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Pattern Recognition of Overnight Intracranial Pressure Slow Waves using Morphological Features of Intracranial Pressure Pulse

Magdalena Kasprowicz, Ph.D.^{a,b,d}, Shadnaz Asgari, Ph.D.^a, Marvin Bergsneider, M.D.^{a,c}, Marek Czosnyka, Ph.D.^d, Robert Hamilton^{a,c}, and Xiao Hu, Ph.D.^{a,c}

^aNeural Systems and Dynamics Laboratory, Department of Neurosurgery, the David Geffen School of Medicine, University of California, 924 La Conte Avenue, Suite 710, CA 90095, Los Angeles ^bInstitute of Biomedical Engineering and Instrumentation, Wroclaw University of Technology, Wyb. Wyspińskiego 27, 50-370 Wroclaw, Poland ^cBiomedical Engineering Graduate Program, Henry Samueli School of Engineering and Applied Science, University of California, CA 90095, Los Angeles ^dAcademic Neurosurgical Unit, Addenbrooke's Hospital, Hills Road, Box CB2 0QQ Cambridge, United Kingdom

Abstract

This study aimed to develop a new approach to detect intracranial pressure (ICP) slow waves based on morphological changes of ICP pulse waveforms. A recently proposed Morphological Clustering and Analysis of ICP Pulse (MOCAIP) algorithm was utilized to calculate a set of metrics that characterize ICP pulse morphology. A regularized linear quadratic classifier was used to test the hypothesis that classification between ICP slow wave and flat ICP could be achieved using features composed of mean values and dispersion of 24 MOCAIP metrics. To optimize the classification performance, three feature selection techniques (differential evolution, discriminant analysis and analysis of variance) were applied to find an optimal set of MOCAIP metrics under different criteria. In addition, we selected three sets of metrics common to those found by combination of two selection methods, to be used as classification features (differential evolution and analysis of variance, discriminant analysis and analysis of variance, and combination of differential evolution and discriminant analysis). To test the approach, a total of 276 selections of ICP recordings corresponding to two patterns without waves and containing slow waves were obtained from overnight ICP studies of 44 hydrocephalus patients performed at the UCLA Adult Hydrocephalus Center. Our results showed that the best classification performance of differentiation of slow waves from the ICP recording without slow waves was obtained using the combination of metrics common to both differential evolution and analysis of variance methods; achieving an accuracy of 89%, specificity 96%, and sensitivity 83%.

Keywords

Intracranial Pressure; Slow Waves; Pulse Morphology; Hydrocephalus; Machine Learning

Introduction

The diagnosis and management of normal pressure hydrocephalus (NPH) remain challenging predominantly due to a lack of reliable methods of selecting candidates for shunt implantation and third ventriculostomy, a procedures that remain to be the most popular surgical treatment but meanwhile are associated with significant complications (Marmarou et al., 2005). Commonly accepted investigations include neuropsychological test, brain imaging, biochemical analysis of cerebrospinal fluid (CSF), etc. Other forms of identifying shunt responders involving studies of intracranial pressure (ICP) have been developed because abnormal ICP dynamics is thought to be associated with NPH (Katzman and Hussey, 1970; Wikkelsø et al., 1982; Eide and Brean, 2006; Eklund et al., 2007; Czosnyka et al., 2008). None of them, however, can definitely differentiate between shunt responders and non-responders. Among these tests, the role of overnight ICP monitoring still remains unclear and intriguing in clinical practice. Of particular interest in analyzing overnight ICP data is the characterization of ICP slow waves, also known as Lundberg's B-waves. It is defined as ICP oscillations with a frequency of 2-0.5/minute and large amplitude (Lundberg, 1960). There is evidence that frequent presence of ICP slow waves predicts a positive outcome after shunt implant (Symon and Dorsch, 1975; Pickard JD, 1980; Raftopoulos et al., 1992). However, the opposite findings have been also reported (Williams et al., 1998; Stephensen et al., 2005; Woodworth et al., 2009). There also exists indirect evidence that certain characteristics of ICP slow waves may contain useful information for correctly diagnosing NPH and predicting shunt response. It was recently found that increased ICP pulse pressure amplitude has a predictive value for shunt response (Eide and Brean, 2006; Czosnyka et al., 2007). However, these authors failed to report whether an increase of ICP pulse pressure amplitude was associated with frequency of slow wave occurrence. It is well known that ICP slow waves usually contain episodes of transient ICP elevation in the positive phase of the wave, during which amplitude of ICP pulses increases (Ellis et al., 2007). Therefore, it is possible that the predictive values associated with increased ICP pulse amplitude stems from occurrence of slow waves. Consequently, investigating the role of ICP pulse amplitude and other ICP pulse morphological metrics (Hu et al., 2008; Hu et al., 2009) in diagnosis and management of NPH patients should ideally be conducted with an awareness of the presence or absence of slow waves.

Unfortunately, detecting the presence of slow waves in an overnight ICP is not straightforward. Despite current advances in computerized data analysis, visual screening of ICP signals to detect slow waves still remains the most common way of overnight ICP analysis. This method is very inaccurate hence it might lead to contradictory conclusions of the predictive value of ICP slow waves. There have been a few studies of the methodologies of detecting ICP slow waves (Hara et al., 1990; Eklund et al., 2001; Walter et al., 2002). However, these methods neglected changes and characteristics of individual ICP pulses during ICP slow waves presence.

In the present work, we proposed a new approach to detect and separate periods of ICP slow waves (BW) from those of flat or nearly flat ICP (NW) in an overnight ICP recording. This approach utilizes the morphological changes of ICP pulses. Our intention was to advance the existing methodology of analyzing overnight ICP recording. This study utilizes an algorithm that automates the process of detecting and designating the three peaks of an ICP pulse (Hu et al., 2009) termed Morphological Clustering and Analysis of ICP Pulse (MOCAIP). We hypothesized that mean values and variations of ICP pulse morphological metrics extracted by the MOCAIP algorithm can be effectively used as input feature vectors to a classification algorithm to distinguish between periods of flat ICP (NW) and those with slow waves (BW). Such a classifier can then be used to construct an automated ICP slow wave recognition algorithm.

