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ORIGINAL RESEARCH

Clinical Characteristics of Auditory Mismatch Negativity in Patients with Chronic Disorders of Consciousness Following Intracerebral Haemorrhage: A Prognostic Prediction Study

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Objective: To examine the clinical features of auditory mismatch negativity (MMN) and its potential utility in prognostic prediction in patients with chronic disorders of consciousness (DOC) following intracerebral haemorrhage (ICH).

Methods: Between September 2023 and July 2024, 24 patients with chronic DOC following ICH were recruited. The Coma Recovery Scale-Revised (CRS-R) was used to assess the patients' level of consciousness, dividing them into vegetative state, minimally conscious state and escaped minimally conscious state groups. Auditory MMN data were collected from each group using an oddball paradigm, and differences in MMN amplitude and latency were compared. Follow-up was conducted 3 months later. Patients were categorised into favourable and unfavourable outcome groups based on the Glasgow Outcome Scale scores. The receiver operating characteristic curve method was utilised to evaluate the prognostic predictive power of significant indicators, establishing cut-off values.

Results: The amplitude of auditory MMN was different in patients with varying levels of consciousness. The MMN amplitude at electrode Cz was associated with prognosis ($P < 0.05$), and the area under the curve was 0.850 (95% CI: 0.79–0.91). Moreover, MMN amplitudes at Cz were dichotomised at a value of 1.19 μV, with a sensitivity and specificity of 87.5% and 80.0%, respectively, for the prognosis prediction. The prediction value improved when combined with the CRS-R and the Glasgow Coma Scale.

Conclusion: Auditory MMN amplitude, particularly at electrode Cz, serves as a reliable prognostic indicator for patients with chronic DOC following ICH. Its integration with clinical scales enhances predictive accuracy, offering valuable insights for clinical decision-making and patient management.

Keywords: chronic disorders of consciousness, auditory mismatch negativity, coma recovery scale-revised, Glasgow coma scale, prognosis, intracerebral haemorrhage

Introduction

Intracerebral haemorrhage (ICH) refers to the non-traumatic rupture of a blood vessel in the brain, resulting in the accumulation of blood in the brain parenchyma.[1] The incidence of ICH is second only to ischemic stroke in all subtypes. According to statistics, the mortality rate of ICH within 30 days of onset is 35%–52%, and half of those who survive

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have sequelae of varying severity.[2] With the advancement of medical technology, patients with ICH can survive following surgical craniotomy and other treatments. However, these patients still suffer nerve damage, such as varying degrees of disorders of consciousness (DOC). When the DOC lasts for more than 28 days, it is termed chronic DOC.[3] In clinical practice, whether patients can wake up and their prognosis are important issues of concern for family members and doctors, meaning it is of great significance to explore appropriate auxiliary tools to evaluate patients' consciousness and prognosis.

The misdiagnosis rate of patients with consciousness status based on behavioral scales is as high as 43%.[4] In addition to behavioral scales, neurophysiological techniques are often used to assess patients' conscious states. Neurophysiological techniques include electroencephalography (EEG) and evoked potentials. Event-related potentials (ERPs) provide a non-invasive method to study the brain's processing of information. Some studies have shown that, as the most representative type of evoked potential, ERPs may have a high temporal resolution in assessing the consciousness and prognosis of patients with chronic DOC.[5]

Mismatch negativity (MMN) is a component of ERPs that reflects the brain's automatic detection of changes in auditory stimuli. This ERP component typically peaks at between 100–250 ms after the onset of stimulation, which are brain responses that are time-locked to specific sensory, cognitive or motor events,[6] and its latency can be extended to 300 ms in patients with severe brain injury.[7] The emergence of MMN indicates that the brain is capable of automatic information processing, even in the absence of conscious attention to the stimulus.[8] Mismatch negativity may be elicited in patients experiencing sleep,[9] deep sedation,[10] anaesthesia[11] and impaired consciousness because its emergence does not require the active attention of the patient's brain, which is the advantage of MMN over other ERP components. Several studies have shown that MMN can be used as a reference indicator when assessing the level of consciousness in patients with DOC.[12,13] The presence and amplitude of MMN are associated with the level of consciousness and prognosis in such patients.[14] However, how to properly apply MMN in clinical practice remains controversial,[15] as the availability of the component is limited by the MMN paradigm and analysis, especially in terms of MMN quantification.

Currently, behavioral measures such as the Glasgow Coma Scale (GCS) and the Coma Recovery Scale-Revised (CRS-R) are the primary tools used to evaluate the prognosis of patients with chronic DOC. However, as noted, the misdiagnosis rate when based on behavioral scales is as high as 43%.[4] Neurophysiological techniques, including EEG and evoked potentials, have been proposed as complementary tools to improve diagnostic accuracy. Among these, MMN has shown promise as a reliable indicator of consciousness and prognosis in patients with DOC.[12–14]

This study examines the clinical features of MMN in patients with chronic DOC following ICH and assesses its potential utility in prognostic prediction. We hypothesise that MMN amplitude, particularly at electrode Cz, can serve as a reliable prognostic indicator and that its integration with clinical scales will enhance predictive accuracy.

