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Physical Characteristics in the New Model of the Cerebrospinal Fluid System

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A B S T R A C T

It is unknown which factors determine the changes in cerebrospinal fluid (CSF) pressure inside the craniospinal system during the changes of the body position. To test this, we have developed a new model of the CSF system, which by its biophysical characteristics and dimensions imitates the CSF system in cats. The results obtained on a model were compared to those in animals observed during changes of body position. A new model was constructed from two parts with different physical characteristics. The »cranial« part is developed from a plastic tube with unchangeable volume, while the »spinal« part is made of a rubber baloon, with modulus of elasticity similar to that of animal spinal dura. In upright position, in the »cranial« part of the model the negative pressure appears without any measurable changes in the fluid volume, while in »spinal« part the fluid pressure is positive. All of the observed changes are in accordance to the law of the fluid mechanics. Alterations of the CSF pressure in cats during the changes of the body position are not significantly different compared to those observed on our new model. This suggests that the CSF pressure changes are related to the fluid mechanics, and do not depend on CSF secretion and circulation. It seems that in all body positions the cranial volume of blood and CSF remains constant, which enables a good blood brain perfusion.

***Key words**: cerebrospinal fluid, model, modulus of elasticity, changes of position*

Introduction

It is generally accepted that the cerebrospinal fluid (CSF) is secreted in greater part (about 70%) by the choroid plexus and in the remaining part (about 30%) by the ependyma inside the brain ventricles[1,2]. Newly formed CSF flows from the ventricles to cisterna magna and subarachnoid space. From the subarachnid space CSF is absorbed passively under the hydrostatic pressure gradient through subarachnoid villi into dural venous sinuses on the brain convexity. Recently there have been numerous studies claiming that CSF can be significantly absorbed into the extracranial lymph[3,4].

Normal CSF pressure in human in a horizontal position varies from 10 to 15 cm H_2O[5]. CSF pressure higher than 20 cm H_2O represents the intracranial hypertension. In accordance to Monroe-Kellie doctrine, normal intracranial pressure depends on the balance of the brain tissue volume, blood volume and the volume of CSF that completely fill the cranial space. If one of these volumes increases, and the remaining two do not decrease proportionally, the increase of the CSF pressure would occur[5]. It is known that the CSF pressure inside the cranium changes depending on the body position. Magnes has shown on a large series of patients that a transient negative CSF pressure appears inside the cranium during shifting of the body from horizontal to upright position[6,7]. Appearance of the transient negative CSF pressure is explained by the simultaneous redistribution of the blood and the CSF from the cranial to the hydrostatically lower parts of the body under the influence of gravity[8–10]. Namely, it is believed that during the verticalisation of the body, the intracranial blood volume decreases due to collapse of veins in the cranium[5,11]. In addition, it is assumed that there is a shift of a smaller volume of the CSF from the cranial to the spinal subarachnoid space[8].

Intracranial dura is fixed to the bone surface, therefore intradural volume in cranium is practically unchangeable. Opposite to that, in the spine, the dura is only partially fixed to the bone and so spinal intradural volume can be significantly changed due to its distensibility. Therefore, the simultaneous decrease of two intra-

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cranial volumes (blood, CSF) during the change of body position should create vacuum inside cranium. According to physics this is not possible. For that reason we assume that during verticalisation of body only the pressure of the CSF inside the cranium is changed whereas volume of the fluids or brain tissue remains unchanged.

In order to test our hypothesis we have constructed a new model of the cerebrospinal system which consists of two parts with different physical characteristics. Namely, this new model is made of a plastic tube with rigid walls closed at one end which represents the cranial part, and a long and narrow rubber baloon which represents the spinal part of the system. Therefore the model has a »cranial« part that cannot change its volume, and a »spinal« part that is able to change volume in each segment. This model is by its dimensions and physical characteristics designed to imitate the CSF system in cats. Pressure changes in two parts of the model during changes of its position from horizontal to vertical were compared with those obtained in lateral ventricle and lumbar subarachnoid space of cats during the same body position changes in our preliminary experiments[12].

In addition, we have tested the physical characteristics of the »cranial« and »spinal« part of the new cerebrospinal system model. Thus, we have subjected the fluid inside the »cranial« part of the model to different forces to demonstrate that without fluid volume changes significant fluid pressure changes can be obtained, and have determined the Young's modulus of elasticity of the rubber baloon, which represents »spinal« part of the model.

