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The relationship between CSF circulation and cerebrovascular pressure-reactivity in normal pressure hydrocephalus

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Summary

Objective. Previously, we documented association between CSF circulation and transcranial-Doppler derived autoregulation in non-shunted patients suffering from hydrocephalus. In the present study we sought to investigate the relationship between the resistance to CSF outflow and pressure-reactivity both in shunted and non-shunted NPH patients.

Material and methods. Sixty-eight patients (47 non-shunted and 21 shunted) with NPH have been examined as a part of routine diagnostic procedure. Resistance to CSF outflow (Rcsf) was measured using a ventricular constant rate infusion test. Cerebrovascular pressure-reactivity was assessed as a moving correlation coefficient (PRx) between coherent 'slow waves' of ICP and arterial blood pressure (ABP). This variable has previously been demonstrated to correlate with the autoregulation of CBF in patients following head injury.

Results. In non-shunted patients cerebrovascular pressure-reactivity (PRx) was negatively correlated with Rcsf ($R = -0.5$; $p < 0.0005$). This relationship was inverted in shunted patients: a positive correlation between PRx and Rcsf was found ($R = 0.51$; $p < 0.03$).

Conclusion. Cerebrovascular pressure-reactivity is disturbed in patients with normal resistance to CSF outflow, suggesting underlying cerebrovascular disease. This result confirms our previous finding where transcranial Doppler autoregulation was investigated. After shunting the pressure-reactivity strongly depends on shunt functioning and deteriorates when the shunt is blocked.

Keywords: Hydrocephalus; autoregulation; CSF flow; shunt.

Introduction

The pathophysiology of hydrocephalus includes three major components: disturbed cerebrospinal fluid (CSF) circulation, poor pressure-volume compensation and the interference of abnormal CSF flux with cerebral blood flow (CBF).

The first component manifests as an impaired outflow or absorption of CSF usually seen in hydrocephalus [2], commonly expressed as an increased resistance to CSF outflow (Rcsf).

The second component, the pressure-volume compensatory reserve, can be regarded as a mechanism by which the cranial cavity adapts to a change in intracranial volume to maintain a stable intracranial pressure (ICP). It is probably predominantly expressed by a buffering capacity of low-pressure compartment of cranial venous volume.

The third component is responsible for a reduction of CBF and an impairment of mechanisms of CBF regulation. It appears that CBF is decreased in patients suffering from NPH, although it remains unclear whether this reduction is a cause or an effect of NPH [1]. It has recently been reported that cerebrovascular reactivity to changes in partial pressure of carbon dioxide in arterial blood and in reaction to acetozolomide are commonly depleted in NPH [3, 7]. In our previous study we demonstrated an association between pressure-autoregulation assessed with transcranial Doppler ultrasonography (TCD) and the resistance to CSF outflow [6]. Our present objective is to study the relationship between the resistance to CSF outflow and cerebrovascular pressure-reactivity in shunted and non-shunted NPH patients.

Material and methods

In this retrospective study we reviewed the data from 68 patients (40 men and 28 women), who presented with clinical and radiological symptoms of NPH (progressive dementia, gait disturbances with or without urinary incontinence, along with communicating hydrocephalus on brain CT/MRI with a bicaudate ratio > 0.25). The age range was 25–86 years (mean 58). 21 patients had a ventriculoperitoneal shunt in-situ at the time of examination. All patients underwent a computerized CSF infusion test being a part of diagnostic procedure in the Addenbrooke's Hospital CSF Clinic. In non-shunted patients the aim was to determine their resistance to CSF

