Does thoracic pump influence the cerebral venous return?

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Zamboni P, Menegatti E, Pomidori L, Morovic S, Taibi A, Malagòni AM, Cogo AL, Gambaccini M. Does thoracic pump influence the cerebral venous return? J Appl Physiol 112: 904–910, 2012. First published December 15, 2011; doi:10.1152/japplphysiol.00712.2011.—We assessed the hemodynamic effects induced by the thoracic pump in the intra- and extracranial veins of the cerebral venous system on healthy volunteers. Activation of the thoracic pump was standardized among subjects by setting the deep inspiration at 70% of individual vital capacity. Peak velocity (PV), time average velocity (TAV), vein area (VA), and flow quantification (Q) were assessed by means of echo color Doppler in supine posture. Deep respiration significantly increases PV, TAV, and Q, but it is limited to the extracranial veins. To the contrary, no significant hemodynamic changes were recorded at the level of the intracranal venous network. Moreover, at rest TAV in the jugular veins was significantly correlated with Q of the intracranial veins. We conclude that the modulation of the atmospheric pressure operated by the thoracic pump significantly modifies the hemodynamics of the jugular veins and of the reservoir of the neck and facial veins, with no effect on the vein network of the intracranial compartment.

METHODS

Forty-four healthy volunteers participated in the study, 21 men and 23 women; mean age was 27.5 ± 5.0 yr. The study was approved by the local ethical committee. All the study participants signed an informed consent.

Assessment of vital capacity. All subjects underwent the assessment of slow vital capacity (VC) according to international guidelines (16). Assessment of VC was performed in the vascular lab of the Vascular Diseases Center, University of Ferrara, prior to assessment of venous hemodynamics, by means of a portable instrument (SpiroPalm, COSMED srl, Roma, Italy). Examination conditions such as time period of the examination and room temperature were the same for all investigated subjects (between 2 and 6 PM; 23°C). The assessed parameters were measured in both sitting and supine positions, because in the supine position VC is reported to be 5–10% less than in an upright position (2). After subject instruction, the assessment of VC was performed with subjects using a mouthpiece and wearing a nose clip and required at least three proper tidal maneuvers. The technician carefully observed that total lung capacity and residual volume were reached. A minimum of three acceptable VC maneuvers were obtained with a difference <0.15 liters. The largest value from at least three acceptable maneuvers was selected.

Method for thoracic pump standardization. Evaluation of the activation of the thoracic pump needed to be standardized for different subjects, who subsequently underwent the assessment of venous hemodynamics. We chose a tidal volume corresponding to 70% of VC to standardize the value of deep inspiration among subjects (22). To this aim, we used an instrument originally designed to exercise respiratory muscles (SpiroTiger, IDIAG AG-Fehraltorf, Switzerland). It avoids, in respect to a spirometer, the effect of hyperventilation induced hypocapnia, which is known to affect the cerebral blood flow. The instrument maintains normocapnia by allowing a partial CO2 rebreathing (15). Furthermore, this instrument allows the subject to check the correct amount of ventilation on the screen. The device consists of a hand-held unit connected to breathing bags of variable sizes, depending on the individual VC previously assessed. Each subject was asked to fully fill and empty the bag by breathing air during the hemodynamic assessment.

Assessment of venous hemodynamic parameters of the intracranial cerebral venous system. The intracranial cerebral venous system is comprised of two main networks of veins, which can be investigated by means of Doppler sonography: 1) the intracranial veins, including the parenchymal network (N3) [basal vein of Rosenthal (BV), Galen vein, deep middle cerebral vein, etc.], and 2) the network of the sinuses of the dura mater (N2) (posterior fossa sinuses: straight sinus (SS), transverse sinus; sinuses of the base of the skull: sphenoparietal and superior petrosus sinus (3, 4, 23, 29)).

