

COMA

SCIENCE GROUP



*Finding words in the silence:  
Detecting consciousness after severe brain injury*

07/10/2025

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COMA

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Coma Science Group (ULiège)



Brain injury inducing coma...  
what's next?

# Various states/levels of consciousness



**Coma**

Eyes  
closed

# Unresponsive Wakefulness Syndrome (UWS)



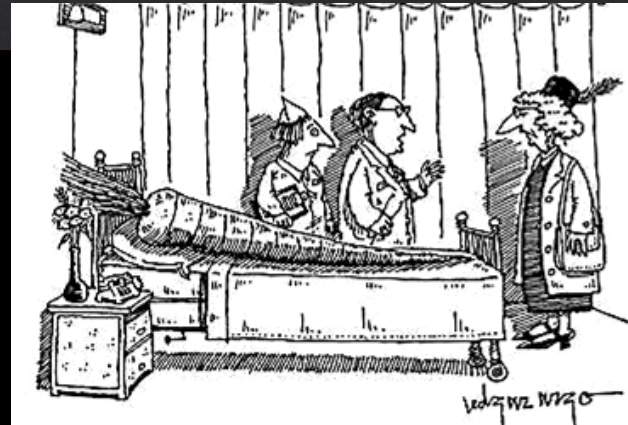
Coma

Eyes closed



VS/UWS

Arousal



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



# Minimally Conscious State (MCS)



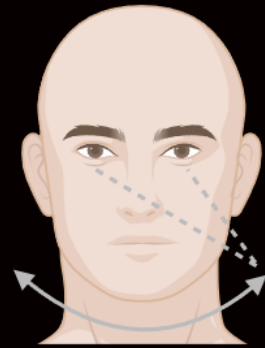
**Coma**

Eyes  
closed



**VS/UWS**

Arousal

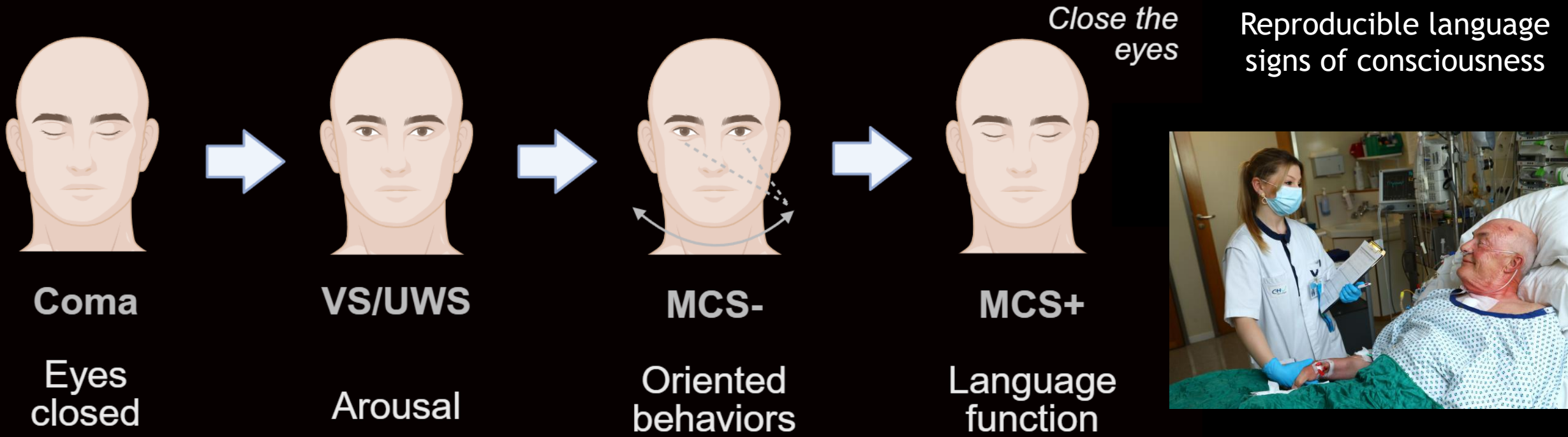


**MCS-**

Oriented  
behaviors

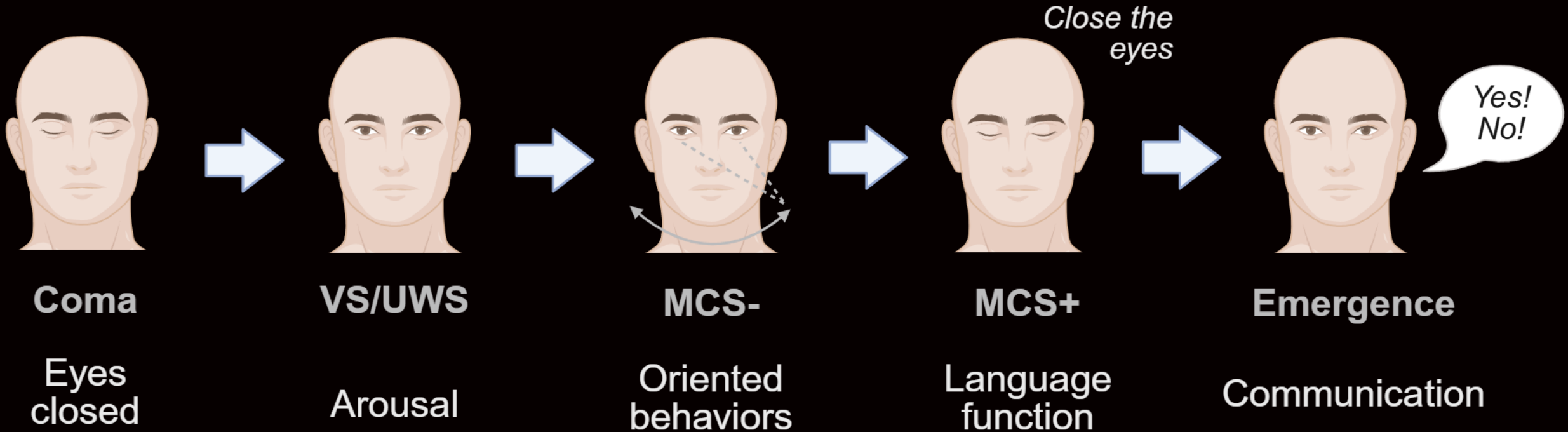


# Minimally Conscious State (MCS)



Command-following  
Intelligible verbalization  
Intentional communication

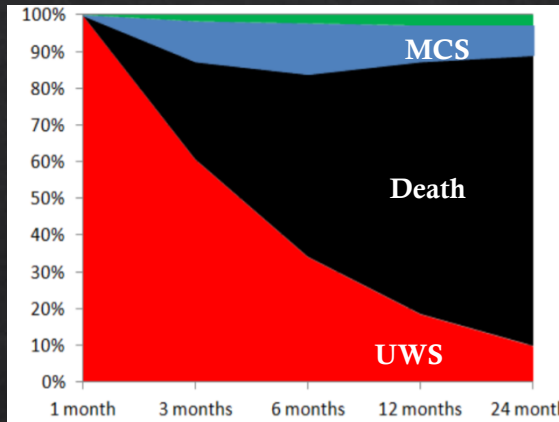
# Emergence from the MCS



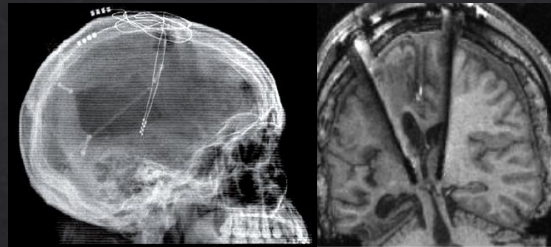
# Why is DoC diagnosis important?

