A Stroke Severity Monitoring System Based on Quantitative Modified Multiscale Entropy

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Abstract—Stroke is the leading cause of death and disability worldwide. This requires significant resources in health-care costs. In addition to physical examination and brain imaging, medical staff need a more quantitative and continuous method to reveal and monitor the severity of patients. This paper proposed a novel stroke severity monitoring system based on a nonlinear method—quantitative modified multiscale entropy (qmMSE). National Institutes of Health Stroke Scale (NIHSS) is adopted as reference of the severity of stroke patients. In the intensive care unit (ICU) admitted acute stroke patients, our proposed qmMSE feature has significant (p-value equals to 0.0026) difference between high NIHSS groups and low NIHSS groups. QmMSE not only highly correlates to NIHSS, but also consists with other clinical parameters, such as stroke volume and Glasgow Coma Scale (GCS). Beside, our proposed method has better significance in patient with ischemic stroke in cortical region. The p-value reaches 0.0008.

Keywords—stroke severity; multiscale entropy; ICU; monitoring;

I. INTRODUCTION

Stroke is the leading cause of death and permanent disability. According to World Health Organization, 15 million people suffer stroke worldwide each year, 5 million die and another 5 million are permanently disabled. A stroke is caused by the interruption of the blood supply to the brain, and is usually diagnosed by carrying out physical examination and studying brain imaging. A physical examination, including taking a medical history of the symptoms and a neurological assessment, helps giving an evaluation of the location and severity of a stroke. The standard score of examiner is the National Institutes of Health Stroke Scale (NIHSS). NIHSS is a reference of the severity of stroke patients; nevertheless, as for stroke severity, we introduce another nonlinear feature—multiscale entropy (MSE).

MSE has been adopted to analyze neurological diseases [4, 6, 7]. Though it provides an outstanding approach from linear features, two problems of MSE application in EEG signal lead to the insignificance of stroke severity inspection-1) the trends in biophysiological signals result in the underestimation of MSE. 2) The coarse graining process causes aliasing in input time series. So, in this paper, we proposed a novel system based on MSE process to give a quantitative index which evaluates stroke severity. It modified the original MSE algorithm to eliminate non-ideal problems and utilize the spatial property of EEG.

In this paper, section II will give an overview of related works about MSE application in EEG domain. The proposed algorithm design and system flow are arranged in section III. Section IV discusses the experiment result, and section V concludes this paper.

II. MSE OF EEG

A. Background

In persuading of new method to process EEG information, MSE was adopted in a lot of research. MSE is a nonlinear method measuring the complexity of a time series. Briefly, the...
MSE method comprises two main steps: 1) coarse-graining the signals into different time scales; 2) sample entropy calculation for each coarse-grained time series. For a given time series \( \{x_i\} \), the coarse-grained time series \( y_j^\tau \) is calculated according to the equation,

\[
y_j^\tau = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i,
\]

where \( \tau \) is the scale factor and \( 1 \leq j \leq \frac{N}{\tau} \). And the sample entropy is described as the ratio of 2-point-match and 3-point-match in series \( y_j^\tau \). The MSE consists of

\[
\text{MSE}_\tau = -\log \left( \frac{3 \text{ - point-match in } y_j^\tau}{2 \text{ - point-match in } y_j^\tau} \right).
\]

Ref. [4] used MSE to extract EEG complexity in autistic spectrum disorders. MSE was also used to assess EEG dynamical complexity in Alzheimer's disease [5]. In addition, EEG signal measures in multi-channel which provides spatial information of brain topography. However, apart from epilepsy detection, EEG is rarely being used to analyze other neurological disorder due to the unreliable specificity and sensitivity.

B. Problem Formulation

MSE was successfully applied in physiological signals. However, the entropy values evaluation is vulnerable to trends [4]. We evaluate sample entropy by counting the number of matched patterns which is determined by a fraction of the standard deviation. Thus, the entropy values will be underestimated due to the increased standard deviation when a trend or a background signal exists.

Another reason why MSE cannot be simply used to diagnose stroke severity is the aliasing problem [5]. The coarse graining process can be regarded as a lowpass filter. As a discrete series analysis tool, sampling rate of a discrete input signal is critical. MSE values may be quite different when analyzing a signal with different sampling frequencies (\( \delta \)). Because of these phenomena, MSE cannot be used in data with different sampling frequency.

III. PROPOSED QUANTITATIVE MODIFIED MSE (QMMSE)

A. Algorithm Design

In order to minimize the influence of trend, the detrending process could be performed prior to calculation of sample entropy. Polynomial fitting or highpass filter are traditional ways for detrending; however, it is difficult to extract trends from physiological signal using traditional methods due to its nonstationary characteristics. Therefore, we use the empirical mode decomposition (EMD) method in our study, since EMD is good at extract nonlinear, nonstationary trends [4].