We chose the BV and the SS for obtaining information, respectively, from the parenchymal veins and sinuses of the dura mater on the basis of the reported success rates of transcranial investigation (3). The intracranial veins and sinuses were studied in supine position by means of echo color Doppler equipment (ESAOTE MyLab 70, Genoa, Italy) through a temporal bone window in the axial plane (probe phased array 2.0–3.0 MHz; PRF 0.7 MHz, insertion of color wall filter for low velocity, and without angle of incidence of the
ultrasonic beam). The intracranial structures were identified according to their anatomic location and the direction of flow as previously described (3, 4, 19, 29). By placing the pulsed wave Doppler sample (PW) in the identified vein, the peak velocity (PV; cm/s) was measured in all 44 subjects; we also assessed in 33 subjects (15 men, 18 women, mean age 30 ± 8.6 yr) the time average velocity (TAV; cm/s), the vein area (VA; mm²), and the flow (Q; ml/min). Measurements were obtained in supine position through either right or left temporal bone window, depending on quality of imaging. Data were collected at rest, after activation of the thoracic pump after 30 s of respiration at individual 70% VC, and during the immediate subsequent expiration phase.

Assessment of blood flow velocity of the extracranial cerebral venous system. The extracranial venous network (N1) is comprised of the internal jugular veins (IJVs) and the vertebral-azygous venous system. The former represent the main cerebral blood collectors in supine position, and were therefore chosen for assessment (17, 18, 21, 24, 25). In N1, J1 is connected by several anatomical anastomosis with the complex network of the facial and neck veins (N4), in turn capable of connecting intra- and extracranial veins (17, 25). All measurements were performed and results noted in supine position at rest, after thoracic pump activation at 70% of subject’s VC, and during the immediate subsequent expiratory phase. Prior to measurement, the subject was placed on a tilt chair and moved to supine position, the head comfortably placed in mid position, without applying any unnecessary pressure to the neck with the probe. For measurement of thoracic pump influence on extracranial venous flow, subjects were asked to breathe into the Spirotiger (described previously) through the mouthpiece and into the breathing bag, which had a previously set volume to 70% of tested individual’s VC, while data were obtained. TAV, VA, and Q were measured in the same 33 subjects defined above at three reference points of the IJVs, on both right and left side. The lower segment of the IJVs is defined J1 (27) and corresponds to the segment close to the junction of the IJVs with the subclavian vein. J2, or the middle segment, is the point where the vein is in an anatomical relationship with the more lateral contour of the thyroid gland. In J3, or the upper segment of the IJV, the measurements were taken as distally as possible in the IJVs, before its passage through the jugular foramen into the skull. Finally, in all 44 subjects, PV was assessed at J2 level. All assessments were done by using a linear array probe 7.5–11 MHz, in the longitudinal aspect, by placing the Doppler sample volume in the middle of the lumen with angle of incidence of the ultrasonic beam 45–60° and PRF not lower than 1.4 MHz (27). Careful placement of the cursor in the middle of the vessel and detailed marking of closer and further vessel wall made it possible to obtain the most precise TAV, VA, and Q measurement. The TAV measurement was obtained from a 4-s cycle by marking the flow spectrum on the screen and using automatic calculation with the software of the ultrasound machine. For obtaining the VA measurement, two cursor points were carefully placed on lumen edges of the near and far vessel walls, perpendicular to the vessel position on the screen. The Q value was automatically calculated from these two measurements.

Statistical analysis. Data are expressed as means ± standard deviations. Data collected from IJVs were analyzed considering the set of all measurements taken in the right and left side, both as separated values corresponding to the different segments J1, J2, J3, and as a whole. Furthermore, on this basis, data from IJVs were also used for analysis considering the mean of all values for each subject.

The normal distribution of the data was verified by the Kolmogorov-Smirnov test. Data were compared using unpaired Student’s t-test, Mann-Whitney test, and Kruskall-Wallis test, as appropriate. To assess the relationship among intracranial and extracranial parameters (considering the mean of all values for each subject) a Pearson correlation analysis was performed. A P value of 0.05 or less was considered statistically significant. Data were analyzed using the software program Medcalc 11.6 (Medcalc Software, Mariakerke, Belgium).

