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Advancing EEG-based assessment of consciousness and cognition in prolonged disorders of consciousness

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Title: Advancing EEG-Based Assessment of Consciousness and Cognition in Prolonged Disorders of Consciousness

Authors: Naomi du Bois¹, Attila Korik¹, Stephanie Hodge², Leah Hudson², Ainjila S. Elahi², Alain Bigirimana³, Natalie Dayan², Jose M. Sanchez-Bornot², Alison McCann⁴, Kudret Yelden⁵, Lloyd Bradley⁶, Krishnan P. S. Nair⁷, Simon Judge⁸, Damon Hoad⁹, Emma Vines⁹, Venu Harilal¹⁰, Sheryl Parke¹⁰, Paul Johnson¹¹, Jacqueline Pogue¹², Emma Dodds¹³, Abayomi Salawu¹⁴, Raymond Carson⁴, Karl McCreadie², Jacqueline Stow⁴, Jacinta McElligott⁴, Aine Carroll^{4,15}, and Damien Coyle^{1,2*}

Affiliations

¹ Bath Institute for the Augmented Human (IAH), University of Bath, Bath, BA2 7AY, UK

² Intelligent Systems Research Centre, Ulster University, BT48 7JL, UK

³ Queens University Belfast, Belfast, BT7 1NN, UK

⁴ National Rehabilitation Hospital, Dublin, A96 RPN4, IRE

⁵ Kings College Hospital, London, SE5 9RS, UK

⁶ Royal Hospital for Neuro-disability, Putney, London, SW15 3SW, UK

⁷ Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, S10 2JF, UK

⁸ Barnsley Hospital NHS Foundation Trust, Barnsley, S75 2EP, UK

⁹ South Warwickshire University NHS Foundation Trust, Rugby, CV21 3SR, UK

¹⁰ Norfolk Community Health and Care NHS Trust, Norwich, NR2 3TU, UK

¹¹ Western Health and Social Care Trust, Derry, BT47 6SB, UK

¹² Northern Health and Social Care Trust, Antrim, BT41 2RL, UK

¹³ Oxford University Hospitals NHS Foundation Trust, Oxfordshire, OX3 9DU, UK

¹⁴ Hull University Teaching Hospitals NHS Trust, Hull, HU3 2JZ, UK

¹⁵ Health Sciences Centre, University College Dublin, Dublin 4, IRE

* Prof Damien Coyle (corresponding author)

Affiliation: Bath Institute for the Augmented Human

Address: Bath Institute for the Augmented Human (IAH), University of Bath, Claverton Down, Bath, BA2 7AY, UK

Email: dhc30@bath.ac.uk

Phone: +441225386896

Abstract

Background: Accurate assessment of residual awareness in patients with Prolonged Disorders of Consciousness (PDoC) remains a major clinical challenge, as conventional behavioural tools can underestimate covert cognition. This study evaluates whether a structured, multi-phase motor imagery Brain–Computer Interface (MI-BCI) protocol provides objective electroencephalography (EEG)-based indicators of awareness that complement behavioural assessments.

Methods: Forty-four participants ($N = 44$) completed repeated imagined-movement tasks using wearable EEG (PDoC: Unresponsive Wakefulness Syndrome (UWS, $n = 14$), Minimally Conscious State (MCS, $n = 17$), Locked-In Syndrome (LIS, $n = 11$); two able-bodied participants as benchmarks; ClinicalTrials.gov: NCT03827187; 30-01-2019). The protocol assessed sensorimotor rhythm modulation, training with and without neurofeedback, and binary question answering across phases. Standard behavioural assessments (CRS-R and WHIM) were administered at each session.

Results: Significant MI-BCI decoding accuracy (DA) is achieved by 73.8% of patients, of whom 90% progress to Q&A testing and frequently exceed the 70% usability threshold, revealing marked inter-individual heterogeneity. For significant MI-BCI runs, LIS outperform MCS ($p = 0.007$) and UWS ($p = 0.048$), while UWS exceed MCS during Q&A ($p = 0.049$), driven by familiar-voice stimuli. Using leave-one-subject-out cross-validation, combining predictions from DA and behavioural assessments improves balanced diagnostic accuracy to 62% (from 55%), increasing sensitivity to MCS (39% to 69%), with a modest reduction in LIS sensitivity (78% to 67%). Task-related activity over sensorimotor and parietal cortices differentiate diagnostic groups.

Conclusions: The structured MI-BCI protocol demonstrates potential as a movement-independent, EEG-based tool for distinguishing UWS, MCS and LIS. Integrating DA and spatial patterns yields diagnostic information that may augment behavioural assessment and advance objective tools for evaluating awareness in PDoC.

Plain language summary

Some people with severe brain injuries seem unresponsive, yet their brains may still show signs of awareness. This study tested a brain-computer system that detects these signs by recording tiny electrical signals from the scalp when a person imagines moving.

We worked with people in different states of consciousness and those with locked-in syndrome, a rare condition marked by complete paralysis, but intact consciousness – across hospitals, care homes, and private homes. The results showed that many could change their brain signals, suggesting intentional thinking, especially those with locked-in syndrome.

These findings show that this kind of brain-computer system could help doctors detect hidden awareness in people who cannot move or speak, and may eventually assist with diagnosis and basic communication.

1 Introduction

2 Disorders of Consciousness (DoC) refer to a spectrum of altered conscious states resulting from an
3 acquired brain injury. When a DoC persists beyond four weeks, it is termed a Prolonged Disorder of
4 Consciousness (PDoC) ¹. Consciousness comprises two components: wakefulness, driven by
5 subcortical arousal systems (primarily the brainstem and thalamus), and awareness, which depends
6 on a distributed frontoparietal network supporting higher-order cognitive processing and perception
7 of self and environment ²⁻⁴. Clinical presentations are on a continuum; coma (no wakefulness or
8 awareness, typically transient); Unresponsive Wakefulness Syndrome (UWS), wakefulness is present
9 but awareness is absent; and the Minimally Conscious State (MCS), wakeful with minimal or
10 fluctuating awareness ¹. In the UK alone, it is estimated that there are between 4,000 and 16,000
11 patients diagnosed with UWS, with up to three times as many living in MCS ⁵. Although not part of the
12 DoC spectrum, Locked-In Syndrome (LIS) can be misdiagnosed as a DoC using behavioural assessment
13 tools, as the condition results in near-total paralysis that can mask preserved awareness ⁶⁻⁸. People
14 with LIS retain consciousness awareness and can typically communicate via eye movements or blinking
15 – although this ability is lost in Complete Locked-In Syndrome (CLIS) due to additional oculomotor
16 impairment ^{7,8}.

17 Several diagnostic tools are available to assess consciousness, including the Coma Recovery Scale-
18 Revised (CRS-R), the Wessex Head Injury Matrix (WHIM), and the Sensory Modality Assessment and
19 Rehabilitation Technique (SMART) ⁹. However, a fundamental limitation shared by all behavioural
20 assessment tools is their reliance on the patient's ability to produce overt motor or verbal responses.
21 For patients with a PDoC, this presents a significant challenge – fluctuations in arousal, sedative side
22 effects of medication, the presence of a tracheotomy, or severe motor impairments may prevent
23 consistent behavioural output. Assessment quality is also influenced by clinician expertise and
24 experience ¹⁰. Consequently, up to 40% of MCS patients are misdiagnosed as being in UWS ^{10,11}.
25 Accurate diagnosis is critical for appropriate prognostication, to maximise quality of life and to guide
26 decisions around longer term continuation of treatment ¹⁰⁻¹³. Misdiagnosis is not limited to PDoC. A
27 survey of forty-four LIS patients in France reported an average diagnostic delay of 78.1 days, with
28 some cases exceeding 1,460 days (four years) – attributed to misinterpretation of symptoms ⁶. These
29 findings highlight the urgent need for objective diagnostic tools that do not rely on motor behaviour
30 or vocalisation alone to assess consciousness.

31 Alternative approaches to behavioural assessment have emerged following advances with
32 neuroimaging techniques. A landmark study by Owen et al. (2006) demonstrated covert awareness in
33 a patient with an apparent UWS by measuring neural responses to motor imagery tasks using
34 functional magnetic resonance imaging (fMRI) ¹⁴. Monti et al. (2010) extended this fMRI-based
35 protocol to achieve yes/no communication ^{14,15}. However, fMRI is costly and not always accessible,
36 prompting the development of alternative methods such as electroencephalography (EEG). Cruse et
37 al. (2011) ¹⁶ demonstrated that EEG, a non-invasive, bedside-compatible method, could detect covert
38 awareness in DoC. Sensorimotor rhythms (SMRs), typically in the 8–12 Hz (μ) and 18–26 Hz (β) ranges,
39 are modulated during both movement and kinaesthetic motor imagery (MI) ¹⁷. Cruse et al. (2011)
40 demonstrated intentional SMR modulation in three UWS patients, indicating misdiagnosis or state
41 transition ¹⁶. Coyle et al. (2015) ¹⁸ moved beyond one-off detection to closed-loop training for MCS
42 patients, using a motor imagery brain-computer interface (MI-BCI), marking a shift toward BCI as a
43 trainable skill. Participants received both auditory and visual real-time feedback across multiple
44 sessions, with auditory feedback (particularly music) shown to improve motor imagery Decoding
45 Accuracy (DA). This study demonstrated the feasibility of MI-BCI training in PDoC populations –

46 catalysing a transition in EEG-based BCI research from passive testing to interactive, real-time systems
47 for PDoC populations ¹⁹.

48 Despite growing support for BCIs in supplementing the CRS-R, the current gold-standard behavioural
49 assessment tool ^{9,20,21}, the Royal College of Physicians (RCP) guidelines continues to recommend
50 behavioural assessments (favouring the CSR-R) ²². The RCP argues that there is not enough evidence
51 for neuroimaging-based methodologies to enter routine clinical practice alone ²². In contrast, the
52 American Academy of Neurology (AAN) and the European Academy of Neurology (EAN) recognise the
53 additive potential of neuroimaging and electrophysiological tools under specific conditions ^{23,24}. All
54 three organisations share concerns, however, regarding standardisation, cost-effectiveness, and real-
55 world feasibility of these technologies ²³. Therefore, ongoing research continues to address these
56 concerns by developing practical, scalable, and clinically integrated solutions.

57 Recent efforts have aimed to broaden the diagnostic capabilities of EEG-based BCIs in (P)DoC. In
58 conjunction with, and subsequent to the Coyle et al. (2015) MI-BCI study, hybrid EEG-based BCI
59 paradigms have been developed that combine visually evoked responses, i.e., the P300 event-related
60 potential (ERP) and the Steady-State Visually Evoked Potential (SSVEP) – to detect command following
61 and preserved reasoning in this population ^{25,26}. This multi-input approach has improved BCI sensitivity
62 and reliability, particularly when supported by advanced classification algorithms ^{18,27–31}. Kim et al.
63 (2022) ³² demonstrated the value of a multi-EEG marker approach to the assessment of cognitive
64 function in a brain-injured paediatric cohort. By combining the EEG correlates of motor command-
65 following and auditory evoked responses, they enabled cognitive profiling in this cohort, reinforcing
66 the diagnostic/prognostic potential for this approach in clinical populations – highlighting the
67 diagnostic potential of integrating multiple neural signals.

68 However, despite these advances, EEG-based MI-BCI systems remain blind to the integrity of the
69 neural networks supporting consciousness. Functional connectivity (FC) analysis offers a systems-level
70 view of the network dynamics that support awareness – including the Default Mode Network (DMN)
71 and the Fronto-Parietal Network (FPN). Research findings show that disruptions in these intrinsic
72 networks are consistently associated with loss of awareness ^{33–38}, while residual or reorganised
73 connectivity in key hubs such as the medial Prefrontal Cortex (mPFC), Posterior Cingulate Cortex (PCC),
74 and dorsolateral Prefrontal Cortex (dlPFC) can distinguish between DoC states ^{39,40}. Furthermore,
75 cortico-thalamic integrity, particularly within the ascending arousal system, is an established neural
76 marker for poor outcomes in acute DoC patients ^{41,42}. Combining FC with EEG-based MI-BCI could
77 move diagnostic tools beyond binary classifiers toward network-informed diagnostics.

78 Building on this foundational work (e.g., Owen *et al.*, 2006 ¹⁴; Cruse *et al.*, 2011 ¹⁶; Coyle et al., 2015
79 ¹⁸), the present study evaluates a multi-phase, longitudinal EEG-based MI-BCI protocol for patients
80 with PDoC and LIS. The study protocol incorporates command-following assessment, real-time
81 neurofeedback, and structured yes/no communication – rolled out in three phases: assessment
82 (sessions 1–2), training and feedback (sessions 3–6), and binary question-answering (sessions 7–
83 10/13). Phase I identifies participants capable of SMR modulation. Phase II provides guided MI practice
84 with auditory feedback to support learning. Phase III investigates participants' binary responses to
85 biographical, numerical, logical, and situational questions using the MI-BCI. The primary focus is to
86 determine whether cognition can be profiled by analysing the aggregate decoding performance within
87 each question category – thereby using the BCI as a scientific instrument to probe domain-specific
88 awareness. Importantly, the outcomes of this phase also provide an indication of the system's
89 potential for future development as a communication mechanism.

90 In addition to EEG-signal classification, used for group-level comparisons of DA – the study
91 incorporates further EEG analyses to probe underlying neural mechanisms of awareness. Specifically,
92 a between-group comparison of the features selected for classification is included, to provide insight
93 into differential neural activation across diagnostic categories – as well as a between-group analysis
94 of functional connectivity, targeting intrinsic networks implicated in awareness, to explore systems-
95 level differences in network integrity between PDoC and LIS participants.

