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Cognitive-Motor Dissociation Following Pediatric Brain Injury

What About the Children?

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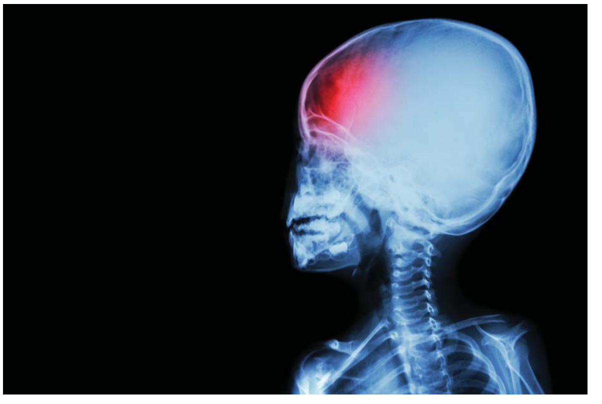

Abstract

Background and Objectives

Following severe brain injury, up to 16% of adults showing no clinical signs of cognitive function nonetheless have preserved cognitive capacities detectable via neuroimaging and neurophysiology; this has been designated cognitive-motor dissociation (CMD). Pediatric medicine lacks both practice guidelines for identifying covert cognition and epidemiologic data regarding CMD prevalence.

Methods

We applied a diverse battery of neuroimaging and neurophysiologic tests to evaluate 2 adolescents (aged 15 and 18 years) who had shown no clinical evidence of preserved cognitive function following brain injury at age 9 and 13 years, respectively. Clinical evaluations were consistent with minimally conscious state (minus) and vegetative state, respectively.

Results

Both participants' EEG, and 1 participant's fMRI, provided evidence that they could understand commands and make consistent voluntary decisions to follow them. Both participants' EEG demonstrated larger-than-expected responses to auditory stimuli and intact semantic processing of words in context.

Discussion

These converging lines of evidence lead us to conclude that both participants had preserved cognitive function dissociated from their motor output. Throughout the 5+ years since injury, communication attempts and therapy had remained uninformed by such objective evidence of their cognitive abilities. Proper diagnosis of CMD is an ethical imperative. Children with covert cognition reflect a vulnerable and isolated population; the methods outlined here provide a first step in identifying such persons to advance efforts to alleviate their condition.

Severe brain injuries are a leading cause of death and disability among children and adolescents. In those who survive, emergence from coma typically results in a disorder of consciousness (DoC).[1] This includes periods with signs of arousal but no clear evidence of awareness of self or

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environment (vegetative state, sometimes known as unresponsive wakefulness syndrome: VS/UWS) and periods with inconsistent evidence of awareness (minimally conscious state, MCS).[1] In adults who are in coma, VS/UWS, or MCS, a lack of observable motor behavior may obscure the presence of high-level cognitive function as revealed by functional neuroimaging and neurophysiologic assessments.[1] In the chronic phase, such studies have reported that 40%–75% of participants with no detectable signs of awareness at the bedside retain high-level cognitive functions.[1] The condition of such patients has been called cognitive-motor dissociation (CMD).[2] Adults with CMD demonstrate significantly better prognosis when identified during early intensive care.[3]

These findings are highly significant both clinically and normatively. In the early stages following injury, accurate diagnoses of preserved or emerging cognitive function can influence decisions about withdrawal of care, the provision of appropriate interventions, and access to rehabilitation.[1,3] In the long term, it is especially important to diagnose residual cognitive function so that families can make informed decisions about augmentative communication strategies and about the appropriate educational and social environments to mitigate the person's isolation.

However, precise diagnosis of emerging cognitive function in DoC is both difficult and error prone[4] and, to date, wholly unaddressed in pediatrics. Current cognitive measures rely on coemergence of motor function—for example, motor control is necessary to demonstrate command-following.[5] This reliance on overt behavior can obscure the presence of residual cognition. In adult DoC, the use of neuroimaging and neurophysiology to inform diagnosis, when available, is now a practice guideline and has been adopted by American Academy of Neurology, American Congress of Rehabilitation Medicine, and National Institute on Disability, Independent Living, and Rehabilitation Research[4] and the European Academy of Neurology.[6] In pediatric DoC, by contrast, only very few attempts[7-11] have been made to apply objective assessments of functional brain activity, and they have provided only circumstantial evidence of covert consciousness as they have not examined brain responses in command-following or language comprehension paradigms. As a result, there is insufficient evidence to develop similar guidelines for pediatric brain injury.

To address this gap, we conducted a systematic, comprehensive, multimodal assessment of cognitive function in 2 adolescents living with chronic DoC following severe brain injuries. We used a battery of behavioral, neurophysiologic, and neuroimaging assessments to diagnose and quantitatively characterize multiple aspects of cognitive function. We expect these tests to be redeployable in a wider range of cases.