To cope with the aliasing problem, first, we have to describe the problem in detail. In the coarse graining step of MSE, the goal of this process is to eliminate the fast temporal fluctuation according to different time scales. The equation aforementioned in section II can be further regarded as a finite impulse response (FIR) filter, and the frequency response is equivalent to a low-pass filter as

\[
H[z] = \frac{1}{\tau} \sum_{k=0}^{\tau-1} z^{-k},
\]

where \( \tau \) is the scale factor, and the magnitude of the frequency response is

\[
|H(e^{j2\pi f})| = \frac{1}{\tau} \frac{\sin(\pi f)}{\sin(\pi f/\tau)},
\]

where \( f \) represents the normalized frequency ranging from 0 cycles per sample to 0.5. The cutoff frequency of FIR filter is 0.5\( \tau \), and the properties of FIR filter are characterized as an ineffective filter with decaying passband, very large transient, and poor attenuation in stopband.

It is necessary to eliminate the fast temporal scales to focus progressively slower time scale. However, aliasing is unavoidable when one represents large quantity of information with small scale of data points. So we decompose the input signal into several mutually exclusive frequency bands using digital filters. These frequency bands are abided by the well-defined EEG rhythmic activity frequency bands, \( \delta \) (1–4Hz), \( \theta \) (4–8Hz), \( \alpha \) (8–13Hz), \( \beta \) (13–30Hz), \( \gamma \) (>30Hz). Then, we adjust the \( F_s \) by resampling the time series. To avoid aliasing by equation (2), we should follow the criteria:

\[
F_{\text{normalized}} = \frac{f_{\text{max}}}{F_s} \leq F_{\text{cutoff}} = \frac{1}{2\tau},
\]

where \( F_{\text{max}} \) stands for the upper bound of each frequency band. In brief,

\[
F_s = 2F_{\text{max}} \times \tau_{\text{max}},
\]

where \( \tau_{\text{max}} \) is the upper bound of selected scale factor. Thus, all of the frequency components of resampled time series are within the passband of the equivalent coarse graining FIR filter. Nothing is left outside the stopband. The block diagram of modified MSE (mMSE) is shown in fig. 1.

Because the structure of brain is nearly symmetric, the complexity is nearly equal in two hemispheres. Topography difference is a good way to represent the stroke severity. To develop topography difference, we subtract the electrodes of the relative location in right hemisphere from left hemisphere in international 10-20 system, that is node1 equals Fp1 minus Fp2, node2 equals F3 minus F4, node3 equals F7 minus F8, and so on. The detail arrangement is shown in fig. 2. Then, subtracted MSE values are quantized by their slope,

\[
\text{qMSE} = \frac{\sum_{r=16}^{20} \text{MSE}_\tau}{5} - \frac{\sum_{r=1}^{5} \text{MSE}_\tau}{5},
\]

Fig. 1. Block diagram of modified MSE (mMSE)
qmMSE is presented below:

The whole process of updating; if the patient is in the control, we could use longer needed, user may shorten the batch length, providing quicker patient is in urgent stage, which means intensive care is can be selected refering to the patients severity in a period of time called batch length. Batch length index. The qmMSE index can continously analyze the stroke quantitative process is carried out, producing the qmMSE being calculated in paralle, the system casts the values on to signal in each channel independently. After the MSE values

Step 1: EEG signal preprocessing

\[ y(t) = H_{bp} \ast x(t), \]

where \( H_{bp} \) is a bandpass filter with passband 1–30 Hz.

\[ y'(t) = \text{Denoise}(y(t)) \]

Denoise process is needed because EEG is vulnerable.

Step 2: EMD detrend

\[ y_{\text{detrend}} = EMD(y'(t)) \]

Step 3: Use FIR to decompose EEG signal into sub-bands

\[ y_\delta = H_\delta \ast y_{\text{detrend}}, \]
\[ y_\theta = H_\theta \ast y_{\text{detrend}}, \]
\[ y_\alpha = H_\alpha \ast y_{\text{detrend}}, \]
\[ y_\beta = H_\beta \ast y_{\text{detrend}}, \]

where \( H_\delta \) (passband 1–4Hz), \( H_\theta \) (passband 4–8Hz), \( H_\alpha \) (passband 8–13Hz) and \( H_\beta \) (passband 13–30Hz).

Step 4: Adaptive resampling

\[ F_\delta = 2F_{\text{max}} \times t_{\text{max}}, \]
\[ z_\delta = \text{resample}(y_\delta, F_\delta), \]
\[ z_\theta = \text{resample}(y_\theta, F_\theta), \]
\[ z_\alpha = \text{resample}(y_\alpha, F_\alpha), \]
\[ z_\beta = \text{resample}(y_\beta, F_\beta). \]

Step 5: MSE

\[ \text{mse}_{1-20} = \text{MSE}(z_\delta) + \text{MSE}(z_\theta) + \text{MSE}(z_\alpha) + \text{MSE}(z_\beta). \]

Step 6: Quantitative process

\[ \text{qmMSE}_1 = \text{slope}(\text{mse}_{\text{f1}} - \text{mse}_{\text{f2}}), \]
\[ \text{qmMSE}_2 = \text{slope}(\text{mse}_{\text{f7}} - \text{mse}_{\text{f8}}), \]
\[ \vdots \]
\[ \text{qmMSE}_6 = \text{slope}(\text{mse}_{\text{01}} - \text{mse}_{\text{02}}). \]

Note that Step1-5 are independent and can process in parallel.