96 This study represents one of the largest EEG-based MI-BCI investigations to date involving patients
97 with UWS, MCS, and LIS/CLIS ($n = 42$). Participants were tested in real-world environments, such as
98 hospitals, care homes, and private residences – enhancing the system’s ecological validity and clinical
99 relevance. Importantly, this work moves beyond one-off detection paradigms by integrating training,
100 communication, and behavioural comparison (CRS-R, WHIM) in a longitudinal framework. The primary
101 objective is to determine whether the structured BCI protocol provides an objective, scalable
102 complement to existing diagnostic frameworks for patients with PDoC. Specifically, we assess whether
103 DA from a two-class imagined-movement task differentiates diagnostic groups (UWS, MCS, and LIS)
104 and reveals consistent neural markers of intentional modulation. In line with the study’s basic-science
105 and diagnostic focus, the final phase involving a structured closed Q&A assesses the feasibility of
106 extending this framework to future applications in understanding cognition in unresponsive patients,
107 and explores whether responses may provide insights into patients’ cognitive state or needs.

108 We demonstrate that most participants achieve significantly above chance level MI-BCI decoding
109 accuracy, with LIS generally achieving higher accuracies than UWS and MCS across paradigms. Group-
110 level modelling identifies DA as a key predictor distinguishing LIS from UWS, while the inclusion of
111 traditional behavioural measures further improves classification. Despite paradigm-dependent
112 variation in DA, overall DA, motor-associative cortical activation patterns, and connectivity features
113 supplement existing behavioural indicators, suggesting that DA offers complementary diagnostic
114 information beyond traditional behavioural assessment. Exploratory analyses using domain-specific
115 question stratification (i.e., grouping yes/no items by cognitive category) revealed promising initial
116 evidence that supports further development of refined BCI-based assessment tools capable of probing
117 distinct cognitive domains and, potentially, enabling more effective communication within this
118 framework.

119 **Methods**

120 **Study sample**

121 This study was registered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT03827187; 30th January, 2019), and included 42
122 patients (aged 17–73 years; 13 females, 29 males). Patients were diagnosed as follows: 14 with
123 unresponsive wakefulness syndrome (UWS), 17 with minimally conscious state (MCS), 10 with locked-
124 in syndrome (LIS), and 1 with complete locked-in syndrome (total LIS participants, $n = 11$). Two able-
125 bodied males (aged 20 and 23) were included as benchmarks (AB, $n = 2$). Previous publications
126 involving subsets of this cohort have reported early findings^{18,43,44}, with a recent preprint reporting on
127 the findings of a separate evaluation⁴⁵. All participants were naïve to the task, with the exception of
128 one MCS participant who had previously taken part in an earlier study by Coyle *et al.* (2015)⁴⁶ that
129 investigated the ability of MCS patients to learn to modulate sensorimotor rhythms through MI-BCI
130 training.

131 Ethical approval was granted by the NHS Health Research Authority (Integrated Research Application
132 System (IRAS) UK and Scotland, Project IDs: 136640 and 247815; Research Ethics Committee (REC)

133 reference: 18/WA/0186; approved 07/10/2020). Ethical approval to conduct this research study in the
 134 Republic of Ireland, was granted by the National Rehabilitation University Hospital (NRH) REC.
 135 Informed consent was obtained from participants or via proxy consent where necessary. The approved
 136 protocol involved experimental procedures that did not include any therapeutic or clinical
 137 intervention; accordingly, the research was conducted as a non-interventional basic science study. All
 138 procedures complied with the Declaration of Helsinki.

139 Clinical consultants screened patients for eligibility and collected consent. For participants lacking
 140 capacity, consent was provided by a consultee, such as the participant's next of kin or legally
 141 authorised carer. Inclusion criteria were a diagnosis of prolonged disorder of consciousness (PDOC),
 142 low awareness states, or (C)LIS. Exclusion criteria included progressive neurological diseases,
 143 uncontrolled epilepsy or pain, medications impairing cognition or causing excessive fatigue, and skull
 144 deformities preventing electrode contact. Sex and gender were not variables under investigation,
 145 however, participants' sex is reported in the population description. The study population did not
 146 include socially relevant subgroupings; therefore, race and ethnicity were not reported.

147 Experimental paradigm

148 Movement imagery tasks were selected for each patient with input from family or clinicians, avoiding
 149 injured brain regions and favouring arm movements when possible. Patients imagined one movement
 150 combination throughout the study: left vs. right arm, right arm vs. feet, or left arm vs. feet. Before
 151 each session, patients were instructed to keep their eyes open, remain still, and avoid teeth grinding.
 152 With consent from a family member or caregiver, a gentle massage between runs was permitted to
 153 rouse the patient if they appeared to fall asleep.

154 **Table 1. Structure of the study phases and associated runs.**

	Run>>>	1	2	3	4
Phase I (Assessment paradigm)	Session 1	A1	F(PN)	-	-
	Session 2	A2	T	F(PN)	-
Phase II (Training and Feedback paradigms)	Sessions 3 - 4	T	T	F(PN)	F(M)
	Sessions 5 - 6	T	F(M)	F(M)	F(M)
Phase III (Q&A paradigm)	Sessions 7 - 8	T	F(M)	Q&A	Q&A
	Sessions 9 – 10	F(M)	F(M)	Q&A	Q&A
	Sessions 11-12	F(M)	Q&A	Q&A	Q&A

155 A = Assessment, F(PN) = Feedback (Pink Noise), T = Training, F(M) = Feedback (Music), Q&A = Question and
 156 Answer session. NOTE: For some participants, training, feedback and Q&A sequencing was adjusted to
 157 accommodate individual progression and responses.

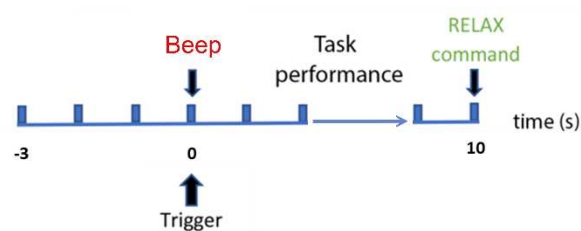
158 The study consisted of three phases (see Table 1).

159 **Phase I (Sessions 1–2):** Assessment of awareness through imagery tasks following cues, plus real-time
 160 Feedback runs. Data were analysed offline (see Offline single-run analysis for BCI calibration for
 161 details). Participants advanced to the next phase when decoding accuracy exceeded 70% or when
 162 task-related DAs were statistically greater than baseline (one-tailed paired t -test, $\alpha = 0.05$). The 70%
 163 threshold corresponds to performance well above the 99% upper bound of the binomial chance level
 164 for 90 trials, providing a conservative operational benchmark for reliable BCI control.

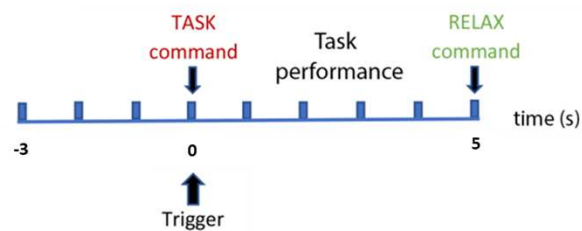
165 **Phase II (Sessions 3–6):** Additional Training and Feedback runs.

166 **Phase III (Sessions 7–10):** Training, Feedback, and Q&A runs.

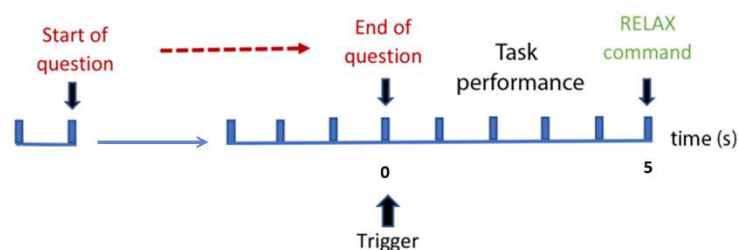
a. Assessment Trial



b. Training/Feedback Trial



c. Q&A Trial



167

168 **Figure 1. Timing of the trials.** a: Assessment. b: Training, and Feedback. c: Q&A. Note: the Q&A task began
 169 with a question. Therefore, the trigger for the start of the task performance period was sent at the end of the
 170 question. Paradigm specific trial instructions are provided in Supporting Information, Supplementary Note 1.

171 Trial timings are presented in Figure 1. Participants who advanced completed 4–13 sessions, each
 172 comprising 1-5 runs, although the number varied depending on health and scheduling. Tasks were
 173 performed without distractions or visual aids once sessions began.

174

175

176 **Experimental procedure**

177 Each daily session (1–2 hours) included 1–5 runs selected from Assessment, Training, Feedback, and
 178 Q&A paradigms. EEG setup was performed at the start of each session. The verbal instructions given
 179 (via headphones) at the start of each task, are provided in Supporting Information: Methods,
 180 Supplementary Note 1. Paradigm Specific Instructions.

181 *Assessment runs:* Patients were verbally and visually instructed to imagine specified movements (e.g.,
 182 lifting a weight with the right arm). Each run followed a block design: six blocks of 15 trials, alternating
 183 between two imagined movements (three blocks per movement). Beeps (0.5s) cued imagery every 8s,
 184 with pre-recorded instructions at block start. Each Assessment run lasted ~17 minutes, including rest
 185 periods. The protocol was adapted from Cruse et al. 2011¹⁶.

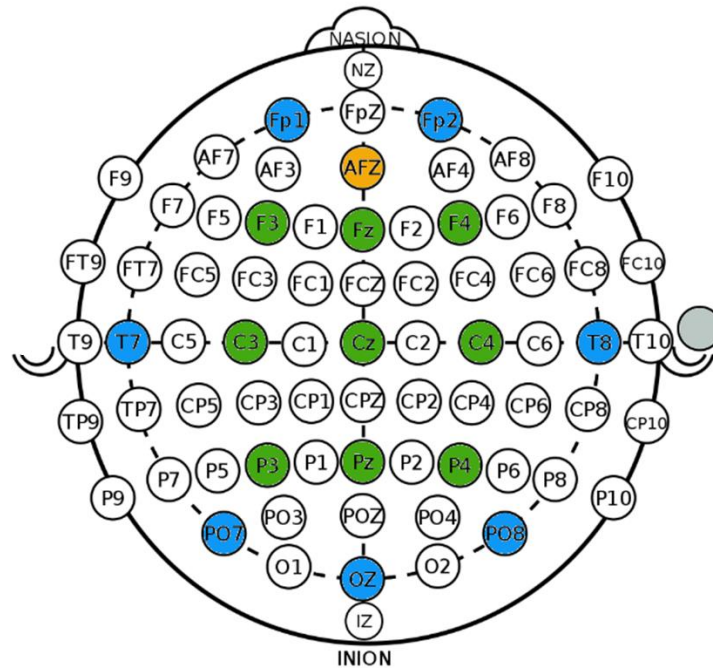
186 *Training runs:* Conducted at the start of each Phase II/III session, Training runs compressed the
 187 Assessment format: 60 randomly ordered trials (30 per movement class) without block structure.
 188 Commands ("Left"/"Right") were given via pre-recorded voice, followed by a 5s imagery period and 3s
 189 relax cue. Each Training run lasted ~8 minutes.

190 *Feedback runs:* Similar to Training runs, but included real-time auditory feedback. Sound (broadband
 191 noise or music) shifted azimuthally between $\pm 90^\circ$ based on correct decoding of imagined movements.
 192 Misclassification led to erratic or misdirected auditory feedback. Runs lasted ~8 minutes

193 *Q&A runs:* Each Q&A run (8–11 minutes) presented 48 yes/no questions from two combined
 194 categories (basic logic, numbers/letters, situational, biographical) using familiar caregiver-recorded
 195 audio to produce self-relevant stimuli which were expected to maximise engagement^{47,48}. Patients
 196 responded by imagining movements associated with "yes" or "no." Task periods lasted 5s, followed
 197 by relax cues. Categories rotated to balance linguistic and numerical content. Questions were adapted
 198 from the Montreal Cognitive Assessment (MOCA)⁴⁹ and in accordance with the National Clinical
 199 Guidelines for PDoC⁵⁰. A full list of the questions for each category is provided in Supporting
 200 Information: Methods, Supplementary Note 2. Questions were personalised by inserting the, correct
 201 (for a "yes" response) or incorrect (for a "no" response), question completion information where there
 202 are blanks in the text. For example, the biographical question set contains the question "Is your name
 203 _____?". This question is asked twice in one biographical questions run – once with the
 204 participant's correct name as a "yes" response question, and once with the participant's incorrect
 205 name as a "no" response. Questions were presented in random order.

206 *Clinical Measures:* Routine CRS-R and WHIM assessments^{51–53}, were conducted daily to compare
 207 behavioural scores with EEG-based BCI performance (i.e., DA). Sessions alternated between morning
 208 and afternoon to account for diurnal variation in patient alertness⁵⁴.

209 *Data Acquisition:* EEG was recorded from 16 channels (Figure 2) with active electrodes using a
 210 g.Nautilus Wireless Research EEG headset⁵⁵. The reference electrode was fixed on the right earlobe
 211 and the ground electrode was positioned over the AFz electrode location according to the
 212 international 10/20 EEG standard. The EEG was filtered (Butterworth, 0.5-100Hz, eighth order), and
 213 sampled (sampling rate: 250Hz, down-sampled to 125Hz).



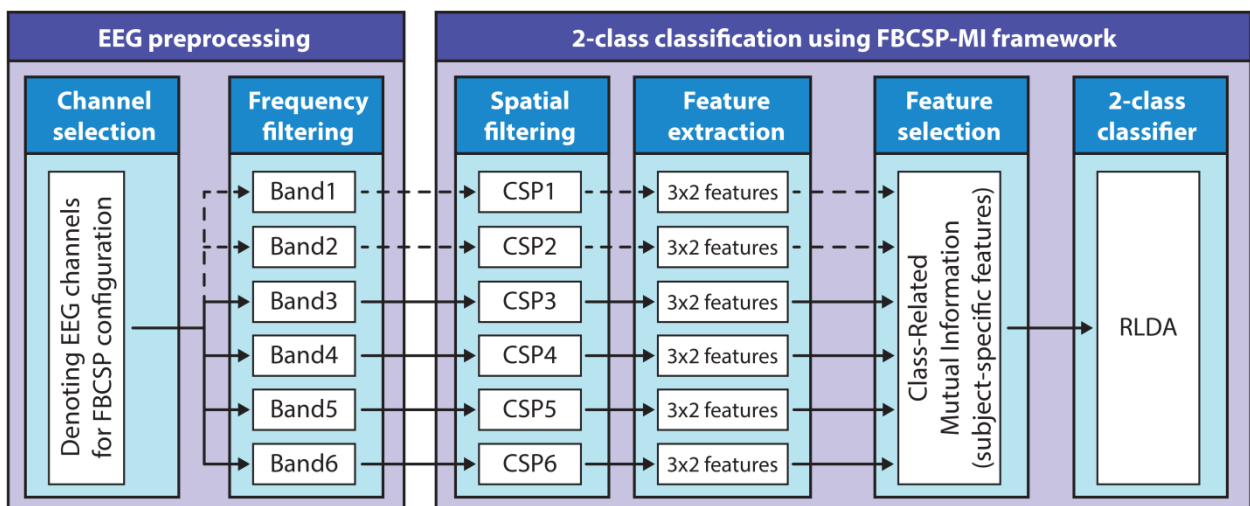
214

215 **Figure 2. EEG montage.** The positions of EEG (blue and green) and ground (orange) electrodes are presented in
 216 this figure. Nine EEG channels covering motor and imagined movement-related cortical areas are indicated in
 217 green. The reference clip was attached to the right ear (as indicated by the circle in grey).