Methods

Participants

Two male adolescent participants, initially referred to an adult DoC research program,[12] participated in this study. They were part of a larger companion study[13] in which they are labeled as participants C and E. Here, they are labeled as participants 1 and 2 (P1 and P2). The companion study reports[13] on 2 EEG tests: event-related potentials (ERPs) in the oddball paradigm (see below) and EEG correlates of motor command-following (MCF-EEG, see below) taken in 8 participants in DoC and 36 participants in other cognitive states. In the current study, we focus on only 2 of the DoC participants by providing a comprehensive profile that includes fMRI motor command-following (MCF-fMRI), EEG correlates of semantic comprehension (N400), fluorodeoxyglucose positron emission tomography, structural MRI, and clinical histories along with the previously reported ERP and MCF-EEG findings. Our criterion for selecting 2 DoC participants for deeper study was that they had positive MCF-EEG despite being unresponsive at the bedside. One additional DoC participant matched these criteria but could not be studied in greater depth, as they were in the acute phase following injury with medical complications that prevented neuroimaging studies.

P1

The participant was 9 years old when he experienced a traumatic brain injury complicated by hypoxemia and associated cardiac arrest. He was a restrained passenger in a motor vehicle collision and was intubated at the scene with a Glasgow Coma Scale of 4. Detailed clinical history is provided in the eMaterial (links.lww.com/CPJ/A333). P1 was 15 and 16 years old during the 2 separate series of testing and imaging for the current study.

P2

The participant was 13 years old when he experienced anoxic brain injury secondary to cardiac arrest. CPR was initiated immediately, and he was intubated in the field and provided 4 separate shocks with an automated external defibrillator for ventricular fibrillation. During hospital stay, he was noted to have supraventricular tachycardia, and an accessory pathway was ablated. Detailed clinical history is provided in the eMaterial (links.lww.com/CPJ/A333). He was 18 years old when he completed the testing and imaging for the current study.

Procedures

To assess neurophysiologic and neuroimaging evidence of command-following, we used a motor imagery task, similar to previous studies in adults[14] and pediatrics,[13] using EEG. We also used both a motor imagery and a spatial navigation task in fMRI, as previously reported in adults.[15] To assess processing of auditory stimuli, we measured auditory evoked potentials (AEP) and P300 ERPs during an oddball stimulus paradigm.[13] To assess semantic comprehension, we measured N400 ERPs elicited by recordings of previously published spoken sentences,[16] as previously applied to healthy populations (age 16–32) and brain-injured populations.

PET, MRI, fMRI, and EEG Data Acquisition

MRI and fMRI data from both pediatric participants were collected with a Siemens MAGNETOM Prisma 3.0 T Scanner at New York-Presbyterian Hospital/Weill Cornell Medical Center between October 2019 and March 2020. Each scan included a sagittal 3D T1 MPRAGE acquisition, as well as sagittal 3D T2 FLAIR with fat saturation, with respective axial and coronal reformats, with a resolution of 0.8 × 0.8 × 0.8 mm. A functional MRI was obtained with a multiband gradient-echo Echo planar imaging sequence with repetition time = 2000 ms, echo time = 30 ms, and 32 slices of 3.74 × 3.74 × 4 mm voxels acquired in interleaved increasing order. PET data were acquired using a 64-slice Biograph mCT PET/CT scanner (Siemens Healthineers, Erlangen, Germany). [18F] FDG PET/CT was obtained with pediatric protocol according to published recommendations, including weight-based FDG dosing and low dose CT following the ALARA principle.[17] In P1, 2 MRI/fMRI sessions were conducted 15 months apart, and a single PET scan was obtained at the later time point. In P2, there was a single time point during which MRI, fMRI, and PET scans were all collected.

Electroencephalographic data (Figures 2 and 4) were recorded from 128-channel HydroCel Geodesic Sensor Net (EGI, Eugene, OR).[18] In P1, a gel-based cap was used, and in P2, a sponge-based cap was used. The impedance of all electrodes was <75 kΩ at the beginning of the recording. The signals were recorded at 1000 Hz with a high-pass filter at 1 Hz to remove drift. Speakers (Micro Innovations 2-piece speaker system) were located at 45° (left/right of the midline) at a distance of 57 cm to the ears. Each speech stimulus was normalized to have equal perceived loudness at a volume of ~70 dB hearing level. Stimulus presentation was conducted using BCI2000 software.[19] Data were acquired with BCI2000, integrated via LabRecorder software (Lab Streaming Layer package), which is a system for unified, time-synchronized measuring. All EEG data reported are from the second visit of P1 and the single visit of P2. See referene 13 for details on the data collection and analysis reported in Figure 3.

