



Brain-Computer Interface and States of Vigilance



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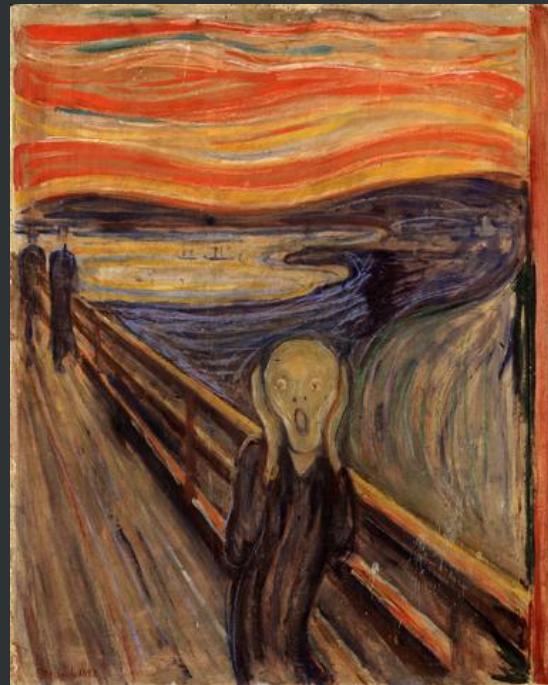
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Crucial question



How to communicate with someone
who *cannot* communicate?

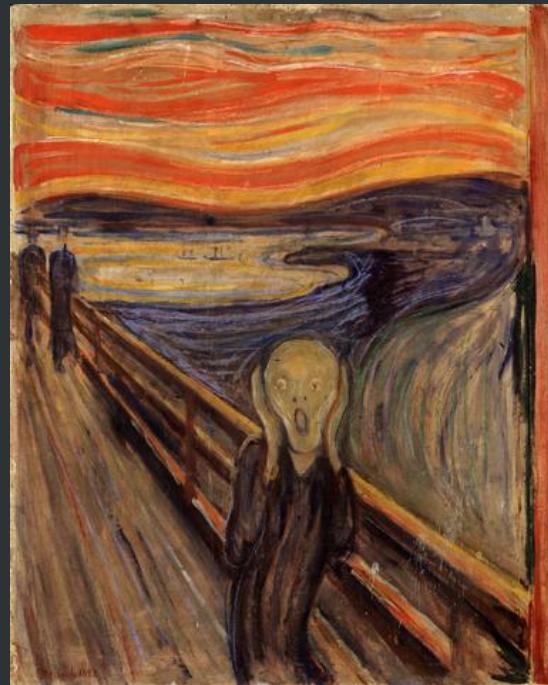




Crucial question



How to communicate with someone
who *cannot* communicate?



... communicate with their brain!



BCI Outline

- 
- A decorative horizontal bar at the bottom of the slide consists of a thick green line followed by six smaller colored squares: dark teal, light green, medium blue, magenta, orange, and dark blue.
1. Identifying the (sub)population
 2. Identifying biomarkers
 3. Modelling (= decoder)
 4. Applications: detection, communication & rehabilitation

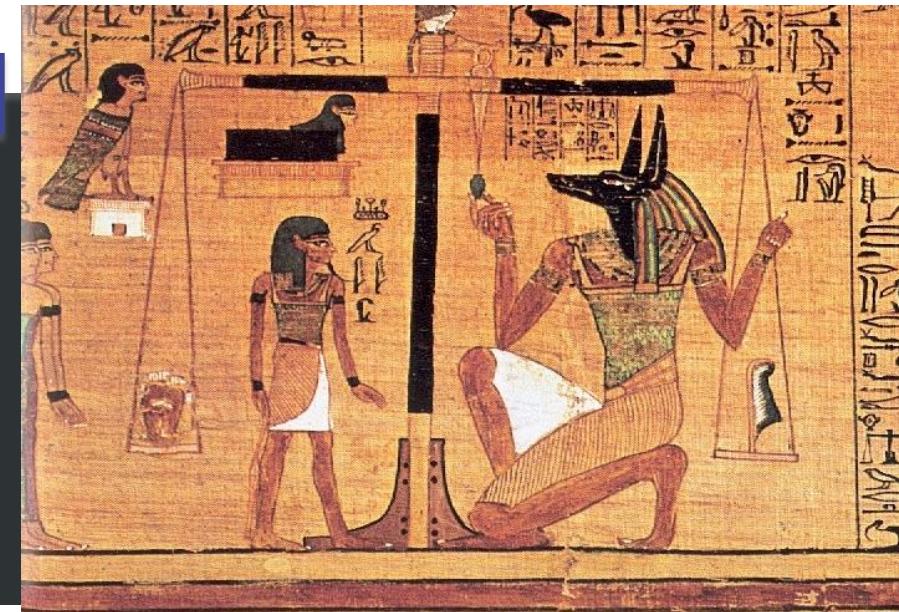


Overview

- 
- A decorative horizontal bar at the bottom of the slide consists of a thick grey line above a thin white line. Along the thin white line are six small colored squares: lime green, dark teal, light green, bright blue, magenta, and dark blue.
1. Identifying the population
 - Disorders of consciousness
 - Clinical diagnoses
 2. Identifying biomarkers
 - Functional neuroimaging and EEG
 3. Modelling
 - Brain-computer interfaces (BCI)
 4. Applications: communication & rehabilitation
 - Conclusions



Disorders of consciousness

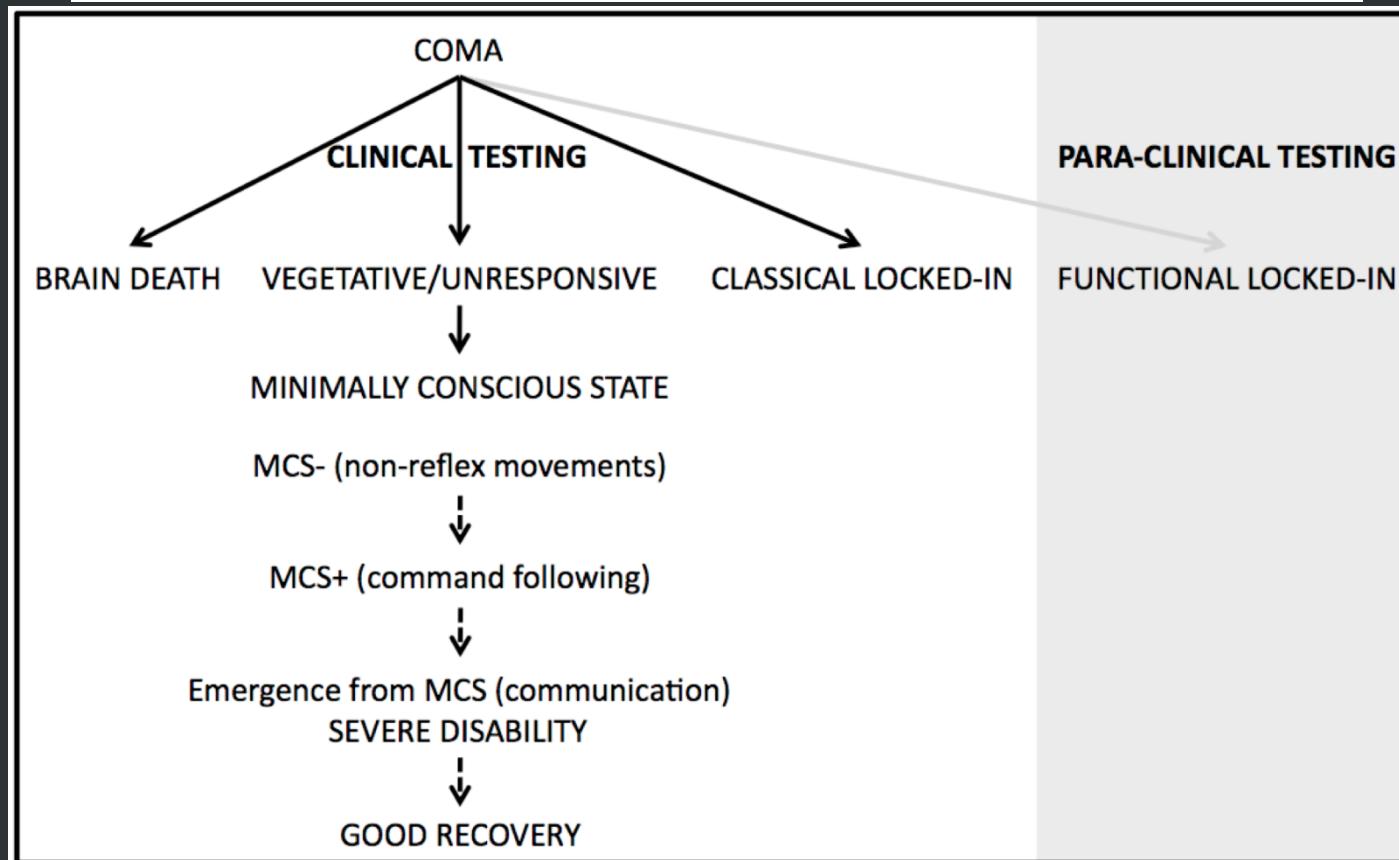


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Disorders of consciousness (DOC)

From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness



A new name for «vegetative»: unresponsive



BMC Medicine

Highly accessed Open Access

Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome

Steven Laureys¹✉, Gastone G Celesia²✉, Francois Cohadon³✉, Jan Larijsen⁴✉, José León-Carrión⁵✉, Walter G Sannita^{6,7}✉, Leon Sazbon⁸✉, Erich Schmutzhard⁹✉, Klaus R von Wild^{10,11}✉, Adam Zeman¹²✉ and Giuliano Dolce¹³✉ for the European Task Force on Disorders of Consciousness¹✉

<http://www.biomedcentral.com/1741-7015/8/68>



"There's nothing we can do...
he'll always be a vegetable."



Disorders of consciousness



Coma: diagnostic criteria (signs)

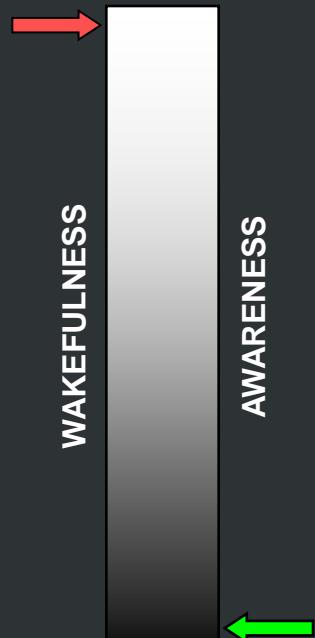


- No eye opening even with stimulation
- No sign of awareness of self or environment
- Transitory state: from 1 hour to ~**1 month**
- Often due to **brainstem** damages
- Respiratory assistance necessary



Vegetative state/Unresponsive wakefulness syndrome

- No sign of awareness of self or environment
- No coherent and voluntary responses to visual, auditive, tactile or nociceptive stimulations
- **Wake-sleep cycle**
- Hypothalamic and brainstem functions (ie, can breathe without help)
- Rarely: vocalizations, emotions
- Can be stable or evolve (or regress...)

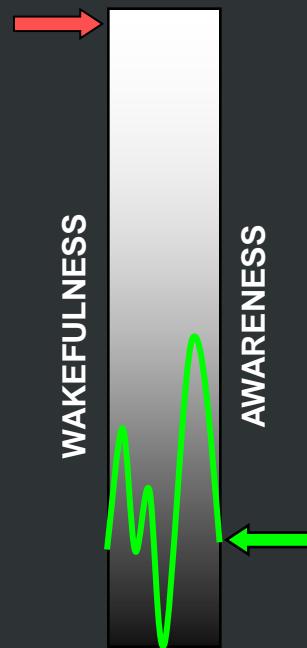


Minimally conscious state

- Awareness of self and environment:
 - Visual **pursuit** and/or fixation (mirror, person or object)
 - Appropriate smiling or crying
 - Object **localization**
 - Object manipulation
 - **Command following**
 - Non-functional communication (out-of-context)
 - Intelligible verbalizations

Emergence from MCS: **functional** communication or functional object use

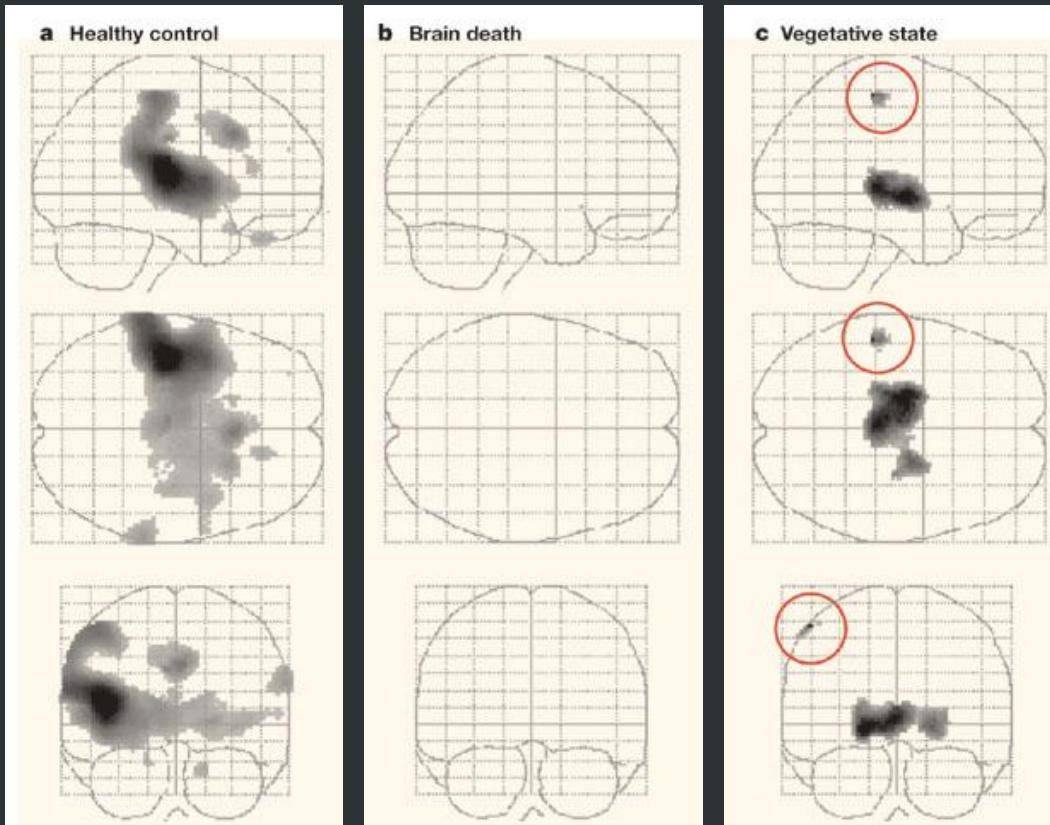
Beware of **aphasia**!



Do they feel pain?



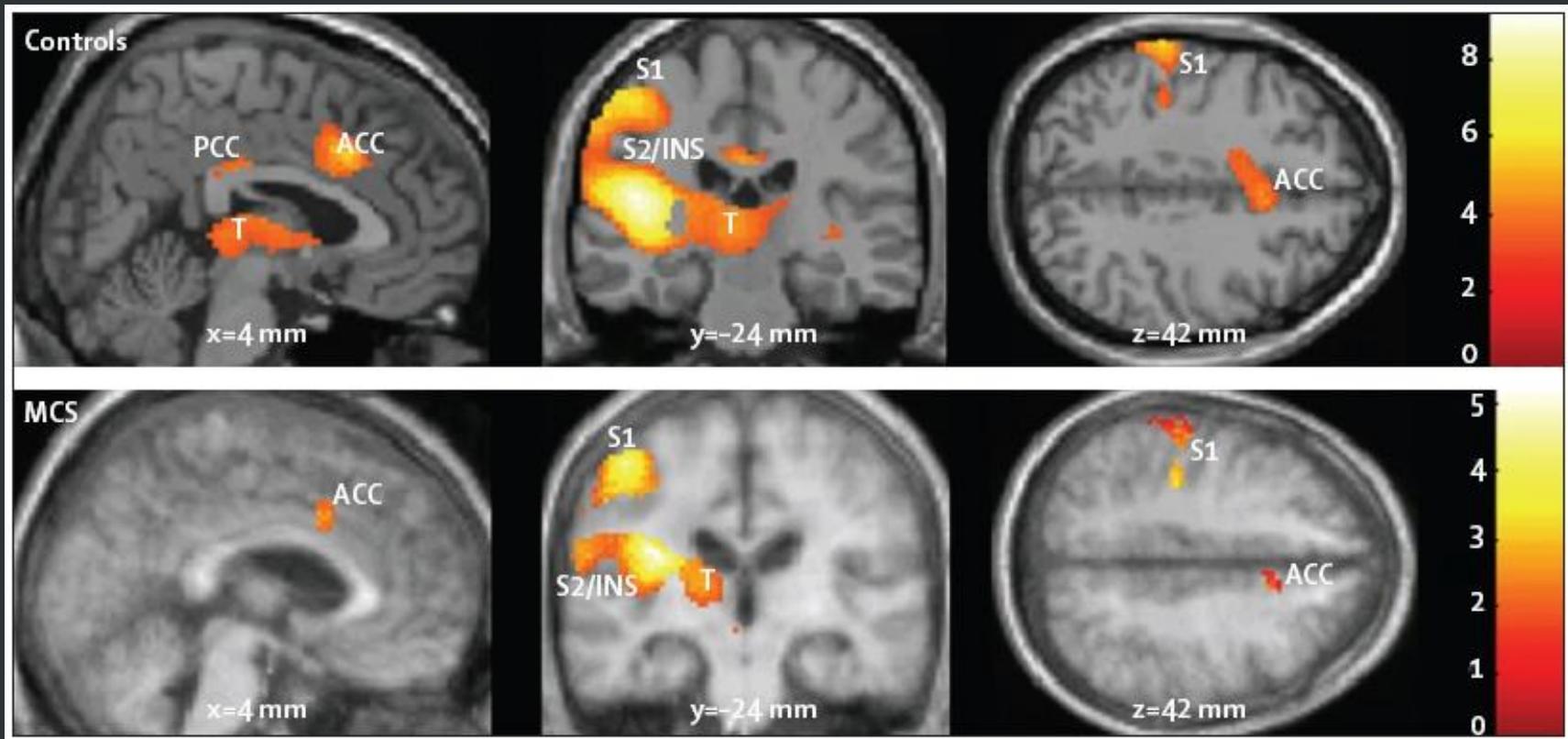
Noxious electrical stimulation



Low level primary sensory area
Activation
But **no secondary sensory** area

⇒ **Functionally disconnected cortical activation**

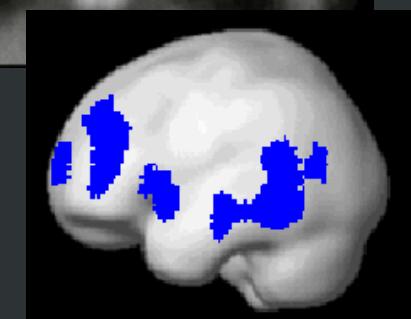
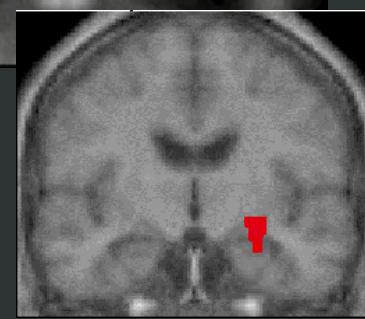
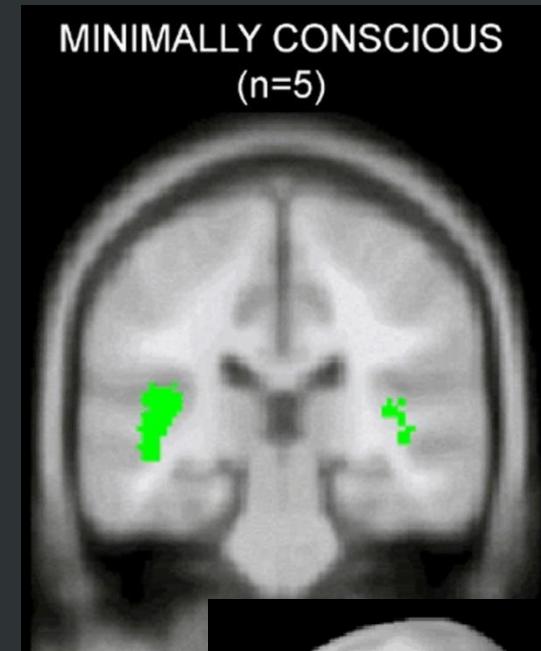
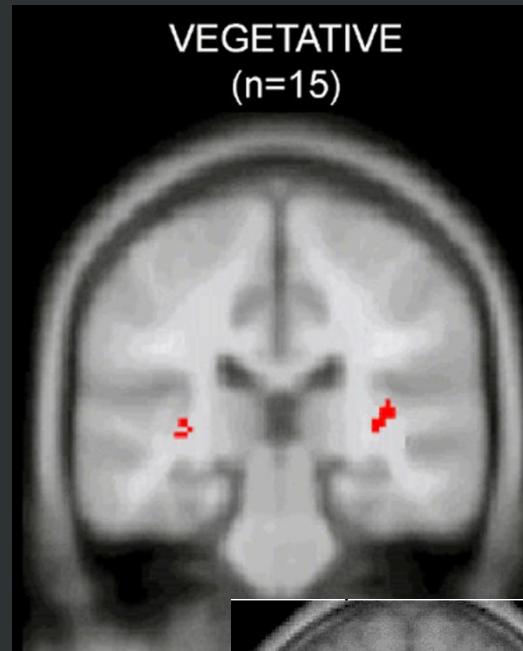
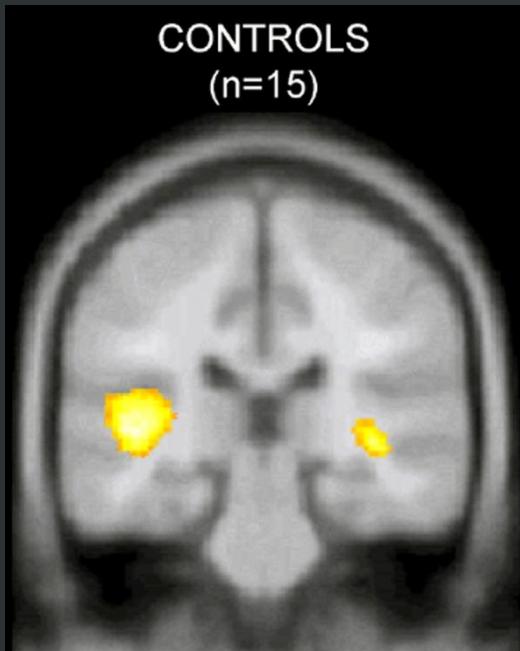
Pain in minimally conscious state



