

# Intracranial pressure wave morphological classification: automated analysis and clinical validation

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## Abstract

**Background** Recently, different software has been developed to automatically analyze multiple intracranial pressure (ICP) parameters, but the suggested methods are frequently complex and have no clinical correlation. The objective of this study was to assess the clinical value of a new morphological classification of the cerebrospinal fluid pulse pressure waveform (CSFPPW), comparing it to the elastance index (EI) and CSF-outflow resistance ( $R_{out}$ ), and to test the efficacy of an automatic ICP analysis.

**Methods** An artificial neural network (ANN) was trained to classify 60 CSFPPWs in four different classes, according to their morphology, and its efficacy was compared to an expert examiner's classification. The morphology of CSFPPW, recorded in 60 patients at baseline, was compared to EI and  $R_{out}$  calculated at the end of an intraventricular infusion test to validate the utility of the proposed classification in patients' clinical evaluation.

**Results** The overall concordance in CSFPPW classification between the expert examiner and the ANN was 88.3 %. An elevation of EI was statistically related to morphological class' progression. All patients showing pathological baseline

CSFPPW (class IV) revealed an alteration of CSF hydrodynamics at the end of their infusion test.

**Conclusions** The proposed morphological classification estimates the global ICP wave and its ability to reflect or predict an alteration in CSF hydrodynamics. An ANN can be trained to efficiently recognize four different CSF wave morphologies. This classification seems helpful and accurate for diagnostic use.

**Keywords** Intracranial pressure · Artificial neural network · Waveform analysis · Morphological classification · Elastance index · Cerebrospinal fluid hydrodynamics

## Introduction

Intracranial pressure (ICP) analysis is critical for the comprehension of the intracranial system's pathophysiological mechanisms and for the management of neurosurgical patients. In the last 5 years, dedicated software has been developed to automatically analyze ICP on the basis of mathematical models [8, 20, 25]. The collection and elaboration of large amounts of data on ICP waveform have therefore been possible, but the clinical value of these data is still a matter of debate. Rather than using complex computational analyses, which would be difficult to reproduce and apply in daily clinical practice, we propose a simple morphological classification of ICP waveforms based on visual criteria.

In 1983, Cardoso [10] described three separate peaks and a notch in the shape of the ventricular CSF pulse pressure waveform (CSFPPW): systolic peak (P1), tidal peak (P2), dicrotic notch (N), and dicrotic peak (P3). It is well known that while in normal conditions the systolic peak is higher than the other two and the dicrotic notch is well evident, in pathological situations, when intracranial compliance decreases, tidal and

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dicrotic peaks exceed the systolic one and the dicrotic notch disappears, thus producing a modification in the shape of the CSFPPW which progressively assumes a sinusoidal morphology (Fig. 1) [13, 23, 36, 37]. Based on the relationship between the three peaks and the notch, we identified four different CSFPPWs (Fig. 1).

This study had two aims. The first was to automatize and objectify the proposed morphological classification using an artificial neural network (ANN), a mathematical model largely applied in pattern recognition or data classification problems [22]. The second aim was to clinically validate the morphological classification, comparing it to conventional indexes of altered intracranial compliance, the elastance index (EI) and the CSF-outflow resistance ( $R_{out}$ ) [2].

## Materials and methods for training the ANN

### Data collection

ICP data obtained from 160 patients admitted to the Institute of Neurosurgery of the Catholic University School of Medicine between September 2009 and September 2012 for different neurosurgical conditions were analyzed. ICP was recorded through an intraventricular catheter and its signal was digitally sampled (128 Hz) and collected by dedicated software, as previously described [2]. Patients were fully informed of the clinical procedure and gave their consent to the intraventricular infusion test and to the use of collected data for scientific purposes.

### Data analyses

#### Expert examiner's analysis

Four hundred eighty-six CSFPPW, representative of the ICP morphology patterns, were selected. Based on the three peaks described by Cardoso et al. [10] (Fig. 1), the senior author (CA) assigned every CSFPPW to one of the following four classes (Fig. 2):

1. class I - *Normal*, if the first peak (P1) exceeds the other two (Fig. 1a);
2. class II - *Potentially pathological*, if the tidal peak (P2) equals or slightly exceeds the first one (P1) and the dicrotic peak equals or is slightly inferior to P1 (Fig. 1b);
3. class III - *Likely pathological*, if the tidal and the dicrotic peaks exceed the first one (Fig. 1c);
4. class IV - *Pathological*, if the tidal and the dicrotic peaks surmount the first one or if the shape of the curve is so rounded as not to permit the identification of the three peaks (Fig. 1d, e).

