Analysis of Intracranial Pressure Signals Using the Spectral Turbulence

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Abstract—**Hydrocephalus includes a range of conditions characterized by clinical symptoms, enlarged ventricles and disorders in cerebrospinal fluid (CSF) circulation. Infusion tests can be used to analyze CSF dynamics in patients with hydrocephalus. In infusion tests, intracranial pressure (ICP) is artificially raised, while the resulting ICP is measured in order to detect CSF circulation alterations. In this study, we analyzed 77 ICP signals recorded during infusion tests using the spectral turbulence (*ST*). Each signal was divided into four artifact-free epochs. The mean *ST*, <*ST*>, and the standard deviation of *ST*, SD[*ST*], were calculated for each epoch. Statistically significant differences were found between the basal phase of the infusion test and the remaining phases using <*ST*> and SD[*ST*] ($p<1.7\cdot10^{-3}$, Bonferroni-corrected Wilcoxon tests). Furthermore, we found significantly higher <*ST*> and significantly lower SD[*ST*] values in the plateau phase than in the basal phase. These findings suggest that the increase in ICP induced by infusion studies is associated with a significant loss of irregularity and variability of the spectral content of ICP signals. In conclusion, spectral analysis of ICP signals could be useful for understanding CSF dynamics in hydrocephalus.**

Keywords—**Hydrocephalus, intracranial pressure, spectral turbulence.**

I. INTRODUCTION

The term hydrocephalus encompasses a range of disorders characterized by clinical symptoms, abnormal brain imaging and derangement of cerebrospinal fluid (CSF) dynamics [1]. The study of intracranial pressure (ICP) and CSF dynamics can help in the decision about performing shunt placement surgery and can also provide valuable information for shunted patient management [2]. Infusion tests are routinely performed to study CSF circulation disorders in patients showing features of hydrocephalus. In infusion tests, CSF pressure is increased by addition of external volume. The resulting ICP is recorded, usually in the lumbar subarachnoidal space [3].

Some therapies in hydrocephalus are based on the ICP time-averaged mean [3], [4]. However, this parameter does not account for all the information included in the ICP waveform and does not provide a deep insight into cerebral autoregulation mechanisms [3], [4]. Several methods have been developed in order to better understand CSF circulation disorders. Some of them rely on the nonlinear [3], [5] or spectral [4], [6], [7] analysis of ICP signals.

In this study we applied the spectral turbulence (*ST*) to characterize ICP signals recorded during infusion tests in patients with hydrocephalus. This is a spectral parameter that quantifies the irregularity of ICP recordings in terms of the degree of similarity between the power spectral density (PSD) of adjacent segments of the ICP signals. *ST* can be regarded as an alternative to other standard irregularity measures, such as entropies or disequilibrium measures [8]. We believe that *ST* could be useful to characterize irregularity patterns during episodes of intracranial hypertension induced by infusion studies. Therefore, the aims of this study were: (i) to analyze the irregularity patterns in ICP signals based on *ST*; (ii) to test whether *ST* could reveal significant differences among phases of the infusion study; and (iii) to introduce an alternative framework to understand brain dynamics in hydrocephalus.

II. SUBJECTS AND ICP DATA RECORDING

ICP signals of 77 patients showing features of hydrocephalus (41 male and 36 female, age 69 ± 14 years, mean ± standard deviation, SD) were recorded during infusion tests at the Department of Neurosurgery of the University Hospital of León (Spain). Infusion tests were performed as a supplementary hydrodynamic study and as a decision aid on the surgical management of patients [3]. Patients or a close relative gave their informed consent to participate in the study, which was approved by the local ethics committee.

Infusion studies were performed using a variant of the Katzman and Hussey method [9]. Under local anesthesia, patients were positioned in the lateral recumbent position and two needles (caudal needle and rostral cannula) were inserted in their lower lumbar region. The caudal needle was connected to an infusion pump (Lifecare® 5000, Abbott Laboratories). The rostral cannula was connected to a pressure microtransducer (Codman® MicroSensorTM ICP transducer, Codman & Shurtleff). The pressure signal from the analog output of the microtransducer monitor was amplified (ML110 Bridge amplifier) and digitized (PowerLab 2/25 Data Recording System ML825, ADI Instruments).