<http://neurology.thelancet.com>

Laureys et al, *Neuroimage*, 2002
Boly et al *Lancet Neurology*, 2008

Auditory perception



DISCONNECTED

CONNECTED

Laureys et al., *Brain*, 2000

Boly et al., *Archives of Neurology*, 2004



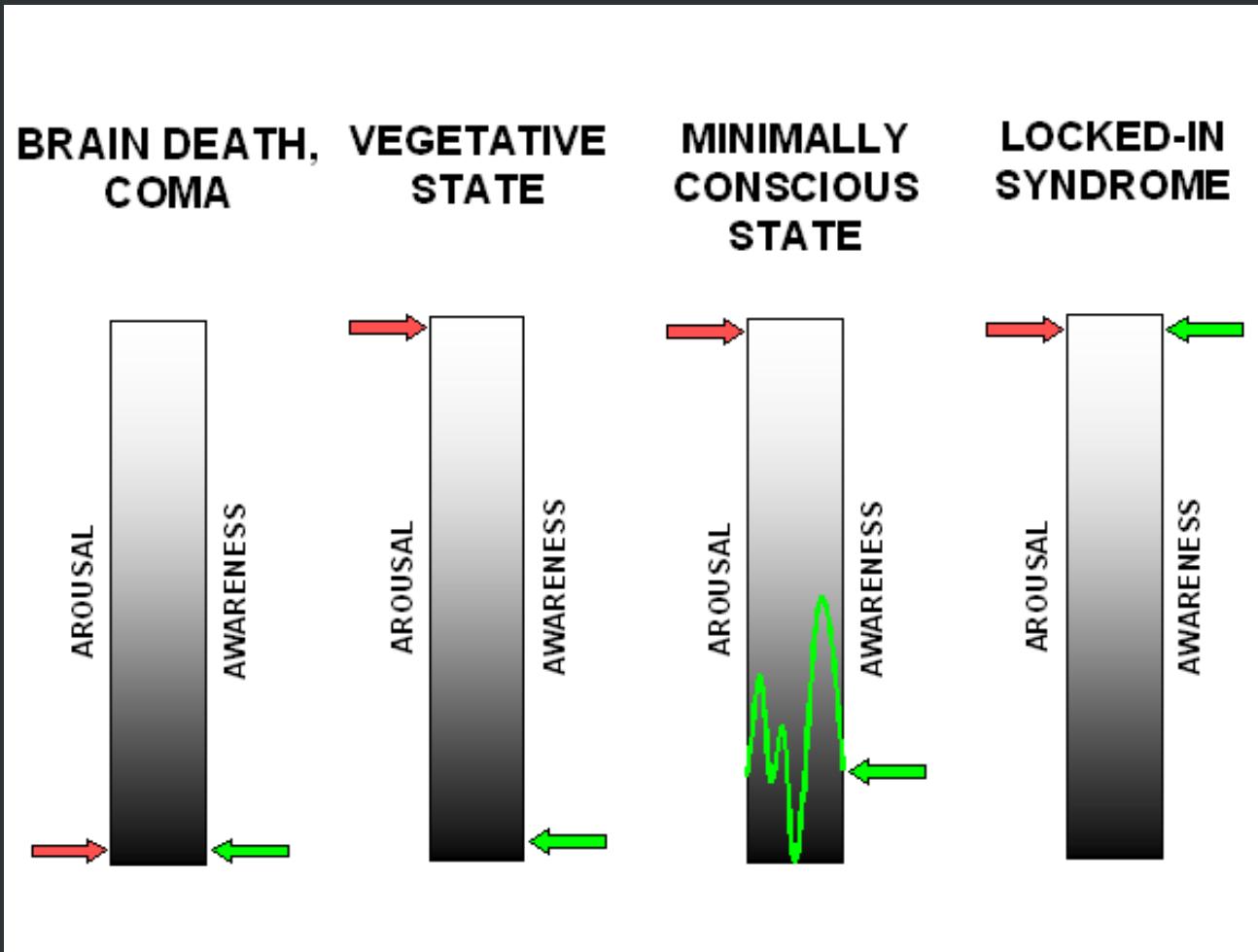
Locked-in syndrome



- Spontaneous eye opening
- Aphony or hypophonia
- Quadriplegia or quadriparesia
- Communication with horizontal or vertical eye movements or blinking
- Preservation of consciousness and cognitive functions



DOC summary



Locked-in syndrome





Clinical Diagnosis

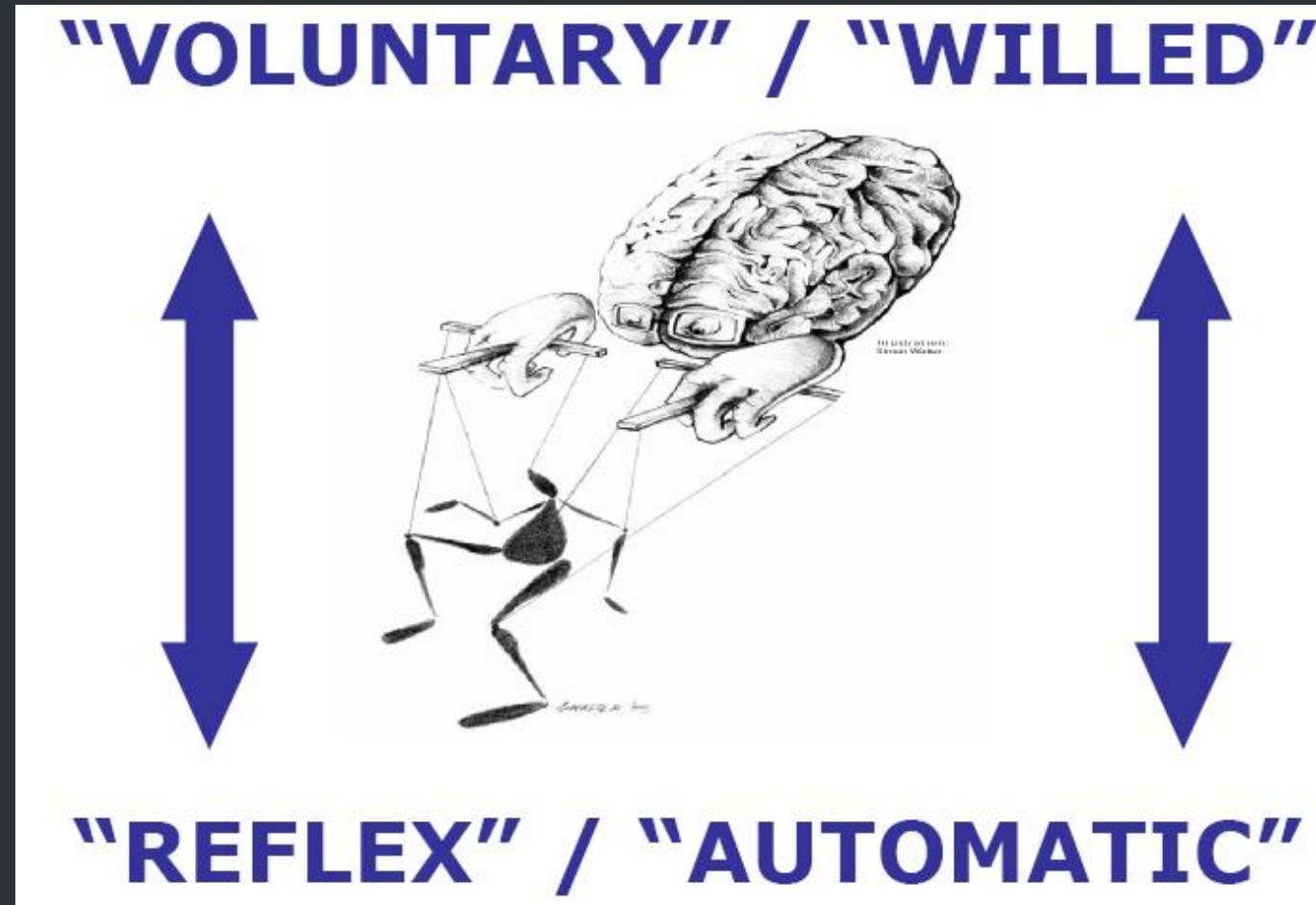


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“Reflex” versus “Voluntary”



“Reflex” versus “Voluntary”





Diagnostic error

n=103 post-comatose patients

- 45 clinical consensus diagnosis 'vegetative state'
- 18 signs of awareness (Coma Recovery Scale-Revise)



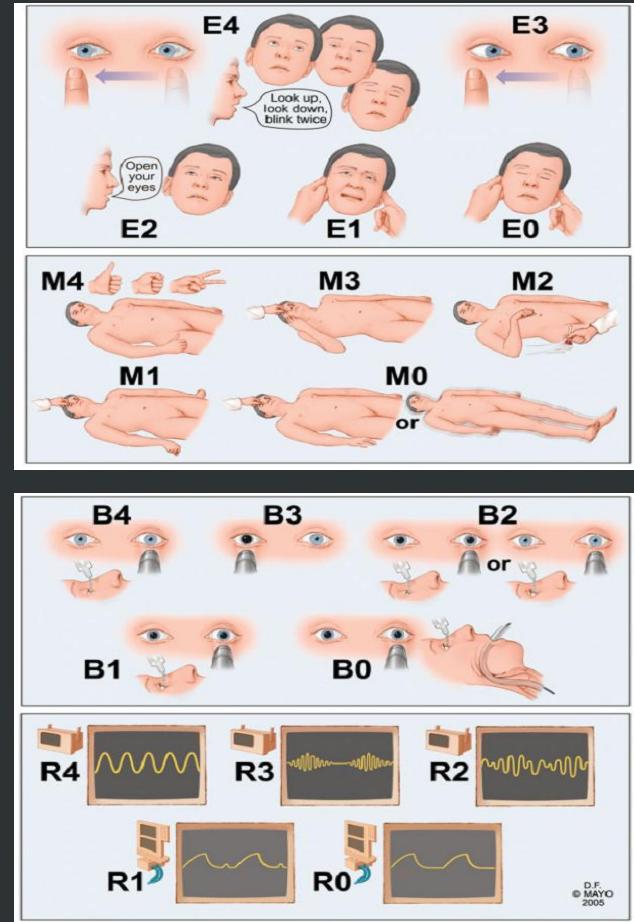
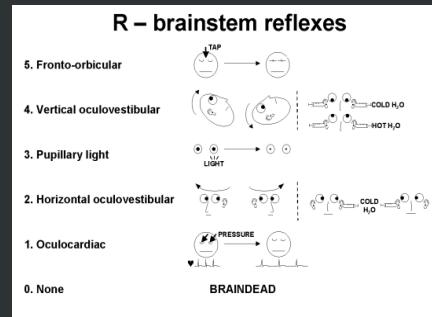
40% potential misdiagnosis





GCS/GLS/FOUR

E – eye opening	
AROUSAL	C. Not assessable
	4. Spontaneous
	3. To speech
	2. To pain
	1. None
T. Not assessable	
AWARENESS	5. Oriented conversation
	4. Confused speech
	3. Inappropriate words
	2. Incomprehensible sounds
	1. None
V – verbal response	
AWARENESS	6. Obeys simple commands
	5. Localizes pain
	4. Withdraws (normal flexion)
	3. Stereotyped flexion
	2. Stereotyped extension
	1. None
M – motor response	



Wijndicks et al., Ann Neurol (2005)
Teasdale G, Jennett B, Lancet (1974)
Born, Acta Neurochir (1988)



GCS, GLS or FOUR?

n=60

GCS : 29 diagnosed
“vegetative”/unresponsive

FOUR : 24 PVS/UWS

Schnakers et al, Annals of Neurology, 2006

n=146

131 intubated (74%)

Inter-rater reliability

- GCS (κ 0.65), GLS (κ 0.66),
FOUR (κ 0.75)

Outcome prediction

- GCS \approx GLS \approx FOUR

Different sensitivity to subpopulations:

- GCS: 71 diagnosed “vegetative”/unresponsive
- FOUR: identified 8 MCS-
(eye tracking - 11%)

Bruno et al, Neurocritical Care, 2011

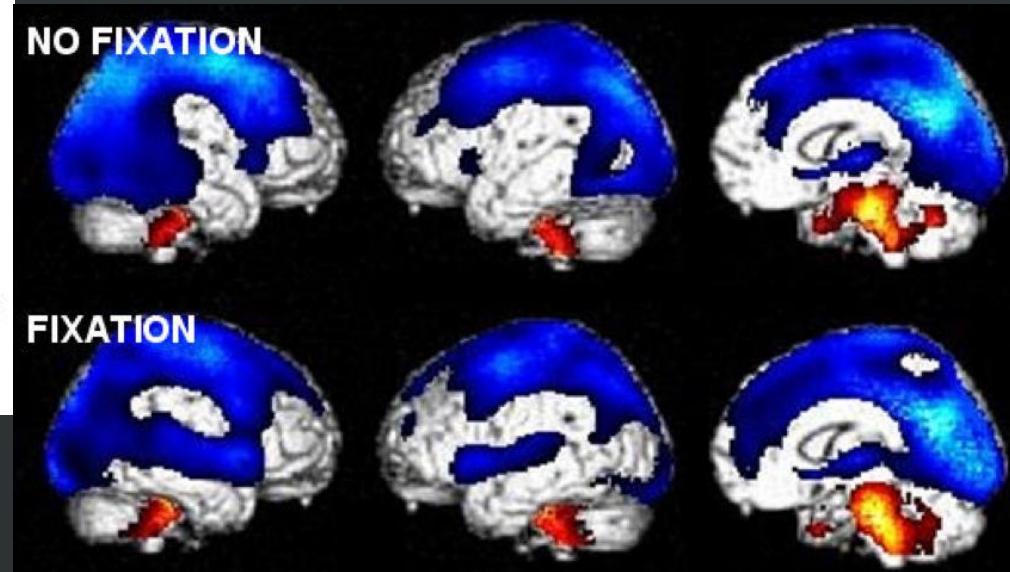
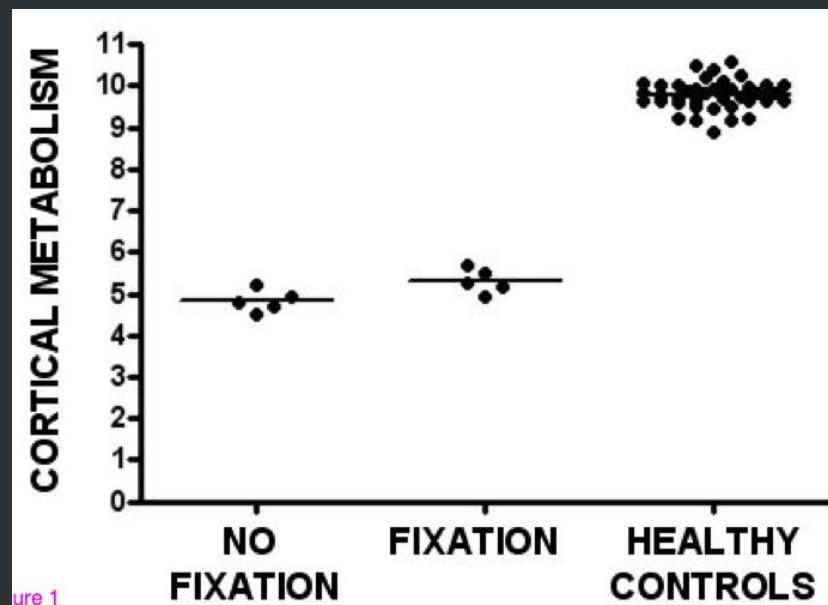


Coma recovery scale revised

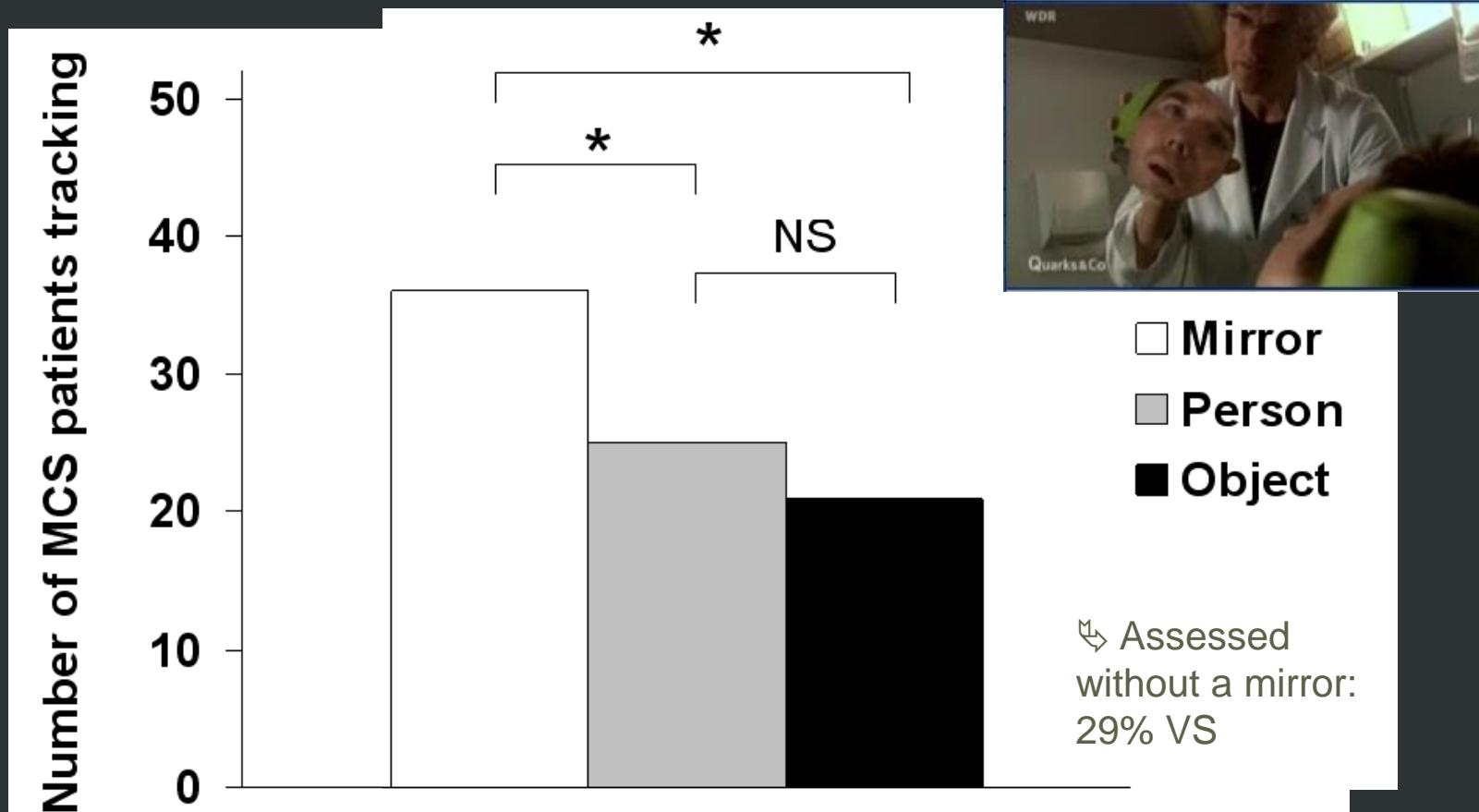


JFK COMA RECOVERY SCALE - REVISED ©2004									
Record Form									
Patient:	Date:								
AUDITORY FUNCTION SCALE									
4 - Consistent Movement to Command *									
3 - Reproducible Movement to Command *									
2 - Localization to Sound									
1 - Auditory Startle									
0 - None									
VISUAL FUNCTION SCALE									
5 - Object Recognition *									
4 - Object Localization: Reaching *									
3 - Visual Pursuit *									
2 - Fixation *									
1 - Visual Startle									
0 - None									
MOTOR FUNCTION SCALE									
6 - Functional Object Use †									
5 - Automatic Motor Response *									
4 - Object Manipulation *									
3 - Localization to Noxious Stimulation *									
2 - Flexion Withdrawal									
1 - Abnormal Posturing									
0 - None/Flaccid									
OROMOTOR/VERBAL FUNCTION SCALE									
3 - Intelligible Verbalization *									
2 - Vocalization/Oral Movement									
1 - Oral Reflexive Movement									
0 - None									
COMMUNICATION SCALE									
2 - Functional: Accurate †									
1 - Non-Functional: Intentional *									
0 - None									
AROUSAL SCALE									
3 - Attention									
2 - Eye Opening w/o Stimulation									
1 - Eye Opening with Stimulation									
0 - Unarousable									
TOTAL SCORE									

Visual fixation = reflex

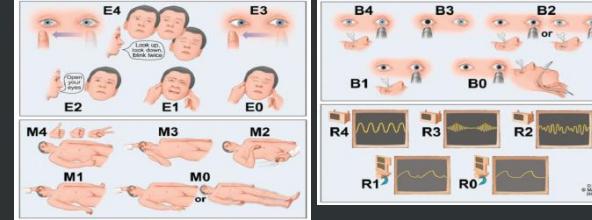


Visual pursuit: use a **mirror!**



New knowledge, new scales

- FOUR
- ↳ Visual subscale → LIS detection



- CRS-R
- ↳ MCS criteria
- ↳ Better diagnosis sensitivity

- Visual pursuit → use a mirror!
- Ambiguous signs of consciousness : e.g. visual fixation

JFK COMA RECOVERY SCALE - REVISED

This form should only be used in association with the "CRS-R ADMINISTRATION AND SCORING GUIDELINES" which provide instructions for the administration of the JFK CRSS-R.