The 486 CSFPPWs formed the neural network training set (Table 1).

### Computer analysis

The direct use of a CSFPPW as input of an ANN was not suitable due to the following aspects:

- i. Wide range of CSFPPWs amplitudes;
- ii. Presence of noise in the measurements of each CSFPPW.

To overcome the above-mentioned points, each CSFPPW was first “normalized”, i.e., scaled so that 0 and 1 were its minimum and maximum value in order to reduce the influence of amplitude on the ICP wave analysis and to emphasize the morphological characteristics. Each normalized CSFPPW underwent an approximation process to find the optimal values for parameters  $a_1, \dots, a_m$  with  $m = 10$  such that the following function

$$y(t) = \sum_{i=1}^m a_i \phi_i(t)$$

where  $\phi_i$  is a radial basis function [28], was able to best approximate a given normalized CSFPPW. Finally, each normalized CSFPPW was mapped onto a vector of ten elements (i.e.,  $a_1, \dots, a_{10}$ ), which was the input of ANN.

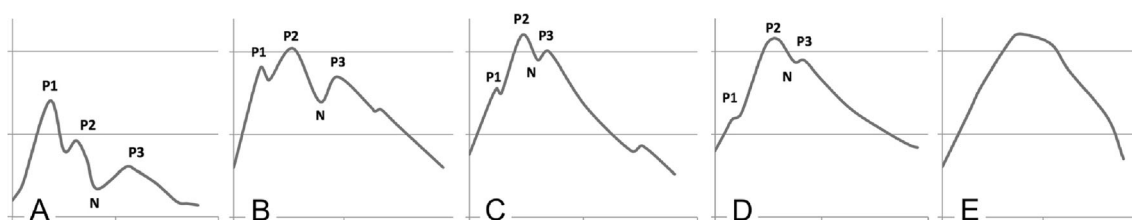
An ANN for pattern recognition was then developed through a training algorithm [34], a procedure targeted to teach the ANN to correctly assign each separate input pattern to one of a finite number of output classes. The training set used in this analysis was constituted by the vectors  $[a_1, \dots, a_{10}]$  of the 486 CSFPPW previously classified by the expert examiner.

### Neural network validation

At the completion of training, the ANN was given 60 new CSFPPW to test its ability in classifying them. The same 60 CSFPPW were presented to the senior author, who was blind to the ANN classification. The results of the two examiners (computer and expert) were then compared.

## Results of artificial neural network training

Table 2 summarizes the results of the classification of the 60 CSFPPW by the expert examiner and the ANN. In summary, the concordance between the two examiners was 53 CSFPPW out of 60 (88.3 %).



**Fig. 1** Morphology of CSF pulse pressure waveform. **a** class I - Normal; **b** class II - Potentially pathological; **c** class III - Likely pathological; **d** and **e** class IV - Pathological. P1 systolic peak, P2 tidal peak, N dicrotic notch, P3 dicrotic peak

**Materials and methods for clinical validation**

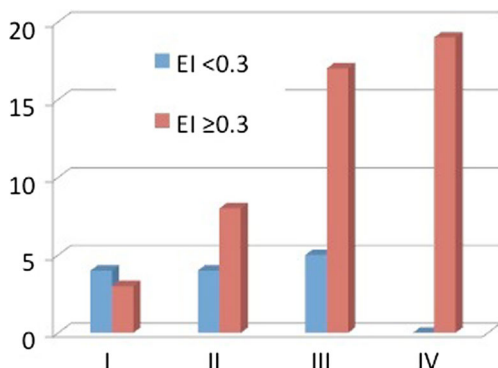
**Patient data analysis**

Sixty patients admitted to the Institute of Neurosurgery of the Catholic University School of Medicine between September 2012 and July 2013 with suspected idiopathic normal pressure hydrocephalus underwent a CSF hydrodynamic evaluation based on the intraventricular infusion test according to a previously described protocol [2]. Three minutes of baseline ICP recording, followed by 30 min of ICP recording during continuous saline solution infusion were obtained. In all patients, 38 males and 22 females, the diagnosis was based on clinical, neuropsychological, and radiological criteria. The average age was 71.5 years (range, 61–84 years).