Materials and Methods

Construction of a new model of craniospinal system and pressure measurement

A new model of CSF system is made of two different materials which enable main biophysical characteristics of the cranial (unchangeable volume) and spinal (changeable volume) part of the CSF system. In construction of the CSF system model, we took into account the anatomical dimensions of the CSF system in cats. »Cranial« part is made of a plastic tube 6 cm long with inner diameter of 0.6 cm and wall thickness of 2.0 mm. This length of a plastic tube with a rigid wall is chosen because it represents the mean distance from the frontal sinuses to foramen magnum, as found in 5 cats by x-rays of the animal skull. »Spinal« part is made of a rubber baloon 31 cm in length (Natural Rubber Latex, Gemar, Casalvieri, Italy). This length is similar to the mean distance between cisterna magna and lumbar subarachnoid space at the level L3 vertebra where the pressure in cats was measured. Measuring cannula in the »cranial« part of the model was placed 4 cm proximally from the lower end of the plastic tube (Figure 1), which corresponded to the distance between the cranial cannula and foramen magnum in cats. Second cannula was placed at the base of the rubber baloon so that the total distance between the two measuring cannulas was 35 cm (Figure 1).

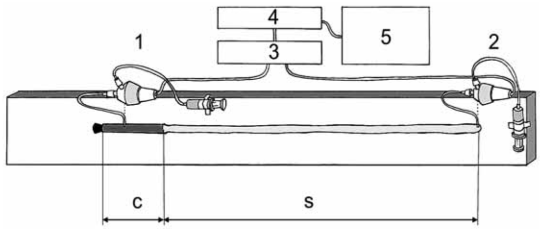

Fig. 1. Scheme of the cerebrospinal fluid system model. C – »cranial« part; S – »spinal« part; 1 – pressure transducer connected to canula in the cranial part of the model; 2 – pressure transducer connected to cannula in the spinal part of the model; 3 – Quand Bridge; 4 – Powerlab/800; 5 – personal computer.

Before measuring the pressures, the model was filled with artificial CSF[13] without the presence of air bubbles and fixed on a board (Figure 1). The pressure transducers (Gould P23 ID, Gould Instruments, Cleveland, OH, USA) were fixed at the same level as the measuring cannulas and connected to the computer via amplifier (QUAD Bridge i PowerLab/800, ADInstruments Ltd., Castle Hill, NSW, Australia). Pressures were measured in horizontal (0°) and upright position (90°). In the preliminary experiments, cats were fixed on a board in prone position. As the board changed its position, the mentioned pressures were measured in both horizontal and upright position in the same way as it was done in the model.

Elasticity examination of the »spinal« part of the model

From a rubber baloon identical to the one from which the »spinal« part of the model was made, the rectangle strap of 0.9 cm in width and 12 cm in length (the wall thickness of the baloon is 0.31 mm) was cut. The strap was than fixed on a stand 70 cm high. On the loose end of the strap, different weights (n=13) of 20 g up to 500 g were fastened and elongation was mesaured. The modulus of elasticity was calculated using the following formula: modulus of elasticity (Y=strain (σ)/deformity (δ)[14], where strain is a ratio of the gravity force (F=mg) and the surface (A), and deformity is a ratio of the change in length (Δl) and the starting length (l).

$$Y = \frac{\sigma}{\delta} = \frac{\frac{mg}{A}}{\frac{\Delta l}{l}}$$

The artificial CSF pressure changes in the »cranial« part under the influence of various forces

A plastic syringe which has the same dimensions as the »cranial« part of model was filled with artificial CSF and its nozzle connected to the pressure transducer (Gould P23 ID, Gould Instruments, Cleveland, OH, USA) which was connected to the computer via amplifier (QUAD Bridge i PowerLab/800, ADInstruments Ltd., Castle Hill, NSW, Australia) (Figure 2).

Two series of fluid pressure measurements were performed. In the first series, the piston of the syringe was faced upwards (Figure 2a) and than weights of 20 g, 100 g and 200 g were consecutively positioned on top of the piston. In the second series, the piston of the syringe was faced downwards (Figure 2c) and than the same weights of 20 g, 100 g and 200 g were hanged on the piston. As we expected, the shift of the piston inside the syringe in both series of experiments was undetectable.