Patient:	Diagnosis:	Etiology:														
Date of Coma:	Date of Admission:															
Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16

ADDITIONAL FUNCTION SCALE

1-4: Compliant Movements to Command
5-8: Noncompliant Movements to Command
9-12: Localization to Sound
13-16: Localization to Pain

VISUAL FUNCTION SCALE

R: Color Recognition *
R: Object Recognition *
R: Object Localizing *
R: Visual Pursuit *
R: Visual Fixation *
R: Visual Startle *

MOTOR FUNCTION SCALE

R: Functional Object Use
R: Unfunctional Object Use
R: Automatic Movement *
R: Chained Manipulation *
R: Spontaneous Movement *
R: Passive Withdrawal
R: Agitated Withdrawal

LESION-UNIVERSAL FUNCTION SCALE

1-2: Inappropriate Verbalization *
1-2: Inappropriate Physical Response *
1-2: Oral Reflexive Movement
1-2: Trunk Reflexes

COMMUNICATION SCALE

1-2: Functional: Auditory
1-2: Functional: Visual
1-2: Nonfunctional: Auditory
1-2: Nonfunctional: Visual

AVOIDANCE SCALE

1-2: Eye Closing with Stimulation
1-2: Eye Opening with Stimulation
1-2: Eye Closing without Stimulation

TOTAL SCORE

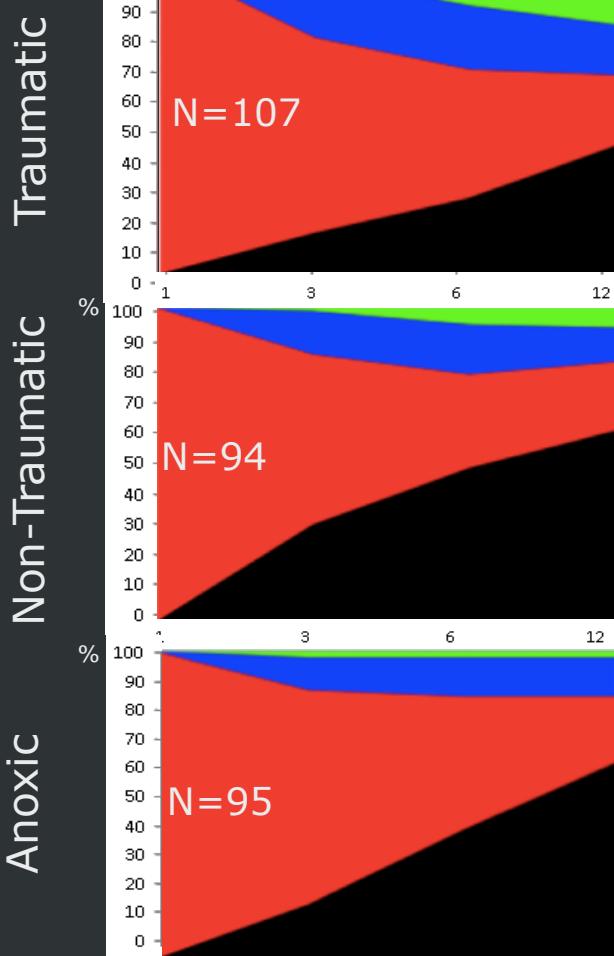
Score emerging from SCS
Interpretation: 1



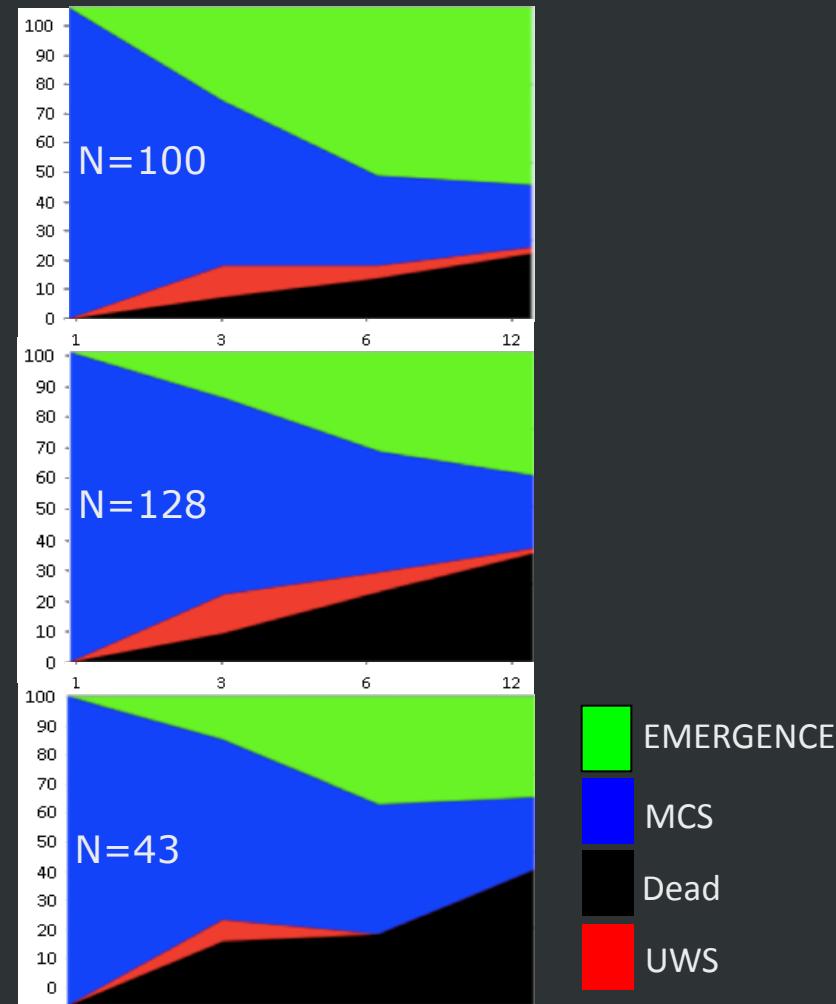
OUTCOME (Projet fédéral Belge)



Unresponsive state (n=296)

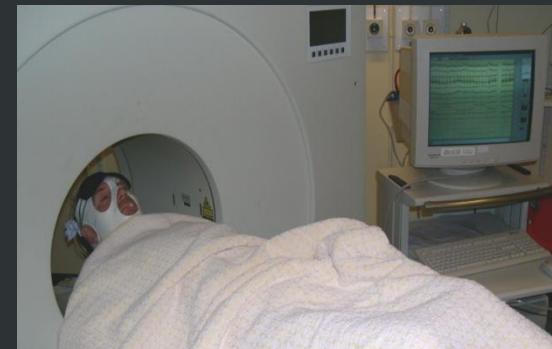
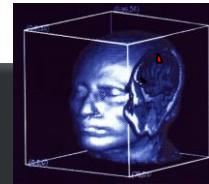


Minimally conscious state (n=271)





Neuroimaging and biomarkers

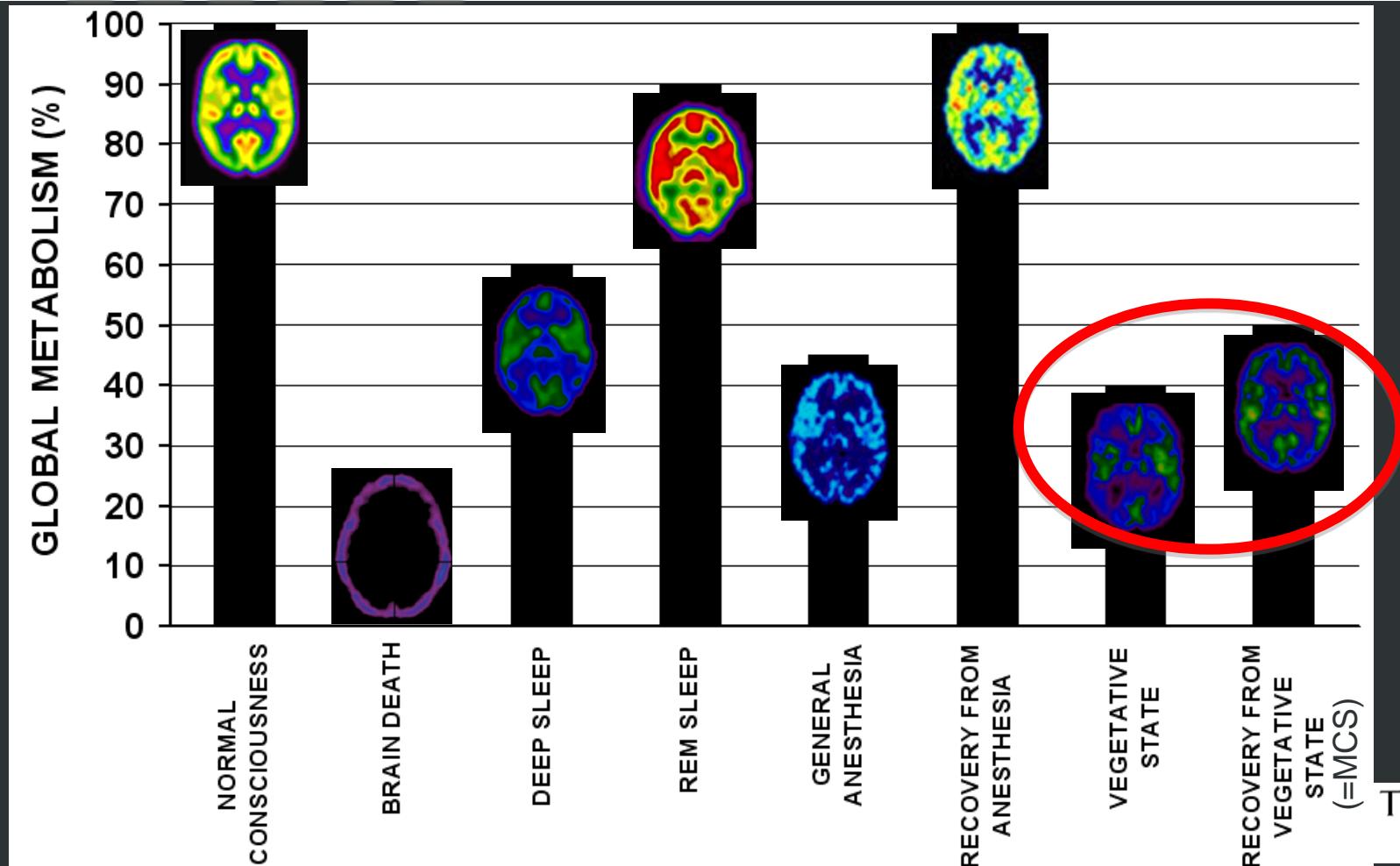


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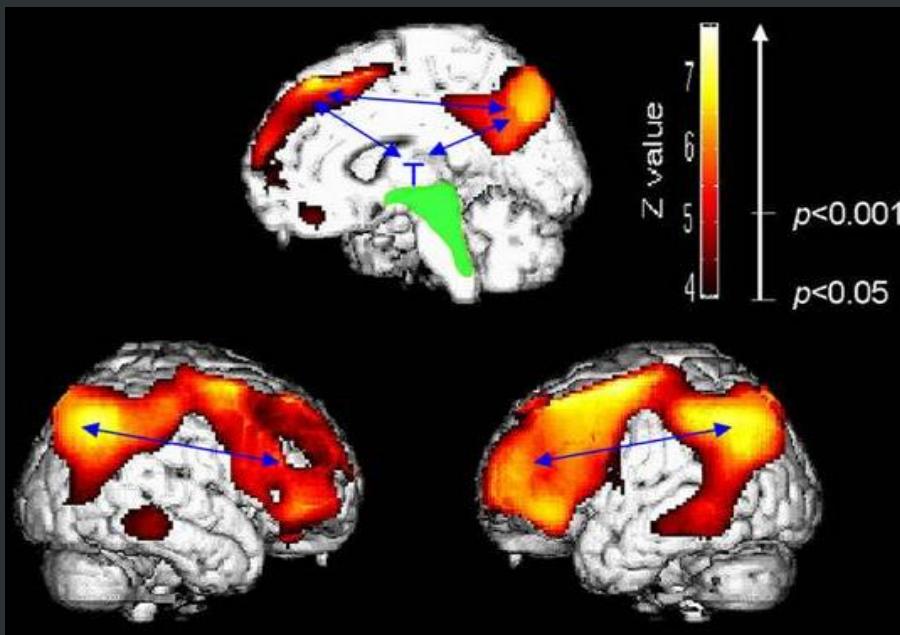
Consciousness ≠ global brain function



Consciousness ≈ frontoparietal

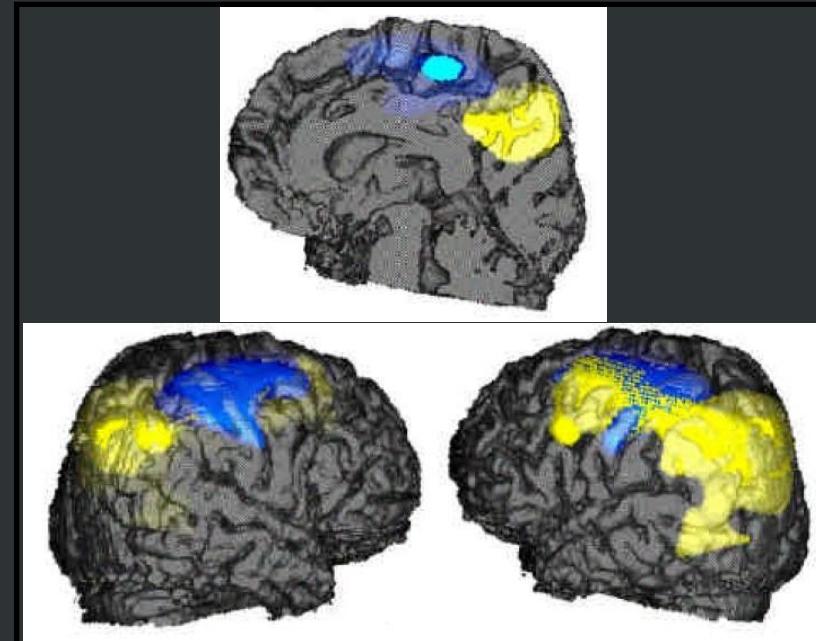


areas that are systematically dysfunctional in the unresponsive state



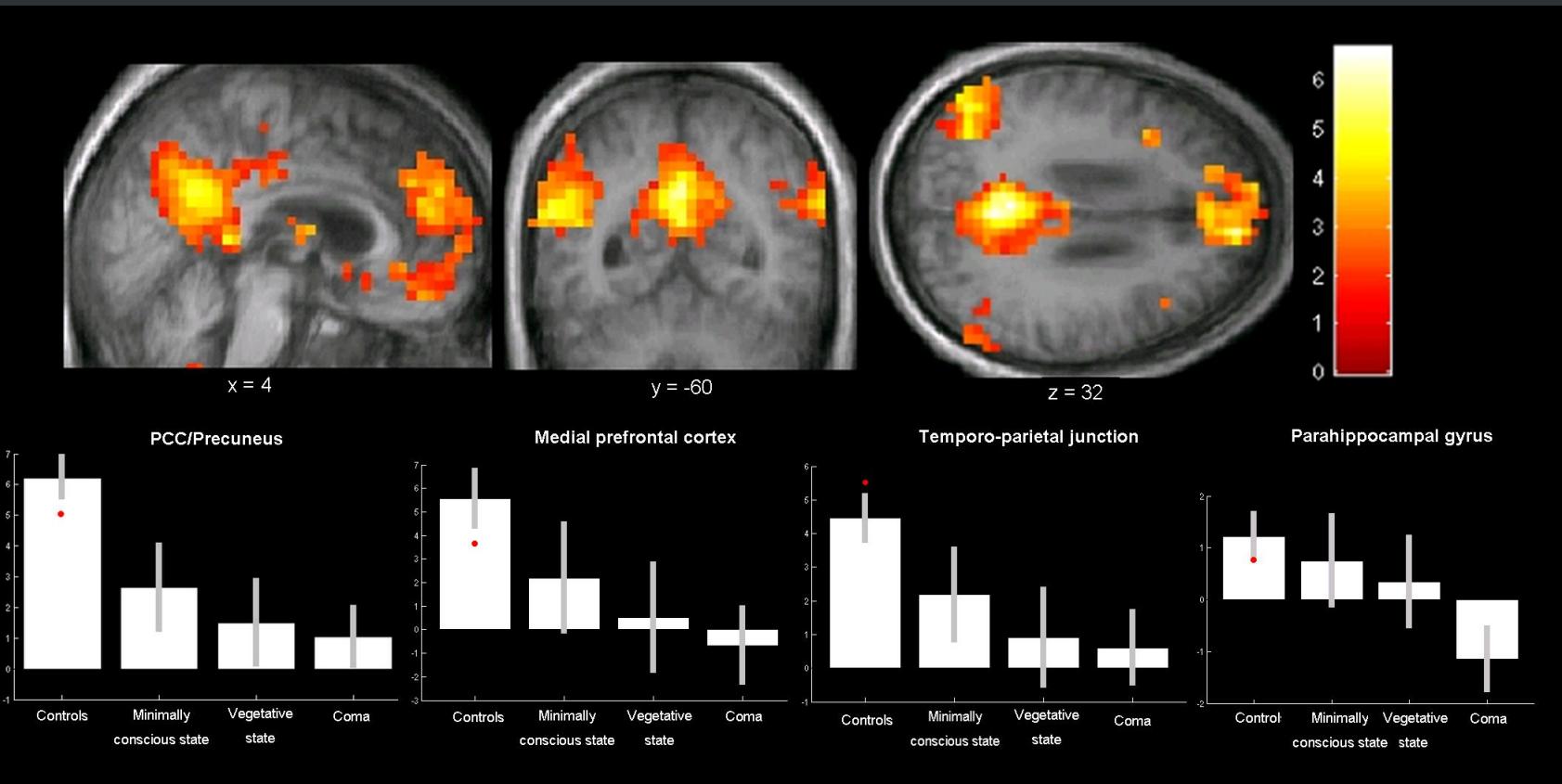
Laureys et al, Neuroimage 1999

areas that recover metabolism **after recovery** from the unresponsive state



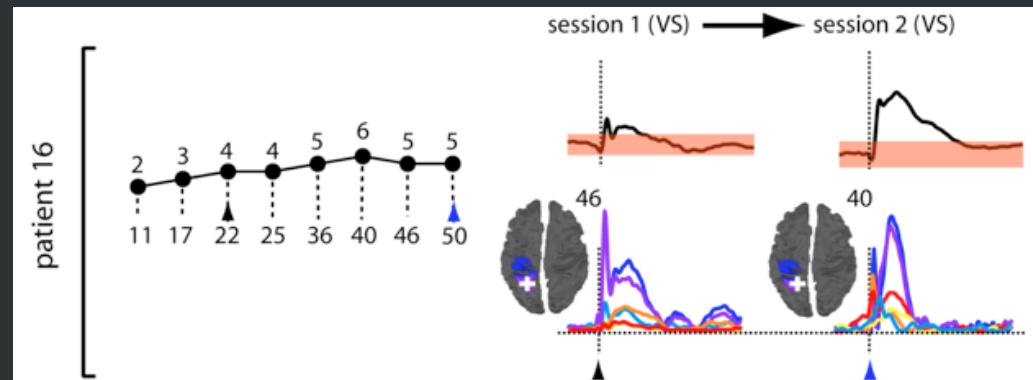
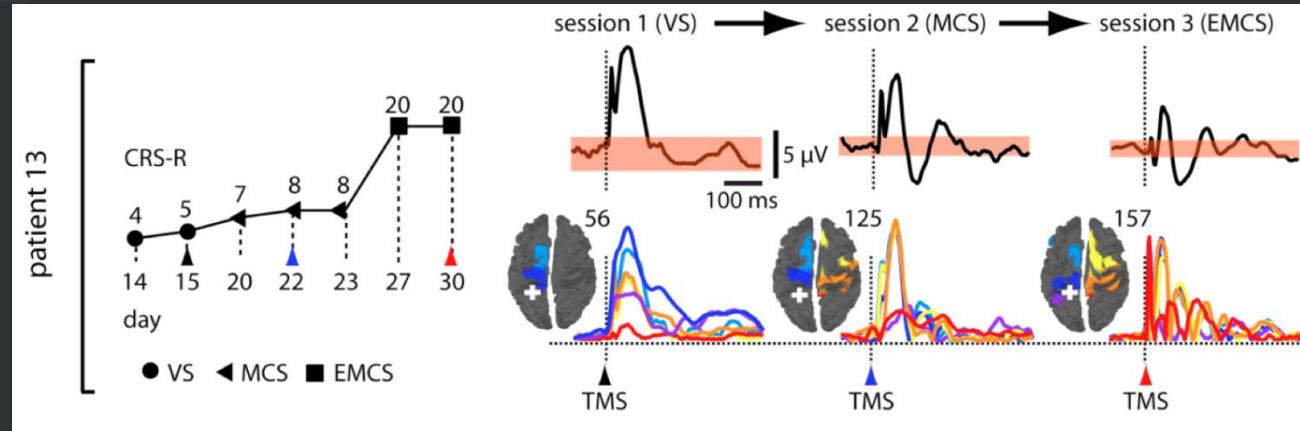
Laureys et al, J Neurol Neurosurg Psychiatry, 1999

“Resting state” fMRI default mode connectivity

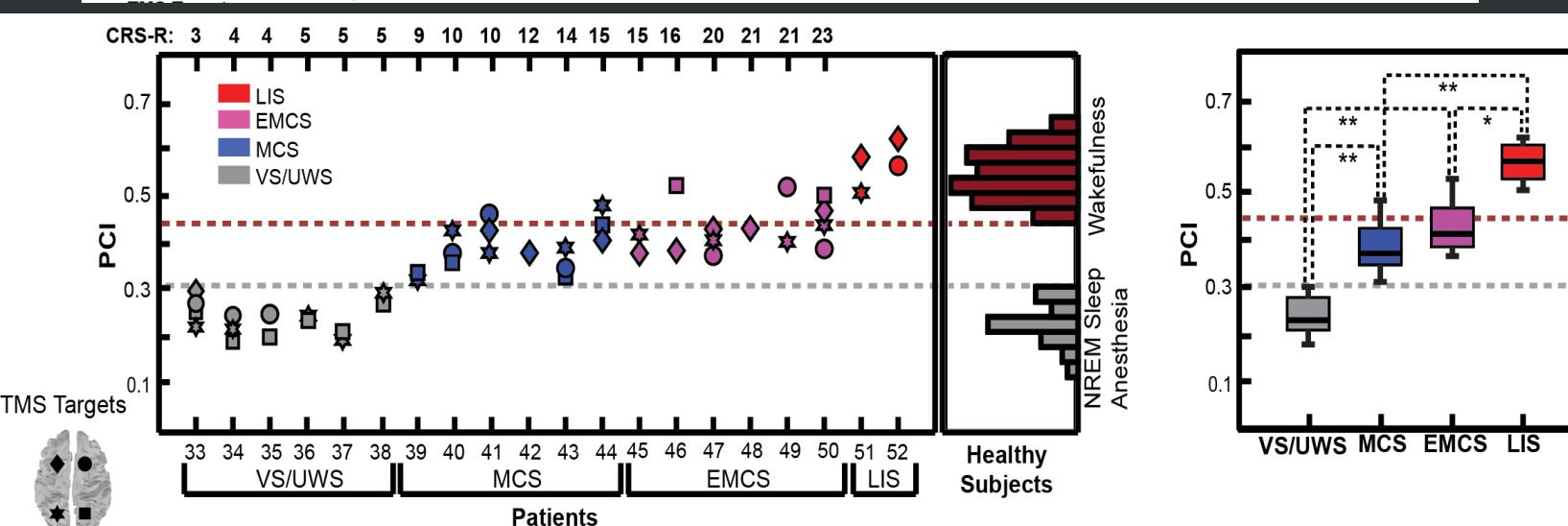
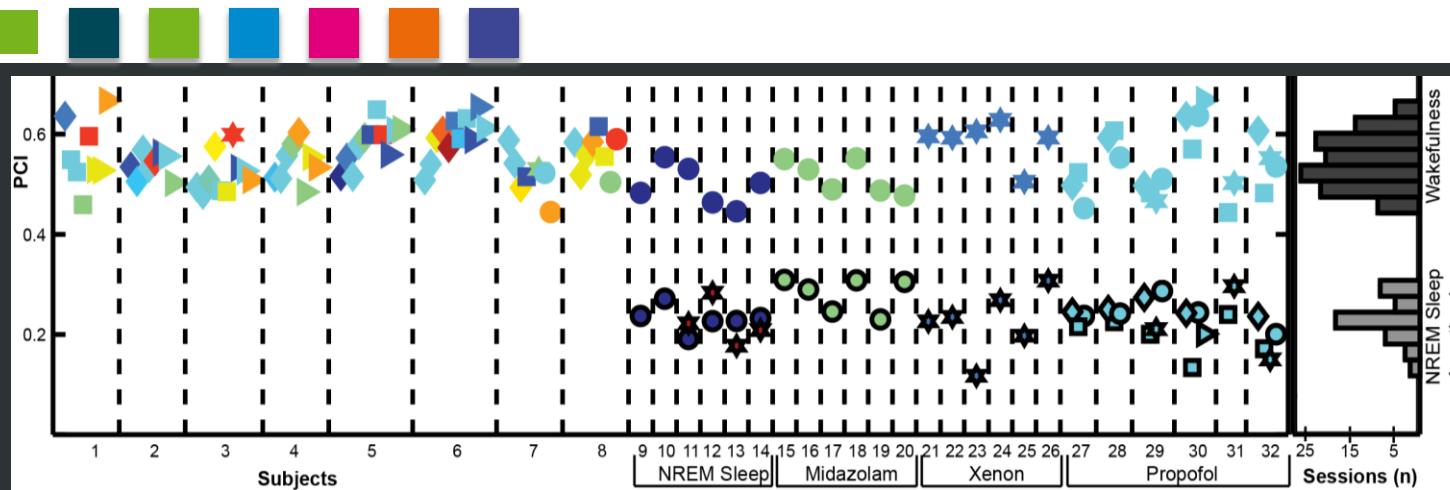


