NeuroImage 297 (2024) 120753

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Exploring the clinical diagnostic value of linguistic learning ability in patients with disorders of consciousness using electrooculography

Xiangyue Xiao [a,b], Junhua Ding [c], Mingyan Yu [a,b], Zhicai Dong [a,b], Sara Cruz [d], Nai Ding [e], Charlène Aubinet [f,g], Steven Laureys [f], Haibo Di [a,b,*], Yan Chen [a,b,*]

[a] International Unresponsive Wakefulness Syndrome and Consciousness Science Institute, Hangzhou Normal University, Hangzhou 311121, China
[b] Key Laboratory of Ageing and Cancer Biology of Zhejiang Province, School of Basic Medical Sciences, Hangzhou Normal University, Hangzhou 311121, China
[c] Department of Psychology, University of Edinburgh, Edinburgh EH8 9YL, UK
[d] The Psychology for Development Research Centre, Lusiada University Porto, Porto 4100-348, Portugal
[e] Key Laboratory for Biomedical Engineering of Ministry of Education, College of Biomedical Engineering and Instrument Sciences, Zhejiang University, Hangzhou 310027, China
[f] Coma Science Group, GIGA Consciousness & Centre du Cerveau, University and University Hospital of Liège, Liège 4000, Belgium
[g] Psychology & Neuroscience of Cognition Research Unit, University of Liège, Liège 4000, Belgium

ARTICLE INFO

Keywords:
Disorders of consciousness
Electrooculography
Diagnosis
Language
Linguistic learning

ABSTRACT

For patients with disorders of consciousness (DoC), accurate assessment of residual consciousness levels and cognitive abilities is critical for developing appropriate rehabilitation interventions. In this study, we investigated the potential of electrooculography (EOG) in assessing language processing abilities and consciousness levels. Patients' EOG data and related electrophysiological data were analysed before and after explicit language learning. The results showed distinct differences in vocabulary learning patterns among patients with varying levels of consciousness. While minimally conscious patients showed significant neural tracking of artificial words and notable learning effects similar to those observed in healthy controls, whereas patients with unresponsive wakefulness syndrome did not show such effects. Correlation analysis further indicated that EOG detected vocabulary learning effects with comparable validity to electroencephalography, reinforcing the credibility of EOG indicator as a diagnostic tool. Critically, EOG also revealed significant correlations between individual patients' linguistic learning performance and their Oromotor/verbal function as assessed through behavioural scales. In conclusion, this study explored the differences in language processing abilities among patients with varying consciousness levels. By demonstrating the utility of EOG in evaluating consciousness and detecting vocabulary learning effects, as well as its potential to guide personalised rehabilitation, our findings indicate that EOG indicators show promise as a rapid, accurate and effective additional tool for diagnosing and managing patients with DoC.

1. Introduction

Disorders of consciousness (DoC) refer to impairments in a person's ability to recognise and perceive their surrounding environment and internal state (Edlow et al., 2021). Depending on the severity of consciousness impairment, patients with DoC are classified into either unresponsive wakefulness syndrome (UWS) or minimally conscious state (MCS) (Giacino et al., 2014). While both exhibit characteristics of arousal, UWS patients lack signs of consciousness, whereas patients with MCS demonstrate fluctuating and minimal levels of consciousness, with occasional awareness of themselves or their environment (Giacino et al., 2014; Giacino et al., 2004). Given the differences in their level of consciousness and residual function, accurate classification is critical for subsequent patient's treatment. Currently, clinical diagnosis of consciousness levels in DoC patients is primarily based on behavioural assessment using the Coma Recovery Scale-Revised (CRS-R) (Giacino et al., 2004; Giacino et al., 2009; Schnakers, 2012). However, varying degrees of external motor and cognitive impairments resulting from brain damage may hinder the manifestation of patients' underlying consciousness. Additionally, the instability of spontaneous movements

* Corresponding authors at: International Unresponsive Wakefulness Syndrome and Consciousness Science Institute, Hangzhou Normal University, Hangzhou 311121, China.
E-mail addresses: dihaibo19@aliyun.com (H. Di), chen_yan@hznu.edu.cn (Y. Chen).

https://doi.org/10.1016/j.neuroimage.2024.120753
Received 28 May 2024; Received in revised form 15 July 2024; Accepted 23 July 2024
Available online 24 July 2024

in DoC patients makes it challenging to distinguish between random and conscious behaviour (Schnakers, 2012; Childs et al., 1993; Wannez et al., 2017). Therefore, relying solely on behavioural performance to assess patients and diagnose DoC may lead to incorrect medical decisions and interfere with the recovery process.

In recent years, an increasing number of studies have successfully used neurological activity monitoring techniques such as Positron Emission Computed Tomography (Stender et al., 2014), functional Magnetic Resonance Imaging (fMRI) (Demertzi et al., 2015), and Electroencephalography (EEG) (Laforge et al., 2020; Golkowski et al., 2017) to assess level of consciousness and predict prognosis in DoC patients (Kondziella et al., 2016; Marino et al., 2016; Snider and Edlow, 2020). For example, Owen and colleagues proposed an active imagination paradigm using fMRI to assess patients' ability to follow commands, their consciousness level, as well as their prognosis (Vogel et al., 2013; Owen et al., 2006). Researchers have also used EEG signals recorded while patients watched or listened to suspenseful movie clips to examine the preservation of patients' hidden capacity for narrative processing (Laforge et al., 2020). However, these existing research methods still need improvement. On the one hand, most of the active paradigms require high levels of language and cognitive abilities from patients, leading to reduced sensitivity (Kondziella et al., 2020) and better suitability for patients with high levels of consciousness. On the other hand, these techniques have limitations in clinical applications due to their radioactive exposure, incompatibility with metal, high cost, time consuming preparation, and difficulty in portability, especially unsuitable for patients with open head injuries or skull defects.

Compared to traditional detection techniques such as EEG, electrooculography (EOG) is more convenient to operate and apply. As a technology for recording eye movements, EOG electrodes are easy to apply without extensive head preparation, and are not affected by factors such as patients' cranial bone defects. However, research using this convenient EOG detection technique for DoC assessment has been relatively limited. Some studies have employed other eye movement detection techniques to examine patients with DoC. For example, one study used eye-tracking technology to assess the preserved reading comprehension ability of patients with MCS and found that they were able to read word and comprehend sentences to some extent (Kwiatkowska et al., 2019). Another study also used eye-tracking signals to assess cognitive functioning in patients with DoC (Kujawa et al., 2022). However, these studies did not directly assess the patients' levels of consciousness, indicating the necessity for further research in this area.

Interestingly, previous studies in healthy subjects have shown that vertical EOG recorded eye movements can track linguistic structure in speech streams similar to cortical neural tracking (Jin et al., 2018). This suggests a potential application of EOG in assessing language processing abilities in DoC patients, which may be partially preserved (deJong et al., 1997; Owen et al., 2005; Laureys et al., 2000). By analysing EEG data, researchers have found specific cortical responses in patients when passively presented with speech stimuli containing different levels of linguistic structures. They suggested that assessing patients' neural tracking of different levels of linguistic structural levels can help to determine the patient's level of consciousness and prognostic outcome (Sokoliuk et al., 2021; Gui et al., 2020). Moreover, the passive paradigm ensures effective assessments even in patients without external behaviour. Therefore, integrating EOG with linguistic assessments could provide a more comprehensive understanding of the preserved functions in DoC patients. However, the linguistic paradigm used in neural tracking studies (common words, phrases, and sentences encountered in daily life) relies on pre-existing language knowledge. The use of this paradigm to assess consciousness in severely brain-injured DoC patients risks producing biased results.

Word acquisition is a crucial component of language learning. Previous researches have employed associative learning methodologies, such as using novel word-referent pairings (Bormann et al., 2020; Kroenke et al., 2013; Tuomiranta et al., 2014), to assess language abilities in subjects, facilitating unbiased assessment unaffected by pre-existing language knowledge. (Peñaloza et al., 2022) This process involves the use of attention, memory, and decision-making abilities. The impact of brain injury on these higher-order functions varies (Giacino et al., 2014), resulting in differences in language learning ability in patients with DoC. Some studies have confirmed that learning abilities are retained in a subset of patients with DoC (Bekinschtein et al., 2009; Kim et al., 2012; Lancioni et al., 2014). Furthermore, studies in healthy individuals have found that linguistic learning effects can be detected by assessing subjects' neural tracking of learned content (Chen et al., 2020). Overall, the research suggests that the linguistic learning paradigm could be used to assess consciousness in patients with DoC.

Therefore, this study aimed to investigate the effectiveness of EOG as a convenient detection technique in assessing linguistic learning abilities, and their relationship to levels of consciousness. By comparing the language learning performance among participants with different levels of consciousness, we aimed to validate the effectiveness of this paradigm for assessing consciousness levels. Specifically, we employed an artificial word learning paradigm. Under the guidance of experimenters, participants learned unfamiliar artificial words, each assigned a corresponding meaningful concept. EOG recordings were taken during auditory linguistic stimuli presentation before and after linguistic learning to analyse and assess subjects' language processing abilities and learning effects in different states of consciousness. We also conducted correlation analyses between learning effects recorded via EOG and EEG to explore the robustness of this metric. Finally, we examined the association between patients' learning abilities and their behavioural assessment scores. By investigating the differences in linguistic learning abilities and their underlying mechanisms in patients with different levels of consciousness, we expect to contribute to develop a convenient clinical tool for the diagnosis of clinical DoC patients.