For each test, a baseline CSFPPW was extracted for morphological classification; final  $R_{out}$  and EI values were calculated by dedicated software, as previously described [2]. The EI was evaluated as normal if  $< 0.3$  and pathological if  $\geq 0.3$  [2]. The  $R_{out}$  value was considered normal if  $\leq 12$  mmHg/ml/min and pathological if  $> 12$  mmHg/ml/min [29, 30].

**Statistical analysis**

Mean patients’ age, average  $R_{out}$ , and average EI within each morphological class were analyzed. The mean values were compared using Student’s *t* test for unpaired data and variance



**Fig. 2** Patients’ EI values over morphological classes. The x-axis shows morphological classes and the y-axis shows the number of patients (units value 5). See Results for details. EI Elastance index

analysis (ANOVA) with Bonferroni correction. The level of significance was established for values of  $p \leq 0.05$ .

**Results of clinical validation**

Table 3 reports  $R_{out}$  and EI values for each patient, together with the morphological class of the CSFPPW recorded at baseline.

**Morphological class and elastance index**

Analyzing class I waves, EI at the end of the infusion test was pathological in three cases out of seven. Among class II waves, EI was pathological in eight of 12 patients. Within class III waves, EI turned out pathological in 17 of 22 tests, while all 19 class IV waves correlated to a pathological EI value. These results are shown in Fig. 2.

Average EI for morphological class was 0.28 for class I (range, 0.02–0.63), 0.37 for class II (range, 0.21–0.63), 0.5 for class III (range, 0.21–1.17) and 0.6 (range, 0.36–1.49) for pathological waves (class IV) (Fig. 4a).

**Morphological class and CSF-outflow resistance**

In class I group, two patients showed  $R_{out} \leq 12$  mmHg/ml/min and five patients had  $R_{out} > 12$  mmHg/ml/min. In class II, six  $R_{out}$  resulted normal, and six resulted pathological. Among class III morphology, three patients had normal  $R_{out}$  compared to 19 patients with a value  $> 12$  mmHg/ml/min. For pathological waves, the test showed a normal  $R_{out}$  in seven cases, while in 12 cases resulted pathological.

Narrowing cut-off values (according to Boon and Borgensen [6, 7]), for  $R_{out} < 8$  mmHg/ml/min one patient had class I wave, two patients were in class II, one in class

**Table 1** Classification of the CSF pulse pressure waveforms (CSFPPW) used to train the artificial neural network

CSFPPW	Total 486
Class I	100
Class II	107
Class III	106
Class IV	173

**Table 2** Comparison of the morphological classification of ICP waveform by the neural network analysis and by the expert examiner

	Expert examiner	Neural network	Unmatched waves	Concordance
Class I	7	7	–	100 %
Class II	12	13	3	75 %
Class III	22	21	4	81.8 %
Class IV	19	19	-	100 %
Total			7	88.3 % (53/60)

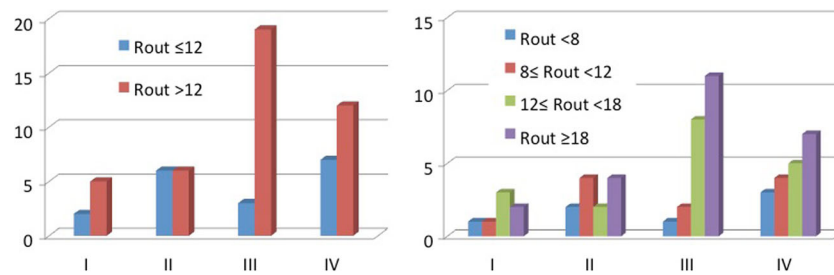
III and three in class IV. For  $R_{out}$  values comprised between 8 and 12 mmHg/ml/min, one wave had normal morphology, four were possible pathological, two were likely and four were pathological at baseline. For  $R_{out}$  comprised between 12 and

18 mmHg/ml/min, three waves were classified as class I, two as class II, eight as class III, and five as class IV. For  $R_{out}$  values greater than 18 mmHg/ml/min, seven waves had pathological morphology, 11 were likely pathological, four

