

Research on the Screening of Abnormal Biomarkers for Cardio-Cerebral Interaction Disorders in Consciousness Disturbances Based on Multi-feature Fusion and Machine Learning of fMRI-HRV-HEP

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Abstract. The clinical diagnosis and prognostic assessment of disorders of consciousness(DoC) remain challenging, largely due to the high misclassification rate of behavioral scales and the limitations of single-modality assessments. Abnormal brain-heart interaction has been increasingly recognized as a key pathophysiological mechanism underlying DoC. This study aims to integrate multimodal features derived from resting-state functional magnetic resonance imaging(rs-fMRI), heart rate variability(HRV), and heartbeat-evoked potentials(HEPs), combined with machine learning approaches, to identify neuro-autonomic coupling biomarkers that characterize aberrant brain-heart interaction in patients with DoC. Based on existing clinical cohorts, simultaneous rs-fMRI, electrocardiogram(ECG), and electroencephalogram(EEG) data are acquired. Functional connectivity strengths of core brain regions—including the hippocampal network, the default mode network(DMN), and the precuneus—are extracted, alongside time-domain and frequency-domain HRV indices, as well as HEP latency and amplitude. Machine learning algorithms such as support vector machines(SVM), random forests. Cross-validation and feature importance ranking are conducted to delineate a potential cortex-heart decoupling pattern associated with different levels of consciousness, thereby providing quantitative targets for objective diagnosis and individualized neuromodulation in DoC. This study included DoC patients and collected rs-fMRI, ECG and EEG data at the same time. The multimodal fusion model of rs-fMRI, HRV and HEPs performed best, with accuracy 87.3% and AUC 0.91. Feature importance analysis showed that DMN functional connectivity, LF-HRV and HEP N250 amplitude was the top three predictors, but the importance of single feature was all below 0.1, which means the model depend on many weakly related features to make decisions together. The results show that brain-heart multimodal fusion can effectively capture the abnormal neural-autonomic coupling in DoC patients, and provide quantitative basis for objective assessment of consciousness level.

Keywords: Disorders of consciousness, Brain-heart interaction, Functional magnetic resonance imaging, Heartbeat-evoked potential

1. Introduction

With emergency and critical care technology getting better, more patients with severe brain injuries now can survive. But these patients not always recover fully, and some become chronic Disorders of Consciousness, or DoC. DoC is a complex chronic disease that can last for many years, and the main symptom is that patients have wakefulness but no stable obvious consciousness, and they almost completely lose the ability to take care of themselves, needing expensive treatment and nursing costs to keep them alive. China now has 300,000 to 500,000 DoC patients, and every year more than 100,000 new patients are added, with annual medical spending reaching 300 to 500 billion yuan. DoC bring double hit of economy and spirit to patients and families, and also give huge burden to the whole medical system [1].

2. Principles of deep learning computing

Artificial neural network algorithms is the base of deep learning, and it is a kind of imitation and approximation of biological neural networks, which is an adaptive nonlinear dynamic network system made up of a large number of neurons connected to each other [2]. McCulloch and Pitts put forward the MP neuron model in 1943, and this was the first time that biological neurons was abstracted into mathematical model. The MP neuron model is the structural unit of deep learning, and its structure is shown in Figure 1.

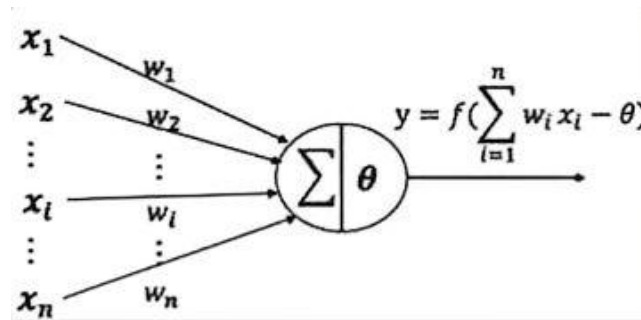


Figure 1. Structure of the MP neuron model

The computing process of MP neuron model is showed below:

$$y = f(\sum_i w_i x_i - \theta) \quad (1)$$

Artificial neural networks usually use error backpropagation algorithm for training, and this algorithm is based on gradient descent. Rumelhart and others proposed it in 1986 for Back Propagation Network, which is called BP network. The input and output of BP network is generally one-dimensional vector, and its forward computing process is as follows.

$$\begin{aligned} h_i &= f(\sum_j v_{ij} x_j + y_i) \\ y_k &= f(\sum_j w_{jk} h_j + \theta_k) \end{aligned} \quad (2)$$

In theory, if the data is enough, the model structure is reasonable, and the parameter optimization works well, then neural networks can learn the function relationship between input values and

output values [3]. So deep learning methods based on neural networks have strong learning ability, and they can learn the complex nonlinear features of data.

