Influence of systemic and cerebral vascular factors on the cerebrospinal fluid pulse waves

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In anesthetized, artificially ventilated dogs, the intracranial cerebrospinal fluid (CSF) pulse waves were studied simultaneously with the central aortic pressure, central venous pressure (CVP), and the sagittal sinus pressure under physiological conditions and in normovolemic arterial hypotension and hypertension, in acute cardiac insufficiency of the right atrium, in raised intracranial pressure (ICP), and in arterial hypoxemia. The physiological CSF pulsations are shown to be mainly arterial in origin. In the diastolic phase, the descending part of the pulse curve can be modified by venous superpositions coinciding with the right atrial “A” wave. With increase of ICP the configuration of the CSF pulsations changes: the venous superpositions disappear and the waves become more and more arterial in shape. Furthermore, the pulse amplitude increases considerably. The same change can be observed when cerebral vessels are dilated by arterial hypoxemia. During cardiac insufficiency and consecutive increase of CVP, the CSF pulse curve is venous in shape and the right atrial “A” wave predominates. In arterial hypotension, CSF pressure decreased. Conversely, in angiotensin-induced systemic arterial hypertension, CSF pressure and its pulse amplitude increased. It is concluded that both systemic arterial blood pressure and cerebrovascular reactivity are major determinants for the shape and the pressure amplitude of the intracranial CSF pulse waves. In the presence of cerebral vasodilatation, systemic arterial blood pressure may be an important factor in raising ICP and altering the brain tissue compliance, because cerebral vascular damping of the arterial pulse is diminished and the arterial pressure head may be directly transmitted to the cerebral capillary bed.

KEY WORDS • cerebrospinal fluid pressure • arterial blood pressure • cerebrospinal fluid pulse wave • cerebrovascular reactivity

Since the basic investigations of Guillaume and Janny18 and Lundberg,27 recording of mean intraventricular cerebrospinal fluid pressure (CSFP) has found wide use in clinical practice for monitoring intracranial pressure (ICP). Neurosurgical interest, however, has hitherto been less intensively focused on the physiology of cerebrospinal fluid (CSF) pulsations and hemodynamically induced changes of the pulse waves. This may be partly explained by the fact that for a long time more casual clinical observations have been based mainly on lumbar pressure measurements. The damping effect of the spinal system and inadequate technical equipment for pressure measuring.
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easily led the clinician to underestimate the importance of rapid pulsations in the intracranial compartment. Moreover, to obtain better knowledge about the origin and dynamics of CSF pulsations, simultaneous polygraphic recordings of CSFP and systemic vascular pressures using sufficiently sensitive pressure transducers are necessary. In the last three decades, only a few experimental studies have been devoted to the physiological intracranial CSF pulsations, and the interpretation of the origin of intracranial CSF pulse waves has remained somewhat controversial. In the present study we are investigating which factors determine the normal intracranial CSF pulse waves and how the shape of the pulse curve changes under pathophysiological conditions, such as systemic arterial hypertension, raised intracranial pressure (ICP), and hypoxic cerebral vasodilatation.

Material and Methods

The present study was performed on 27 anesthetized, artificially normoventilated, healthy mongrel dogs with a mean body weight of 30 kg. Anesthesia was induced with sodium pentobarbital (10 mg/kg body weight) and maintained with 0.4 vol% halothane. Artificial ventilation was carried out by means of an Engstroem respirator,* and the CO₂ concentration in the respiratory air was measured on a Hartmann-Braun Uras infrared CO₂ analyzer.†

For blood sampling and pressure-recording both femoral arteries and veins were dissected and cannulated with polyethylene catheters pushed into the thoracic part of the aorta and the superior vena cava, respectively. The superior sagittal sinus was exposed through a median burr hole in the frontal region and after occlusion of major draining diploic veins a cannula was inserted into the sinus. The burr hole was then sealed with acrylic. The cisterna magna was punctured percutaneously with a double-barrelled needle for simultaneous pressure recording and infusion of artificial CSF. All pressures were measured by Statham transducers‡ with the experimental animal in the horizontal prone position and the reference point for pressure recording at the level of the right atrium. The pressure transducers were connected to an eight-channel multiscriptor polygraph 19§ that permitted the recording of both pressure pulse waves and electronically determined mean pressures.