2. Materials and methods

2.1. Participants

Patients with DoC and healthy controls (HC) participated in the current study. All participants were right-handed, native speakers of Mandarin Chinese and provided written informed consent. This study was approved by the Ethics Committee of the Hangzhou Normal University.

2.1.1. Patients

Fifty-one patients with DoC were recruited from three medical institutions: Shanghai Yongci Rehabilitation Hospital, rehabilitation units of Hangzhou Wujing Hospital, and Zhejiang Rehabilitation Medical Centre. Forty-eight patients (38 males) were included in the final analysis. They met the following inclusion criteria: (i) diagnosed with MCS or UWS according to the CRS-R (26 MCS and 22 UWS); (ii) presence of the auditory startle reflex; (iii) no history of hearing or visual impairment prior to brain injury; (iv) no history of neurological or psychiatric disease prior to brain injury; (v) aged over 18 years; (vi) at least 28 days post-onset [mean = 14.04 months; standard deviation (SD) = 6.78; range: 3–35 months]. The mean age of patients with MCS was 61.00 years (SD = 11.74; range: 37–81 years), and the mean age of patients with UWS was 51.64 years (SD = 15.44; range: 25–75 years). Thirty-one patients suffered from non-traumatic brain injury (NTBI) and 17 patients suffered from traumatic brain injury (TBI). Background information on the DoC patients is shown in Table 1.

2.1.2. Healthy controls

Twenty-four HC subjects were recruited from the local community of each medical institution. And all subjects were included in the final analysis (16 males). The subjects had a mean age of 58.46 years (SD = 11.36; range: 32–75 years), normal hearing and vision, and no history of brain injury, psychiatric or neurological disease.

Table 1
The demographic and clinical information of 48 patients with DoC.

Patient ID	Diagnosis	Age (years)	Gender	Aetiology	Time since injury (months)	CRS-R score
sub001	UWS	75	M	NTBI	13	7
sub003	MCS-	44	M	NTBI	35	11
sub004	MCS-	66	M	TBI	11	12
sub005	UWS	71	M	TBI	10	5
sub006	UWS	41	F	NTBI	8	8
sub007	UWS	37	M	NTBI	11	7
sub008	MCS-	67	M	TBI	14	10
sub009	MCS-	81	M	NTBI	16	11
sub010	UWS	34	M	NTBI	12	5
sub011	MCS-	59	F	NTBI	4	10
sub012	MCS+	70	F	TBI	14	19
sub013	MCS-	50	M	NTBI	18	9
sub014	MCS-	47	M	TBI	4	10
sub015	MCS-	37	M	NTBI	4	8
sub016	UWS	42	M	NTBI	7	7
sub017	MCS+	66	M	TBI	13	11
sub018	UWS	41	M	NTBI	5	7
sub019	MCS+	66	F	TBI	15	18
sub020	UWS	33	M	TBI	15	7
sub021	MCS-	53	M	NTBI	8	12
sub022	UWS	55	M	TBI	12	7
sub023	UWS	54	M	TBI	3	7
sub024	MCS-	67	F	NTBI	12	12
sub025	UWS	73	M	NTBI	18	2
sub026	UWS	25	F	NTBI	9	7
sub027	UWS	52	M	TBI	15	7
sub028	UWS	29	F	NTBI	10	7
sub029	UWS	71	M	NTBI	32	8
sub030	UWS	67	M	TBI	26	7
sub031	MCS-	77	M	NTBI	20	12
sub032	UWS	55	M	NTBI	13	7
sub033	UWS	56	M	NTBI	10	6
sub034	MCS+	72	F	NTBI	10	15
sub035	UWS	68	M	TBI	22	7
sub037	MCS-	51	M	TBI	12	11
sub038	MCS-	75	M	TBI	18	14
sub039	MCS-	50	M	NTBI	23	11
sub040	MCS-	51	M	NTBI	11	13
sub041	UWS	65	M	NTBI	10	7
sub043	UWS	51	F	NTBI	16	7
sub044	MCS-	68	M	NTBI	20	9
sub045	MCS-	72	M	NTBI	19	12
sub046	MCS-	52	M	TBI	9	13
sub047	MCS-	66	M	NTBI	16	13
sub048	UWS	41	M	NTBI	21	7
sub049	MCS-	64	F	NTBI	18	11
sub050	MCS-	71	M	NTBI	22	12
sub051	MCS-	44	M	NTBI	10	9

CRS-R = Coma Recovery Scale-Revised; DoC = disorders of consciousness; F = female; M = male; MCS = minimally conscious state; N/A = data not available; NTBI = non-traumatic brain injury; TBI = traumatic brain injury; UWS = unresponsive wakefulness syndrome.

The DoC patients and HC were comparable in age ($F = 0.275$, $P = 0.602$) and gender distribution ($\chi^2 = 1.333$, $P = 0.248$).

2.2. Clinical assessments

This study used the CRS-R (Giacino et al., 2004; Kondziella et al., 2020) behavioural scale to assess patients' levels of consciousness. Six subscale scores of the CRS-R were generated to assess their specific cognitive abilities, including Auditory function, Visual function, Motor function, Oromotor/verbal function, Communication, and Arousal. Following guideline recommendations, each patient underwent at least five behavioural assessments within ten days prior to EOG data collection. These assessments were conducted by two medically trained personnel who had received professional training. The highest total score from the assessments was recorded as the final assessment score. Clinical raters and data analysts were blinded to ensure unbiased assessment.

2.3. Procedures

2.3.1. Stimuli

We used a speech stream consisting of five artificial words as experimental stimuli. These artificial words were constructed from Mandarin syllables, which were nonsense words, and semantically unrelated to each other. To generate these artificial words, we selected five common trisyllabic real Mandarin words, all of which were nouns, with each syllable occurring in only one word (i.e., "cháng jǐng lù", "xī hóng shì", "tuī xiāo yuán", "diàn yùn dǒu", "fǔ wò chēng" for giraffe, tomato, salesman, iron, and for push-up). There were significant differences in the initial phonemes, final phonemes, and tones at the corresponding positions in each word. Subsequently, by randomly shuffling the syllables at the same positions within the real words, we obtained five trisyllabic artificial words (i.e., "cháng xiāo shì", "xī wò dǒu", "tuī jǐng chēng", "diàn hóng lù", "fǔ yùn yuán").

We then concatenated all the artificial words in random order, ensuring that the same word was not repeated immediately. The stimulus speech stream was generated using the Neospeech synthesiser (http://www.neospeech.com/, the male voice). Within the speech stream, the transition probability between adjacent syllables within each word was kept at 1, and word boundaries at 0.25. The total stimulus consisted of 800 artificial words, totalling 2400 syllables, with each syllable lasting 250 ms. Syllables were concatenated without acoustic gaps between them, resulting in a presentation rate of 4 Hz for each syllable and 1.33 Hz for each trisyllabic word (Fig. 1A). To prevent participants from arbitrarily grouping every three syllables into single words from the start, we added 7–8 random syllables at both the beginning and end of the speech sequence. These additional syllables were randomly selected from those constituting the artificial words, while also ensuring that the generated sequence consisted entirely of nonsense words that were semantically unrelated to each other.

The entire speech stream lasted for 10 min and 3.75 s. To increase participants' attention, we adjusted the formant shift ratio of 10 syllables and modulated them into "anomalous syllables" with a higher pitch perception for use in the target detection task during the experiment. All stimuli were presented using the Psychtoolbox MATLAB toolbox (Brainard, 1997).

2.3.2. Experimental design

The experiment spanned two days, involving linguistic learning and the recording of EOG and EEG data. Prior to the experiment, participants were unfamiliar with the artificial words they were about to learn. They listened to a speech sample extracted from the experimental speech stream containing "anomalous syllables". After listening to the sample, participants were informed about the anomalous syllables and given detailed explanations to help them understand.

Participants were then instructed to keep their eyes open and to remain focused and still during the presentation of the speech stream. Participants were also required to perform a target detection task while listening to the experimental stimuli. Due to functional impairments in patients, they were asked to imagine squeezing their right hand when hearing "anomalous syllables", while healthy participants were instructed to make a keypress response instead. Throughout the experiment, participants wore headphones to listen to speech streams.

The formal experiment consisted of alternating artificial word listening tasks with EOG/EEG recording and artificial word learning sessions (Fig. 1B). In the first phase of the experiment, participants' EOG/EEG were recorded during speech stream presentations before they engage in artificial word learning. During this phase, participants were required to listen attentively to the experimental speech stream and complete a target detection task as instructed. This phase served as the pre-learning recording.