## Prognosis

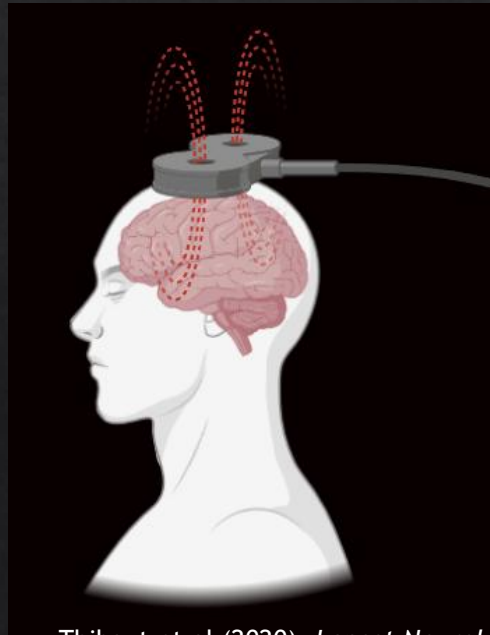
VS/UWS



## Therapeutic

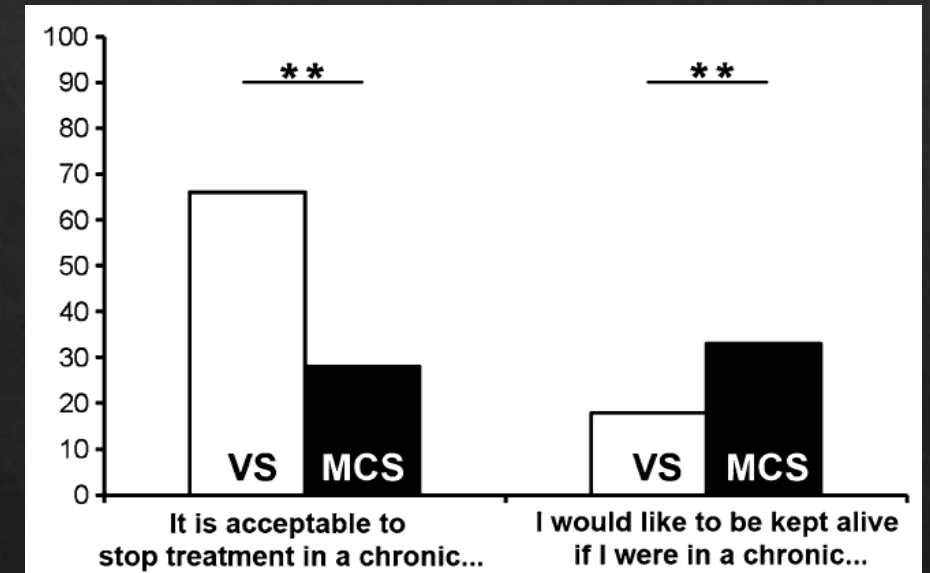


Schiff et al (2007), *Nature*



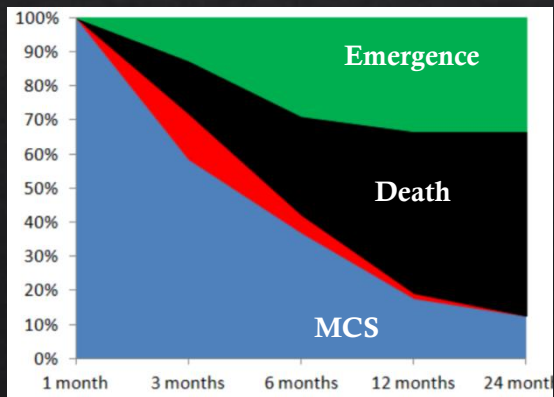
Thibaut et al (2020), *Lancet Neurol*

## Ethical aspects



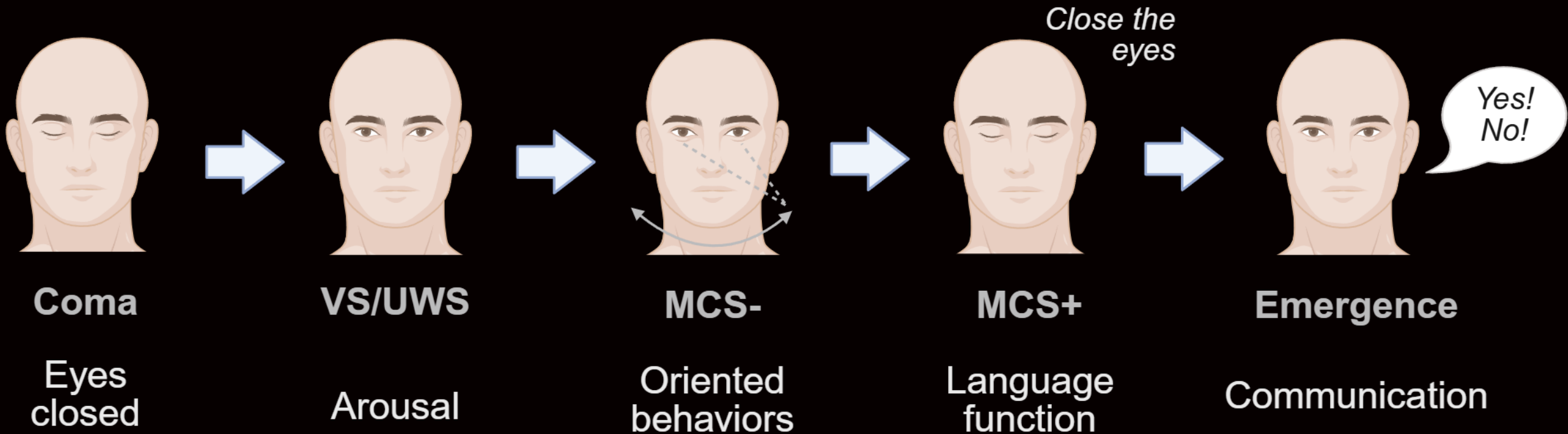
Demertzi et al (2011), *J Neurology*

MCS



Cassol et al, *unpublished data*

# Misdiagnosis rates



Disorders of Consciousness (DoC)

→ 30-40% risk based on clinical consensus

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

<b>Patient:</b>	<b>Diagnosis:</b>									
<b>Date of onset:</b>	<b>Date of Admission:</b>									
<b>Date</b>										
<b>Assessment</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>					
<b>AUDITORY FUNCTION SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
4 – Consistent Movement to Command <sup>■</sup>										
3 – Reproducible Movement to Command <sup>■</sup>										
2 – Localization to Sound										
1 – Auditory Startle										
0 – None										
<b>VISUAL FUNCTION SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
5 – Object Recognition <sup>■</sup>										
4 – Object localization: Reaching <sup>*</sup>										
3 – Visual Pursuit <sup>*</sup>										
2 – Fixation <sup>*</sup>										