The animal preparations were divided into five groups:

Group 1. In Group 1 (6 dogs), arterial blood pressure was lowered by controlled intravenous injections of trimethaphan until mean arterial blood pressure (MABP) had dropped to 40 mm Hg. During this hypotensive state, hypercapnia was induced by inhalation of 5% CO₂, and CO₂ reactivity of the cerebral vessels was tested by measuring global cerebral blood flow (CBF) by the nitrous oxide method as modified by Bernsmeier and Siemons. In this modification, cerebral arterial and venous blood was withdrawn slowly and steadily at a rate of 1 ml/min by motor pumps for 10 minutes. The CBF measurements were carried out after steady-state conditions had been achieved for 30 minutes.

Group 2. In Group 2 (3 dogs), the effect of angiotensin-induced systemic arterial hypertension on the intracranial CSF pulsations was tested.

Group 3. In Group 3 (2 dogs), acute cardiac right atrial insufficiency was produced by rapid intravenous hyperinfusion.

Group 4. In Group 4 (10 dogs), ICP was gradually increased by infusing mock CSF into the cisterna magna while keeping MABP and central venous pressure (CVP) constant. The CBF data of this group have been reported in another publication.¹⁸

Group 5. In the last group (6 dogs), arterial hypoxemia was produced by reducing oxygen and adding nitrogen to the inhaled gas mixture leaving arterial CO₂ pressure (PaCO₂) normocapnic and MABP normotensive. The hypoxic arterial oxygen pressure (PaO₂) level (mean PaO₂, 35 torr) was maintained for about 20 minutes; CBF measurements were

†Infrared CO₂ analyzer manufactured by Hartmann-Braun, Frankfurt/Main, West Germany.
‡P37 and CEC 4-327-L223 transducers manufactured by Statham Laboratories, Inc., Hato Rey, Puerto Rico.
§Eight-channel multiscriptor polygraph 19 manufactured by Hellige, Freiburg, West Germany.

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### TABLE 1

**Cerebral blood flow and mean CSFP in six dogs**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Normocapnic Arterial Normotension</th>
<th>Normocapnic Arterial Hypotension</th>
<th>Hypercapnic Arterial Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean arterial blood pressure (mm Hg)</td>
<td>107.5 ± 7.5</td>
<td>46.2 ± 3.9*</td>
<td>47.0 ± 3.1*</td>
</tr>
<tr>
<td>arterial CO₂ pressure (mm Hg)</td>
<td>37.3 ± 1.2</td>
<td>37.2 ± 1.9</td>
<td>81.3 ± 7.1*</td>
</tr>
<tr>
<td>cerebral blood flow (ml/100 gm/min)</td>
<td>66.3 ± 13.1</td>
<td>32.8 ± 5.1†</td>
<td>57.9 ± 14.8†</td>
</tr>
<tr>
<td>cerebrospinal fluid pressure (mm Hg)</td>
<td>10.3 ± 1.6</td>
<td>5.5 ± 1.6†</td>
<td>6.3 ± 1.3†</td>
</tr>
</tbody>
</table>

*Difference from resting values statistically significant at \( p < 0.001 \).
†Difference from resting values statistically significant at \( p < 0.01 \).

Arterial pH, pressure of CO₂ and O₂, standard bicarbonate, and base excess were checked in short intervals throughout all experimental runs. In all preparations the body temperature of the experimental animals was kept close to 36°C.

**Results**

Base-line tracings made under physiological conditions, that is, in the absence of raised ICP and in arterial normotension and normocapnic normoxia show two distinct CSFP pulsations: larger sinusoidal and smaller rapid peak-shaped waves (Figs. 1 and 2). The slow rhythmic waves are also reflected in the sagittal sinus pressure (SSP) and CVP, and are synchronous with the frequency of respiration. The rapid CSFP wave is composed of a steep increase, a small dicrotic peak on the slope of the initial pressure rise, and some more or less distinct smaller peaks on the following lower part of the wave. The amplitude of the initial high peak varies between 1 and 2 mm Hg. The peak-shaped CSFP waves are mirrored in the sinus pressure pulsations, but both CSF and sagittal sinus pulse waves are different from the central venous pulsations. The initial high CSFP peak virtually coincides with the systolic pressure increase of the systemic arterial blood pressure (SABP). The following CSFP peaks at the end of the diastole are venous superpositions (central venous "A" wave) originating in the right atrium.