Consciousness ≈ connectivity

EEG-TMS



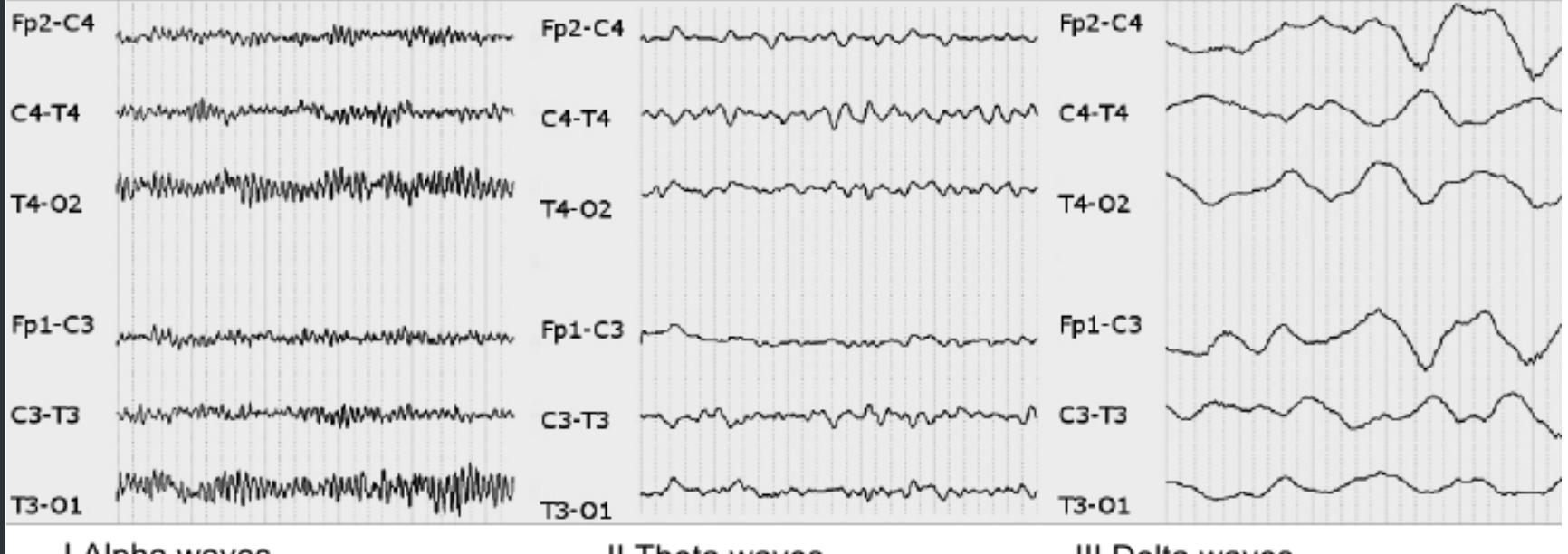
Consciousness ≈ integration?



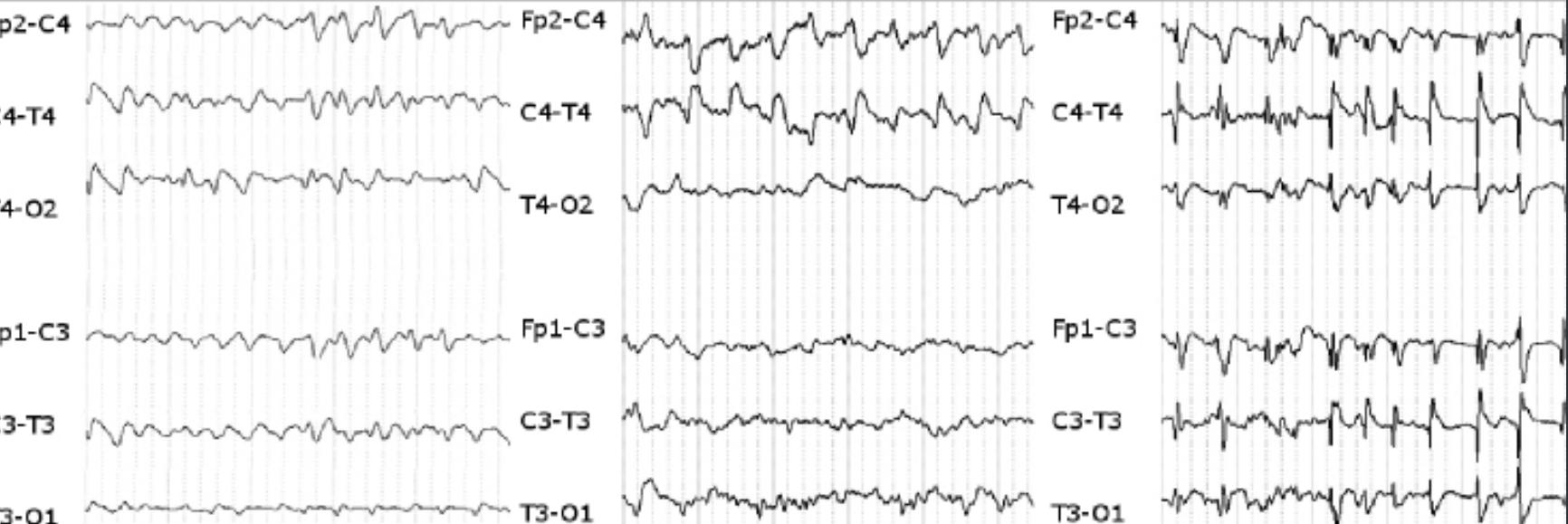
Electroencephalography: Slowing



EEG Patterns



Electroencephalography: Epilepsy



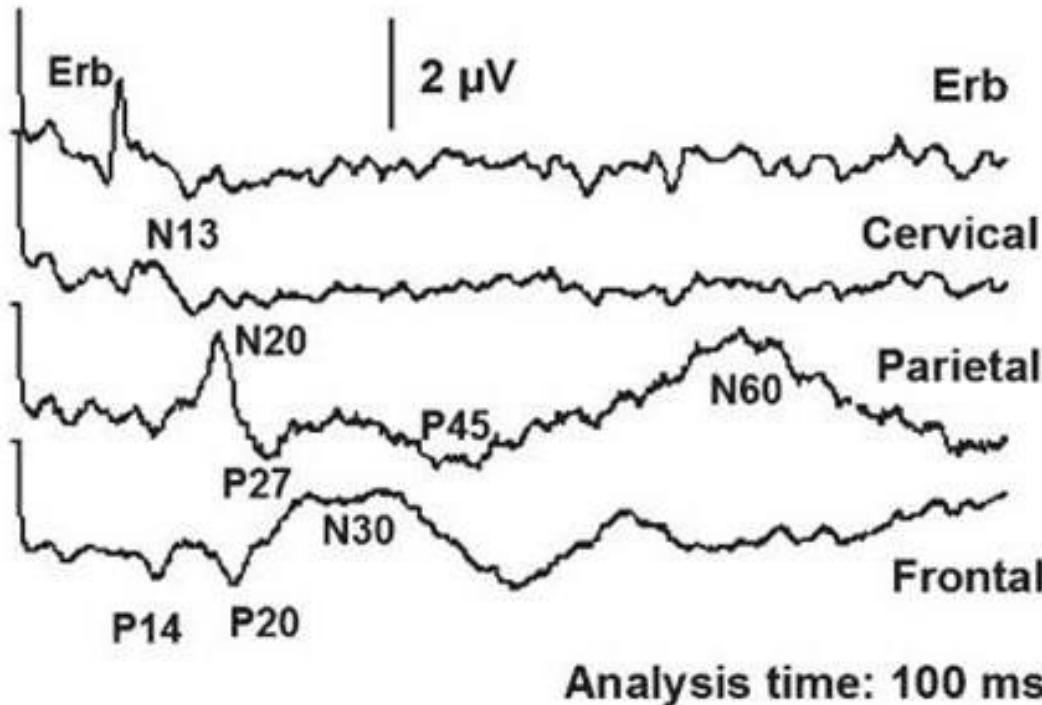
IV Triphasic waves

V Focal epileptiform
activity

VI Generalized epileptiform
activity

Event-related potentials (ERP)

SEPs (median-nerve stimulation, wrist)

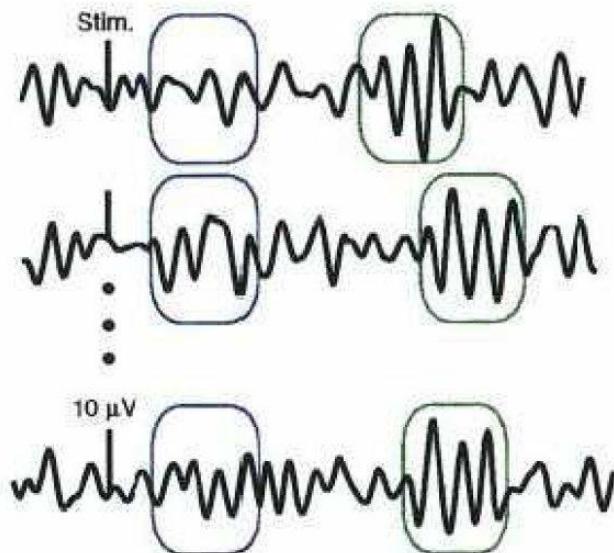


- Activity onset **following sensory** stimulation
- **Evoked** potentials vs **Induced** potentials
- P = positive
- N = negative
- Number = time after stimulus onset (msec)

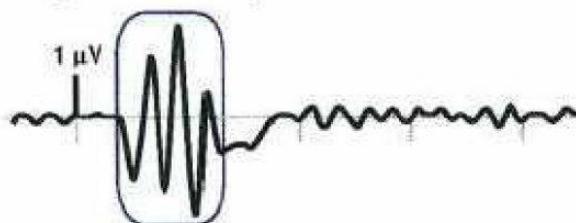
Event-related potentials - Averaging



A Single-trials



B Time average : evoked potential



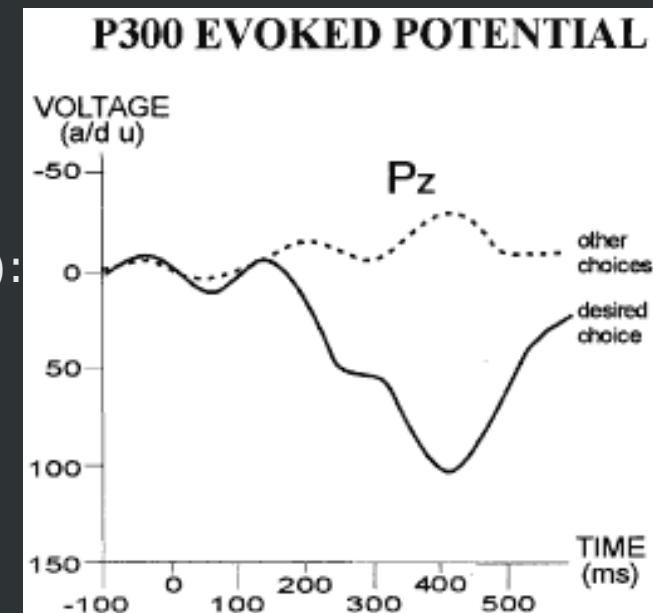
- Average potential across trials / subjects
- Need to synchronize potentials: **locking** time
 - 2 types of locking:
 - **evoked**: lock at **stimulus onset** time (left squares)
 - **induced**: lock at **potential's peak** (right squares)

Adapted from Tallon-Baudry and Bertrand,
1999

P300 = biomarker of surprise



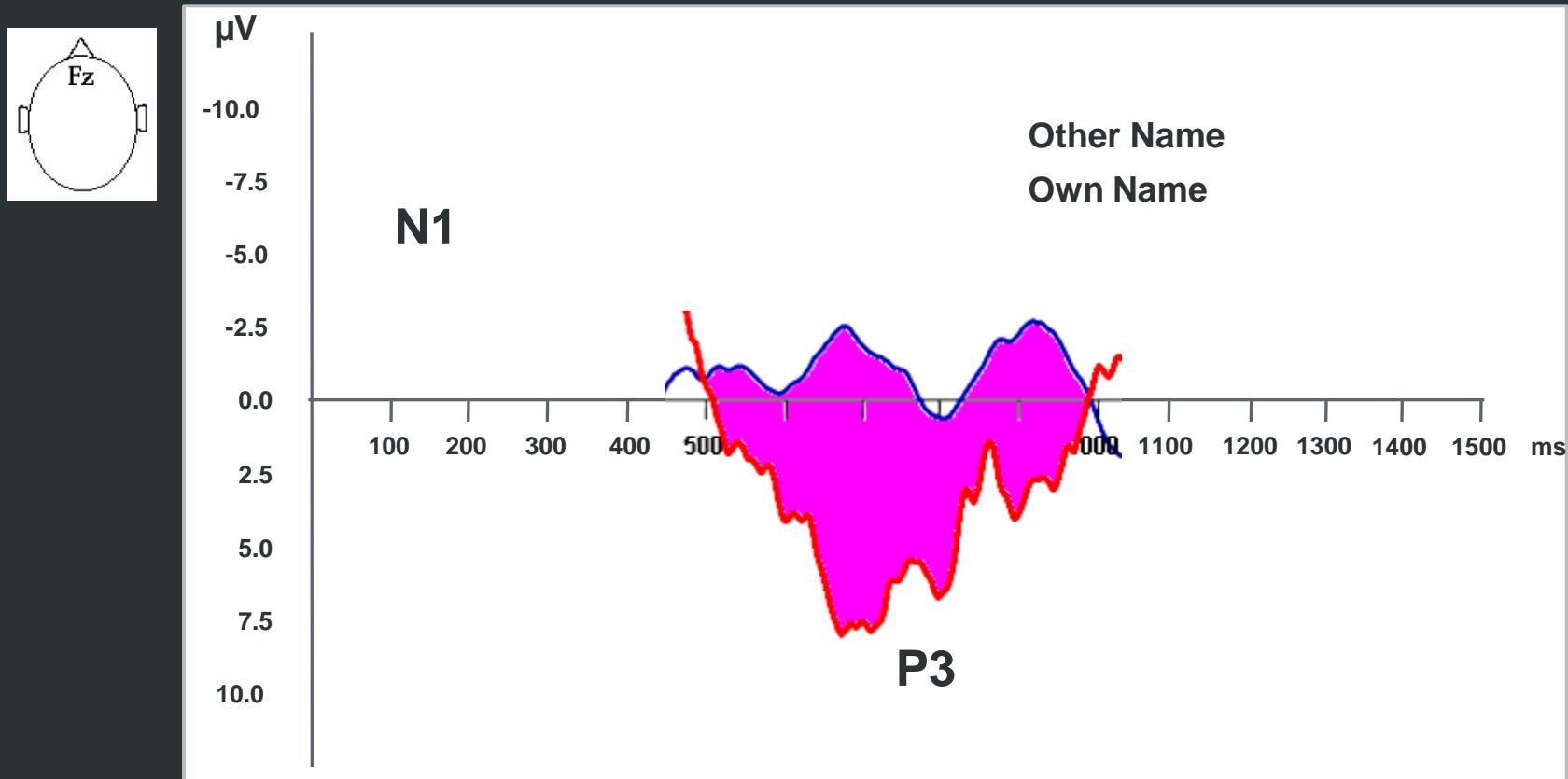
- P300 = ~**300** msec **positive** wave after stimulus onset
- General **biomarker** of **surprise**
- Happens in all sensory modalities, often studies in visual or **auditory**
- Two subtypes:
 - P3a = new stimulus, amplitude \propto surprise (beware of habituation!)
 - P3b = memorize and wait until item appears.
Amplitude \propto task complexity, vigilance, motivation, stimulus rarity, etc...
- **Oddball** paradigm (see also von Restoff or Sternberg):
 1. Ask subject to remember an item
 2. Present several stimuli sequentially
 3. Present the item to be remembered
 4. Capture P3b
- Beware: surprise => P3, but **P3 \neq surprise!**



Late ERP / Late Positive Component



Minimally conscious state



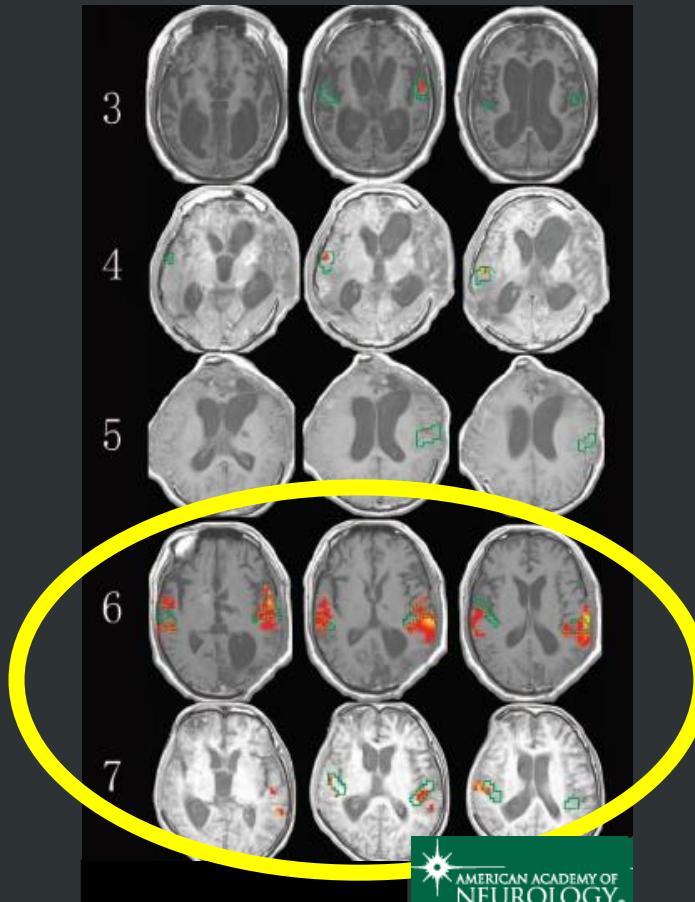
Predicting outcome in chronic DOC



Unresponsive Wakefulness syndrome?

ACTIVATION
TO THE OWN
NAME

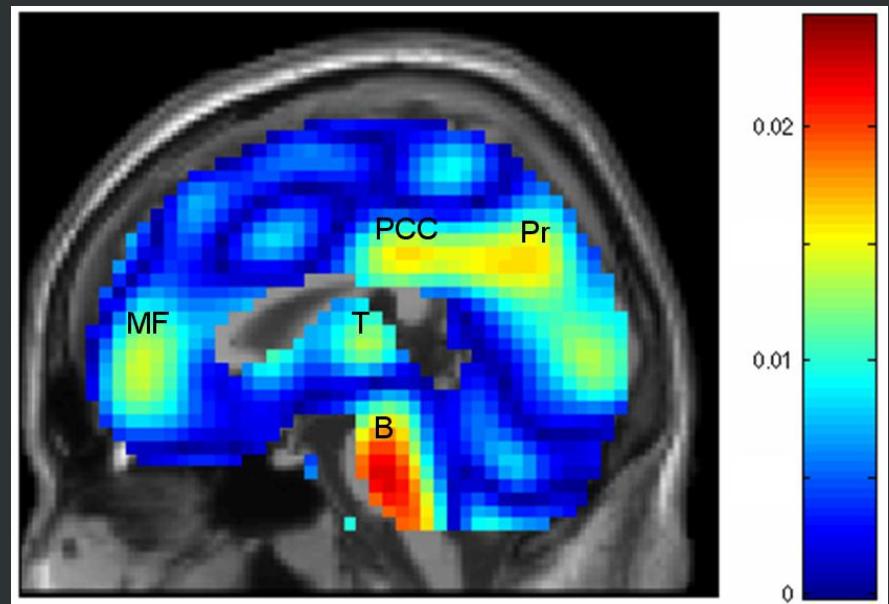
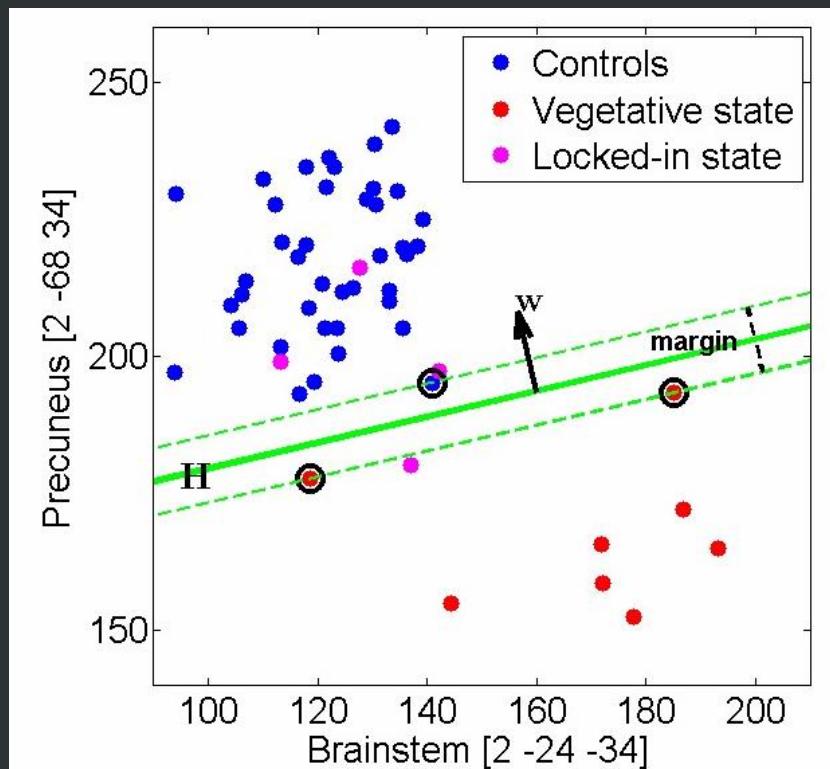
ATYPICAL
'HIGH LEVEL'
CORTICAL
ACTIVATION