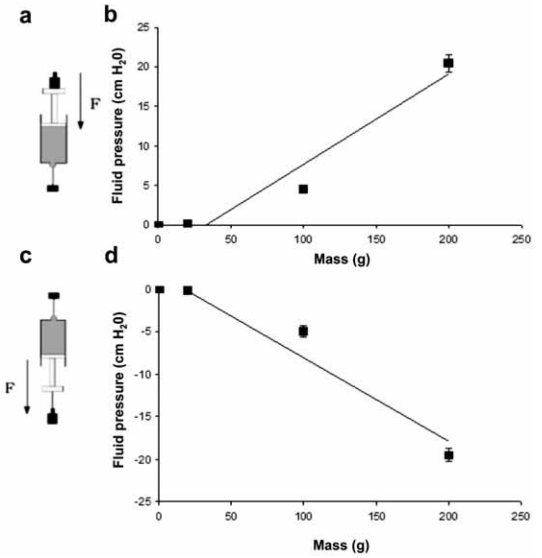

Fig. 2. Changes in fluid pressure (cm H_2O) inside the injection syringe during pressing (a,b) or pulling out the piston (c,d) by burdening it with weights of 20 g, 100 g and 200 g. The points are mean value of seven measurements, while the vertical lines are S.E.M.

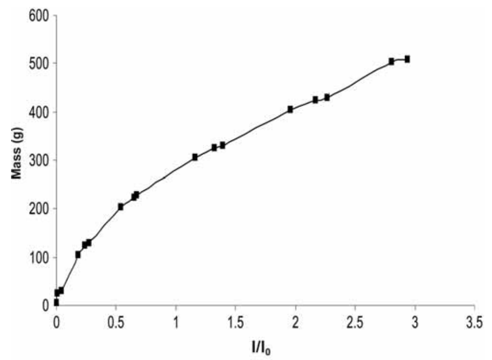

Fig. 3. Deformity (l/l_0 – A ratio between the measured length change and the starting lenght) of the »spinal« part of a cerebrospinal system model in a longitudinal direction during burdening with weights of different masses (g). A single typical experiment is shown.

Statistical analysis

All data were presented as means ± standard error of mean (SEM). Statistical significance of differences was determined by Student *t* test and $p<0.05$ was considered statistically significant.

Results

Figures 2a and 2b show an increase of artificial CSF pressure inside the plastic syringe without any measureable artificial CSF volume changes. On the other side, Figures 2c and 2d show decrease of artificial CSF pressure without any detectable fluid volume changes inside the plastic syringe. Observed pressure changes were dependent on the weights used. This clearly implies that within »cranial« part of our model it is possible to create significant changes in the fluid pressure (from –20 cm H_2O to + 20 cm H_2O) without any significant changes in the fluid volume.

Figure 3 shows a typical experiment in which the modulus of elasticity of the »spinal« part of our model is determined. By burdening the strap of rubber balloon with weights of smaller mass (up to 125 g), the obtained modulus of elasticity Y_1 was 1.417×10^6 N/m^2. Using the weights of larger masses, the occurred modulus of elasticity Y_2 was 0.458×10^6 N/m^2.

Table 1 shows the values of fluid pressure changes in »cranial« and »spinal« part of the model in horizontal and upright position, as well as values of CSF pressure in lateral ventricle and lumbar subarachnoid space in 4 cats during preliminary experiments[12]. In horizontal position the pressures in the »cranial« and »spinal« part of the model were similar (Table 1). In horizontal position the CSF pressures in the lateral ventricle (15.1±1.2 cm H_2O) and in the lumbar subarachnoid space (14.2±1.3 cm H_2O) in cats were also similar and did not statistically differ ($p<0.1$). The pressure inside the »cranial« part in upright position was negative or subatmospheric (–4.1±0.1 cm H_2O) and in the »spinal« part it was positive (31.0± 0.1 cm H_2O). In cats in the upright position the CSF

TABLE 1

CHANGES IN PRESSURE (CM H_2O) OF THE FLUID INSIDE THE »CRANIAL« AND »SPINAL« PART OF THE MODEL (N=5) AND CHANGES IN CSF PRESSURE INSIDE THE LATERAL VENTRICLE (LV) AS WELL AS IN THE LUMBAR SUBARACHNOID SPACE (LSS) IN CATS (N=4) WHILE CHANGING POSITION FROM HORIZONTAL TO VERTICAL (90°). MEAN VALUES OF PRESSURES±STANDARD ERROR OF THE MEAN ARE PRESENTED.