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The analog to digital converter was connected to a computer in order to visualize and record the ICP signals. After 5 minutes of baseline recording, a Ringer solution at a constant infusion rate of 1.5 ml/min was infused until a plateau was reached. After the infusion stopped, CSF pressure was recorded until it decreased towards baseline levels [3]. For each recording, a neurosurgeon selected four artifact-free epochs, representative of four phases of the infusion test:

- Epoch 0 (E0) corresponds to the basal phase.
- Epoch 1 (E1) is representative of the early infusion phase and usually describes an ascending slope.
- Epoch 2 (E2) corresponds to the plateau phase.
- Epoch 3 (E3) represents the recovery phase, once the infusion has stopped and the ICP signal returns slowly to basal state levels.

ICP recordings were acquired with a sampling frequency of 100 Hz. The recordings were also processed using a finite impulse response (FIR) bandpass filter with cut-off frequencies 0.1 Hz and 10 Hz. This frequency range was chosen in order to minimize the influence of the DC component and preserve the relevant spectral content [7].

III. Methods

A. Calculation of Spectral Turbulence

A Fourier analysis was carried out in order to characterize the spectral content of ICP signals. Biomedical signals are intrinsically non-stationary [10]. Thus, we analyzed the ICP signals using the short-time Fourier transform (STFT), since it takes into account their time-varying properties. Each ICP signal was divided into N_T segments of 5 s (length L= 500 samples) with an overlap of 4 s [3], [7]. The power spectral density (PSD) was calculated as the Fourier transform of the autocorrelation function in each temporal window [8], [11]. The PSD was normalized to a scale from 0 to 1 leading to the normalized PSD, $PSD_n^{(i)}(f)$, in each temporal interval i ($i = 1,\ldots,N_T$).

From PSD_n different time-frequency parameters can be calculated. ST is a measure that quantifies the spectral changes of the signal over time [12]. It is based on calculating the PSD_n map and comparing adjacent spectra by means of the correlation coefficient [12], [13]. It can be defined as:

$$ST^{(i)} = \rho\left[PSD_n^{(i)}(f), PSD_n^{(i+1)}(f)\right], \quad i = 1,\ldots,N_T - 1, \qquad (1)$$

where $\rho[\cdot]$ denotes the Pearson correlation coefficient between $PSD_n^{(i)}(f)$ and $PSD_n^{(i+1)}(f)$.

The mean (<ST>) and the standard deviation (SD[ST]) of ST were subsequently calculated from the time series formed by the temporal evolution of ST. <ST> summarizes the average degree of similarity between the spectral content of adjacent time slices, while SD[ST] describes the lack of homogeneity in correlation around the mean value [14]. An average value of <ST> and SD[ST] in the four artifact-free epochs was obtained for each subject. We will denote by <$ST0$> to the average value of ST in E0, by <$ST1$> to the mean ST value in E1, by <$ST2$> to the mean ST value in E2 and by <$ST3$> to the mean ST value in E3. Similarly, SD[$ST0$], SD[$ST1$], SD[$ST2$] and SD[$ST3$] represent the value of SD[ST] in E0, E1, E2 and E3, respectively.

B. Statistical Analysis

An initial exploratory analysis was performed to study the data distribution. The Kolmogorov–Smirnov test with Lilliefors significance correction and the Shapiro–Wilk test were used to assess the normality of <ST> and SD[ST] in the four artifact-free epochs. Variables did not meet parametric test assumptions. Thus, the non-parametric Friedman test was used to determine whether statistically significant interactions (α=0.01) could be found between epochs of the infusion test [15]. *Post hoc* analyses were carried out using the Wilcoxon signed rank test with Bonferroni correction to account for multiple comparisons (α=0.01/6=$1.7\cdot10^{-3}$) [15].

