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Amplitude of the Pulsatile Component of a Photoplethysmographic Waveform as an Optical Marker of Cerebrovascular Reactivity: Experimental Verification in Animal Model

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Abstract: Imaging photoplethysmography (PPG) is useful method for monitoring intracranial blood-flow during vasodilatation tests. Our experiments with rats revealed that an increase of PPG pulsatile component is reliable marker of cerebrovascular reactivity.

1. Introduction

Assessing cerebral perfusion is critical for the management of patients with cerebrovascular pathology. This assessment is important both for diagnosing the severity of hemodynamic disorders, and for the purpose of prognosis. Moreover, it can be useful to determine the tactics and control of treatment, including revascularizing surgery of the brain. It is known that a degree of vascular reactivity can be evaluated during provocative tests with either carbon dioxide [1] or inhibitor of carbonic anhydrase [2], each resulting in efficient vasodilation. Several instrumental methods, such as Positron Emission Tomography, Magnetic Resonance Imaging, Doppler Ultrasound, and others are currently used to reveal changes in blood supply to problem areas of the brain [2–4]. However, these techniques have a number of limitations that impede their intraoperative use, where the operation speed of the equipment, its technical simplicity and ease of control, the size and contactless mode of operation play a decisive role. At the same time, the technology of imaging photoplethysmography (IPPG) meets all the above requirements [5-7].

The aim of our study was to reveal features of IPPG as a method for assessing the cerebrovascular reserve during vasodilation tests in the course of neurosurgical interventions, and to identify reliable optical markers of vascular reactivity.

2. Methods

The study was carried out in a series of acute experiments with Wistar rats in accordance with the ethical guidelines of the International Association for the Study of Pain, the Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes. Adult male animals (n = 23) were anaesthetized by intraperitoneal injection with a mixture of urethane and a-chloralose at an initial dose of 800/60 mg/kg. Surgical preparation of rats for the experiment included tracheostomy, cannulation of the femoral vein and artery, fixation of the head in a stereotaxic device, and the formation of two closed cranial windows, for which both parietal bones were thinned to ensure visualization of intracranial vessels. During each experiment, the following physiological parameters were continuously monitored: electrocardiogram, systemic blood pressure (BP), heart rate (HR), body temperature, and end-tidal CO_2. Seven animals remained on spontaneous breathing while 16 were transferred to artificial pulmonary ventilation after muscle relaxation (pipcuronium bromide, 0.9 mg / kg, i.v.). Parameters of cortical blood flow were measured by using custom-made IPPG system consisted of a digital monochrome camera and illumination block [7]. The latter contained eight green LEDs ($\lambda = 530 \pm 25$ nm) mounted

around the camera lens (25 mm focal length) in such a way as to ensure uniform illumination of the rat's cortex through the cranial window.

The animals were divided into two groups: the first (n = 15, of which 8 with artificial pulmonary ventilation) received inhibitor of carbonic anhydrase dorzolamide (2 mg, i.v.), and the second (n = 8, all with artificial pulmonary ventilation) inhaled air mixture containing 5% of CO_2. Inhalation of the gas mixture in rats of the second group was carried out sequentially for 30, 60 and 120 seconds with a ten-minute interval between inhalations. During each test, two IPPG parameters were continuously evaluated: the normalized amplitude of the pulsatile component (APC) of the PPG waveform and its slowly varying DC component (also known as optical intrinsic signal, OIS). IPPG parameters were assessed before, during and after either dorzolamide administration or CO_2 inhalation. Non-parametric tests with multiplicity correction were used for identifying significance of changes in systemic (BP, HR) and local (APC, OIS) hemodynamics caused by the functional tests.

3. Results

Dorzolamide injection in all rats led to a significant increase in APC (36 ± 17%, $p < 0.001$) accompanied by a decrease in end-tidal CO_2 concentration (32 ± 7%, $p < 0.001$), whereas reaction of the mean ABP did not reveal statistically significant changes (5.7 ± 14.3%, $p = 0.09$, Wilcoxon sign-rank test). Above-mentioned changes began to appear immediately during the first minute of dorzolamide infusion and reached a steady state within one minute after the completion of dorzolamide administration. Similarly, inhalation of CO_2 of any duration also resulted in significant increase in APC, which was developing within 10-15 seconds after its onset. However, in contrast to the first group of rats, end-tidal CO_2 was increasing in the second group. Moreover, it was found that both 30-s and 60-s inhalation led to increase in systemic BP, whereas its changes were biphasic during 120-s inhalation: the initial phase of increase was replaced by a phase of decrease followed by normalization after hypercapnia cessation.

4. Conclusions

In this study, we demonstrated feasibility of using IPPG as a contactless method for express analysis of changes in intracranial blood flow caused by well-known vasodilating interventions. It is worth noting that regardless of the type of vasodilatation provocation (CO_2 or dorzolamide) and the method of its administration (inhalation or injection), there has always been a significant increase in the APC parameter. It should be especially noted the rate of development of this change and its severity in both experimental groups of animals. Therefore, an increase in APC of the PPG waveform can be considered a reliable optical marker of preserved cerebrovascular reactivity, which makes it possible to quickly assess the functional reserve of cerebral blood flow. The data obtained in our study can be translated into clinical practice and used as a diagnostic tool, in particular, in revascularizing neurosurgery.

5. Funding

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