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The Effect of Craniotomy on the Intracranial Hemodynamics and Cerebrospinal Fluid Dynamics in Humans

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Abstract—The goal of the research was to study the effect of the trephination of the human cranial cavity on the intracranial hemodynamics and cerebrospinal fluid (CSF) dynamics. The sample comprised 11 patients of a neurosurgical clinic in whom a trephine opening in the cranial bones was made for medical indications. In these patients, at rest and during an appropriate functional load, we recorded pulse changes in blood circulation (by transcranial Doppler sonography) and in the ratio between the pulse fluctuations in the blood and CSF volumes (by rheoencephalography) before and after surgery. Simultaneous recording of these parameters followed by computer pattern and phase analyses allowed evaluation of the complex biomedical compliance of the cranium during successive phases of the cardiac rhythm: the inflow of arterial blood, the redistribution of blood/CSF volumes, and the outflow of venous blood. Analysis of the results showed a beneficial influence of craniotomy on the intracranial hemodynamics and CSF dynamics. This was reflected in an increase in the cranial compliance, which increased the pulse increment in the volume of the arterial blood in the skull almost twofold. After craniotomy, the cross-flow of CSF between the cranial and spinal cavities decreased significantly, giving way to volumetric compensatory translocations of blood and CSF within the cranial cavity per se during the cardiac cycle, which increased the intracranial utilization of the energy of the cardiac output and contributed to the outflow of venous blood from the cranium. The results suggest a beneficial effect of craniotomy on the physiological mechanisms of the circulatory and metabolic maintenance of the brain activity.

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INTRODUCTION

Craniotomy has a long history and is of interest for a number of reasons. With respect to the brain blood circulation, the skull integrity was shown to be important for its normal functioning. Disturbance of this integrity should influence the ratio of the function of the vascular and cerebrospinal fluid (CSF) systems of the brain [1, 2], and, therefore, the circulatory and metabolic maintenance of its function. Craniotomy is usually performed during neurosurgery, and the trephine opening remains, as a rule, in the postsurgical period. It is obvious that the disturbance of the skull integrity caused by trephination changes radically the intracranial hemodynamics and CSF dynamics. However, these changes and their consequences have been poorly studied. Thus, there are still no distinct pathophysiological indications for leaving the trephine opening unclosed for some period after surgery or for its closing at the end of surgery or a certain period after it.

One aspect of craniotomy is of special interest. It belongs more to the realm of archaeology than to that of physiology or medicine and relates to some findings of skulls dating from two to three thousand years ago with traces of craniotomies. It is difficult to say what the aim of such craniotomies was; however, there is an opinion that they were performed for medical purposes. In any case, direct evidence has been obtained recently that subjects 40–50 years of age may have a significantly decreased capacity of the CSF system [3]. Therefore, changes in the hemodynamics and CSF dynamics caused by craniotomy may be beneficial for the circulatory and metabolic maintenance of the brain activity.

A. Feilding and P. Halvorson are supporters of this idea, and they placed it at the basis of a comprehensive study on the effect of craniotomy on hemodynamics and CSF dynamics. The results of this research are reported below. We should note that this study is, to our knowledge, one of the first fundamental physiological studies on craniotomy.

METHODS

Craniotomy may influence the function of the intracranial hemodynamics and CSF dynamics, as well as the interaction of these two systems. Therefore, the study of this problem requires an integrated approach based on simultaneous recording of physiological parameters of the activity of these systems. The methodological approach in this case may be simultaneous recording of the transcranial Doppler sonogram (TCD) and the rheoencephalogram (REG) on the same data carrier, analysis of the results during the cardiac cycle at rest and under the conditions of functional load, and comparison of the results before and after craniotomy. This integrated method has been used successfully in comparative physiological studies aimed at revealing age-related changes in the coupling of the intracranial hemodynamics and CSF dynamics [3–5]. In these papers, the tools and computer software used are described, including the principles of data standardization and analysis.