IV. EXPERIMENT RESULTS

A. Data Collection

Patients with acute stroke were prospectively recruited. 62 patients were admitted within 24 hours in stroke ICU of National Taiwan University Hospital (NTUH) with clinical information registered. Clinical information includes age, sex, medication, heart rate, blood pressure and other habit such as smoking or drinking. Other scale like NIHSS, Glasgow Coma Scale (GCS) and modified Rankin Scale (mRS) are also measured. Research was approved by the ethical committee of the NTUH.

The entry criteria of our stroke ICU including ischemic stroke (IS) patients receiving thrombolytic therapy, intracerebral hemorrhage (ICH) patients receiving aggressive blood pressure (BP) control, severe neurological deficits (e.g. NIHSS score higher than 8), stroke in evolution, or medical conditions requiring intensive care (e.g. respiratory failure). All stroke patients received standard intensive care and monitoring of vital signs (pulse rate, BP and continuous electrocardiogram (EKG), respiratory rate, oxygen saturations, and temperature).

We excluded patients who had anoxic–ischemic brain injury following cardiac arrest, traumatic intracranial hemorrhage or subarachnoid hemorrhage as their prognostic factors may be different from those for IS and ICH. Other exclusion criteria include patients with a score of more than 2 on modified Rankin Scale (mRS) prior to the stroke, fever or severe active infection at admission, history of symptomatic cardiac failure (exertional dyspnea, leg edema, and etc), unable to obtain continuous EKG signals, atrial blood pressure (ABP) and EEG within 48 hours after admission, poor quality (artifacts) of EKG, ABP or EEG signals and unwilling to have clinical data collection and follow up.

B. Statistical Analysis

To evaluate the accuracy of our severity measurement, qmMSE index is compared with 24-h NIHSS. The NIHSS is used by healthcare providers to objectively quantify the
impairment caused by a stroke. A higher score is indicative of some level of impairment. The maximum possible score is 42, with the minimum score being a 0. The stroke patients are then separated into two groups – NIHSS≤21 and NIHSS>21. Two-sampled t-test in Matlab was adopted to determine if two sets of data are significantly different from each other. The results of traditional DAR, MSE direct implement and qmMSE are list in fig. 3 and TABLE I.

Fig. 4 is the box plot of two severity groups of DAR, traditional MSE and qmMSE. The linear feature, DAR, shows rough difference between low severity and high severity groups, and the traditional MSE show more significance but still doesn’t reach the criteria of p-value 0.05. On the other hand, qmMSE distinguish two groups with a significant p-value of 0.0026. Moreover, not only NIHSS but also GCS and stroke volume are consistent with the qmMSE result.

As we narrow down to more specific type of stroke, ischemic patients with lesion side on one hemisphere. QmMSE shows good ability in determine the severity of this category. Fig. 5 shows the box plot of qmMSE of two severity groups with ischemic stroke patients. A p-value of $8 \times 10^{-4}$ (N=22) indicates high significance. In the same category, traditional MSE has a p-value of 0.15, which still can’t meet the significant level, so can’t DAR.

V. CONCLUSION

In our work, we proposed a novel signal processing flow based on nonlinear method, MSE, to reveal the stroke severity. QmMSE solves the problems in original MSE and utilizes the spatial property of EEG. It significantly distinguishes patients with low severity from high severity in terms of NIHSS. The result of t-test shows significant statistical differences (p-value = 0.0026, N=62), which means the result of qmMSE is highly consistent with physical examination. Moreover, for ischemic stroke patients, qmMSE shows more significant result with p-value equals to 0.0008. Therefore, qmMSE can be a continuous and quantitative tool to monitor stroke severity in ICU-admitted acute stroke patients.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>P-VALUE OF QEEG IN GROUPING OF NIHSS</th>
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<tbody>
<tr>
<td>Significant: P&lt;0.05</td>
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<tr>
<td>P-value of Two-sampled T-test in Matlab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DAR</td>
</tr>
<tr>
<td>All (N=62)</td>
<td>0.312</td>
</tr>
<tr>
<td>Ischemic (N=22)</td>
<td>0.448</td>
</tr>
</tbody>
</table>

Fig. 4. Box plot of two groups with NIHSS≤21 and NIHSS>21 of (1) DAR, (2) traditional MSE and (3) qmMSE.

Fig. 5. Box plot of qmMSE of two severity groups with ischemic stroke patients.

REFERENCES