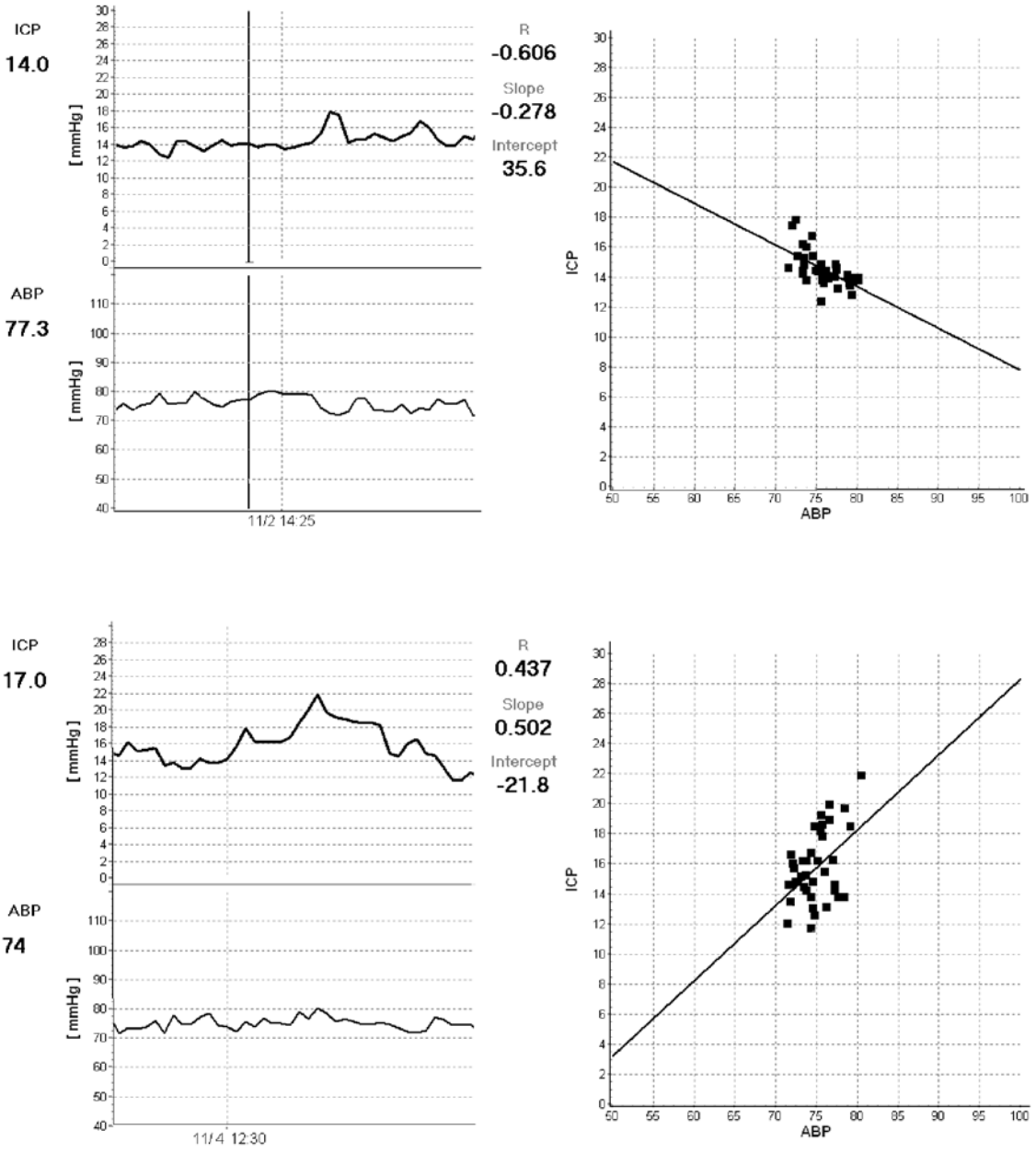

Fig. 1. Relationship between slow waves of arterial pressure (*ABP*) and intracranial pressure (*ICP*). Upper panel: *PRx negative* indicating good pressure-reactivity. Lower panel: *PRx positive* indicating poor pressure-reactivity

outflow, which is one of the predictors of response to shunting. In shunted patients the aim was to assess the shunt function in-vivo, as they had the persistence or recurrence of some clinical signs. This examination is a part of routine diagnostic procedure in our hospital. Data were analyzed retrospectively and anonymity and confidentiality were maintained throughout.

Two needles, which were used for the infusion and the pressure measurement, were placed either into a subcutaneous reservoir that was connected to the intraventricular catheter or into the shunt antechamber. Before the infusion was started, baseline ICP was recorded for 10 minutes. The infusion of a normal saline solution was then started at a rate of 1.5 ml/min or 1 ml/min. When a steady state of ICP plateau was reached, the infusion was stopped. The recording was continued until ICP decreased to a steady baseline level. During the whole period of recording a Finapress finger cuff measured the arterial pressure (ABP).

An IBM-compatible personal computer recorded and processed the data during the infusion test, to obtain mean CSF pressure, pulse wave amplitude of CSF pressure and to calculate the resistance to CSF outflow. ICP and ABP waveforms were processed during the infusion test to obtain an additional index describing cerebrovascular pressure-reactivity (PRx). The index is based on the concept of assessing vascular responses by observing repetitively the reaction of ICP to spontaneous fluctuations of ABP [4]. Using computational