Materials and methods

Patient and data preparation

Pre-shunt operative overnight intracranial pressure (ICP) recordings performed in 44 patients (18 females and 26 males) hospitalized at the UCLA Adult Hydrocephalus Center. The mean age of the patients was 68 ± 17 years (range $32 \div 94$ years). All patients presented ventricular dilatation evidenced on brain imaging (CT or MRI scan). Hydrocephalus was diagnosed for all patients based on brain scan and clinical picture (gait disturbance, urinary incontinence, and dementia). An insertion of the ICP sensor and data acquisition were approved by the local IRB committee and an informed consent was obtained from each patient or from their family member. An intraparenchymal ICP microsensor (Codman and Schurtleff, Raynaud, MA) was inserted in the right frontal lobe. Simultaneous recordings of ICP and ECG signals were performed using either a PowerLab™ SP-16 acquisition system (ADInstruments, Colorado Springs, CO) connected to the analog outputs of both the Codman ICP Express Box and the GE bedside monitor or the BedMaster™ system that acquires data from bedside monitors. A different sampling rate was used by the acquisition systems PowerLab™ - 400 Hz and BedMaster™ - 240 Hz.

The signal recordings were visually screened by 3 independent experts to select both BW and NW patterns. Figure 1 (a) presents an example of ICP overnight monitoring where, initially fairly stable ICP recording transforms into clearly distinguishable slow waves with relatively high amplitude and asymmetrical shape (long ascending phase followed by rapid decrease of ICP). In our study, small ICP slow waves with amplitude less than 6 mm Hg were classified as NW pattern. As both patterns of ICP (BW and NW) might occur repetitively during overnight monitoring in the same patient, we included several selections from the same study. The total number of selected patterns was 276 (NW-131 and BW-145).

MOCAIP algorithm

ICP pulse shape was quantitatively characterized by 24 metrics (Table1) calculated based on Morphological Clustering and Analysis of ICP Pulse (MOCAIP) algorithm. Details of this algorithm were precisely described in another publication (Hu et al., 2009). The input signal to the algorithm includes ICP and ECG. First, the ICP pulses are detected. To achieve this, MOCAIP utilizes an ECG QRS detection technique (Afonso et al., 1999) integrated with an ICP pulse extraction method (Hu et al., 2008). Then, the representative pulse is extracted from a sequence of consecutive ICP pulses using a clustering method. An averaged pulse obtained from the largest cluster is called a dominant pulse. The sequence of dominant pulses calculated from 30 seconds of the ICP recording including both NW and BW is presented in Fig.1(b). The clustering approach and averaging process effectively reduce influence of noise and artifacts in the ICP signal originating from patient movement, coughing, transportation, ICP sensor detachment, and amplifier devices. However, the dominant pulse should be invalid in the case that the whole segment is noisy. Therefore, the MOCAIP algorithm utilizes a reference ICP pulse library to further help recognize legitimate dominant ICP pulses. As the validation process is successfully completed, the MOCAP detects a set of sub-peak candidates that are detected as either inflection points or local maximas. The average number of candidate peaks as reported in our original study (Scalzo et al., 2009) was 5.67 per pulse. In the next step, the peak designation process is applied to determine three peaks (P_1 , P_2 , P_3) from the set of candidate peaks in each valid dominant pulse. Finally, the set of ICP pulse metrics based on the determined peaks are calculated: amplitudes (dP_1 , dP_2 , dP_3) and their ratios (dP_{12} , dP_{13} , dP_{23}), latencies (L_T , L_1 , L_2 , L_3) and their differences (L_{12} , L_{13} , L_{23}), curvatures ($Curv_m$, $Curv_1$, $Curv_2$, $Curv_3$), their ratios ($Curv_{12}$, $Curv_{13}$, $Curv_{23}$), slope of ascending phase (slope), decay time constant (RC) and mean and diastolic value of ICP (mICP and diasICP, respectively). As is shown in Fig.

1(c) and (d), the shape as well as the dispersion of ICP pulse waveforms change when the ICP pattern transforms from NW to BW. Hence, the values of MOCAIP metrics, calculated for each dominant pulse are more spread out during BW than NW. Therefore we calculated, besides mean values of 24 MOCAIP metrics, standard deviations (S.D.) of mean of every MOCAIP feature for every selection (about 10 minutes of raw ICP data) to capture morphological changes of ICP pulse waveforms during B wave occurrence.

Feature selection

We used a simple regularized linear quadratic classifier (Webb, 2002) to test the hypothesis that ICP slow waves (BW) can be separated from NW based on morphological changes of ICP pulse waveforms. The performance of the classification experiment was evaluated by standard measures: sensitivity (Se), specificity (Spe), positive predictivity (PPV), and accuracy (Ac). Twenty four morphological metrics for every dominant ICP pulse (extracted from 30 seconds of ICP signal) were calculated using above described MOCAIP algorithm. The full set of input metrics consisted of 24 mean values and 24 standard deviations of MOCAIP metrics calculated from each selection. As using full 48-dimension feature vector may cause over-fitting the data and the possible correlations among metrics might decrease classification performance, a subset of ICP metrics is needed. In the present work, we investigated three different methods of feature selection and an additional three based on all combinations of pairs of the three methods.