**Influence of Systemic Arterial Blood Pressure**

In the present animal preparations, intracranial CSF mean pressure was about 8 to 10...
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mm Hg. This value is consistent with data obtained in anesthetized dogs by other investigators. With a controlled stepwise decrease of MABP from 100 to about 45 mm Hg, mean CSFP fell to about 5 mm Hg (p < 0.01), and CBF decreased by about 50% as compared to the resting state (p < 0.01). However, when PaCO₂ was elevated from 36 to 80 torr by inhalation of 5% CO₂, CBF markedly increased, indicating that the cerebral vessels still responded to the CO₂ stimulus in deep normovolemic arterial hypotension. In spite of increased blood flow, mean CSFP was not significantly elevated (see Table 1). In three normoxic normocapnic dogs, SABP was increased by controlled intravenous infusion of angiotensin. The CSFP and its pulse amplitude increased with the elevation of the SABP (Fig. 3). The ICP increase was small at MABP levels of 130 and 150 mm Hg, respectively, but marked at 180 mm Hg (Table 2). When an insufficiency of the right atrium with a consecutive increase of right atrial pressure and CVP was produced by massive hyperinfusion, mean CSFP increased (Table 3), CSF pulsations rapidly became more and more venous in shape, and the right atrial “A” wave predominated (Fig. 4).

![Fig. 2. Base-line tracing of the cerebrospinal fluid pressure (CSFP). Respiration was recorded by using the infrared CO₂ analyzer, which determined the CO₂ concentration in the inspired and expired air of the experimental animal. Note the larger sinusoidal respiratory waves of the CSF pulsations.](image)

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Increase of mean CSFP during artificially elevated arterial blood pressure in three dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Arterial Blood Pressure (mm Hg)</td>
<td>Cerebrospinal Fluid Pressure (mm Hg)</td>
</tr>
<tr>
<td>95</td>
<td>7</td>
</tr>
<tr>
<td>130</td>
<td>9</td>
</tr>
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<td>95</td>
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<td>150</td>
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<tr>
<td>106</td>
<td>11</td>
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<td>180</td>
<td>22</td>
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</table>

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Elevation of central venous pressure and its influence on CSFP and MABP in two dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Venous Pressure (mm Hg)</td>
<td>Cerebrospinal Fluid Pressure (mm Hg)</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>10</td>
<td>14</td>
</tr>
</tbody>
</table>
FIG. 3. Tracing shows the intracranial pressure (ICP) raised by angiotensin, even at moderate arterial hypertension (MABP about 130 torr). Note the increase of cerebrospinal fluid pulse amplitude (CSFP) with the rise of systemic arterial blood pressure (SABP).

FIG. 4. Tracing shows predominance of right atrial "A" wave in the CSF pulsations in cardiac insufficiency. Right atrial pressure (RAP) increased after rapid intravenous hyperinfusion. SABP = systemic arterial blood pressure, CSFP = cerebrospinal fluid pressure.
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Influence of Raised Intracranial Pressure

When ICP was increased by progressively infusing artificial CSF into the cisterna magna, the rapid peak-shaped pulse waves of the CSF pulsations markedly changed their configuration. The venous superpositions completely disappeared and CSF pulse waves reflected the shape of the central aortic pressure wave, even at moderately increased ICP, that is, 20 to 30 mm Hg (Fig. 5). Another very constant finding was the increase in CSF pulse amplitude during increasing ICP (Fig. 6). On the other hand, a progressive decrease of the elevated CSF pulse amplitude could be observed during the reduction of intracranial hypertension (Fig. 7).

Influence of Hypoxic Cerebral Vasodilatation

At a PaO₂ of about 35 torr, the increase of mean CSFP was moderate but statistically significant. The pressure increase was due to marked cerebral hyperemia (see Table 4). In spite of the moderate increase of CSFP, the effect of hypoxemia on the CSF pulse wave amplitude and the configuration of the curve was similar to that of artificially induced marked intracranial hypertension. Venous superpositions disappeared and the CSF pulse curve showed only large peaks with high amplitudes (Fig. 8).

Discussion

Physiologically, the intrathoracic pressure changes during respiration are known to exert a marked influence on the systemic vascular pressures. During expiration the pressure in the superior vena cava system increases,

![Influence of Raised Intracranial Pressure](image)

**FIG. 5.** Tracing of the cerebrospinal fluid pressure (CSFP) curve after ICP had been increased and maintained at a mean pressure of about 20 torr. Note the arterial shape of the CSF pulse, even in moderate intracranial hypertension. SABP = systemic arterial blood pressure.

**TABLE 4**

Results of dynamic testing in normocapnic normoxia and normocapnic hypoxemia in six dogs

<table>
<thead>
<tr>
<th>Factors</th>
<th>Normoxia</th>
<th>Hypoxemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean arterial blood pressure (mm Hg)</td>
<td>108.3 ± 5.1</td>
<td>105.0 ± 7.8</td>
</tr>
<tr>
<td>arterial oxygen pressure (mm Hg)</td>
<td>121.2 ± 17.1</td>
<td>34.6 ± 6.4*</td>
</tr>
<tr>
<td>cerebral blood flow (ml/100 gm/min)</td>
<td>58.0 ± 8.9</td>
<td>132.0 ± 29.5†</td>
</tr>
<tr>
<td>cerebrospinal fluid pressure (mm Hg)</td>
<td>10.0 ± 1.4</td>
<td>15.0 ± 3.5‡</td>
</tr>
</tbody>
</table>

*p <0.001.
†p <0.01.
‡p <0.05.

