Continuous Monitoring of the Complexity of Intracranial Pressure After Head Injury

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Abstract Multiscale entropy (MSE) has been increasingly used to investigate the complexity of biological signals. Our previous study demonstrated that the complexity of mean intracranial pressure (ICP), assessed by MSE based on the whole recording periods, is associated with the outcome after traumatic brain injury (TBI). To improve the feasibility of MSE in a clinical setting, this study examined whether the complexity of ICP waveforms based on shorter periods could be a reliable predictor of the outcome in patients with TBI. Results showed that the complexity of ICP slow waves, calculated in 3-h moving windows, correlates with the outcome of patients with TBI. Thus, the complexity of ICP may be a promising index to be incorporated into multimodal monitoring in patients with TBI.

Keywords Complexity • Intracranial pressure • Multiscale entropy • Outcome • Traumatic brain injury

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Introduction

The physiological function of an organism is regulated by complex interacting systems. To maintain homeostasis, the interacting network reacts to an ever changing environment and therefore produces complexity. Loss of complexity may signify the inability to adapt to the harsh environment and lead to subsequent death. Indeed, reduced physiological complexity has been associated with mortality in critically ill patients [1–3]. Our previous study also demonstrated that the complexity of mean intracranial pressure (ICP) is associated with the outcome after traumatic brain injury (TBI) [4]. Given that the complexity of ICP in our previous study was calculated by multiscale entropy (MSE) based on whole recording periods, the clinical utility may be limited. In this study, we computed the complexity of ICP waveforms based on shorter time series to investigate whether this method could provide a reliable and even early predictor of the outcome in patients with TBI.

Materials and Methods

This retrospective analysis is based on 325 patients with TBI who were admitted to the Neurosciences Critical Care Unit, Addenbrooke's Hospital, Cambridge, United Kingdom, between 2002 and 2010. Digital recordings from these patients were sampled at a frequency of 30 to 200 Hz using ICM+ software (Cambridge, UK). The complexity of ICP was calculated by MSE over two different, moving time windows:

1. 300-s periods, including the complete 100-Hz sampled ICP waveforms
2. A 3-h window of mean ICP series (comprising mean ICP values calculated every 10 s)

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Multiscale entropy was calculated as described previously [5, 6]. In brief, the MSE analysis comprises several steps:

1. Constructing a set of coarse-grained time series by different time scales
2. Calculating sample entropy [7] of each coarse-grained time series
3. Plotting the sample entropy of each coarse-grained time series as a function of time scales to obtain the MSE curve

The area under the MSE curve represents the complexity of the time series.

The pressure reactivity index (PRx), a validated index of cerebrovascular reactivity, was obtained from the moving correlation coefficient between the changes of arterial blood pressure and ICP. Outcome determined 6 months after head injury using the Glasgow Outcome Scale (GOS) was used for analysis. The relationship between the complexity of ICP and the patient-averaged values of derived parameters, including PRx, was examined. Interval data were compared using one-way ANOVA or Kruskal–Wallis nonparametric tests where appropriate. A multiple logistic regression model was used to identify the independent predictors with the dichotomized outcome. Receiver operating characteristic (ROC) curves were obtained and the area under the curve was analyzed for the ability of the parameters to predict mortality. $P<0.05$ was considered to represent a significant difference.

Results

Observation of the Complexity During Increased ICP

During a plateau wave, the complexity of ICP decreased compared with the baseline. The complexity of ICP returned, while the elevated ICP was resolved (Fig. 1).

The Complexity of ICP Calculated Over Two Different Time Windows

Differences in the complexity of ICP waveforms calculated over 300-s windows did not reach significance ($P=0.058$) between groups classified by GOS. In contrast, the differences in the complexity of the mean ICP in the first 3 h after the beginning of monitoring were significant across different GOS groups ($P=0.004$). Moreover, the average complexity calculated in 3-h windows was able to differentiate patients across different GOS groups ($P=0.0000005$). Reduction in the complexity of ICP in 3-h windows could predict death (area under the ROC curve=0.713) and was identified as a significant independent predictor of mortality in a multivariate logistic regression model including covariates such as age, sex, Glasgow Coma Scale, ICP, cerebral perfusion pressure, and PRx ($P=0.00008$).

Discussion

In this study we demonstrated that the complexity of ICP calculated in 3-h moving windows correlated significantly with the outcome after TBI. On the other hand, the correlation between the complexity of ICP calculated in 300-s windows and the outcome did not reach statistical significance.

Similar to our previous study [4] we used a 10-s moving average filter to obtain the mean ICP fluctuations in 3-h windows. Therefore, the respiratory and pulse wave components of ICP waveforms were effectively removed and the complexity of ICP obtained from 3-h windows reflects almost solely the complexity of slow waves. In accordance with our previous results the average complexity calculated in 3-h windows was able to differentiate patients across different GOS groups and it was identified as an independent predictor of mortality. Furthermore, we have demonstrated that the complexity of the mean ICP in the first 3 h has a significant predictive power of outcome even though the significance is less pronounced compared with the average complexity.

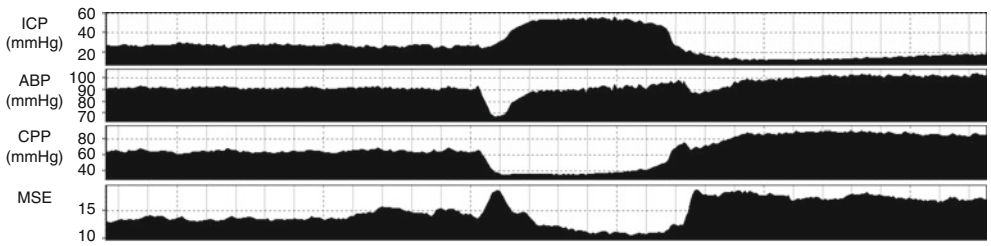

Fig. 1 Time-related changes in intracranial pressure (*ICP*), arterial blood pressure (*ABP*), cerebral perfusion pressure (*CPP*), and the complexity of ICP calculated by multiscale entropy (*MSE*) during a plateau wave

While the ICP signal was resampled to 100 Hz using band-limited interpolation, we demonstrated that the complexity of ICP decreased during a plateau wave and this is consistent with the findings of previous studies [8, 9]. However, the differences in the complexity of the complete ICP waveforms calculated over 300-s windows did not reach significance between different outcome groups. This indicates that although the complexity of ICP pulse waves decreases during elevated ICP, this phenomenon does not translate into better or worse outcomes in TBI patients. Indeed, none of the previous studies focusing on the complexity of ICP pulse waves [8, 9] could demonstrate its relationship with the outcome.

Based on the findings of our previous study and this study, we believed that the complexity of ICP slow waves may be a promising predictor of prognosis in TBI patients. By shortening the time window from the whole recording period to 3-h moving windows, we make the complexity of ICP slow waves more applicable in a clinical setting. As slow waves have a frequency range from 0.05 to 0.008 Hz [10], efforts can be made to shorten the time windows and increase the precision of the complexity, looking at the optimal frequency. Although, slow waves are thought to be generated by the cerebrovascular changes in response to changes in cerebral blood volume, their presence may or may not be associated with pathological processes. Therefore, the complexity of slow waves may not have a corresponding pathological meaning. Another limitation should be addressed in this study. This is a retrospective study and it is impossible to control and investigate the influence of treatments or medications on the complexity of intracranial pressure.

Conclusion

Our results suggest that reduced complexity of ICP slow waves, calculated in 3-h moving windows, might predict death in TBI patients.

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Conflict of Interest Statement We declare that we have no conflict of interest.

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