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Effect of infusion tests on the dynamical properties of intracranial pressure in hydrocephalus

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ABSTRACT

Background and objective: Hydrocephalus comprises a number of conditions characterised by clinical symptoms, dilated ventricles and anomalous cerebrospinal fluid (CSF) dynamics. Infusion tests (ITs) are usually performed to study CSF circulation and in the preoperatory evaluation of patients with hydrocephalus. The study of intracranial pressure (ICP) signals recorded during ITs could be useful to gain insight into the underlying pathophysiology of this condition and to further support treatment decisions. In this study, two wavelet parameters, wavelet turbulence (*WT*) and wavelet entropy (*WE*), were analysed in order to characterise the variability, irregularity and similarity in spectral content of ICP signals in hydrocephalus.

Methods: One hundred and twelve ICP signals were analysed using *WT* and *WE*. These parameters were calculated in two frequency bands: B_1 (0.15–0.3 Hz) and B_2 (0.67–2.5 Hz). Each signal was divided into four artefact-free epochs corresponding to the basal, early infusion, plateau and recovery phases of the IT. We calculated the mean and standard deviation of *WT* and *WE* and analysed whether these parameters revealed differences between epochs of the IT.

Results: Statistically significant differences ($p < 1.70 \cdot 10^{-3}$, Bonferroni-corrected Wilcoxon signed-rank tests) in pairwise comparisons between phases of ITs were found using the mean and standard deviation of *WT* and *WE*. These differences were mainly found in B_2.

Conclusions: Wavelet parameters like *WT* and *WE* revealed changes in the signal time-scale representation during ITs. Statistically significant differences were mainly found in B_2, associated with ICP pulse waves, and included a higher degree of similarity in the spectral content, together with a lower irregularity and variability in the plateau phase with respect to the basal phase.

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1. Introduction

Adult hydrocephalus encompasses a heterogeneous group of disorders occurring in a wide range of ages, severity of symptoms and physiological states [1]. Patients with hydrocephalus generally show clinical symptoms, ventriculomegaly and anomalous cerebrospinal fluid (CSF) dynamics [1,2]. Normal pressure hydrocephalus (NPH) can appear as a primary condition [3] or as a consequence of subarachnoid haemorrhage, traumatic brain injury (TBI) or meningitis [1,3]. Implantation of a CSF shunt is the main treatment option [4]. However, not all patients improve after surgery and their condition becomes challenging for neurosurgeons [1,5]. Despite the recent advances, treatment is sometimes based on a limited knowledge of the underlying pathophysiology [6]. Therefore, the study of intracranial pressure (ICP) and CSF dynamics can provide valuable information on the management of patients with hydrocephalus [7].

Lumbar infusion tests (ITs) are frequently performed in the preoperatory evaluation of subjects who show features of NPH [8]. In ITs, ICP is artificially raised by the injection of fluid in the lumbar CSF space. Then, pressure is recorded and the resistance to CSF outflow is calculated [8]. Additionally, the applications of ITs include the assessment of shunt function [9], the analysis of metabolic changes in periventricular white matter [10] and the study of the haemodynamic response associated with ICP [11].

Traditionally, therapies derived from ICP monitoring relied on the time-averaged mean, as this parameter has been related to pathological patterns [12]. However, it does not account for all the information contained in the ICP waveform and does not clarify the pathophysiology underlying NPH [8,12]. For this reason, prior research has been devoted to the development of alternatives to study ICP. Some of them were based on non-linear methods, including approximate entropy [13], multiscale entropy [14] and Lempel–Ziv complexity [8,15]. Results revealed that intracranial hypertension was associated with a lower ICP signal complexity in children with TBI [13,15] and in adults with hydrocephalus [8]. Moreover, reduced complexity seems to be linked to poor outcome after TBI [14]. On the other hand, previous studies addressed the spectral analysis of ICP signals [11,16–18]. Thereby, the reconstruction of an ICP signal from its first harmonic was accomplished [17]. The relationship between resistance to CSF outflow and three spectral components of the ICP waveform was also analysed [11]. Finally, the study of very low frequency components of the ICP signal (slow waves) has also received interest [16]. In our previous research, we addressed the spectral analysis of ICP recordings from ITs using median frequency and relative power [18]. The morphology of ICP pulse waveforms has also been analysed to characterise ICP dynamics [19–21]. The Morphological Clustering and Analysis of ICP Pulse (MOCAIP) algorithm has been proposed to detect ICP pulse waveform peaks based on ICP and electrocardiographic (ECG) signals [20]. This approach has also been used in a later study to determine whether the morphology of ICP pulse waves could be helpful to detect slow waves in overnight recordings [19]. Besides, the relationship between the shape of intracranial pulse waves and brain compliance has been analysed in the control of a hydrocephalus shunt [21].

Recent studies proposed an alternative spectral representation of ICP signals using the wavelet transform. This is a suitable methodology due to the non-linear, non-stationary and multiscale aspects of cerebral haemodynamics [22]. In this sense, some authors used the wavelet transform to analyse the instantaneous phase difference between arterial blood pressure (ABP) and ICP [22]. The wavelet spectrograms have been also analysed in long-term ICP recordings and ITs [23]. Parameters like windowed wavelet entropy and relative wavelet entropy, have been also used to study ICP signal irregularity in patients with hypertension [24].

The present study represents a novel approach to analyse the effectiveness of several wavelet-based measures in characterising the variability, irregularity and similarity in spectral content of ICP signals in hydrocephalus. Initially, a time-scale representation of ICP signals was obtained by means of the continuous wavelet transform (CWT). Then, two parameters were calculated: wavelet turbulence (*WT*) and wavelet entropy (*WE*). They were analysed in two frequency bands: B_1 (0.15–0.3 Hz), related to respiratory blood pressure oscillations [25]; and B_2 (0.67–2.5 Hz), related to ICP pulse waves [25]. Thus, we tried to address the following research questions: (i) Are the proposed parameters useful to analyse the dynamical properties of ICP signals recorded during ITs? and (ii) Can the proposed parameters be useful to evaluate the influence of respiratory and pulse waves of the ICP waveform in NPH?

2. Materials and methods

2.1. Patients

A database of 112 ICP signals recorded during ITs at the Department of Neurosurgery of the University Hospital of León (Spain) was analysed. The recordings belonged to patients with hydrocephalus (65 male and 47 female, age 74 ± 14 years, mean ± standard deviation, SD). Ventriculomegaly was observed in all patients (Evans index ≥ 0.30). Participants presented different combinations of Hakim's triad: gait disturbances, cognitive deterioration and urinary incontinence [9]. Lumbar ITs were performed as a supplementary hydrodynamic study to help in the decision on the surgical management of patients [8]. Table 1 summarises the data of the population under study.

All patients or a close relative gave their informed consent to be included in the study. The study was approved by the Ethics Committee at the University Hospital of León (Spain).

Table 1 – Data recorded from the subjects under study.

Characteristic	Value (median [IQR])
Number of subjects (n)	112
Age (years)	74 [63–80]
Ventricular size (Evans index, E)	0.37 [0.35–0.41]
Basal pressure (P_0) (mm Hg)	7.71 [5.53–11.10]
Basal amplitude (A_0) (mm Hg)	2.73 [1.57–3.46]
Plateau pressure (P_p) (mm Hg)	24.95 [18.57–32.67]
Plateau amplitude (A_p) (mm Hg)	9.74 [5.93–13.85]
Outflow resistance (R) (mm Hg ml^{-1} min)	11.21 [7.34–14.98]

IQR: interquartile range.