The second phase of the experiment consisted of two parts. First, an

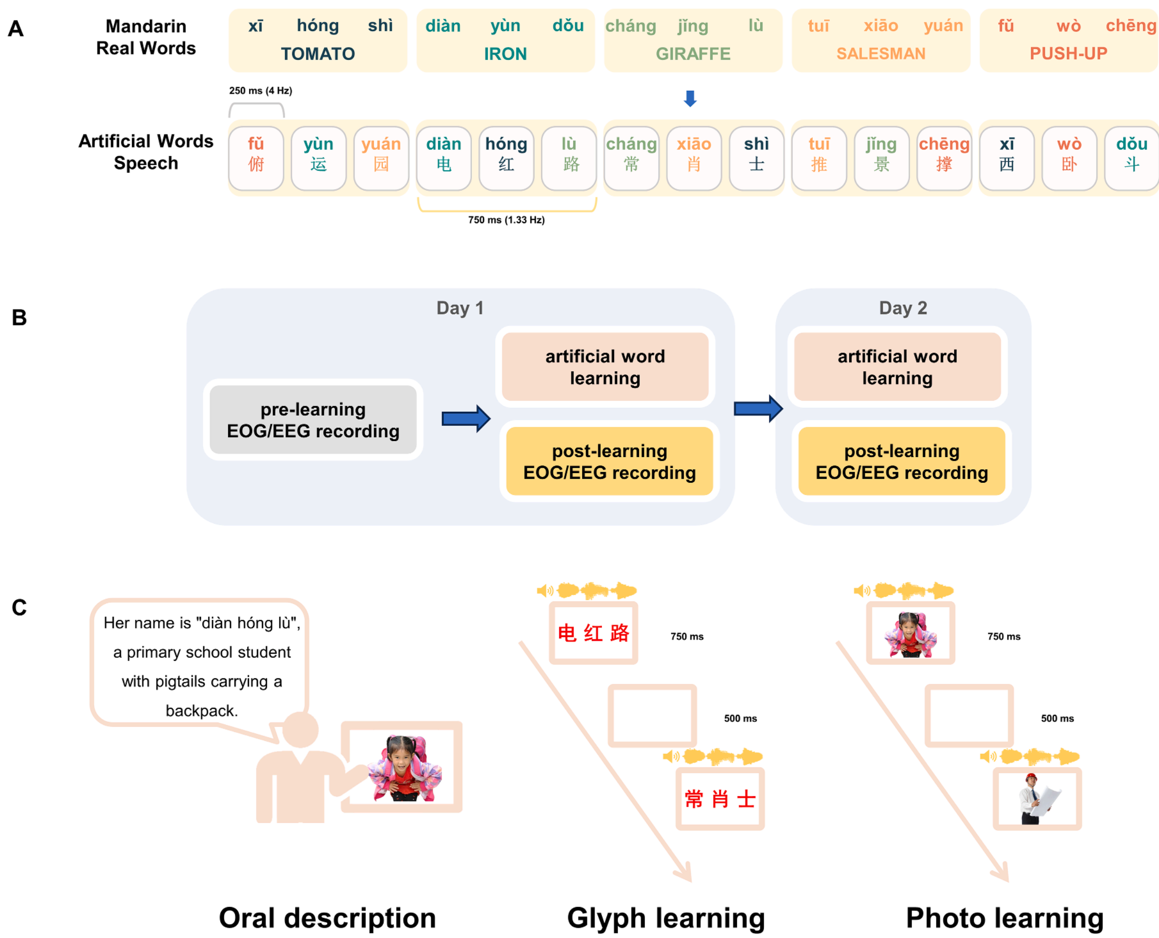

Fig. 1. Stimuli and procedures for the artificial word learning experiment. (A) The auditory stimulus stream consisted of five trisyllabic artificial words. The artificial words were generated by randomly shuffling the syllables within five trisyllabic real Mandarin words. Each syllable was presented at 4 Hz, and each artificial word at 1.33 Hz. (B) The experiment was conducted on two consecutive days. It included listening tasks with EOG/EEG recording before artificial word learning, and two alternating sessions of artificial word learning, and listening tasks with EOG/EEG recording after learning. (C) Artificial word learning included: a 2-min oral description by the experimenter of the characters represented by the artificial words; 3-min of glyph learning; and 3-min of photo learning. Each artificial word was presented auditorily for 750 ms with a 250 ms interval between the presentation of the glyph and the photo.

eight-minute session of artificial word learning was conducted, in which five artificial words were identified and learned as the names of five fictional characters (Fig. 1C). Using graphic materials, the experimenter provided a 2 min oral description of all the characters represented by the artificial words, including their names, physical characteristics, and occupations. Participants then completed two 3-min learning tasks: glyph learning and photo learning. Specifically, each artificial word was audio presented for 750 ms along with the corresponding Chinese character or photo of the character. Two consecutive artificial words were separated by a 500 ms of silence and black screen. The five artificial words were repeated a total of 144 times. After completing the artificial word learning, participants underwent another round of listening tasks with EOG/EEG recording, consistent with the pre-learning recording, as the post-learning recording.

On day 2, the third phase of the experiment involved a second round of artificial word learning and EOG/EEG recording during the presentation of speech streams. Both procedures were consistent with those used the second phase of the experiment.

2.4. *Electrophysiological data recording*

During the experimental sessions, electrophysiological data were collected from all participants while they were in their optimal state throughout the day. EOG/EEG responses were recorded continuously at a sampling rate of 1000 Hz using a 32-channel BrainAmp EOG/EEG system (Brain Products GmbH, Munich, Germany). The EOG electrodes were placed below the right eye to record vertical EOG signals. EEG signals were recorded according to the international 10–20 system. All data were then preprocessed using custom MATLAB scripts and the EEGLAB toolbox (version 14.1.2). Signals were filtered from 0.3 to 40 Hz using a Butterworth filter. Independent component analysis (ICA) was then applied to remove artifacts. All data, initially referenced online to the FCz during acquisition, were then re-referenced to the average mastoid recording (left and right mastoid) and resampled at 80 Hz.

2.4.1. *Data feature extraction*

To explore the neural tracking of rhythmic speech structures, frequency domain analysis was performed on the data. First, to remove the potential onset and offset effects and to focus on steady-state responses, the neural activity corresponding to the random syllables presented at the beginning and end of each speech sequence was not analysed. Next, the 10-min continuous data were segmented into 50 epochs of 12 s each. Since the syllables in the speech stream were presented at a constant rate, each epoch corresponded to the presentation of 16 trisyllabic words. The signals from the 50 epochs were then averaged and transformed from the time domain to the frequency domain using the discrete Fourier transform function. Inter trial phase coherence (ITPC) analysis was then used to assess the degree of neural synchronisation at different frequencies. It is defined as follows:

$$\mathrm{ITPC}(f) = \frac{1}{n}\left(\sum_{k=1}^{n}\cos(\theta_k)^2 + \sum_{k=1}^{n}\sin(\theta_k)^2\right)$$

ITPC values ranged from 0 to 1, with higher values indicating greater phase consistency of neural responses across trials at that frequency, and thus greater neural synchrony.

2.5. Learning effect analysis

To accurately reflect the participants' learning effects, the ITPC values at the word-rate of 1.33 Hz were compared between the two post-learning recordings. The recording with the highest ITPC value was selected to represent the participant's after learning performance, and for the subsequent analysis.

Additionally, to control for the effect of individual variations in syllable identification ability on the estimation of word identification ability, we quantified individual word learning efficiency by the Word Learning Index (WLI) using the following formula:

$$\mathrm{WLI} = \frac{\mathrm{ITPC}_{\text{word frequency}}}{\mathrm{ITPC}_{\text{syllable frequency}}}$$

2.6. Statistical analysis

To confirm the successful linguistic tracking effect for our experiment, a series of paired *t*-tests were conducted. ITPC values at word-rate and syllable-rate were compared to the average of the two adjacent frequencies. To deal with multiple comparisons, a Bonferroni correction was applied to determine whether there were significant spectral peaks at these two frequencies for each group of participants. To validate the results, more paired *t*-tests were done on the ITPC values between the word-rate and the average of the eight adjacent frequencies (i.e., ± 0.33 Hz) and on the frequency of the first harmonic of the word-rate (i.e., 2.67 Hz).

A two-way repeated measures analysis of variance (ANOVA) was then performed to analyse ITPC values separately at word-rate and syllable-rate to examine learning effects within each group. Learning stage (i.e., before and after learning stages) was treated as a within-subject factor, while group (i.e., HC, MCS, and UWS) was treated as a between-subjects factor. Where significant main effects were identified, post-hoc multiple comparisons were performed using Bonferroni-corrected *t*-tests. In the case of a significant interaction, paired *t*-tests were conducted on the ITPC values at that frequency before and after learning within each group of participants to investigate specific learning effects. To directly assess the efficiency of word learning, we used the chi-squared test to compare whether the trends of change in WLI (ITPC of word-rate/ITPC of syllable-rate) before and after learning were consistent across the different groups. To ensure that the observed vocabulary learning effects in the MCS group, as detected by EOG, were not solely driven by patients with a higher level of consciousness (i.e., MCS+ patients), we excluded all MCS+ patients ($n = 4$) and conducted the paired *t*-test and WLI analyses again to examine whether the MCS-patients ($n = 22$) exhibited similar learning effects to the healthy controls.