Materials and Methods

Patients

Between September 2023 and July 2024, patients with chronic DOC following ICH were selected for Handan Central Hospital's Rehabilitation Medicine and Neurosurgery Department. The following were requirements for inclusion: (1) ICH verified by magnetic resonance imaging or computed tomography; (2) repeated assessment by clinicians to confirm the presence of impaired consciousness, with specific standards based on the diagnosis and assessment of DOC,[16] including multiple evaluations of the patient's level of consciousness (eg GCS score <8 or CRS-R score <20);[16] (3) duration of onset ≥28 days, vital signs were stable; and (4) provided informed consent. The exclusion criteria included (1) known hearing impairment; (2) During the MMN examinations, the patient take sedative and hypnotic drugs; and (3) incomplete clinical data. (4) Adverse events occurred, such as scalp infections.

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Handan Central Hospital ([2024] Ethical Review Research No.014). All legal guardians provided informed consent and willingly participated in the study.

Table 1 Diagnostic Standard for Vegetative State, Minimally Conscious State, and Escaped Minimally Conscious State Patients

CRS-R Function	VS	MCS	EMCS
Auditory	≤2	3-4	/
Visual	≤1	2-5	/
Motor	≤2	3-5	6
Verbal	≤2	2	/
Communication	≤0	1	2
Arousal	≤2	3	/

Notes: Note that to classify a patient as VS all five measurement score criteria were met, while for MCS or EMCS the presence of any of the measurement criteria was enough to consider the patient as MCS or EMCS.

Clinical Evaluation

Patients were divided into the vegetative state (VS) group, minimally conscious state (MCS) group and escaped minimally conscious state (EMCS) based on the CRS-R scores.[17] During the first week of the trial, two experienced neurologists conducted five CRS-R assessments on the recruited patients at various times. The final CRS-R score was determined by taking the highest score. The CRS-R was used to evaluate patients with DOC in six aspects: communication and arousal, and auditory, visual, motor and verbal functions. The criteria used for the inclusion of patients in the VS, MCS and EMCS groups are presented in Table 1.

Mismatch Negativity Paradigm

A classical oddball auditory paradigm was used to elicit MMN. This paradigm presents a widely used experimental design in cognitive neuroscience, particularly for studying auditory processing and attention. In this paradigm, participants are presented with a series of auditory stimuli, where the majority of the stimuli (standard stimuli) are repeated frequently, and a smaller number of deviant stimuli are presented infrequently. The standard stimuli and deviant stimuli differ in specific characteristics, such as duration, frequency or intensity. The brain automatically detects these deviant stimuli, even in the absence of conscious attention, resulting in the MMN response. In addition, here, it included two different forms of pure sound, each lasting 75 ms for the standard stimuli and 35 ms for the deviant stimuli. In this paradigm, 750 pure sound stimuli (comprising 80% standard stimuli and 20% deviant stimuli; sound pressure level: 80 dB, frequency: 800 Hz) were presented to every patient to elicit the MMN response.[18] The sound stimuli were presented randomly, although there were at least three standard stimuli between two consecutive deviants. The sound was delivered through headphones. The whole examination lasted 15 minutes.

Event-Related Potential Data Acquisition

Scalp ERP examinations were performed at the patient's bedside, when they were free from visible body shaking. Data were recorded at two electrodes (Fz and Cz) according to the 10/20 international system using a Gongtong Medical event-related potentiometer (GT-Spectrum 5, Moscow, Russia). All electrode impedance was maintained below 5 KX, and an online 3–30 Hz bandpass filter was used to sample at 1000 Hz. Data were referenced with the mean potential at electrodes M1 and M2.

Event-Related Potential Data Processing and Mismatch Negativity Analysis

Raw ERP data with amplitudes exceeding 500 μV were automatically rejected, thereby eliminating eye movements and other artifacts. The data of 100 ms before stimulation and 500 ms after stimulation were extracted, and the average values of standard response and deviation response were calculated. The former is mainly used for baseline correction.

Mismatch negativity is derived by subtracting the standard stimulus waveform from the waveform caused by the deviant stimulus, following established procedures for MMN extraction.[19] The amplitude of the MMN at electrodes Fz and Cz, referred to as "FzMMNA" and "CzMMNA", respectively, were measured as the peak-to-peak amplitude from the onset of the N1 component to the most negative peak of the MMN within the 100–250-ms time window. These measurements were crucial for assessing the differences in automatic auditory processing among patients with varying levels of consciousness. The final results of each parameter were confirmed manually based on the actual condition, ensuring accurate identification of the MMN components.

Finally, ERP components such as N1 and MMN were calculated via an automatic algorithm using the GT-Spectrum 5 software (Gongtong Medical). This algorithm identifies and measures the peaks of the ERP components based on predefined criteria. Specifically, the presence of N100 is a prerequisite for measuring the MMN component. The most negative peak (peak of the MMN component) within the 100–250-ms time window was identified and measured. The final results of each parameter were confirmed manually based on the actual condition to ensure accurate identification of the MMN components.

Outcome Assessment

The treatment process for patients involved standard medical care for chronic DOC following ICH, including but not limited to supportive care, prevention and management of complications, and rehabilitation therapies as deemed appropriate by their healthcare team. The specific interventions were tailored to each patient's condition and needs.

For outcome assessment, the Glasgow Outcome Scale (GOS) was utilised, with levels ranging from 1 to 5, where higher levels indicate better outcomes. The GOS results were obtained through structured telephone follow-up interviews conducted by trained assessors, 3 months after the MMN examinations. During these interviews, detailed information about the patient's functional status and level of independence was collected to determine their GOS score.