![Influence of Hypoxic Cerebral Vasodilatation](image)

**FIG. 6.** Tracing shows increase of CSF pulse amplitude related to controlled infusion of artificial CSF into the cisterna magna.

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Fl. 7. Tracing shows decrease of the CSF pulse amplitude during stepwise withdrawal of CSF from the cisterna magna.

whereas during inspiration CVP drops. The basic physiological mechanism of this pressure effect has been extensively reviewed by Manoach, et al.\textsuperscript{28,29} In clinical practice, the effect of respiratory movements on CSF dynamics has recently been studied in hydrocephalic children by Yamada, et al.\textsuperscript{40} The respiratory pressure variations are transmitted to the intracranial CSFP via the CVP and are reflected as large sinusoidal waves superimposed on the rapid CSF pulsations. In the presence of a spinal block in the lower thoracic or lumbar spine, a dissociation of the respiratory waves may occur. Whereas the intracranial CSF waves follow the respiratory pressure variations of the superior vena cava system, the pressure fluctuations in the subarachnoid lumbar space display a phase displacement according to the respiratory pressures in the inferior vena cava; during inspiration the pressure rises, on expiration the pressure falls.\textsuperscript{2} This clearly demonstrates the major role of the systemic venous pressure in transmitting the respiratory intrathoracic pressure changes to the CSF spaces. The rapid pulsations of the intracranial CSF pressure, however, are different from the pattern of the genuine CVP fluctuations known to originate in the right atrium. Even the pressure waves in the superior sagittal sinus do not reflect the CVP changes, but resemble the intracranial CSF pulsations. This fact has also been observed by other investigators.\textsuperscript{41} Moreover, since the experimental investigations of Weed and Flexner,\textsuperscript{89} it is known that under physiological conditions intracranial CSFP and SSP are closely linked and that only a small pressure difference of about 2 mm Hg exists between the CSF space and the sinus. This may explain why the cerebral pulsations must be reflected almost to the same degree in the curves of both the CSF and the sinus pressures, provided that an obstruction of the cerebral venous outflow tract is absent. In markedly elevated ICP, however, CSFP and SSP may exist under very different pressures,\textsuperscript{3,15,39} whereas the cortical venous pressure parallels the rise in CSFP\textsuperscript{19} and reflects increased intracranial pulsations.\textsuperscript{38}

Under certain pathophysiological conditions, such as cardiovascular disturbances with right atrial insufficiency and increased CVP, the CSFP pulsations become more and more venous in shape and finally the "A" wave of the right atrium predominates. This has been shown previously also by experimentally induced atrioventricular block and by occlusion of the main pulmonary artery.\textsuperscript{1} However, in contrast to the assumption of Hamit, et al.\textsuperscript{17} the present investigations demonstrate that under physiological con-

![Fig. 7. Tracing shows decrease of the CSF pulse amplitude during stepwise withdrawal of CSF from the cisterna magna.](image)

![Fig. 8. Tracings show CSF pulsations during (left) normoxia (PaO\textsubscript{2} 120 torr), (center) moderate hypoxemia (PaO\textsubscript{2} about 60 torr), and (right) profound hypoxemia (PaO\textsubscript{2} 35 torr). Note the disappearance of venous superpositions and the steep arterial shape of CSF pulsations in the presence of hypoxia.](image)
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ditions the intracranial CSF pulse wave is not primarily venous but arterial in origin. This has already been stated by other investigators.\textsuperscript{1,8,10,38} Even the dicrotic notch of the arterial pulse may be mirrored in the CSFP curve.\textsuperscript{12,41} The arterial origin of the physiological CSF pulsations is further suggested by the present finding that mean CSFP, the result of the "diastolic" ICP and of the corresponding pressure wave amplitude, dropped in arterial hypotension and did not increase in hypercapnic hyperemia as long as the systemic blood pressure was kept hypotensive.