A similar methodological approach was used in this study, including the application of the REG electrodes in the frontomastoidal position and the focusing of the TCD sensor on segment M-1 of the base of the medial cerebral artery. Moreover, a certain adaptation of the methodological approach was necessary, taking into account the specific character of the study. First, the research protocol included only strictly standardized functional tests with targeted effects on the arterial and venous vascular systems, as well as on the CSF dynamics. Brief voluntary apnea was used to affect the cerebral arteries, which caused significant changes in the oxygen balance and significant vasodilatation in the brain as soon as within 10 s, as was shown in our previous studies [6]. Beginning from the 20th to 25th second, shifts in systemic hemodynamics were observed, which were reflected in the TCD parameters. Therefore, a pulse cycle recorded 15–20 s after the beginning of the test was chosen for analysis.

To determine the role of the venous system in the interaction of the vascular and CSF systems before and after craniotomy, comparative analysis of the pulse cycles of the TCD and REG during the phases of deep inspiration and expiration was performed, during which significant changes in the filling of the cranial cavity with venous blood occurred according to our experimental [7] and clinical [8] studies. Stuckey's test was used for functional testing of the CSF system: pressing onto the abdominal region causes the transfer of CSF from the spinal cavity into the skull, which, in turn, causes reaction of the cerebral vessels. Therefore, for evaluating the role of the CSF cross-flow to the cranial cavity, we analyzed the cardiac cycle that occurred 3–5 s after the beginning of the functional test to minimize the effect of the vascular response because its latency was 5–7 s [9].

The specific features of the ratio between the pulse waves of the TCD and the REG recorded before and after craniotomy using these two functional tests were revealed using phase analysis based essentially on the analysis of the relative changes in these parameters in different phases of the cardiac cycle. For this purpose, three zones were distinguished in the pulse changes in the TCD and the REG standardized with respect to the amplitude and duration (Fig. 1I).

The first zone was the range of the anacrotic increase in these parameters during the beginning of the TCD elevation to its maximum. This was the period of dilatation of the skull as a structural system, which involved not only the bones of the skull and their conjunctions, but also the meninges and the biomechanical properties of its vascular system. In other words, all these factors determine the cranial compliance (CC), according to the terminology introduced by Marmarou [10]. The relative unit for this parameter used in the methodological modification of the present study was the slope of the straight line that approximated the TCD/REG ratio during the anacrotic period (Fig. 1IIa).

The second zone was a section of the pulse cycle where changes in the TCD and REG differed significantly from each other. Moreover, an increase in one of these parameters could be accompanied by a decrease in the other. This zone reflects compensatory cross-flows of CSF inside the cranial cavity and between the cavities in the skull and spine. It lasts from the maximum of the pulse wave of the TCD to the beginning of a zone of quick and almost synchronous decrease in the TCD and REG. The differentiation of the direction of compensatory cross-flows of CSF within this zone of the cardiac cycle is possible if the direction of changes in the REG is taken into consideration. If the pulse decrease in the TCD occurred immediately after achievement of the maximum and was accompanied by elevation of the REG curve, i.e., by a further decrease in the electrical resistance between the REG electrodes, and after that it decreased more slowly than the TCD, this meant that CSF (a medium with a high electrical conduction) remained within the skull. If the pulse decrease in the TCD (after achievement of the maximum) was accompanied by a comparatively more intense decrease in the REG, i.e., by an increase in the electrical resistance, this meant that the CSF was squeezed out from the skull into the spinal cavity. The diagram is shown in Fig. 1IIb, where $+\Delta$REG indicates an increase in the electrical conduction upon completion of its changes in the first zone and $-\Delta$REG indicates its more pronounced decrease simultaneously with the pulse decrease in the TCD. Hence, a value of the ratio $\Delta\text{REG}/\Delta\text{TCD} < 0$ means a predominant outflow of CSF from the cranial cavity in the area of the compensatory changes in the filling of the cranial cavity with blood, whereas a ratio $\Delta\text{REG}/\Delta\text{TCD} > 0$ shows that the cross-flow of the CSF is restricted to the cranial cavity. If the value of $\Delta\text{REG}/\Delta\text{TCD}$ approaches zero, this is an indicator of equilibrium in the cross-flow of the CSF within the cranial cavity, as well as between the cranial and spinal cavities. Taking into account the fact that changes in the pulse curve of the TCD in the second zone always have the same direction, it is appropriate to use for evaluating the direction of the CSF compensatory cross-flows the modulus of the value of the TCD change, whereas, for evaluating the changes in the CSF mobility in general, before and after craniot-