**Table 3** Patients' data, divided into CSFPPW class of morphology

	Pt	Age	EI	$R_{out}$		Pt	Age	EI	$R_{out}$	
Class I	1	61	0.02	14.48	Class II	8	72	0.56	28.98	
	2	75	0.23	19.78		9	65	0.21	4.16	
	3	63	0.16	13.39		10	80	0.29	14.3	
	4	68	0.63	10.64		11	77	0.63	5.49	
	5	63	0.05	3.80		12	71	0.30	15.09	
	6	68	0.52	30		13	82	0.35	8.86	
	7	69	0.37	15.22		14	68	0.38	30	
Mean values		66.7	0.28	15.33	15	76	0.40	19.27		
Class III	20	72	0.21	7.08	Class IV	16	73	0.24	11.31	
	21	61	0.42	14.22		17	73	0.26	18.27	
	22	76	0.45	30		18	73	0.48	10.3	
	23	66	0.51	16.09		19	73	0.42	10.24	
	24	73	0.53	30		Mean values		73.5	0.37	14.68
	25	76	0.63	28.27		42	73	0.67	21.32	
	26	77	0.43	30		43	60	0.60	16.6	
	27	80	0.54	14.77		44	82	0.37	30	
	28	63	0.28	16.81		45	71	1.49	2.77	
	29	63	0.63	12.8		46	67	0.59	16.36	
	30	72	1.17	30		47	62	0.40	12.31	
31	77	0.32	9.4	48	74	0.52	17.43			
32	71	0.21	30	49	64	0.72	5.25			
33	76	0.89	14.63	50	71	0.57	7.53			
34	73	0.93	30	51	78	0.63	8.81			
35	73	0.71	30	52	63	0.37	9.23			
36	73	0.22	10.08	53	82	1.00	11.43			
37	75	0.47	12.56	54	84	0.94	30			
38	73	0.31	30	55	64	0.40	30			
39	72	0.29	30	56	77	0.40	12.58			
40	68	0.32	16.86	57	63	0.36	9.43			
41	71	0.60	30	58	72	0.53	18.42			
Mean values		71.8	0.50	21.52	59	75	0.56	30		
					60	79	0.36	30		
					Mean values	71.6	0.60	16.81		

EI and  $R_{out}$  at the end of intraventricular infusion test are reported. EI elastance index,  $R_{out}$  Resistance to cerebrospinal fluid outflow, CSFPPW cerebrospinal fluid pulse waveform



**Fig. 3** Patients'  $R_{out}$  values over morphological classes ( $R_{out}$  values are expressed in mmHg/ml/min). The  $x$ -axis shows morphological classes and the  $y$ -axis shows the number of patients (units value 5). See Results for details.  $R_{out}$  CSF outflow resistance

potentially pathologic, and two had normal morphology (as shown in Fig. 3).

In the first class,  $R_{out}$  mean value was 15.33 mmHg/ml/min (range, 3.8–30), in class II it was 14.68 mm Hg/ml/min (range, 4.16–30), in class III 21.52 mmHg/ml/min (range, 7.08–30) and in class IV 16.81 mm Hg/ml/min (range, 2.77–30) (Fig. 4b).

### Results of statistical analysis

Mean patients' age did not differ statistically among the morphological classes. No correlation between mean age or average  $R_{out}$  value and increased morphological CSFPPW class was observed.

A progressive rise in average EI values with increasing morphological class was evident (Fig. 4a). The difference between class I mean EI and class III mean EI was statistically significant (according to Student's  $t$  test), as well as between class I mean EI and class IV mean EI (Student's  $t$  test and variance analysis). The difference between class II mean EI value and class IV mean EI value was statistically significant according to Student's  $t$  test.

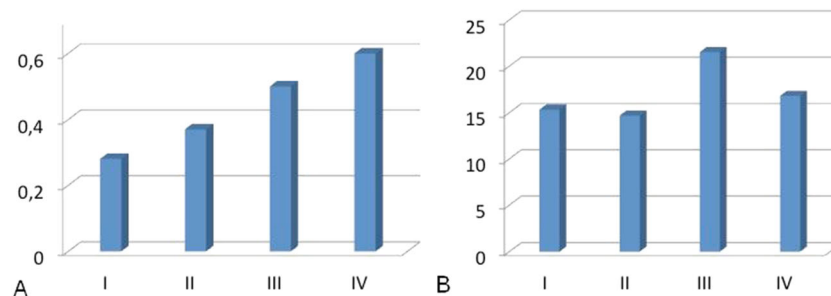
### Discussion

Intracranial pressure behavior is crucial for understanding the pathophysiological mechanisms of the intracranial system,

assuming that dynamic changes in ICP reflect the system ability to counterweight for changes in intracranial volume. The alteration of ICP mean values is usually monitored in neurosurgical units, although it is a "late" event in the pathophysiological cascade [33] and is not always present in pathological conditions, such as in normal pressure hydrocephalus. Given the complexity of the intracranial system, it becomes evident that a thorough analysis cannot ignore examination of ICP morphology, as suggested by other authors [11, 19].