	Model		Cat	
	»cranial« space (cm H_2O) (n=5)	»spinal« space (cm H_2O) (n=5)	LV(cm H_2O) (n=4)	LSS (cmH_2O) (n=4)
Horizontal position	11.3±0.1	12.1±0.1	15.1±1.2	14.2±1.3
Vertical position	–4.1±0.1	31.0±0.1	–3.9±0.2	33.5±1.1

pressure was also negative in lateral ventricle (–3.9±0.2 cm H_2O), and positive in the lumbar subarachnoid space (33.5±1.1 cm H_2O). In an upright position the CSF pressures in lateral ventricle and lumbar subarachnoid space of cats were not statistically different from fluid pressures observed inside the »cranial« and »spinal« part of our new model ($p<0.1$).

Discussion

Existing CSF system models given in literature so far were made of glass pipes in the entire length of the craniospinal system, which were completely closed, or closed at one end using a small piece of plastic material[5]. Graphic analysis of the pressures inside these models was used to attempt to explain the changes in CSF pressures observed in animals and humans during changes of body position. However, there is no data refering to measurement of pressure changes in models themselves.

Unlike the above mentioned models, our model completely imitates the pressure changes inside the CSF system of living organisms in different body positions (Table 1). Namely, our new model has main anatomic and biophysical features of the CSF system in cats. The model consits of the »cranial« part 6 cm in length (the distance between frontal sinuses and foramen magnum in cats, see Material and Methods) whose volume cannot be changed (rigid plastic tube) and »spinal« part 31 cm in length (around 30 cm is the average distance from foramen magnum to the L3 vertebra in cats) whose volume can be changed (oblong rubber baloon) (Figure 1).

Prior studies show that spinal intradural volume, contrary to intradural volume inside the cranium, can be considerably changed[15]. In the cranium dura is firmly attached to the bone and intradural volume cannot be changed significantly. On the other hand, the spinal dura is only partially attached to the vertebrae and is separated from the bone by an epidural space filled with venous plexus and fatty tissue. So it was observed that the lumbar space significantly changes in different physiological states (hyperventilation, hypoventilation, pressure applied to the abdomen)[15,16]. These changes of lumbar space volume enable filling and emptying of venous plexuses that adapt to the changes of intradural volume. Data in literature show that spinal space, by its ability to change volume, participates from 30 to 80% in the compensation of the pressure increase inside the cranium[17,18].

Hystologic structure of the spinal dura mater enables changes of both volume and pressure in accordance with our hypothesis and shown results. Namely, the dura is made of collagenous and elastic fibers. Collagenous fibers are mostly directed in longitudinal direction and stretched mostly in that direction. However, the elastic fibers are intertwined in all directions. This structure enables two important physiological characteristics: a) plasticity, important during the volume load b) elasticity, important for the protective role of dura. Earlier studies have shown that dura is stretched in two phases, and therefore has two moduli of elasticity[19,20]. The elastic fibers stretch under smaller loads, while the elongation of collagenous fibers occurs under the larger loads. Therefore, the spinal dura can stretch in transversal direction at any part depending on the burden. Our model is constructed in the same way. Testings of the elastic features of a rubber baloon that represents the »spinal« part of the model show that we have chosen a proper material to use in our model. As it is shown in the Figure 3, the »spinal« part of the model has two moduli of elasticity, similar to spinal dura of the dogs. Values of these elastic moduli in our model ($Y_1 = 1.417 \times 10^6$ N/m^2; $Y_2 = 0.458 \times 10^6$ N/m^2) have the same order of magnitude as elastic moduli determined on the stripes of the spinal dura in dogs ($Y_1 = 3.99 \times 10^5$ N/m^2; $Y_2 = 4.6 \times 10^7$ N/m^2)[19].

We assumed that the changes of the CSF pressure inside the cranium occur according to the law of fluid mechanics. Namely, it is possible to apply this law in the same way on the CSF inside the cranium as well as on the fluid inside a tube with a rigid wall closed at the upper end and opened at the lower end under the affect of gravity. The fate of fluid inside the mentioned tube should be the same as of the CSF inside the cranium because intracranial space is surrounded by a rigid wall (skull), and opened at the lower end (foramen magnum) when the body is in an upright position. Since there is no leakage from the tube in that position, as in our model, it is clear that inside the tube hydrostatic pressure is lower than the atmospheric pressure. According to the law of fluid mechanics, inside that tube the pressure is negative and has the value of the distance from the point of pressure measurement to the tube opening[21].

