Identification of delirium in neurocritically ill patients based on behavioral patterns of facial expressions Clinical study protocol of the study

Project Name: Identification of delirium in neurocritically ill patients based on facial expression behavior patterns Project Leader/Responsible Department: Huang Huawei/Department of Critical Care Medicine

Project entrusted unit: Beijing Tiantan Hospital Affiliated to Capital Medical University

Project undertaking unit: Beijing Tiantan Hospital Affiliated to Capital Medical University

Project Sponsor: Beijing Tiantan Hospital Affiliated to Capital Medical University

Study Duration: 2023/01 - 2025/12

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Summary of the plan

Project name	Identification Study of Delirium in Neurocritically Ill Patients Based on Facial Expression Behavior Patterns
Research objectives	Through a three-year project, a large sample of neurocritically ill patients was included in the Department of Critical Care Medicine of Beijing Tiantan Hospital Affiliated to Capital Medical University, and the facial expression behavior of patients with severe neurodelirium was digitally analyzed by machine learning algorithms, and a delirium classification model based on facial expression behavior was constructed, so as to realize the accurate and efficient diagnosis of delirium in neurocritically ill patients through facial expression behavior recognition.
Study design	Prospective diagnostic study
Total number of cases	3180 people
	Inclusion criteria: Admitted to the comprehensive ICU of Beijing Tiantan Hospital from January 2023 to January 2025 Patients with severe neurology who are in intensive care in the ward, including patients after neurosurgery, stroke patients, and patients admitted to the ICU for monitoring and treatment due to other neurological diseases, and sign an informed consent form.

Case selection	Exclusion Criteria: 1) Age less than 18 years; 2) Persistent coma (GCS) before surgery and within 7 days after surgery （≤ 8 points) unable to perform delirium evaluation; 3) Severe dementia or severe cognitive impairment or mental illness that cannot be evaluated for delirium; 4) Not alive in the ICU for more than 24 hours; 5) Patients with facial paralysis, post-traumatic facial deterioration, etc., which may have a serious impact on facial recognition; 6) Exclude patients with dementia, Parkinson's, depression, etc., which may affect facial emotional expressions.
Treatment options	Critically ill patients in the ICU who met the inclusion criteria were evaluated for delirium and their facial features were recorded using software. Algorithm technology is used to learn to simulate facial features of patients with delirium.
Efficacy evaluation	*Effectiveness evaluation indicators (primary and secondary efficacy indicators):* Construction and evaluation of delirium model in patients with severe neuropathy based on expression behavior patterns

	Safety evaluation index: diagnostic research, not involving safety evaluation
Statistical methods	The time frequency of expression behavior and the dynamic change rate of expression behavior between the delirium group and the non-delirium group, as well as the differences in different high-level features, were expressed as mean and standard deviation. The Shapiro-Wilk test is used to confirm that the data conforms to a normal distribution. Therefore, the independent sample t-test was used for comparison between the two groups with normally distributed data, and the one-way analysis of variance was used for comparison between multiple groups. The Mann-White U test was used for comparison between the two groups of non-normally distributed data. $P<0.05$ is the difference and is statistically significant. Through machine learning, the advantages and disadvantages of different models are examined, and three metrics are used: correctness, sensitivity, and intentionality. Sensitivity represents the number of subjects who are predicted to be normal and the real situation is normal/the total number of normal groups, that is, the strength of the model's ability to identify normal groups. Specificity refers to the number of subjects predicted to have delirium and the real situation is delirium/review of the delirium group, that is, the strength of the model to identify the delirium group.
Study duration	2023/01 - 2025/12

Ⅰ. Research background

Through a three-year project, a large sample of neurocritically ill patients was included in the Department of Critical Care Medicine of Beijing Tiantan Hospital Affiliated to Capital Medical University, and the facial expression behavior of patients with severe neurodelirium was digitally analyzed by machine learning algorithms, and a delirium classification model based on facial expression behavior was constructed, so as to realize the accurate and efficient diagnosis of delirium in neurocritically ill patients through facial expression behavior recognition. By summarizing the research results, writing and publishing academic papers, and participating in domestic academic exchanges, the delirium face recognition software is promoted, which provides new ideas for the clinical prevention and treatment of POD.