1 – Visual Startle										
0 – None										
<b>MOTOR FUNCTION SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
6 – Functional Object Use <sup>†</sup>										
5 – Automatic Motor Response <sup>*</sup>										
4 – Object Manipulation <sup>*</sup>										
3 – Localisation to Noxious Stimulation <sup>*</sup>										
2 – Flexion Withdrawal										
1 – Abnormal Posturing										
0 – None										
<b>OROMOTOR/VERBAL FUNCTION SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
3 – Intelligible Verbalization <sup>■</sup>										
2 – Vocalization/Oral Movement										
1 – Oral Reflexive Movement										
0 – None										
<b>COMMUNICATION SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
2 – Functional: Accurate <sup>†</sup>										
1 – Non-functional: Intentional <sup>■</sup>										
0 – None										
<b>AROUSAL SCALE</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>	<b>#</b>	<b>TCC</b>
3 – Attention										
2 – Eye Opening w/o Stimulation										
1 – Eye Opening with Stimulation										
0 – Unarousable										
<b>TOTAL SCORE</b>										

\* Denotes Minimally Conscious State Minus (MCS-)  
 ■ Denotes Minimally Conscious State Plus (MCS+)  
 † Denotes emergence from Minimally Conscious State (eMCS)  
 TCC Test Completion Code