Automated consciousness classifier



“Relevance Vector Machine” on FDG-PET data in DOC





Overview

- 
-
- 1. Identifying the population
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 - 3. Modelling
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 - Conclusions



Brain-Computer Interface

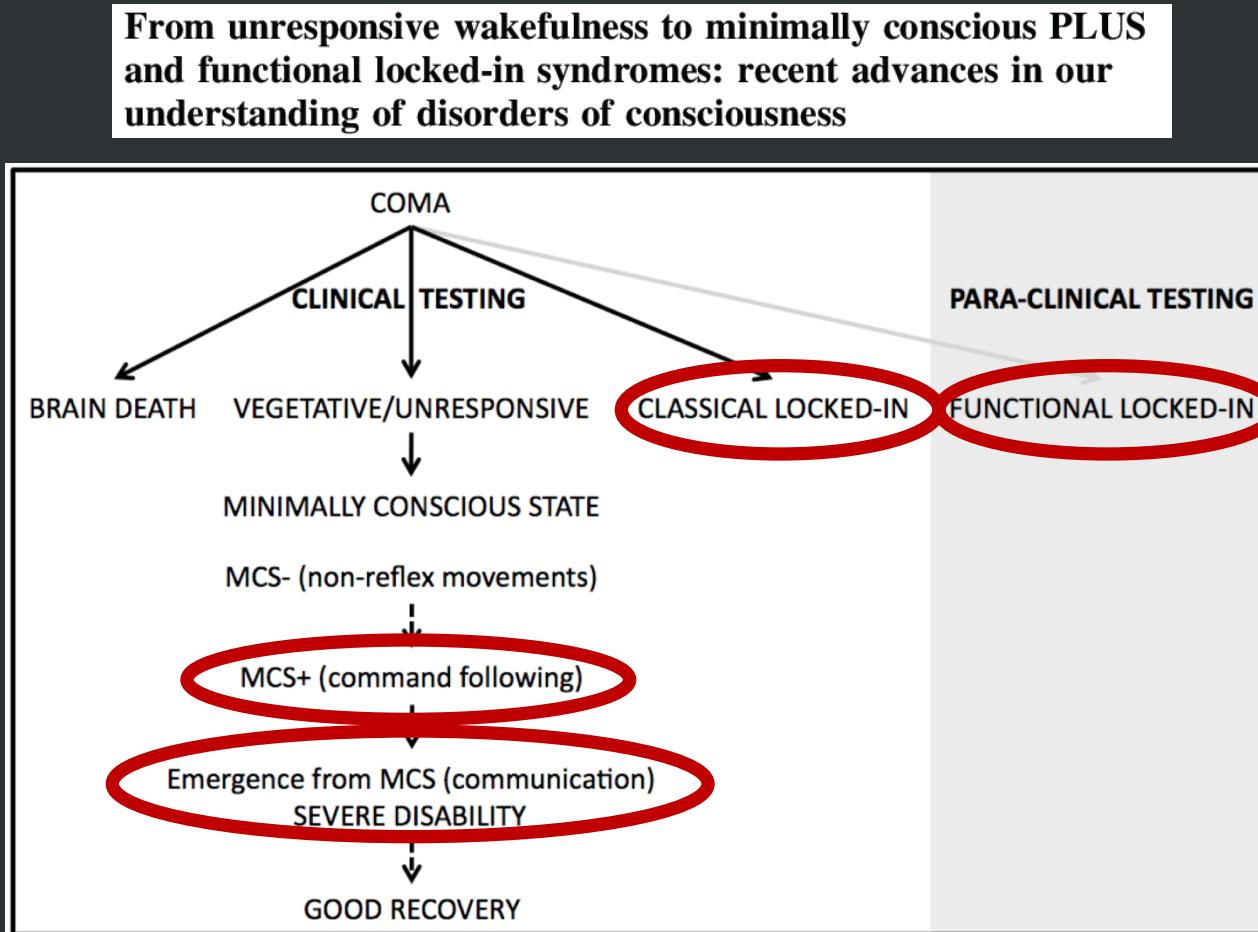


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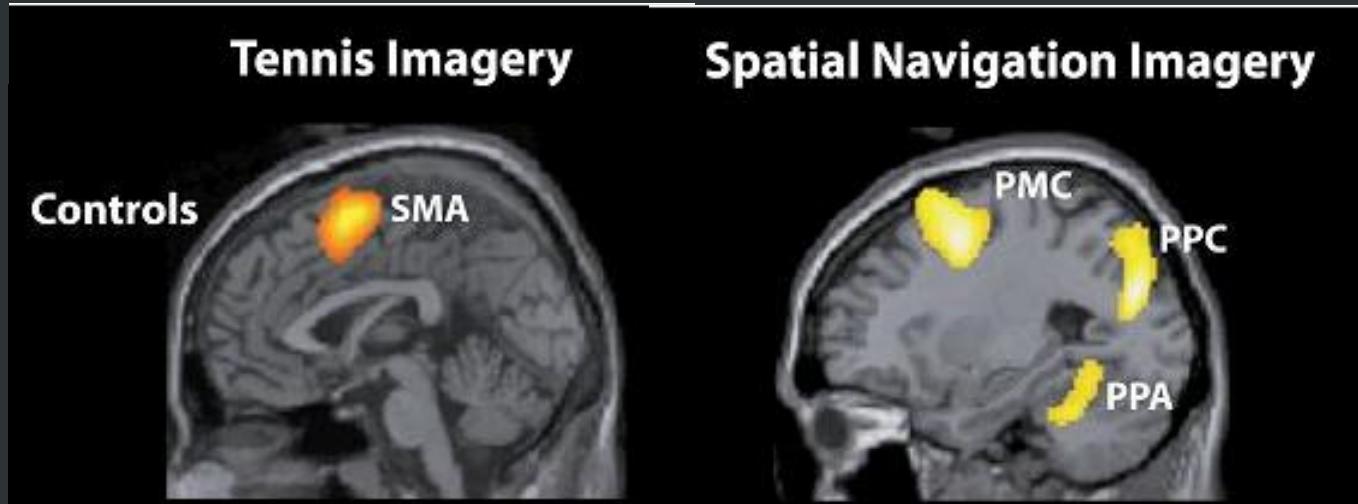
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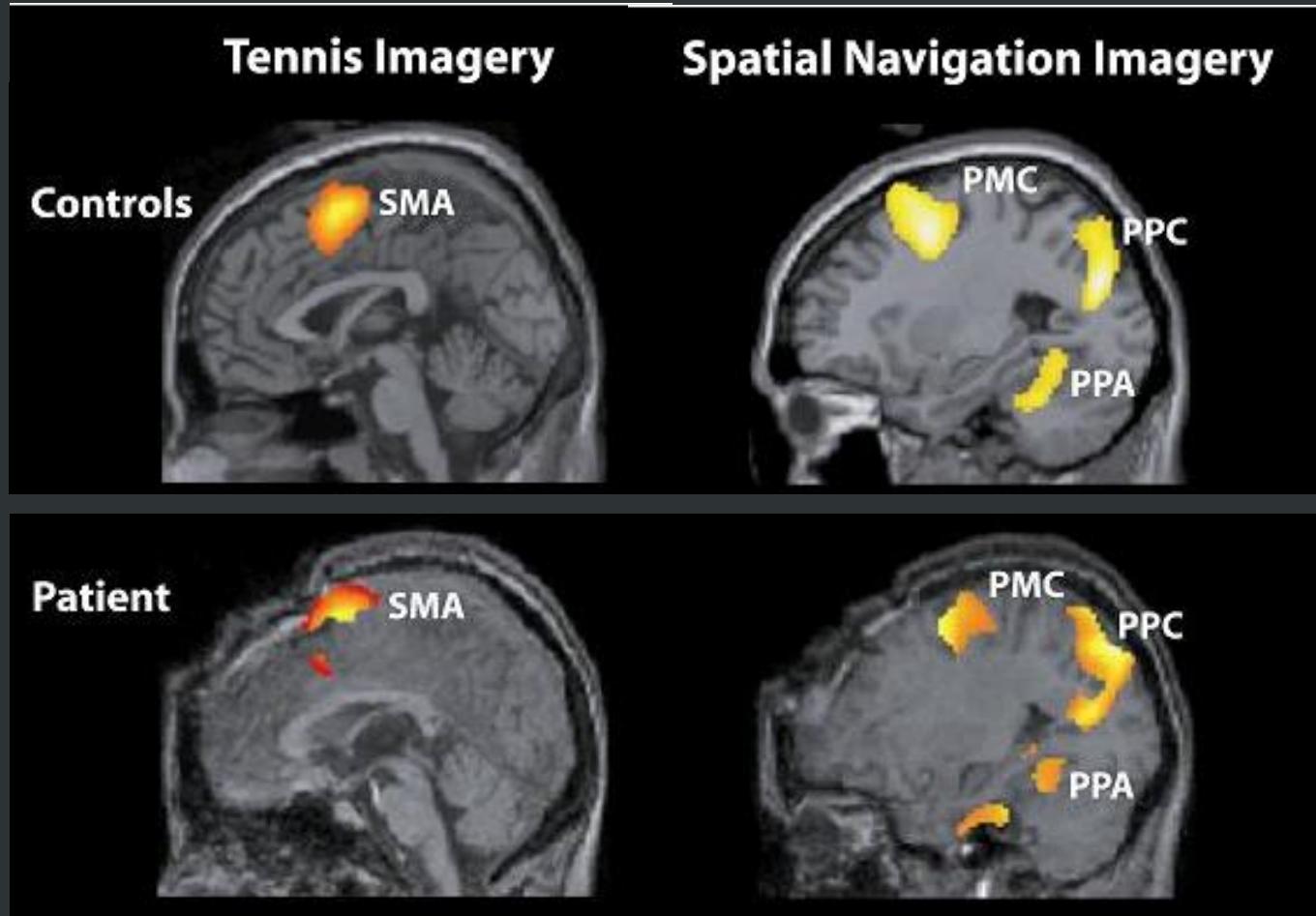


fMRI proof of concept



- 30-seconds period of mental imagery/resting
- Each imagery task was repeated 10 times.

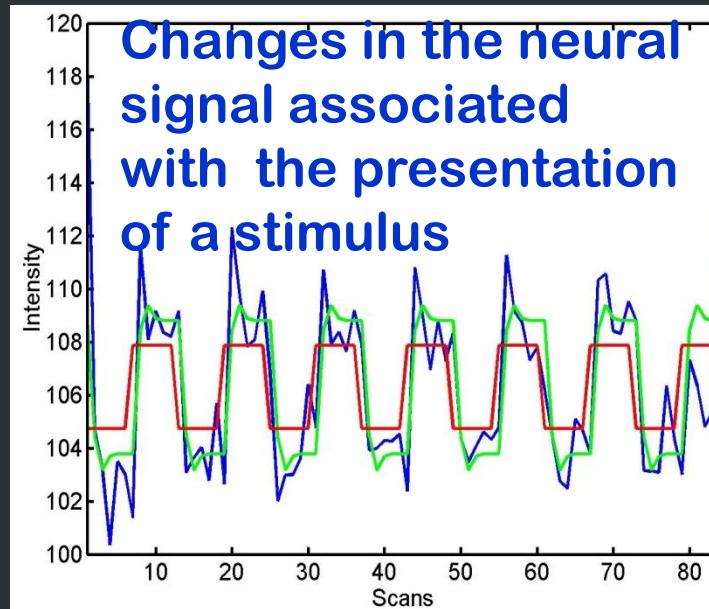
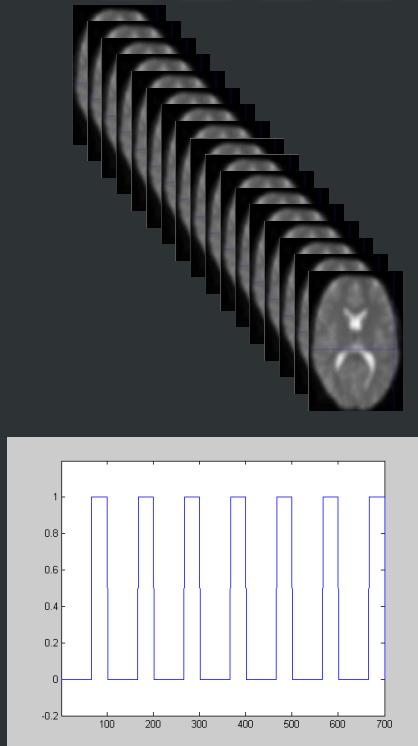
fMRI proof of concept



Boly et al, *NeuroImage* 2007

Owen, Coleman, Boly, Davis, Laureys and Pickard, *Science*, 2006

Statistical parametric mapping



Design matrix

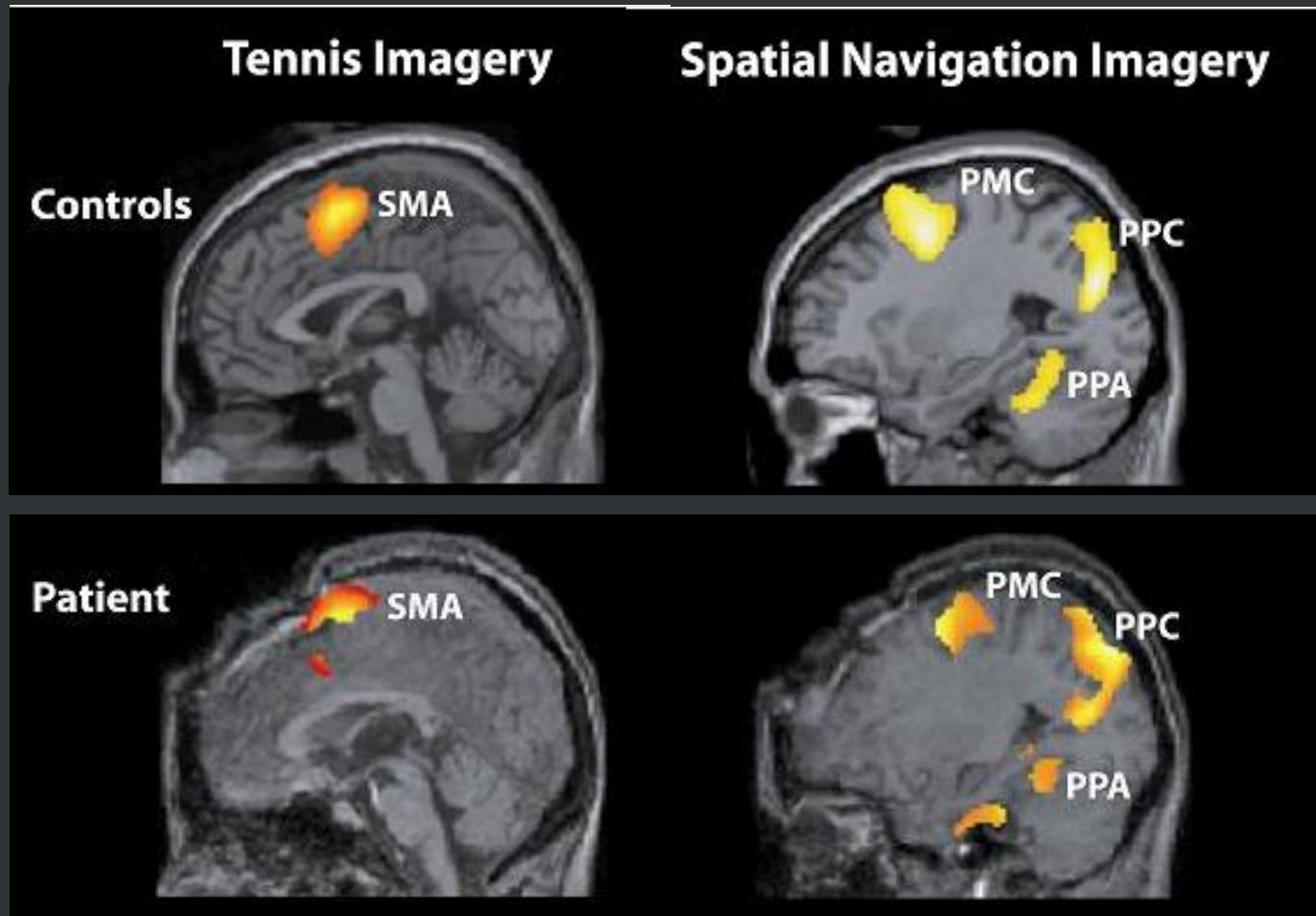


General Linear Model

$$Y = X \times \beta + \epsilon$$

Model and predictions!

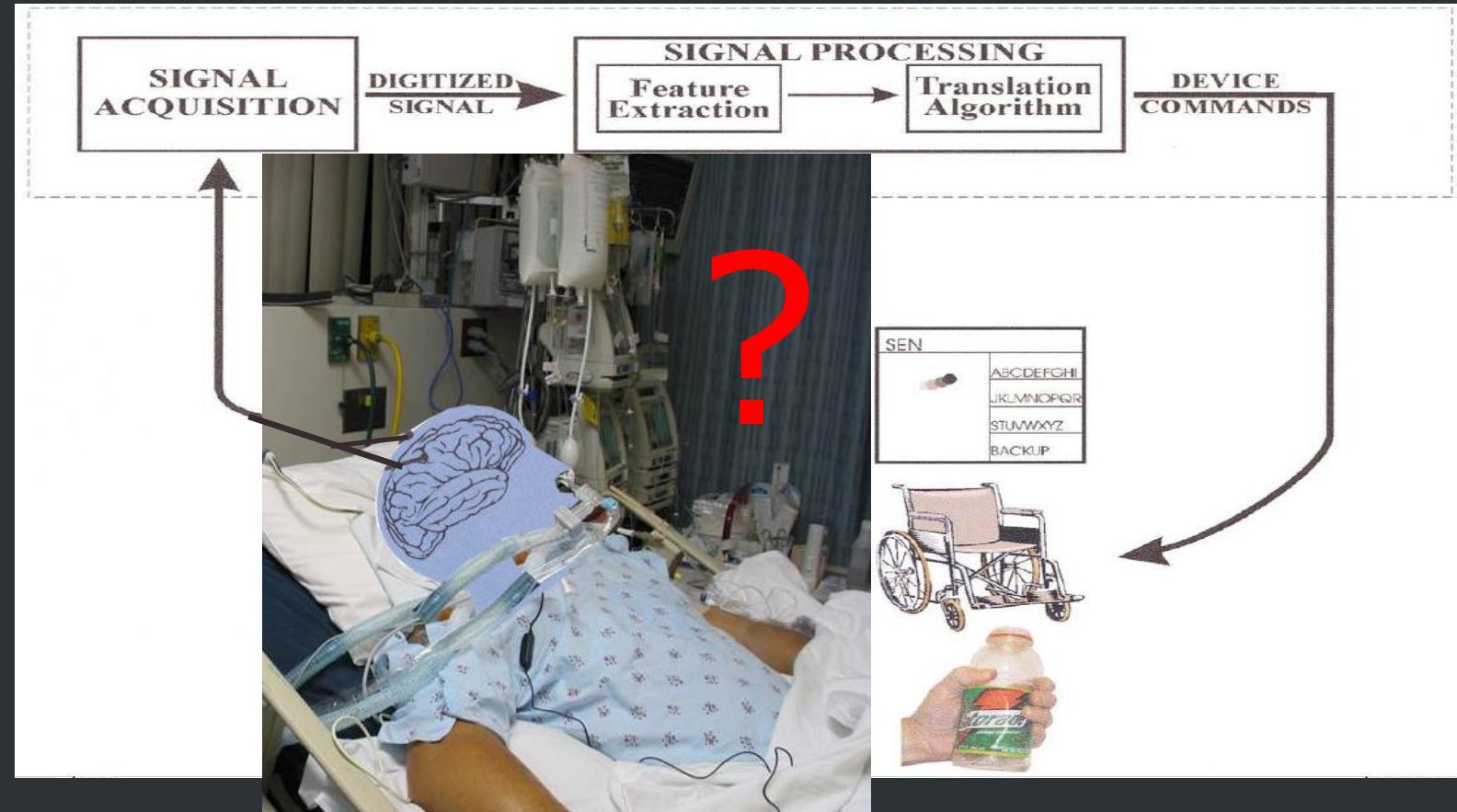
Result of SPM



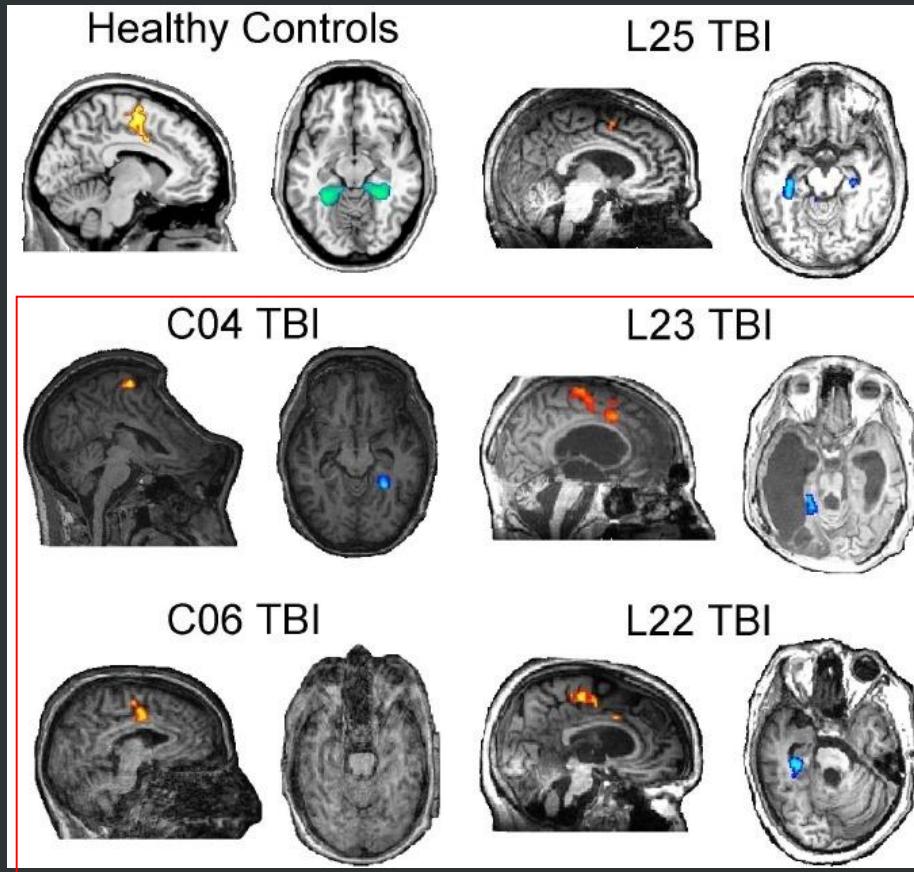
Boly et al, *NeuroImage* 2007

Owen, Coleman, Boly, Davis, Laureys and Pickard, *Science*, 2006

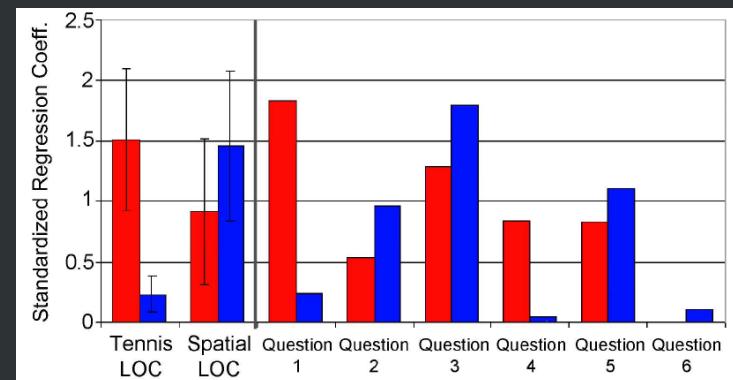
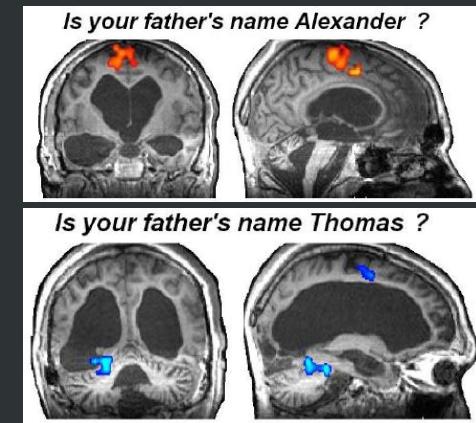
Brain – Computer Interface: from neural signal to model to BCI