Stimuli and Tasks

Motor Command-Following (EEG)

Similar to previous studies in adults[14] and pediatrics,[13] in the motor imagery task, participants alternately heard the commands "Keep opening and closing your right/left hand," and "stop and relax" (interleaved 8 trials of the left hand; 8 trials of the right hand; 16 trials of rest). Each trial consisted of prerecorded commands in a female voice; commands lasted approximately 2 seconds, providing participants with 13 seconds to perform the mental imagery task (trials were delivered 15 seconds apart). In P1, there were a total of 3 sessions over 3 days, and in P2, there were 4 sessions over 4 days.

Motor and Nonmotor Command-Following (fMRI)

We used experimental designs similar to previous fMRI studies used to detect command-following in DOC participants, notably motor imagery and spatial navigation.[15] For the spatial navigation task, the participant was asked to imagine walking around the rooms of their house. For the motor imagery task, the patient was asked to move their (his or her) left arm. The patient was asked to perform alternating sessions of repeated rest-imagery cycles. A period of rest or imagery lasted 16 seconds each, with the rest-imagery cycle repeated 8 times. In P1, a single session of each task was conducted, at each of 2 time points, 15 months apart. For P2, 2 sessions were acquired for each task during the same scan.

Auditory Oddball

This EEG paradigm, frequently used in both adults[20] and pediatrics,[13] consists of frequent standard tones with randomly interspersed but infrequent deviant tones and other auditory stimuli. It requires no participation from the participant beyond passive listening. Although both sounds trigger ERPs, the ERPs time-locked to standards and those time locked to oddballs exhibit robustly detectable differences. See reference 13 for details.

Semantic Processing (EEG Event-Related Potentials)

Previously published sentences[16] composed of 6–8 words were used.[21] This stimulus, which consists of 320 congruent trials (e.g., "Apples and cherries are a type of fruit.") and 320 incongruent trials (e.g., "A wild pig is called a shirt."), has previously been applied to healthy populations (age 16–32)[22] and brain-injured populations.[23] The interstimulus interval between the sentences was 3.5–4.5 seconds. All stimuli were spoken by a young female English native speaker. All sounds had a sampling rate of 44.1 kHz, a resolution of 32 bits, and were presented at a sound level of ~70 dB. In P1, there were a total of 5 sessions over 4 days, and in P2, there were 3 sessions over 3 days.

Data Analysis

EEG Data Preprocessing and ERP Analyses

EEG data processing was as described in a previous study[13] and is included in the eMaterial (links.lww.com/CPJ/A333).

Analysis of Semantic Event-Related Potentials

For the semantic processing ERP analysis, data were segmented into 1000 ms epochs time-locked to the onset of the auditory target word (200 ms prestimulus and 800 ms poststimulus). Mean amplitudes were calculated for each stimulus type for each individual at the Cz electrode site. We calculated the *t* test statistics between the congruent and the incongruent condition at each time point.

Spectral Analysis of Motor Command-Following EEG

Analysis of command-following EEG data is as described in a previous study[13] and is included in the eMaterial (links.lww.com/CPJ/A333).

fMRI Analyses

The fMRI data were preprocessed using the CONN toolbox.[24] Functional preprocessing included realignment, slice-timing correction, segmentation and intensity normalization, and 6-mm full-width at half-maximum smoothing. BOLD data were high-pass filtered using a cutoff of 128 seconds to remove slow signal fluctuations. The analysis was performed with SPM12 (Wellcome Trust Center for Neuroimaging, London, UK) using a general linear model (GLM) with a canonical hemodynamic response function (HRF) to assess task vs rest activations.[25] To identify auditory responses to the verbal commands, a new condition block design was created with an impulse of 0 length at the beginning of each verbal command (both start and stop commands) and convolved with an HRF. For each scan, contrasts between periods of active imagery with periods of rest were calculated, with 8 periods of imagery and rest for P1 and P2. The GLM and contrasts were performed twice for P2, separately for each session and with sessions concatenated. Contrasts were performed across all voxels in the brain. Thresholded statistical *t*-value maps were plotted. All *p* values reported are uncorrected.

Standard Protocol Approvals, Registrations, and Patient Consents

All procedures were approved by the institutional review boards (IRBs) of Weill Cornell Medicine and Blythedale Children's Hospital. Parental consents were obtained as per IRB protocols.

Data Availability

Data and stimuli from this study are available from the corresponding author on reasonable request.

Results

Behavioral Assessment

P1 was assessed at 2 time points 15 months apart using the standardized neurobehavioral assessment Coma Recovery Scale–Revised (CRS-R)[5]; the first assessment was 5 years after injury. He demonstrated a consistent startle to visual threat but no evidence of an ability to fixate on objects or track them visually through space. He likewise consistently responded to sounds in his environment with generalized facial and limb movements, and in addition, he showed evidence of orienting toward the sound. He consistently demonstrated spontaneous vocalizations, but there was no evidence of verbal communication or comprehension through command-following. His examination was inconsistent across time points: his response to the presentation of pain (nail bed pressure) ranged from localized movement of a nonstimulated limb toward the painful stimulus during the first assessment (suggesting emergence to MCS)—to unspecific movement in multiple limbs in the second assessment (more characteristic of VS/UWS). The CRS-R total score at visit 1 was 10 and at visit 2 was 7.