218 A user datagram protocol (UDP) managed communication between a MATLAB Simulink⁵⁶ module
 219 (that was used for EEG data acquisition and online signal processing), and the experimental protocol
 220 controller application presented in the Unity 3D Game Engine⁵⁷.

221 Offline signal processing

222 Offline analysis and BCI calibration were performed using a filter-bank common spatial patterns
 223 (FBCSP) and mutual information (MI)-based feature selection framework^{58,59} following a structure
 224 similar to Korik *et al.*⁶⁰. This calibrated model was used to provide auditory feedback in online runs.
 225 FBCSP is a well-established EEG classification method for distinguishing between imagined
 226 movements^{61,62}, as shown in Figure 3.



227

228 **Figure 3. Structure of the applied FBCSP-MI based 2-class classification method.** The block diagram illustrates
 229 the signal processing framework, including filter bank common spatial patterns and mutual information
 230 (FBCSP-MI) based features selection modules, and a regularized linear discriminant analysis (RLDA) 2-class
 231 classifier. The analysis performed using three different sets of frequency bands, involving four adjacent bands
 232 from the six pre-processed bands (i.e., delta, theta, mu, low-beta, high-beta, low-gamma bands). The
 233 illustrated setup represents the highest four-band option.

234 EEG signals were filtered into six standard frequency bands [0.5–4 Hz (delta), 4–8 Hz (theta), 8–12 Hz
 235 (mu), 12–18 Hz (low beta), 18–28 Hz (high beta), 28–40 Hz (low gamma)] using Simulink FIR filters⁵⁶
 236 (band-pass attenuation: 0 dB; band-stop: 60 dB). For each participant and run, FBCSP-MI calibration
 237 involved testing combinations of:

- 238 1. Two EEG channel sets [16-channel full coverage; 9-channel motor cortex-focused]
- 239 2. Three frequency band sets ([delta–low beta], [theta–high beta], [mu–low gamma], each
 240 comprising four adjacent bands from the six preprocessed bands, see Figure 3**Error!**
 241 **Reference source not found.**)
- 242 3. Classification windows of 1 s and 2 s
- 243 4. Between 4–10 of the highest ranked MI-selected features

244 Feature extraction and classification

245 *Epoching:* For each run, task-relevant EEG segments were extracted from -3s to +5s relative to the
 246 onset of the motor imagery cue. These epochs were extracted from the frequency-filtered dataset
 247 and processed separately for each EEG channel configuration.

248 *Spatial Filtering (CSP):* A common spatial patterns (CSP) method was applied to maximise
 249 discriminability between two motor imagery classes. CSP generates a set of spatial filters that
 250 maximise the variance of EEG signals from one class while minimising it for the other^{63,64}. Each filter
 251 corresponds to a row in a linear transformation matrix applied to the band-pass filtered EEG signals.
 252 For each frequency band, three CSP filter pairs (six filters total) were retained. These were selected
 253 based on their ability to produce the highest variance separation between classes.

254 *Feature Extraction:* CSP-filtered signals were transformed into feature vectors using a sliding window
 255 of either 1 s or 2 s (depending on the FBCSP-MI setup), with a 40 ms step size between windows. For
 256 each window, the feature vector was calculated as the natural logarithm of the signal variance:

$$\bar{\omega} = \log(\text{var}(E)) \quad (1)$$

257 where, $\bar{\omega}$ is the feature vector and E is the CSP-transformed EEG signal.

258 *Feature Selection (Mutual Information):* Features were ranked and selected using a "best individual
 259 feature" algorithm based on mutual information (MI)⁵⁹. The MI between each feature and the class
 260 label was computed using a fixed quantisation level of 3. For each configuration, 4 to 10 features with
 261 the highest MI values were retained for classification (evaluated across multiple configurations).

262 *Classification (RLDA):* Selected features were classified using regularised linear discriminant analysis
 263 (RLDA), implemented via the RCSP toolbox⁶⁴. RLDA constructs a linear decision boundary (hyperplane)

264 that separates the two classes. Classification output is determined by the sign of the feature vector's
265 projection onto the weight vector:

- 266 • Positive output → Class 1
- 267 • Negative output → Class 2

268 The classifier's decision confidence is proportional to the distance from the hyperplane ⁶⁵.

269 *MI-BCI Performance Evaluation:* Decoding accuracy (DA) values were computed for each setup (1 s vs.
270 2 s window, channel configuration, frequency band set, and number of features). These were
271 compared across configurations to 1. determine the optimal BCI calibration per participant and 2. to
272 maximise sensitivity at the individual level to detect evidence of intentional sensorimotor modulation
273 within a BCI framework.

274 Offline single-run analysis for BCI calibration

275 Each combination of FBCSP-MI setup parameters (channel set, frequency band set, classification
276 window length, and number of features) was evaluated independently for every participant and run.
277 Classification performance was assessed using six-fold cross-validation (CV). The configuration yielding
278 the highest peak DA in the task period was selected as optimal for that participant and run (see Feature
279 extraction and classification).

280 *Time-Varying Decoding Accuracy Calculation:* For each fold, DA was calculated at each time point,
281 generating a time-resolved accuracy curve. The baseline (reference) interval was defined from -1000
282 ms to 0 ms before the task cue. Although motor imagery tasks were cued at 0 ms and nominally
283 expected between 0 to 5000 ms, the task interval was defined from 400 ms to 7000 ms post-cue. This
284 adjusted window accounts for potential stimulus-related activity in the first 400 ms (which could
285 confound motor imagery signals), and known latency in PDoC patient responses, which may extend
286 beyond 5s post-cue ⁶⁶. A 200 ms moving average smoothing was applied to each DA time-series to
287 reduce short-term variance.

288 *Peak DA Extraction:* For both reference and task intervals, the smoothed DA curve was scanned to
289 identify the maximum DA value (smoothed peak). A final peak DA was then selected from the non-
290 smoothed DA curve as the local maximum within a ± 150 ms (300 ms total) window centred on the
291 smoothed peak. This two-step process reduced the likelihood of selecting spurious DA spikes in
292 otherwise low-accuracy regions.

293 *Statistical Comparison of Task vs. Baseline DAs:* Task and baseline DAs were compared using a one-
294 tailed paired *t*-test across CV folds, to test the hypothesis that DA during the task interval was higher
295 than baseline. A statistically significant result at $\alpha=0.05$ indicated that classifier performance during
296 motor imagery exceeded baseline variability. Runs without significant task-related increases indicated
297 non-engaged runs. Following initial group analyses that focused specifically on differences in DA,
298 subsequent analyses were conducted only on runs with significant DA. This procedure ensures that
299 significant results reflect intentional modulation rather than random variability.

300 *Evaluation Against Chance:* Although the theoretical chance level for two-class classification is 50%,
301 actual chance levels can be influenced by trial count, label distribution, and temporal correlations ⁶⁷.
302 To assess whether observed DA exceeded chance performance, a permutation test was conducted:

- 303 • 100 permutations of the trial labels (class 1 vs. class 2) were generated.

- 304 • For each permutation, the full six-fold CV procedure was repeated, producing 100 time-
 305 resolved random DA curves.
- 306 • At each time point, the empirical p -value was calculated as:

$$p = \frac{|\{D' \in \hat{D} : ac(D') \geq ac(D)\}| + 1}{n + 1} \quad (2)$$

307 where, \hat{D} is a set of n -randomised versions D' of the original data D , and $ac(D)$ is the accuracy
 308 achieved with the non-randomised data⁶⁸. The null hypothesis (that observed DA could be obtained
 309 by chance) was rejected for $\alpha = 0.05$. Time-resolved DA curves from both the original data and the
 310 permutation baseline were plotted together for visual comparison.

311 *Paradigm-Wise Performance Tracking*: Peak DA values from each experimental paradigm
 312 (Assessment, Training, Feedback, Q&A) were extracted for each participant and session. These were
 313 visualised in separate plots to monitor consistency across paradigms.

314 Frequency and topographical contribution analysis

315 To explore which frequency bands and EEG channels contributed most to class separation, the CSP
 316 filter outputs and associated mutual information (MI) weights were analysed post-calibration.

317 *Band-wise Contribution (Heatmap Basis)*: At each time point t , the contribution of frequency band b
 318 to classification was computed as the average MI weight of all features n_b within that band:

$$M_{b,t} = \frac{\sum_{n_b} M_{b,t}^{n_b}}{N_b} \quad (3)$$

319 where $M_{b,t}^{n_b}$ is the MI weight of feature n_b at time t , and N_b is the number of features from band b .

320 *Topographical Contribution per Band*: To generate spatial maps of DA-relevant EEG activity, CSP filter
 321 outputs were weighted by their MI scores:

$$F_{b,n_b,i,t} = C_{i,t}^{b,n_b} M_t^{b,n_b} \quad (4)$$

322 where $F_{b,i,t}$ is the cumulative contribution of EEG channel i within frequency band b at time t . This is
 323 computed by summing over all features n_b from band b , where each feature's contribution $F_{b,i,t}^{n_b}$ is
 324 the product of the CSP transformation value $C_{i,t}^{b,n_b}$ for channel i , and its mutual information weight
 325 M_t^{b,n_b} . Thus, Equation 1 aggregates these weighted contributions:

$$F_{b,i,t} = \sum_{n_b} F_{b,i,t}^{n_b} \quad (5)$$

326 *Multi-band Channel Contribution*: To integrate across all frequency bands, a composite score for
 327 each channel was computed as:

$$F_{i,t} = \frac{\sum_b F_{i,t}^b}{N} \quad (6)$$

328 where N is the number of bands.

329 *Task vs. Baseline Topographical Difference:* Finally, to isolate spatial patterns specifically related to
330 motor imagery (vs. baseline activity), the difference between multi-band contributions at peak task
331 and baseline times was computed:

$$F_{i,t_1-t_0} = F_{i,t_1} - F_{i,t_0} \quad (7)$$

332 where, F_{i,t_1-t_0} represents the difference in multi-band contributions for EEG channel i between the
333 task period (F_{i,t_1}) and the reference period (F_{i,t_0}).

334 The topographical maps using mutual information weighted CSP filters are calculated at the sensor
335 level using MATLAB⁶⁹ and the location of source activity are estimated and plotted using the sLORETA
336 software package⁷⁰.

337 Online BCI configuration

338 In online runs, real-time auditory feedback was generated using the optimised FBCSP-MI configuration
339 selected during offline calibration (see previous sections). For each time point t within a trial n , the
340 classifier produced a time-varying signed distance (TSD) – a scalar value representing the projection
341 of the feature vector onto the RLDA decision boundary^{71,72}. The TSD value was computed as described
342 in 8:

$$TSD_t^n = \mathbf{w}^T \bar{\omega}^n - a_0 \quad (8)$$

343 where, \mathbf{w}^T is the transposed weight vector (slope of the RLDA hyperplane), $\bar{\omega}^n$ is the feature vector
344 at time t in trial n , and a_0 is the bias term (intercept of the RLDA hyperplane).

345 *Interpretation of TSD:* The sign of the TSD determines the predicted class (e.g., left vs. right imagery),
346 and the magnitude of the TSD reflects the classifier confidence, which was mapped to the extent of
347 auditory feedback movement (e.g., how far the sound panned toward the left or right ear).

348 *Bias correction:* To reduce systematic classification bias and improve feedback stability, the TSD was
349 de-biased online by subtracting a rolling average of TSD values over the preceding 35 seconds. This
350 dynamic correction helped stabilise the feedback direction over time, particularly in cases of class
351 imbalance or drift.

352 Offline analysis of Q&A category results

353 To explore the feasibility of the SMR-BCI system as a communication tool for patients with PDoC,
354 offline analysis examined whether DA varied as a function of participant group, question category,
355 and experimental paradigm. The groups included patients diagnosed with UWS, MCS, LIS, and AB
356 controls. The four question categories consisted of biographical, numerical, logical, and situational
357 content. Experimental paradigms included assessment, training, feedback, and Q&A runs.

358 The analysis replicated the methods described in the Offline Single-Run Analysis for BCI Calibration,
359 applying the same procedures for feature extraction, classification, cross-validation, and peak DA
360 calculation. For Q&A runs specifically, trials were grouped by question category, and DA was
361 computed separately for each participant and group. These results were then compared across groups
362 and categories to identify patterns in BCI communication performance. Additionally, all Q&A trials
363 across the four categories were pooled into a general 'question category' to assess overall decoding
364 performance within each participant group. An exploratory analysis was performed to evaluate the
365 question-level accuracies. For each question category (Biographical, Situational, Basic Logic,
366 Numbers/Letters) and participant group (UWS, MCS, LIS, AB), we computed confusion matrices
367 comparing target to decoded class, using smoothed peak DA as the decision metric in the task and
368 reference periods separately. From these matrices we derived overall question-level accuracy, per-
369 class bias indices, and per-class false-negative and miss rates.