IV. Results

We calculated the PSD for the 5-s segments in which each ICP recording was divided. The evolution of ST over time was then computed from PSD_n. Finally, the mean values (<$ST0$>, <$ST1$>, <$ST2$> and <$ST3$>) and the standard deviations (SD[$ST0$], SD[$ST1$], SD[$ST2$] and SD[$ST3$]) of ST in the four artifact-free epochs were obtained.

Table 1 summarizes the mean values of the epoch length, CSF pressure, <ST> and SD[ST]. These values were averaged over the 77 subjects in our database. These results show that the lowest <ST> value was obtained in the basal phase, then increased during infusion to reach the highest values in the plateau phase and, finally, decreased in the recovery phase. In the case of SD[ST], the highest SD[ST] values were obtained for the basal phase, then decreased during infusion towards the lowest SD[ST] values, obtained in the plateau phase. Finally, SD[ST] increased again during the recovery phase. These evolutions are depicted in Fig. 1.

The Friedman test revealed significant interactions among <ST> values ($\chi^2(3)$=55.89, p=$4.27\cdot10^{-12}$<0.01) and SD[ST] values ($\chi^2(3)$=23.14, p=$3.78\cdot10^{-5}$<0.01). In order to analyze these interactions, *post hoc* analyses were carried out using the Wilcoxon signed rank test with Bonferroni correction. Statistically significant differences were found between the following pairs: <$ST0$> vs. <$ST1$>, <$ST0$> vs. <$ST2$>, <$ST0$> vs. <$ST3$>, SD[$ST0$] vs. SD[$ST1$], SD[$ST0$] vs. SD[$ST2$] and SD[$ST0$] vs. SD[$ST3$]. These results are

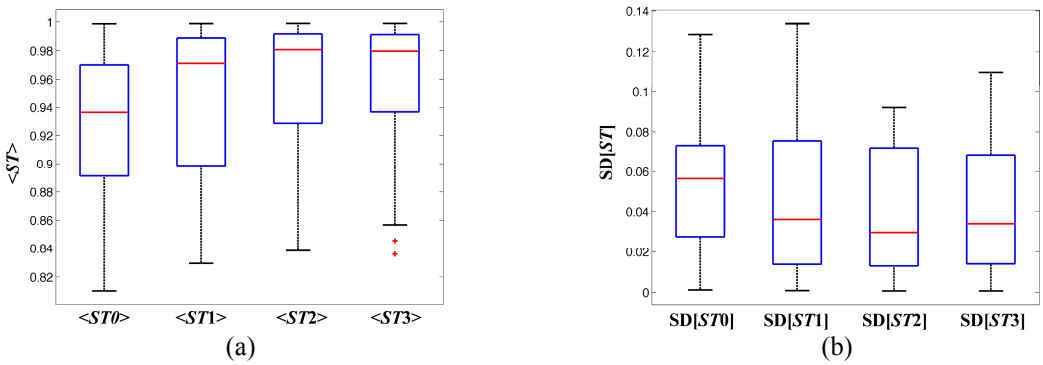

Fig. 1 Boxplots displaying the distribution of <*ST*> and SD[*ST*] in the four artifact-free epochs. (a) <*ST*>. (b) SD[*ST*].

summarized in Table 2, where the statistically significant values have been highlighted.

V. Discussion

In this study, we analyzed the changes produced in *ST* during infusion studies in patients with hydrocephalus. <*ST*> and SD[*ST*] were calculated for the four artifact-free epochs in which the infusion study was divided.

Our results showed that significant differences were found between the basal phase and the remaining phases of the infusion tests using <*ST*>. It is noteworthy that a significant increase in <*ST*> was found in the plateau phase with respect to the basal phase. This suggests that intracranial hypertension due to volume loading results in a significantly higher degree of similarity in the spectral content. Besides, <*ST*> can be considered as an indirect measure of the irregularity of the signal [14]. Thus, the increase in <*ST*2> with respect to <*ST*0> is associated with an irregularity loss in E2 with respect to E0. This result correlates with the decrease in Lempel-Ziv (LZ) complexity between the plateau and basal phases of infusion studies found in [3]. Decreased complexity during episodes of intracranial hypertension has also been found in pediatric patients with traumatic brain injury [5]. Certainly, irregularity and complexity are linked, focusing on different signal characteristics. They can be regarded as complementary measures to quantify the degree of disorder in infusion tests.