Ⅱ. Research objectives

1. Main objective: To digitally analyze the facial expression behavior of patients with severe delirium by machine learning algorithm, and to construct a delirium classification model based on expression behavior.

Ⅲ. Research design types, principles and test steps

1. Study design

This study is a prospective diagnostic study

2. Sample size and research plan

According to previous literature studies, based on the advanced characteristics related to facial expressions and behaviors in patients with severe delirium. The sensitivity of predicting delirium is between 75% and 85%, and the specificity is between 80% and 90%, respectively, according to our previous studies and previous studies, the incidence of delirium in patients with severe neuropathy is about 20%, the test level is a=0.05, the certainty is 80%, and the sample size of patients with severe neuropathy is calculated according to the PASS software to be 2891 cases. The number is 3180 cases. At present, the department has 75 beds and treats more than 4,000 patients annually Basic satisfaction.

3. Research duration: 3 years

4. Subject selection

Inclusion criteria: Critically ill patients admitted to the comprehensive ICU ward of Beijing Tiantan Hospital for intensive care from January 2023 to January 2025, including patients after neurosurgery, stroke patients, and patients admitted to the ICU for monitoring and treatment due to other neurological diseases, and signed the informed consent form.

Exclusion criteria include: 1) age less than 18 years; 2) Persistent coma (GCS ⩽ 8 points) before surgery and within 7 days after surgery, unable to evaluate delirium; 3) Severe dementia or severe cognitive impairment or mental illness that cannot be evaluated for delirium; 4) Not alive in the ICU for more than 24 hours; 5) Patients with facial paralysis, post-traumatic facial damage that may have a serious impact on facial recognition; 6) Exclude patients with dementia, Parkinson's, depression, and other conditions that may affect facial emotional expressions.

Ⅳ Research methods

(1) Delirium assessment process: After the patient is admitted to the ICU, delirium assessment and facial behavior data are collected every day at 8:00 – 10:00 and 20:00 - 22:00. Assessment Diagnosis by an experienced specialist using the gold standard DSM-V for delirium measurement. Assessment completed Video data collection of facial expression behavior was carried out within 5 minutes.

(2) The gold standard DSM-V for delirium measurement specifically includes: 1) attention and consciousness disorders, respectively, which represent decreased attentional directing, concentration, maintenance, and switching abilities, and decreased orientation to the environment; 2) Impaired attention and consciousness progressed within hours or days, and the condition fluctuated within 1 day; 3) Companion Cognitive dysfunction such as memory, orientation, language, visuospatial or perceptual impairment; 4) When not in a coma, it cannot be explained by other pre-existing neurocognitive disorders; 5) There is evidence related to delirium, such as drug poisoning or withdrawal. Other symptoms that may occur

may include altered arousal, disorientation, disturbed thinking, inappropriate speech or mood, disturbed sleep-wake cycles, hallucinations, and psychomotor alterations.

(3) Identification of facial expression behavior patterns in delirium people

① Design an experimental paradigm for facial expressions and behaviors of delirium people for data collection According to the diagnostic criteria of delirium, changes in attention and consciousness and disturbed thinking are important conditions, so the experimental paradigm we designed should reflect the feedback of different facial expressions and behaviors when patients have consciousness disorders, attention deficits and thought disorders. We used the questions on consciousness, attention, and thinking assessment in the classic delirium assessment tool CAM-ICU as stimulus material. These stimulus materials are integrated into a mobile application software to take pictures of the patient's facial expressions answering a question as subsequent analysis data. Among them, the questions for examining attention are "I will read you 10 numbers, when you hear the number 8, please pinch my hand, 6-8-5-9-8-3-8-8-4-7" and "Please stretch out these fingers (the examiner stretches out a few fingers in front of the patient), and now extend the same finger with the other hand (the examiner does not demonstrate)"; The question of examining thinking is: "Do stones float on water?" Are there fish in the sea? Is a pound heavier than two pounds? Can a hammer be used to drive nails? "or" Can leaves float on water? Are there elephants in the sea? Can two pounds be used to saw? "While recording the video recording

during the question, the examiner also records the correctness of the answer on the software so that it can be associated with the recorded expression. The consciousness situation can be dynamically presented throughout the video recording process. Through the mobile application software, the collected data can also be standardized and constrained, and preprocessing operations such as face cropping, alignment, and data enhancement can be completed.