To further assess the usefulness of EOG ITPC in measuring linguistic learning ability in DoC patients, we conducted separate Pearson correlation analyses for the word-rate and syllable-rate. The "ITPC-difference" was defined as the change in ITPC values before and after learning for each measure. These analyses examined the relationship between EOG ITPC-difference and the EEG ITPC-difference within each patient, with the aim of exploring the association between EOG ITPC and commonly used biomarkers.

Finally, we also examined the relationship between the linguistic learning effects represented by EOG ITPC and the behavioural performance of the patients. The linguistic learning effect of each patient was indicated by the difference in EOG ITPC before and after learning (ITPC-difference). We conducted two-tailed Spearman correlation analyses between the total score and subscale scores of the CRS-R and the ITPC-difference at word-rate and syllable-rate.

3. Results

3.1. EOG tracking effects of linguistic features

By comparing the EOG's ITPC spectral responses at word and syllable rates with their adjacent frequencies, we observed different tracking effects before and after learning in the HC, MCS and UWS groups (Table 2; Fig. 2A). Specifically, the HC group displayed no significant peak at the word-rate before learning ($t = 1.625$, Bonferroni corrected $P = 0.236$), whereas significant peak at this frequency emerged after learning ($t = 3.766$, Bonferroni corrected $P = 0.002$). For the MCS group, we found a similar peak tendency, with no obvious peak at the word-rate before learning ($t = 0.765$, Bonferroni corrected $P = 0.903$), but significant peak emerging after learning ($t = 2.521$, Bonferroni corrected $P = 0.037$). For the UWS group, the peaks in the word-rate were not significant regardless of the learning stage (before learning: $t = 2.251$, Bonferroni corrected $P = 0.070$; after learning: $t = 1.967$, Bonferroni corrected $P = 0.125$). In contrast, there were significant peaks in syllable-rate for all groups regardless of learning stage ($t > 2.917$, Bonferroni corrected $P < 0.029$). To confirm the robustness of the significant effect of linguistic tracking, we compared the word-rate ITPC values with a wider range of neighbouring frequencies (the average of the eight adjacent frequencies). The results were consistent with the previously described findings in each group (HC/MCS word-rate before learning: $t < 2.384$, Bonferroni corrected $P > 0.052$; HC/MCS word-rate after learning: $t > 3.563$, Bonferroni corrected $P < 0.003$; UWS word-rate before/after learning: $t < 2.322$, Bonferroni corrected $P > 0.061$). Additionally, we tested for the significance of peaks at the first harmonic of the word rate (i.e., 2.67 Hz). We found a significant peak at the harmonic in the HC group after learning (before learning: $t = 1.996$, Bonferroni corrected $P = 0.116$; after learning: $t = 2.403$, Bonferroni corrected $P = 0.049$). However, no significant peaks at the harmonic were observed before learning in the HC group or before and after learning in the two patient groups ($t < 2.204$, Bonferroni corrected $P > 0.074$).

3.2. EOG learning effects of linguistic features

To examine the learning effect of linguistic features in each group, we performed two-way repeated measures ANOVA analyses on the EOG's ITPC values for both word-rate and syllable-rate conditions. Specifically, these ANOVA tests compared the ITPC values before and after learning across the HC, MCS, and UWS groups within each frequency condition.

Table 2
Tracking the effects of each linguistic feature's ITPC spectral peaks at different learning stages.

Learning stage	HC		MCS		UWS	
	t	*P*	*t*	*P*	*t*	*P*
Word-rate						
before learning	1.625	0.236	0.765	0.903	2.251	0.070
after learning	3.766	0.002**	2.521	0.037*	1.967	0.125
Syllable-rate						
before learning	4.658	0.000***	5.414	0.000***	3.342	0.009**
after learning	6.417	0.000***	2.917	0.015*	3.774	0.029*

Paired *t*-tests were conducted to examine whether the neural response at the word and syllable frequencies was significantly stronger than the average of the two adjacent frequency bins. HC = healthy control; MCS = minimally conscious state; UWS = unresponsive wakefulness syndrome; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (Bonferroni corrected P value threshold).

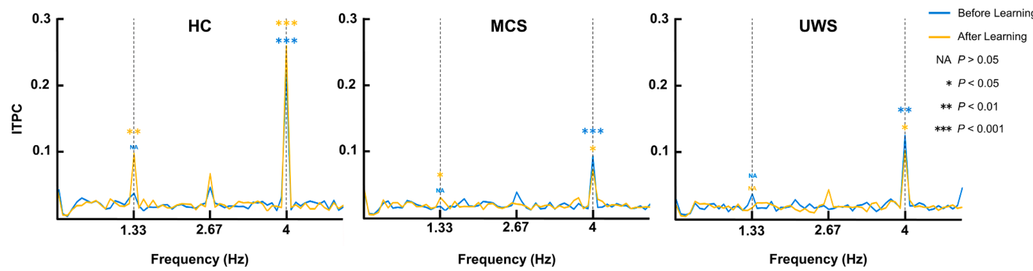

Fig. 2. EOG spectrograms in each group. The ITPC spectra of the EOG responses for the HC, MCS, and UWS groups, showing trends before and after the artificial word learning, illustrate the changes in ITPC values across different frequencies. HC = healthy control; ITPC = inter-trial phase coherence; MCS = minimally conscious state; UWS = unresponsive wakefulness syndrome.

3.2.1. *Learning effects of word*

The results of the ANOVA on the ITPC values at the word-rate showed significant main effects of learning stage ($F = 8.327$, $P = 0.005$) and group ($F = 8.741$, $P < 0.001$). Further post-hoc multiple comparisons revealed that word-rate ITPC values were significantly higher after learning than before learning (Bonferroni corrected $P = 0.005$) (Fig. 3A). Compared to the MCS group (Bonferroni corrected $P < 0.001$) and the UWS group (Bonferroni corrected $P = 0.040$), participants in the HC group exhibited higher word-rate ITPC values. There was no significant difference between the MCS and UWS groups (Bonferroni corrected $P = 0.443$) (Fig. 3B).

We also observed a significant interaction effect between learning stage and group for ITPC values at the word-rate ($F = 3.327$, $P = 0.042$) (Fig. 3C). This suggests that the patterns of change in word-rate ITPC values varied across the three groups at different learning stages. To further investigate the specific learning effects within each group, we conducted paired *t*-tests on the before and after learning word-rate ITPC values for each group separately. The results showed that for the HC group, word-rate ITPC values increased significantly after learning ($t = 2.495$, Bonferroni corrected $P = 0.020$). Similarly, the MCS group showed the same learning effect, with a significantly higher ITPC value after learning ($t = 2.612$, Bonferroni corrected $P = 0.015$). In contrast, no significant change was observed in the UWS group across different learning stages ($t = 0.416$, Bonferroni corrected $P = 0.682$) (Fig. 3D). Additionally, to test whether the learning effects observed in the MCS group were driven only by a few patients with a higher level of consciousness (i.e., MCS+, $n = 4$), we re-evaluated the learning effects by excluding these MCS+ patients and focusing on the remaining MCS- group ($n = 22$). We found that the MCS- patients still exhibited similar learning effects, with a significant increase in word-rate ITPC values after learning ($t = 2.432$, $P = 0.024$).

3.2.2. *Learning effects of syllable*

The results of the ANOVA on the ITPC values at the syllable-rate showed the significant main effect of group ($F = 8.489$, $P = 0.001$). Post-hoc multiple comparisons revealed that the HC group had higher ITPC values at the syllable-rate compared to the MCS group (Bonferroni corrected $P < 0.001$) and the UWS group (Bonferroni corrected $P = 0.029$) (Fig. 3F). No significant main effect of learning stage ($F = 0.286$, $P = 0.594$) (Fig. 3E) or significant interaction effect ($F = 0.661$, $P = 0.519$) (Fig. 3G) was observed.

3.2.3. *Learning effects of word/syllable ratio*

The ratio of word-rate and syllable-rate ITPC values (i.e., WLI) reflects word learning effects controlling for syllable-rate differences (Fig. 4). The results showed that 70.83 % of the HC participants showed increased WLI values after learning compared to before learning, and 80.77 % of the MCS patients exhibited increased WLI after learning. In contrast, only 40.91 % of the UWS patients showed an increase in WLI after learning.

Chi-squared tests revealed that, compared to the UWS group, a significantly higher proportion of subjects in the HC group ($\chi^2 = 4.182$, $P = 0.041$) and the MCS group ($\chi^2 = 8.078$, $P = 0.004$) exhibited increased WLI values after learning. No significant difference was found between the HC and MCS groups ($\chi^2 = 0.675$, $P = 0.411$). Additionally, we found that 77.27 % of MCS- patients exhibited increased WLI values after learning, a proportion similar to that of the HC group ($\chi^2 = 0.247$, $P = 0.619$) and significantly higher than that of the UWS group ($\chi^2 = 6.017$, $P = 0.014$).