In addition to the GOS, other baseline clinical data were systematically gathered at the time of enrollment. This included demographic information such as age and sex, as well as medical history details, such as the duration of the disorder, any prior surgeries (eg decompressive craniectomy) and scores on clinical scales such as the CRS-R and the GCS. These data were meticulously recorded in the patients' study files, ensuring a comprehensive understanding of their clinical profiles and facilitating accurate analysis and interpretation of the study results.

Statistical Processing

Statistical analysis was performed using IBM SPSS Statistics software (IBM, Armonk, NY, USA). Measurement data conforming to normal distribution were expressed as mean ± standard deviation. One-way ANOVA was used across the three groups, and a post-hoc comparison was made. Data not conforming to normal distribution were expressed as median (first quartile, third quartile), and the Mann–Whitney *U*-test was used for comparisons. Following the previously mentioned univariate analysis, a multiple logistic regression analysis was performed on the statistically significant components to determine the independent prognostic factors. Sensitivity, specificity and Youden's index were used to evaluate the predictive accuracy of the categorical variables (sensitivity + specificity − 1 = Youden index). To assess the prediction effect of continuous variables, the area under the curve (AUC) was computed and the receiver operating characteristic (ROC) curve was shown.

Results

Comparison of Baseline Information and Event-Related Potential Parameters Among the Groups

Twenty-four patients who met the criteria were included in this study. No patients were lost to follow-up, although three of the patients were removed from the study without N1 induction. No adverse events were reported. Twenty-one patients (mean age: 54.62 ± 2.79 years; 14 male patients) were included in the analysis. The time from ICH onset to performing ERP ranged from 28 to 163 days (74.95 ± 8.852). The enrolled patients were classified as having VS (n = 3), MCS (n = 15) or EMCS (n = 3) based on the clinical behavioral criteria and the CRS-R score. The baseline information and ERP

parameters of the DOC groups were compared (Table 2). Here, MMN displayed a tendency for a slow rise in wave amplitude as the level of impaired consciousness decreased (Table 2). Additional data was discovered: FzMMNA and CzMMNA were substantially lower in the VS group than in the MCS group ($P < 0.01$); CzMMNA was considerably lower in the VS group than in the EMCS group ($P < 0.001$); and FzMMNA did not differ statistically between the two groups ($P > 0.05$). For FzMMNA and CzMMNA, there was no statistically significant difference between the MCS group and the EMCS group ($P > 0.05$) (Table 3 and Figure 1). Age, sex, duration, FzMMNL and CzMMNL did not differ statistically significantly across the groups ($P > 0.05$).

Comparison of Baseline Information and Event-Related Potential Parameters Between Good Prognosis and Poor Prognosis Groups

A univariate study of clinical characteristics and prognosis revealed a strong correlation between prognosis and the GCS score, CzMMNA and overall CRS-R score ($P < 0.05$). There were no significant differences in age, course of disease, FzMMNA, FzMMNL and CzMMNL between the two groups ($P > 0.05$) (Table 4 and Figure 2).

Table 2 Baseline Clinical Characteristics and ERP Parameters of Patients

Characteristic	VS (n=3)	MCS (n=15)	EMCS (n=3)	Total (n=21)
Age, years	54.67 ± 13.013	57.13 ± 8.196	42.00 ± 26.627	54.62 ± 2.79
Sex, male/female	3/0	8/7	3/0	14/7
Duration from ICH onset, days	49.00 ± 16.063	82.20 ± 44.127	64.67 ± 31.644	74.95 ± 8.852
Hemorrhage location				–
Basal ganglia	3	5	2	10
Cerebral hemisphere		8	1	9
Brainstem		1		1
Cerebellar	1	1	2	4
Hemorrhage volume, mL	30-50	20-40	10-30	Range: 10-50
Admission NIHSS score	37.33 ± 2.52	29.87 ± 3.16	22.67 ± 2.52	Mean: 28.5 ± 5.2
Treatment				
Conservative	2	7	3	-
Surgical	1	8	0	-
Complications	Infection (n=1)	Seizures (n=2)	None	-
CRS-R total score	5.67 ± 2.517	11.67 ± 3.155	17.33 ± 3.055	11.5 ± 4.2
GCS	6.67 ± 2.517	9.87 ± 1.598	11.67 ± 1.528	9.5 ± 2.1
FzMMNA, μV	0.657 ± 0.153	1.387 ± 0.302	2.703 ± 0.589	1.45 ± 0.87
FzMMNL, ms	167.67 ± 34.962	174.87 ± 41.560	178.33 ± 51.404	173.6 ± 43.1
CzMMNA, μV	0.676 ± 0.196	1.504 ± 0.339	1.927 ± 0.564	1.37 ± 0.65
CzMMNL, ms	157.67 ± 6.807	166.67 ± 36.707	180.00 ± 50.922	168.1 ± 38.2

Note: Values are presented as mean ± standard deviation or as specified.
Abbreviations: NIHSS, National Institutes of Health Stroke Scale; CRS-R, Coma Recovery Scale-Revised; GCS, Glasgow Coma Scale; FzMMNA, amplitude of MMN at electrode Fz; FzMMNL, latency of MMN at electrode Fz; CzMMNA, amplitude of MMN at electrode Cz; CzMMNL, latency of MMN at electrode Cz.