As a simple approach, we compared the means of each single metric between the two groups: NW and BW using the classic analysis of variance (V). We then selected those metrics to be used as features for classification that demonstrated significant difference between the two groups. This method only analyzes the importance of a single metric (SM), neglecting the possible correlation among the other metrics. As there was more than one selection from the same patient included to this study, we averaged the data over multiple selections of the same ICP pattern (BW or NW) in each patient, which resulted in total 76 selections (44 NW and 32 BW). The level of significance for ANOVA analysis was set at 0.001. The log transformation of the majority of data was done to meet the assumptions of ANOVA (normal distribution and homogeneity of variance).

In contrast to the first approach, it may be the case that certain combination of ICP metrics may have better discrimination power even if its individual constituent metric does not pass the analysis of variance test. Therefore, it may be more meaningful to search for best combinations. Due to the sheer number of possible combinations of the 48 metrics (more than 140 trillion), a random search algorithm was needed to find the optimal solution within a reasonable amount of time. Implementing the differential evolution algorithm (DE) provided efficient and reasonably robust results (Price and Storn, 1997). DE has been proven to perform well on a wide variety of problems presenting powerful performance in terms of solutions optimality and feature selection (Price et al., 2005, Khushaba RN et al., 2009, Xingshi H et al., 2009).

Average of the Se and PPV was used as the objective function for DE algorithm to maximize, whose values were found by the standard leave-one-patient-out cross validation procedure (Webb, 2002.). A real number within [0, 1] was used to encode whether to select a particular ICP metric such that a metric is selected if the corresponding number is greater than 0.5. Besides the 48 metrics, two tunable parameters for the classifier: differential weight (F) and crossover probability (α) set at recommended values 0.95 and 0.9, respectively (Price and Storn, 1997), were also incorporated to the optimization process. In other words, DE searches the best solution within a 50-dimension hyper-cube. The choice of these two tunable DE parameters can affect the performance to some degree. Therefore, we cannot claim that the performance obtained in this study is the best one that can be achieved

using the DE algorithm. This issue remains to be studied using some recent techniques (Pedersen, 2010).

In comparing the computational advanced DE algorithm with standard dimensionality reduction technique we utilized discriminant analysis (DA) to select suitable features for BW and NW differentiation. The forward discriminant step-wise approach was used (McNitt-Gray et al., 1995, McLachlan, 2004). At each step of analysis 48 MOCAIP metrics were reviewed and evaluated to determine which one will contribute most to the discrimination between groups: NW and BW. The step-wise procedure was controlled by F value and tolerance value. Tolerance was calculated as $1-R^2$ of the respective metric with all other metrics included in the current model and the F to enter was set at recommended value 4.0 (Costanza and Afifi, 1979, McNitt-Gray et al., 1995). To remove potentially redundant variables from the model the minimum tolerance value was set at 0.01. We repeated the step-wise procedure 44 times, in every run the samples from one patient were excluded and the selections from the remaining 43 patients were used to build the discriminant model.

In addition to selecting features based on the DE algorithm, DA technique, and analysis of variance (V), three sets of possible useful features were chosen from those that overlapped the two sets selected by: DE+V, DA+V, DE+DA.

Classification performance

We repeated classification experiment seven times: first time for the set of optimal ICP metrics chosen by DE algorithm, second time for the set of ICP metrics selected based on analysis of variance (V), the third time for these metrics picked by step-wise DA approach and the next three runs were repeated for the metrics overlapped two sets: DE+V, DA+V and DE+DA, and finally we used only one parameter – S.D. of mean ICP to confirm possible advantage of using combination of metrics over single metric (SM). We used a bootstrapping cross-validation procedure (BB) to evaluate the performance of each classification experiment (Webb, 2002) because the leave-one-patient-out cross-validation was used to derive the objective function for the DE approach. To compare the performance of classification for different sets of metrics, we ran the bootstrapping procedure 25 times to calculate average and S.D. of performance metrics including Se, Spe, PPV and Ac. Once again we used the ANOVA technique ($p < 0.001$) to compare the performance of these seven independent classification experiments. The flowchart of classification algorithm is presented in Fig.2.

Results

Table 2 provides the information regarding each of the 48 metrics averaged over multiple selections of the same ICP pattern in each patient (mean and S.D. of MOCAIP metrics) calculated for both patterns: NW and BW. 'V' denotes metrics selected based on ANOVA technique, 'DE' metrics obtained from optimization procedure, 'DA' metrics selected by discriminant analysis, and finally metrics overlapped two of above-mentioned sets are tagged 'DE+V', 'DA+V', or 'DE+DA'. The classification performance (Se, Spe, PPV and Acc) from bootstrapping cross-validation process (BB) averaged over 25 repetitions for DE, V, DA, DE+V, DA+V, DE+DA and SM is presented in Fig.3 (a-d). Mean time for these calculation was 155 ± 35 sec.

Differential evolution (DE)

Sixteen metrics were chosen based on differential evolution algorithm (labeled as 'DE' in Table 2). Most of them were related to peak amplitudes (S.D. of: dP_2 , dP_{12} , dP_{13} , dP_{23} , mean values of: dP_{12} , dP_{13}), latencies (mean values of: L_T , L_1 , L_2-L_1 , L_3-L_2 , S.D. of: L_T ,

L_1, L_3-L_1) and S.D. of: total curvature ($Curv_T$) diastolic ICP (dICP) and mean ICP (mICP). Based on the cross validation results, BW can be distinguished from NW with specificity $96.7 \pm 0.2\%$, sensitivity $73.6 \pm 0.3\%$, accuracy $84.5 \pm 0.2\%$, and positive predictivity $96.1 \pm 0.2\%$ (Fig.3(a-d)).