# Coma Recovery Scale-Revised (CRS-R)

## ANNALS of Neurology

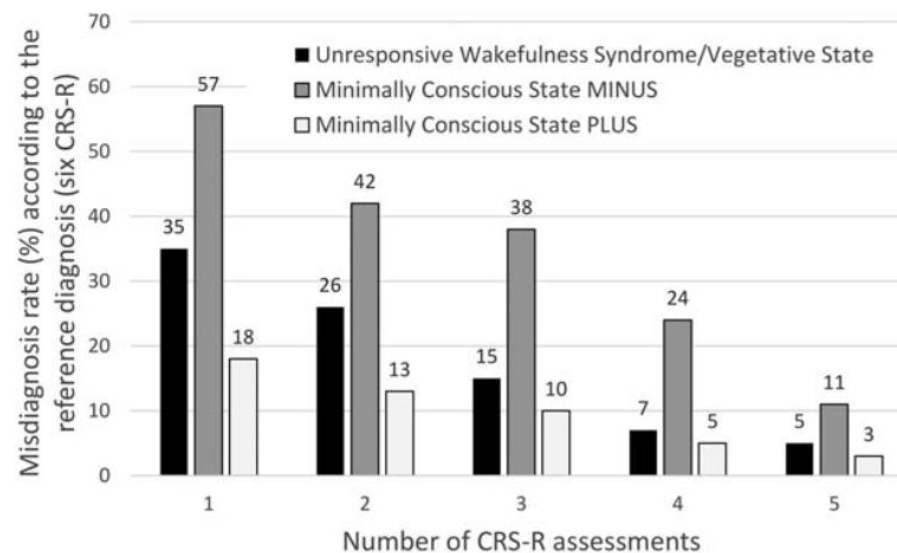


FIGURE 1: Misdiagnosis rates (%) of patients after n CRS-R assessments according to the diagnosis. CRS-R = Coma Recovery Scale-Revised.

5% misdiagnosis after 5 assessments



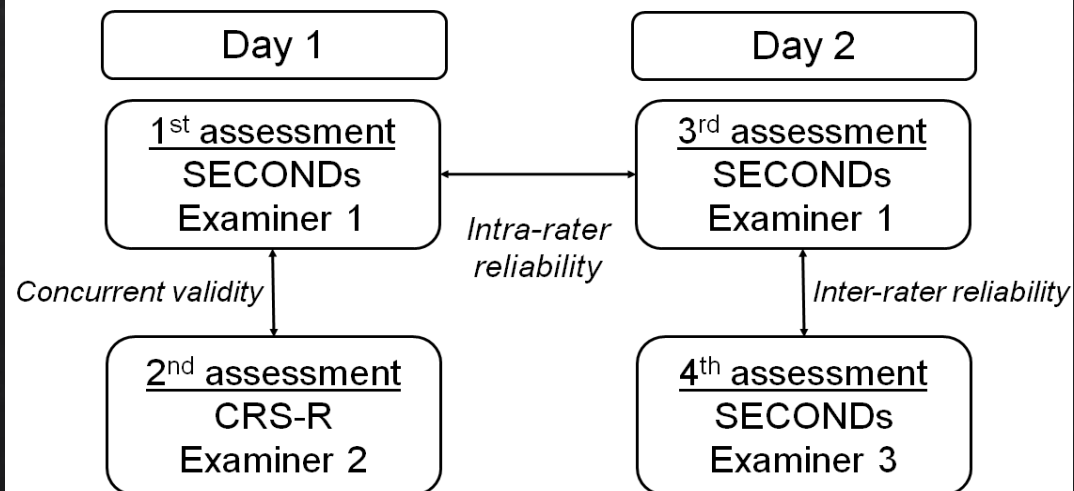
# Validation of the SECONDS

- 57 chronic DoC patients
- 3 examiners “blind” to clinical info
- Randomized order

> Ann Phys Rehabil Med. 2020 Sep 26;S1877-0657(20)30160-3. doi: 10.1016/j.j.rehab.2020.09.001.  
Online ahead of print.

## Simplified Evaluation of CONsciousness Disorders (SECONDS) in individuals with severe brain injury: a validation study

Charlène Aubinet<sup>1</sup>, Helena Cassol<sup>2</sup>, Olivier Bodart<sup>2</sup>, Leandro R D Sanz<sup>2</sup>, Sarah Wannez<sup>2</sup>, Charlotte Martial<sup>2</sup>, Aurore Thibaut<sup>2</sup>, Géraldine Martens<sup>2</sup>, Manon Carrière<sup>2</sup>, Olivia Gosseries<sup>2</sup>, Steven Laureys<sup>2</sup>, Camille Chatelle<sup>2</sup>