② Digital analysis of expression behavior patterns in people with severe delirium

We will use the collected data to quantitatively analyze the facial expression behavior patterns of delirium people. Since AU is produced by the movement of facial muscle masses, it may be more behaviorally interpretable than other traditional image features. Therefore, in this study, we propose a quantification method for typical expression behavior based on AU features. The details are as follows: 1) First, through the description of delirium symptoms through previous literature, compared with normal people, delirium patients have special behavior patterns in emotional cognition and emotional feedback. Therefore, according to the classification of delirium and the specific manifestations in each classification, we divided the facial expressions of the subjects into the following three categories: agitation (including fright, excitement, euphoria), calmness, and apathy (including drowsiness and lethargy). According to the AU involved in looking for the above emote in the FACS documentation. Among them, the calm expression is used as the initial expression and used as a reference for comparison with the rest of the expressions. The so-called calm expression is defined as when the facial muscle mass is not very active, or the exercise intensity is low, the face does not

produce expression behavior, which is the so-called calm expression. The remaining AUs involved in the emoji are as follows:

2) The 2400 frames of data of each video are precisely divided into the typical facial expressions described above, i.e. by realization. Each expression on each frame of the video data calculates a value, and in each frame. The values of all expressions represent the main expressions and subordinate expressions produced by the above faces cause. Therefore, we need to distinguish the main expression at each frame moment, ignore the subordinate expressions, and label each frame of expression behavior with a classification label. 3) The number of occurrences of typical facial expressions under stimulation and their proportion in each video were calculated separately to measure the time-frequency ratio of facial expressions, so as to explore the emotional feedback of delirium patients. The amplitude characteristics of AU are used to quantify the dynamic change rate of expression behavior, so as to reflect the sensitivity of delirium patients' emotional feedback. The purpose of this paper is to verify the expression behavior patterns of delirium patients from the digital level.

(3) To construct high-level features related to facial expressions and behaviors in patients with severe delirium. Taking the time-frequency ratio of expression behavior and the dynamic change rate of expression behavior as objects, we construct the advanced characteristics of delirium in the time domain and frequency domain of AU signal, which are mainly divided into three aspects: statistical features, rate characteristics and dynamic characteristics. Among them, the statistical characteristics include: the time frequency of expression behavior, the

number of occurrences of maximal points, and the number of occurrences of singular points; The rate characteristics include the rate feature of expression behavior change, the average gradient feature of the maximum point, the average gradient feature of the singular point, and the HHT frequency feature. Dynamic features are maximal point gradient FDHH features and singular point gradient FDHH features. A total of 9 types of features are involved. These features are described in detail below:

1) Characteristics of the time frequency of expression behaviors: We hypothesize that the number of excited, fearful or euphoric expressions in agitated delirium is higher than that of normal people, while the number of unconcerned and emotionless expressions in apathetic delirium is higher than that of normal people. Therefore, we take the expression ratio number as a high-level feature, that is, the number of times the subject's various expressions appear under the stimulus question are entered into the classifier to calculate.

2) Characteristics of the rate of change in facial expression behavior: The physical meaning of AU is the movement of muscle masses, which in turn are related to facial behavior. Since the rate of change of expression behavior is difficult to measure by feature indexes, in this experiment, we measure the dynamic change rate of expression behavior by the average gradient of its amplitude and AU, and classify it as a constructed high-level feature.

3) Characteristics of the maximum value point: In the original video data, there may be no significant difference in expression between the delirium group and the normal population in many time periods, and the difference in the corresponding AU signal value may not be large. Therefore, we should consider capturing the "key points" in the expression behavior, that is, extracting the maximum value of the AU feature as a secondary feature. The maximum value point in this study represents the maximum degree of deformation of the action unit under the stimulus problem. We extract the relevant AUs involved in different facial expressions, count the number of their maximum value points, and then classify them as high-level characteristics for delirium recognition.