RESULTS

As reported in Fig. 1, the VC assessed in the first phase of our study in investigated subjects was without significant differences in both sitting and supine positions. The complete set of hemodynamic parameters at the level of the BV was successfully measured in 67% of subjects and at the SS in 45%. Both IJVs were successfully investigated in all subjects. Table 1 shows the PV assessed in the different segments of the cerebral venous system at rest and after standardized deep inspiration. In the IJVs, the deep inspiration significantly increased the PV from 52.8 ± 19.4 to 72.5 ± 26.9, whereas in both the intracranial venous networks did not (Fig. 2). The same behavior has been confirmed by the analysis of the other parameters describing venous hemodynamics and are given in Table 2. TAV, VA, and Q are reported at rest and at 70% VC in all the segments comprising the cerebral venous system, also including the percentage rate of variation measured in the two respiratory conditions under study. We do not show flow parameters assessed during the immediate subsequent expiratory phase because they were significantly different than at deep respiration. Significant changes were found in the TAV assessed at rest and at deep inspiration, respectively, at the upper and mid level of the IJVs and in the IJVs as a whole. In the latter, despite the big variability among individuals, which characterizes the cerebral venous return, we recorded an increased TAV rate of more than 50% (P < 0.008). Interestingly, we did not record only increased PV and TAV under 70% VC in the IJVs, but also assessed a significant increase of the Q at
the activation of the thoracic pump, either in J2 and along the entire IJVs, where the average variation was even 80% more (Table 2). To the contrary, no significant changes were recorded at the level of the intracranial venous networks N3 and N2, where we simply found a trend toward significance in the Q of the SS (Table 2).

By comparing the flow trace of the BV with those recorded in the SS and IJVs of Fig. 2, it can be clearly seen the modulation induced by the vis a fronte by approaching the chest. The BV trace is almost linearly constant and there is little modulation induced by deep respiration in the SS trace, whereas the magnitude of the flow modulation induced by the pump is very well apparent in the IJVs. This is further confirmed by the TAV values reported in Table 3, showing significantly increased values of TAV along the IJVs from the jugular foramen to the base of the neck, with a sequential increase in velocity from J3 to J2 and from J2 to J1 (Fig. 3). This supports the presence of a significant modulation reasonably induced by the atrium and pleural negativity on the IJVs.

We analyzed our findings according to sex, with no significant differences between men and women at rest and at 70% VC in all the examined veins (data not shown).
Table 2. Values of all parameters measured in the intracranial and extracranial systems of 33 subjects under study at rest and after activation of the thoracic pump normalized to 70% of vital capacity

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TAVrest (cm/s)</th>
<th>TAV70%VC (cm/s)</th>
<th>BV (mm^2)</th>
<th>SS (mm^2)</th>
<th>IJVs-J3</th>
<th>IJVs-J2</th>
<th>IJVs-J1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Values are means ± SD (n = 66)</td>
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</tr>
</tbody>
</table>

Values are means ± SD. BV (n = 66); SS (n = 66). J3, J2, J1, upper, medium, and lower segment of IJVs, respectively. P value of comparison among the three measurements (Kruskall-Wallis test).

Analysis of the relationship between intra- and extracranial venous hemodynamics. Further analysis was performed to investigate the presence of correlations between hemodynamic parameters in the extra- and intracranial venous networks. In Table 4 the correlation between the TAV in the IJVs and the Q measured in the intracranial veins are given. Interestingly, the TAV of the IJVs measured at all levels at rest correlates with Q recorded in the BV and in the SS at rest. The correlation between TAV of the IJVs and SS is maintained also under deep inspiration, but surprisingly, at the level of the BV under deep respiration the relationship becomes an inverse correlation, reaching level of significance when the TAV recorded at the upper level of the IJVs is matched with the Q at the level of N3 (r = −0.47; P = 0.05).

