lower resting cerebral oxygen saturation and lower middle cerebral artery blood flow. Repeated exposure to 10% $O_2$ resulted in less pronounced increases in cerebral blood flow, cerebrovascular permeability, heart rate, and ventilatory response than younger subjects [8]. The reviewed literature found that describing the cerebral response using only one parameter was not sufficient. Changes in $PaCO_2$ in response to hypoxia can independently alter cerebral blood flow. Therefore, the same $SpO_2$ level does not necessarily mean the same cerebral perfusion in individuals with different ventilatory responses.

In the elderly, changes in adaptation to hypoxia are not limited to the cerebral blood vessels. Age-specific differences in peripheral hypoxic vasodilation, sympathetic nerve activity, and compensatory tachycardia have also been observed [9–11]. Although sympathetic activity is

increased in both young and old individuals during systemic hypoxia, compensatory increases in heart rate are less pronounced in the elderly group [9]. Peripheral vasodilation has also been reported to decrease with age in acute hypoxemia [11]. These data suggest that it is not possible to assess cerebral perfusion separately from cardiac output, systemic blood pressure, and peripheral vascular responses.

The data on intermittent hypoxia have been more heterogeneous than those on acute hypoxia. A systematic review identified seven published studies and five registered studies in elderly individuals. Existing studies have shown that brain tissue oxygenation, middle cerebral artery blood flow velocity, and cerebrovascular permeability are improved with some protocols, but results are not consistent between protocols [14].

In a small pilot study in elderly participants with mild cognitive impairment, brain tissue oxygenation and cerebral vasodilation to hypoxemia were increased after eight weeks of intermittent hypoxia [13]. This finding cannot be directly extrapolated to the healthy elderly population, as it was obtained in a study with seven participants.

In a randomized study in individuals aged 62–79 years, cerebrovascular reactivity to $CO_2$ was not significantly increased after 24 sessions compared with controls [15]. This finding suggests that hypoxemia reactivity, $CO_2$ reactivity, and basal cerebral blood flow are not fully interchangeable measures. The results of the analysis allowed us to distinguish the following physiological trends:

| Physiological indicator | Direction determined in old age | Sources |
|---|---|---|
| Basal cerebral blood flow | Lower in most studies | [4, 5, 19, 20] |
| Cerebrovascular reactivity to $CO_2$ | Decrease or regional differences | [5, 6, 17] |
| CBF response to hypoxia | The amplitude is limited | [7, 8] |
| Brain tissue oxygenation | Differences in basal level and hypoxic dynamics | [8, 13] |
| Cardioventilatory response | Slower in the older group | [8, 9] |
| Effects of intermittent hypoxia | Depends on the protocol, not the same | [13–16, 18] |

## DISCUSSION

The results of the analysis showed that the changes in cerebral hemodynamics in aging cannot be interpreted as a single-directional phenomenon of “decreased cerebral blood flow”. Basal CBF, reactivity to $CO_2$, vasodilator response to hypoxia and autoregulation represent different physiological mechanisms. Lower basal CBF in the elderly group may be associated with changes in metabolic demand, arterial blood vessel structure, $PaCO_2$ level and neurovascular coupling characteristics. De Vis et al. reported that the reduction in the difference between age and CBF when $EtCO_2$ was included in the statistical model indicated the importance of this factor [4]. Therefore, the failure to control respiratory gases when comparing elderly and young groups may lead to incorrect physiological conclusions.

Vasodilation in hypoxia is provided by several parallel mechanisms. Current physiological data suggest a link between NO synthase, erythrocyte-derived S-nitrosothiol signaling, potassium channels, prostaglandins, and ROS [3]. Several of these systems may change simultaneously in old age. Therefore, explaining the decline in cerebral reactivity solely by endothelial NO deficiency is incomplete.

The results of intermittent hypoxia cannot be interpreted in the same way. Controlled short-term hypoxia can activate adaptive responses, but the number of sessions, the duration of the hypoxic phase, the minimum $SpO_2$, the mode of exchange with normoxia or hyperoxia, and the initial functional state of the participants will change the result. A 2024 systematic review also indicated the need for standardization of protocols [14]. $SpO_2$ and heart rate are not sufficient to assess the cerebral hypoxic response in elderly individuals. Simultaneous recording of middle cerebral artery blood flow velocity by transcranial Doppler, brain tissue oxygenation by NIRS, arterial pressure, and respiratory gases allows us to separate the cerebral and systemic components of the hypoxic response.

Another limitation of the available studies is the large age difference between the "elderly" groups. In some studies, the average age is 60–65 years, in others it is over 70 years. The 2025 Cerebral Autoregulation Review also suggests that the effects of aging are not the same as chronological age, but are modified by factors such as hypertension, vascular stiffness, and cognitive status [17]. Therefore, when assessing the hemodynamic response to hypoxic stress, it is important to consider the age, blood pressure, functional status, and hypoxia dose of elderly participants within a single protocol.

## CONCLUSION

Literature review has shown that there are age-specific functional differences in basal cerebral blood flow, cerebrovascular reactivity, and vasodilatory response to hypoxia in the elderly. Cerebral blood flow and the amplitude of cardioventilatory compensation during hypoxic exposure may be limited in the elderly group. Cerebrovascular changes after intermittent hypoxia are not uniform and depend on the characteristics of the protocol used. In the physiological assessment of hypoxic stress in the elderly, it is reasonable to analyze $SpO_2$, arterial pressure, and heart rate in conjunction with cerebral blood flow and brain tissue oxygenation.

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