**Duration SECONDS:**

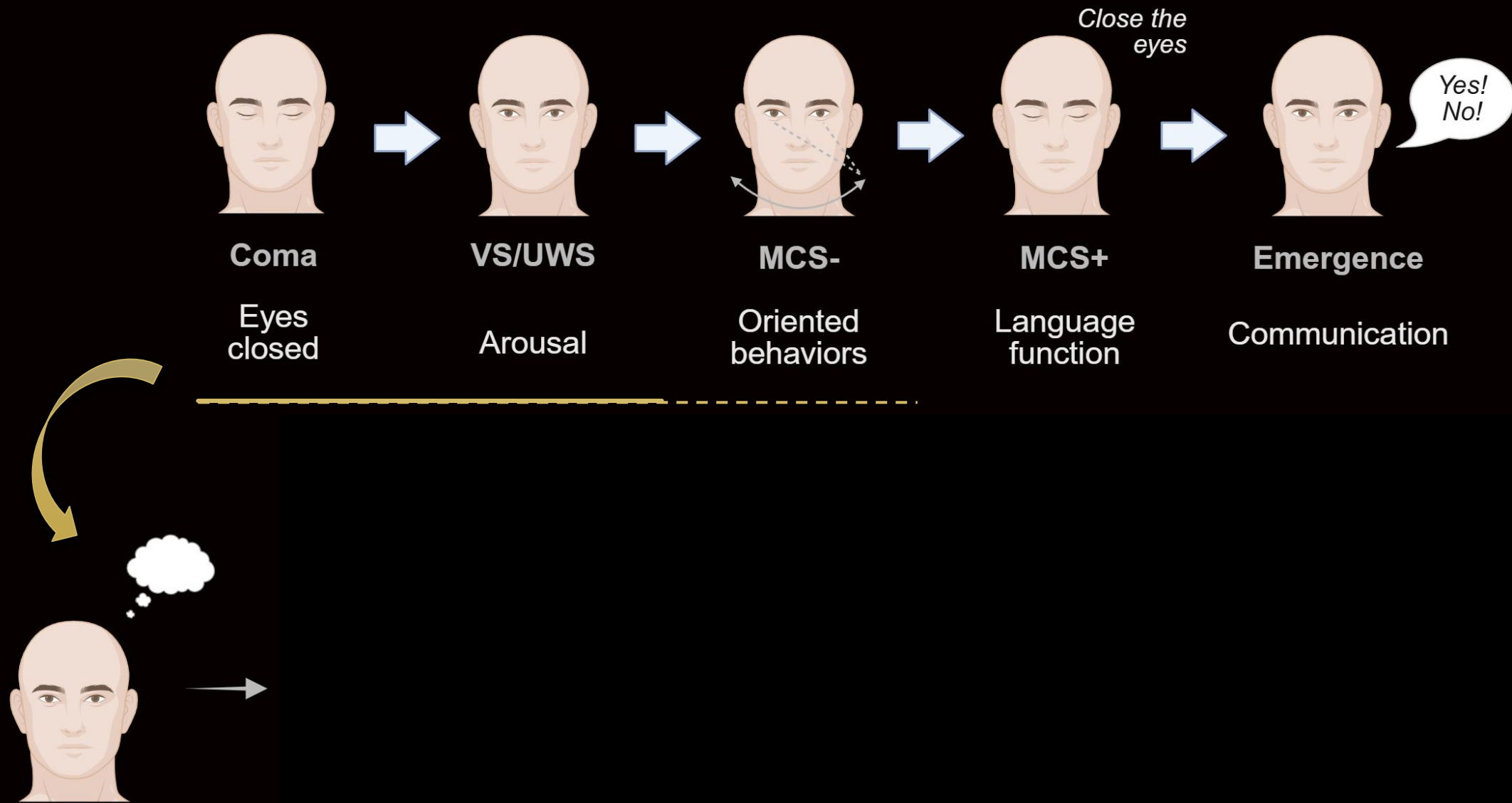
**7 min (CRS-R: 17 min)**

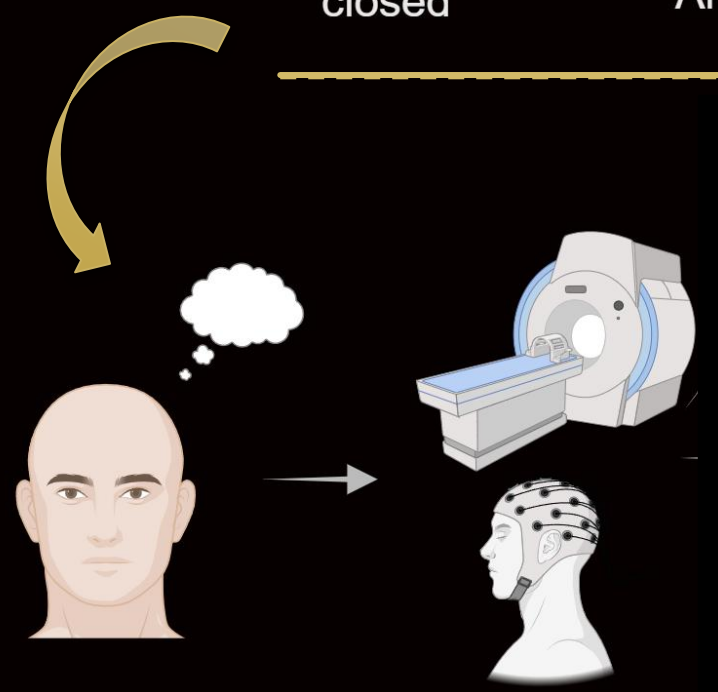
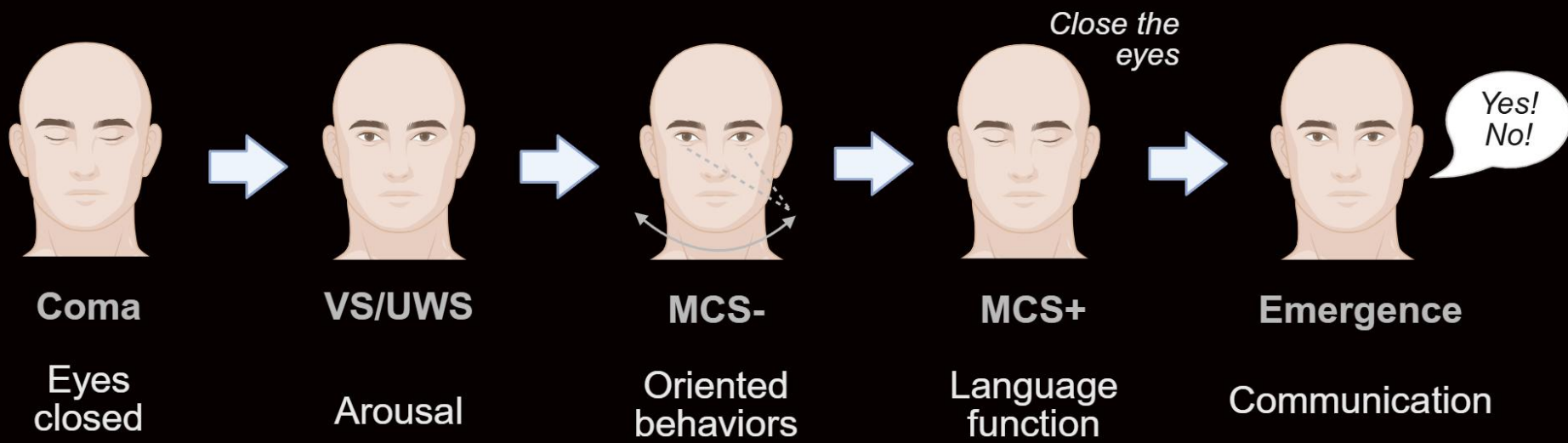
- **Concurrent validity:**
- CRS-R vs. SECONDS same day :  $\kappa = 0.78$  (substantial)
- CRS-R vs. SECONDS best:  $\kappa = 0.85$  (almost perfect)
- **Intra-rater reliability:**  $\kappa = 0.85$  (almost perfect)
- **Inter-rater reliability:**  $\kappa = 0.85$  (almost perfect)