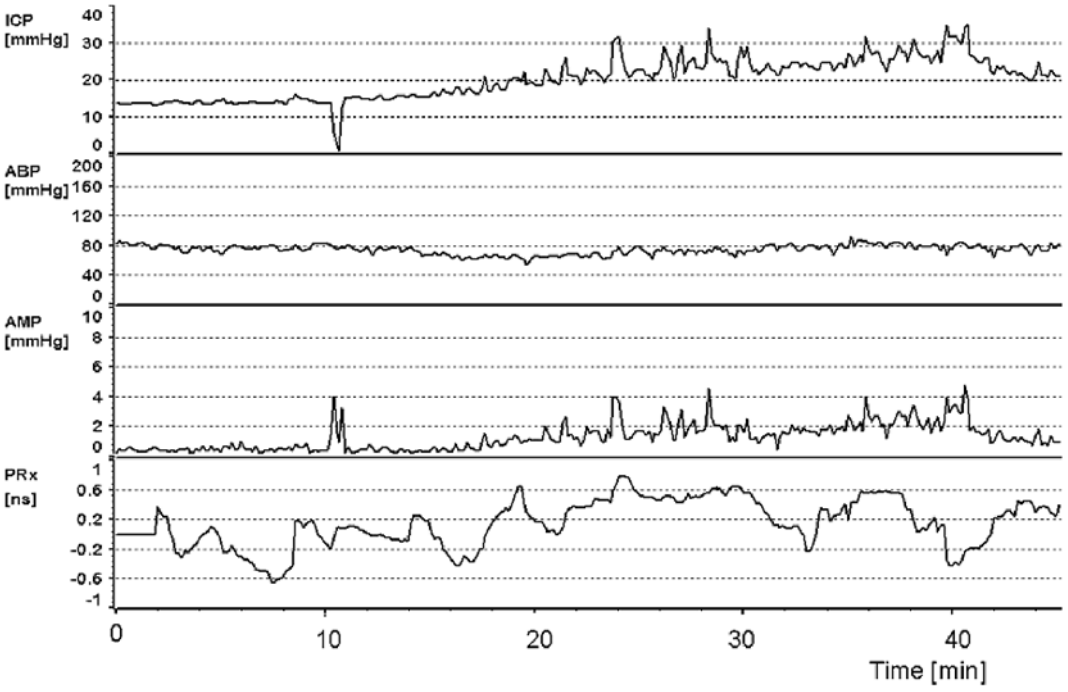

Fig. 2. Example of data recorded during the infusion test. Infusion of 1 ml/min started at 14 minutes and continued until the 40th minute. *ICP* Intracranial pressure, *ABP* arterial pressure, *AMP* pulse amplitude of ICP, *PRx* pressure reactivity index

methods PRx was determined by calculating the correlation coefficient between 40 consecutive, time-averaged (over 6 sec periods) data points of ICP and ABP. A positive PRx signifies a positive gradient of the regression line between the slow components of ABP and ICP, which has been shown to be associated with a passive behavior of a non-reactive vascular bed. A negative value of PRx reflects normal reactive cerebral vessels, as ABP waves provoke inversely correlated waves in ICP (Fig. 1). This index correlates well with indices of autoregulation based on transcranial Doppler ultrasonography. Furthermore, abnormal values of PRx indicative of poor autoregulation have been demonstrated to be predictive of a poor outcome following head injury [4].

Calculated variables were averaged over 10-min. periods at the baseline and during the plateau phase of infusion (Fig. 2) and a non-parametric paired test (signed-rank) was used for comparison of time-averaged values at the baseline and during the elevated ICP within the phase of constant rate infusion. Regression analysis was used, after checking the normal distribution of data, to compare compensatory and cerebrovascular-reactivity indices with the resistance to CSF outflow, separately for shunted and non-shunted patients.

Results

The measured parameters responded to the change in mean ICP between the baseline and the infusion. The mean values and standard deviations are given in Table 1 together with the significance levels for the differences (paired signed-rank test).

In the group of non-shunted patients 28 had a resistance to CSF outflow above 13 mmHg of which 12 above 18 mmHg/(ml/min). In the group of shunted patients 9 tests evaluated the shunt as functioning normally and 5 tests revealed a shunt blockage [5]. In 8 cases 'possible under drainage' was revealed (i.e. Rcsf was increased in comparison to the hydrodynamic resistance of the shunt, but lower than 10 mmHg/(ml/min)).

Table 1. *ICP, ABP and derived parameters before and during infusion*

	At the baseline	During infusion	P value
ICP [mmHg]	7.7 (5.7)	23.1 (10.1)	$2.47 * 10^{-12}$
ABP [mmHg]	85 (28)	92 (36)	0.000247
CPP [mmHg]	76.8 (28)	67.6 (34.3)	0.00019
PRx	0.11 (0.21)	0.18 (0.26)	0.047
Magnitude of B waves [mmHg]	0.71 (0.76)	2.26 (1.23)	0

Of all the CSF compensatory parameters derived from the infusion test, the resistance to CSF outflow (Rcsf) and the baseline ICP demonstrated significant associations with cerebrovascular reactivity (PRx): In non-shunted patients, the regression between PRx and Rcsf indicated a negative linear relationship ($R = -0.5$; $p < 0.0005$) (Fig. 3a).