Discriminant analysis (DA)

Based on DA step-wise analysis 13 metrics were selected at least once during 44 runs: dP_3 (1), $Curv_T$ (1), S.D. of $Curv_T$ (1), S.D. of $Curv_2$ (1), L_2 (2), L_1 (3), S.D. of LT (6), S.D. of dP_1 (8), $Curv_2$ (10), L_3-L_2 (29), S.D. of Slope (36), $Curv_3$ (40), S.D. of mean ICP (44). Numbers in brackets denote how many times a particular metric was selected. These metrics, which occurred most often (more than 10 times) were then used as input vector to the classifier. The final set consisted of 5 metrics: $Curv_2$, L_3-L_2 , $Curv_3$, S.D. of Slope, S.D. of mean ICP. Only one of these metrics (S.D. of mICP) was selected for every 44 discriminant models. The classification performance values for discrimination between NW and BW were: sensitivity $76.3 \pm 0.4\%$, specificity $91.6 \pm 0.2\%$, positive predictivity $91.0 \pm 0.2\%$ and accuracy $83.6 \pm 0.2\%$ (Fig. 3(a-d)).

Analysis of variance ANOVA (V)

ANOVA test showed that 13 metrics were significantly different between NW and BW (labeled as 'V' in Table 2). Only three of them were related to mean values (dP_2 , dP_3 and $Curv_2$) and the rest were associated with dispersion range – S.D. of: peak amplitudes (dP_1 , dP_2 , dP_3), and their ratios (dP_{12} and dP_{13}), curvatures ($Curv_T$ and $Curv_2$), slope of ascending part of ICP pulse waveforms and diastolic and mean ICP. No significant difference was found in latencies between BW vs. NW. Despite statistically significant separation in means, the noticeable overlap of samples exists as demonstrated in Fig.4 (a-c), where the distribution of three metrics divided into 2 groups: NW and BW were compared. Two of presented metrics with evident overlap (Fig.4 (b) and (c)) were not selected by DE algorithm, although they were selected by ANOVA test and in case of. S.D. of Slope (Fig. 4 (b)) also by DA. S.D. of mean ICP was chosen by all methods (DE, DA, V). This metric, as presented in Fig.4 (a), has a smaller amount of overlapping between NW and BW.

The performance values for differentiation between BW vs. NW for V set were: specificity $88.4 \pm 0.6\%$ sensitivity $84.4 \pm 0.3\%$, accuracy $86.2 \pm 0.3\%$ and positive predictivity $90.8 \pm 0.4\%$ (Fig.3(a-d)).

Differential evolution + Anova (DE+V)

There were six overlapping metrics (highlighted with gray in Table 2) between these two sets of features found by the DE and the V methods. None of the overlapped metrics was related to mean value of MOCAIP metrics. The D+V subset consists only of S.D. of following MOCAIP metrics dP_2 , dP_{12} , dP_{13} , $Curv_T$, dICP, mICP. The performance metrics for DE+V were: specificity $96.3 \pm 0.3\%$, sensitivity $83.0 \pm 0.5\%$, accuracy $88.9 \pm 0.3\%$ and positive predictivity $96.6 \pm 0.3\%$ (Fig.3(a-d)).

Discriminant analysis + Anova (DA+V) and Differential evolution + Discriminant analysis (DE+DA)

There were three metrics overlapping two sets of features selected by DA and V methods: $Curv_2$, S.D. of Slope and S.D. of mean ICP and two metrics common to both DE and DA sets: L_3-L_2 and S.D. of mean ICP. The classification performance metrics for DA+V were: sensitivity $71.0 \pm 0.4\%$, specificity $91.2 \pm 0.2\%$, positive predictivity $90.9 \pm 0.2\%$, accuracy $80.6 \pm 0.2\%$ and for DE+DA were: sensitivity $72.2 \pm 0.3\%$, specificity $93.6 \pm 0.2\%$, positive

predictivity $92.7 \pm 0.2\%$, accuracy $82.4 \pm 0.2\%$. These results were significantly worse than these achieved based on DE+V set (Anova; $p < 0.001$, Fig.3 (a-d)).

Single parameter analysis (SM)

The S.D. of mean ICP shows relatively small overlap between NW and BW groups (Fig. 4(a)) and was chosen by all feature selection methods DE, DA and V. Moreover S.D. of mean ICP was the only parameter which was selected during each 44 runs of DA step-wise procedure. The sensitivity ($71.0 \pm 0.4\%$) and accuracy ($82.1 \pm 0.2\%$) achieved for SM were significantly lower than those obtained for other feature sets: DE, DA, V, DE+V, DE+DA (Anova $p < 0.001$) with the exception of these calculated for DA+V set. The accuracy calculated based on SM was significantly higher than for DA+V set (Anova $p < 0.001$) and the sensitivity did not differ from this calculated for DA+V (Anova, $p > 0.05$). However, the specificity ($94.5 \pm 0.2\%$) and positive predictivity ($93.5 \pm 0.2\%$) obtained for SM were lower only than these calculated for DE and DE+V- Fig.3(a-d)).

Since accuracy of classification experiment for V+DE is the highest (88.9%) and the number of input metrics is reasonable small (6 metrics), we ranked this method as the best for separating BW from NW.

Discussion

We presented a new approach to distinguish ICP slow waves from flat ICP in an overnight recordings based on analysis of morphological changes of ICP pulse waveforms. The dispersion of dominant pulses of flat or nearly flat ICP recordings (NW) and that of ICP slow waves (BW) differs significantly. Therefore, we also evaluated their spread about mean to capture the variations of ICP pulse components during slow waves in addition to their mean values of MOCAIP metrics. According to our results, the changes in six morphological metrics (S.D. of: dP_2 , dP_{12} , dP_{13} , $Curv_T$, $dICP$, $mICP$) were sufficient to distinguish between BW from NW with high specificity 96.2% and acceptable accuracy 88.9%.