4) Singularity characteristics: A certain derivative of the original signal suddenly changes at a certain moment, which is called singular signal, which can represent many characteristics of the signal and is an indispensable and important part of the original signal. Detect the singularity of the signal, find and determine the location of the singularity of the

signal value, and judge the singularity of the point. However, due to the influence of external environmental noise, the signal of singular point presents non-stationary characteristics, so it is very difficult to process such signals. In order to study the changes in the signal curve carrying important information, we will combine the Lipshitz exponent and wavelet transform theory to construct singular point features.

5) Hilbert-Huang Transform (HHT) frequency characteristics: In order to study the relevant information of AU amplitude time signals on the frequency threshold, we perform the HHT transform on the signal. Firstly, the Empirical Mode Decomposition (EMD) method of the signal is used to decompose the original AU signal into several IMF functions. Then apply the Hilbert transform to each IMF component, The corresponding Hilbert spectrum is obtained, and then the subband energy and center frequency of each IMF component are calculated. The energy ratio of each IMF component is multiplied by the average frequency to obtain the final HHT frequency characteristic index.

6) Feature dynamic history histogram features based on gradients (Feature dynamic history histogram, (FDHH): Firstly, the maximum point gradient sequence and the singular point gradient sequence of each AU are extracted, and then the absolute value difference is calculated for the adjacent feature point gradient series, and then the threshold is set, and the absolute value difference is set as "0" or "1", and the binary value sequence is defined as different PM modes according to the difference in the number of consecutive "1" in the above figure and the final histogram features are obtained.

④Construction and evaluation of delirium model in patients with severe neuropathy based on expression behavior patterns. We send the advanced features of each of the above six different feature sets, including the time frequency feature of expression behavior, the rate of change of expression behavior, the statistical number of maximum point statistics, the average gradient feature of the maximum value point, the statistical number of singularity points, the average gradient feature of singularity, the HHT frequency feature, the FDHH dynamic feature based on the maximum point gradient, and the FDHH dynamic feature based on the singularity point gradient into the classifier to establish a model for classification. In order to reduce randomness and chance bias, the classification process will strictly abide by the "tenfold cross-validation" criterion, and divide the samples into training samples and test samples, which are not related to each other and intersect as null. The training sample is only used to train the classifier and does not participate in any testing experiments. The test sample is only used to detect the classification effect of features, and does not participate in any training tasks. Finally, the performance metrics of the models, namely correctness, sensitivity, and specificity, will be evaluated, and the advantages and disadvantages of the models will be examined.

Ⅴ. Concomitant medication

Not.

Ⅵ. Observation indicators and inspection time

Delirium assessment process: After the patient was admitted to the ICU, delirium assessment and facial behavior data were collected every day at 8:00 – 10:00 and 20:00 - 22:00 respectively. The assessment is made by an experienced specialist using the gold standard DSM-V for delirium measurement. Video data collection of facial expression behavior will be carried out within 5 minutes after the assessment is completed.

Ⅶ Follow-up time

not

Ⅷ. Clinical evaluation

(1) Objective efficacy evaluation: construct a delirium classification model based on facial expression behavior

(2) Safety indicators: None

Ⅸ Pre-assessment of project risks and risk disposal plans

Adverse events refer to adverse medical events that occur after the subject receives the test drug, but it does not necessarily have a causal relationship with the treatment. The investigator should record all adverse events that occur during drug treatment in the case report form, including type, diagnosis time, duration, and consequences. Any adverse events should be followed up until remission or treatment termination.

Predictable adverse events in this study included: None

Adverse events were handled according to clinical routine. When the treating physician deems it necessary, the dose of the trial drug may be temporarily or permanently reduced, or the trial drug may be temporarily or permanently discontinued. and record these situations in the case report form.

For predictable adverse events in this study, management measures include: None

Serious adverse events

When serious adverse events occur, the investigational drug must be stopped immediately and treatment must be given. In this study, serious adverse events are those that result in:

1. Causes death

2. Life-threatening (risk of immediate death)

3. Prolong the subject's hospital stay or readmission to the hospital

4. Persistent or significant disability/incapacity

5. Other important medical events that the investigator deems to be reportable

Any serious adverse events occurring in the trial, whether related to the trial drug or not, should be reported to the Ethics Committee within 24 hours of being informed. If the test drug causes death, the test should be stopped immediately, reported to the ethics

committee as soon as possible, and recorded in detail, and the information should be properly preserved. Any adverse events are followed up until remission or treatment termination.