Table 3 Comparison of Amplitude at Fz and Cz Between Three Groups

Index	VS	MCS	EMCS	F	P	P^a	P^b	P^c
FzMMNA(uV)	0.657±0.153	1.387±0.302	2.7033±0.589	20.287	0.008	0.003	0.168	0.345
CzMMNA(uV)	0.676±0.196	1.504±0.339	1.927±0.564	9.774	0.001	0.002	<0.001	0.079
CRS-R, Total score	5.67±2.517	11.67±3.155	17.33±3.055	10.773	<0.001	0.006	<0.001	0.009
GCS	6.67±2.517	9.87±1.598	11.67±1.528	6.716	0.007	0.009	0.002	0.115

Notes: P^a: p value for comparison between VS and MCS; P^b: p value for comparison between VS and EMCS; P^c: p value for comparison between MCS and EMCS.

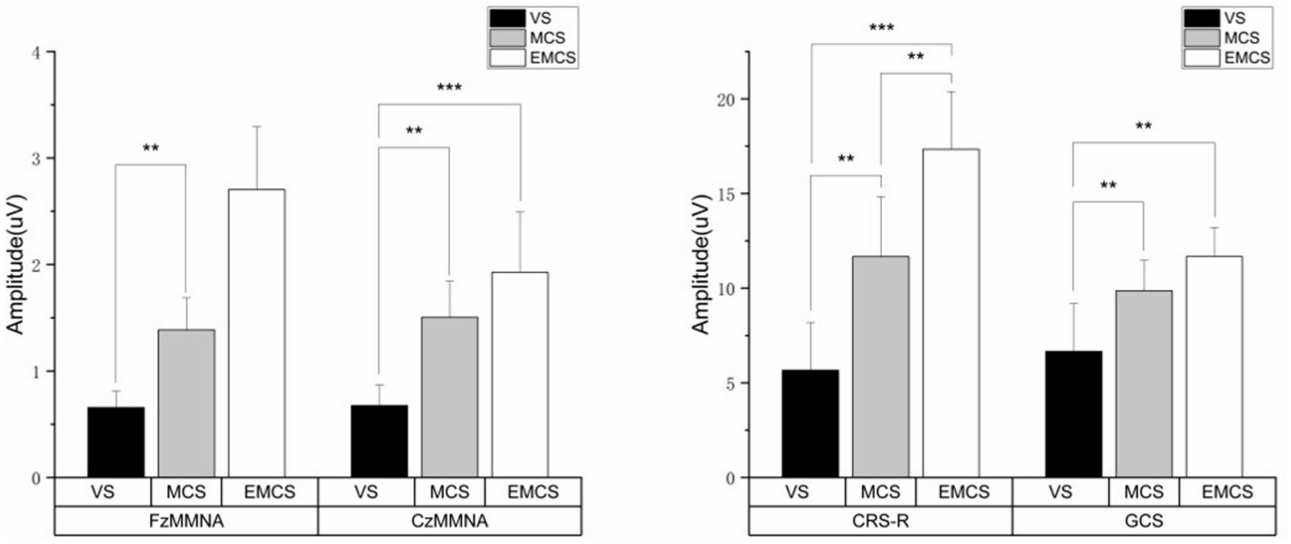

Figure 1 FzMMNA, CzMMNA, the total score of CRS-R, and GCS data were pair-to-pair compared among the three groups.
Notes: **P<0.01, ***P<0.001.

Multiple Logistic Regression Analysis

The logistic regression analysis, which excluded CRS-R due to collinearity with CzMMNA and incorporated additional baseline clinical factors, revealed that admission National Institutes of Health Stroke Scale (NIHSS) score (odds ratio [OR]: 1.15, 95% CI: 1.02–1.30, P = 0.023) and haemorrhage location (cerebral vs others; OR: 2.10, 95% CI: 1.10–4.03, P = 0.026) were significant independent predictors of prognosis in patients with chronic DOC following ICH. Complications (yes vs no) also showed a trend towards significance (OR: 3.20, 95% CI: 1.20–8.53, P = 0.021). However, age, sex, duration of disorder, haemorrhage volume and CzMMNA did not reach statistical significance as independent predictors in this model (Table 5).

Coma Recovery Scale-Revised, Glasgow Coma Scale and CzMMNA Accuracy in Predicting the Awakening of Patients

The updated ROC analysis, utilising the revised prediction model with significant clinical factors, demonstrated that the combined model, including admission NIHSS score, haemorrhage location, complications and other variables, had an AUC of 0.85 (95% CI: 0.79–0.91, P < 0.001), indicating good predictive accuracy for patient prognosis. Individually,

Table 4 Relationship Between Clinical Factors and Prognosis of Patients with Chronic Disorders of Consciousness After Intracerebral Hemorrhage

Index	Good Prognosis	Poor Prognosis	Z	P
Number of cases	16	5		
Age, Y	60.50(51.00,66.25)	53.00(47.5,53.50)	−1.778	0.75
Duration, Days	71.50(33.50,98.75)	66.00(46.50,117.00)	−0.248	0.804
CRS-R, Total score	14.00(9.25,15.75)	8.00(5.50,10.50)	−2.120	0.034
GCS	10.00(9.25,11.75)	7.00(5.50,9.50)	−2.496	0.013
FzMMNA	1.315(1.083,1.813)	1.09(0.570,1.795)	−0.992	0.321
FzMMNL	184.50(129.00,204.75)	146.00(139.00,218.50)	−0.083	0.934
CzMMNA	1.54(1.323,1.865)	1.05(0.581,1.365)	−2.312	0.021
CzMMNL	167.5.00(127.00,199.75)	160.00(141.50,190.50)	0.000	1.000

