WHAT DO YOU NOTICE ABOUT THESE IMAGES?

controls  sleep  coma  anesthesized monkey

(Boly et al., 2008)
SO YOU FELL INTO A COMA
A HANDY GUIDE TO PREDICTING RECOVERY
WHAT DO YOU NOTICE ABOUT THESE IMAGES?

Default mode activation in different states of consciousness

(Boly et al., 2008)
CONSCIOUSNESS

Fully conscious (now, hopefully)
Sleep (unconscious, aware)
Coma (unconscious, unaware)
AROUSAL & AWARENESS

- Two main components of consciousness
  - **Awareness** = content of consciousness
    - Self-awareness
    - External awareness
      - Usually anti-correlated – one dominates
  - **Arousal** = level of consciousness
- Usually positively correlated

Laureys, Owen, & Schiff (2004)
WHAT IS A COMA?

- Coma ~ prolonged state of unconsciousness where individuals cannot respond to stimuli in the environment
  - Cannot consciously think, lack awareness of their surroundings
  - Basic life support functions are intact (breathing and circulation)

- **Arousal and awareness are low**
AROUSAL & AWARENESS

Figure 2. Arousal and awareness, the two components of consciousness in coma, vegetative state, minimally conscious state, and locked-in syndrome.

Laureys, Owen, & Schiff (2004)
AROUSAL & AWARENESS

Laureys, Owen, & Schiff (2004)

Figure 2. Arousal and awareness, the two components of consciousness in coma, vegetative state, minimally conscious state, and locked-in syndrome.
Figure 2. Arousal and awareness: the two components of consciousness in coma, vegetative state, minimally conscious state, and locked-in syndrome.

Laureys, Owen, & Schiff (2004)
WHAT CAUSES A COMA?

• Head trauma (car accident or fall)
• Underlying illness
• Infection
• Tumor
• Toxins
• Stroke
• Oxygen deprivation (i.e. from cardiac arrest)
  • Hypoxia, anoxia
CAUSES

• More than 50% of comas are related to head trauma or disturbances in circulatory system
  • Trauma = brain swelling
  • Can cause brain to push down on brain stem, damaging the reticular activating system (RAS), which is responsible for arousal and awareness
CAUSES

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• Anatomy lesson:
CAUSES

- More than 50% of comas are related to head trauma or disturbances in circulatory system
  - Trauma = brain swelling
  - Can cause brain to push down on brain stem, damaging the reticular activating system (RAS), which is responsible for arousal and awareness
- Hemorrhage
  - Epidural hemorrhage (in skull, outside dura)
  - Subdural hemorrhage (inside dura, but not in brain tissue)
  - Subarachnoid hemorrhage (adjacent to brain tissue)
  - Intracerebral hemorrhage (in brain tissue)
CAUSES

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PROGNOSIS

• Generally, comas are temporary
• Rarely lasting more than 2-4 weeks
• Recovery can vary – some patients recover full autonomy and function and some require physical therapy and some only recover basic functions

• About ~40% of patients with disorders of consciousness are misdiagnosed
→ We need a more accurate assessment of consciousness!
GLASGOW COMA SCALE

- Measures the depth or severity of coma

<table>
<thead>
<tr>
<th>Motor response</th>
<th>Verbal response</th>
<th>Eye opening</th>
</tr>
</thead>
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<tr>
<td>Obeys commands</td>
<td>6</td>
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<tr>
<td>Localizes pain</td>
<td>5</td>
<td>Oriented</td>
</tr>
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<td>Withdrawals from pain</td>
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<td>Confused, disoriented</td>
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<tr>
<td>Abnormal flexion posture</td>
<td>3</td>
<td>Inappropriate words</td>
</tr>
<tr>
<td>Extensor posture</td>
<td>2</td>
<td>Incomprehensible</td>
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<td>None</td>
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<td>None</td>
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</tbody>
</table>
(SOME) TYPES OF COMA (-ISH) DISORDERS

- **Minimally conscious state** – inconsistent but clearly-distinguishable behavioral signs of consciousness
- **Persistent vegetative state** – patient is unaware of surroundings, cannot move voluntarily (breathing and circulation intact)
- **Locked-in syndrome** – person is totally paralyzed except for the eye muscles, but remains awake and alert with normal brain function (very rare)
- **Medically induced** – used to protect the brain from swelling after injury, doctors administer controlled anesthetic, only happens in ICU
- **Brain death** – irreversible unconsciousness with complete loss of brain function
LOCKED-IN SYNDROME

Prog Brain Res, 2005;150:495-511.

The locked-in syndrome: what is it like to be conscious but paralyzed and voiceless?