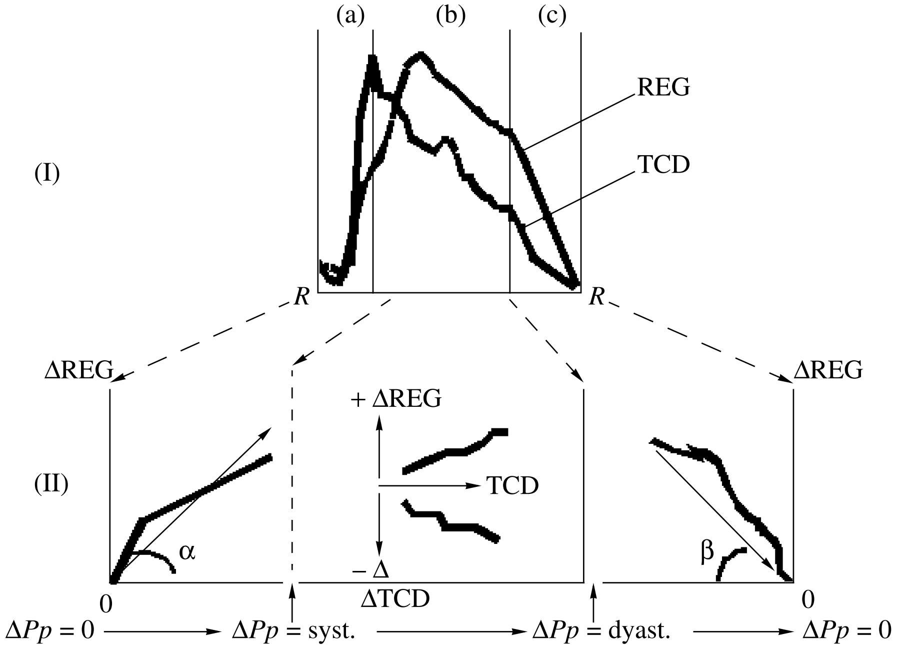

Fig. 1. The principle of the pattern and phase analysis of the pulse waves of transcranial Doppler sonography (TCD) and rheoencephalography (REG) recorded simultaneously. (I) Initial curves normalized with respect to the duration of the RR interval and the amplitude. (II) Zones distinguished in the curves: (a) the zone of systolic increase in the TCD and REG, the phase diagram of which (IIa) characterizes the total compliance of the skull; (b) the phase diagram reflects the mobility and direction of the pulse transfer of the CSF, which characterizes (IIb) compensatory CSF dynamics; (IIc) parameters of the outflow of venous blood from the skull. At the bottom, a scale of the pulse pressure (*Pp*), systolic (syst.) and diastolic (dyast.), is shown.

omy at rest or during functional loads, the moduli of the TCD and REG should be compared.

In order to present the curves in Fig. 1II in a diagram with a common abscissa, the direction of the axes in Figs. 1IIb and 1IIc should be changed to the opposite because, in Fig. 1IIa, the pulse change in the TCD reaches its maximum, after which it decreases to the initial level in Figs. 1IIb and 1IIc. These procedures were not difficult to perform using the Canvas 6 software. The relative scale of the pulse pressure combined for the curves given in Fig. 1II is shown at the bottom of Fig. 1.

The third zone of changes in the ratio between the TCD and the REG is approximately the last quarter of the cardiac cycle and characterizes the outflow of blood from the skull. The slope of the approximating curve reflects the intensity and completeness of the pulse outflow of venous blood from the skull (Fig. 1IIc), which is determined by the difference between the intracranial pressure and the pressure in the precava, which is related largely to the respiratory phase. The most suitable unit for estimating this parameter is the slope of a line that approximates a descending segment of the curve of the phase diagram.

Taking into consideration the biophysical bases of the methods applied, we can reasonably interpret changes in the REG/TCD ratio within the cardiac cycle in volume–pressure terms, as far as the pulse fluctuations in the REG reflect volumetric changes in the liquid medium in the skull, whereas the pulse fluctuations in the TCD are proportional to the pulsations of the intracranial pressure, reasoning from Poiseuille's law, which is true for the given case.

Simultaneously with the TCD and REG, the respiratory movements of the chest and the ECG were recorded in order to determine the limits of the cardiac cycle and consider the respiratory phase. The integrated analysis of the results also involved data on the mean values of the linear blood velocity in the medial cerebral artery and the value of the index *Pi*, which allowed the estimation of the cerebral blood supply.