Proposed approach is a step forward to automate analysis of overnight ICP recording. Despite advance in computerized methods of data analysis, no tools exist to help analyze the overnight ICP recordings. Recently, a few automatic algorithms for calculation of slow waves present of ICP recording have been described (Hara et al., 1990; Eklund et al., 2001; Walter et al., 2002). Most of them utilized spectral analysis using fast Fourier Transform (FFT) and band pass filtering to identify slow waves ICP oscillations. However, ICP B waves changes with time in amplitude and duration therefore using linear methods like FFT to analyze non-stationary signal (ICP) may lead to misleading and inaccurate results. Moreover, information derived from these methods ignores potentially important knowledge about changes in morphology of ICP pulse waveform during ICP slow wave occurrence.

At present stage of our effort to automate a long term ICP recording analysis, a set of features discriminating between NW and BW was determined and the classification performance was estimated. Since the usefulness of this approach was confirmed, in the next step a fully automatic algorithm for BW recognition in continuous recorded data can be developed. In our study we took into consideration only segments of 'clean' episodes of BW and NW. In clinical practice, however, ICP recording may contain a mix of both NW and BW patterns and can be also contaminated by noise and artifacts. MOCAIP algorithm deals effectively with poor quality data by, one, utilizing a clustering procedure to extract a representative ICP pulse from each segment of data and two, by incorporating a reference library of validated ICP pulses to aid a recognition of nonartificial pulses (Hu et al., 2009).

The compound pattern including both types of NW and BW however can be classified with less accuracy than these presenting profound BW.

As we demonstrated in our study, the performance of classification experiment depends on choice of an optimal set of metrics that can be achieved using different feature selection methods. We used three different methods to select the optimal subset of metrics: differential evolution algorithm (DE), discriminant analysis (DA) and classic analysis of variance (V). The highest sensitivity (84.4%) but at the same time the lowest specificity (88.4%) were obtained using V method. The opposite results were achieved using the DE method: sensitivity was the lowest (73.6%) and specificity was the highest (96.7%) – Fig. 3(a) and (b). The sensitivity (76.3%) and specificity (91.6%) obtained for DA set were intermediate to these achieved for both DE and V methods (Fig. 3 (a-d)). Such a discrepancy between DE and V methods can be explained by possible mutual correlation among MOCAIP metrics. Analysis of variance technique is insensitive to dependency among the MOCAIP metrics because the significant difference in mean was evaluated independently for each single metric. While the DE algorithm explores the possible dependency among ICP metrics, it, however, does not penalize the size of final feature vector. It resulted in a feature vector of the greatest dimension. Step-wise discriminant analysis (DA) in turn is computationally similar to analysis of variance and furthermore allows to study the difference in two groups with respect to several features simultaneously as well as to control the dependence of the features. Nevertheless, the accuracy (86.6%) obtained for a set of metrics selected by DA was lower than both DE and V.

Based on our experiments, using DE in conjunction with V to derive the final set of metrics leads to the best classification results. The combination of methods: DA+V as well as DE +DA did not improve the classification performance. Combining DE and V methods appeared to be complementary in our study, however it may be highly specific and depends on the data base. Given the limited amount of data in the present study, either the high dimension feature vector obtained based on DE method or a set of metrics selected by standard DA step-wise approach, have proven not to generalize well by the bootstrapping test because a 6-dimension subset of the metrics included in those found by both DE and V achieved a much better sensitivity while not sacrificing the specificity.

Our results here suggest that feature selection is a critical step not to be neglected in pattern recognition studies.

The final list of 6 metrics selected by DE+V (S.D. of: dP_2 , dP_{12} , dP_{13} , $Curv_T$, $dICP$, $mICP$) reflects the most salient changes associated with ICP increase due to slow waves. We found that amplitude of P_2 component notably increases during ICP slow wave occurrence (hence S.D. of dP_2), which is also associated with increase in total curvature of the pulse (hence S.D. of $Curv_T$). Amplitude of P_1 , most probably related to systole of arterial pressure (Carrera et al., 2009), shows relatively moderate increase during BW in comparison with both dP_2 and dP_3 (hence S.D. of dP_{12} , S.D. of dP_{13}). Our findings are in accordance with existing literature (Cardoso et al., 1983; Miller et al., 1987; Czosnyka et al., 2007), however the interpretation remains difficult as the origin of the three ICP sub-peaks has not been established yet. Possibly, P_2 may be dependent upon the intracranial compliance (Germon, 1988) and an increase in amplitude of P_3 , as ICP evolves from a no-wave state to a slow wave state, reflects an increase in venous pressure (P_v), which in turn, strives to balance the increase in ICP (Chopp et al., 1983); however this explanation needs further confirmative study.

The proposed method is not limited to analyze overnight ICP recordings for hydrocephalus patients but can be also applied to any group of patients for whom continuous monitoring of

ICP is acquired. It was recently reported that low percentage of occurrence of ICP slow waves in patients after head injury is associated with fatal outcome (Balestreri et al., 2005). Hence the assessment of B wave content could be helpful to detect head injury patients at higher risk. Though, it may be likely that the combination of useful metrics for recognition between stable and unstable ICP recording is different for head injury patients and hydrocephalic ones. Hence the usefulness of proposed methodology for head injury patients needs to be confirmed in future studies.

In summary, the new approach presented here can be utilized to automate analysis of overnight ICP data. It can not only provide morphological information of ICP pulses but also can associate these pulse morphological changes within the context of whether slow waves occur. The results reported here can be still improved considering that further studies on different feature selection methods and more advanced forms of classifiers could potentially improve the performance of pattern recognition of ICP slow waves.