370 Statistics and Reproducibility

371 All statistical analyses were performed using R-studio (version version 4.4.2)⁷³. Two-tailed tests were
372 used unless otherwise specified, with a 95% confidence interval (CI) applied throughout. Statistical
373 results are reported using exact p -values where available; adjusted post-hoc comparisons are labelled
374 and presented using standard threshold notation. The Shapiro–Wilk test is used to assess normality,
375 and Levene's test evaluates the homogeneity of variances across groups. Prior to hypothesis testing,
376 data are screened for outliers using the interquartile range (IQR) method. Outliers are retained unless
377 they clearly influence the variance or distribution of the data, as such cases may reflect clinically
378 meaningful variability rather than artefactual noise, given the heterogeneity of PDoC populations. To
379 account for potential influence from these values, robust statistical approaches are employed.
380 Specifically, for analyses of variance Welch's ANOVA is applied to mean DA data when assumptions of
381 normality are met, as it is robust to unequal variances and sample sizes. The Kruskal–Wallis test is
382 applied to median DA data, as it is appropriate for non-normally distributed data that may include
383 meaningful extreme values. To control for Type I error across pairwise comparisons, where omnibus
384 effects are significant, Games-Howell post-hoc tests are conducted for Welch's ANOVA, and Dunn's
385 post-hoc tests with Holm correction are performed for the Kruskal-Wallis analyses. In addition,
386 planned Welch contrasts are included to test a priori hypotheses comparing (1) UWS against the
387 combined mean of MCS and LIS, and (2) MCS against LIS. In each case, sample size (including n per
388 group), means and standard deviations are reported descriptively in the Supporting Information,
389 Supplementary Table 1 (a) and (b)). These tables include the AB group as a benchmark. While not
390 included in the inferential analyses, descriptive data for the AB group are provided to illustrate the
391 performance of all diagnostic groups relative to healthy individuals. For further visualisation, the AB
392 group is included in Figure 5-Figure 6, and Figure 9. For all analyses of DA data, unless specified, only
393 DA values for significant runs were used, i.e., motor imagery (MI) -BCI runs where peak DA during the
394 task period was significantly higher than the corresponding peak baseline DA (one-tailed t -test, $\alpha =$
395 0.05; consistent with our directional hypothesis, see *Statistical Comparison of Task vs. Baseline DAs* in
396 Methods Section, Offline single-run analysis for BCI calibration). In between-group analyses and
397 correlations, each participant constitutes one independent observation. In linear mixed-effects model
398 (LMM) analyses, repeated measures of DA across paradigms are treated as within-subject replicates
399 (statistically modelled via random intercepts).

400 Bivariate associations were evaluated using Pearson's correlation. Partial correlations were computed
401 to control for group membership, which was entered as a categorical variable using dummy coding.
402 To examine DA across task paradigms within each group, a LMM was fitted with *task paradigm* as a
403 fixed effect and participant as a random intercept to account for repeated measures. Model

404 assumptions of normality, homoscedasticity, and linearity were assessed using residuals versus fitted
 405 values and Q–Q plots. Where significant effects of paradigm were identified, estimated marginal
 406 means (EMMs) were computed, and pairwise comparisons between paradigms were performed using
 407 Holm-adjusted p-values to control for Type I error. Bivariate associations were evaluated using
 408 Pearson’s correlation. Partial correlations were computed to control for group membership, which
 409 was entered as a categorical variable using dummy coding.

410 To predict diagnostic category (UWS, MCS, LIS), a multinomial logistic regression was performed using
 411 DA, CRS-R, and WHIM scores as predictors, with injury type (Traumatic = 1; Non-Traumatic = 0) and
 412 time since injury (in months) included as covariates. Model performance was evaluated using leave-
 413 one-subject-out (LOSO) cross-validation, in which the model was trained on all participants except
 414 one, and then used to predict the diagnosis of the held-out participant. This procedure was repeated
 415 for each participant to provide subject-level out-of-sample predictions. Overall, accuracy, balanced
 416 accuracy, and macro-F1 scores were calculated from the aggregated LOSO predictions, with
 417 uncertainty quantified via exact and bootstrap confidence intervals. To explore whether integrating
 418 DA and behavioural measures improves diagnostic prediction, we performed a post-hoc ensemble
 419 analysis that combined three single-measure models – DA, CRS-R, and WHIM, each fitted with the
 420 same covariates as the main multinomial model. Using leave-one-subject-out (LOSO), we obtained
 421 held-out predictions and class probabilities for every participant from each model. For the ensemble,
 422 the final predicted class for each participant was determined by majority vote across the three models;
 423 in cases of a three-way tie, we applied probability-based tie-breaking by averaging per-class
 424 probabilities and choosing the maximum. Ensemble performance (accuracy, balanced accuracy,
 425 macro-F1, and class-wise recall with confidence intervals) was computed from these LOSO-derived
 426 predictions to allow direct comparison with the individual predictor measures and the combined
 427 multinomial model.

428 Topographical analysis methods

429 Topographical contributions of cortical regions were assessed using data from runs with statistically
 430 significant DA. For each task period, common spatial pattern (CSP) weights were multiplied by their
 431 corresponding mutual information (MI) scores to determine the contribution of each electrode.
 432 Following the interpretive framework proposed by Haufe et al. (2014)⁷⁴, these MI-weighted CSP values
 433 are treated as activation patterns (i.e., estimates of each sensor’s relative contribution to classification
 434 performance), rather than as direct representations of cortical source activity. To aid qualitative
 435 visualisation, these sensor-level activation patterns were optionally projected into source space using
 436 sLORETA; this step was exploratory and not intended as a quantitative inverse solution. Accordingly,
 437 scalp-level MI-weighted CSP maps remain the primary analytical result. Electrodes were grouped by
 438 cortical region: frontal (F3, Fz, F4), left-temporal (T7, C3), right-temporal (C4, T8), sensorimotor (C3,
 439 Cz, C4), parietal (P3, Pz, P4), and occipital (PO7, Oz, PO8)⁷⁵.

440 For each paradigm (assessment, training, feedback, Q&A), MI-weighted CSP values are averaged
 441 across electrodes within each cortical region and then across participants, such that each participant
 442 contributes one independent observation per region to the group-level comparisons.

443 Functional Connectivity analysis methods

444 Functional connectivity (FC) differences between diagnostic groups were evaluated during motor
 445 imagery (MI) task performance, using source-level, frequency-specific connectivity measures. The
 446 analysis aimed to identify how task-evoked network dynamics varied across diagnostic categories.

447 The networks of interest included the Default Mode Network (DMN), Fronto-Parietal Network (FPN),
 448 Auditory Network, and Thalamocortical Network, due to their respective roles in endogenous
 449 awareness^{39,76}, executive control^{39,77}, exogenous awareness and auditory processing^{33,39,78}, and
 450 thalamocortical information integration^{39,79,80}. Nodes used for each network were defined as follows
 451 – DMN: medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC); FPN: left and right
 452 dorsolateral prefrontal cortex (l-dlPFC, r-dlPFC), and left and right inferior parietal lobule (l-IPL, r-IPL);
 453 Thalamocortical: left and right thalamus (l-Thal, r-Thal); and Auditory: left and right superior temporal
 454 gyrus (l-STG, r-STG). The Montreal Neurological Institute (MNI) coordinates for the locations of the
 455 nodes are presented in Supporting Information: Additional Exploratory Results, Supplementary Table
 456 6), replicated from the Aubinet et al. (2018) study examining resting-state FC in a cohort of MCS
 457 patients³⁹.

458 Connectivity was computed within six frequency bands: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12
 459 Hz), low-beta (12–18 Hz), high-beta (18–28 Hz), and low-gamma (28–40 Hz). Data were epoched into
 460 1-second windows centred on the peak DA time point within each significant MI trial. Only runs that
 461 showed statistically significant DA were included.

462 EEG source localisation was performed using the New York head model⁸¹, which incorporates
 463 standard electrode positions and a forward model aligned to the Montreal Neurological Institute
 464 (MNI) template⁸². In this template, the forward model is constrained to a priori selected dipoles with
 465 perpendicular orientation to the cortical surface. The dipole locations are represented by the network
 466 nodes of interest listed in Supplementary Table 6. To solve the source localisation problem, eLORETA
 467 was applied, as it provides zero localisation error under ideal conditions^{83,84} and an estimated
 468 localisation error of ~1 cm for general scenarios^{85–87}. The inverse solution equations followed from
 469 the formulation described in equations Eq. 32 and Eq. 37 by Pascual-Marqui et al. (2007)⁸⁸, using a
 470 regularisation parameter $\alpha = 0.01$.

471 FC was estimated between the predefined cortical nodes using imaginary coherence (iCOH). iCOH
 472 quantifies the strength of phase coupling between two source signals, while minimising spurious
 473 effects from volume conduction and common source artifacts⁸⁹.

474 The iCOH measure between signals $x(t)$ and $y(t)$ at frequency f was computed as:

$$\text{iCOH}_{xy}(f) = \frac{\text{Im}[S_{xy}(f)]}{\sqrt{S_{xx}(f) S_{yy}(f)}} \quad (9)$$

475 where, $S_{xy}(f)$ is the cross-spectrum between x and y , $S_{xx}(f)$ and $S_{yy}(f)$ are their respective power
 476 spectrum values at f , and $\text{Im}[\cdot]$ denotes the imaginary component.

477 Group-level FC differences were assessed using Spectral Functional Connectivity Difference (SFCD)
 478 matrices, derived from the iCOH signed values computed between all the 66 paired interactions of
 479 twelve predefined cortical nodes (regions) across 6 frequency bands. Firstly, epoched regional activity
 480 was concatenated for all the participants in each diagnostic group, then the FC metric was estimated
 481 for each group and SFCD matrices were obtained from the group differences. In parallel, a non-
 482 parametric max-statistics approach was implemented using a Monte Carlo permutation test (1000
 483 replications). Here, the condition labels were shuffled prior to the calculation of a surrogate SFCD,
 484 finally resulting in a single value corresponding to the maximum absolute difference value of SFCD
 485 elements, for each replication. Under the null hypothesis of non-differences between the conditions,
 486 this non-parametric max-statistic test, provides a distribution for the evaluation of significant

487 differences between the conditions while controlling for multiple comparisons. Significant differences
488 were tested with a threshold of $\alpha = 0.01$.

489 Manuscript editing

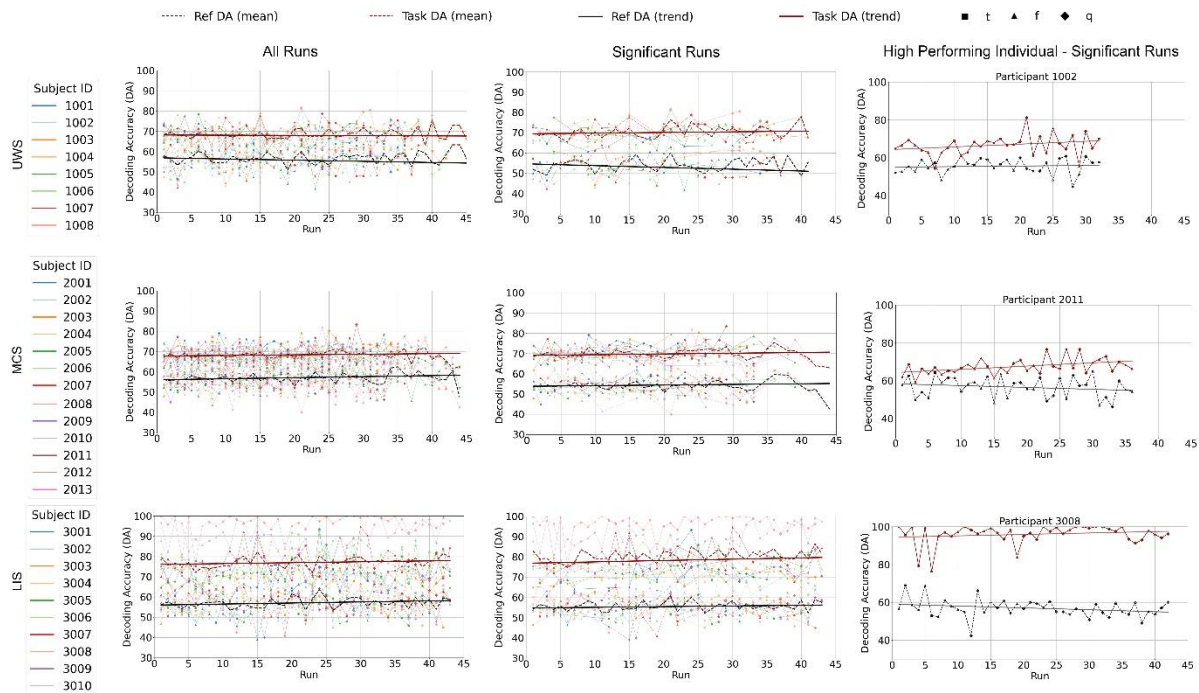
490 To improve clarity and conciseness, manuscript editing was aided by ChatGPT (OpenAI, San Francisco,
491 CA). All content was reviewed and verified by the authors for accuracy and appropriateness.

492 Results

493 Decoding accuracy examples and metrics

494 AB participants served as a benchmark representing optimal MI-BCI performance, providing a
495 reference framework for interpreting diagnostic group outcomes. Following Phase I (assessment), 8
496 of 14 UWS, 13 of 17 MCS, 10 of 11 LIS patients, and both AB participants progressed to Phase II
497 (training and feedback; $N = 33$, 73.8% of patients passed assessment). Having completed Phase II, 6
498 UWS, 12 MCS, 10 LIS, and both AB participants advanced to Phase III (Q&A; $N = 30$, 90% of patients
499 progressed to Q&A). The number of sessions completed by each patient varied between 4 and 13 –
500 however, all patients who progressed to Phase III (Q&Q) completed a minimum of 9 sessions. The two
501 AB participants completed 4 and 5 sessions, respectively – one completed 20 runs (including 4 Q&A),
502 and the other completed 15 runs (including 2 Q&A). Decoding Accuracy (DA) refers to the percentage
503 of correctly classified imagined movements – and throughout the analyses, ‘significant runs’ refer to
504 MI BCI runs where DA during the task period was significantly higher than during the corresponding
505 baseline (one-tailed t-test, $\alpha = 0.05$).