Author information

Abstract

The locked-in syndrome (pseudocoma) describes patients who are awake and conscious but selectively deefferented, i.e., have no means of producing speech, limb or facial movements. Acute ventral pontine lesions are its most common cause. People with such brainstem lesions often remain comatose for some days or weeks, needing artificial respiration and then gradually wake up, but remaining paralyzed and voiceless, superficially resembling patients in a vegetative state or akinetic mutism. In acute locked-in syndrome (LIS), eye-coded communication and evaluation of cognitive and emotional functioning is very limited because vigilance is fluctuating and eye movements may be inconsistent, very small, and easily exhausted. It has been shown that more than half of the time it is the family and not the physician who first realized that the patient was aware. Distressingly, recent studies reported that the diagnosis of LIS on average takes over 2.5 months. In some cases it took 4-6 years before aware and sensitive patients, locked in an immobile body, were recognized as being conscious. Once a LIS patient becomes medically stable, and given appropriate medical care, life expectancy increases to several decades. Even if the chances of good motor recovery are very limited, existing eye-controlled, computer-based communication technology currently allow the patient to control his environment, use a word processor coupled to a speech synthesizer, and access the worldwide net. Healthy individuals and medical professionals sometimes assume that the quality of life of an LIS patient is so poor that it is not worth living. On the contrary, chronic LIS patients typically self-report meaningful quality of life and their demand for euthanasia is surprisingly infrequent. Biased clinicians might provide less aggressive medical treatment and influence the family in inappropriate ways. It is important to stress that only the medically stabilized, informed LIS patient is competent to consent to or refuse life-sustaining treatment. Patients suffering from LIS should not be denied the right to die - and to die with dignity - but also, and more importantly, they should not be denied the right to live - and to live with dignity and the best possible revalidation, and pain and symptom management. In our opinion, there is an urgent need for a renewed ethical and medicolegal framework for our care of locked-in patients.
Figure 1. Flow chart of cerebral insult and coma. Vegetative state typically follows a coma; after 1 month the term "persistent vegetative state" is used; after 3 months for a non-traumatic insult or 1 year for a traumatic insult some authors use the term "permanent vegetative state", which implies no chance of recovery.
SO YOU FELL INTO A COMA

1. Assess underlying cause of coma (trauma, stroke, etc.)
2. Assess depth or severity of coma (Glasgow rating scale)
3. Recover vs. Permanent vegetative state/ brain death
TREATMENTS

• Depends on the underlying cause

• Prevent infections, provide nutrition, maintain physical health

• Physical therapy is used to prevent bone, joint, or muscle deformities

.......... How can we tell who will/can recover?
Default mode activation in different states of consciousness

(Boly et al., 2008)
IMAGING

• Measuring brain activity to assess levels of consciousness

• Functional magnetic resonance imaging (fMRI)
  • Measures blood-oxygenation levels (BOLD signal)

• Positron emission tomography (PET)
  • Measures brain metabolism

• Electroencephalogram (EEG)
  • Detects electrical activity at the surface of the brain
IMAGING: FMRI

- Measuring brain activity to assess levels of consciousness

- Default mode network/ functional resting state
  - Posterior cingulate cortex/ precuneus, medial prefrontal cortex, bilateral temporoparietal junctions

- Slow but spatially accurate
IMAGING: PET

- Measuring brain activity to assess levels of consciousness

- PET scans: measuring brain metabolism
  - Uses a radioactive tracer - can be targeted to specific molecules (glucose analogs are common)
EEG

- Measuring brain activity to assess levels of consciousness
- EEG: measuring electrical activity at the surface of the brain
- Fast but spatially ambiguous (vs. fMRI)
CEREBRAL METABOLISM IN VARIOUS STATES OF CONSCIOUSNESS

Laureys, Owen, & Schiff (2004)
CEREBRAL METABOLISM IN VARIOUS STATES OF CONSCIOUSNESS

Laureys, Owen, & Schiff (2004)
CEREBRAL METABOLISM IN VARIOUS STATES OF CONSCIOUSNESS

% cerebral metabolism in various states of consciousness

Normal vs. Coma vs. Locked-in

Laureys, Owen, & Schiff (2004)
While reviewing the clinical applications of fMRI, Dr. Owen had a “crisis of confidence”
fMRI confirms what we know from brain mapping studies, but it isn’t doing anything new
There really aren’t any clinical applications

Let’s try something new: fMRI in comatose patients
CASE STUDIES

- Patient: age 26, female
- Cause: viral infection, resulting in vegetative state
- PETscan
- fusiform face area (FFA) → familiar faces

CASE STUDIES

• Patient: age 26, female
  • Cause: viral infection, resulting in vegetative state
  • PET scan
  • fusiform face area (FFA) → familiar faces

• Patient: age 30, male
  • Cause: stroke
  • Moving from visual to auditory tests
  • Prompt: “the dates and pears are in the bowl”
    • Ambiguity forces the brain to work harder and shows up in fMRI patterns during comprehension