The ICP wave morphology depends on arterial pressure waveform, as the result of interaction between the pulsatile arterial pressure and intracranial compartments, i.e., the brain tissue, the CSF, and the arterial and the venous blood [41]. According to Anile [1] and Baledent [5], the intracranial arterial pulsation is transmitted through the CSF to the veins in order to nearly simultaneously compensate the intracranial volume variation with an equivalent pulsatile venous outflow. CSF pulsation derives from the transmission of arterial pulsation on cerebral veins and is therefore dependent on cerebrovascular bed resistance. In pathological conditions, the venous compartment, by the Starling's resistor, offers a variable resistance against the arterial pulse wave transmission that modifies the CSFPPW contour [1].

ICP pulse detection and waveform analysis have been the focus of attention for more than 30 years. Chopp and Portnoy [12, 13, 36, 37] proposed a morphological evaluation of the ICP wave using spectral analysis. Morgalla [33] applied evaluation of systolic, diastolic, and pulse pressure amplitude in ICP analysis software.



**Fig. 4** Mean EI values and mean  $R_{out}$  values over morphological classes. **a** Mean EI values are shown on the  $y$ -axis and morphological classes are on the  $x$ -axis. **b** Mean  $R_{out}$  values are shown on the  $y$ -axis and

morphological classes are on the  $x$ -axis ( $R_{out}$  values are expressed in mmHg/ml/min). EI Elastance Index,  $R_{out}$  CSF outflow resistance



More recently, in line with the increasing impact of technology in medicine, automatic systems approaches, performing a large amount of complex calculations on a single CSFPPW, have been presented.

The software MOCAIP (MORphological Clustering and Analysis of Intracranial Pressure), developed at the University of California, extrapolates from a group of consecutive waves a “dominant pulse”, artifact free, that should summarize all of the ICP characteristics. The algorithm analyzes the other CSF waves, comparing them to this ideal wave, and determining on each one more than 120 metrics [3, 4, 24, 25, 38, 39]. P1, P2, and P3 peaks are assigned using statistical models. This system requires simultaneous ECG recording, analyzes a “medium” wave, not a real one, and is not reliable in those cases where a wave’s morphology is so irregular or “monotonous” that peak identification is hard to achieve. The meaning attributed to the different forms of intracranial pressure wave, moreover, has not yet been clarified or standardized.

Another multiparametric analysis was described by Galeano and coworkers [8, 9, 20], who reported correct automatic peak identification, as related to an expert examination, in 64 % of cases.

In a strongly technological era, the temptation is to record and analyze a large amount of data. Nonetheless, this does not necessarily provide better results in terms of correct classification: data reduction possibly leads to a more easily interpretable categorization. With this purpose, a morphological analysis, founded on clinical experience and examination of CSF wave peaks relationship, has been suggested in this study. The differences in correlation between the three peaks in a single ICP wave depict the progressive decline in intracranial compliance, i.e., the ability of the intracranial system to react to volume changes with minimal pressure change. The pressure wave transmitted from the arterial systolic pulsation (P1) “bumps” into a less compliant (more resistant) compartment, made by the intracranial venous system and the cerebral parenchyma with the capillary network. This reverberates on the pressure waveform, with a progressive increase of P2 and P3 compared to P1, up to a rounded waveform where any peak or notch is no more detectable.

Many authors investigated ICP waveform changes during intracranial hypertension using spectral analysis [14, 23, 35, 41]. To the best of our knowledge, there is only one study from Li et al. [27] that analyzes the relationships between peaks P1, P2, and P3 using a visual criterion and correlates them to a progressive increase in mean ICP, speculating that different waves morphologies could reflect the residual compensatory capacity of the brain.