506 Examples of decoding accuracy dynamics and associated spectral contributions for individual
507 participants from each diagnostic group are provided in the Supporting Information: Methods
508 (Supplementary Figure 6). As shown there, significant task-related modulation of brain activity is
509 reflected by DA peaks exceeding baseline and permutation-derived chance levels, with corresponding
510 time-frequency maps highlighting sensorimotor rhythm contributions, typically within mu and beta
511 bands. These examples serve to illustrate the physiological basis of decoding accuracy and validate
512 the feature-selection and classification approach used in the main analyses.



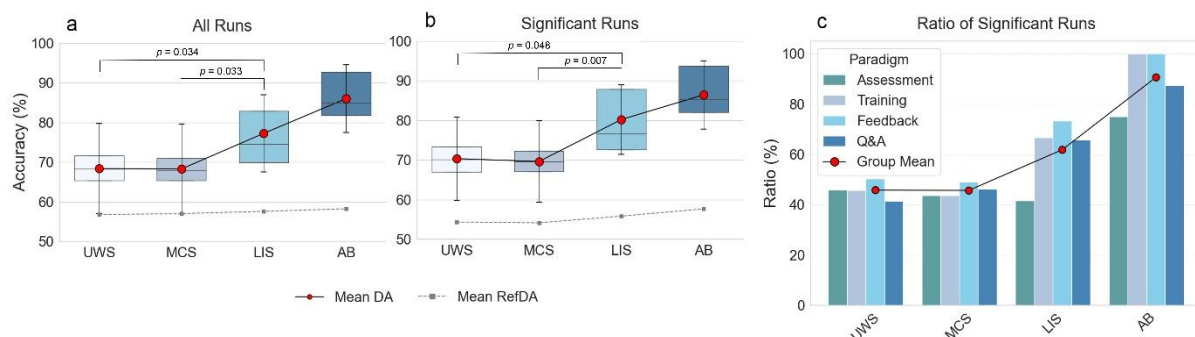
513

514 **Figure 4. Decoding accuracy (DA) across runs for all participants.** Graphs are displayed according to diagnostic
 515 category (top row – UWS; middle row – MCS; bottom row – LIS), shown separately for all runs (left-hand
 516 column) and runs reaching statistical significance (middle column); group-level trajectories for Ref DA (black)
 517 and Task DA (red), including participant traces (see subject ID for each group), mean trajectories (dashed), and
 518 participant-averaged linear trends (solid). Representative high-performing individuals, illustrating stable high
 519 performance and task-reference separation, are presented in the right-hand column.

520 Inspection of participant- and run-specific DA, visualised in Figure 4, reveal substantial variability in
 521 both initial performance and longitudinal patterns across runs and sessions. Some LIS participants
 522 demonstrated consistently high task decoding accuracy throughout the protocol, whereas others
 523 exhibited gradual improvements over time (see trendlines in Figure 4). Strong task-related DA was not
 524 uniformly accompanied by corresponding changes in reference/baseline decoding accuracy,
 525 particularly for PDoC participants, indicating that task-specific modulation and baseline performance
 526 can vary independently across these individuals. Together, these patterns illustrate overall
 527 heterogeneity in MI-BCI performance expression across participants, regardless of diagnostic
 528 category.

529 Group analysis

530 Decoding accuracy (DA) was calculated for each participant and paradigm (assessment, training,
 531 feedback, Q&A) using the procedure described in the *Offline Single-Run Analysis* section. Subsequent
 532 group comparisons were based on these calculated DA values and conducted in two ways: (1) using
 533 all runs (Figure 5a), and (2) using only runs where task-related DA significantly exceeded baseline DA
 534 (one-tailed t-test, $\alpha = 0.05$; Figure 5b).



535

536 **Figure 5. Illustration of the comparison of DA values obtained for each group (UWS, MCS, LIS, AB).** DA values
 537 obtained from (a) all runs ($n = 1233$ run/33 participants; UWS = 293/8, MCS = 472/13, LIS = 433/10, AB = 35/2)
 538 and (b) runs showing a significant task-related peak (one-tailed t -test comparing task vs. reference interval, α
 539 = 0.05; $n = 681$ run/31 participants; UWS = 138/8, MCS = 211/13, LIS = 299/10, AB = 33/2). Boxplots display
 540 the data distribution for each group, showing the interquartile range (25th–75th percentile) with the median
 541 as a horizontal line. Individual data points represent DA values from multiple runs per participant, illustrating
 542 within-group variability. Red circles mark group mean DA, with vertical error bars showing ± 1 SD. Black circles
 543 and solid lines connect mean task-related DA across groups, while grey squares and dashed lines indicate
 544 mean DA during the reference interval. Panel (c) illustrates the proportion of significant runs per paradigm
 545 (assessment, training, feedback, and Q&A), by group. Bars represent the mean percentage of significant runs
 546 for each group and paradigm. Individual data points represent proportions from each participant's runs,
 547 illustrating within-group variability. Red points and connecting lines indicate group-level averages across
 548 paradigms. Exact P values for diagnostic group comparisons are displayed in the figure.

549 A Kruskal-Wallis test on data from all runs revealed a significant group effect ($H_{(2)} = 12.047$, $p = 0.0012$,
 550 $\epsilon^2 = 0.36$). Dunn post hoc comparisons with Holm correction showed the LIS group achieved
 551 significantly higher DA than both MCS ($p = 0.033$) and UWS ($p = 0.034$) groups, with no significant
 552 difference between MCS and UWS. Restricting the analysis to significant runs (Figure 5b) confirmed
 553 group differences (Kruskal-Wallis: ($H_{(2)} = 10.026$, $p = 0.007$, $\epsilon^2 = 0.29$). Dunn post hoc tests with Holm
 554 correction again showed higher DA in the LIS group compared to MCS ($p = 0.007$), and UWS ($p = 0.048$).
 555 Figure 5c shows the proportion of significant runs per paradigm and group. A Kruskal-Wallis test was
 556 used to evaluate diagnostic group variance in the proportion of significant runs across paradigms and
 557 did not find significant group differences ($H_{(2)} = 4.65$, $p = 0.098$, $\epsilon^2 = 0.12$).

558 Descriptive statistics for both tests indicated that the AB group's mean and median were higher than
 559 those of the diagnostic groups, providing a benchmark for interpreting patients' MI results (Supporting
 560 Information, Supplementary Table 1(a)).

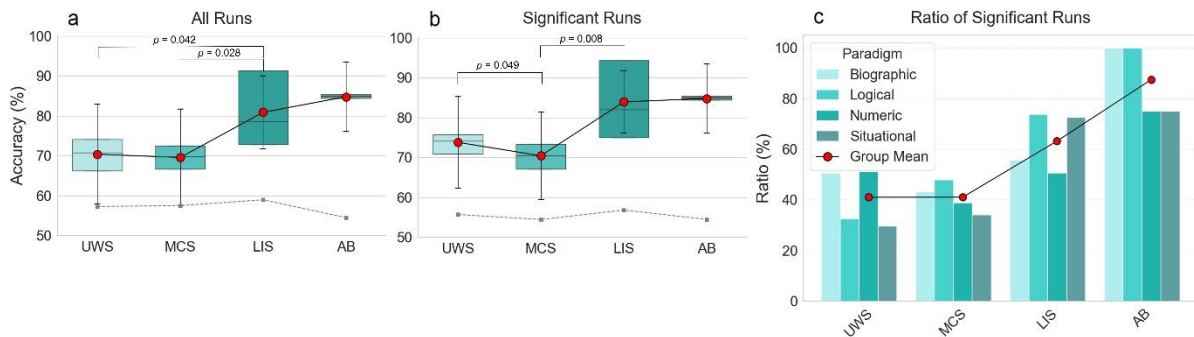
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562 Q&A question category analysis, across diagnostic groups

563 In the Q&A phase, the MI-BCI was used primarily as a cognitive assessment tool to examine whether
 564 participants with PDoC could intentionally modulate neural activity in response to different categories
 565 of questions (biographical, logical, numerical, and situational). While the diagnostic potential of the
 566 framework is the focus of the earlier phases, this phase was designed to probe domain-specific
 567 awareness and intentional modulation, with the results also providing initial indications of future
 568 potential as a communication aid for patients with PDoC and CLIS.

569 Welch ANOVAs revealed significant group differences (all runs; $F_{(2, 13.69)} = 4.64$, $p = 0.029$, $\omega^2_{adj} = 0.3$,
 570 significant runs; ($F_{(2, 13.52)} = 7.94$, $p = 0.005$, $\omega^2_{adj} = 0.46$). Games-Howell post-hoc tests revealed that,
 571 with all runs included, LIS had higher DA than MCS ($p = 0.028$) and UWS ($p = 0.042$). When analyses

572 included significant runs only, DA was higher for the UWS group compared to the MCS group ($p =$
 573 0.049) and not compared with the LIS group. A significant difference was also observed between the
 574 LIS and MCS groups ($p = 0.008$).



575

576 **Figure 6. Comparison of decoding accuracy (DA) values obtained for Q&A categories, across groups (UWS,**
 577 **MCS, LIS, AB).** DA values obtained from (a) all runs ($n = 297$ run/30 participants; UWS = 57/6, MCS = 112/12,
 578 LIS = 124/10, AB = 4/2) and (b) runs showing a significant task-related peak (one-tailed t -test comparing task
 579 vs. reference interval, $\alpha = 0.05$; $n = 169$ run/29 participants; UWS = 26/5, MCS = 51/12, LIS = 88/10, AB = 4/2).
 580 Boxplots display the data distribution for each group, showing the interquartile range (25th–75th percentile)
 581 with the median as a horizontal line. Individual data points represent DA values from multiple runs per
 582 participant, illustrating within-group variability. Red circles mark group mean DA, with vertical error bars
 583 showing ± 1 SD. Black circles and solid lines connect mean Q&A task-related DA across groups, while grey
 584 squares and dashed lines indicate mean DA during the reference interval. Panel (c) illustrates the proportion of
 585 significant runs per Q&A category (Biographical, Basic Logic (Logic), Numbers and Letters (Numeric), and
 586 Situational), by group. Bars represent the mean percentage of significant runs for each group and question
 587 category. Individual data points represent proportions from each participant's runs, illustrating within-group
 588 variability. Red points and connecting lines indicate group-level averages across paradigms. Exact P values for
 589 diagnostic group comparisons are displayed in the figure.

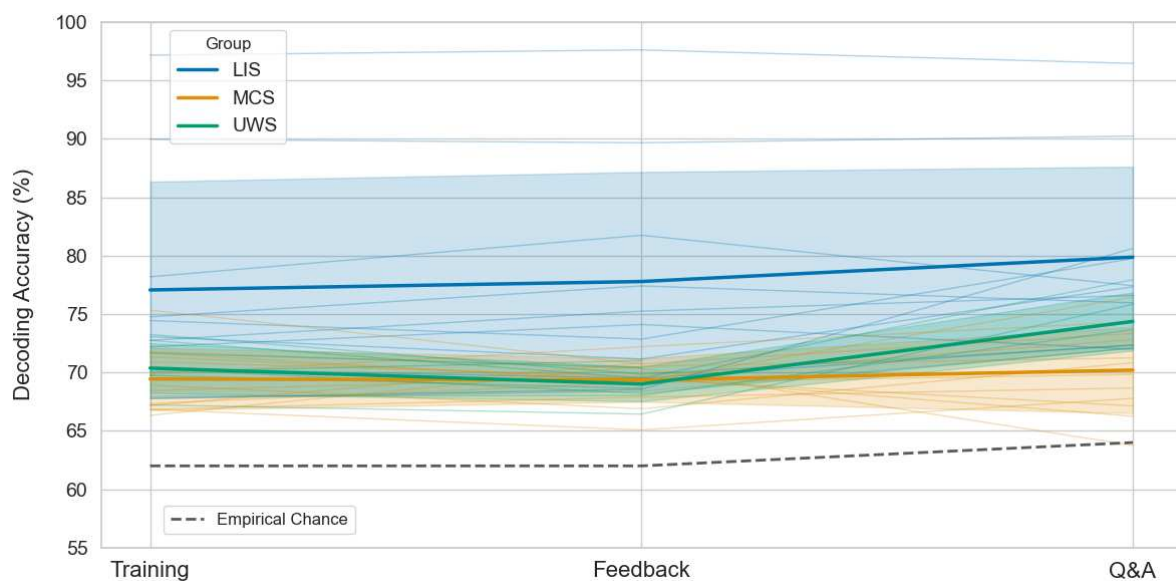
590 The proportion of significant runs by question category is illustrated in (Figure 6c). Again a Kruskal-
 591 Wallis test evaluating diagnostic group variance in the proportion of significant runs across question
 592 categories and did not find significant group differences ($H_{(2)} = 4.98$, $p = 0.083$, $\epsilon^2 = 0.12$). Descriptive
 593 statistics for Q&A session performance, based on both all runs and significant runs only, show higher
 594 mean and median values for the AB group, again providing a normative reference for evaluating
 595 patient performance (Supporting Information, Supplementary Table 1(b)). Exploratory analyses of
 596 question-level accuracies computed using confusion matrices, across cognitive categories are
 597 provided in Supporting Information: Additional Exploratory Results. Supplementary Tables 4 (a and b)
 598 summarise the accuracy of decode responses, with interpretive guidance provided in Supplementary
 599 Note 3. Supplementary Table 5, together with Supplementary Note 4 and 5, summarises question-
 600 level accuracy rankings by group. UWS and MCS participants achieved mean accuracies of 76-78%,
 601 and LIS participants exceeded 80%, whereas accuracies derived from baseline intervals were
 602 substantially lower 54-65.5%).

603 Paradigm-specific differences in MI-BCI Decoding Accuracy across diagnostic 604 groups

605 A linear mixed-effects model (LMM) was fitted with task paradigm as a fixed effect and participant as
 606 a random intercept, to test whether MI-BCI performance varied across task paradigms. The model
 607 included significant MI-BCI runs only. The assessment paradigm was excluded because it employed a

608 block design, which introduces temporal correlations that may inflate classification performance by
 609 capturing slow signal drift rather than stimulus-specific neural responses⁹⁰. As this repeated-measures
 610 analysis focuses on within-subject variation, including a structurally different paradigm would
 611 confound the comparison. Consequently, the training paradigm (no feedback) was used as the
 612 reference condition.