P2's arousal and responsiveness were assessed using the CRS-R during his single assessment for this study, almost 5 years after injury. His clinical presentation was consistent with VS/UWS as he demonstrated sustained wakefulness with startle to sound, abnormal posturing to pain, and spontaneous vocalizations. He did not respond to any visual stimuli or demonstrate any evidence of verbal comprehension, functional object use, or communication. The CRS-R total score was 6.

Structural and Metabolic Markers of Brain Injury

MRI and FDG PET/CT imaging revealed changes in brain structure and cerebral metabolism consistent with severe traumatic (P1) and hypoxic-ischemic (P2) brain injuries (Figure 1). In P1, MRI demonstrated moderate frontal-predominant parenchymal volume loss with corresponding PET findings of disproportionately decreased FDG avidity in the bilateral frontal cortex. In P2, MRI demonstrated marked generalized parenchymal volume loss with superimposed disproportionate volume loss in the left frontal, temporal, and parietal operculum; PET additionally demonstrated a disproportionate decrease in FDG avidity in the bilateral parietal precuneus, left greater than right lateral parietal convexity, and bilateral calcarine cortex.

EEG Correlates of Motor Command-Following

During attempted hand movement to command, contralateral desynchronization of EEG sensory-motor rhythms was seen in both participants, manifested as a reduction in bandpower in the alpha frequency band (Figure 2). In P1, positive responses were seen to attempted movement of the left hand (permutation test: $p = 0.04$) but not right ($p = 0.67$); in P2, positive responses were seen to attempted movement of both hands ($p = 0.01$ left; $p = 0.03$ right).

fMRI Correlates of Motor and Nonmotor Command-Following

We further evaluated motor and nonmotor command-following abilities using fMRI (Figure 2). In P1, a differential response (command vs rest) was observed in bilateral Brodmann Area 6 ($p < 0.005$, uncorrected); imagined spatial navigation elicited significant activation at the occipito-parietal junction ($p < 0.001$, uncorrected). In P2, no significant responses were observed to either command type.

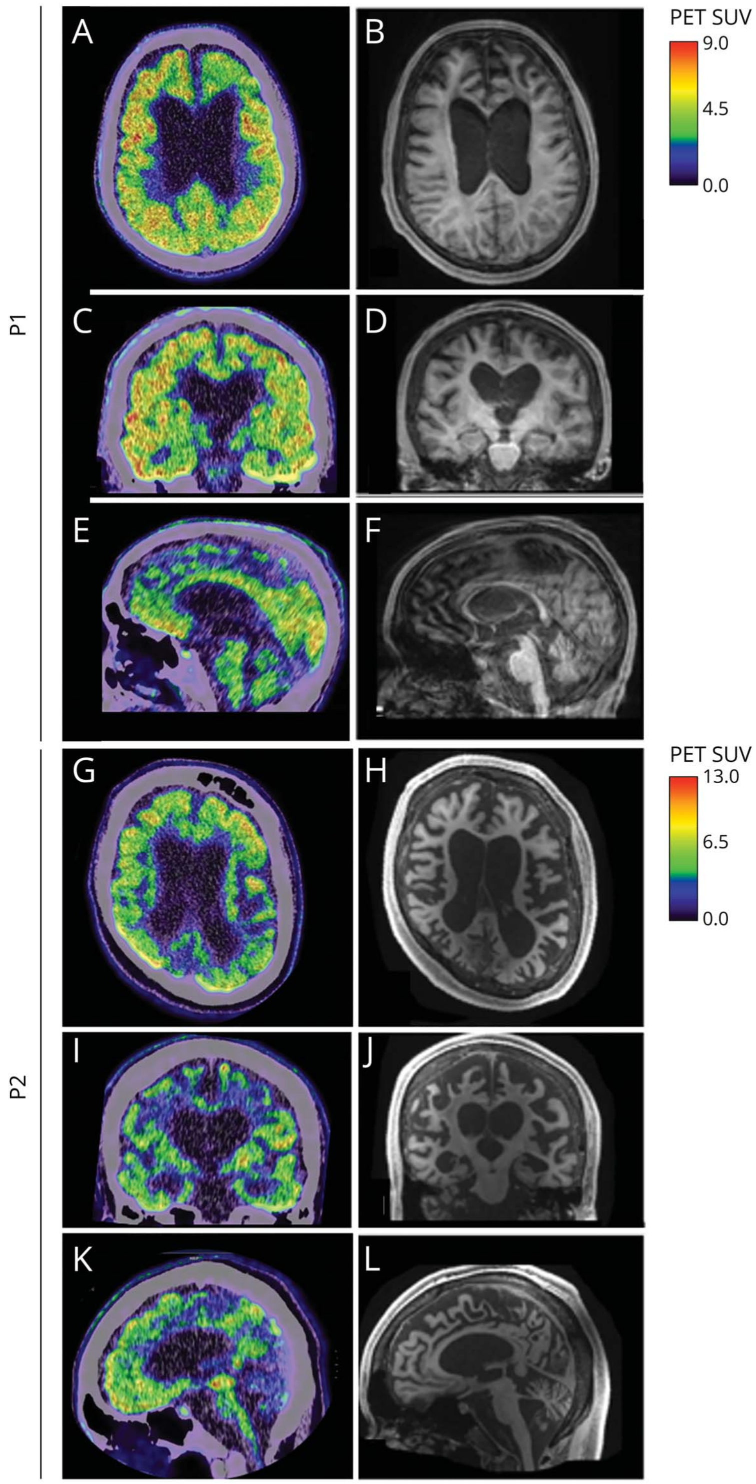
EEG Correlates of Auditory Stimulus Processing