This study was performed on patients of the neurosurgical clinic of the Institute of the Human Brain, Russian Academy of Sciences, with a diagnosis of space-occupying lesions of various etiologies for whom neurosurgery including craniotomy was indicated and in whom the trephine opening had to remain open for a certain period after surgery. A group of 11 patients was examined. The parameters mentioned above were recorded before surgery and during eight to ten days of postoperative supervision. We selected patients with the minimal possible extent of surgical trauma to the brain. During the postoperative period, most of the patients were examined repeatedly two or three times in order to increase the reliability of the data and to follow up changes in the parameters studied at different stages of the postoperative period, up to two months.

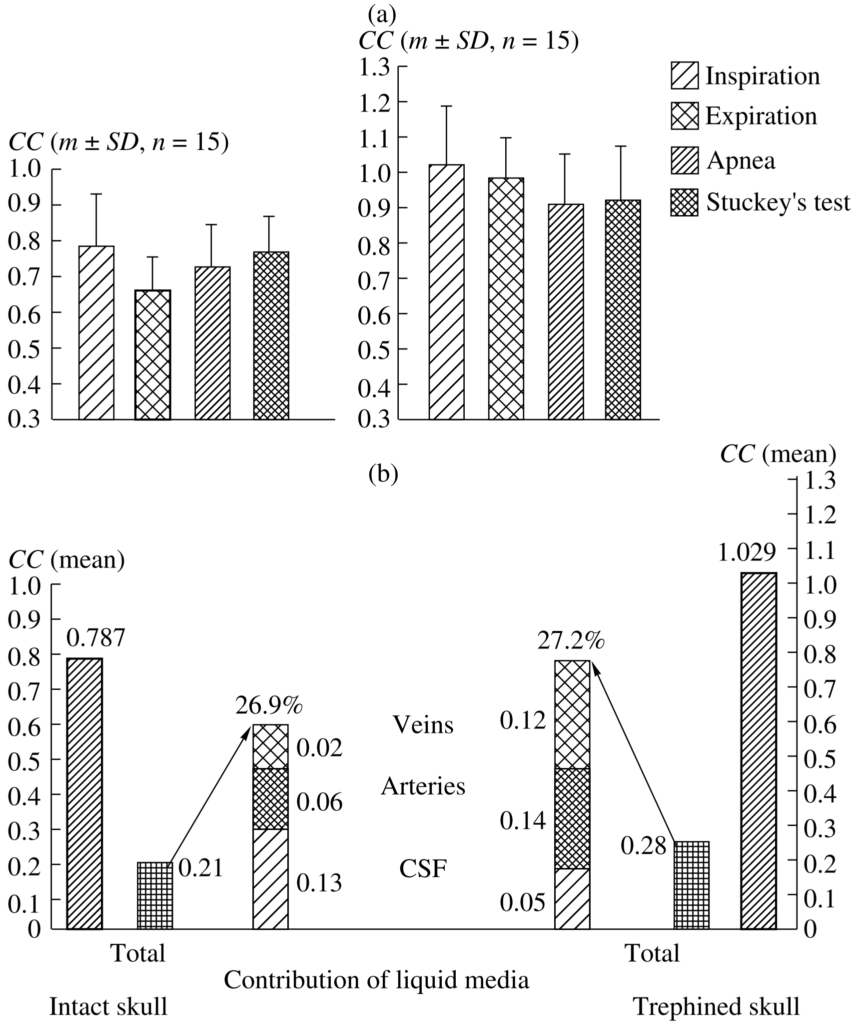

Fig. 2. Parameters of the total compliance of the intact and trephined cavity of the skull under the influence of hemodynamics or CSF dynamics tests: (a) the liquid component of this parameter; (b) before and after craniotomy.

RESULTS AND DISCUSSION

The research showed that most of the parameters studied changed significantly after craniotomy. First, this applies to their ratio. When the parameters recorded increased almost linearly, the TCD/REG ratio approximated a straight line, the slope of which was 0.78 ± 0.18 before surgery (*m* ± *SD*, *n* = 15) and equaled the mean normal value of this parameter in the given age group [3]. After craniotomy, this parameter, which characterized the total CC (*CC*), increased to 1.04 ± 0.22 (*m* ± *SD*, *n* = 15), i.e., increased by approximately 20%.