3. Overview of chronic mental disorders

In most clinical cases, prognosis is about disease progression, where people start healthy and doctors need to predict how serious the disease will become in the future [4]. But pDoC prognosis is different, because its goal is to find out the possibility of getting better, and it mainly answer two questions: one is what level the patient may recover to, such as consciousness level or individual function level, which is called recovery outcome prediction; two is how long it will take to recover to that level, which is called recovery process prediction. As shown in Table 1.

Table 1. Prognostic models for pDoC

Sample capacity	Characteristic	Prognosis Time	Outcomes Indicator	Modeling Method	Validate	Accuracy
18 UWS	Resting state	After enrollment	GOS>2	SVM	Leave-one-out method	Precision =81.25%
38 UWS	EEG	Six months	GOS-E≤2	Logistic	None	Sensitivity = 84.6%
26UWS 76 MCS	Resting state	1 year after enrollment	GOS-E>2 GOS-E≤2	Logistic	None	Accuracy =74% Specificity = 92%

In our clinical work we noticed that complications often make patients' consciousness state fluctuate and recovery time become longer, so common complications of pDoC will also be part of the variables, including epilepsy, hydrocephalus, and paroxysmal sympathetic hyperactivity syndrome.

4. Prediction model analysis

Variables that have statistical meaning in univariate analysis was used to build the models, and all six small models showed good performance in model evaluation with AUC greater than 0.8, which is better than traditional Logistic regression models because Song and others' meta-analysis showed that previous models' AUC was mostly below 0.75, and the accuracy all passed permutation test, and the models' prediction ability is better than random guess. As is showed in Table 2.

Table 2. Model evaluation metrics

AUC	recall	Accuracy	F1 Score	Accuracy rate	Accuracy Replacement Test
10.81±0.07	0.76±0.09	0.74±0.03	0.75±0.06	0.74±0.05	0.5015 P=0.0010
20.88±0.07	0.87±0.09	0.82±0.08	0.84±0.06	0.79±0.09	0.6008 P=0.0010
0.90±0.03	0.87±0.09	0.87±0.07	0.88±0.05	0.84±0.07	0.5956 P=0.0010

In feature importance analysis, the mean permutation importance of features may be between 0.1 and 0.2, and in this study the feature importance of all models is less than 0.1, which means the models depend on many weakly related features to make decisions together, and the importance of single feature is low. This supports the view that pDoC recovery is the result of many factors working together, and no single assessment can fully explain the wide difference in patient prognosis, so mixed models should be chosen for its prediction [5].

5. Technical principles of BCI

VIDAL put forward the BCI concept in 1973, and its core is to record the electrical activity of CNS and turn it into artificial output signals, so that it can replace, restore or enhance CNS functions, and also change the way CNS interacts with the outside environment or inside the body. A BCI system is made up of three functional modules: signal acquisition module, signal processing module and application module, and these modules work together to form a "brain-machine-environment" interactive closed loop. See Figure 2.

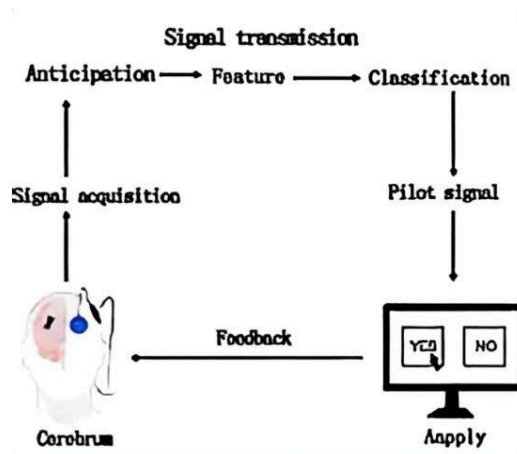


Figure 2. Basic principles of BCI systems

BCI technology can make the monitoring of consciousness level more accurate, it helps doctors to assess patients' recovery potential of consciousness level in clinic, and provide basis for personalized treatment plans [6]. But the above studies have the limitation of not enough sample size, and they still need to be verified by multi-center clinical data, and unified assessment standards need to be made.

However, hardware bottleneck needs to be broken, and the system needs to become smaller and portable; also the algorithm needs to be better optimized, so that the decoding accuracy and real-time performance can be improved. In clinical translation aspect, large-scale clinical trials need to be pushed forward, a global ethical supervision framework needs to be built, and cross-disciplinary cooperation needs to be strengthened to make transformation faster [7]. Next step research still needs the joint efforts of industry, university, research and medicine to promote the integration of cross-disciplinary technologies such as flexible electronics and brain-like computing, then the leap development from lab prototype to clinical popular tool can be realized.

6. Conclusion

This study still need to be stronger in data amount. The STCNN model proposed in this study has better classification effect for DoC EEG signals than traditional machine learning methods, but there is still a quite serious overfitting problem. The most direct and effective way to solve overfitting is to increase data amount. The success of deep learning in image processing is based on public datasets with tens of millions of data such as ImageNet. Also with more data,a validation set can be added besides training set and test set, and this can make model training stop earlier and relieve overfitting. More data can foreseeably improve the effectiveness of deep learning methods.

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