3.3. *Correlation of EOG with other biomarkers*

We examined the correlation between the linguistic learning effects reflected in the EOG and EEG of each patient, respectively, under both word-rate and syllable-rate conditions. It was found that at the word-rate there was a significant positive correlation between the EOG ITPC-difference and the EEG ITPC-difference ($r = 0.317$, $P = 0.028$), suggesting agreement between the two detection measures in reflecting the learning effects of artificial words (Fig. 5A). However, for the syllable-rate (Fig. 5B), no significant correlation was observed between the EOG ITPC-difference and the EEG ITPC-difference ($r = 0.079$, $P = 0.595$).

3.4. *Correlation between learning effect and behavioural performance*

Following the correlation analysis between the patients' linguistic learning effects of EOG and their behavioural performance as reflected in various scales (Table 3), it was found that, at the word-rate, the EOG ITPC-difference showed a significant positive correlation with the "Oromotor/Verbal Function" sub-scale score of the CRS-R ($\rho = 0.370$, $P = 0.010$) (Fig. 5C). However, for the syllable-rate, no significant association was observed between the EOG ITPC-difference and this sub-scale score (Fig. 5D; $\rho = -0.136$, $P = 0.358$), nor with other behavioural scores ($|\rho| < 0.226$, $P > 0.122$).

4. Discussion

Evaluating residual learning ability and levels of consciousness in DoC patients has important implications for clinical diagnosis and management. We compared the learning patterns between different groups of DoC patients and HC by analysing behavioural and EOG data recorded during speech stream presentation before and after a language learning task. The results showed that patients in the MCS group exhibited learning patterns similar to those of HC, as both groups showed neural tracking of artificial word frequencies after linguistic learning compared to before learning. However, neural tracking of artificial word frequency in the UWS group did not demonstrate significant differences between learning stages. In addition, EOG data showed significant synchronisation with traditional EEG measures in detecting linguistic learning effects. Furthermore, EOG-detected learning effects were significantly correlated with scores on the "Oromotor/Verbal Function" subscale of the CRS-R. These results support the

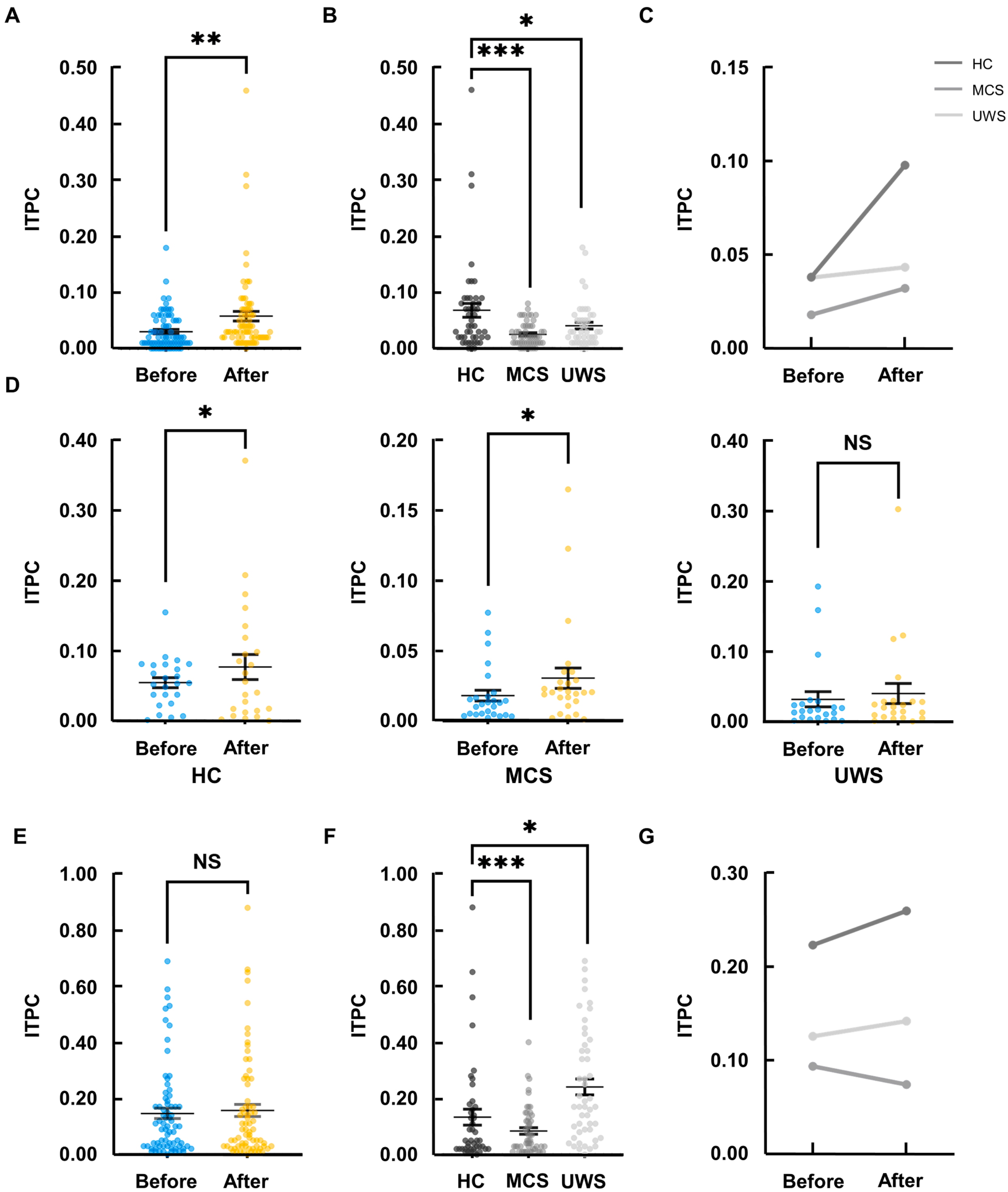

Fig. 3. Comparisons of word and syllable rate ITPC across learning stages in each group. (A) Post-hoc comparisons of word-rate ITPC between different learning stages. Mean and SEM are depicted. Significant difference was observed between learning stages. (B) Post-hoc comparisons of word-rate ITPC between groups. Mean and SEM are depicted. Significant differences were observed between groups. (C) Word-rate ITPC across learning stages and participant groups. A significant interaction indicates that ITPC developed differently between groups across stages. (D) Paired *t*-tests of ITPC values between learning stages for each participant group. (E) Post-hoc comparisons of syllable-rate ITPC between different learning stages. Mean and SEM are depicted. No significant difference was observed. (F) Post-hoc comparisons of syllable-rate ITPC between each group. Mean and SEM are depicted. Significant differences were observed between groups. (G) Syllable-rate ITPC across learning stages and participant groups. No significant interaction was observed. After = after learning; Before = before learning; HC = healthy control; ITPC = inter-trial phase coherence; MCS = minimally conscious state; NS = not significant; UWS = unresponsive wakefulness syndrome; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (Bonferroni corrected P value threshold).

Fig. 4. WLI changes in each group. The numbers in the figure represent the count of participants in each group (HC, MCS, UWS) who showed an increase or no increase in WLI values after the learning task. The background color intensity indicates the percentage of participants within each group corresponding to these counts, as shown by the adjacent color bar. HC = healthy control; MCS = minimally conscious state; UWS = unresponsive wakefulness syndrome; WLI = Word Learning Index.

ability of EOG signals to detect linguistic learning effects in our participants and suggest the potential clinical application of this approach, which combines linguistic learning and electrophysiological methods in the assessment of the level of consciousness in patients with DoC.

4.1. Assessment of linguistic learning effectiveness

Linguistic learning is a process that requires the integration of sensory, neural networks and motor systems. Through learning, our familiarity with phonology, grammar and lexical knowledge is enhanced, which improves language processing abilities (Batterink and Paller, 2017; Vanden Bosch der Nederlanden et al., 2022). In line with this, we here showed that semantic and orthographic knowledge associated with the artificial words increased their neural tracking. Moreover, previous research has found that, in healthy individuals, the acquisition of linguistic knowledge would lead to neural tracking effects in the processing of higher-level linguistic structures (Chen et al., 2020). Our results showed that before linguistic learning, no significant neural tracking at the word-rate was observed in any group. This further confirms that without learning, higher linguistic structures hidden in speech would not be identified or captured.

Our findings revealed that, after learning, the healthy control (HC) group exhibited significant learning effects, affirming the paradigm's general applicability. We also observed that although a high proportion of participants in this group showed an increase in the word/syllable ratio after learning, some did not demonstrate this effect. This could be attributed to some healthy participants experiencing fatigue or distraction during the latter part of the after learning EOG recording, leading to decreased attention to experimental stimuli. This reduction in attention could result in a weaker neural response to word frequencies and a stronger response to rhythmic syllable frequencies, ultimately affecting the manifestation of the WLI increase.