The changes in these values during functional tests (Fig. 2a) were very informative. For example, comparison of the *CC* values in the phases of inspiration or expiration enables assessment of the relative contribution of the venous blood filling of the skull. Comparison of the same parameters in the phase of apnea allows assessment of the relative contribution of the arterial blood system of the brain to the *CC*. Comparison of the results of Stuckey's test permit evaluation of the relative contribution of the CSF mobility. The absolute values of these data are shown in Fig. 2b, from which it is clear that the contributions of the arterial, venous, and CSF systems change significantly after craniotomy. However, the relative integrated contribution of the liquid components of the cranial cavity remained unchanged after craniotomy. It can be seen from the diagram that craniotomy affected predominantly the redistribution of the volumes of arterial and venous blood and CSF in the skull, which contributed to additional compliance of the skull and ensured its sufficient capacity during a pulse increase in the blood pressure. Thereby, sufficient cerebral blood circulation in the diastole phase was ensured, as is the case in some other organs lacking rigid envelopes. We should also note that this led to a relative (almost twofold) increase in the pulse arterial blood volume followed by a significant increase in the oxygen supply to brain tissues.

Maintenance of the brain blood supply in the phase of diastole possibly depends on the CSF mobility in the

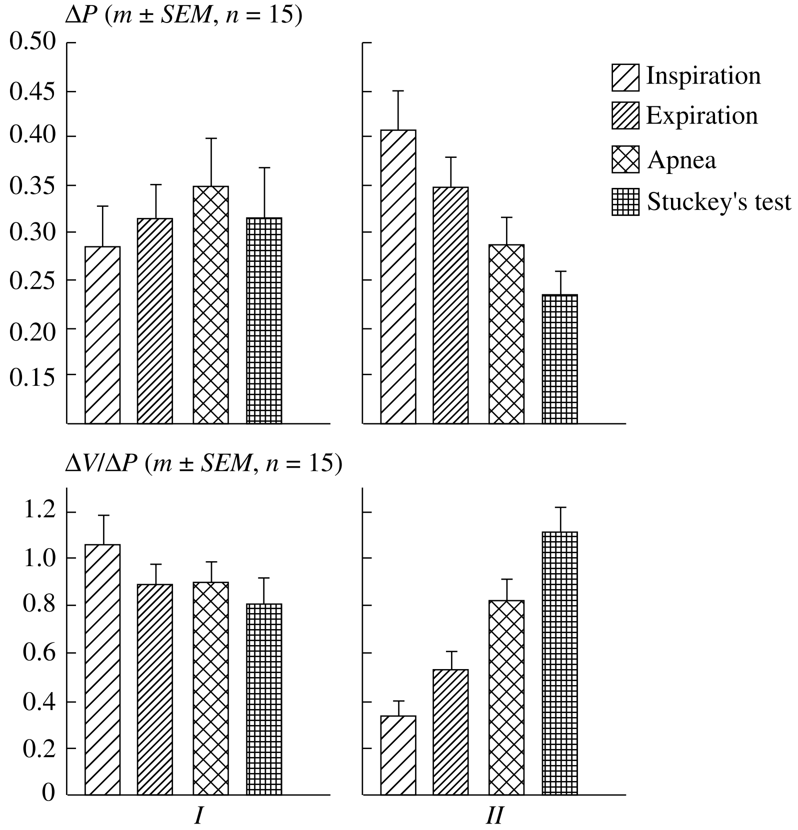

Fig. 3. Parameters of the CSF mobility: relative variation in the CSF pressure (Δ*P*) and the volume-to-pressure ratio (Δ*V*/Δ*P*) in the phase of volumetric compensations under the influence of functional tests (a) before and (b) after craniotomy.