Another contributing but probably minor factor relating to the hypotensive decrease of cerebral perfusion pressure may be the reduction in CSF formation. It has recently been shown by Carey and Vela\textsuperscript{6} in dogs that CSF production fell by about 40% when MABP was decreased to 60 mm Hg. The importance of SABP both for the height and the configuration of the intracranial CSF pulsations becomes most evident in the presence of a progressive decrease of cerebrovascular resistance, that is, in cerebral vasodilatation that occurs in hypercapnia and hypoxemia and during autoregulation of CBF in raised ICP. With progressive cerebral vasodilatation the damping of the SABP in the brain is diminished and consequently the transmission of the arterial pressure head to the cerebral capillary bed is increased. This undamped transmission is readily reflected by an increase of the CSF pulse amplitude and by the completely arterial shape of the pulse waves. A marked elevation of the CSF pulse amplitude in raised ICP has been observed by several investigators\textsuperscript{4,8,10,12,38,41} and is probably due to changed cerebral tissue compliance.

One major factor in cerebral bulk compliance seems to be cerebrovascular reactivity. In the presence of decreased cerebrovascular resistance, arterial hypertension will lead to an increase of the cerebral pulse amplitude and thus must exert a very unfavorable influence on the ICP. It has been shown that in intracranial hypertension the undamped transmission of raised systemic blood pressure to the dilated cerebral vascular bed favors the propagation of brain edema.\textsuperscript{21,22,32,84} Furthermore, it has been demonstrated in animal preparations that in raised ICP the so-called volume-pressure response (the increase of ventricular CSFP following the artificial rise of CSF volume by injecting very small amounts of artificial CSF into the lateral ventricles) can be considerably intensified by arterial hypertension.\textsuperscript{24} Löfgren\textsuperscript{26} has demonstrated that variations in mean arterial pressure in the range of 25 to 230 mm Hg produced approximately a fivefold change in the elastance of the brain. The damping of the arterial pulse by the cerebral vascular tone seems to be a rather sensitive mechanism: Kaufman, et al.\textsuperscript{29} have recently shown in mongrel dogs subjected to CSF drainage of one of the lateral ventricles that on the side of the shunted ventricle the CSF pulse amplitude was slightly lower than in the opposite lateral ventricle. Moreover, in his studies of the CSFP volume curve in dogs, Löfgren\textsuperscript{26} has observed that even at a CSFP of about 15 mm Hg a small volume increment rapidly transforms the intracranial system "to a state of high elastance." This observation fits well with the present CSFP curves, which displayed a rapid attenuation of venous pulse superpositions and a purely arterial shape even at a moderate (about 20 mm Hg) increase of ICP. This change of pulse-wave configuration and amplitude was more marked, even at lower ICP levels, when the cerebral vasculature was dilated by systemic hypoxemia.

The significance of cerebrovascular reactivity for the configuration of the CSF pulse curve and intracranial bulk compliance should also be considered in cases of hypertensive encephalopathy. Whereas physiologically, an increase of arterial blood pressure is met by a corresponding vasoconstriction of the cerebral vessels due to autoregulation which keeps CBF constant, a "break-through" of the vasoconstriction with forced vasodilatation may occur in hypertensive encephalopathy.\textsuperscript{11,14,18,23,37} Under such conditions it is conceivable that arterial hypertension may increase ICP. It has been observed long ago that CSFP may be elevated in hypertensive patients,\textsuperscript{30} and consistent with the present findings Adolph, et al.\textsuperscript{1} have demonstrated in animal preparations that after rapid intravenous injection of norepinephrine, CSFP rose coincident with the increase in arterial blood pressure before any change in CVP occurred. A similar effect on brain tissue pressure has been observed by Clark, et al.\textsuperscript{7} The present data suggest that the increase of CSFP is more marked beyond the upper limit of autoregulation, that is,
beyond 160 to 180 mm Hg arterial mean pressure.

Clinically, it should be borne in mind that the SABP may be an important factor in raising ICP, particularly in hypercapnic or hypoxic cerebral vasodilatation and in vasomotor paralysis. Thus, it must be questioned whether the Cushing reflex really is a beneficial mechanism protecting the brain against further ischemic and hypoxic damage. Recent experimental investigations do not prove this to be the case. In monitoring intracranial CSF pressure in neurosurgical patients, special interest should be focused not only on the height of mean CSFP, but also on the pressure pulse curve, because the configuration and pulse amplitude of the CSF pulsations can be regarded to a certain extent as an index of the state of intracranial elastance or cerebral bulk compliance. Furthermore, a progressive change of the arterial shape of the pressure curve to one more like that of CVP can be an early sign of cardiac failure and insufficient cerebral perfusion. Thus, tracing the intracranial CSF pulsations may be a useful additional method for controlling intracranial hypertension and evaluating intensive-care therapy.

References

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