Communication using Tennis Test



Imagine **Tennis** to answer 'YES'
 Imagine **Navigating** to answer 'NO'





Communication



05/01/2015

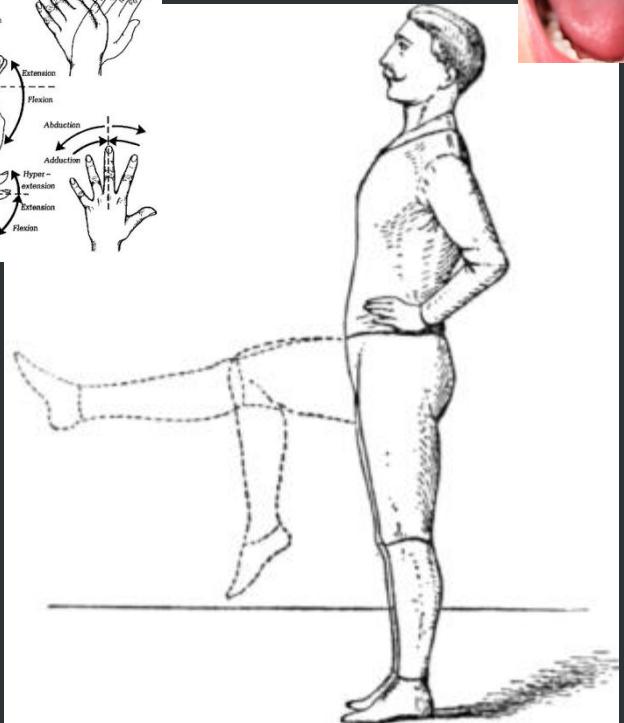
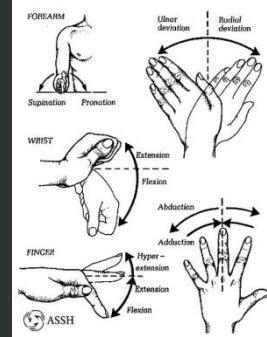
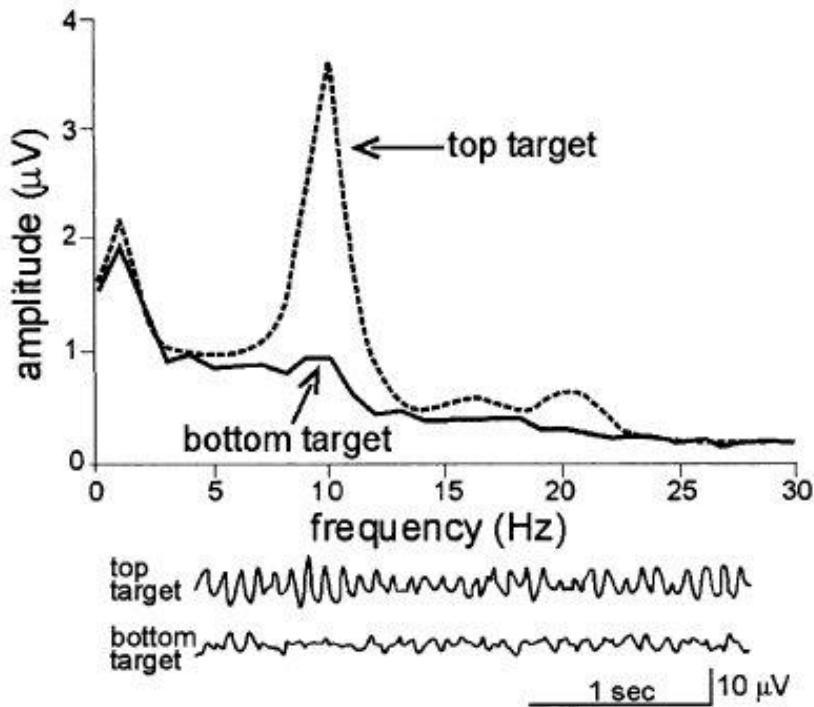
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University of Liège, Belgium

CHU
de Liège 1907-2007
20 ans

Université
de Liège
ULG

Sensorimotor rythms

SENSORIMOTOR RHYTHMS





EEG-based Brain Computer Interfaces

"MOVE YOUR FOOT"



"MOVE YOUR HAND"

HEATHY
CONTROL
SUBJECT



"VEGETATIVE"
UNRESPONSIVE
PATIENT



www.thelancet.com



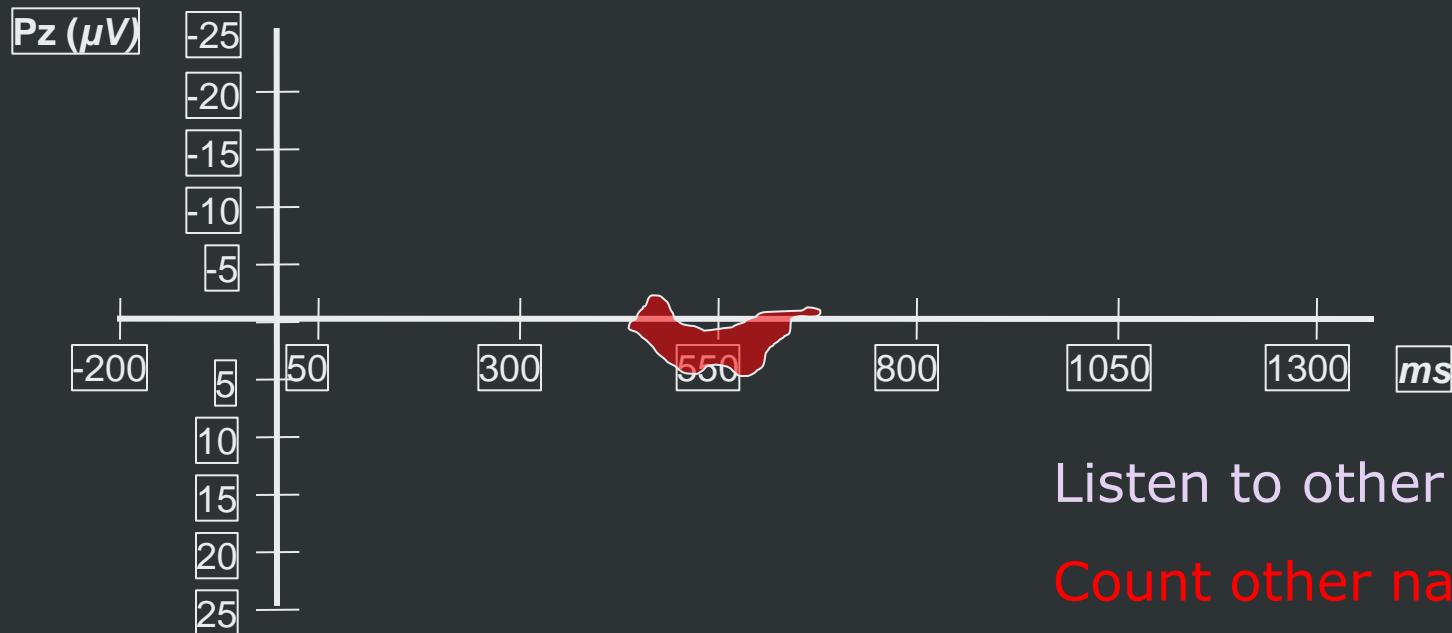
Cruse et al, *Lancet* 2012
3/16 VS/UWS (19%)
- 2/5 traumatic (40%)
- 1/11 non-traumatic (9%)

Cruse et al, *Neurology* 2012
7/23 MCS (30%)
- 7/15 traumatic (49%)
- 0/8 non-traumatic (0%)

ERP proof of concept



Coma or total Locked-in syndrome?



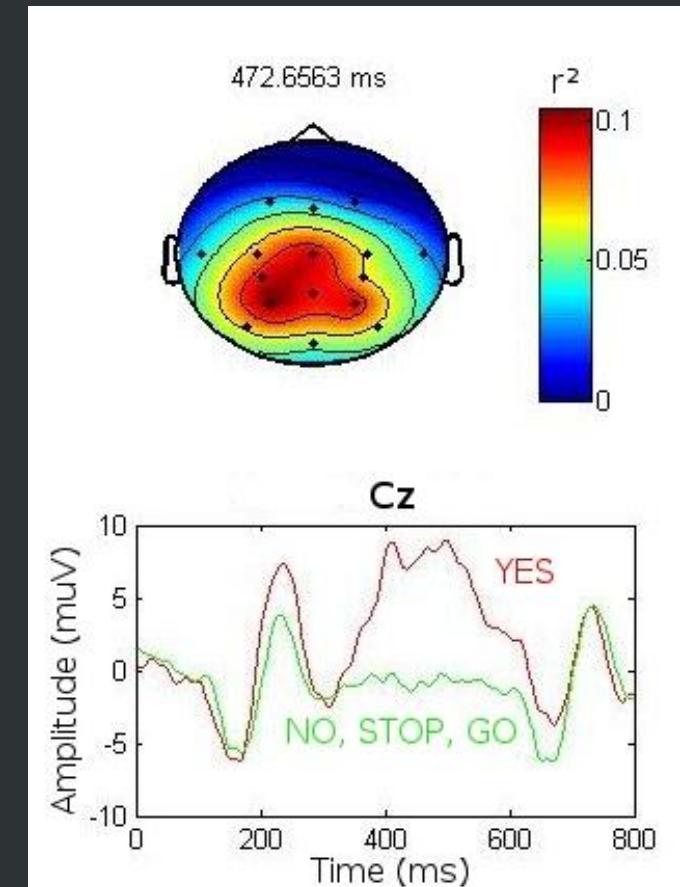
Listen to other name

Count other name

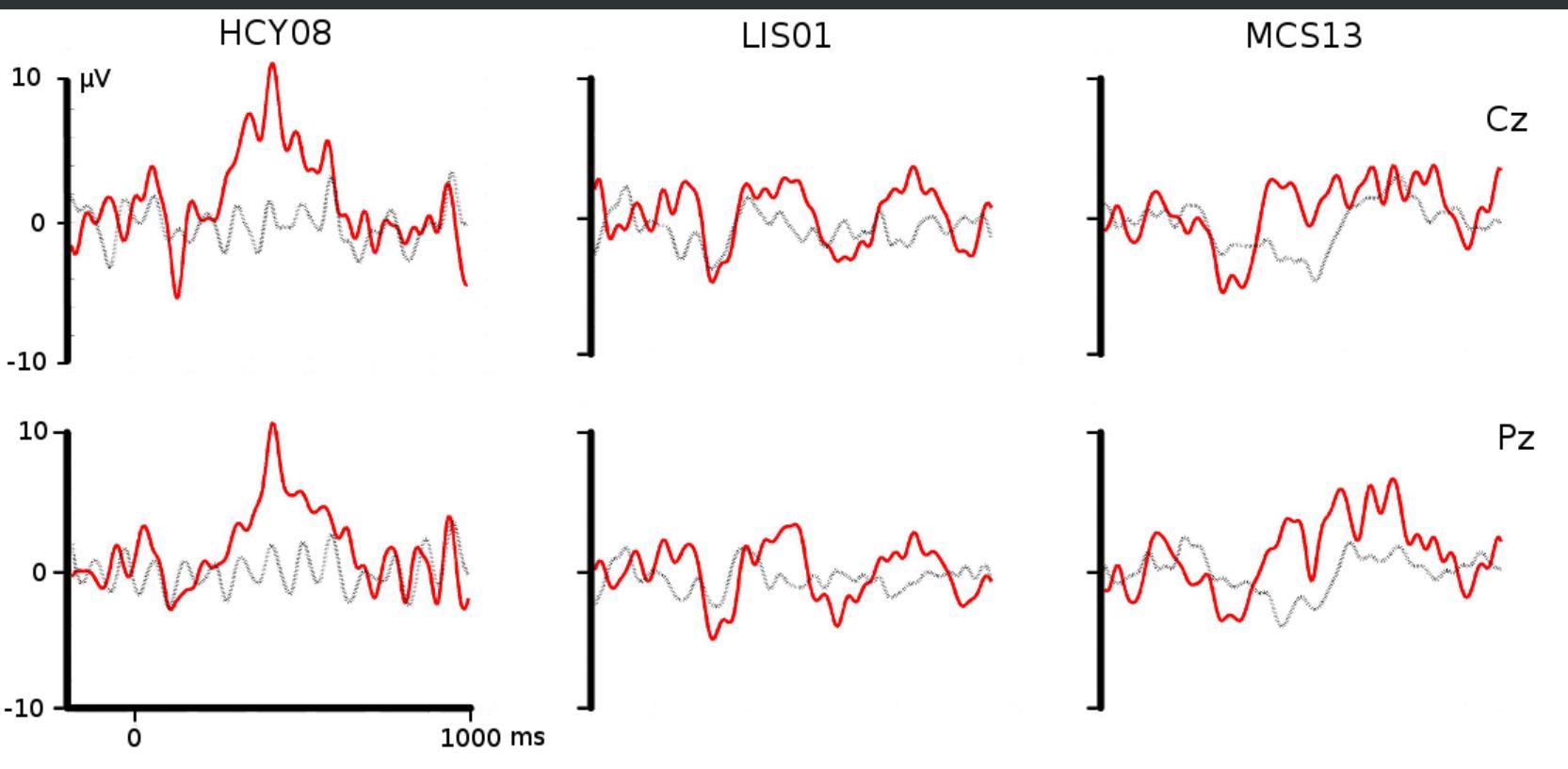
Listen to own name

Count own name

Auditory P300

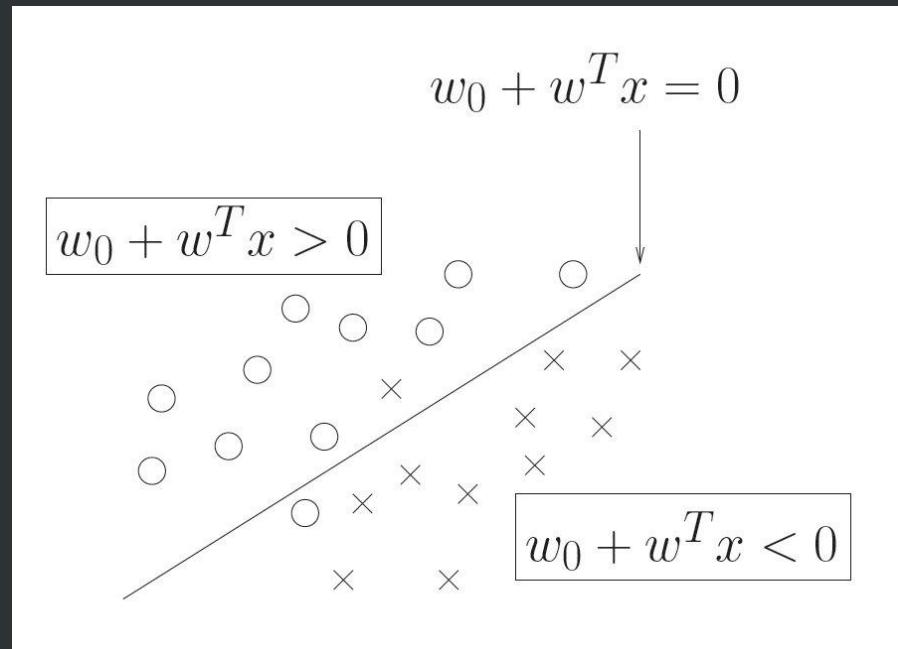


Evoked potentials





- Training set
- Classifier
 - Linear discriminant analysis
 - Step-wise LDA

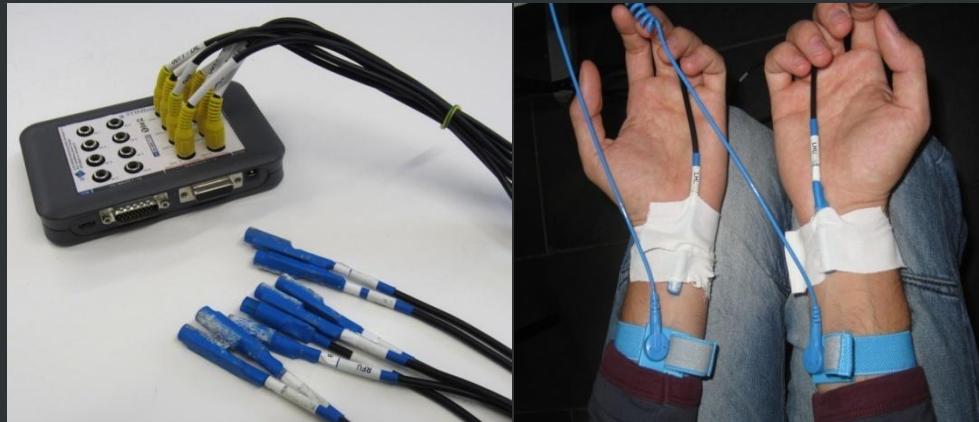


Auditory P3 results

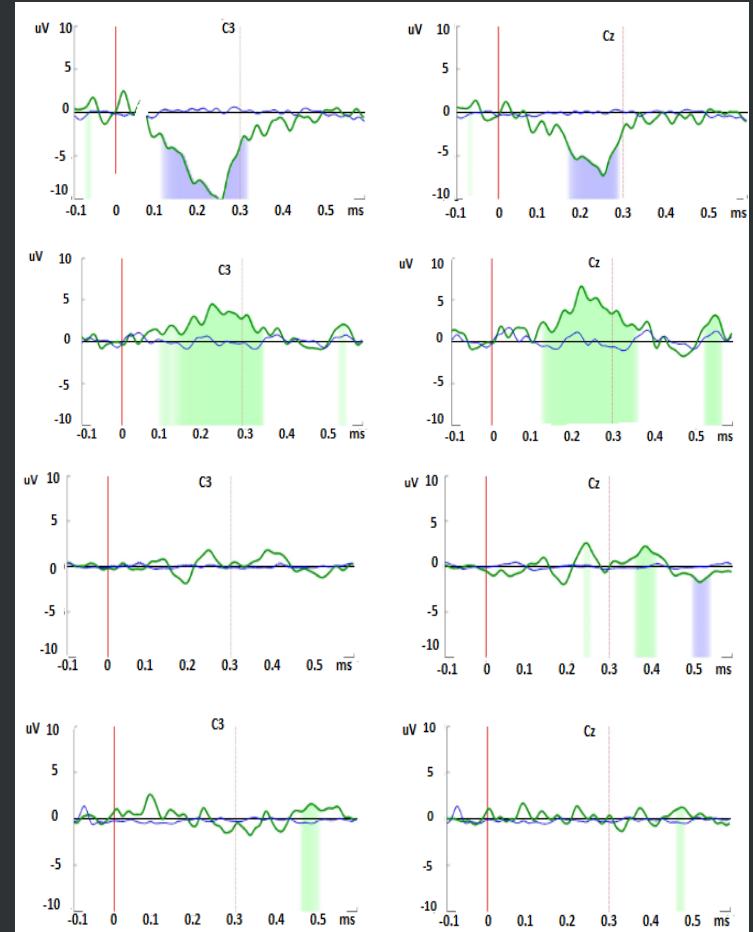


Subject	online [%]	online	offline [%]	offline [correct]
MCS01	37.5	3/8	8	1/12
MCS03	30.0	3/10	36	5/14
MCS04	50.0	5/10	21	3/14
MCS05	20.0	2/10	36	5/14
MCS02	40.0	4/10	28	4/14
MCS06	22.2	2/9	0	0/13
MCS07	10.0	1/10	50	7/14
MCS08	30.0	3/10	36	4/14
MCS09	30.0	3/10	43	6/14
MCS10	40.0	4/10	36	5/14
MCS11	10.0	1/10	50	7/14
MCS12	28.6	2/7	18	2/11
MCS13	0.0	0/10	57	8/14
VS01	30.0	3/10	14	2/14
VS02	40.0	4/10	28	4/14
VS03	30.0	3/10	0	0/14