Results in Table 2 also show that significant differences were found between E0 and the remaining phases of the infusion test using SD[*ST*]. Besides, our results showed a significant decrease in SD[*ST*2] with respect to SD[*ST*0]. These findings suggest that there is a significantly lower variability in the spectral content when CSF pressure reaches the range of intracranial hypertension. This variability reduction could be linked to the decrement in data dispersion found in previous studies on infusion tests [3], where lower SD values in LZ complexity were found in the plateau phase than in the basal phase.

The decreased irregularity and variability during episodes of intracranial hypertension found in this study might be explained from an early Cushing response mediated by a moderate rise in ICP during infusion studies [3], [16]. This early Cushing response elicits a moderate rise in arterial blood pressure, a mild decrease in cerebral perfusion pressure, a reduction of cerebral blood flow and an increase in the heart rate variability without a modification of its mean value [16]. These processes could affect the shape of the

Table 1 Mean values of the epoch length, CSF pressure, <*ST*> and SD[*ST*] for the four artifact-free epochs

Parameter	E0	E1	E2	E3
Length (s)	175 ± 54	300 ± 49	497 ± 139	199 ± 50
CSF pressure (mm Hg)	8.247 ± 3.747	16.241 ± 5.446	25.381 ± 8.975	16.381 ± 5.978
<*ST*>	0.930 ± 0.048	0.950 ± 0.049	0.957 ± 0.047	0.956 ± 0.045
SD[*ST*]	0.055 ± 0.030	0.042 ± 0.033	0.040 ± 0.029	0.039 ± 0.029

Table 2 *Z* statistics and *p*-values associated with the Wilcoxon tests for <*ST*> and SD[*ST*]

Parameter	E0 vs. E1		E0 vs. E2		E0 vs. E3		E1 vs. E2		E1 vs. E3		E2 vs. E3	
	Z	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*
<*ST*>	-5.69	**$1.28\cdot10^{-8}$**	-6.00	**$1.93\cdot10^{-9}$**	-6.27	**$3.54\cdot10^{-10}$**	-2.93	$3.40\cdot10^{-3}$	-2.08	$3.74\cdot10^{-2}$	-1.37	0.17
SD[*ST*]	-4.71	**$2.49\cdot10^{-6}$**	-4.62	**$4.18\cdot10^{-6}$**	-5.00	**$5.62\cdot10^{-7}$**	-0.47	0.64	-1.13	0.26	-0.57	0.57

ICP waveform in the plateau phase and influence the irregularity and variability of ICP signals. It has also been suggested that decreased irregularity is associated with greater system isolation [17]. It has been stated that increased hypertension and severity of brain injury produce physiological uncoupling between the cardiovascular and the autonomic system [18] and, thereby, decreased irregularity. These mechanisms have been suggested as a possible explanation for the decreased complexity in E2 reported in [3], which is related to the loss of variability found in our study.

Finally, some limitations merit further consideration. In this study, spectral analysis was performed on a heterogeneous group of patients showing features of hydrocephalus. Since this study is focused on assessing whether *ST* could derive alternative measures from ICP signals, heterogeneity in patient population should not be regarded as a serious drawback. It would also be desirable to test the proposed method on a larger set of ICP signals.

VI. Conclusion

In summary, <*ST*> and SD[*ST*] reveal changes in the ICP signal spectrum during stress episodes. Our findings suggest that the evolution of CSF pressure in infusion studies is characterized by a significant loss of irregularity and variability. We conclude that spectral measures, such as *ST*, may help to gain further insight into brain dynamics in hydrocephalus. Future research should explore other spectral parameters in order to obtain complementary information to better understand CSF dynamics in hydrocephalus.

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