X Quality control and quality assurance of research

(1) Researchers and medical staff

1. Conduct training on the research plan before the start of the experiment, and strictly follow the plan during the trial.

2. All drugs and materials used in clinical research must be subject to quality control, regular inspection,

ensure that it is in good condition;

3. The Ethics Committee has the right to audit clinical research for the purpose of

ensuring the authenticity of clinical research records and complying with the

provisions of the clinical research protocol.

(2) Subjects

1. Explain the benefits and risks of the investigational drug in detail to each potential subject;

2. Informed consent must be signed by the patient or an authorized representative;

3. Subjects can withdraw from the trial at any time after inclusion.

(3) Termination of the trial

1. In the event of death due to the investigational drug, the trial shall be terminated and reported to the Ethics Committee. heavy

The New Start Trial requires ethics committee approval;

2. When all patients have completed inclusion and follow-up, and the data collection is complete, the principal investigator will decide to terminate the trial

Examine.

XI Data preservation

The cognitive assessment data, imaging data, and postoperative cognitive assessment results of the patients were stored by the main research.

XII. Data security supervision

Clinical research will formulate corresponding data security monitoring plans according to the size of the risk. All adverse events should be recorded in detail, handled appropriately and tracked until they are properly resolved or the condition is stable, and serious adverse events and unexpected events should be reported to the Ethics Committee, competent departments, sponsors and drug administration departments in a timely manner according to regulations. The principal investigator conducts a regular cumulative review of all adverse events and holds investigator meetings if necessary to assess the risks and

benefits of the study. Studies greater than minimal risk will have an independent data monitor review the study Data monitoring, high-risk research will establish an independent data security monitoring committee to monitor the accumulated security data and efficacy data to make recommendations on whether to continue the study.

XIII. Statistical processing

The time frequency of expression behavior and the dynamic change rate of expression behavior between the delirium group and the non-delirium group, as well as the differences between different high-level features, were expressed as mean and standard deviation. The Shapiro-Wilk test is used to confirm that the data conforms to a normal distribution. Therefore, the independent sample t-test was used for the comparison of the normally distributed data between the two groups, and the single-factor variance analysis was used for the comparison between multiple groups. The Mann-White U test was used for the comparison of the data between the two groups. $P<0.05$ is the difference and is statistically significant. Through machine learning, the advantages and disadvantages of different models are examined, and three metrics are used: correctness, sensitivity and intentionality. Sensitivity represents the number of subjects predicted to be normal and the real situation is normal/the total number of normal groups, that is, the strength of the model's ability to identify normal groups. Specificity represents the number of subjects predicted to have delirium and the real

situation is delirium/a review of delirium groups, that is, the strength of the model to identify delirium groups.

XIIII Ethical considerations

Before the study begins, the clinical study is carried out after the ethics committee approves the trial protocol. Before each subject is selected for this study, the investigator is responsible for comprehensively introducing the purpose, procedures and possible risks of this study to the subject or his legal representative, as well as the corresponding information of alternative treatment, and signing a written informed consent form. The personal privacy and data confidentiality of the subjects will be protected during the research process.

Describe the study's consideration of the informed process and how to ensure that the subject is fully informed and given

Subjects have sufficient time to consider and voluntarily choose to agree to participate in the study to avoid inducement and inappropriateness of the subject

Effect.

XV: Data confidentiality

Confidentiality of subject information, data protection, intellectual property rights, research summaries, publication communications, etc.

XVI: Participants

name	Title/Major	task	GCP Training (time Period)
Huang Huawei	Deputy Chief Physician/ICU	Project design, delirium assessment	September 2018
Zhang Guobin	Associate Chief Physician/Neurosurgery	Project design, sample collection, data collation and analysis, article writing	August 2019
An bamboo forest	Senior engineer/	image preprocessing, algorithm design and implementation	

Zhang Xiaokang	PhD Candidate/Neurosurgery	Cognitive assessment, data collation and analysis, and clinical follow-up	November 2021
Li Hao arrived	PhD Candidate/Neurosurgery	Cognitive assessment, data collation and analysis, and clinical follow-up	
Ying Yuzhe	Master's Degree/Neurosurgery	Cognitive assessment, data collation and analysis, and clinical follow-up	