As regards DoC patients, we observed that MCS patients, like HC, exhibited significant learning effects, indicating that both groups had

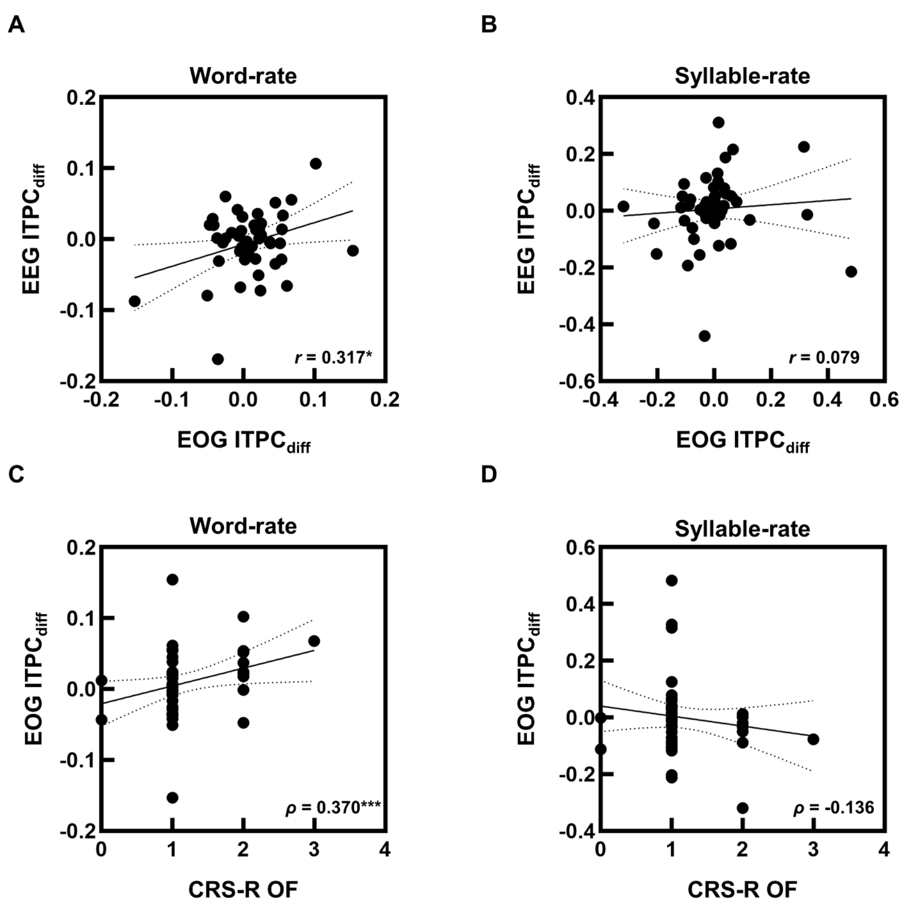

Fig. 5. Correlation analysis between EOG ITPC-difference and EEG ITPC-difference, and relationship with CRS-R scores. (A) A significant positive correlation was observed between EOG ITPC-difference and EEG ITPC-difference at word-rate in DoC patients. (B) No correlation was observed between EOG ITPC-difference and EEG ITPC-difference at syllable rate in DoC patients. (C) EOG ITPC-difference showed a significant positive correlation with the score on the "Oral motor/verbal function" subscale of the CRS-R at word-rate in DoC patients. (D) No significant association was found between EOG ITPC-difference and the score on the "Oral motor/verbal function" subscale of the CRS-R at syllable-rate in DoC patients. $ITPC_{diff}$ = the change in inter-trial phase coherence values before and after learning for each measure; $^{*}P < 0.05$, $^{***}P < 0.001$(Bonferroni corrected P value threshold).

Table 3
The correlation between behavioural scale scores and changes in ITPC values before and after learning for each linguistic feature.

Learning effects under different frequency		CRS-R Tot	CRS-R AF	CRS-R VF	CRS-R MF	CRS-R OF	CRS-R C	CRS-R AR
Word-rate ITPC-difference	ρ-value	0.080	−0.043	−0.035	0.068	0.370	0.226	−0.131
	P-value	0.590	0.772	0.815	0.647	0.010**	0.122	0.375
Syllable-rate ITPC-difference	ρ-value	−0.211	−0.109	−0.088	−0.195	−0.136	−0.142	−0.153
	P-value	0.150	0.460	0.552	0.185	0.358	0.335	0.299

CRS-R Tot = Total score of the CRS-R scale; CRS-R AF = Auditory Function subscale of the CRS-R scale; CRS-R VF = Visual Function subscale of the CRS-R scale; CRS-R MF = Motor Function subscale of the CRS-R scale; CRS-R OF = OroMotor/Verbal Function subscale of the CRS-R scale; CRS-R C = Communication subscale of the CRS-R scale; CRS-R AR = Arousal subscale of the CRS-R scale; **$P < 0.01$ (Bonferroni corrected P value threshold).

completed the extraction of linguistic structures through learning. The majority of individuals within this group also demonstrated an increase in WLI values after learning. This finding suggests that the MCS patients may still retain some degree of learning ability and consciousness, although their performance may differ from that of HC. Previous neuroimaging, electrophysiological, or behavioural studies have all demonstrated that MCS patients retain some language processing ability (Kwiatkowska et al., 2019; Rohaut et al., 2015; Aubinet et al., 2022; Nigri et al., 2017; Schiff et al., 2005; Balconi and Arangio, 2015; Boly et al., 2004). Other research suggests that even without explicit learning, MCS patients with some level of consciousness would show statistical learning of word structure similar to HC (Xu et al., 2023). To note, compared with healthy controls, such a learning effect is still weaker in MCS patients. For example, they did not show an effective tracking at the harmonic frequency as healthy controls and exhibited lower ITPC values compared to heathy controls. This may be because that their brain connectivity and integrative capacities are still impaired compared to healthy controls due to brain damage. Additionally, individual variability and fluctuations in consciousness levels among MCS patients (Giacino et al., 2014) might lead to less consistent neural responses to linguistic stimuli.

In contrast, UWS patients did not show a similar learning pattern during the learning process, with the proportion of individuals showing an increase in WLI post-learning close to the chance level (50 %). This may reflect that their severely impaired level of consciousness may affect their linguistic learning ability. Although UWS patients may retain some language processing abilities (Kotchoubey et al., 2014; Beukema et al., 2016), they still lack relatively advanced language processing abilities (Gui et al., 2020). Studies of sleep and deep anaesthesia also demonstrate the lack of advanced language processing abilities in completely unconscious subjects (Koelsch et al., 2006; Makov et al., 2017).

4.2. Neural tracking effects of syllables

Neural tracking of syllables refers to the human brain's recognition and response to rhythmic variations in auditory stimuli. The temporal envelope containing the acoustic prosody of speech would elicit regular cortical activity in the listener, resulting in neural tracking manifested as neural oscillations synchronised with the frequency of the temporal envelope (Li et al., 2019; Kerlin et al., 2010; Lalor and Foxe, 2010). Research suggests that cortical tracking of speech temporal envelopes is an automatic, non-attentive process, with synchronised neural oscillations primarily reflecting auditory encoding in response to these rhythmic acoustic features (Prinsloo and Lalor, 2022). Neural tracking of speech envelopes has been observed in studies involving native and non-native languages, as well as non-linguistic stimuli (Lalor and Foxe, 2010; Kubanek et al., 2013; Ding et al., 2016; Zou et al., 2019).

Since cortical tracking of syllable frequency is an automatic process that does not require learning, it can be inferred that even when consciousness is impaired, the human brain can still engage in neural entrainment. This is consistent with the results of our study in that, regardless of the participants' levels of consciousness, significant neural tracking corresponding to syllables frequency can be observed when exposed to speech streams composed of syllables of constant frequency. Moreover, the successful tracking of syllable frequency also manifests the validity of our experimental paradigm.

4.3. Application of EOG in the consciousness assessment

Previous studies have demonstrated the potential of EEG signals in assessing subjects' lexical learning abilities (Chen et al., 2020; Batterink, 2020; Ding et al., 2018). In this study, we found that EOG signals could successfully track the learning effects of artificial words and synchronise with EEG signals at 1.33 Hz. This finding validates the ability of EOG to synchronously track linguistic structures with the cortex (Jin et al., 2018), and further demonstrates the accuracy of our paradigm used to assess subjects' linguistic learning effects.

Our paradigm shows promise for clinical applications. On the one hand, language processing abilities are closely related to levels of consciousness. Previous research has indicated that residual language processing abilities in patients may point to their level of consciousness (Owen et al., 2005; Sokoliuk et al., 2021; Gui et al., 2020). In line with this, our language learning paradigm has demonstrated effectiveness in detecting consciousness levels, particularly in patients with higher consciousness levels (i.e., MCS patients). On the other hand, the paradigm's efficacy can be evaluated using EOG alone. The practicability and low effort required to record EOG demonstrate that this approach could be qualified for use in a hospital ward to complement standard behavioural assessments. Integrating this paradigm into daily hospital routines could enhance the accuracy of consciousness assessments and potentially improve patient care by providing additional insights into their cognitive and linguistic processing abilities.