In Figure 3, we compare the responses to the oddball paradigm in both participants against 10 other pediatric participants with brain injuries.[13] We note that, in comparison to participants in DoC who had no evidence of motor command-following, both P1 and P2 had larger AEPs to the frequent standard stimuli, as well as larger P300 responses in the difference wave between standard and rarer deviant stimuli. Their magnitudes are comparable to those of a group of children who had emerged from DoC and were categorized as being in a confusional state—see reference 13 for details, including results on a broader spectrum of cognitive recovery states.

EEG Correlates of Semantic Processing

Both participants exhibited a normal N400 ERP (Figure 4). This negative deflection at 400 ms latency is specific to words that are semantically incongruent with the preceding sentence context, as compared with congruent words.

Figure 1 Structural and Metabolic Integrity



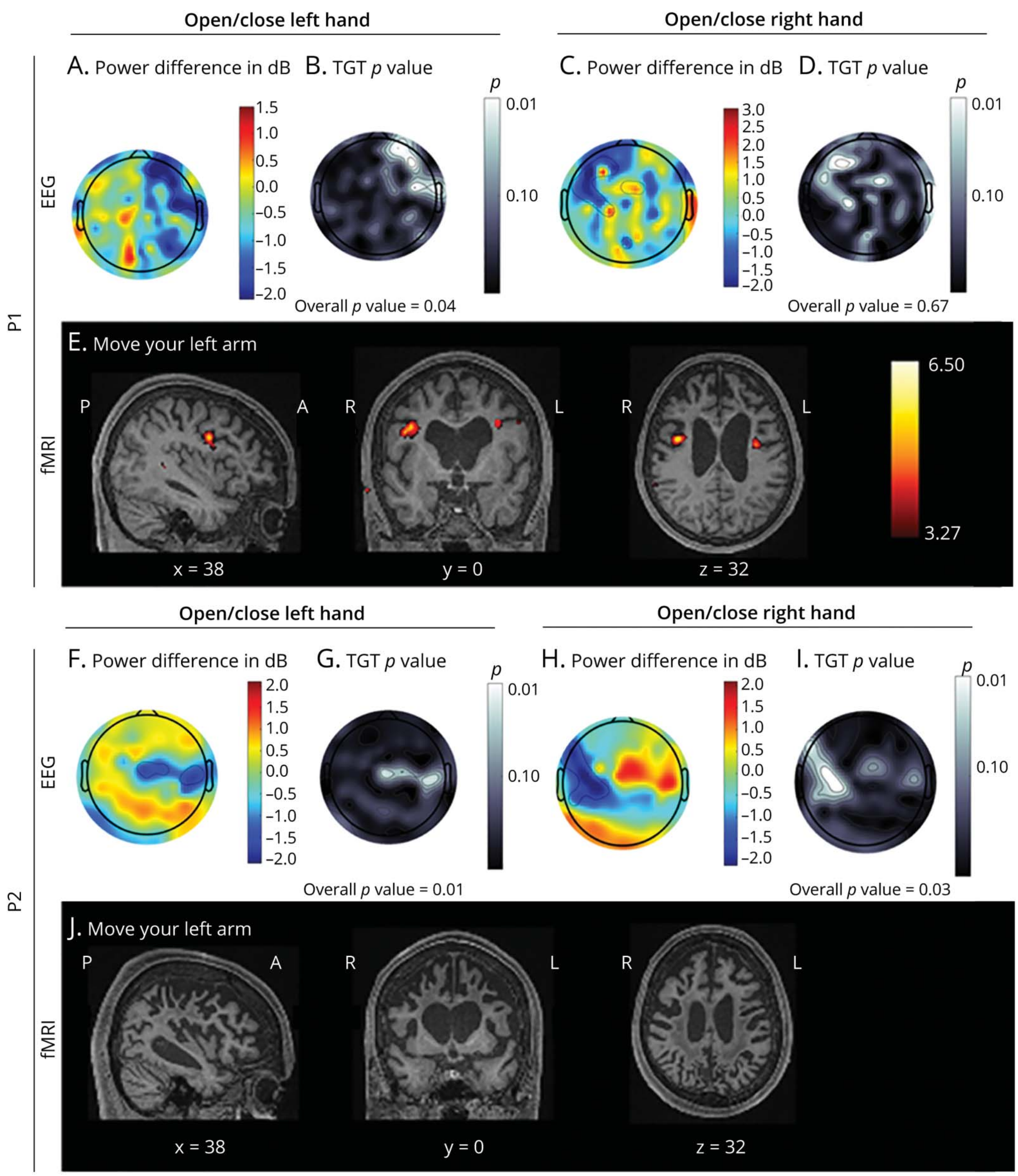
Left panels A–F: 16-year-old male P1 (traumatic brain injury at age 9). Right panels G–L: 18-year-old male P2 (anoxic brain injury at age 13). Panels A, C, and E for P1 and Panels G, I, and K for P2 show axial, coronal, and sagittal fused PET/CT windowed at 0–9 standardized uptake value (SUV) for P1 and 0–13 SUV for P2; Panels B, D, and F for P1 and Panels H, J, and L for P2 show the corresponding T1 MPRAGE MRI.