Compared to mathematical software, the method developed in this study appears easier to apply in daily activity. The visual criterion has the advantage of immediacy in contrast to parameters identified by statistical calculations. This classification can be applied to an ICP pressure monitor

recording, available in every neurosurgical unit, without the need for further technical support. As there is still no evidence as to which ICP wave variables are significant, mathematical functions encoding all morphological multiplicity are rather complicated, probably not exhaustive, and certainly not efficient. This categorization does not analyze a single wave component, but estimates the global ICP wave and its ability to reflect or predict an alteration of CSF hydrodynamics.

Moreover, the ANN, allowing pattern recognition even if the input does not rigidly comply to all the parameters given for classification, can be helpful when in the CSFPPW P3 is difficult to recognize or when there are more than three clear peaks. Automation eliminates operator-dependent bias and makes this categorization accessible to every neurosurgeon, irrespective of his/her experience in ICP waveform analysis. Overall, the proposed automatic classification system appears easy to apply and reliable for diagnostic use. Disagreement between the expert examiner classification and the ANN, inferior to 12 %, is probably imputable to the apparent morphological similarity between class II and class III waves. We believe, however, that the system could be improved by increasing the number and variability of training data.

The clinical relevance of ICP wave categorization is still a matter of debate. Mariak [31, 40] proposed an ANN-mediated ICP signal processing. Analysis of a “sufficiently long” segment of ICP signal, combined with clinical information and instrumental data (transcranial Doppler, measurement of vegetative parameters, etc.), reached 70 % rate of judgments consistent with expert scoring in level of risk of clinical conditions. A waveform pattern classification similar to the one proposed here has been described by Elixmann [18]. The results of their algorithm, used in the evaluation of 13 suspected NPH patients’ infusion tests, showed correct classification compared to visual judgment in 88 %. At least in one illustrative patient, the waveform patterns correlate with mean pressure, compliance, and pressure amplitude measured during the infusion test.

In this study, the relevance and efficiency of the morphological classification were provided by comparison to well-known parameters of CSF hydrodynamics alteration, EI and  $R_{out}$ .

We found that the increase of the average EI value from class I to class IV significantly correlated with the progressive pathological changes in a wave’s morphology, while no association was highlighted between morphological classes and  $R_{out}$  values. This is in line with the growing call into question of  $R_{out}$  diagnostic and prognostic usefulness [6, 15, 21, 29]. In the debate between supporters [26, 32] and detractors [2, 17, 30] of  $R_{out}$  reliability in patients selection for neurosurgical intervention, we believe that normal-pressure hydrocephalus, at least in its idiopathic form, is not a simple disorder of CSF absorption [16]. For this reason, the  $R_{out}$  value should not be used as a single evaluation parameter because it is probably

not able by itself to demonstrate an alteration in complex CSF hydrodynamics.

In our opinion, it is very interesting that all patients with a pathological baseline CSFPPW (class IV) showed an alteration of CSF dynamics at the end of their infusion tests. We can speculate that, at least in some cases, hydrodynamic CSF alterations can be highlighted by a short baseline registration, thus avoiding infusion test performance.

Moreover, data obtained from the analysis of Classes II and III, respectively associated with altered CSF dynamics in 66.6 and 77.3 % of the cases, are remarkable. We ascribe these results to the ability of CSFPPWs to reflect an alteration of the intracranial system that is not clearly manifested in basal conditions, but evident after stress test. This hence validates the definition of “potentially pathological” and “likely pathological” waves.

## Conclusions

The preliminary data of this study suggest that changes in the shape of the ICP wave are informative on an incoming or established alteration of the intracranial system; ICP wave morphological analysis can predict the results of a more invasive method of compliance measurement. In addition, automatic ANN categorization allows the transition from a subjective evaluation of the ICP waveform to an objective classification, simplifying the diagnostic process, which does not depend on the operator’s experience.

Future studies are needed to achieve greater reliability of the neural network analysis and to discover new quantifiable ICP wave parameters to clarify how the intracranial system is regulated and possibly prevent or rapidly manage an alteration in its homeostasis.