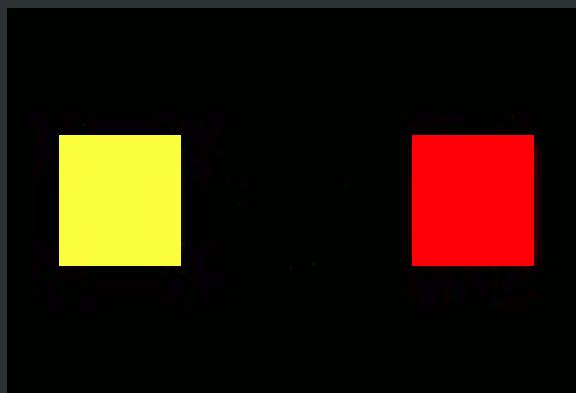
Vibrotactile stimulation



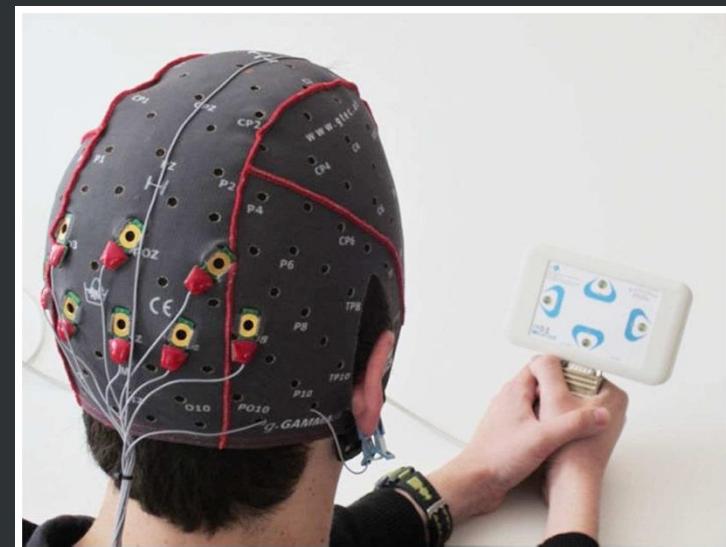
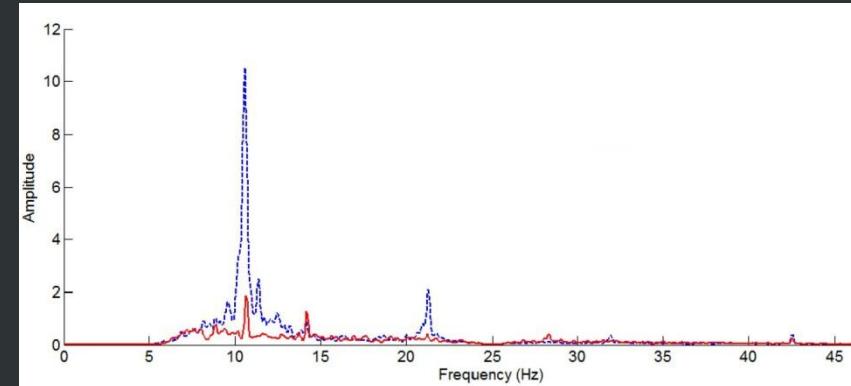
- 6 LIS patients
- 5/6 with visual deficit
- All able to elicit a P3



Steady state evoked potential



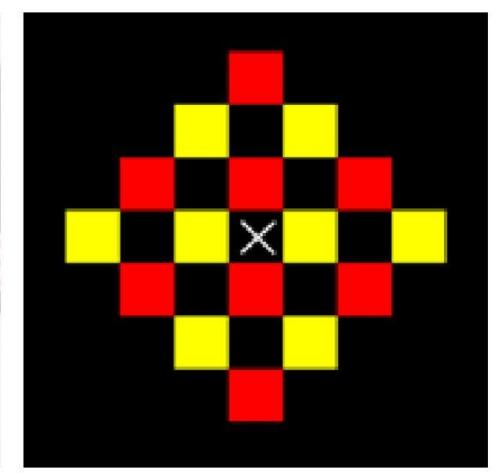
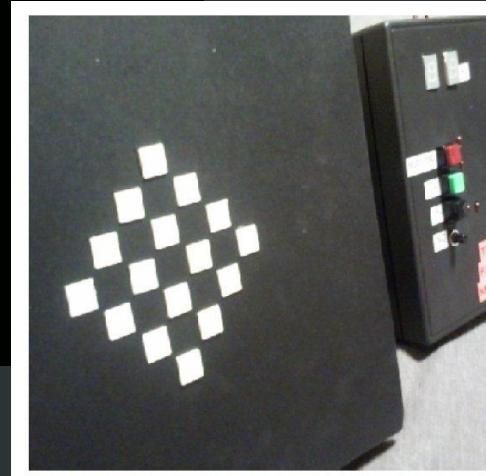
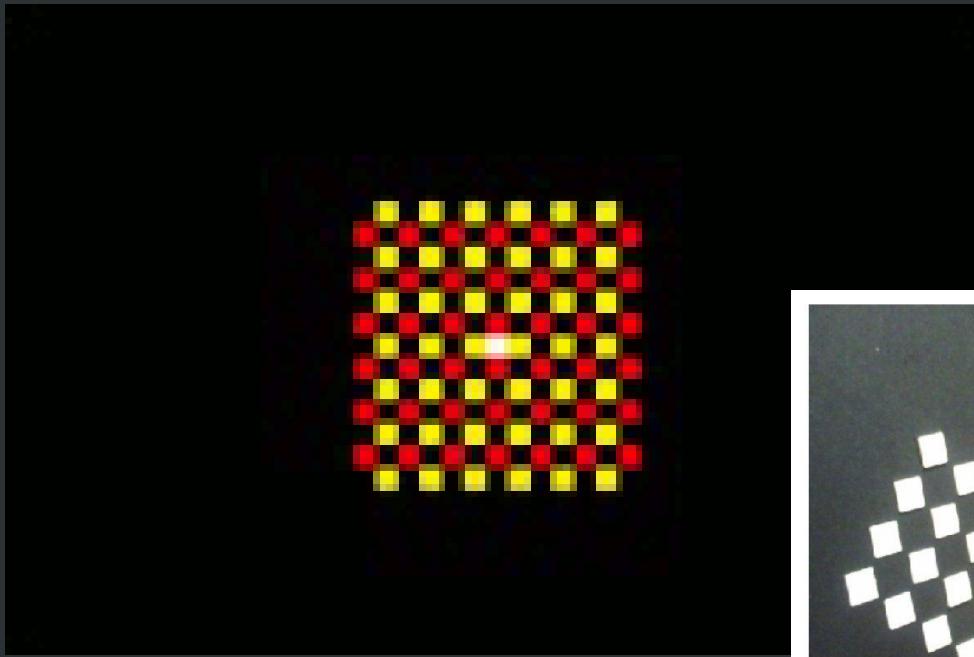
Lesenfants et al., 2011
Guger et al., 2012





Covert SSVEP

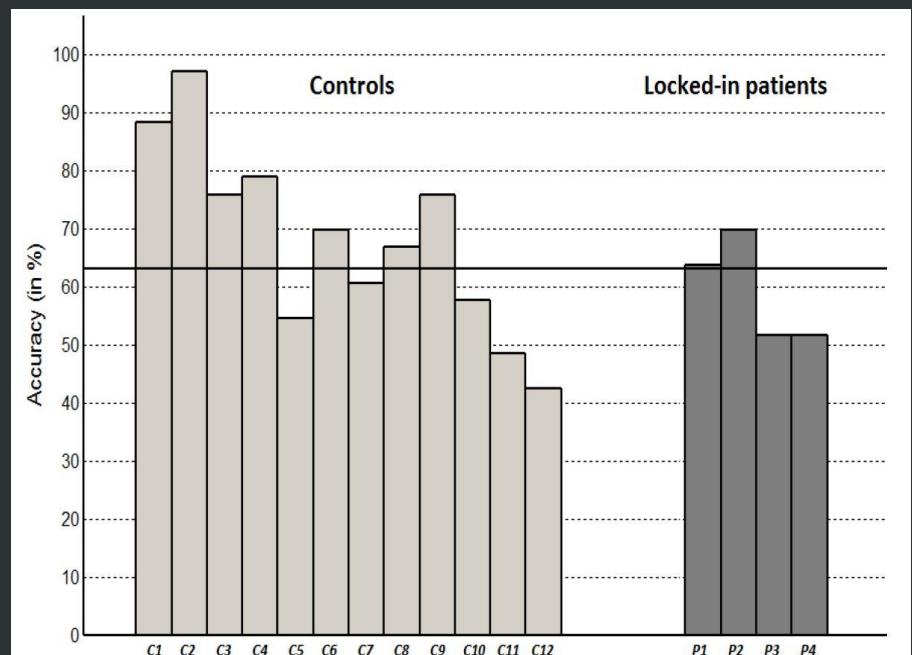
Use covert attention



Covert SSVEP



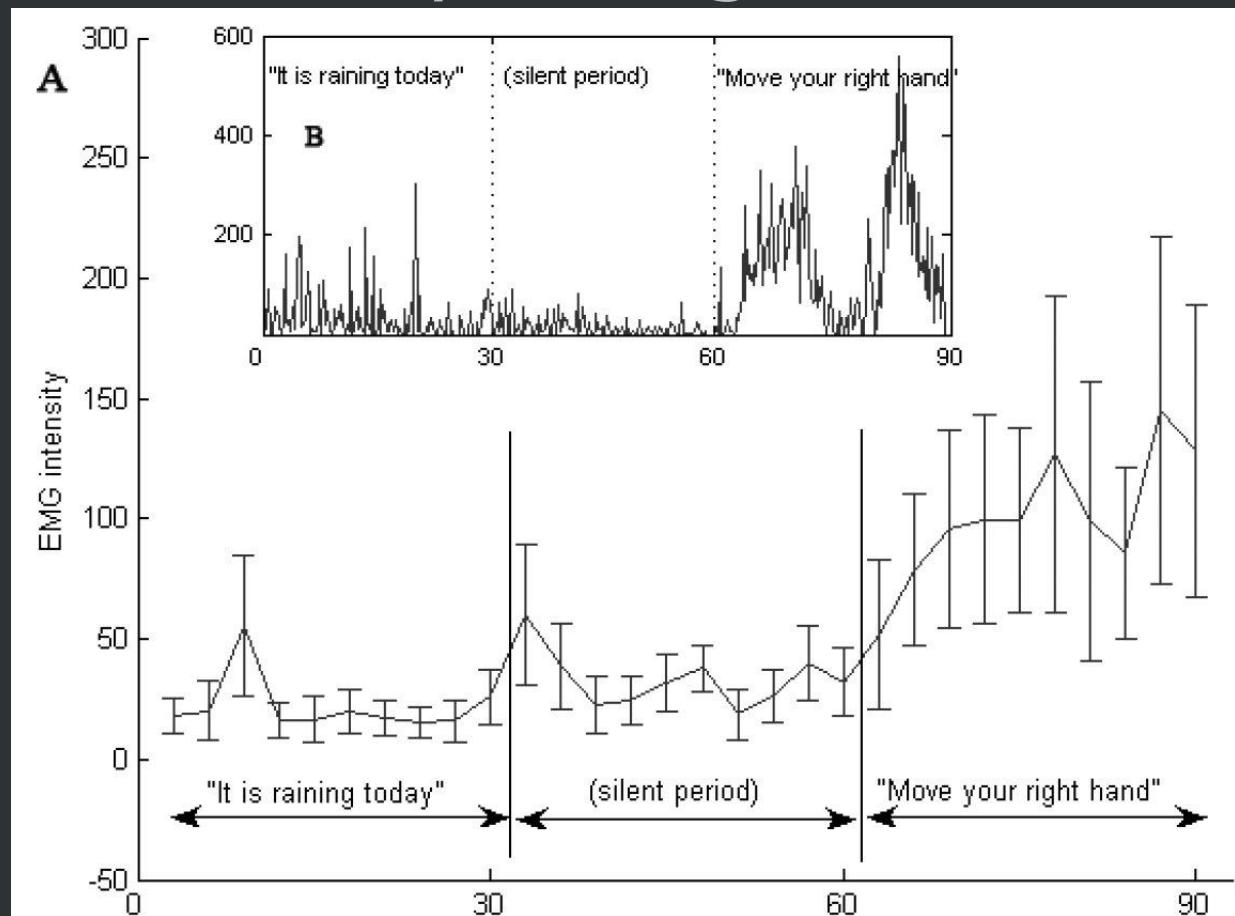
- 7/12 above chance level
- 5/12 communication
- 1/4 LIS communication



EMG of command following



« Move your right hand »





Rehabilitation

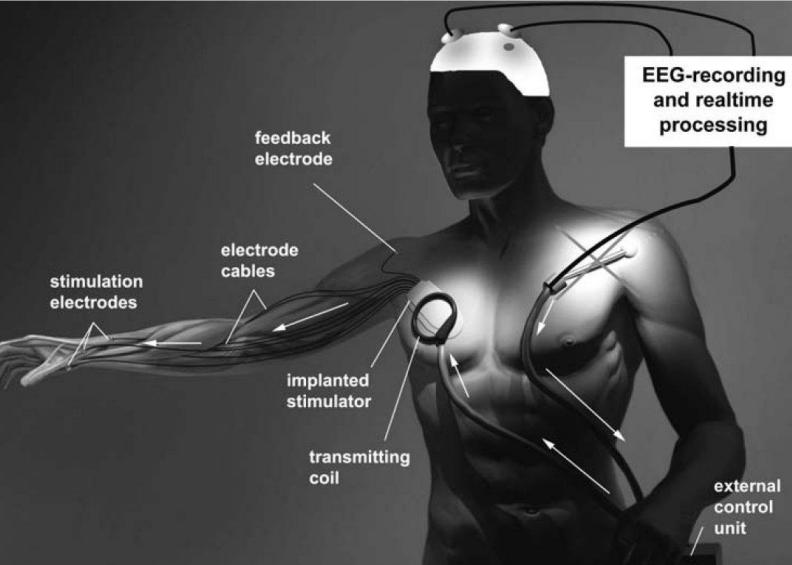


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Neuroprosthetics



Rupp and Gerner, 2007



Pfurtscheller, et al., 2008

- High cervical spinal cord injuries - below C4 (C1-3 are too vital)
- Speed performance of these systems is low
- Training, training, training

Linear model prosthetic arm.. in 85 days!

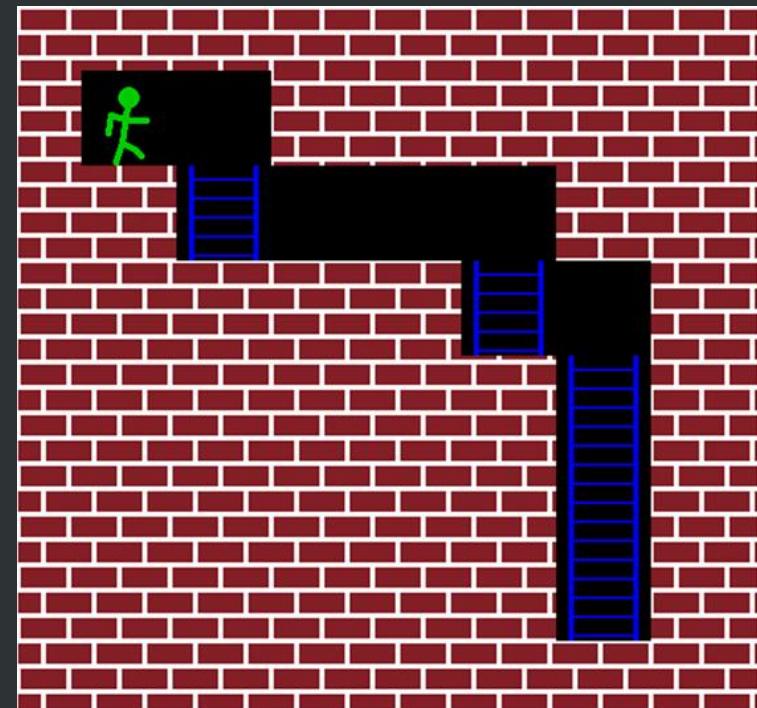
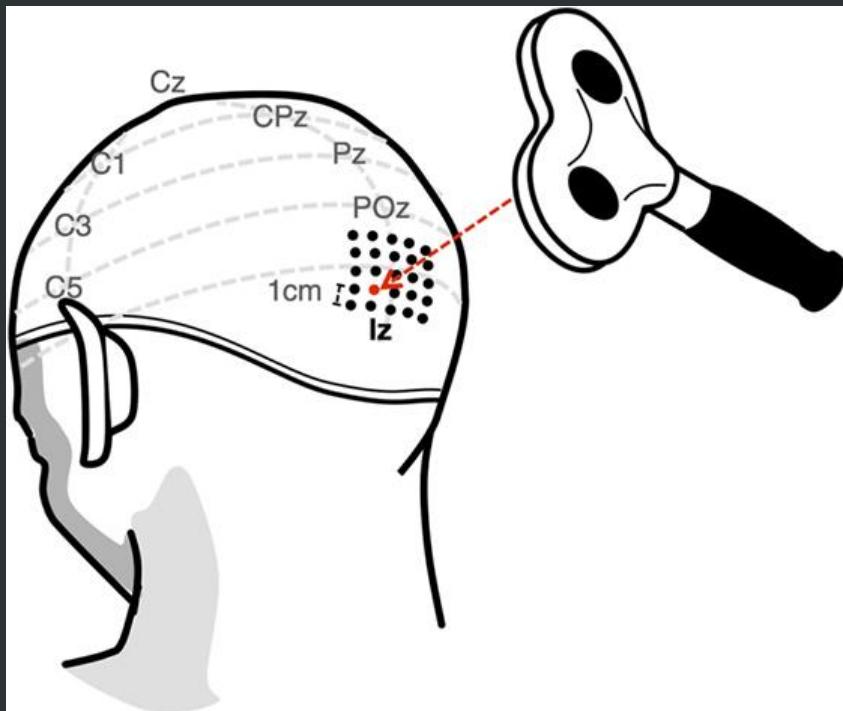


Feedback



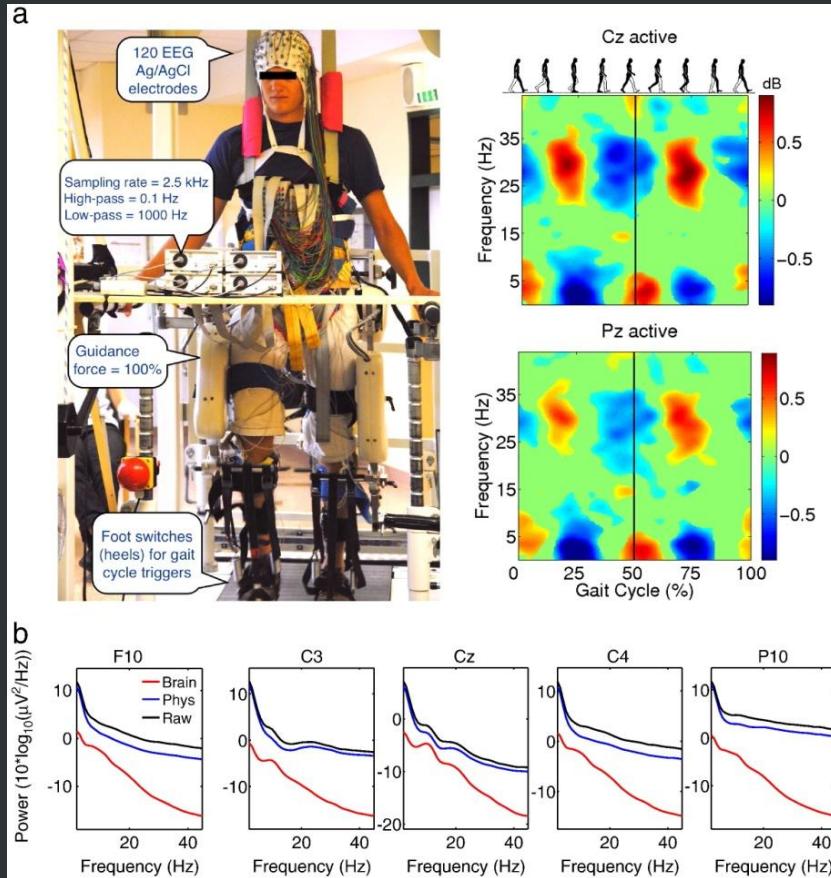
- Ecological feedback
- Recruit and/or reinforce patient's sensorimotor experience

Direct brain stimulation to harness brain's plasticity for rehabilitation



Hidden maze game
92% success with TMS inputs, 15% without!

Information on the process



- Recruited process (brain/motoneurons)
- Recruited muscles
- Hybrid

Do we really need to access the brain? Intention decoding



Repin, 1888
Yarbus, 1967
Faisal et al, 2015

Do we really need the brain? Intention decoding

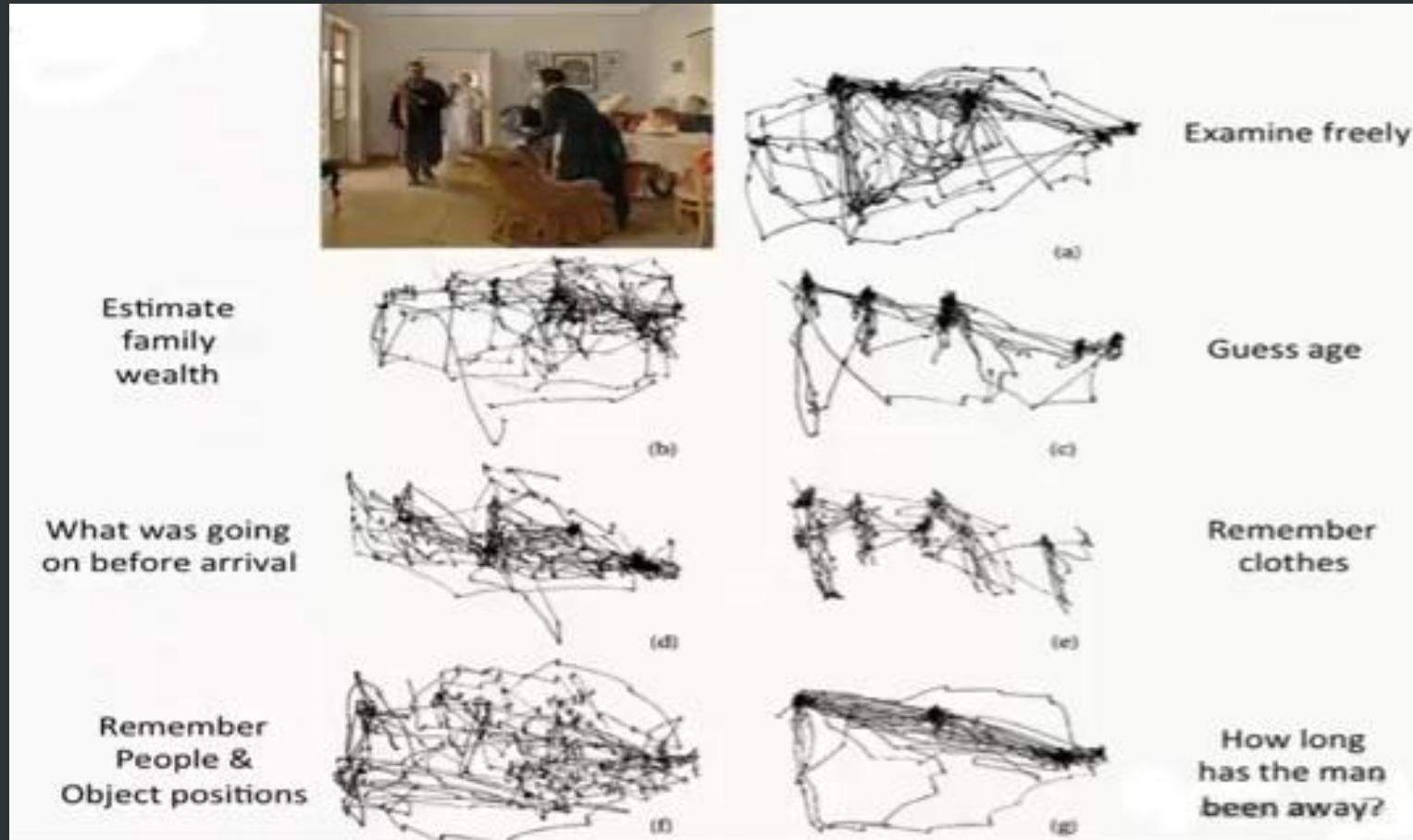


Repin, 1888

Yarbus, 1967

Faisal et al, 2015

Do we really need the brain? Intention decoding



Repin, 1888

Yarbus, 1967

Faisal et al, 2015

Do we really need the brain? Intention decoding



Pupil dilation for locked-in patients
(Stoll et al, 2013)