Discussion

The current findings provide convergent evidence for cognitive-motor dissociation in 2 adolescents who had remained in DoC over several years. The results illustrate that CMD arises in pediatric patients with severe brain injuries and raise many troubling questions in light of the very limited existing published literature on pediatric DoC.[4]

As shown by our neurophysiologic and neuroimaging assessments of motor command-following, both participants could understand commands sufficiently to follow them

Figure 2 Command-Following Using EEG and fMRI

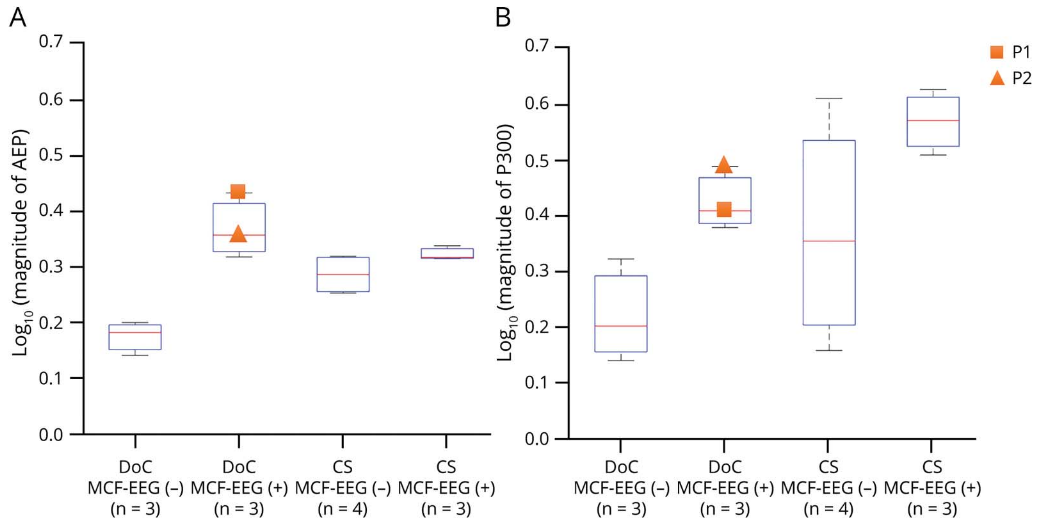


Scalp maps show changes in EEG spectral power during attempted hand movement in the alpha (8–12 Hz) frequency band. EEG results are show from P1's session 3 (panels A–D) and P2's session 2 (F–I): colored scalp maps display average difference in log spectral power between attempted movement and baseline at rest. Grayscale maps represent the *p* value of a two-group test performed separately at each electrode position. Overall *p* value is from a 1-sided permutation test of a statistic reflecting contralateral desynchronization (reduction in EEG spectral power) and ipsilateral synchronization (increase in power). Panels (E) and (J) show bilateral fMRI responses in BA6 to the command "Move your left arm" (highlighting activation in the right hemisphere in the leftmost panel) for the second of P1's 2 sessions and P2's single session, respectively; colors indicate significant *t*-statistics.

accurately without physical cues, make a voluntary decision to follow them, and remain focused on the task instructions (positive fMRI results in P1, positive EEG in both participants). Such evidence of command-following, derived from EEG or fMRI as proxies for absent behavioral responses, has been the distinguishing feature of CMD.[2] Our previous report[13] on the current participants as part of a larger sample also showed positive EEG results in motor command-following in one further participant in DoC. It is important to note that false-negative command-following results are common both in fMRI[26,27] and, independently, in EEG.[14] This is even true in uninjured subjects, but especially so in people with brain injury because of the greater fluctuations in arousal. The positive predictive value of these tests far outweighs their negative predictive value—therefore, we ascribe no particular interpretation to P2's negative fMRI results.