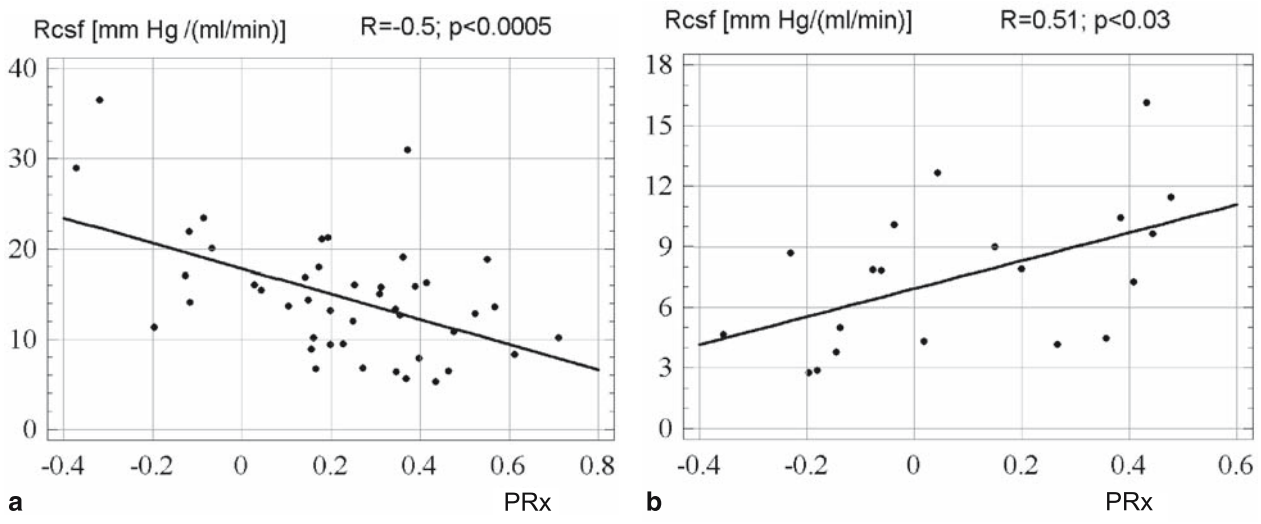

Fig. 3. (a) Relationship between PRx and resistance to CSF outflow in non-shunted patients (n = 44). (b) Relationship between PRx and resistance to CSF outflow in shunted patients (n = 20)

In shunted patients, we observed an opposite relationship between PRx and Rcsf: both parameters were positively associated ($R = 0.51$; $p < 0.03$) (Fig. 3b).

There was no correlation between PRx and ventricular size (bicaudate ratio), opening ICP, Rcsf or elastance coefficient of the intracranial space.

Following the infusion study 27 patients with increased Rcsf were shunted. 14 of them improved 6 did not show any signs of improvement (1 of them got worse). 8 patients were not available for the follow-up. When PRx was compared between improved and non-improved patients it appeared that it indicated nearly significantly ($p = 0.082$) worse pressure-reactivity in patients who did not improve ($PRx = 0.25 \pm 0.23$) in comparison to patients who demonstrated improvement ($PRx = 0.050 \pm 0.21$).

Discussion

The negative correlation between cerebrovascular pressure reactivity (PRx) and Rcsf for non-shunted patients was in agreement with our previous findings about CBF autoregulation assessed using transcranial Doppler ultrasonography. We found that patients with a higher Rcsf tended to have a better autoregulation than patients with a lower Rcsf. Similarly, in the present study, patients with higher Rcsf had better pressure-reactivity (lower PRx). This paradoxical finding was attributed to the possible higher rate of cerebrovascular disease in patients with ventricular dilatation and normal circulation of CSF. Consequently, such patients tend not to exhibit clinical improvement after shunting. The shunt cannot restore normal conditions of cerebral vascular reactivity (and hence improvement of CBF) when the problem lies only or predominantly within the cerebrovascular tree. In hydrocephalus, where there is a pathological link between disturbed CSF circulation (manifested by increased Rcsf) and reduced CBF, shunting can improve CSF distribution and hence CBF.

The relationship between PRx and Rcsf in shunted patients was found to be positive, i.e. inverse to the negative correlation between these two parameters in non-shunted patients. This indicates that the shunt may influence cerebrovascular haemodynamics.

The presented data suggest an association between the three pathophysiological components of hydrocephalus: CSF circulation and haemodynamic reactivity. We found a positive relationship between PRx and Rcsf in shunted patients, which is opposed to the negative relationship between these two parameters in non-shunted patients. This indicates an interference of the shunt with cerebrovascular haemodynamics.

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