CASE STUDY: PATIENT 23

• Because fMRI’s require a few sections to register changes in blood flow, patients have to focus for 30 seconds on their answer and rest for 30 seconds, with lots of repetition

  • (This is a realllllly long time & requires a lot of effort and concentration)

Imagine playing tennis

http://www.sciencemag.org/content/347/6220/915.full
Imagine walking through your house

http://www.sciencemag.org/content/329/5994/1351.full.html
CASE STUDY

• Prompt: imagine playing tennis and walking through the rooms of your house

Normal result: activity in supplementary motor area and parahippocampal gyrus

CASE STUDY

- Patient: age 23, female
- Cause: traffic accident, unresponsive 5 months
- Prompt: imagine playing tennis and walking through the rooms of her house

Dr. Owen: “this woman’s brain activity shows she is conscious”

A LARGER STUDY

- 5 out of 54 patients in a vegetative or minimally conscious state respond with brain activity approaching normal.
- **Yes** and **no** questions: imaging playing tennis for yes, navigating your house for no.
- Ask questions the scoring technician doesn’t know:

  - Is your father’s name Thomas? No
  - If your father’s name Alexander? Yes
  - Do you have any brothers? Yes
  - Do you have any sisters? No
SUMMARY

Patterns of activation in:

supplementary motor (playing tennis = yes)

parahippocampal gyrus (walking through your house = no)

For patient vs. control
CRITICISMS

- Dr. Nachev criticizes the work for assuming “consciousness is a binary phenomenon”
  - Patients can show limited responsiveness without being conscious

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  • Patients can show limited responsiveness without being conscious

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• [Link to Scientific American article]
CRITICISMS

• Dr. Nachev criticizes the work for assuming “consciousness is a binary phenomenon”
  • Patients can show limited responsiveness without being conscious

• Dr. Owen agrees consciousness is not an “on or off thing”, but is an emergent property of many brain modules working together

→ “emergent property” refers to the properties that come out of a system, which are more than the sum of its parts
  → A property that a collection or complex system has, but the individuals parts do not

RESPONSE TO CRITICISM

1. A person needs long-term memory to know what tennis is
2. Short-term memory to remember the question and intend to give an answer
   → Enough modules are at work to qualify as “conscious”

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RESPONSE TO CRITICISM

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   • Dr. Owen takes a “know it if you see it approach”, and is not worried about defining a threshold
   • Responding to commands and questions is an “undeniably conscious activity”
     • Dr. Owen estimates about 20% of vegetative patients are capable of communicating
     • “What we’re seeing here is a population of totally locked-in patients”

“In the end, if they say they have no reason to believe the patient is conscious, I say ‘fine, but I have no reason to believe you are either’” – Dr. Owen

FAMILY’S RESPONSE

• For one family member, technology could “steal the hope” she had that her relative would recover.

• Another family member felt dread for another reason: her daughter might actually have had some awareness during years of being considered vegetative.

“For us it would just make us feel so much worse. My heart would bleed for Lavenna to think there’s been something going on there all this time and she’s still trapped where she is... and when I hear something like that [fMRI] I think... my poor girl, you’ve been suffering, I would see it as suffering, like the mental torture... And a feeling of uncertainty and almost dread in a way... it’s not something that I could personally put Lavenna through.”

“We’d feel so guilty that we haven’t tried harder to get through to her, but yet we know that everything has been done, you know...
FOLLOW-UP ON DR. OWEN’S PATIENTS

• So far, the technology has done little
  • The first patient in the tennis study died last year
  • Patient 23 was only assessed once (for logistical and financial reasons)
• Even if a person in a vegetative state is “found”, there is no guarantee he/she will be able to return to a normal life

• However, clarifying a patient’s state of consciousness helps families deal with tragedy

“They want to know what the diagnosis really is so they can move on and deal with that”

“Doubt and uncertainty are always bad things”
FAMILY’S RESPONSE

“Scientists can say ‘yes there’s something going on there but I’m sorry Mrs. X we can’t do anything to help your daughter out of it”

It’s not practical to be hooked up to an fMRI all the time – expense and access are an issue

“If you knew your loved one could communicate ... that would be great, [but] how do you accommodate that ... you can’t have someone in an MRI scanner for the rest of their life ... [what] if there is something there but there’s not a damn thing that we can do to get to her to reach her.”