All of the above suggests that the fate of fluid inside the »cranial« part of the model in an upright position should be similar to the fate of fluid inside the plastic syringe in experiments shown in Figure 2c. Namely, in these experiments the direction of forces applied to the fluid is the same as the direction of gravity. This force direction causes negative fluid pressure without any changes of fluid volume inside the plastic syringe (Figure 2d).

If our hypothesis is correct, than the CSF pressure during the verticalization of the body would be as negative as is the value of the distance between the measuring cannula and foramen magnum (Figure 1). The measuring cannulas in a model, as well as in animals, were set at a distance of 4 cm from the opening of the plastic tube (»cranial« space in a model) and from foramen magnum in cats. Therefore, according to our hypothesis a result of –4 cm H_2O during verticalization was expected. As it is clearly shown, the results (Table 1) did not statistically differ from the expected value neither in a model, nor in experimental animals. Minor deviations of pressure are a consequence of the CSF pressure pulsations.

According to our hypothesis and experiments shown in Figure 2a and 2b, we expected the pressure at the bottom of the »spinal« part of model in the upright position to be positive. This pressure should correspond to the hydrostatic difference between the point of the pressure measurement and the point where the »cranial« and »spinal« part of the model are joined. The length of the

»spinal« part of the model was 31 cm. During the verticalization the pressure in that part of the model was 31.0±0.1 cm H_2O. In cats, an average distance from foramen magnum to the lumbar subarachnoid space at the L3 vertebra level was 33 cm, whereas the CSF pressure at that point in the upright position amounted to 33.5±1.1 cm H_2O. Therefore, the values of pressures measured in a model and in experimental animals correspond with the values, expected according to our hypothesis, to the dimensions of the spinal spaces in cats.

Our results suggest that decrease of pressure inside the cranium can occur without any significant change of fluid volume (cerebral blood and CSF). This means that blood and CSF volumes inside the cranium are constant and are not influenced by the changes in body position. It seems to us that this is an exceptionally important evolutionary feature of cranial space as it enables good brain perfusion during standing in an upright position as well as bipedal walking.

These results oppose the classic hypothesis of CSF physiology, according to which the CSF is secreted inside the ventricles and from there CSF flows unidirectionally to the subarachnoid space where it is absorbed into the dural sinuses of the brain or into the extradural lymph[2,5]. Accoring to our hypothesis, in an upright position the pressure inside the ventricles would be negative and amount to approximately –10 cm H_2O in humans, whereas it would be around 0 cm H_2O in cisterna magna. According to the laws of physics, the CSF cannot flow from the region of the lower to the region of the higher pressure. Therefore, in the upright position CSF could not flow from the ventricles to the cisterna magna. Observed results are in accordance with the experimental results obtained on cats[22–25], and with the new hypothesis of CSF physiology, by which the CSF volume is determined by the gradients of hydrostatic and osmotic forces between blood, CSF and cells of the central nervous system[22–24, 26–28].

In conclusion, these results indicate that physical characteristics of the new model of CSF correspond to those observed in animal models. Hence, the changes in CSF pressure during the changes of body position in cats do not differ from the changes of fluid pressure observed in our model. This suggests that the changes of CSF pressure during the changes of body position occur in accordance to the law of fluid mechanics.