The problem of false-negative command-following results motivates additional tests that could contribute to a CMD diagnosis via assessment of independent aspects of cognition. Furthermore, tests that characterize residual and recovered cognitive abilities quantitatively and in greater detail, beyond mere detection of the presence or absence of covert cognition, are needed to facilitate appropriate communication with

Figure 3 EEG Correlates of Auditory Stimulus Processing

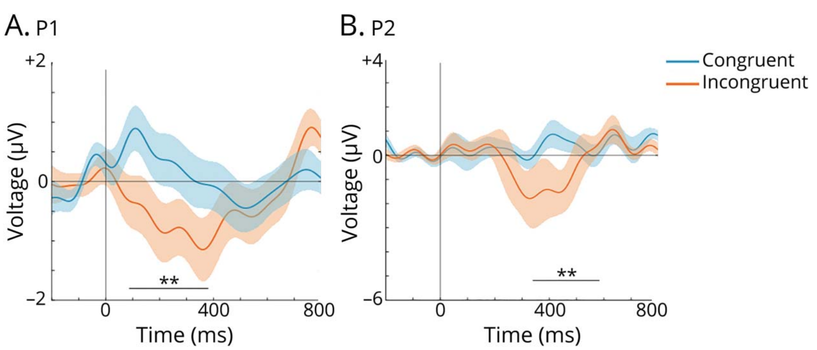


The log noise-corrected magnitudes of the auditory evoked potential (AEP, A) and P300 event-related potential (ERP, B) are shown for P1 and P2 in comparison with 10 other pediatric participants with brain injury.[13] Participants are split into 4 groups according to whether they were in a disorder of consciousness (DoC) or had emerged from DoC into confusional state (CS) and whether they had positive or negative EEG findings in motor command-following (MCF-EEG + or –).

people in CMD. For these reasons, we augment the command-following findings by reporting EEG-based assessments of auditory and rudimentary attentional processing using an oddball paradigm, and of language processing using spoken sentence stimuli. The auditory oddball test is described in more detail and validated in a larger sample across the full spectrum of cognitive recovery following brain injury, in a companion study.[13] In this larger cohort of patient participants, the P300 measure is more consistently related to positive EEG correlates of motor command-following (including the 2 participants in this study) compared with AEP measures. Evidence of language processing was provided by EEG measurements that demonstrated intact processing of word meaning (typical N400 ERPs in response to semantically incongruent words at the end of a sentence). Throughout the years in which these 2 participants had remained in DoC, attempts at communication and therapy had remained uninformed by any such objective evidence of their auditory processing and language comprehension. This vividly highlights the crucial gap in current clinical practice.

Each of the tests has previously been shown to be informative in DoC research studies on adults. Functional MRI or EEG correlates of attempted movement to command have been used to detect awareness and motor planning in the absence of overt, purposeful movements.[14,28] Task-based brain signal analytics can reveal CMD in 15–20% of patients judged unresponsive on clinical examination.[1] Variation in the amplitude of the AEP has been linked to arousal and selective attention,[29] allowing identification of residual consciousness in severely brain-injured adults.[30] Absent, reduced-amplitude or longer-latency AEPs are associated with poorer outcomes following adult traumatic brain injury.[31] In the oddball difference wave, 2 components (the N200[32] and P300[20]) are considered to be dependent on attention to target discrimination[20] and information processing. In adults, the P300 has been used to

Figure 4 Time-Locked EEG Correlates of Semantic Processing



From a single representative session with P1 (A) and another with P2 (B), event-related potentials from electrode position Cz are shown time-locked to the onset of the last word in a sentence, which is either semantically congruent (blue) or incongruent (orange) with the preceding sentence context. Time points at which there was a statistically significant difference ($p < 0.05$) between conditions are indicated with a black line and asterisks.

improve diagnosis and prognostication in severe brain injury.[31,33] The N400 has been shown to be preserved (albeit at reduced amplitude) in the group mean data from adults in VS/UWS and MCS. This has previously been presented as unreliable on an individual-patient basis in DoC[34] because of its low negative predictive value. However, when present, it is predictive of positive outcomes.[23,34]