BRAIN-COMPUTER INTERFACES (BCI)

• Behaviors or thoughts trigger measurable changes in brain activity, which can be converted into a signal
  • Not dependent on motor responses (which are often not possible)

→ More accurate diagnoses & better patient care

http://www.medicalnewstoday.com/articles/192522.php
Probing command following in patients with disorders of consciousness using a brain-computer interface

Dorothee Lulé, Quentin Noirhomme, Sonja C. Kleih, Camille Chatelle, Sebastian Halder, Athena Demertzis, Marie-Aurélie Bruno, Olivia Gossieres, Audrey Vanhaudenhuyse, Caroline Schnakers, Marie Thonnard, Andrea Soddu, Andrea Kübler, Steven Laureys

ARTICLE INFO

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Keywords:
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EEG
BCI
P300
Standard oddball

HIGHLIGHTS

- Brain–computer interfaces (BCIs) are suggested for testing cognitive abilities in patients with disorders of consciousness.
- Brain injured patients can present distorted ERP in response to an oddball but detectable with a BCI.
- Brain injured patients can demonstrate command following with a BCI.

ABSTRACT

Objective: To determine if brain–computer interfaces (BCIs) could serve as supportive tools for detecting consciousness in patients with disorders of consciousness by detecting response to command and communication.

Methods: We tested a 4-choice auditory oddball EEG–BCI paradigm on 16 healthy subjects and 18 patients in a vegetative state/insensitive wakefulness syndrome, in a minimally conscious state (MCS), and in locked-in syndrome (LIS). Subjects were exposed to 4 training trials and 10–12 questions.

Results: Thirteen healthy subjects and one LIS patient were able to communicate using the BCI. Four of those did not present with a P3. One MCS patient showed command following with the BCI while no behavioral response could be detected at bedside. All other patients did not show any response to command and could not communicate with the BCI.

Conclusion: The present study provides evidence that EEG based BCI can detect command following in patients with altered states of consciousness and functional communication in patients with locked-in syndrome. However, BCI approaches have to be simplified to increase sensitivity.

Significance: For some patients without any clinical sign of consciousness, a BCI might bear the potential to employ a “yes–no” spelling device offering the hope of functional interactive communication.

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FAMILY’S RESPONSE

Many families alluded to better everyday care and support for patients as they live lives bound by their condition as more important than grand technological development.

While new technological advances are exciting science, not everyone is so excited that it will change their life and that of their loved one.

FOLLOW-UP ON DR. OWEN’S PATIENTS

• Should these results influence a family or clinician’s decision to end a life?

• If a patient answers questions, they move from the “possibly allowed to die” to the “not generally allowed to die” category”, says Owens

• Some families will have hope and solace, but some may feel burdened by ambiguous communication
ETHICAL CONCERNS

• How do you decide whether to continue treatment/maintenance?

• In the even of:
  • Brain death
  • Permanent vegetative state
  • Recovery is not likely (low chances of regaining consciousness) as measured via brain scans

• What do you consider to be “alive”?

• What about religious beliefs?
• What about financial issues?
ETHICAL CONCERNS

• Should we “ask” patients if they want to be kept alive?

• How can you be sure they understand the complexities of that question?
  • Issues of “informed consent”

• How reliable does your question/answer method have to be?
LEGAL CONCERNS

• The law:
  
  • You can refuse treatment that would sustain your life
  
  • But what about when you lack legal capacity to make that decision (i.e. loss of consciousness)?
    • Parents & legal guardians usually have to make those decisions for minors
    • For adults with no guardian, most states provide no clear answer as to who can make decisions for them
LEGAL CONCERNS

• When are you allowed to withdraw treatment?

• Possible courses of action
  • Active vs. passive euthanasia
    • Withdrawing treatment vs. refusing or abstaining treatment
  • “Do not resuscitate (DNR)” orders
  • Palliative care = focus on providing relief from symptoms (mostly pain)
LEGAL CONCERNS

• Priority is usually given to the individual when making these decisions
  • “living wills” = directives for patient care when the patient is unresponsive/unable to communicate

• Providers can refuse to comply if they face an issue of conscience, but must make a reasonable effort to transfer the individual into the care of a provider who will comply
Dr. Owen:

“It’s too early to think about such applications”

“We need to be absolutely sure that we know what to do with the answers before we go down this road” he warns.

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Podcast:
http://www.nature.com/news/neuroscience-the-mind-reader-1.10816

GLOBAL BRAIN METABOLISM

• At highest levels of awareness, global brain metabolism is intermediate.

• At low and high brain metabolism, awareness is low.

**FIGURE 1.** Relationships between global brain metabolism and awareness. The link between global brain energy consumption and awareness is complex. Evidence exists that both states of extremely low and extremely high global brain metabolism are associated with small amounts of awareness. An intermediate level of brain metabolism, corresponding to a proper balance between inhibitory and excitatory neural activity, seems to be necessary to allow the genesis of awareness.
LEGAL CONCERNS

- Documentation of death through brain studies is required when:

1. Organs will be removed for transplantation
2. The patient's death may become a criminal matter (ex. trauma from car accident)
3. Information is necessary to resolve disagreements between physician and family members