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References

- Afonso VX, Tompkins WJ, Nguyen TQ, Luo S. ECG beat detection using filter banks. *IEEE Trans. Biomed. Eng.* 1999; 46(2):192–202. [PubMed: 9932341]
- Balestreri M, Czosnyka M, Steiner LA, Hiler M, Schmidt EA, Matta B, Menon D, Hutchinson P, Pickard JD. Association between outcome, cerebral pressure reactivity and slow ICP waves following head injury. *Acta Neurochir. Suppl.* 2005; 95:25–28. [PubMed: 16463814]
- Cardoso ER, Rowan JO, Galbraith S. Analysis of the cerebrospinal fluid pulse wave in intracranial pressure. *J. Neurosurg.* 1983; 59(5):817–821. [PubMed: 6619934]
- Carrera E, Kim DJ, Castellani G, Zweifel C, Czosnyka Z, Kasprowicz M, Smielewski P, Pickard J, Czosnyka M. What shapes pulse amplitude of intracranial pressure? *J. Neurotraum.* 2009; 27(2): 317–24.
- Chopp M, Portnoy HD, Branch C. Hydraulic model of the cerebrovascular bed: an aid to understanding the volume-pressure test. *Neurosurgery.* 1983; 13(1):5–11. [PubMed: 6877565]
- Costanza MC, Afifi AA. Comparison of stopping rules in forward stepwise discriminant analysis. *J. Amer. Stat. Assn.* 1979; 368(74):777–785.
- Czosnyka M, Czosnyka Z, Keong N, Lavinio A, Smielewski P, Momjian S, Schmidt EA, Petrella G, Owler B, Pickard JD. Pulse pressure waveform in hydrocephalus: what it is and what it isn't. *Neurosurg. Focus.* 2007; 22(4):E2. [PubMed: 17613191]
- Czosnyka Z, Czosnyka M, Lavinio A, Keong N, Pickard JD. Clinical testing of CSF circulation. *Eur. J. Anaesthesiol. Suppl.* 2008; 42:142–145. [PubMed: 18289432]
- Eide PK, Brean A. Intracranial pulse pressure amplitude levels determined during preoperative assessment of subjects with possible idiopathic normal pressure hydrocephalus. *Acta Neurochir.* 2006; 148(11):1151–1156. discussion 1156.
- Eklund A, Agren-Wilsson A, Andersson N, Bergenheim AT, Koskinen LO, Malm J. Two computerized methods used to analyze intracranial pressure B waves: comparison with traditional visual interpretation. *J. Neurosurg.* 2001; 94(3):392–396. [PubMed: 11235941]
- Eklund A, Smielewski P, Chambers I, Alperin N, Malm J, Czosnyka M, Marmarou A. Assessment of cerebrospinal fluid outflow resistance. *Med. Biol. Eng. Comput.* 2007; 45(8):719–735. [PubMed: 17634761]

- Ellis T, McNamers J, Aboy M. Pulse morphology visualization and analysis with applications in cardiovascular pressure signals. *IEEE Trans. Biomed. Eng.* 2007; 54(9):1552–1559. [PubMed: 17867347]
- Germon K. Interpretation of ICP pulse waves to determine intracerebral compliance. *J Neurosci Nurs.* 1988; 20(6):344–351. [PubMed: 2975310]
- Hara K, Nakatani S, Ozaki K, Ikeda T, Mogami H. Detection of the B waves in the oscillation of intracranial pressure by fast Fourier transform. *Med. Inform. (Lond).* 1990; 15(2):125–131. [PubMed: 2214918]
- Hu X, Xu P, Lee DJ, Vespa P, Baldwin K, Bergsneider M. An algorithm for extracting intracranial pressure latency relative to electrocardiogram R wave. *Physiol. Meas.* 2008; 29(4):459–471. [PubMed: 18354246]
- Hu X, Xu P, Scalzo F, Vespa P, Bergsneider M. Morphological clustering and analysis of continuous intracranial pressure. *IEEE Trans. Biomed. Eng.* 2009; 56(3):696–705. [PubMed: 19272879]
- Katzman R, Hussey F. A simple constant-infusion manometric test for measurement of CSF absorption. I. Rationale and method. *Neurology.* 1970; 20(6):534–544. [PubMed: 5463608]
- Khushaba, RN.; Al-Ani, A.; Al-Jumaily, A. *Advances in Neuro-Information Processing*. Vol. 5506. Springer; Berlin, Heidelberg: 2009. Feature Subset Selection Using Differential Evolution; p. 103–110.
- Lundberg N. Continuous recording and control of ventricular fluid pressure in neurosurgical practice. *Acta Psychiatr. Scand. Suppl.* 1960; 36(149):1–193. [PubMed: 13764297]
- McLachlan, JG. *Discriminant analysis and statistical pattern recognition*. Wiley-Interscience; NY: 2004. Wiley Series in Probability and Statistics
- McNitt-Gray MF, Huang HK, Sayre JW. Feature selection in the pattern classification problem of digital chest radiograph segmentation. *IEEE Trans Med Imaging.* 1995; 14(3):537–47. [PubMed: 18215858]
- Marmarou A, Black P, Bergsneider M, Klinge P, Relkin N. Guidelines for management of idiopathic normal pressure hydrocephalus: progress to date. *Acta Neurochir. Suppl.* 2005; 95:237–240. [PubMed: 16463856]
- Miller JD, Peeler DF, Pattisapu J, Parent AD. Supratentorial pressures. Part I: Differential intracranial pressures. *Neurol. Res.* 1987; 9(3):193–197. [PubMed: 2891068]
- Pedersen, MEH. *Tuning & Simplifying Heuristical Optimization* (PhD thesis). University of Southampton, School of Engineering Sciences, Computational Engineering and Design Group; 2010.
- Pickard, JD.; Matheson, M.; Shulman, K.; Marmarou, A.; Miller, JD., et al. *Intracranial Pressure IV*. Springer-Verlag; Berlin: 1980. Intraventricular pressure waves - the best predictive test for shunting in normal pressure hydrocephalus; p. 498–500.
- Price K, Storn R. Differential evolution. *Dr Dobb's Journal.* 1997; 22:18–20. 22, 24, 78.
- Price, K.; Storn, R.; Lampinen, J. *Natural Computing Series*. Springer Berlin Heidelberg; Berlin: 2005. Differential evolution. A practical approach to global optimization.
- Raftopoulos C, Chaskis C, Delecluse F, Cantraine F, Bidaut L, Brothi J. Morphological quantitative analysis of intracranial pressure waves in normal pressure hydrocephalus. *Neurol. Res.* 1992; 14(5):389–396. [PubMed: 1362253]
- Scalzo F, Xu P, Asgari S, Bergsneider M, Hu X. Regression analysis for peak designation in pulsatile pressure signals. *Med. Biol. Eng. Comput.* 2009; 47:967–7. [PubMed: 19578916]
- Stephensen H, Andersson N, Eklund A, Malm J, Tisell M, Wikkelso C. Objective B wave analysis in 55 patients with non-communicating and communicating hydrocephalus. *J Neurol. Neurosurg. Psychiatry.* 2005; 76(7):965–970. [PubMed: 15965203]
- Symon L, Dorsch NW. Use of long-term intracranial pressure measurement to assess hydrocephalic patients prior to shunt surgery. *J. Neurosurg.* 1975; 42(3):258–273. [PubMed: 1117323]
- Walter M, Kiefer M, Leonhardt S, Steudel WI, Isermann R. Online analysis of intracranial pressure waves. *Acta Neurochir. Suppl.* 2002; 81:161–162. [PubMed: 12168292]
- Webb, AR. *Statistical pattern recognition*. second ed.. John Wiley & Sons, Ltd; West Sussex, England: 2002.