We also found that the synchrony of EEG and EOG neural oscillations at 4 Hz (i.e., the syllable frequency) was not significant. A possible explanation for this result is that EEG and EOG, as different physiological indicators, record different cognitive components, leading to inconsistent performance at this frequency. Syllables are primarily recognised based on their rhythmicity rather than the process of lexical learning. Therefore, the discrepancy between the 1.33 Hz and 4 Hz results may indicate that the EOG result at 4 Hz reflects the patients' lexical learning ability, rather than a general similarity between EOG and EEG signals.

4.4. Correlation between linguistic learning and behavioural assessments

The assessment of Oromotor/Verbal subscale of the CRS-R subscale may to some extent reflect the language recovery of patients with DoC. Our study found a positive correlation between patients' learning of advanced linguistic structures and their scores on this subscale. This correlation may be due to the preservation of the patients' language function as measured by this behavioural scale, which may reflect the recovery of linguistic learning ability.

In addition, the Communication subscale, as one of the subscales that can reflect the subjects' speech function, is also crucial for indicating the recovery of the patients' language function. However, in this study, we found that its scores showed only a positive correlation trend with the learning effects detected by EOG. This may be because the scoring criteria of the Communication subscale require relatively high and explicit language processing abilities from the patients (Giacino et al., 2004). For patients in the stage of global functional impairment (MCS and UWS), their residual language functions were difficult to reflect in this subscale due to confounding factors such as motor/attention impairments. Therefore, we speculate that in the early stages of recovery of consciousness in DoC patients, the Oromotor/Verbal function subscale may be more sensitive in detecting the recovery of patients' language functions.

4.5. Future directions

Studies have suggested the possibility of using higher-level linguistic structures (e.g., phrases, sentences) to further assess patients' linguistic learning abilities. For example, Getz et al. (Getz et al., 2018) observed from MEG data that only subjects who understood the language content showed neural tracking of phrase structure, highlighting the importance of abstract knowledge of phrase structure for linguistic structure recognition.

Our study included both MCS+ and MCS- patients, but the small sample size of MCS+ patients precluded detailed subgroup analyses and limited the ability of this study to examine the effectiveness of this paradigm in differentiating between MCS subgroups. Future research should include a larger sample size of MCS+ patients to enable more statistically balanced and robust analyses. Incorporating higher-level linguistic structures into our learning paradigm may further discriminate subgroups of MCS patients, with MCS+ patients potentially retaining greater language processing capacity (Aubinet et al., 2022).

4.6. Conclusions

In conclusion, by dynamically monitoring explicit language learning processes using the EOG indicator, we found that MCS patients exhibited learning patterns similar to HC in linguistic learning. In contrast, UWS patients did not show this learning capability. Additionally, we validated the consistency of the EOG indicator with other traditional measures in detecting lexical learning effects. Furthermore, we found a correlation between lexical learning effects of EOG and Oromotor/Verbal function. These findings provide evidence for the use of EOG as a rapid and accurate technique for assessing residual cognition in DoC patients and provide potential biomarkers for personalised rehabilitation interventions for patients with DoC.

CRediT authorship contribution statement

Xiangyue Xiao: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Junhua Ding:** Writing – review & editing, Validation, Formal analysis. **Mingyan Yu:** Writing – review & editing, Validation, Data curation. **Zhicai Dong:** Methodology, Data curation. **Sara Cruz:** Writing – review & editing, Validation. **Nai Ding:** Methodology, Conceptualization. **Charlène Aubinet:** Writing – review & editing. **Steven Laureys:** Supervision. **Haibo Di:** Supervision, Resources. **Yan Chen:** Writing – review & editing, Validation, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors report no competing interests.

Data availability

The dataset of the current study is available from the corresponding authors Dr. Haibo Di and Dr. Yan Chen and upon reasonable request and with permission of Hangzhou Normal University. However, restrictions apply, and the data are not publicly available.

Acknowledgements

This study was supported by the National Natural Science Foundation of China [82201332], the Natural Science Foundation of Zhejiang Province [LQ22H090002], and the National Key Research and Development Program of China [2022YFC3601200]. SC was supported by national funds through the FCT – The Portuguese Foundation for Science and Technology, I.P., under the Project UIDB/04375/2020.

References

Aubinet, C., Chatelle, C., Gosseries, O., et al., 2022. Residual implicit and explicit language abilities in patients with disorders of consciousness: a systematic review. Neurosci. Biobehav. Rev. 132, 391–409. https://doi.org/10.1016/j.neubiorev.2021.12.001.

Balconi, M., Arangio, R., 2015. The relationship between coma near coma, disability ratings, and event-related potentials in patients with disorders of consciousness: a semantic association task. Appl. Psychophysiol. Biofeedb. 40, 327–337. https://doi.org/10.1007/s10484-015-9304-y.

Batterink, L., 2020. Syllables in sync form a link: neural phase-locking reflects word knowledge during language learning. J. Cogn. Neurosci. 32, 1735–1748. https://doi.org/10.1162/jocn_a_01581.

Batterink, L.J., Paller, K.A., 2017. Online neural monitoring of statistical learning. Cortex 90, 31–45. https://doi.org/10.1016/j.cortex.2017.02.004.

Bekinschtein, T.A., Shalom, D.E., Forcato, C., et al., 2009. Classical conditioning in the vegetative and minimally conscious state. Nat. Neurosci. 12, 1343–1349. https://doi.org/10.1038/nn.2391.

Beukema, S., Gonzalez-Lara, L.E., Finoia, P., et al., 2016. A hierarchy of event-related potential markers of auditory processing in disorders of consciousness. Neuroimage: Clin. 12, 359–371. https://doi.org/10.1016/j.nicl.2016.08.003.

Boly, M., Faymonville, M.-E., Peigneux, P., et al., 2004. Auditory processing in severely brain injured patients: differences between the minimally conscious state and the persistent vegetative state. Arch. Neurol. 61, 233–238. https://doi.org/10.1001/archneur.61.2.233.

Bormann, T., Seyboth, M., Machleb, F., Weiller, C., 2020. Learning of novel compound nouns – A variant of lexical learning that requires intact verbal short-term memory. Cortex 124, 23–32. https://doi.org/10.1016/j.cortex.2019.08.024.

Brainard, D.H., 1997. The Psychophysics toolbox. Spat. Vis. 10, 433–436.

Chen, Y., Jin, P., Ding, N., 2020. The influence of linguistic information on cortical tracking of words. Neuropsychologia 148, 107640. https://doi.org/10.1016/j.neuropsychologia.2020.107640.

Childs, N.L., Mercer, W.N., Childs, H.W., 1993. Accuracy of diagnosis of persistent vegetative state. Neurology 43, 1465. https://doi.org/10.1212/WNL.43.8.1465.

deJong, B., Willemsen, A., Paans, A., 1997. Regional cerebral blood flow changes related to affective speech presentation in persistent vegetative state. Clin. Neurol. Neurosurg. 99, 213–216. https://doi.org/10.1016/S0303-8467(97)00024-3.

Demertzi, A., Antonopoulos, G., Heine, L., et al., 2015. Intrinsic functional connectivity differentiates minimally conscious from unresponsive patients. Brain 138, 2619–2631. https://doi.org/10.1093/brain/awv169.

Ding, N., Melloni, L., Zhang, H., et al., 2016. Cortical tracking of hierarchical linguistic structures in connected speech. Nat. Neurosci. 19, 158–164. https://doi.org/10.1038/nn.4186.

Ding, N., Pan, X., Luo, C., et al., 2018. Attention is required for knowledge-based sequential grouping: insights from the integration of syllables into words. J. Neurosci. 38, 1178–1188. https://doi.org/10.1523/JNEUROSCI.2606-17.2017.

Edlow, B., Claassen, J., Schiff, N., Dm, G., 2021. Recovery from disorders of consciousness: mechanisms, prognosis and emerging therapies. Nat. Rev. Neurol. 17, 135–156. https://doi.org/10.1038/s41582-020-00428-x.

Getz, H., Ding, N., Newport, E.L., Poeppel, D., 2018. Cortical tracking of constituent structure in language acquisition. Cognition 181, 135–140. https://doi.org/10.1016/j.cognition.2018.08.019.

Giacino, J.T., Fins, J.J., Laureys, S., Schiff, N.D., 2014. Disorders of consciousness after acquired brain injury: the state of the science. Nat. Rev. Neurol. 10, 99–114. https://doi.org/10.1038/nrneurol.2013.279.

Giacino, J.T., Kalmar, K., Whyte, J., 2004. The JFK coma recovery scale-revised: measurement characteristics and diagnostic utility. Arch. Phys. Med. Rehabil. 85, 2020–2029. https://doi.org/10.1016/j.apmr.2004.02.033.

Giacino, J.T., Schnakers, C., Rodriguez-Moreno, D., et al., 2009. Behavioral assessment in patients with disorders of consciousness: gold standard or fool's gold? Prog. Brain Res. 177, 33–48. https://doi.org/10.1016/S0079-6123(09)17704-X.