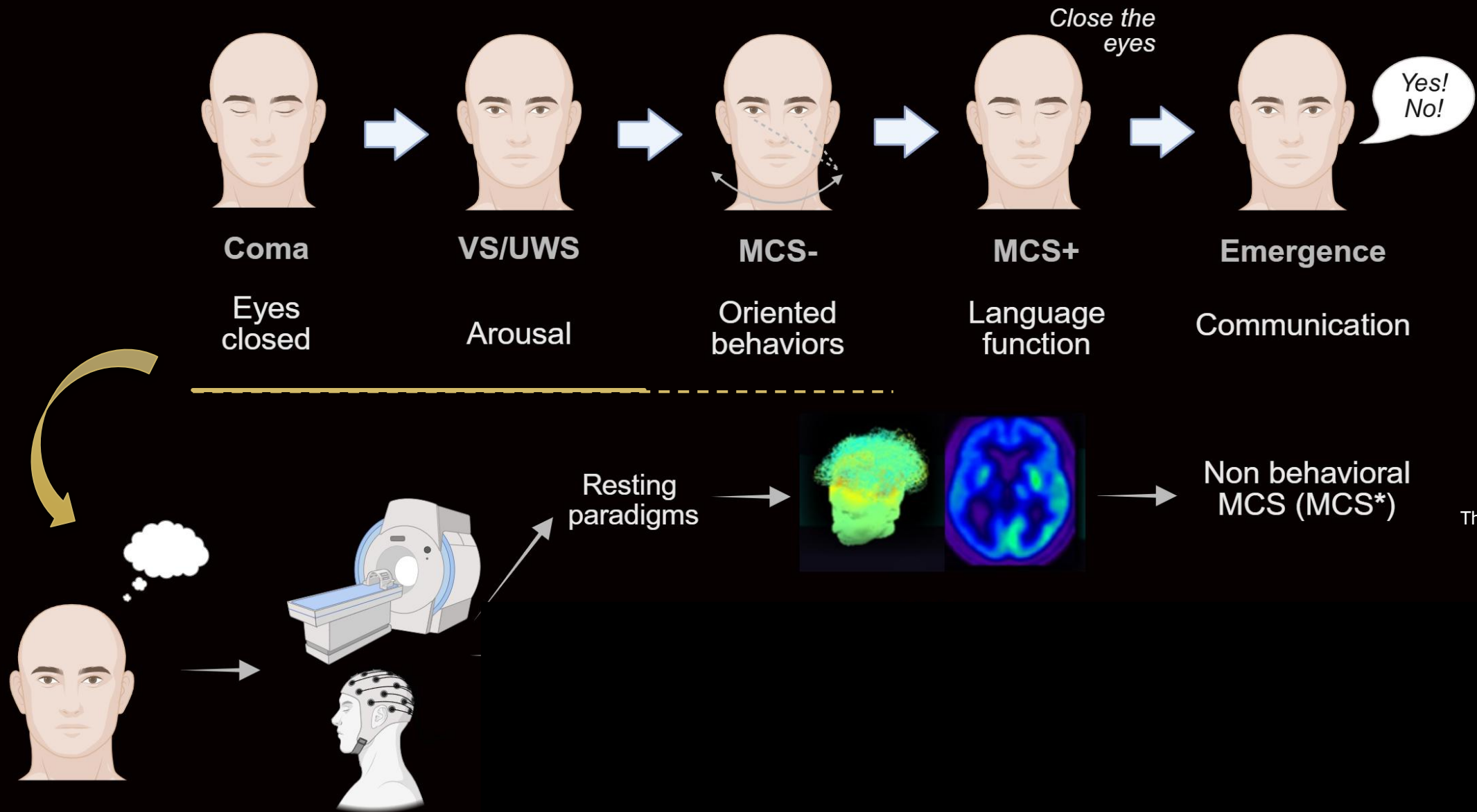


# Covert consciousness

*Unresponsiveness does not equate unconsciousness*







Thibaut et al. (2021),  
Ann Neurol

# Prediction of recovery

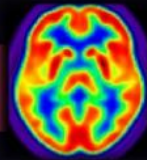
## Bedside behavioral assessment

## Positron emission tomography (PET)

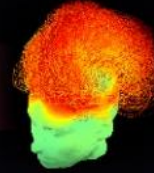
## Electroencephalography (EEG)

## Prognosis after 1 year

Control

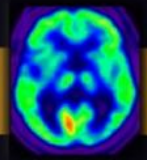


Control

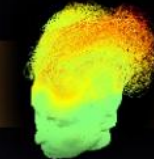


Minimally conscious

n=87

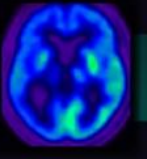


Minimally conscious state

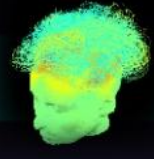


Unresponsive

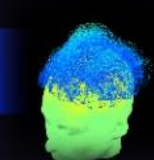
n=16  
n=48  
n=32



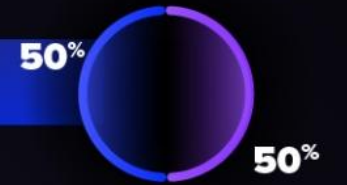
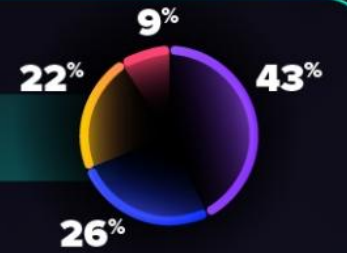
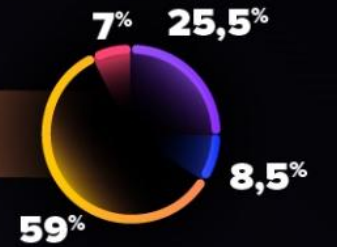
Minimally conscious state \*