613 For the UWS group, adding random intercepts did not significantly improve model fit ($p = 0.13$),
 614 whereas including task paradigm as a fixed effect significantly improved fit compared to the null model
 615 ($p = 1.76 \times 10^{-6}$, see green band in Figure 7). Pairwise comparisons showed higher DA during Q&A
 616 compared to training ($p = 0.002$) and feedback ($p = 1.22 \times 10^{-6}$), with no difference between training
 617 and feedback ($p = 0.12$). The Intraclass Correlation Coefficient (ICC) indicated a low between-
 618 participant variance (ICC = 0.076).



619

620 **Figure 7. Mean DA across task paradigms (Training, Feedback, and Q&A) for significant runs only, shown**
 621 **separately for diagnostic groups (UWS, $n = 8$; MCS, $n = 13$; LIS, $n = 10$).** Thin lines represent individual
 622 participants, illustrating within-group variability. Bold lines and shaded bands denote group-level means ± 1 SD.
 623 The dashed line indicates empirical chance levels for each paradigm, computed using the “better-than-
 624 random” binomial rule⁹¹. Group colours: UWS = green, MCS = orange, LIS = blue.

625 In contrast, random intercepts significantly improved model fit for both the MCS ($p = 0.009$) and the
 626 LIS ($p = 2.76 \times 10^{-77}$) group, while paradigm had no significant effect on DA in either group ($\alpha = 0.05$).
 627 Pairwise comparisons were not significant ($\alpha = 0.05$). However, between-participant variance was low
 628 in the MCS group (ICC = 0.103), suggesting that most variability occurred within individuals across
 629 trials (as opposed to paradigms); while in the LIS group, ICC was high (0.731), indicating that inter-
 630 individual differences were the dominant source of variation in DA.

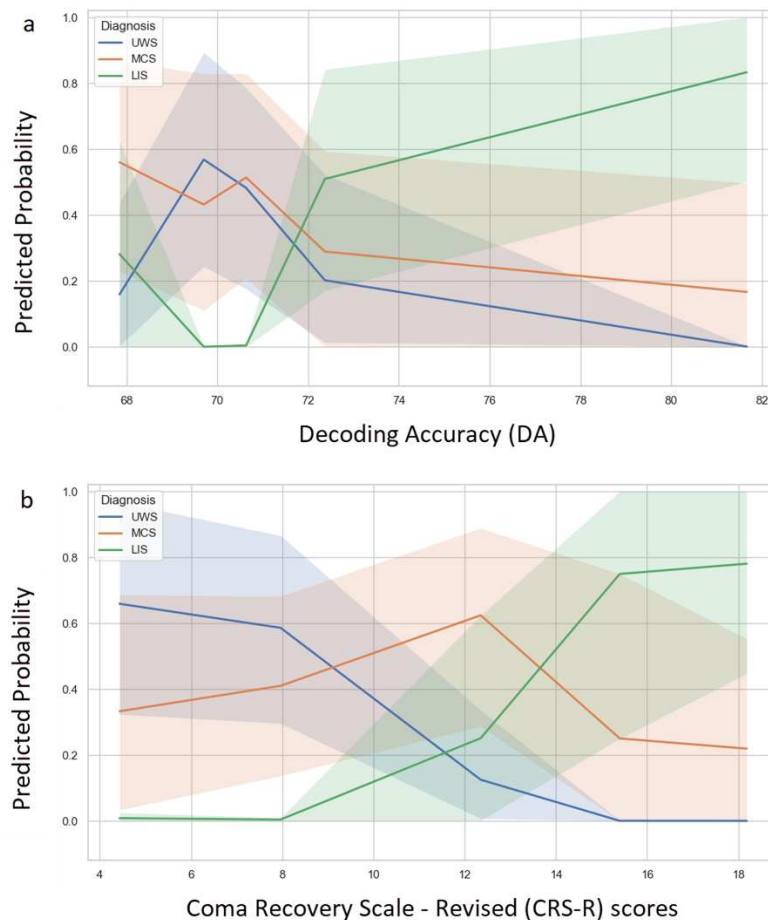
631 Between-participant variance was low for the MCS group (ICC = 0.103) but high for the LIS group (ICC
 632 = 0.731), indicating that variability in DA for LIS was driven mainly by inter-individual differences. In
 633 contrast, MCS variability arose primarily within participants across trials rather than across paradigms.

634 These results suggest that only the UWS group was sensitive to paradigm differences, whereas inter-
 635 individual variability among LIS patients accounted for the majority of variance in DA (see blue band
 636 in Figure 7).

637 Analysis of Decoding Accuracy and CRS-R and WHIM assessment scores

638 CRS-R and WHIM scores were strongly correlated (Pearson's $r(28) = 0.66$, $p = 6.94 \times 10^{-5}$, 95% CI [0.40,
639 0.82]), indicating substantial agreement between both behavioural assessment measures. Partial
640 correlations between participants peak DA and CRS-R and WHIM scores, controlling for diagnostic
641 group, revealed DA was significantly associated with WHIM (partial Pearson's $r(28) = 0.43$, $p = 0.02$),
642 but not with CRS-R ($p = 0.89$) measures. Group differences in both CRS-R and WHIM scores were
643 significant, indicating both measures significantly differentiate between the diagnostic groups. For
644 CRS-R: Welch ANOVA; $F_{(2, 17.55)} = 42.61$, $p = 1.84 \times 10^{-7}$, $\omega^2_{adj} = 0.8$ (Games-Howell comparisons; UWS
645 MCS $p = 0.002$; UWS vs LIS $p = 5.6 \times 10^{-7}$; MCS vs LIS $p = 0.012$). For WHIM: Welch ANOVA; $F_{(2, 15.55)} =$
646 11.42 , $p = 8.87 \times 10^{-4}$, $\omega^2_{adj} = 0.53$ (Games-Howell comparisons; UWS vs MCS $p = 0.012$; UWS vs LIS $p =$
647 0.004 ; MCS vs LIS $p = 0.018$). However, given the CRS-R and/or WHIM (and/or similar) measures were
648 employed to form the diagnosis, these results are not surprising. At issue is whether diagnoses formed
649 using assessment measures that require overt behavioural responses are accurate.

650 Therefore, to evaluate the predictive value of DA, CRS-R, and WHIM for diagnostic classification, we
651 fitted a multinomial logistic regression model with diagnosis (UWS, MCS, LIS) as the outcome. UWS
652 was set as the reference category. The model included DA, CRS-R, and WHIM as predictors, with injury
653 type (TBI vs. non-TBI) and time since injury (IOT) included as covariates. To provide subject-level
654 external validation, predictive performance was estimated using leave-one-subject-out (LOSO) cross-
655 validation. This approach ensured that each participant's diagnosis was predicted from a model
656 trained on all other participants, avoiding within-sample bias. A balanced accuracy of 55.4% (CI: 38-
657 73%) was observed, indicating moderate classification performance across groups – correctly
658 identifying 4/8 UWS, 5/13 MCS, and 7/9 LIS cases. The model performed best for LIS classification
659 (recall = 77.78%, CI: 45-94%), and was weaker for MCS (recall = 38.46%, CI: 18-64%). While predictive
660 metrics were modest and uncertainty wide, the LIS group shows the clearest separation from UWS
661 (see Figure 8). A complimentary full-sample association analysis found MI-BCI DA has the strongest
662 association with LIS relative to UWS, followed by CRS-R however, as association analyses are not cross-
663 validated, this finding cannot be taken as evidence of out-of-sample predictive performance.



664
 665 **Figure 8. Predicted probabilities of clinical diagnosis (UWS, MCS, LIS) derived from a multinomial logistic**
 666 **regression model as a function of (a) average decoding accuracy (DA) and (b) CRS-R score.** The model was
 667 fitted using participant-level averages within each diagnostic group. Lines show model-estimated probabilities
 668 with 95% bootstrapped confidence intervals. Colours denote diagnostic groups (UWS = blue, MCS = red, LIS =
 669 green).

670 As an exploratory post hoc analysis, we examined whether combining all three single-measure models
 671 – DA, CRS-R, and WHIM (each fitted with the same covariates as the main multinomial model) –
 672 improves classification relative to any single predictor measure. Using LOSO held-out predictions,
 673 single-modality balanced accuracies were 57.3% for DA, 49.4% for CRS-R, and 59.4% for WHIM. A
 674 three-model majority-vote ensemble with probability-based tie-breaking achieved a balanced
 675 accuracy of 61.81% ((95% CI: 43-80.4), macro-F1 = 0.633, and class-wise recalls of 50.0% (UWS), 69.2%
 676 (MCS), and 66.7% (LIS).

677 A ~5% improvement in diagnostic accuracy is achieved when integrating MI-BCI DA as a metric
 678 alongside behavioural (CRS-R, WHIM) predictor measures; most notably improving recall for the
 679 intermediate MCS group – while acknowledging the wide uncertainty around the estimates. However,
 680 the reduced predictive performance for LIS in the integrated ensemble model suggests that MI-BCI DA
 681 alone remains the most robust predictor of LIS.

682 Brain topography analysis

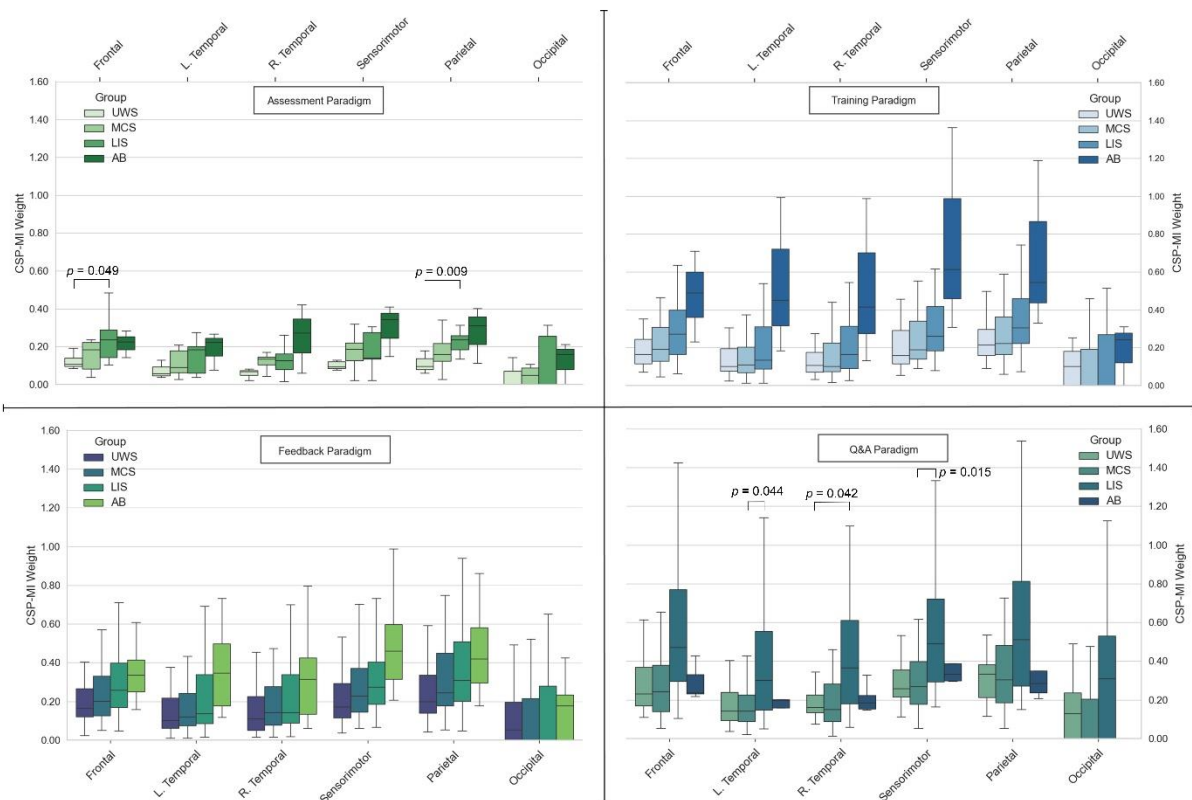
683 Topographical maps were visually inspected to identify brain regions contributing most to MI task
 684 classification. These maps represent sensor-level activation patterns derived from MI-weighted CSP

685 values, indicating relative discriminative contributions of each electrode rather direct neural source
 686 estimates ⁷⁴. sLORETA projections provide a qualitative visualisation to assess whether scalp-level
 687 contributions corresponded to expected sensorimotor regions. Task-related activity was calculated as
 688 the difference between common spatial patterns-mutual information (CSP-MI) weights during task
 689 and baseline periods, for each group. In the AB (benchmark) group, activity was consistently localised
 690 to sensorimotor and somatosensory regions across paradigms (see Supplementary Figure 1(d)). In
 691 contrast, the PDoC and LIS groups (particularly PDoC) showed more spatially diverse and less
 692 stereotyped patterns (Supplementary Figure 1(a–c)).

693

694 Group differences in regional CSP-MI activity were evaluated through an analysis of task-related CSP-
 695 MI weights across six cortical regions; frontal, left temporal, right temporal, sensorimotor, parietal,
 696 and occipital – within each paradigm (full details in Methods; significant results in Supporting
 697 Information, Supplementary Data 1 (F) and descriptive statistics in Supplementary Data 1 (G).)