- Wikkelso C, Andersson H, Blomstrand C, Lindqvist G. The clinical effect of lumbar puncture in normal pressure hydrocephalus. *J Neurol. Neurosurg. Psychiatry.* 1982; 45(1):64–69. [PubMed: 7062072]
- Williams MA, Razumovsky AY, Hanley DF. Comparison of Pcsf monitoring and controlled CSF drainage diagnose normal pressure hydrocephalus. *Acta Neurochir. Suppl.* 1998; 71:328–330. [PubMed: 9779221]
- Woodworth GF, McGirt MJ, Williams MA, Rigamonti D. Cerebrospinal fluid drainage and dynamics in the diagnosis of normal pressure hydrocephalus. *Neurosurgery.* 2009; 64(5):919–925. discussion 925-916. [PubMed: 19404152]
- Xingshi, H.; Qingqing, Z.; Na, S.; Yan, D. Feature Selection with Discrete Binary Differential Evolution. *Artificial Intelligence and Computational Intelligence; International Conference; Shanghai.* 7-8 Nov. 2009; p. 327-30.

Figure 1.

An example of nearly flat ICP recording (NW- no slow wave pattern) followed by clearly distinguishable ICP slow waves (BW). **a.** row ICP data **b.** sequence of dominant pulses calculated from 30 sec of row ICP signal **c.** low dispersed overlapped dominant pulses calculated for NW- **d.** high dispersed overlapped dominant pulses calculated for BW.

Figure 2.

A block diagram of feature selection and classification procedure. Input metrics to the algorithm consist of 24 mean values and 24 standard deviations of MOCAIP metrics. Three feature selection techniques: differential evolution algorithm (DE), discriminant analysis (DA) and analysis of variance (V) were applied to obtain three sets of MOCAIP metrics (DE-16 features; DA-5 features, V-13 features). Six metrics overlapped DE+V sets, three metrics overlapped DA+V sets and two metrics were common to DE+DA sets. For each set (DE, V, DE+V, DA+V, DE+DA) bootstrapping cross-validation procedure was used to evaluate the performance metrics of classification experiment (sensitivity, specificity, positive predictivity, accuracy).

Figure 3.

Mean $\pm$ 95%CI of classification performance metrics: **a.** sensitivity, **b.** specificity, **c.** positive predictivity and **d.** accuracy calculated based on 25 repetitions of bootstrapping procedure for: DE – 16 features selected by differential evolution algorithm, DA – 5 features selected by discriminant analysis, V – 13 features selected by analysis of variance, DE+V – 6 metrics overlapped both sets DE and V, DA+V – 3 metrics overlapped both sets DA and V, DE+DA – 2 metrics overlapped both sets DE and DA and SM- single metric (SDmICP).

Figure 4.

Mean $\pm$ 95%CI – first column, scatter plot – second column **a.** S.D. of mean ICP **b.** S.D. of Slope **c.** dP2 divided into two groups NW (no ICP slow waves) and BW (ICP slow waves). The title of each subplot in second column depicts whether the metric was selected or not by differential evolution algorithm DE(+) or DE(-) respectively, or/and by discriminant analysis DA(+) or DA(-) or/and by analysis of variance V(+) or V(-). The overlap of distribution despite significant difference in mean between NW and BW can be clearly seen on b, c.

Table 1

MOCAIP metrics that can be extracted after identifying the peaks of ICP pulses using the MOCAIP algorithm.

MOCAIP Metric Group		Metrics
	Amplitude	Absolute	mICP, dP ₁ , dP ₂ , dP ₃ , diasICP
		Ratio	dP ₂ / dP ₁ (dP ₁₂), dP ₃ / dP ₁ (dP ₁₃), dP ₃ / dP ₂ (dP ₂₃)
	Time Interval	Absolute	L _T , L ₁ , L ₂ , L ₃
		Relative	L ₂ - L ₁ , L ₃ - L ₁ , L ₃ - L ₂
	Pulse Curvature	Absolute	Curv ₁ , Curv ₂ , Curv ₃ , Curv _m
		Ratio	Curv ₂ / Curv ₁ (Curv ₁₂), Curv ₃ / Curv ₁ (Curv ₁₃), Curv ₃ / Curv ₂ (Curv ₂₃)
	Slope		(P ₁ - diasICP)/ L ₁
	Decay time constant		L _x where dP _x = 0.37 dP ₃

Table 2

Mean value $\pm$ S.D. and Mean Standard Deviation $\pm$ S.D. of MOCAIP metrics calculated for NW (no ICP slow wave pattern – 44 patients) and BW (ICP slow wave pattern – 32 patients). ‘V’ - metrics selected by analysis of variance (Anova, $p < 0.001$). ‘DE’ - metrics selected by differential evolution algorithm. ‘DA’ - metrics selected by discriminant analysis. ‘V+DA’ denotes features selected by both DA and V, ‘DE+DA’ denotes features selected by both DE and DA and ‘DE+V’ denotes features selected by both V and DE as highlighted.