Model of thoracic pump influence on cerebral venous hemodynamics. To express the influence of thoracic pump at rest and activation of the respiratory muscles on cerebral venous return we propose a hemodynamic lumped model describing qualitatively the cerebral venous return. Since the lumped model basically describes venous networks, we refer to N3 for the BV, to N2 for the SS, to N1 for the IJVs, and finally, to N4 for the neck and facial veins. Models describing intracranial dynamics and cerebrovascular control are already available in the literature (6, 7, 11–14, 20). Here, by using the same methodology, we describe qualitatively the cerebral venous return in relation to vis a fronte to explain the data collected in the present experiment (Fig. 4).

DISCUSSION

The concept of vis a fronte is widely accepted in human physiology and medicine (9, 18, 19). However, no data are available on changes in venous hemodynamics at rest and after deep inspiration along the main intracranial and extracranial veins, comprising the highly complex cerebral system. Data are probably lacking because of the difficulty of measuring and comparing the amount of the thoracic pump activation among subjects. The novelty of our study is to propose a methodology permitting to standardize “deep inspiration” with a precise quantification comparable among different subjects. We herein propose a normalized deep inspiration settled at 70% VC in all the subjects admitted to the study. Once standardized, we measured the PV and found the blood attraction of the thoracic pump to be the more reliable hemodynamic parameter, as well as other hemodynamic parameters, TAV, Q, and VA, which can be assessed noninvasively by means of Doppler sonography (1, 3, 10, 19, 21, 29).

Our findings measured at rest demonstrate that all the values of the investigated venous hemodynamic parameters are higher...
as the veins are anatomically closer to the chest, confirming the primary role of vis a fronte as a motor mechanism. The activation of the thoracic pump through deep inspiration seems to further elicit blood return from the brain, but limitedly to the extracranial segments. PV, TAV, and Q are significantly higher in the IJVs during respiratory muscular contraction of the chest (Tables 2 and 3; Figs. 2 and 3). In contrast, respiratory mechanism does not significantly influence venous hemodynamics in the intracranial segments, either parenchymal vein, or in the dural sinuses. We did not find any significant variation of velocity and Q in respect to the measurement performed at rest. Because no variation in blood velocity and Q were measured in the intracraniap venous segments, apparently there is no explanation of the increased Q in the IJVs measured especially between J3 and J2 level (Table 2). Specifically in these segments the outlets of facial and neck veins into the internal jugulars are located. For this reason we may assume that the increased Q can be explained by an aspiration of blood from the N4 toward the main collector, induced by deep inspiration. We know that the atmospheric pressure is an important component of transmural pressure for the extracranial venous network and can be modulated by deep inspiration; on the other hand, the skull prevents any modulation of the atmospheric pressure in the intracranial veins. To understand such experimental results we can now make use of the developed hemodynamic model (see APPENDIX). The model accounts for the finding that during deep inspiration the flow increases within the IJVs (Eq. 1) whereas such phenomenon is not measured in the intracranial veins. The blood velocity in the IJVs increases because of the increased flow. The increased velocity of the blood produces a pressure decrease at the outlets of network N4 (Fig. 4). The variation in time of the pressure drop at this level, because of the deep inspiration activation, induces a flow from the neck and facial veins. Such a flow is attributable to the blood contained in the neck veins capacities (i.e., venous compliance) that, according to Eq. 2, flow in the IJVs when the pressure drop changes over time. In conclusion, the model supports the hypothesis that cerebral venous return is driven by the thoracic pump. In addition, the flow discontiuity between the intracranial compartment (N3, N2) and the IJVs (N1) during the deep inspiration is explained by the compliance of the neck and facial veins (N4). The emptying of N4 during active respiration toward N1 explains the increased Q in the IJVs in the absence of Q variation from the intracranial networks as an alternative source of blood.