cranial cavity and between the cranial and spinal cavities. The integrated CSF mobility can be assessed by comparing the relative values of the TCD changes after the achievement of the maximum values (the second zone of the cardiac cycle), which corresponds to a pulse pressure drop and to a proportional decrease in the intracranial pressure with volumetric changes seen in the REG (Fig. 3). Figure 3 shows that craniotomy significantly changed the relative value of the volumetric CSF changes ΔREG/ΔTCD, which corresponds to Δ*V*/Δ*P*, as well as the *ΔP* value: the former decreased by a factor of more than 2, and the latter increased by 40% on average. However, during the functional tests, the difference between these values for the intact and trephined skull disappeared. This indicates that the increase in the volumetric reserve capacities of the cranial cavity after trephination was reduced under the conditions of an increase in its blood filling or in the CSF volume due to external action. This was most evident during Stuckey's test, when the Δ*P* value dropped below and the Δ*V*/ΔP ratio increased above the level of these parameters in the intact skull. The direction of changes in the Δ*V*/Δ*P* ratio shows that the compensatory cross-flows of CSF between the cranial and spinal cavities in most cases (about 70%) significantly decreased after craniotomy. In addition, the number of cases of balanced hemodynamics and CSF dynamics at rest increases. However, variations in this parameter in different phases of the respiratory cycle and under the influence of the functional test increased after craniotomy. These data mean that craniotomy activates compensatory cross-flows of CSF, which contributes to the most complete utilization of the energy of the systolic output for maintaining the brain blood supply. Moreover, the influence of various factors on the intracranial hemodynamics and CSF dynamics, e.g., respiratory movements, increases, which is evidenced by an increase in the REG respiratory waves. Therefore, we can expect that, under certain conditions, the influence of some external factors on the body can destabilize the system of circulatory support of the brain activity. The blood outflow from the skull can be characterized by the slope of the dependence ΔREG/ΔTCD (the descending part of the pulse pressure curve, the third zone of the pulse cycle, Fig. 1IIb). In general, this dependence can be represented as a line with a relatively small slope reflecting the rate of blood outflow from the skull. A more intense blood outflow from the skull was observed in the case where the CSF cross-flows during the cardiac cycle were restricted by the rigidity of the cranial cavity. This state contributes to the transfer of some energy of the systolic output via

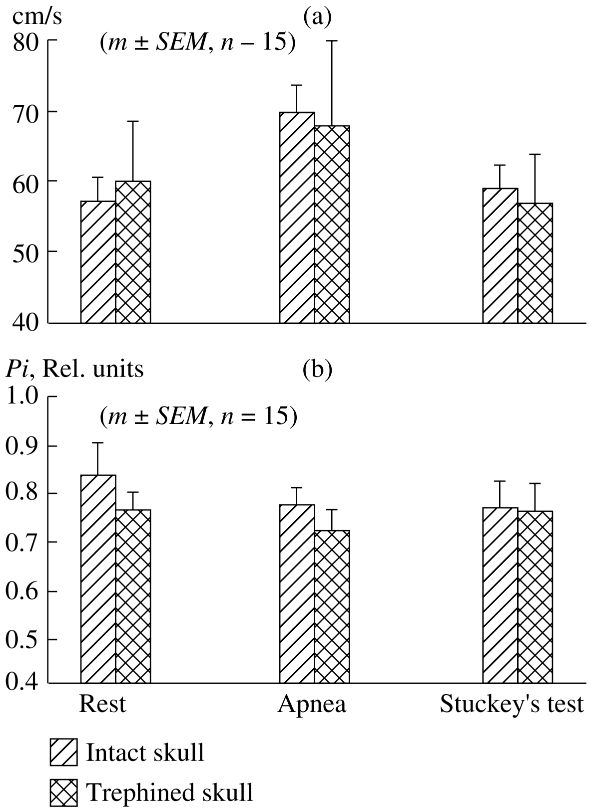

Fig. 4. Changes (a) in the blood circulation rate (cm/s) at the base of the medial cerebral artery and (b) in the pulsation index *Pi* at rest, during apnea, and during Stuckey's test.

CSF directly to the veins, thus facilitating blood outflow from the skull [11]. If the pulse CSF outflow to the spinal cavity increases, the venous outflow from the skull decelerates, which can affect the function of the intracranial blood circulation. In general, our results on the pulse cross-flows of the CSF are similar to the data obtained by means of phase-contrast nuclear magnetic resonance imaging [12, 13] or by simulation [14]. We should note that, despite some negative features, these procedures have a higher resolution compared to the methodology used in the present study, thus giving a more detailed idea of the CSF cross-flow, which is undoubtedly important but does not change essentially the notions on the effect of craniotomy on the intracranial hemodynamics and CSF dynamics described earlier.