MOCAIP metrics	Mean $\pm$ S.D.		Standard Deviation $\pm$ S.D.	
	NW (44)	BW (32)	NW (44)	BW (32)
dP_1 [mm Hg]	4.20 $\pm$ 1.60	5.34 $\pm$ 2.16	0.25 $\pm$ 0.12	0.62 $\pm$ 0.37
dP_2 [mm Hg]	5.26 $\pm$ 2.03	7.90 $\pm$ 3.44	0.46 $\pm$ 0.17	1.57 $\pm$ 0.90
dP_3 [mm Hg]	3.79 $\pm$ 1.69	5.95 $\pm$ 2.84	0.46 $\pm$ 0.18	1.33 $\pm$ 0.74
dP_{12} [mm Hg/mm Hg]	1.28 $\pm$ 0.31	1.50 $\pm$ 0.41	0.07 $\pm$ 0.03	0.15 $\pm$ 0.09
dP_{13} [mm Hg/mm Hg]	0.92 $\pm$ 0.31	1.13 $\pm$ 0.36	0.09 $\pm$ 0.04	0.15 $\pm$ 0.09
dP_{23} [mm Hg/mm Hg]	0.71 $\pm$ 0.11	0.75 $\pm$ 0.09	0.04 $\pm$ 0.03	0.04 $\pm$ 0.02
L_T [ms]	110.2 $\pm$ 33.92	114.4 $\pm$ 32.30	2.55 $\pm$ 1.51	3.4 $\pm$ 1.88
L_1 [ms]	100.1 $\pm$ 12.28	103.2 $\pm$ 10.30	4.39 $\pm$ 2.26	5.94 $\pm$ 2.63
L_2 [ms]	232.5 $\pm$ 28.69	244.4 $\pm$ 29.97	6.65 $\pm$ 4.30	7.72 $\pm$ 3.44
L_3 [ms]	369.4 $\pm$ 33.89	368.6 $\pm$ 35.97	6.19 $\pm$ 2.68	8.08 $\pm$ 3.56
L_2-L_1 [ms]	132.4 $\pm$ 28.44	141.2 $\pm$ 31.26	7.68 $\pm$ 4.16	8.99 $\pm$ 3.31
L_3-L_1 [ms]	269.3 $\pm$ 32.21	265.4 $\pm$ 35.18	7.81 $\pm$ 3.03	10.09 $\pm$ 4.48
L_3-L_2 [ms]	136.9 $\pm$ 23.77	124.2 $\pm$ 19.17	8.02 $\pm$ 5.10	10.11 $\pm$ 4.92
$Curv_T \cdot 10^{-3}$ [1/mm Hg]	3.08 $\pm$ 2.10	3.77 $\pm$ 2.55	0.17 $\pm$ 0.14	0.39 $\pm$ 0.27
$Curv_1 \cdot 10^{-3}$ [1/mm Hg]	4.89 $\pm$ 6.97	3.82 $\pm$ 6.28	1.20 $\pm$ 1.14	1.90 $\pm$ 2.63

MOCAIP metrics	Mean $\pm$ S.D.		Standard Deviation $\pm$ S.D.	
	NW (44)	BW (32)	NW (44)	BW (32)
Curv ₂ * 10 ⁻³ [1/mm Hg]	5.40 $\pm$ 4.06	9.46 $\pm$ 6.95	0.85 $\pm$ 0.51	2.26 $\pm$ 1.61
Curv ₃ * 10 ⁻³ [1/mm Hg]	3.20 $\pm$ 3.06	3.44 $\pm$ 3.27	0.58 $\pm$ 0.35	1.12 $\pm$ 1.13
Curv ₁₂ * 10 ⁻³ [1/mm Hg]	46.35 $\pm$ 61.34	98.33 $\pm$ 164.89	110.81 $\pm$ 189.11	212.63 $\pm$ 342.97
Curv ₁₃ * 10 ⁻³ [mm Hg/mm Hg]	20.79 $\pm$ 29.34	30.72 $\pm$ 63.69	51.21 $\pm$ 98.53	66.91 $\pm$ 127.94
Curv ₂₃ * 10 ⁻³ [mm Hg/mm Hg]	2.09 $\pm$ 4.70	1.82 $\pm$ 6.12	3.35 $\pm$ 9.98	5.87 $\pm$ 26.78
Slope [mm Hg/s]	43.00 $\pm$ 18.44	52.89 $\pm$ 20.69	2.38 $\pm$ 1.13	5.72 $\pm$ 3.15
RC [mm Hg]	40.55 $\pm$ 15.67	42.85 $\pm$ 16.47	4.46 $\pm$ 30.1	4.67 $\pm$ 3.27
Diastolic ICP [mm Hg]	1.43 $\pm$ 4.90	3.74 $\pm$ 5.68	0.57 $\pm$ 0.17	1.51 $\pm$ 0.66
Mean ICP [mm Hg]	3.93 $\pm$ 4.98	7.34 $\pm$ 6.49	0.68 $\pm$ 0.22	2.14 $\pm$ 0.98
				V
				V+DA
				DA
				V+DA
				DE+V
				DE+V+DA