698



699

700 **Figure 9. Clustered boxplots illustrating CSP–MI weights across brain regions for each diagnostic group**
 701 **(UWS, MCS, LIS, AB) and paradigm: Assessment (top left), Training (top right), Feedback (bottom left), and**
 702 **Q&A (bottom right). Each box represents the distribution of CSP-MI weights across individual runs (multiple**
 703 **runs per participant) within each group and brain region, with boxes showing the interquartile range (25th–75th**
 704 **percentile) and horizontal lines marking the median. Whiskers extend to 1.5× the interquartile range, and**
 705 **outliers are not displayed. Colours denote diagnostic groups as indicated in the legend. Exact P values for**
 706 **diagnostic group comparisons are displayed in the figure. See Supplementary Data 1 (H) for full details on the**
 707 **graphed units of observation.**

708 The results show group differences in MI-weighted CSP values emerged only in brain regions
 709 contributing to MI task classification during the Assessment and Q&A paradigms, with higher MI-
 710 weighted CSP values distinguishing LIS from PDoC groups (as illustrated in Figure 9). Notably, during

711 the Assessment paradigm the difference in MI-weighted CSP values between LIS and UWS in the
 712 parietal region was significant (Welch ANOVA and Games-Howell post-hoc, $F_{(2, 11.8)} = 7.16, p = 0.009,$
 713 $\omega^2_{adj} = 0.45, LIS > UWS, p = 0.009$) – and during the Q&A paradigm, the difference between LIS and MCS
 714 in the sensorimotor region was significant (Kruskal-Wallis and Dunn post-hoc tests with Holm
 715 correction; $H_{(2)} = 8.801, p = 0.012, \epsilon^2 = 0.28, LIS > MCS, p = 0.015$). These results suggest that LIS
 716 participants produce stronger and more discriminable motor imagery-related activation patterns
 717 compared with PDoC patients, particularly early on in the protocol, as well as in the Q&A task which
 718 requires a yes/no response to a question as opposed to simple command following.

719 Functional connectivity

720 Exploratory source-level FC analyses suggested group differences largely consistent with known
 721 thalamo-frontal and DMN–FPN disruptions in UWS compared with MCS and LIS. These patterns were
 722 most evident in the alpha band, extending into the theta band for UWS–LIS comparisons during the
 723 Q&A task (see Supplementary Figure 7). Given the low-density (16-channel) montage, these source-
 724 space results are presented as exploratory only; full details are reported in Supporting Information:
 725 Additional Exploratory Results, comprising Supplementary Tables 6 and 7, Supplementary Note 6, and
 726 Supplementary Figure 7. The main conclusions are instead supported by sensor-level and aggregate
 727 source-space summaries.

728 Discussion

729 The current study evaluated a multi-phase MI-BCI protocol across four groups: patients with
 730 Prolonged Disorders of Consciousness (PDoC) (unresponsive wakefulness syndrome (UWS, $n=14$) and
 731 minimally conscious state (MCS, $n=17$), Locked-In Syndrome (LIS, $n = 11$) and able-bodied controls (AB,
 732 $n = 2$). The AB participants were included as descriptive benchmarks of the upper bound of decoding
 733 performance under limited session exposure, rather than as part of the formal inferential tests, since
 734 they completed fewer sessions than the patients. As expected, descriptive statistics show they
 735 achieved the highest decoding accuracies (DAs); however, peak performances in some diagnostic
 736 groups occasionally approached these benchmark levels^{92,93}. All primary statistical analyses and
 737 conclusions remain focused on the diagnostic groups (UWS, MCS, LIS).

738 The three-phase protocol comprised: Phase I, assessment of initial motor imagery (MI) modulation;
 739 Phase II, MI training with neurofeedback; and Phase III, binary question–response testing using closed
 740 questions from specific categories, designed to evaluate the potential for cognitive profiling and
 741 domain-specific awareness with the MI-BCI framework. Overall, 8/11 UWS, 13/17 MCS, and 10/11 LIS
 742 patients (73.8% of recruited patients) achieved significant DA during Phase I, with 6/8 UWS, 12/13
 743 MCS and 10/10 LIS (90% of the patients who passed the Assessment phase) completing phase III –
 744 suggesting volitional modulation of brain activity was preserved in a high proportion of patients within
 745 this study cohort. An evaluation of diagnostic group differences in the proportion of significant runs,
 746 across (a) paradigms and (b) question categories, revealed no significant effects, suggesting
 747 comparable (a) motor imagery capacity and (b) potential ability to communicate yes-no answers,
 748 across diagnostic groups (see Figure 5(c) and Figure 6(c)). The latter interpretation remains theoretical
 749 and requires further empirical testing to assess whether patients can reliably use motor imagery to
 750 communicate yes-no responses on a single trial basis however the results demonstrate the average
 751 overall response to repetitions of questions may enable, albeit slow, communication.

752 As illustrated in Figure 4, group averages can obscure inter-individual variability – masking individuals
 753 whose MI-BCI performance is substantially better than is suggested by their diagnostic group mean.
 754 The marked heterogeneity in MI-BCI performance across PDoC groups reinforces the growing

755 consensus that preserved covert awareness may be underestimated in patients with PDoC, when
756 assessment relies on tools that require overt behavioural responses^{96–98}. Furthermore, the presence
757 of exceptionally high-performing LIS participants highlights the potential for some individuals with LIS
758 to approach maximal DA, in a short time-frame. Such cases motivate the development of responder-
759 focused, individually tailored MI-BCI protocols.

760 In binary motor imagery BCIs, classification accuracies of approximately 70% are commonly adopted
761 as a criterion for reliable control, reflecting statistically significant performance above chance and
762 practical usability, while higher accuracies (≥ 75 –80%) are typically required for sustained online or
763 clinical applications^{67,94,95}. Here, we report within-run cross-validation accuracies, as the primary
764 focus is group-level comparative analysis. Nevertheless, the individual results shown in Figure 4 are
765 indicative of performance that exceeds the commonly adopted criterion level for BCI utilisation. It
766 should be noted, however, that inter-run and inter-session variability, which is more pronounced in
767 these participant groups due to factors such as fluctuating awareness, fatigue, and engagement,
768 makes it more difficult to assume reliable cross-run DA.

769 The multi-stage protocol adopted in this study, incorporating real-time continuous feedback, is
770 intended as a stepping stone toward training participants to produce reliable single-trial responses.
771 The gradual performance improvements observed in a subset of participants (Figure 4) suggest that
772 feedback-driven learning and sustained engagement can enhance MI control. These findings indicate
773 that performance may further improve with extended exposure, real-time adaptive feedback, and
774 motivational engagement paradigms.

775 When statistical analyses of group variance in DA only included significant runs, the difference in
776 overall DA between the LIS and UWS groups was significant ($p = 0.048$), whereas their DA during the
777 Q&A sessions did not differ ($p = 0.13$). In contrast, the difference in DA between the LIS and MCS
778 groups remained consistently significant. While there was no overall DA difference between the MCS
779 and UWS groups ($p = 0.87$), a significant difference emerged between these PDoC groups during the
780 Q&A sessions ($p = 0.049$). This pattern suggests that, when analyses were performed using only
781 significant runs, UWS participants performed marginally better than the MCS group during Q&A
782 sessions, thereby narrowing the apparent MI performance gap with the LIS group. Further support for
783 this finding was provided by the significant variation in Q&A MI performance compared to Training
784 and Feedback, in the UWS group (see Figure 7). Notably, the Q&A task presented pre-recorded
785 questions spoken by a familiar caregiver or relative. The suggestion is that emotionally salient auditory
786 input potentially enhanced cognitive engagement in UWS patients, consistent with prior evidence
787 showing that meaningful stimuli can activate residual cortical networks in UWS despite widespread
788 disconnection⁹⁹. That this paradigm-specific effect emerged only in UWS indicates a potential
789 moderating effect of emotionally salient stimuli on BCI engagement in lower awareness states.
790 Additionally – or alternatively – the UWS participants may collectively exhibit more awareness than
791 previously assumed, which was not evident through standard behavioural diagnostic tests but became
792 observable over time, via movement-independent responses using the MI-BCI.

793 Grouping questions into distinct cognitive categories enabled assessment of category-specific
794 decoding accuracy as a means of probing differential conscious awareness, rather than validating the
795 MI-BCI as a communication channel per se. The randomised presentation and balanced phrasing of
796 Yes/No questions minimised the likelihood of auditory or linguistic confounds in significant runs. In
797 addition, all auditory cues were temporally and procedurally separated from the MI task window,
798 identical across conditions, and too brief to account for sustained decoding differences; occasional
799 tactile re-alerting occurred only between runs. These controls make it unlikely that the observed MI-
800 specific effects were driven by auditory or arousal-related factors, although we acknowledge this as a

801 potential limitation. These preliminary findings indicate that MI-BCI responses may offer a window
802 into preserved cognitive processing in participants with PDoC. Future studies will implement
803 counterbalanced Yes/No mappings, auditory-control conditions, and formal multiplicity corrections to
804 further substantiate and refine this approach.

805 A multinomial modelling framework was used to examine the relative contributions of MI-BCI DA and
806 behavioural measures to diagnostic classification. Under leave-one-subject-out (LOSO) cross-
807 validation, overall classification accuracy was modest (Balanced Accuracy; 55.41%), with DA and CRS-
808 R contributing independently to differentiation from UWS. Whereas CRS-R scores showed lower
809 sensitivity for LIS, DA achieved higher recall for LIS cases (77.8%) and provided clearer separation of
810 LIS from UWS and MCS in predicted probabilities compared to CRS-R (see Figure 8). A post-hoc
811 ensemble combining DA, CRS-R and WHIM predictions improved balanced accuracy to 63.21% (95%
812 CI: 44–80%), with MCS predictive accuracy increasing from 38.46% in the multinomial model to
813 69.23% in the ensemble. Previous MI-BCI studies in PDoC populations have primarily used the CRS-R
814 as the comparative behavioural measure, as this measure is considered the clinical gold standard for
815 assessing responsiveness^{100–102}. However, by including the WHIM, our findings reveal that DA
816 correlates significantly with WHIM scores ($p = 0.02$) but not with CRS-R scores ($p = 0.89$). The WHIM
817 contributed the least to diagnostic classification in the multinomial logistic regression, whereas both
818 DA and CRS-R showed significant predictive power. Nonetheless, combining all three measures
819 modestly improved model performance. Given that the CRS-R aggregates behaviour into broad
820 categorical levels, while the WHIM provides a finer-grained, context-sensitive measure of
821 spontaneous and goal-directed responses, these findings suggest that WHIM may more closely reflect
822 the neural substrates underlying covert command-following detected by MI-BCI. At the same time,
823 each measure appears to capture distinct aspects of residual function, together improving diagnostic
824 sensitivity. Together, these results suggest that MI-BCI can complement existing clinical standards for
825 the assessment of patients with PDoC, improving diagnostic accuracy.

826 Regarding analyses at the sensor and source space, analysis of spatial features derived from task-
827 related activity over sensorimotor and parietal cortices further supports distinctions between
828 diagnostic groups. CSP-MI weights applied for feature selection over these motor-associative areas of
829 cortex differentiated LIS and PDoC groups, specifically distinguishing LIS from UWS during the
830 Assessment paradigm (parietal; $p = 0.009$) and LIS from MCS during the Q&A paradigm (sensorimotor;
831 $p = 0.015$). These findings implicate the sensorimotor-parietal network in the preserved capacity for
832 motor imagery and volitional modulation in LIS – and more broadly confirm the role of these networks
833 in MI-BCI control; demonstrating that BCI performance reflects physiologically meaningful activation,
834 rather than random variance. Exploratory FC analyses suggested network-level alterations in UWS
835 relative to MCS and LIS, most prominently involving thalamo-frontal and DMN–FPN interactions (see
836 Supporting Information: Additional Exploratory Results, Supplementary Tables 6 and 7,
837 Supplementary Note 6, and Supplementary Figure 7). These patterns were most evident during
838 cognitively demanding tasks such as the Q&A paradigm – and align with known mechanisms of
839 impaired awareness in DoC^{38,41,42}. Although limited by the 16-channel montage, these exploratory
840 findings support the idea that task-based FC can reveal context-specific neural disruptions relevant to
841 residual awareness, complementing the main sensor-level and behavioural results.

842 Taken together, the convergence of decoding, spatial, and preliminary functional connectivity findings
843 underscores the diagnostic potential of this multi-phase MI-BCI protocol as a clinically viable tool to
844 augment existing behavioural based protocols. However, several limitations should be acknowledged.
845 While this study represents the most comprehensive MI-BCI protocol trialled in a PDoC population to
846 date, involving fifteen NHS hospitals in the UK and the NRH in Ireland in patient recruitment – unequal

847 group sizes constrained some statistical comparisons, though the analysis of all MI-BCI runs achieved
848 91% power ¹⁰³, and large effect sizes were found for the analyses of group variance based on MI-BCI
849 DA values. Although improvements were made to BCI parameter updating and paradigm sequencing
850 compared to previous work ¹⁸, future performance may benefit from fully adaptive BCI systems
851 capable of real-time adjustment to a participant's mental state ¹⁰⁴.

852 EEG instability due to non-stationary brain states, linked to fatigue, arousal, medication, or learning –
853 remains a challenge, often resulting in covariate shift ^{105,106}. Changes were observed in the evolution
854 of frequency responses and feature importance, sometimes introducing features that degraded
855 performance. DA could likely be improved through more fine-grained, participant-specific band
856 optimisation, with adaptive classifiers ¹⁰⁷, feature adaptation ¹⁰⁸, or data space adaptation ^{109,110} also
857 representing promising strategies to mitigate these effects. The current protocol included per-session
858 recalibration; however, if a prior session's BCI setup outperformed the new calibration, the previous
859 model was reused. While this maximised neurofeedback quality, it may have compromised patient
860 learning, as classifier features could vary across sessions. Future work should develop globally
861 optimised training data selection and automation for classifier updates.

862 Furthermore, although concurrent EMG was not recorded, visual inspection did not reveal sustained
863 artefacts consistent with muscle activity. Given the severe motor impairment of participants,
864 systematic EMG contamination is unlikely. Nevertheless, the integration of EMG and eye-tracking
865 would benefit future research, to further rule out residual movement influences.

866 Additionally, while the FC analysis revealed interactions involving thalamo-frontal regions, these
867 findings are exploratory and should be interpreted cautiously given the 16-channel EEG configuration
868 and limited spatial resolution. Future work employing high-density EEG or beamformer-based inverse
869 solutions (e.g., Atlantis Source Connectivity Toolbox (ASCT)) ^{111–113}, will be required to substantiate
870 these observations. Additionally, while imaginary coherence (iCOH) is robust to volume conduction
871 and well-suited for non-parametric testing, it has interpretive limitations. iCOH detects non-zero
872 phase-lagged coupling but cannot reliably infer temporal directionality – signals with vastly different
873 delays (e.g., 10 ms vs 90 ms) can yield identical values ¹¹⁴. Although faster communication is often
874 assumed in low-frequency bands, this assumption is not always valid. Techniques like Phase Slope
875 Index or Granger Causality could offer richer insights but are themselves limited (e.g., GC's
876 vulnerability to volume conduction ¹¹⁵).