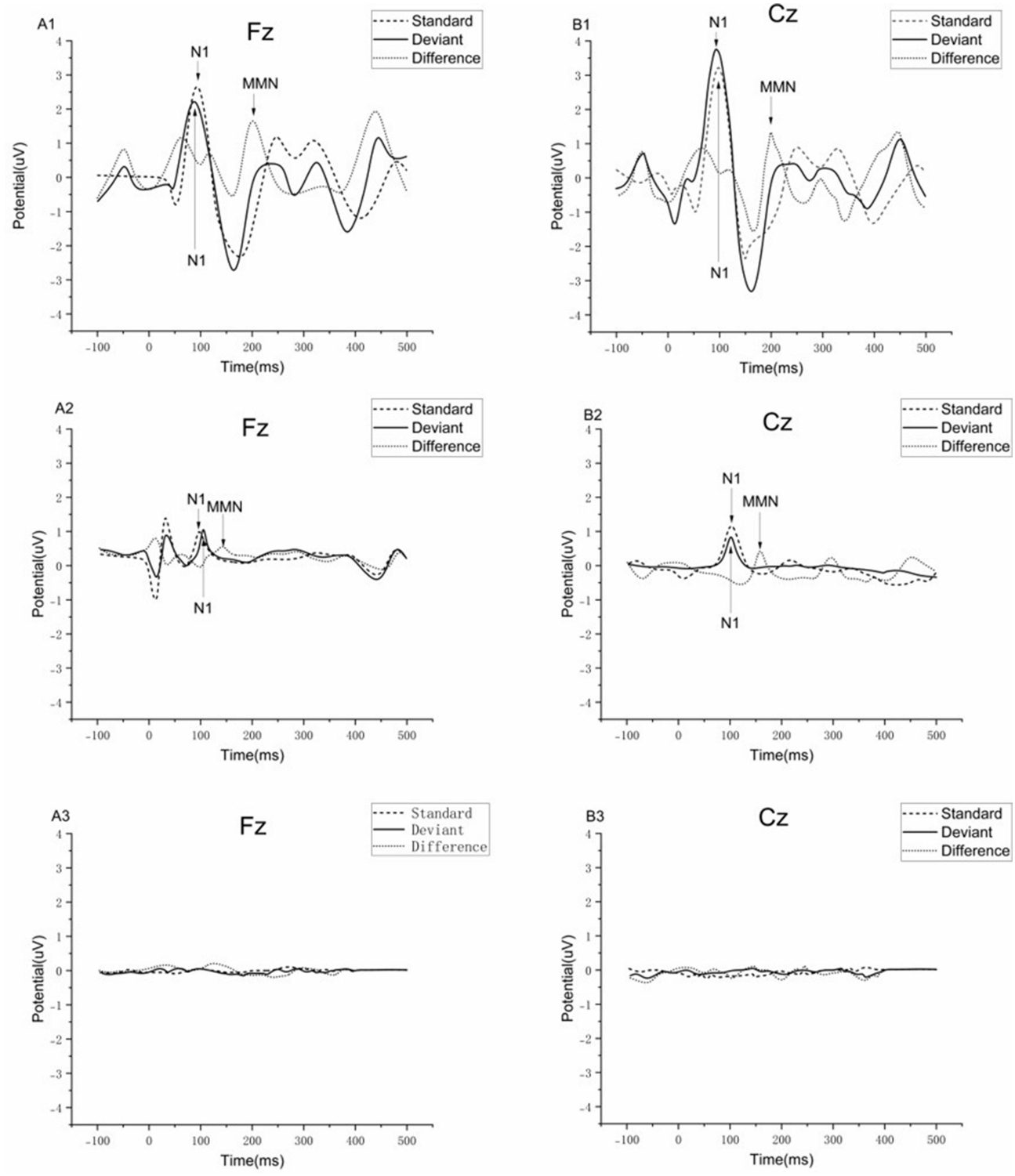

Figure 2 (**A1** and **B1**) MMN waveforms of patients with favorable outcomes at electrodes Fz and Cz; (**A2** and **B2**) MMN waveforms of patients with unfavorable outcomes (N100 present) at electrodes Fz and Cz; (**A3** and **B3**) MMN waveforms of patients with N100 absent.
Abbreviation: MMN, mismatch negativity.