Craniotomy does not change significantly the blood circulation at the base of the medial cerebral artery or the pulsation index. However, the response of the cerebral arteries to breath-holding somewhat weakens (Fig. 4). This points to some reduction in the cerebrovascular reactivity after craniotomy.

Follow-up of the patients after craniotomy demonstrated that the effects of the craniotomy shown earlier were retained during the whole period of monitoring; however, by the end of the second month after the craniotomy, they had somewhat decreased.

Since surgical trauma to the brain accompanies craniotomy, the natural question arises of whether it can bias the data recorded during the postsurgical period. It is difficult to give a direct answer to this question. However, comparison of variations in the parameters recorded before and after craniotomy in different patients showed the absence of significant differences in their relative values. This fact allows us to suggest that surgical trauma to the brain does not have a significant impact on the dynamics of the fluid in the craniospinal space. The results of examination of patients with minimal brain trauma or its absence also confirmed this conclusion, though these cases were rare. Moreover, we could not entirely exclude the possibility of the influence of brain trauma on the data recorded, at least because other authors [15, 16] have considered brain trauma to be the most acceptable explanation for a decrease in cerebrovascular reactivity after craniotomy. We also could not find a dependence of the results on the size or location of the trephine opening. Apparently, since the dimensions of a trephine opening necessary for brain neurosurgery are rather large, variations in them do not influence considerably the results obtained. The influence of the location of the trephine opening on the parameters of the intracranial hemodynamics and CSF dynamics is also not clear yet. In respect to the biophysical organization of the intracranial hemodynamics and CSF dynamics and the modeling results [9], the location of the trephine opening should not affect substantially the function of these systems, taking into consideration their globality. However, this question needs special investigation.

Consequently, the data presented above show that changes in the intracranial hemodynamics due to craniotomy mainly influence the compliance of the skull as a biomechanical system, the ratio between the pulse changes in the liquid media in the skull, and the CSF mobility. The physiological assessment of these changes may be performed by comparing the rate of the blood inflow to the brain due to pulsations with the mean blood flow through the brain. In fact, the pulse increment in the blood volume in the cranial cavity under normal conditions equals, according to calculations, 30–35% of the total blood volume flowing through the brain during a cardiac cycle. It is known that 20% of the minute blood volume goes to the brain and that with a mean blood flow of 50 ml/(100 g min) the minute blood volume flowing through a brain of average size (approximately 1200 g) is about 600 ml. Thus, at a pulse rate of 60 beats/min, the brain consumes about 10 ml of the systolic output, with a pulse volume component of 4 ml.

This implies that even slight changes in the skull capacity for pulse blood volume, as little as 0.2–0.3% of the total cranial cavity space, may influence significantly its blood supply. Indeed, a change in the total skull capacity by 1 ml can change the total cerebral blood flow by 10%. A simple calculation shows that, if the skull capacity increases by 20% after craniotomy, the trephined skull can receive more blood (by 0.8 ml on average) than before craniotomy. Consequently, according to our study, the cerebral blood flow may increase after craniotomy by approximately 8–10%, which agrees with the known experimental data [9]. Hence, if a certain cerebrovascular insufficiency was observed in an intact skull, craniotomy could contribute to normalization of the brain blood supply. If the brain blood supply before craniotomy were sufficient, the excessive perfusion would be compensated by the physiological mechanisms of self-regulation of the cerebral blood flow. In this case, an increased intracranial cerebrovascular reserve will be retained.

CONCLUSIONS

In summary, we can conclude that alterations in the integrity of the skull caused by craniotomy significantly affect the intracranial hemodynamics and CSF dynamics. We may interpret the data of our study as an increase in the functional activity of these physiological systems. As a result, the volume of arterial blood flowing into the skull during systolic elevation of arterial pressure increases, which results in an increased supply of the brain tissue with oxygen. Craniotomy changes the dynamic relationship between the liquid media (arterial and venous blood and CSF), thus contributing to optimization of the functional mechanism responsible for the circulatory and metabolic support of the brain activity. Taking into consideration the fact that most brain diseases are related to disturbances in its hemodynamics and/or CSF dynamics and, as a result, to disturbance in the oxygen supply to the brain cells, we can suppose, with some caution, a possible therapeutic effect of craniotomy in some diseases. However, for confirmation, this assumption requires further research in this field.

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