Although accurate diagnosis of pediatric CMD is clearly important, the life of such children is not improved by its identification alone, without providing specific targets for improving rehabilitation or communication strategies.[35] The proximate goal, in the absence of further motor recovery, is to restore meaningful communication with family and caregivers, allowing reintegration into the community.[36] This is both clinically significant and a mandate of the Americans with Disabilities Act.[37] Moving both clinical care and research in the direction of this goal, unfortunately, remains a challenge even for adults with CMD. In adults, attempts have been made using motor imagery in fMRI[38] and EEG[39] to build a brain-computer interface (BCI) allowing 2-way communication. Apart from isolated reports, very little progress has been made—importantly, patients with CMD demonstrate difficulties converting command-following responses into communication signals. Similar BCI methods have had some limited success in patients with locked-in syndrome; however, unlike the special case of locked-in syndrome, CMD is more generally characterized by concomitant injuries across a broad range of cerebral functions.[12] Therefore, significant challenges remain to be surmounted in both adult and pediatric CMD, among which accurate diagnosis is just the first step. With our results, we demonstrate possible active BCI channels—motor imagery and spatial imagery. Establishing a range of options, as we have shown, may be a necessary first step in achieving individualized communication solutions for this heterogeneous and underserved population.

Future work will also need to address 4 challenges. First, we require deeper knowledge of the effects of trauma on the developing brain. For example, as described elsewhere,[13] we noted that P1's AEP had a longer latency more characteristic of his age at injury (9 years) than at testing (15 years). It is unclear whether this reflects stunting of brain development. Second, rigorous validation studies are required to determine the reliability of additional assessments (beyond motor command-following) in identifying CMD—this might include, for example, passive language paradigms that have previously been used in pediatric DoC studies.[7–11,13] Third, the current research and clinical infrastructure needs to expand to allow neuroimaging and neurophysiologic studies for pediatric subjects with brain injury. Finally, we require a better understanding of which of the wide range of possible injury and disease mechanisms allow for, or preclude, CMD.[2] We have incomplete knowledge even concerning the ways in which different injury and disease mechanisms might impact the various tests (such as command-following) that we use to infer CMD. This limitation significantly impacts the immediate generalizability of the present findings and of similar results in pediatrics and adults alike.

In summary, the accurate diagnosis of CMD is challenging, and the condition is unrecognized in children. Our study demonstrates proof of principle for identifying CMD in children and adolescents and lays out a hierarchical toolset for individualized assessments. As these and similar results emerge, they should shape the way new patients are assessed, and chronic patients reassessed. Even as the implications for treatment remain to be finalized, the immediate impact of such assessments will be to guide the way in which clinicians and caregivers talk to people in DoC. This toolset should be expanded still further, validated, and adapted to ensure applicability in younger children. The proximate goal should be to produce a reliable clinical algorithm for detecting covert consciousness in people of all ages. Concerted efforts to translate these research tools into practicable bedside assessments constitute a clinical and ethical imperative[40] and should be a focus of future work. Emerging technologies can be envisioned that may help remedy these conditions and affirm the rights of the child to autonomy and self-determination.[41] Seen from this perspective, the present findings set a major challenge to improve the standard of care for children and adolescents with severe brain injuries to bring the international evidence base and practice recommendations in line with those emerging for adults.[4]

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Nayoung Kim, PhD	Department of Radiology, Weill Cornell Medicine, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; and analysis or interpretation of data

Continued

Appendix (continued)

Name	Location	Contribution
James O'Sullivan, PhD	Department of Radiology, Weill Cornell Medicine, New York	Analysis or interpretation of data
Emily Olafson, BA	Department of Radiology, Weill Cornell Medicine, New York	Analysis or interpretation of data
Eric Caliendo, MD	Department of Rehabilitation Medicine, Weill Cornell Medicine, New York	Drafting/revision of the manuscript for content, including medical writing for content
Sophie Nowak, BA	Blythedale Children's Hospital, Valhalla, NY	Major role in the acquisition of data
Henning U. Voss, PhD	Department of Radiology, Weill Cornell Medicine, New York	Analysis or interpretation of data
Ryan Lowder, BA	Department of Rehabilitation Medicine, Weill Cornell Medicine, New York	Major role in the acquisition of data
William D. Watson, PhD	Blythedale Children's Hospital, Valhalla, NY	Drafting/revision of the manuscript for content, including medical writing for content, and study concept or design
Jana Ivanidze, MD	Department of Radiology, Weill Cornell Medicine, New York	Analysis or interpretation of data
Joseph J. Fins, MD	Division of Medical Ethics, Weill Cornell Medicine and New York Presbyterian Weill Cornell Medical Center	Drafting/revision of the manuscript for content, including medical writing for content
Nicholas D. Schiff, MD	Department of Neurology and BMRI, Weill Cornell Medicine, New York	Drafting/revision of the manuscript for content, including medical writing for content, and study concept or design
N. Jeremy Hill, DPhil	National Center for Adaptive Neurotechnologies, Stratton VA Medical Center; Department of Electrical and Computer Engineering, State University of New York at Albany, NY	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and analysis or interpretation of data
Sudhin A. Shah, PhD	Department of Radiology, Weill Cornell Medicine, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

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