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Table 5 Multiple Logistic Regression of Factors Associated with Prognosis Within 3 months After MMN Examination

Predictor Variable	OR (95% CI)	P-value
Age	1.02 (0.98–1.07)	0.314
Sex (Male vs Female)	1.56 (0.45–5.31)	0.478
Duration of Disorder (Days)	0.99 (0.96–1.02)	0.512
Admission NIHSS Score	1.15 (1.02–1.30)	0.023
Hemorrhage Location (Cerebral vs Others)	2.10 (1.10–4.03)	0.026
Hemorrhage Volume (mL)	1.01 (0.99–1.03)	0.345
Complications (Yes vs No)	3.20 (1.20–8.53)	0.021
CzMMNA (μV)	1.05 (0.98–1.13)	0.167

Table 6 ROC Analysis

Variable	AUC (95% CI)	P-value
Admission NIHSS Score	0.78 (0.65–0.91)	0.042
Hemorrhage Location (Cerebral vs Others)	0.72 (0.59–0.85)	0.018
Complications (Yes vs No)	0.75 (0.62–0.88)	0.031
CzMMNA (μV)	0.68 (0.55–0.81)	0.105
Combined Model (All Variables)	0.85 (0.79–0.91)	<0.001

admission NIHSS score (AUC: 0.78, 95% CI: 0.65–0.91, P = 0.042) and haemorrhage location (AUC: 0.72, 95% CI: 0.59–0.85, P = 0.018) were moderately accurate predictors, while complications (AUC: 0.75, 95% CI: 0.62–0.88, P = 0.031) also contributed to the predictive model. Moreover, CzMMNA alone had a lower AUC of 0.68 (95% CI: 0.55–0.81, P = 0.105), suggesting limited predictive value when not combined with other clinical factors (Table 6 and Figure 3).

Discussion

This study offers several novel contributions to the field of DOC following ICH. First, by focusing specifically on the chronic DOC population post-ICH, we address a gap in the literature, as this specific aetiology has not been extensively studied. Our findings provide clinicians with valuable insights and practical tools for managing these patients. Second, we determined a specific cut-off amplitude value for MMN at electrode Cz (1.19 μV), which serves as a reliable prognostic indicator with high sensitivity and specificity. This quantification avoids the subjectivity of visual assessments and enhances the objectivity of prognosis prediction. Third, this study demonstrates that integrating MMN amplitude with clinical scales (eg CRS-R and GCS) significantly improves predictive accuracy. This multimodal approach offers a more comprehensive assessment of patient prognosis compared with using MMN or clinical scales alone. Lastly, by highlighting the potential of MMN as a prognostic tool in the clinical setting for patients with ICH, this study supports more targeted interventions and better patient management. Overall, this study provides specific and practical insights for the prognosis of chronic DOC following ICH, advancing the clinical application of MMN in this context.

Disorders of consciousness represent a frequent and serious sequela following ICH.[20] While various assessment techniques exist, current clinical scales have notable limitations. The CRS-R, though useful for differentiating VS, MCS and EMCS, carries a 22% error rate in clinical judgment.[21] Similarly, while the GCS correlated with consciousness levels in our ICH cohort (P < 0.05),[22] its utility is often compromised in intubated patients.[23] These limitations underscore the need for more objective neurophysiological markers.

Auditory MMN, generated primarily in temporal and frontal cortices,[24] reflects automatic auditory processing through memory trace and change detection mechanisms. Our findings align with previous work demonstrating MMN's clinical relevance in DOC.[12–14] Specifically, we observed significant MMN amplitude differences across consciousness levels (VS < MCS < EMCS, P < 0.05), corroborating Fischer's early observations in comatose patients[25] and Wijnen's findings