## Compliance with ethical standards

**Funding** No funding was received for this research.

**Conflict of interest** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

**Ethics approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

1. Anile C, Bonis PD, Ficola A, Santini P, Mangiola A (2011) An experimental study on artificially induced CSF pulse waveform morphological modifications. *Neurol Res* 33:1072–1082
2. Anile C, De Bonis P, Albanese A, Di Chirico A, Mangiola A, Petrella G, Santini P (2010) Selection of patients with idiopathic normal-pressure hydrocephalus for shunt placement: a single-institution experience. *J Neurosurg* 113:64–73
3. Asgari S, Bergsneider M, Hamilton R, Vespa P, Hu X (2011) Consistent changes in intracranial pressure waveform morphology induced by acute hypercapnic cerebral vasodilatation. *Neurocrit Care* 15:55–62
4. Asgari S, Xu P, Bergsneider M, Hu X (2009) A subspace decomposition approach toward recognizing valid pulsatile signals. *Physiol Meas* 30:1211–1225
5. Baledent O, Fin L, Khuoy L, Ambarki K, Gauvin AC, Gondry-Jouet C, Meyer ME (2006) Brain hydrodynamics study by phase-contrast magnetic resonance imaging and transcranial color Doppler. *J Magn Reson Imaging* 24:995–1004
6. Boon AJ, Tans JT, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HA, Avezaat CJ, de Jong DA, Gooskens RH, Hermans J (1997) Dutch normal-pressure hydrocephalus study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid. *J Neurosurg* 87:687–693
7. Borgesen SE, Gjerris F (1982) The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus. *Brain* 105: 65–86
8. Calisto A, Bramanti A, Galeano M, Angileri F, Campobello G, Serrano S, Azzerboni B (2009) A preliminary study for investigating idiopathic normal pressure hydrocephalus by means of statistical parameters classification of intracranial pressure recordings. *Conf Proc IEEE Eng Med Biol Soc* 2009:2629–2632
9. Calisto A, Galeano M, Serrano S, Azzerboni B (2013) A new approach for investigating intracranial pressure signal: filtering and morphological features extraction from continuous recording. *IEEE Trans Biomed Eng*
10. Cardoso ER, Rowan JO, Galbraith S (1983) Analysis of the cerebrospinal fluid pulse wave in intracranial pressure. *J Neurosurg* 59: 817–821
11. Carrera E, Kim DJ, Castellani G, Zweifel C, Czosnyka Z, Kasparowicz M, Smielewski P, Pickard JD, Czosnyka M (2010) What shapes pulse amplitude of intracranial pressure? *J Neurotrauma* 27:317–324
12. Chopp M, Portnoy HD (1980) Analysis of intracranial pressure waveforms, comparison to the volume pressure test. *Biomed Sci Instrum* 16:149–158
13. Chopp M, Portnoy HD (1980) Systems analysis of intracranial pressure. Comparison with volume-pressure test and CSF-pulse amplitude analysis. *J Neurosurg* 53:516–527
14. Contant CF Jr, Robertson CS, Crouch J, Gopinath SP, Narayan RK, Grossman RG (1995) Intracranial pressure waveform indices in transient and refractory intracranial hypertension. *J Neurosci Methods* 57:15–25
15. Delwel EJ, de Jong DA, Avezaat CJ (2005) The prognostic value of clinical characteristics and parameters of cerebrospinal fluid hydrodynamics in shunting for idiopathic normal pressure hydrocephalus. *Acta Neurochir (Wien)* 147:1037–1042
16. Di Rocco C, Pettorossi VE, Caldarelli M, Mancinelli R, Velardi F (1978) Communicating hydrocephalus induced by mechanically increased amplitude of the intraventricular cerebrospinal fluid pressure: experimental studies. *Exp Neurol* 59:40–52
17. Eide PK, Sorteberg W (2005) Preoperative spinal hydrodynamics versus clinical change 1 year after shunt treatment in idiopathic