Golkowski, D., Merz, K., Mlynarcik, C., et al., 2017. Simultaneous EEG-PET-fMRI measurements in disorders of consciousness: an exploratory study on diagnosis and prognosis. J. Neurol. 264, 1986–1995. https://doi.org/10.1007/s00415-017-8591-z.

Gui, P., Jiang, Y., Zang, D., et al., 2020. Assessing the depth of language processing in patients with disorders of consciousness. Nat. Neurosci. 23, 761–770. https://doi.org/10.1038/s41593-020-0639-1.

Jin, P., Zou, J., Zhou, T., Ding, N., 2018. Eye activity tracks task-relevant structures during speech and auditory sequence perception. Nat. Commun. 9, 5374. https://doi.org/10.1038/s41467-018-07773-y.

Kerlin, J.R., Shahin, A.J., Miller, L.M., 2010. Attentional gain control of ongoing cortical speech representations in a "cocktail party". J. Neurosci. 30, 620–628. https://doi.org/10.1523/JNEUROSCI.3631-09.2010.

Kim, E.J., Park, J.M., Kim, W.H., et al., 2012. A learning set up for detecting minimally conscious state (MCS). Ann. Rehabil. Med. 36, 428–431. https://doi.org/10.5535/arm.2012.36.3.428.

Koelsch, S., Heinke, W., Sammler, D., Olthoff, D., 2006. Auditory processing during deep propofol sedation and recovery from unconsciousness. Clin. Neurophysiol.: Offic. J. Int. Federat. Clin. Neurophysiol. 117, 1746–1759. https://doi.org/10.1016/j.clinph.2006.05.009.

Kondziella, D., Bender, A., Diserens, K., et al., 2020. European academy of neurology guideline on the diagnosis of coma and other disorders of consciousness. Eur. J. Neurol. 27, 741–756. https://doi.org/10.1111/ene.14151.

Kondziella, D., Friberg, C.K., Frokjaer, V.G., et al., 2016. Preserved consciousness in vegetative and minimal conscious states: systematic review and meta-analysis. J. Neurol. Neurosurg. Psychiatr. 87, 485–492. https://doi.org/10.1136/jnnp-2015-310958.

Kotchoubey, B., Yu, T., Mueller, F., et al., 2014. True or false? Activations of language-related areas in patients with disorders of consciousness. Curr. Pharm. Des. 20, 4239–4247.

Kroenke, K.-M., Kraft, I., Regenbrecht, F., Obrig, H., 2013. Lexical learning in mild aphasia: gesture benefit depends on patholinguistic profile and lesion pattern. Cortex 49, 2637–2649. https://doi.org/10.1016/j.cortex.2013.07.012.

Kubanek, J., Brunner, P., Gunduz, A., et al., 2013. The tracking of speech envelope in the human cortex. PLoS ONE 8, e53398. https://doi.org/10.1371/journal.pone.0053398.

Kujawa, K., Żurek, A., Gorączko, A., Zurek, G., 2022. Application of high-tech solution for memory assessment in patients with disorders of consciousness. Front. Neurol. 13, 841095 https://doi.org/10.3389/fneur.2022.841095.

Kwiatkowska, A., Lech, M., Odya, P., Czyżewski, A., 2019. Post-comatose patients with minimal consciousness tend to preserve reading comprehension skills but neglect syntax and spelling. Sci. Rep. 9, 19929. https://doi.org/10.1038/s41598-019-56443-6.

Laforge, G., Gonzalez-Lara, L.E., Owen, A.M., Stojanoski, B., 2020. Individualized assessment of residual cognition in patients with disorders of consciousness. Neuroimage: Clin. 28, 102472 https://doi.org/10.1016/j.nicl.2020.102472.

Lalor, E.C., Foxe, J.J., 2010. Neural responses to uninterrupted natural speech can be extracted with precise temporal resolution. Eur. J. Neurosci. 31, 189–193. https://doi.org/10.1111/j.1460-9568.2009.07055.x.

Lancioni, G.E., Bosco, A., Olivetti Belardinelli, M., et al., 2014. Assessing learning as a possible sign of consciousness in post-coma persons with minimal responsiveness. Front. Hum. Neurosci. 8, 25. https://doi.org/10.3389/fnhum.2014.00025.

Laureys, S., Faymonville, M.-E., Degueldre, C., et al., 2000. Auditory processing in the vegetative state. Brain 123, 1589–1601. https://doi.org/10.1093/brain/123.8.1589.

Li, X., Shao, X., Xia, J., Xu, X., 2019. The cognitive and neural oscillatory mechanisms underlying the facilitating effect of rhythm regularity on speech comprehension. J. Neuroling. 49, 155–167. https://doi.org/10.1016/j.jneuroling.2018.05.004.

Makov, S., Sharon, O., Ding, N., et al., 2017. Sleep disrupts high-level speech parsing despite significant basic auditory processing. J. Neurosci. 37, 7772–7781. https://doi.org/10.1523/JNEUROSCI.0168-17.2017.

Marino, S., Bonanno, L., Giorgio, A., 2016. Functional connectivity in disorders of consciousness: methodological aspects and clinical relevance. Brain Imaging Behav. 10, 604–608. https://doi.org/10.1007/s11682-015-9417-1.

Nigri, A., Catricalà, E., Ferraro, S., et al., 2017. The neural correlates of lexical processing in disorders of consciousness. Brain Imaging Behav. 11, 1526–1537. https://doi.org/10.1007/s11682-016-9613-7.

Owen, A.M., Coleman, M.R., Boly, M., et al., 2006. Detecting awareness in the vegetative state. Science 313, 1402. https://doi.org/10.1126/science.1130197.

Owen, A.M., Coleman, M.R., Menon, D.K., et al., 2005. Residual auditory function in persistent vegetative state: a combined PET and fMRI study. Neuropsychol. Rehabil. 15, 290–306. https://doi.org/10.1080/09602010443000579.

Peñaloza, C., Martin, N., Laine, M., Rodríguez-Fornells, A., 2022. Language learning in aphasia: a narrative review and critical analysis of the literature with implications for language therapy. Neurosci. Biobehav. Rev. 141, 104825 https://doi.org/10.1016/j.neubiorev.2022.104825.

Prinsloo, K.D., Lalor, E.C., 2022. General auditory and speech-specific contributions to cortical envelope tracking revealed using auditory chimeras. J. Neurosci. 42, 7782–7798. https://doi.org/10.1523/JNEUROSCI.2735-20.2022.

Rohaut, B., Faugeras, F., Chausson, N., et al., 2015. Probing ERP correlates of verbal semantic processing in patients with impaired consciousness. Neuropsychologia 66, 279–292. https://doi.org/10.1016/j.neuropsychologia.2014.10.014.

Schiff, N.D., Rodriguez-Moreno, D., Kamal, A., et al., 2005. fMRI reveals large-scale network activation in minimally conscious patients. Neurology 64, 514–523. https://doi.org/10.1212/01.WNL.0000150883.10285.44.

Schnakers, C., 2012. Clinical assessment of patients with disorders of consciousness. Arch. Ital. Biol. 150, 36–43. https://doi.org/10.4449/aib.v150i2.1371.

Snider, S.B., Edlow, B.L., 2020. MRI in disorders of consciousness. Curr. Opin. Neurol. 33, 676–683. https://doi.org/10.1097/WCO.0000000000000873.

Sokoliuk, R., Degano, G., Banellis, L., et al., 2021. Covert speech comprehension predicts recovery from acute unresponsive states. Ann. Neurol. 89, 646–656. https://doi.org/10.1002/ana.25995.

Stender, J., Gosseries, O., Bruno, M.-A., et al., 2014. Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study. Lancet 384, 514–522. https://doi.org/10.1016/S0140-6736(14)60042-8.

Tuomiranta, L., Grönroos, A.-M., Martin, N., Laine, M., 2014. Vocabulary acquisition in aphasia: modality can matter. J. Neuroling. 32, 42–58. https://doi.org/10.1016/j.jneuroling.2014.08.006.

Vanden Bosch der Nederlanden, C.M., Joanisse, M.F., Grahn, J.A., et al., 2022. Familiarity modulates neural tracking of sung and spoken utterances. Neuroimage 252, 119049. https://doi.org/10.1016/j.neuroimage.2022.119049.

Vogel, D., Markl, A., Yu, T., et al., 2013. Can mental imagery functional magnetic resonance imaging predict recovery in patients with disorders of consciousness? Arch. Phys. Med. Rehabil. 94, 1891–1898. https://doi.org/10.1016/j.apmr.2012.11.053.

Wannez, S., Heine, L., Thonnard, M., et al., 2017. The repetition of behavioral assessments in diagnosis of disorders of consciousness. Ann. Neurol. 81, 883–889. https://doi.org/10.1002/ana.24962.

Xu, C., Li, H., Gao, J., et al., 2023. Statistical learning in patients in the minimally conscious state. Cereb. Cortex 33, 2507–2516. https://doi.org/10.1093/cercor/bhac222.

Zou, J., Feng, J., Xu, T., et al., 2019. Auditory and language contributions to neural encoding of speech features in noisy environments. Neuroimage 192, 66–75. https://doi.org/10.1016/j.neuroimage.2019.02.047.