Table 4. Relationship between Q values and extracranial TAV values measured at rest and after activation of the thoracic pump normalized to 70% VC in 33 subjects under study

<table>
<thead>
<tr>
<th></th>
<th>Q BV Rest</th>
<th>Q BV 70% VC</th>
<th>Q SS rest</th>
<th>Q SS 70% VC</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>TAV IJVs-J3-J2-J1 rest</td>
<td>0.56</td>
<td>0.005</td>
<td>0.03</td>
<td>0.88</td>
</tr>
<tr>
<td>TAV IJVs-J3-J2-J1 70%VC</td>
<td>0.18</td>
<td>0.43</td>
<td>0.45</td>
<td>0.04</td>
</tr>
<tr>
<td>TAV IJVs-J3 rest</td>
<td>0.58</td>
<td>0.002</td>
<td>0.20</td>
<td>0.38</td>
</tr>
<tr>
<td>TAV IJVs-J2 rest</td>
<td>0.32</td>
<td>0.17</td>
<td>0.18</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Values in bold are significant (P < 0.05).
A possible limitation of our study is the success rate of detection by ultrasound of the dural sinuses, reducing the magnitude of our statistical sample. However, the objective technical difficulties of transcranial Doppler assessment of the hemodynamics into the SS were previously described, and our success rate of assessment is not different from that previously reported (3, 19, 29). Also VA measurement of the intracranial veins is based on the color spot contouring. Although this has the advantage to being a noninvasive assessment, it is not considered a highly accurate measurement. However, the VA did not show significant changes and seems to be a less significant parameter. A further discrepancy in our findings might be the lack of significant increase in both the Q and TAV measured at the lower level of IJVs, the J3 level (Table 2). This data can be explained by the presence of the jugular valve in ~90% of human subjects, leading to significant turbulences (17) (Fig. 3). Of course, both the valve leaflets and the turbulent flow may affect the measurements, creating a segment of discontinuity in the venous outflow from the brain. Finally, one more limitation of our conclusions could be the intracranial veins located behind the orbit. It should be expected that cavernous and petrosus sinuses, differently from the deep paracavernous veins and sinuses, could be modulated by respiration, but our investigation did not involve these venous segments (28).

Conclusions. We conclude that the thoracic pump influences cerebral venous return because at rest the velocity of the IJVs is related to the Q of the intracranial veins, although the traces did not show any modulation, as clearly shown by the straight wave exhibited by the BV (Fig. 2). Active respiration further significantly increases all the hemodynamic parameters of the IJVs thanks to modulation of the atmospheric pressure, something lacking in the intracranial compartment because the skull prevents any action on veins on behalf of the atmospheric pressure.

APPENDIX

The thoracic pump produces a pressure $P_T$. In this model $P_T$ is attributable to the rest thoracic pump pressure $P_R$ plus the pressure induced by the 70% deep inspiration $P_{70\%}$. We consider $P_R$ as constant in time, whereas the deep inspiration pressure $P_{70\%}$ is a periodic function of time. The total pressure due to thoracic pump is then given by $P_T(t)=P_R+P_{70\%}(t)$.

At rest, the deep inspiration pressure $P_{70\%}=0$ so the flow $Q_I$ in N1 (IJV) is due to the entrance flow $Q_{VIC}$ from N2 and N3. The activation of the deep inspiration pump gives rise to a significant change of the pressure difference $\Delta P$. Such change over time generates two different effects:

The pressure drop in N1 is $\Delta P = P_T - P_V$, and the flow $Q_I$ is given by:

$$Q_I = \frac{\Delta P}{R_I}$$

Since $P_{70\%}$ is negative, $\Delta P$ during deep inspiration is greater (in module) than $\Delta P$ at rest, hence the flow $Q_I$ increases during deep inspiration.

The variation in time of $\Delta P$ allows the blood stored in N4 capacity to generate the flow $Q_N$. In fact, the velocity of the blood in N1 increases as effect of the increased flow, which in turns produces a decrease of $P_V$. The pressure difference $\Delta P = P_V - P_N$ at N4 increases in module and the flow $Q_N$ is given by:

$$Q_N = -C_N \frac{d}{dt} (\Delta P)$$

The flow $Q_N$ joins $Q_I$, which during the deep inspiration becomes $Q_I = Q_{VIC} + Q_N$. Finally, the flow $Q_{VIC}$ is left unchanged because the increased pressure difference is compensated by the flow $Q_N$.

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DISCLOSURES

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AUTHOR CONTRIBUTIONS


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