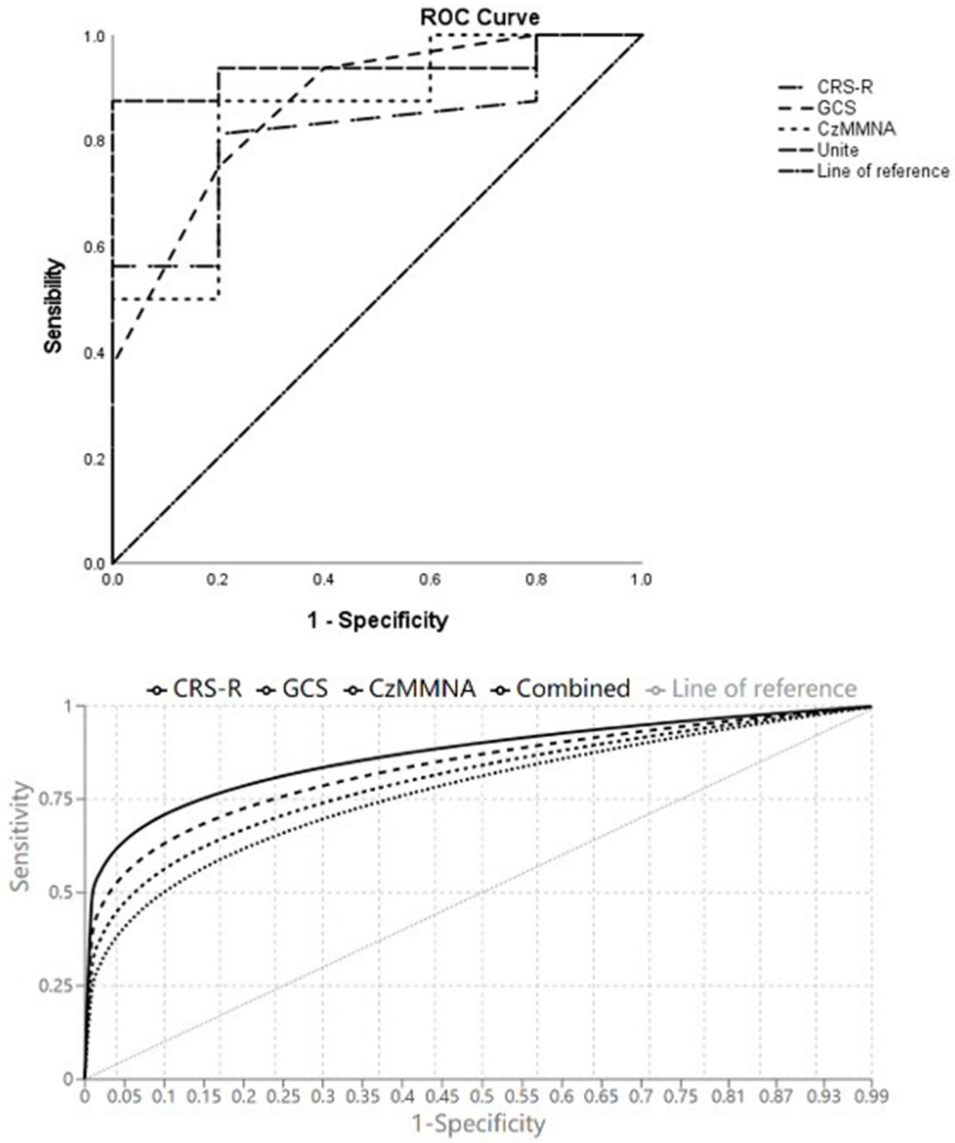

Figure 3 Receiver operating characteristic (ROC) curves for predicting outcomes in patients with chronic disorders of consciousness after intracerebral hemorrhage using different clinical indicators.

in vegetative states.[26] However, unlike Shao's report,[13] we found no significant correlation between MMN latency and consciousness levels, potentially due to the known variability in latency measurements.[27,28]

The choice of patients with ICH reflects this aetiology's growing clinical importance, representing 24% of stroke cases in China.[29] Our results extend previous MMN research in other aetiologies,[30,31] identifying a clinically useful Cz amplitude cutoff (1.19 μV), with 87.5% sensitivity and 80% specificity for 3-month prognosis. The absence of Fz amplitude correlations may relate to frontotemporal craniectomies performed in 17 patients,[7] though this surgical necessity reflects real-world practice. Importantly, combining CzMMNA with CRS-R and GCS scores enhanced predictive accuracy (AUC = 0.938), supporting Wang's[32] advocacy for multimodal assessment approaches.

However, several limitations warrant consideration. First, the modest sample size may affect generalisability, and second, visual MMN identification introduces subjectivity, particularly in noisy clinical environments. Third, the heterogeneous patient population reflects clinical reality but may obscure subtle effects. Future studies should expand sample sizes, standardise stimulus paradigms and explore automated MMN quantification methods to address these limitations.

Conclusions

In summary, MMN amplitude effectively distinguishes consciousness states (particularly VS and MCS) in patients with ICH and shows prognostic potential at electrode Cz. Combined with the GCS and CRS-R, it enhances predictive accuracy, suggesting that multimodal assessment will be crucial for future ICH consciousness evaluation.

Data Sharing Statement

All data generated or analyzed during this study are included in the article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Handan Central Hospital [(2024) Ethical Review Research No.014]. All patients provided informed consent and willingly participated in the study.

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Disclosure

None of the authors have any personal, financial, commercial, or academic conflicts of interest in this work.

References

1. Puy L, Parry-Jones AR, Sandset EC, et al. Intracerebral haemorrhage. *Nat Rev Dis Primers*. 2023;9(1):14. doi:10.1038/s41572-023-00424-7
2. Casolla B, Cordonnier C. Intracerebral haemorrhage, microbleeds and antithrombotic drugs. *Rev Neurol*. 2021;177(1–2):11–22. doi:10.1016/j.neurol.2020.05.008
3. Giacino JT, Katz DI, Schiff ND, et al. Practice guideline update recommendations summary: disorders of consciousness: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research. *Arch Phys Med Rehabil*. 2018;99(9):1699–1709. doi:10.1016/j.apmr.2018.07.001
4. Schnakers C, Vanhaudenhuyse A, Giacino J, et al. Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. *BMC Neurol*. 2009;9(1):35. doi:10.1186/1471-2377-9-35
5. André-Obadia N, Zyss J, Gavaret M, et al. Recommendations for the use of electroencephalography and evoked potentials in comatose patients. *Neurophysiol Clin*. 2018;48(3):143–169. doi:10.1016/j.neucli.2018.05.038
6. Grimm S, Escera C, Slabu L, et al. Electrophysiological evidence for the hierarchical organization of auditory change detection in the human brain. *Psychophysiology*. 2011;48(3):377–384. doi:10.1111/j.1469-8986.2010.01073.x
7. Wang X, Fu R, Xia X, et al. Spatial properties of mismatch negativity in patients with disorders of consciousness. *Neurosci Bull*. 2018;34(4):700–708. doi:10.1007/s12264-018-0260-4
8. Kropotov JD, Alho K, Näätänen R, et al. Human auditory-cortex mechanisms of preattentive sound discrimination. *Neurosci Lett*. 2000;280(2):87–90. doi:10.1016/s0304-3940(00)00765-5
9. Nashida T, Yabe H, Sato Y, et al. Automatic auditory information processing in sleep. *Sleep*. 2000;23(6):821–828. PMID: 11007449. doi:10.1093/sleep/23.6.1i
10. Azabou E, Rohaut B, Porcher R, et al. Mismatch negativity to predict subsequent awakening in deeply sedated critically ill patients. *Br J Anaesth*. 2018;121(6):1290–1297. doi:10.1016/j.bja.2018.06.029
11. Simpson TP, Manara AR, Kane NM, et al. Effect of propofol anaesthesia on the event-related potential mismatch negativity and the auditory-evoked potential N1. *Br J Anaesth*. 2002;89(3):382–388. doi:10.1093/bja/89.3.382
12. Zhang K, Li K, Zhang C, et al. The accuracy of different mismatch negativity amplitude representations in predicting the levels of consciousness in patients with disorders of consciousness. *Front Neurosci*. 2023;17:1293798. doi:10.3389/fnins.2023.1293798
13. Shao H, Deng W, Du R, et al. Mismatch negativity and P300 in the diagnosis and prognostic assessment of coma and other disorders of consciousness. *Neurocrit Care*. 2024;42(1):185–195. doi:10.1007/s12028-024-02058-3
14. Qin P, Di H, Yan X, et al. Mismatch negativity to the patient's own name in chronic disorders of consciousness. *Neurosci Lett*. 2008;448(1):24–28. doi:10.1016/j.neulet.2008.10.029
15. Schall U. Is it time to move mismatch negativity into the clinic? *Biol Psychol*. 2016;116:41–46. doi:10.1016/j.biopsycho.2015.09.001
16. Gill-Thwaites H, Elliott KE, Munday R. SMART - Recognising the value of existing practice and introducing recent developments: leaving no stone unturned in the assessment and treatment of the PDOC patient. *Neuropsychological Rehabilitat*. 2018;28(8):1242–1253. doi:10.1080/09602011.2017.1310113