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REFERENCES

1. BRODBELT A, STOODLEY M, Br J Neurosurg, 21 (2007) 510. — 2. JOHANSON CE, DUNCAN JA, KLINGE PM, BRINKER T, STOPA EG, SILVEBERG GD, Cerebrospinal Fluid Res, 5 (2008) 10. — 3. JOHNSTON M, ZAKHAROV A, KOH L, ARMSTRONG D, Neuropathol Appl Neurobiol, 31 (2005) 632. — 4. KOH L, ZAKHAROV A, NAGRA G, ARMSTRONG D, FRIENDSHIP R, JOHNSTON M, Anat Embryol, 211 (2006) 335. — 5. DAVSON H, WELCH K, SEGAL MB, Physiology and pathology of the cerebrospinal fluid (Churcill Livingstone, Edinburgh, 1987). — 6. MAGNES B, J Neurosurg, 44 (1976) 687. — 7. MAGNES B, J Neurosurg, 44 (1976) 698. — 8. MAGNES B, Surg Neurol, 10 (1978) 45. — 9. ALPERIN N, LEE SH, SIVARAMAKRISHNAN A, HUSHEK SG, J Magn Reson Imaging, 22 (2005) 591. — 10. ALPERIN N, HUSHEK SG, LEE SH, SIVARAKRISHNAN A, LICHTOR T, Acta Neurochir (Wien), 95 (2005) 177. — 11. ROSNER MJ, COLEY IB, J Neurosurg, 65 (1986) 636. — 12. KLARICA M, RADOŠ M, ERCEG G, OREŠKOVIĆ D, BULAT M, Clin Neurol Neurosurg, 110 (Suppl 1) (2008) 8. — 13. MERLIS JK, Am J Physiol, 131 (1940) 67. — 14. ARTHUR W, FENSTER SK (Eds) Mechanics (Holt, Reinhart and Winston, New York, 1969). — 15. MARTINS AN, WILEY JK, MYERS PW, J Neurol Neurosurg Psychiatry, 35 (1972) 468. — 16. HOGAN QH, PROST R, KULIER A, TAYLOR ML, LIU S, MARK L, Anesthesiology, 84 (1996) 1341. — 17. MARMARAU A, SHULMAN K, LAMORGESE J, J Neurosurg, 43 (1975) 523. — 18. LOFGREN J, ZWETNOW NN, Acta Neurol Scandinav, 49 (1973) 575. — 19. TUNTURI AR, J Neurosurg, 47 (1977) 391. — 20. TUNTURI AR, J Neurosurg, 48 (1978) 975. — 21. LANDAU LD, LIFSHITZ EM, Fluid mechanics (Elsevier Butterworth-Heinemann, Oxford, 2005). — 22. OREŠKOVIĆ D, WHITTON PS, LUPRET V, Neurosci, 41 (1991) 773. — 23. OREŠKOVIĆ D, KLARICA M, VUKIĆ M, Med Hypotheses, 56 (2001) 622. — 24. OREŠKOVIĆ D, KLARICA M, VUKIĆ M, Neurosci Lett, 327 (2002) 103. — 25. KLARICA M, OREŠKOVIĆ D, BOŽIĆ B, VUKIĆ M, BUTKOVIĆ V, BULAT M, Neurosci, 158 (2009) 1397. — 26. BULAT M, Dynamics and statics of the cerebrospinal fluid: the classical and a new hypothesis. In: AVEZAAT CJJ, EJINDHOVEN JHM, MAAS AIR, TANS JTJ (Eds) Intracranial pressure VIII (Springer-Verlag, Berlin, 1993). — 27. BULAT M, KLARICA M, Period Biol, 107 (2005) 147. — 28. BULAT M, LUPRET V, OREŠKOVIĆ D, KLARICA M, Coll Antropol, 32 (Suppl 1) (2008) 43.

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FIZIKALNE OSOBINE NOVOG MODELA CEREBROSPINALNOG LIKVORA

S A Ž E T A K

Nije poznato koji sve čimbenici uvjetuju promjene tlaka likvora unutar kraniospinalnog sustava pri promjeni položaja tijela. Kako bismo to ispitali izradili smo novi model likvorskog sustava koji svojim biofizičkim karakteristikama i dimenzijama imitira likvorski sustav u mačaka te usporedili rezultate dobivene na modelu i životinjama pri promjeni položaja iz horizontalnog u uspravni. Novi model je izrađen iz dva dijela. »Kranijski« dio je izrađen od plastične cijevi i ne može mijenjati svoj volumen, dok je »spinalni« dio izrađen od duguljastog gumenog balona sličnog elastičnog modula kao spinalna dura pa može mijenjati volumen u svakom segmentu. Pri uspravljanju modela u »kranijskom« dijelu dolazi do pojave negativnog tlaka bez promjene volumena tekućine unutar tog prostora, a u »spinalnom« dijelu tlak tekućine odgovara visini hidrostatskog tlaka što je u skladu s zakonom o mehanici fluida. Promjene tlaka likvora kod promjene položaja mačke ne razlikuju se od promjena tlaka tekućine opažene u modelu. To ukazuje kako su promjene tlaka likvora odvijaju u skladu s zakonom o mehanici fluida i ne ovise o sekreciji i cirkulaciji likvora.