Repin, 1888
Yarbus, 1967
Faisal et al, 2015



Conclusion



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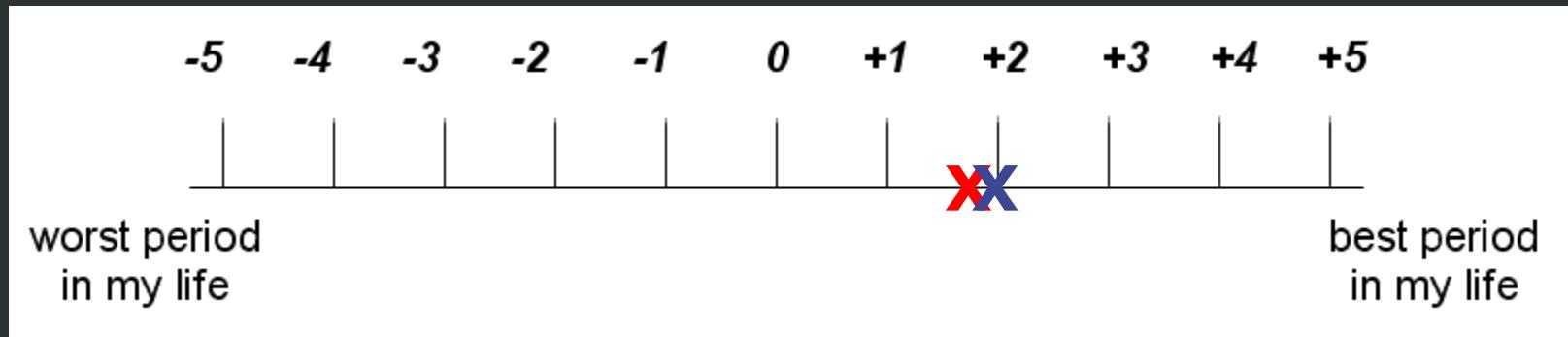


BCI for DOC and other pathologies

- 
- A decorative horizontal bar at the bottom of the slide consists of several colored squares: light green, dark teal, medium green, light blue, magenta, orange, and dark blue.
- BCIs may enable the detection of response to command and communication
 - Results need to be interpreted with great caution
 - Statistical validation
 - Be aware of **false negative**
 - Numerous challenges: subpopulation identification, feature extraction, hardware restrictions, physical restrictions (lots of **noise!**), expensive, etc.
 - Results could have a high impact on rehabilitation strategies, **quality of life and prognosis**
 - **Exciting era for BCI, lots of AI models and wonderful technological advances!**

Quality of life

Anamnestic Comparative Self Assessment (Bernheim et al)



X Locked-in patients average n=70

X Matched healthy controls average n=70



Further information



- See previous slides for references
- Books:
 - The neurology of consciousness: cognitive neuroscience and neuropathology, Laureys, Steven, Olivia Gosseries, and Giulio Tononi, Academic Press, 2015.
- Videos, documentaries:
 - **Charlie Ford Coma 1 to 7**
 - Holly's Road To Recovery - A TBI Survivor
 - Human Neuroscience in the wild – Aldo Faisal – FSC 2016



Thank you!



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MRI: DTI & spectroscopy

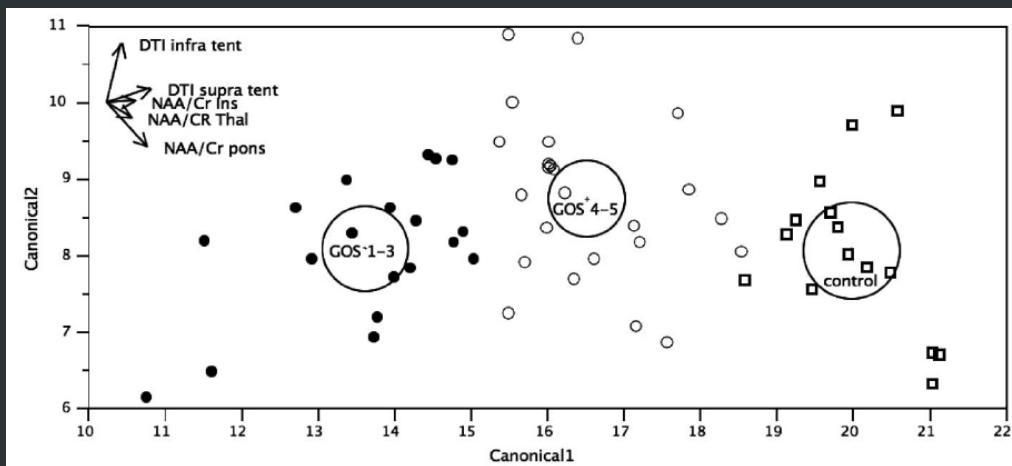
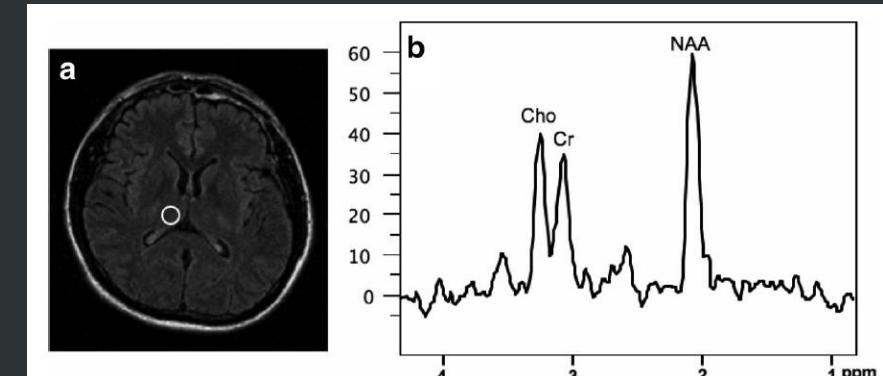
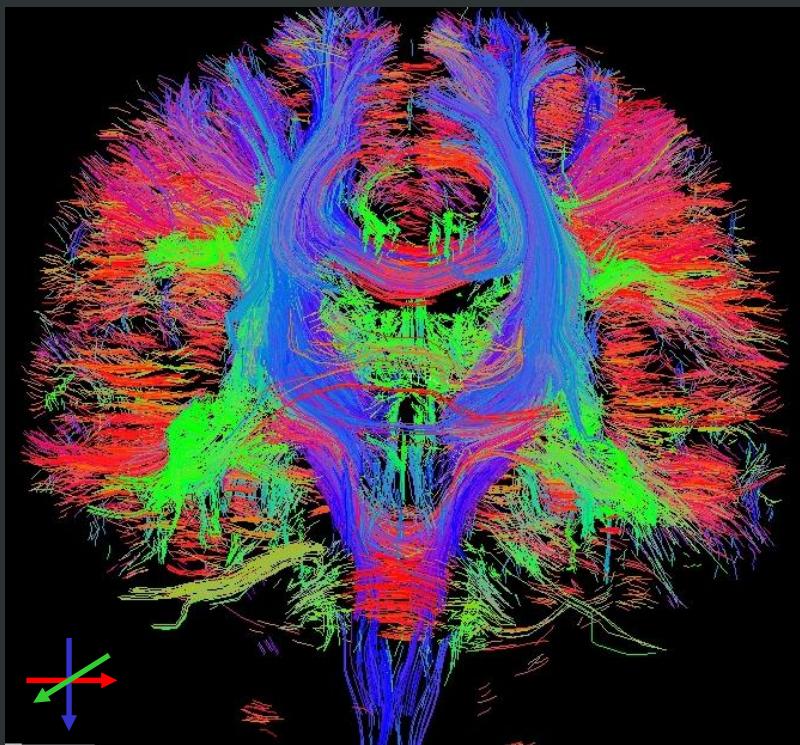
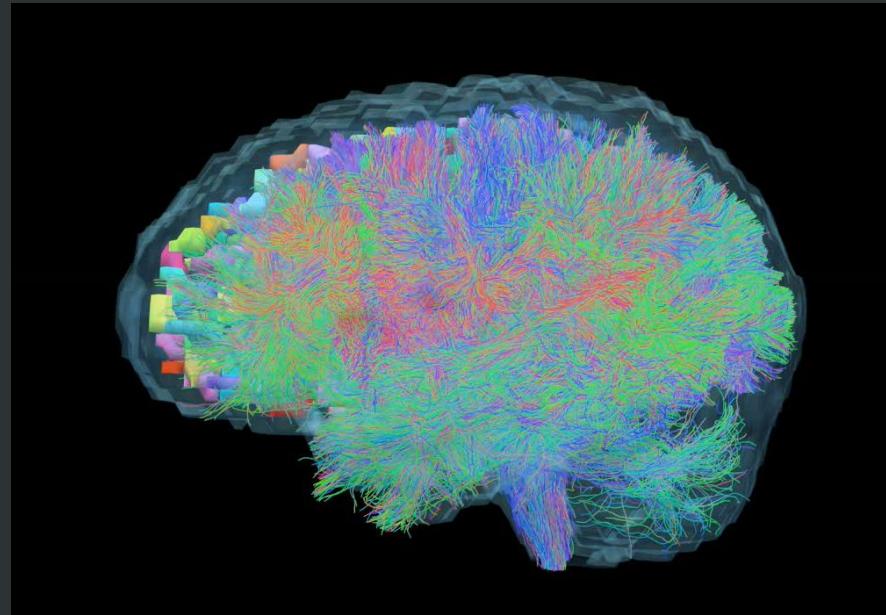
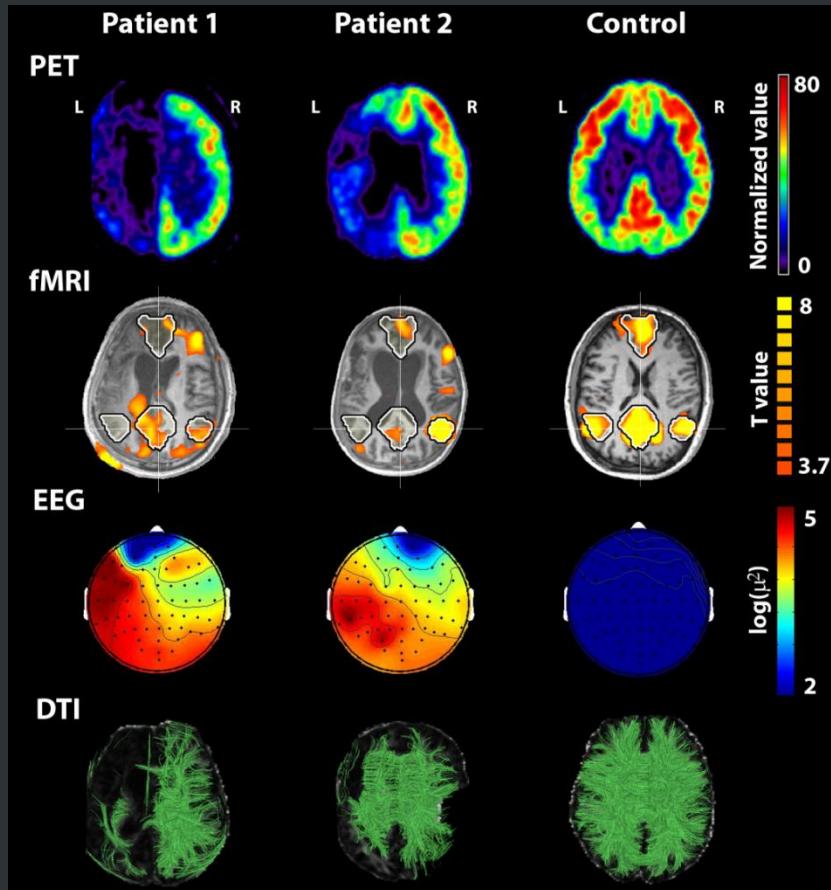


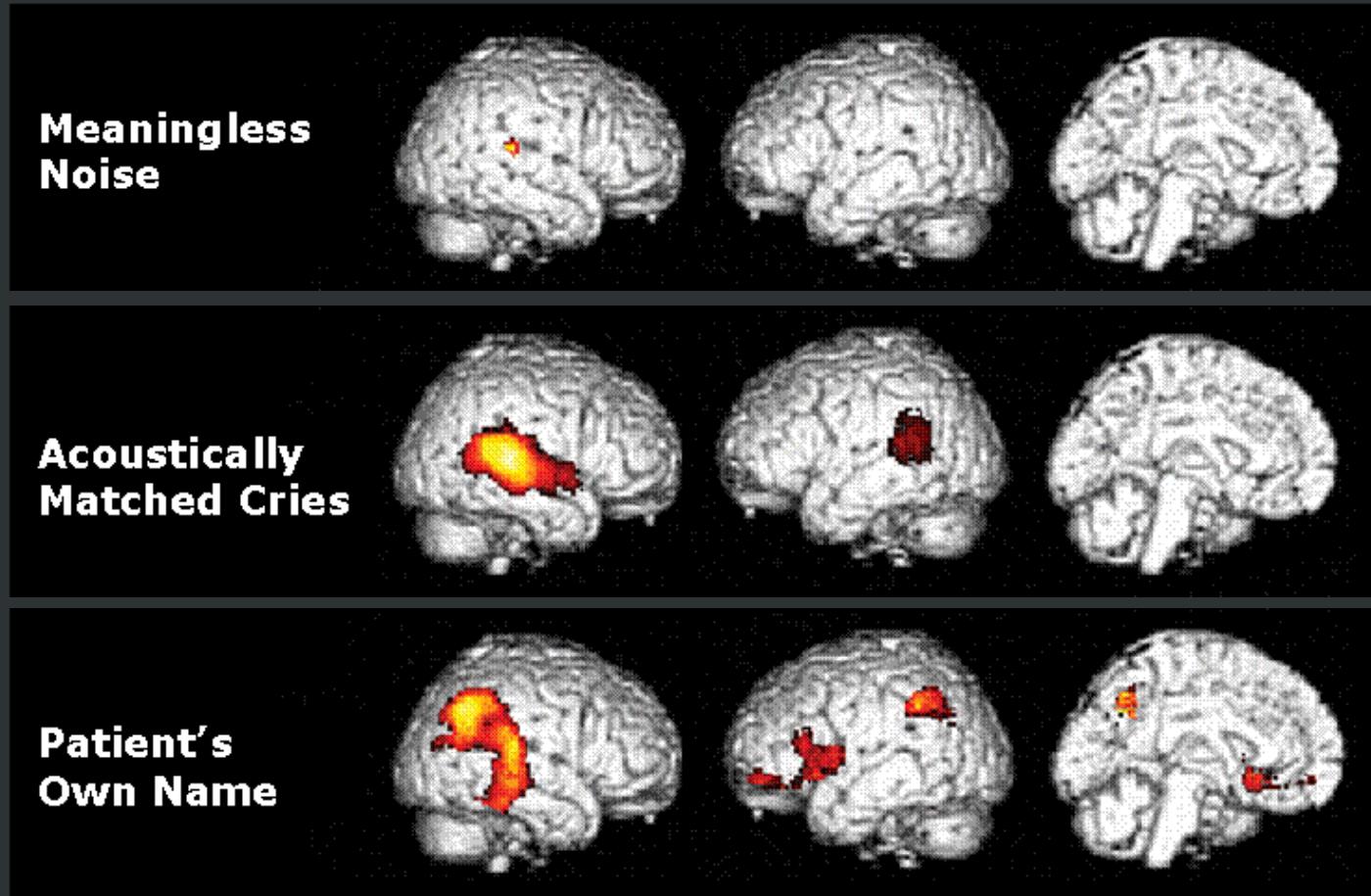
Figure 5. Linear discriminant analysis. Plotting the two discriminant functions (or canonical roots) against each other separated the GOS 1–3 group (unfavorable outcome, *closed circles*), the GOS 4–5 group (favorable outcome, *open circles*), and the control group (*open squares*). NAA, *N*-acetyl aspartate; *Cr*, creatine; *GOS*, Glasgow Coma Scale; *DTI*, diffusion tensor imaging.

Combining neuroimaging approach



Erik Ziegler, *Cyclotron Art Committee*

Emotions in MCS patients





Statistical analysis



- Statistical analysis of latency, amplitude
- For all derivations and potentials
- ANOVA, t-test
- Group level



BCI features



- Synchronous/asynchronous
- Dependent/independent
- Robust to artifacts



Challenges



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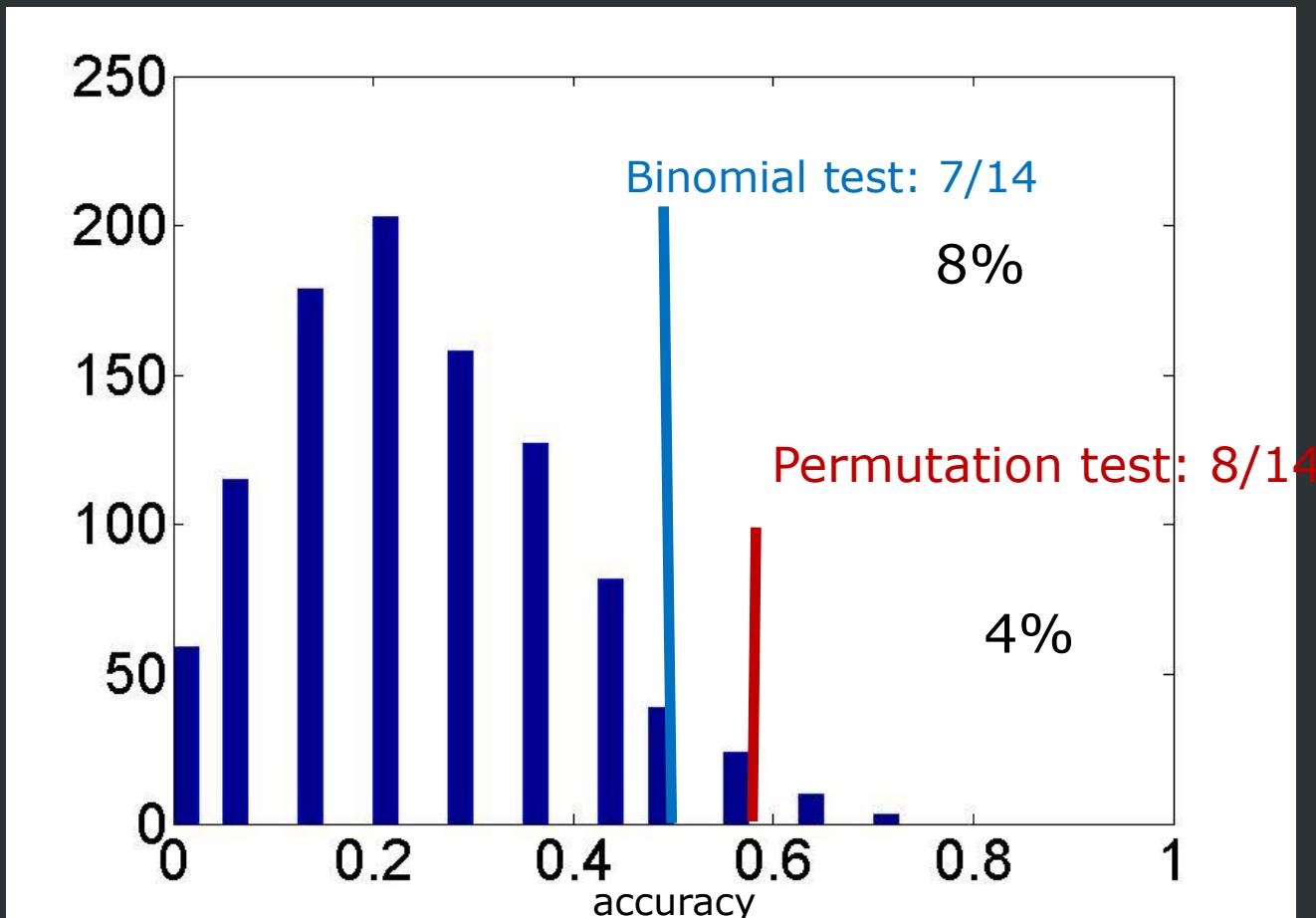


Should we trust the machine?



A Soddu

Statistical test: auditory P3





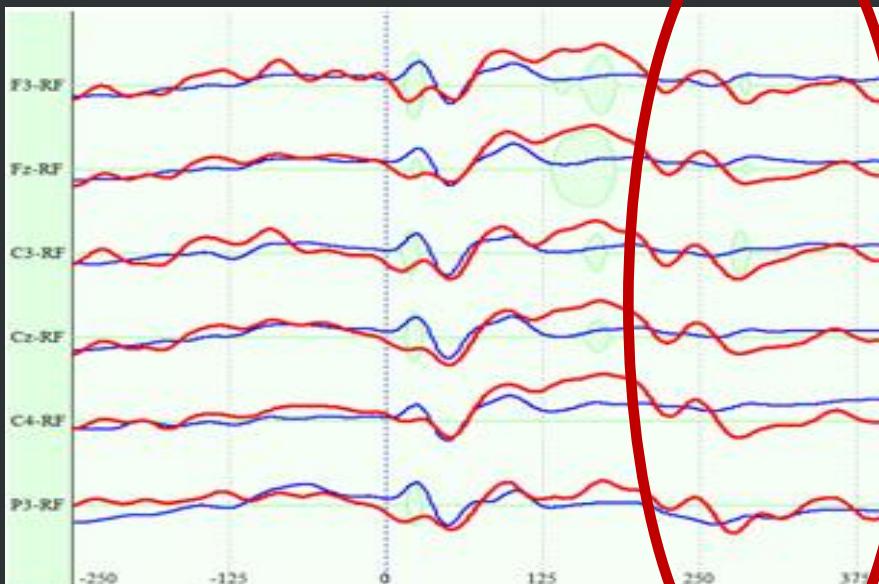
False Negative



References	Technique used- Brain response	False negative /Number of MCS+
Monti, et al. 2010	fMRI- imagery	17/18
Bardin et al., 2011	fMRI - imagery	2/5
Schnakers et al.	EEG- P3	2/9
Lulé et al. , 2012	EEG-P3	5/6
Goldfine et al, 2011	EEG-motor imagery	1,5/3

Feedback and motivation

Passive P3



Active P3



Feedback and motivation



- Always give the feedback in a positive way
- Goal oriented task
- Lots of tricky issues, see Sellers et al., 2010



BCI Limits for home use



- Not usable by non-technical personal
- Do not provide basic communication capacities (just binary: yes/no)
- Not easily configured for the needs of each user
- Not suited to periodic long-distance technical oversights