Intensive Care Med (2012) 38:925–927
DOI 10.1007/s00134-012-2572-6

EDITORIAL

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Brain compliance: the old story with a new 'et cetera'

Received: 27 March 2012
Accepted: 27 March 2012
Published online: 18 April 2012

This editorial refers to the article available at:
doi:10.1007/s00134-012-2571-7.

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Legions of clinical neuroscientists have, in addition to monitoring primary brain modalities such as intracranial pressure (ICP) or brain tissue oxygenation, been dreaming for decades of being able to use validated secondary modalities able to describe brain homeostasis more precisely and to anticipate brain function deterioration.

One of these is the so-called '*brain compliance*', a parameter introduced very early with the advent of interest in the brain pressure–volume relationship [1]. Great masters in the field, such as Douglas Miller [2] and Anthony Marmarou [3], conducted the first important experimental and clinical studies which ultimately resulted in measurements of pressure–volume response or pressure volume index (PVI), obtained using bolus injection, being introduced into the clinical arsenal of methods for studying brain compliance. From the school of Prof. Miller emerged Ian Piper, who developed the method of rapid repetitive micro-changes in intracerebral volume [4], which was subsequently introduced into clinical practice through the industrial application known as the 'Spiegelberg Brain Compliance Monitor'. This approach involves the use of an intraventricular small balloon which is able to induce continuous repetitive volumetric impulses. The apparatus subsequently calculates compliance as a change in volume divided by change in ICP and monitors it over longer periods, even days and weeks after the initial injury. A number of clinical studies have been conducted that compare brain compliance to clinical status, outcome, other brain modalities, among others [5, 6]. The net weight of enthusiasm included in conclusions drawn from these studies is difficult to express in only a few words, but our personal impression is that it is rather low key. One of the main reasons for this lack of enthusiasm is that brain compliance is strictly inversely proportional to ICP; therefore, with continuous ICP monitoring the compliance per-se does not add an extraordinary amount of new information. Translating compliance to PVI, which is invariant to mean ICP, is complex due to the unknown reference pressure [7]. Thus, the management of the hydrocephalus situation is theoretically easier, but even here brain compliance or elasticity/PVI has never been seriously used in clinical practice. Of the more contemporary studies, the paper by Tissell et al. [8] linking high elasticity with a better outcome of third ventriculostomy in patients suffering from non-communicating hydrocephalus is worth mentioning.

Attempts have also been made to assess compliance indirectly in many forms using ICP waveform analysis, high-frequency centroid [9] (rule: lower centroid, lower compliance), or the P2/P1 ratio [10] (P2 and P1 are distinctive peaks of the ICP pulse waveform, with P1 being the percussion peak and P2, the tidal peak). From among the purely non-invasive methods, one interesting idea worth mentioning has been to look at the cochlear channel pressure pulse waveform [11], although this method has never been widely introduced into clinical practice. Quite recently, brain compliance has

been assessed by magnetic resonance imaging (MRI)-based volume–pressure accounting [12].

What is brain compliance? This question would be simple to answer if the brain were a closed balloon. We need to inflict change in volume and measure the pressure response. The trouble with this approach is that in the brain, part of the compartmental volumes are 'trapped' inside the craniospinal space, such as brain tissue and, over short periods, slowly circulating cerebrospinal fluid (CSF). However, in contrast, cerebral blood flows through the system at a high rate. Consequently, any attempt to inflict cerebrospinal volumetric change easily leads to compensation, according to Monro–Kellie doctrine, by the migration of a certain amount of blood from the brain venous pool. Therefore, introducing a change in the intracerebral volume by bolus injection of CSF or an expanding intraventricular balloon leads primarily to the measurement of brain venous compliance. Apart from venous compliance, the CSF pool also has a limited space for compensation by expanding into the lumbar space against venous plexi inside the lumbar channel. Slow changes in CSF volume during lumbar infusion studies [13] are probably suited better to account for this component of brain compliance. The third component can be associated with the high-pressure brain arterial pool. This volume is regulated actively through the modulation of tension in the smooth muscles of brain vessels. The influence of this compliance can most strikingly be observed at the level of an extremely elevated ICP, when cerebral arteries tend to collapse passively, being previously maximally dilated ('critical closing pressure' [14]). Such a phenomenon leads to temporal decrease in the slope of a steep pressure volume curve [1], which was observed by Prof. Miller as a 'terminal' increase in PVI at a low level of cerebral perfusion pressure (CPP) in patients after head injury [15].

In summary, brain compliance is a sum (it is not certain whether it is an algebraic sum) of three compliances:

$$C_{\text{brain}} = C_{\text{venouspool}}(\text{ICP}, P_{\text{ss}}, \text{CVP}) \; ' + ' \; C_{\text{CSFpool}}(\text{ICP}, \text{CVP}, P_0) \; ' + ' \; C_{\text{arterialpool}}(\text{CPP}),$$

where P_{ss} is sagittal sinus pressure, CVP is the central venous pressure, P_0 is the ICP reference pressure, and '+' is the symbol of the 'non-algebraic' sum.

Therefore, the resulting brain compliance is hypothetically a function (non-linear!) of many brain compartmental pressures. Obviously, other vascular factors, such as regulation of cerebral blood flow, tension of arterial smooth muscles, partial pressure CO_2, endothelial function, brain hydration, metabolism, among others, play important role.

The ICP pulse amplitude (AMP), slope of the amplitude–pressure regression, or RAP index (correlation coefficient between slow changes in AMP and mean ICP) are interesting parameters; the difficulty is that none of these describes brain compliance directly. The AMP is equivalent to a pressure–volume response measured with an unknown volume-load, i.e. brain fraction of heart stroke volume. The AMP/ICP regression slope is proportional to brain elasticity multiplied by the same stroke volume [16, 17]. The RAP index shows where the craniospinal 'working point' is placed on the pressure–volume curve (on the linear part, exponential part, or above the 'critical ICP' when the PVI secondarily increases and arterial blood volume is compromised [18]).

It is, by all means, interesting to study all of these modalities after a head injury, but using them to infer changes in 'brain compliance' is a risky intellectual exercise. Changes in the AMP and AMP/ICP slope are affected mainly by cerebrovascular regulation, while changes in RAP roughly describe the brain compensatory reserve (RAP = 0 at low ICP: good compensatory reserve; RAP = 1 at moderately increased ICP: poor compensatory reserve, such as during brain swelling after traumatic brain injury; RAP negative at high ICP: state of deeply deteriorated CBF/CBV regulation). Many authors have described values of AMP, AMP/ICP slope, and RAP after head injury and subarachnoid hemorrhage (clinical status, outcome, state of autoregulation, etc.) [18–20] without reference to the term 'brain compliance'.

In this issue of *Intensive Care Medicine*, Howells et al. [21] compare different measures of cerebrospinal compensatory reserve in a cohort of patients with traumatic brain injury both before and after extreme medical and surgical therapies. The strong point of this study is that it characterizes the response to medication: the described measures of ICP waveform are dependent on the type of surgery and thiopental administration. This is very interesting article that provides useful information, with the exception that the first sentence of the Conclusion in the Abstract is not valid. At least one co-author who participated in the referring process (MC) feels guilty about missing this point.

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