17. Giacino JT, Kalmar K, Whyte J. The JFK coma recovery scale-revised: measurement characteristics and diagnostic utility. *Arch Phys Med Rehabil*. 2004;85(12):2020–2029. doi:10.1016/j.apmr.2004.02.033
18. Honbolygó F, Zulauf B, Zavogianni MI, et al. Investigating the neurocognitive background of speech perception with a fast multi-feature MMN paradigm. *Biol Futur*. 2024;75(1):145–158. doi:10.1007/s42977-024-00219-1
19. Lundin NB, Burroughs LP, Kieffaber PD, et al. Temporal and spectral properties of the auditory mismatch negativity and p3a responses in schizophrenia. *Clin EEG Neurosci*. 2023;54(4):409–419. doi:10.1177/15500594221089367
20. Jang SH, Chang CH, Jung YJ, et al. Relationship between impaired consciousness and injury of ascending reticular activating system in patients with intracerebral hemorrhage. *Stroke*. 2019;50(8):2234–2237. doi:10.1161/STROKEAHA.118.023710
21. Bodien YG, Carlowicz CA, Chatelle C, et al. Sensitivity and specificity of the coma recovery scale--revised total score in detection of conscious awareness. *Arch Phys Med Rehabil*. 2016;97(3):490–492.e1. doi:10.1016/j.apmr.2015.08.422
22. Kondziella D, Bender A, Diserens K, et al. European Academy of Neurology guideline on the diagnosis of coma and other disorders of consciousness. *Eur J Neurol*. 2020;27(5):741–756. doi:10.1111/ene.14151
23. Selioutski O, Auinger P, Siddiqi OK, et al. Association of the verbal component of the GCS with mortality in patients with encephalopathy who are not undergoing mechanical ventilation. *Neurology*. 2022;98(5):e533–e540. doi:10.1212/WNL.0000000000013127
24. Näätänen R, Escera C. Mismatch negativity: clinical and other applications. *Audiol Neurootol*. 2000;5(3–4):105–110. doi:10.1159/000013874
25. Fischer C, Morlet D, Bouchet P, et al. Mismatch negativity and late auditory evoked potentials in comatose patients. *Clin Neurophysiol*. 1999;110 (9):1601–1610. doi:10.1016/s1388-2457(99)00131-5
26. Wijnen VJ, van Boxtel GJ, Eilander HJ, et al. Mismatch negativity predicts recovery from the vegetative state. *Clin Neurophysiol*. 2007;118 (3):597–605. doi:10.1016/j.clinph.2006.11.020
27. Morlet D, Bouchet P, Fischer C. Mismatch negativity and N100 monitoring: potential clinical value and methodological advances. *Audiol Neurootol*. 2000;5(3–4):198–206. doi:10.1159/000013881
28. Cruse D, Chennu S, Chatelle C, et al. Relationship between etiology and covert cognition in the minimally conscious state. *Neurology*. 2012;78 (11):816–822. doi:10.1212/WNL.0b013e318249f764
29. Wu S, Wu B, Liu M, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol*. 2019;18 (4):394–405. doi:10.1016/S1474-4422(18)30500-3
30. Rodriguez RA, Bussière M, Froeschl M, et al. Auditory-evoked potentials during coma: do they improve our prediction of awakening in comatose patients? *J Crit Care*. 2014;29(1):93–100. doi:10.1016/j.jcrc.2013.08.020
31. Zhou L, Wang J, Wu Y, et al. Clinical significance of mismatch negativity in predicting the awakening of comatose patients after severe brain injury. *J Neurophysiol*. 2021;126(1):140–147. doi:10.1152/jn.00658.2020
32. Wang XY, Wu HY, Lu HT, et al. Assessment of mismatch negativity and P300 response in patients with disorders of consciousness. *Eur Rev Med Pharmacol Sci*. 2017;21(21):4896–4906.