- normal pressure hydrocephalus patients. *Br J Neurosurg* 19:475–483
18. Elixmann IM, Hansinger J, Goffin C, Antes S, Radermacher K, Leonhardt S (2012) Single pulse analysis of intracranial pressure for a hydrocephalus implant. *Conf Proc IEEE Eng Med Biol Soc* 2012:3939–3942
  19. Foltz EL, Aine C (1981) Diagnosis of hydrocephalus by CSF pulse-wave analysis: a clinical study. *Surg Neurol* 15:283–293
  20. Galeano M, Calisto A, Bramanti A, Angileri F, Campobello G, Serrano S, Azzerboni B (2011) Classification of morphological features extracted from intracranial pressure recordings in the diagnosis of normal pressure hydrocephalus (NPH). *Conf Proc IEEE Eng Med Biol Soc* 2011:2768–2771
  21. Gjerris F, Borgeesen SE (1992) Current concepts of measurement of cerebrospinal fluid absorption and biomechanics of hydrocephalus. *Adv Tech Stand Neurosurg* 19:145–177
  22. Haykin SS (1999) *Neural networks: a comprehensive foundation*. Prentice Hall Upper Saddle River, NJ
  23. Hirai O, Handa H, Ishikawa M, Kim SH (1984) Epidural pulse waveform as an indicator of intracranial pressure dynamics. *Surg Neurol* 21:67–74
  24. Hu X, Glenn T, Scalzo F, Bergsneider M, Sarkiss C, Martin N, Vespa P (2010) Intracranial pressure pulse morphological features improved detection of decreased cerebral blood flow. *Physiol Meas* 31:679–695
  25. Hu X, Xu P, Scalzo F, Vespa P, Bergsneider M (2009) Morphological clustering and analysis of continuous intracranial pressure. *IEEE Trans Biomed Eng* 56:696–705
  26. Kahlon B, Sundbarg G, Rehnrona S (2002) Comparison between the lumbar infusion and CSF tap tests to predict outcome after shunt surgery in suspected normal pressure hydrocephalus. *J Neurol Neurosurg Psychiatry* 73:721–726
  27. Li JR, He WW, Yao JJ, Wen XL (1993) Classification of pulse waveform of cerebral spinal fluid during intracranial pressure monitoring. *Chin Med J (Engl)* 106:809–813
  28. Light WA, Science and Engineering Research Council (Great Britain) (1991) *Advances in numerical analysis*. Clarendon Press; Oxford University Press, Oxford
  29. Malm J, Jacobsson J, Birgander R, Eklund A (2011) Reference values for CSF outflow resistance and intracranial pressure in healthy elderly. *Neurology* 76:903–909
  30. Malm J, Kristensen B, Karlsson T, Fagerlund M, Elfverson J, Ekstedt J (1995) The predictive value of cerebrospinal fluid dynamic tests in patients with idiopathic adult hydrocephalus syndrome. *Arch Neurol* 52:783–789
  31. Mariak Z, Swiercz M, Krejza J, Lewko J, Lyson T (2000) Intracranial pressure processing with artificial neural networks: classification of signal properties. *Acta Neurochir (Wien)* 142:407–411
  32. Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T, Dunbar J (2005) Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients. *J Neurosurg* 102:987–997
  33. Morgalla MH, Stumm F, Hesse G (1999) A computer-based method for continuous single pulse analysis of intracranial pressure waves. *J Neuro Sci* 168:90–95
  34. Nocedal J, Wright SJ (1999) *Numerical optimization*. Springer, New York
  35. Piper IR, Chan KH, Whittle IR, Miller JD (1993) An experimental study of cerebrovascular resistance, pressure transmission, and craniospinal compliance. *Neurosurgery* 32:805–815
  36. Portnoy HD, Chopp M (1981) Cerebrospinal fluid pulse wave form analysis during hypercapnia and hypoxia. *Neurosurgery* 9:14–27
  37. Portnoy HD, Chopp M, Branch C, Shannon MB (1982) Cerebrospinal fluid pulse waveform as an indicator of cerebral autoregulation. *J Neurosurg* 56:666–678
  38. Scalzo F, Asgari S, Kim S, Bergsneider M, Hu X (2010) Robust peak recognition in intracranial pressure signals. *Biomed Eng Online* 9:61
  39. Scalzo F, Xu P, Asgari S, Bergsneider M, Hu X (2009) Regression analysis for peak designation in pulsatile pressure signals. *Med Biol Eng Comput* 47:967–977
  40. Swiercz M, Mariak Z, Krejza J, Lewko J, Szydlak P (2000) Intracranial pressure processing with artificial neural networks: prediction of ICP trends. *Acta Neurochir (Wien)* 142:401–406
  41. Takizawa H, Gabra-Sanders T, Miller JD (1987) Changes in the cerebrospinal fluid pulse wave spectrum associated with raised intracranial pressure. *Neurosurgery* 20:355–361

## Comment

Nucci and coworkers describe their automated analysis and clinical validation of intracranial pressure wave morphological classification in 60 patients. As the authors themselves point out in the discussion, the clinical relevance of ICP wave morphological analysis is still unsettled. However, studies like the present one, combining ICP pulse waveform assessment with the options created by the rapidly increasing computer technology, should help us to get a better evaluation of this approach.

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