877 Although anecdotal, feedback from families suggests a possible therapeutic benefit from engaging
878 with the MI-BCI system. Some patients appeared to become aware of their influence on the system,
879 potentially stimulating cognitive activity. This aligns with the observed shift in FC profiles between
880 UWS and MCS patients during the Q&A task – becoming more similar to UWS-LIS differences,
881 suggesting possible adaptive effects that merit further investigation (Supplementary Figure 7).

882 Regarding the the support for the integration of DA and the CRS-R to improve diagnostic prediction,
883 these findings should be interpreted cautiously given the broad confidence intervals, and the potential
884 instability of parameter estimates in multinomial models with small group counts. Although LOSO
885 cross-validation mitigates within-sample bias, it remains an internal validation procedure; external
886 replication in larger, independent cohorts will be essential to confirm the robustness and
887 generalisability of these classification patterns.

888 A key limitation of the study design concerns the inclusion threshold applied during Phase I:
889 participants had to achieve a mean DA > 70% and/or a significant DA peak (one-tailed *t*-test, $\alpha = 0.05$)
890 during the task versus baseline. Given that participants were initially classified using behavioural

891 assessments – known to produce misdiagnoses, especially in UWS^{10,11} – this introduces diagnostic
892 circularity. To truly evaluate the MI-BCI’s potential, future protocols should use updated clinical
893 diagnoses, blind researchers to these diagnoses during testing, and remove assessment thresholds to
894 avoid sampling bias. A second related important limitation which warrants acknowledgement, is that
895 the paired-samples *t*-test used to assess whether DA during the task exceeded baseline DA at the fold
896 level does not assume independence of CV folds. This test was retained for descriptive consistency,
897 and comparison with alternative statistical methods indicated that our conclusions are robust to the
898 choice of inference procedure (see Supporting Information: Methods, Supplementary Table 3).

899 While the exploratory analysis of the question-level accuracy attained for the illustrative case is of
900 considerable interest in view of the potential for communication-relevant applications – the findings
901 should be interpreted cautiously, as the analysis is based on a snapshot sample of one per group,
902 and the confusion matrices were computed from offline results. Future work will be needed to test
903 the reliability and practicality of MI-BCI use for communication in larger and more systematic
904 designs.

905 Furthermore, practical constraints also introduced variability. While improving ecological validity,
906 conducting sessions across hospitals, care homes, and private homes also created inconsistencies in
907 intersession intervals and testing environments. The inherent instability of PDoC patients further
908 complicates standardisation. Ideally, recordings would occur during each patient’s considered peak
909 arousal window, but this is often impractical due to logistical constraints. While our protocol already
910 included multiple recording sessions per participant, collecting data across additional sessions could
911 further increase the likelihood of assessing each patient during their optimal state of awareness. Runs
912 identified as significant—or sessions yielding the highest number of significant runs—may indicate
913 periods of peak arousal or cognitive responsiveness, suggesting that denser longitudinal sampling
914 could enhance sensitivity to intra-individual fluctuations in conscious state.

915 In conclusion, despite some limitations, the study findings highlight the transformative potential of
916 this multi-phase motor imagery BCI protocol in reshaping diagnostic practice for patients with severe
917 motor and cognitive impairments. By uncovering covert cognitive capacities often missed by standard
918 behavioural assessments, the protocol enables a more nuanced differentiation across clinical
919 categories. Therefore, integrating DA as a metric, with CRS-R and WHIM behavioural indices, offers a
920 more comprehensive assessment framework, improving diagnostic precision and sensitivity to
921 residual awareness, particularly for LIS classifications. Furthermore, analysis of MI-weighted CSP
922 values over motor-associative cortical regions indicates that motor imagery-related activation is
923 preserved to a greater extent in LIS than in PDoC, consistent with decoding results showing that LIS
924 participants consistently achieved the highest DA – a generally significant group effect confirming
925 preserved volitional control despite total motor paralysis. In contrast, paradigm-specific neural
926 signatures proved more informative for distinguishing patients with PDoC. Notably, a significant boost
927 in DA among UWS patients during the familiar-voice Q&A paradigm suggests that emotionally salient
928 stimuli can transiently unlock hidden awareness. Although the functional connectivity (FC) analysis
929 was exploratory, distinct thalamo–frontal and DMN–FPN network alterations were revealed in UWS,
930 and to a lesser extent, in MCS, relative to LIS. These patterns are consistent with established markers
931 of impaired awareness in disorders of consciousness^{38,41,42}. Together, DA, CSP-MI features, and
932 connectivity metrics capture complementary facets of brain function, indicating that an interactive,
933 personalised BCI approach holds promise as a scalable, movement-independent diagnostic tool – that
934 may eventually support clinical decision-making and give voice to those otherwise unable to
935 communicate.

Data availability

The data that support the findings of this study are available here: <https://doi.org/10.15125/BATH-01632>¹¹⁶. This anonymised dataset includes electroencephalography (EEG) recordings, descriptive variables, and session-level Coma Recovery Scale-Revised (CRS-R) and Wessex Head Injury Matrix (WHIM) scores. All data contained within the repository are provided under controlled access. Access will be granted upon reasonable request, which should include a brief description of the proposed research use, confirmation of relevant ethical approval where applicable, and agreement to data use conditions that prohibit data redistribution or use beyond the approved scope. Requests should be directed to the corresponding author (Prof D. Coyle, dhc30@bath.ac.uk) and will be reviewed on a case-by-case basis. A response will typically be provided within two weeks of receipt of a complete request. The source data graphed in Figures 4-9 and Supplementary Figure 7 are provided in Supplementary Data 1 (worksheets Supplementary Data A-E, H and I, respectively).

Code availability

The offline signal processing code used during the current study to analyse a single participant/run is available here: <https://doi.org/10.15125/BATH-01632>¹¹⁶. The code contained in the repository provides an analysis framework developed for the EEG data files also in this repository. Therefore, this code is provided under controlled access to ensure appropriate use within the approved methodological context. Access will be granted upon reasonable request, which should include a brief description of the proposed research use, confirmation of relevant ethical approval where applicable, and agreement to data use conditions that prohibit data redistribution or use beyond the approved scope. Requests should be directed to the corresponding author (Prof D. Coyle, dhc30@bath.ac.uk) and will be reviewed on a case-by-case basis. A response will typically be provided within two weeks of receipt of a complete request. Statistical analyses were performed using R-studio (version 4.4.2)⁷³.

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Author contributions

The authors confirm their contribution to the paper as follows: D. C., K. M., A. M., K. Y., J. S., J. M., and A. C., study conception and design; A. M., K. Y., J. M., A. C., R. C., L. B., S. N., S. J., D. H., E. V., V. H., S. P., P. J., J. P., E. D., J. S., and A. S., participant recruitment; D. C., S. H., L. H., N. D., A. S. E., and N. B., data collection; D. C., A. K., A. D. B., and K. M., development of the Brain-Computer Interface software and feedback systems; J. M. S., development of the functional connectivity (FC) pipeline; D.C. and A.K., development of the motor-imagery task related EEG data analysis framework and analysis to extract decoding accuracies (DAs), plus FC analysis; D.C and N. B., statistical analysis to determine group differences. D. C., A. K., and N. B., interpretation of results; D. C., A. K., J. M. S., and N. B., draft manuscript preparation. A. K., preparation of figures 3, 4, 9, and Supplementary Figures 1-4; N. B., preparation of remaining figures and tables; All authors reviewed the results and approved the final version of the manuscript.

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Competing Interests

Prof Damien Coyle, Chief Investigator on this project, is the founder, Chief Executive Officer, and a shareholder of NeuroCONCISE Ltd., a company involved in the development of neurotechnology and wearable electroencephalography (EEG) systems.

Figure Captions and Main Tables

Figure Captions

Figure 1. Timing of the trials. a: Assessment. b: Training, and Feedback. c: Q&A. Note: the Q&A task began with a question. Therefore, the trigger for the start of the task performance period was sent at the end of the question. Paradigm specific trial instructions are provided in Supporting Information, Supplementary Note 1.

Figure 2. EEG montage. The positions of EEG (blue and green) and ground (orange) electrodes are presented in this figure. Nine EEG channels covering motor and imagined movement-related cortical areas are indicated in green. The reference clip was attached to the right ear (as indicated by the circle in grey).

Figure 3. Structure of the applied FBCSP-MI based 2-class classification method. The block diagram illustrates the signal processing framework, including filter bank common spatial patterns and mutual information (FBCSP-MI) based features selection modules, and a regularized linear discriminant analysis (RLDA) 2-class classifier. The analysis performed using three different sets of frequency bands, involving four adjacent bands from the six pre-processed bands (i.e., delta, theta, mu, low-beta, high-beta, low-gamma bands). The illustrated setup represents the highest four-band option.

Figure 4. Decoding accuracy (DA) across runs for all participants. Graphs are displayed according to diagnostic category (top row – UWS; middle row – MCS; bottom row – LIS), shown separately for all runs (left-hand column) and runs reaching statistical significance (middle column), with representative high-performing individuals highlighted (right-hand column). Left and middle columns show group-level trajectories for Ref DA (black) and Task DA (red), including participant traces (see subject ID for each group), mean trajectories (dashed), and participant-averaged linear trends (solid). Right column shows single-participant examples illustrating stable high performance and task-reference separation.

Figure 5. Illustration of the comparison of DA values obtained for each group (UWS, MCS, LIS, AB). DA values obtained from (a) all runs ($n = 1233$ run/33 participants; UWS = 293/8, MCS = 472/13, LIS = 433/10, AB = 35/2) and (b) runs showing a significant task-related peak (one-tailed t-test comparing task vs. reference interval, $\alpha = 0.05$; $n = 681$ run/31 participants; UWS = 138/8, MCS = 211/13, LIS = 299/10, AB = 33/2). Boxplots display the data distribution for each group, showing the interquartile range (25th–75th percentile) with the median as a horizontal line. Individual data points represent DA values from multiple runs per participant, illustrating within-group variability. Red circles mark group mean DA, with vertical error bars showing ± 1 SD. Black circles and solid lines connect mean task-related DA across groups, while grey squares and dashed lines indicate mean DA during the reference interval. Panel (c) illustrates the proportion of significant runs per paradigm (assessment, training, feedback, and Q&A), by group. Bars represent the mean percentage of significant runs for each group and paradigm. Individual data points represent proportions from each participant's runs, illustrating within-group variability. Red points and connecting lines indicate group-level averages across paradigms. Statistical significance of diagnostic group differences is indicated by asterisks: * $p < 0.05$, ** $p < 0.01$.

Figure 6. Comparison of decoding accuracy (DA) values obtained for Q&A categories, across groups (UWS, MCS, LIS, AB). DA values obtained from (a) all runs ($n = 297$ run/30 participants; UWS = 57/6, MCS = 112/12, LIS = 124/10, AB = 4/2) and (b) runs showing a significant task-related peak (one-

tailed t-test comparing task vs. reference interval, $\alpha = 0.05$; $n = 169$ run/29 participants; UWS = 26/5, MCS = 51/12, LIS = 88/10, AB = 4/2). Boxplots display the data distribution for each group, showing the interquartile range (25th–75th percentile) with the median as a horizontal line. Individual data points represent DA values from multiple runs per participant, illustrating within-group variability. Red circles mark group mean DA, with vertical error bars showing ± 1 SD. Black circles and solid lines connect mean Q&A task-related DA across groups, while grey squares and dashed lines indicate mean DA during the reference interval. Panel (c) illustrates the proportion of significant runs per Q&A category (Biographical, Basic Logic (Logic), Numbers and Letters (Numeric), and Situational), by group. Bars represent the mean percentage of significant runs for each group and question category. Individual data points represent proportions from each participant's runs, illustrating within-group variability. Red points and connecting lines indicate group-level averages across paradigms. Statistical significance of diagnostic group differences is indicated by asterisks: * $p < 0.05$, ** $p < 0.01$.

Figure 7. Mean DA across task paradigms (Training, Feedback, and Q&A) for significant runs only, shown separately for diagnostic groups (UWS, MCS, LIS). Thin lines represent individual participants, illustrating within-group variability. Bold lines and shaded bands denote group-level means ± 1 SD. The dashed line indicates empirical chance levels for each paradigm, computed using the “better-than-random” binomial rule 91. Group colours: UWS = green, MCS = orange, LIS = blue.

Figure 8. Predicted probabilities of clinical diagnosis (UWS, MCS, LIS) derived from a multinomial logistic regression model as a function of (a) average decoding accuracy (DA) and (b) CRS-R score. The model was fitted using participant-level averages within each diagnostic group. Lines show model-estimated probabilities with 95% bootstrapped confidence intervals. Colours denote diagnostic groups (UWS = blue, MCS = red, LIS = green).

Figure 9. Clustered boxplots illustrating CSP–MI weights across brain regions for each diagnostic group (UWS, MCS, LIS, AB) and paradigm: Assessment (top left), Training (top right), Feedback (bottom left), and Q&A (bottom right). Each box represents the distribution of CSP–MI weights across individual runs (multiple runs per participant) within each group and brain region, with boxes showing the interquartile range (25th–75th percentile) and horizontal lines marking the median. Whiskers extend to $1.5\times$ the interquartile range, and outliers are not displayed. Colours denote diagnostic groups as indicated in the legend. Statistical significance of diagnostic group differences is indicated by asterisks: * $p < 0.05$, ** $p < 0.01$.

Main Tables

Table 1. Structure of the study phases and associated runs.

Editorial Summary: Du Bois et al. use a structured, multiphase brain–computer interface to test how people with severe brain injuries can modulate brain activity through imagined movements. The results show that decoding these signals provides objective evidence of awareness and diagnostic information beyond traditional behavioural assessments.

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