Unresponsive wakefulness syndrome

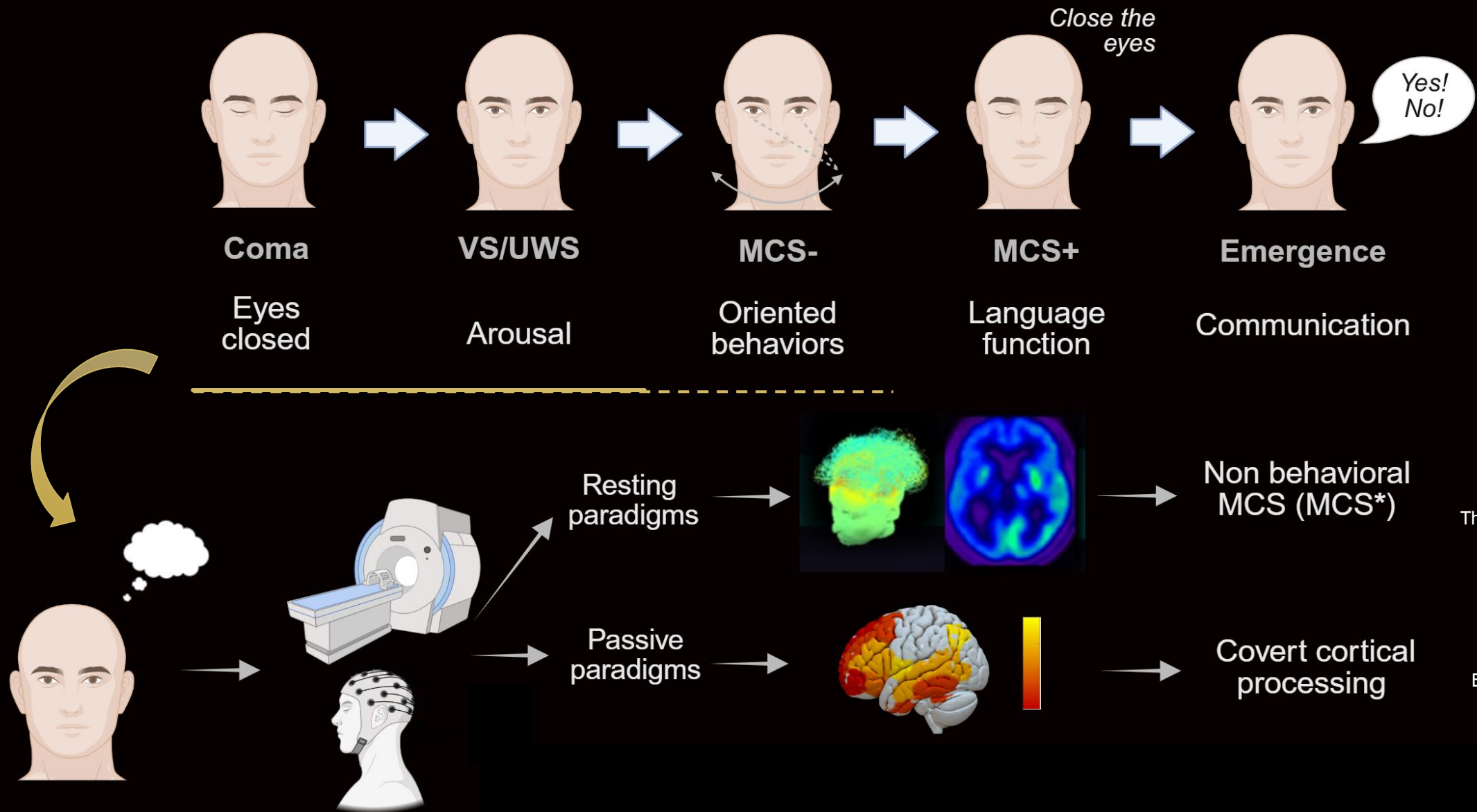


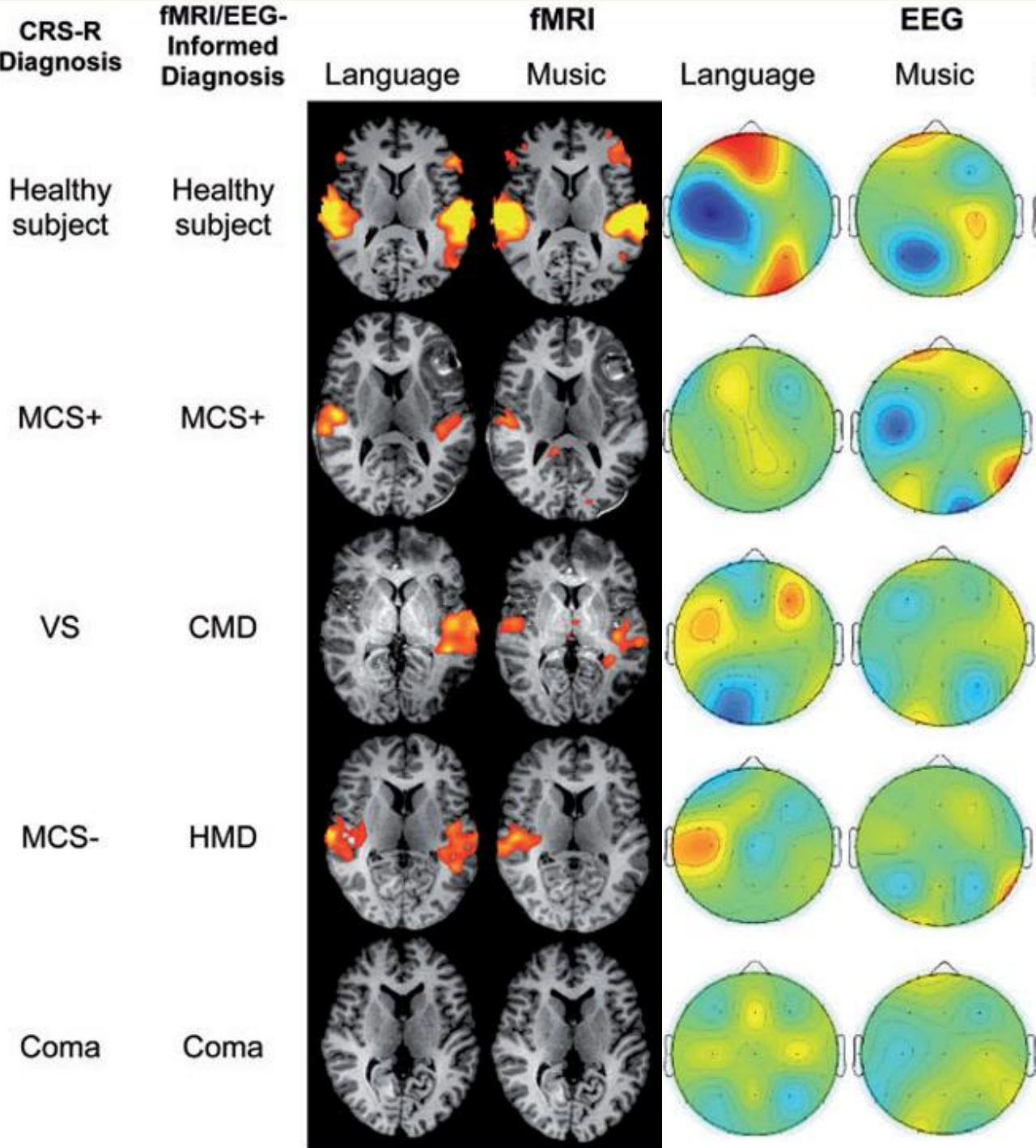
- Dead
- Unresponsive wakefulness syndrome
- Minimally conscious state
- Emergence



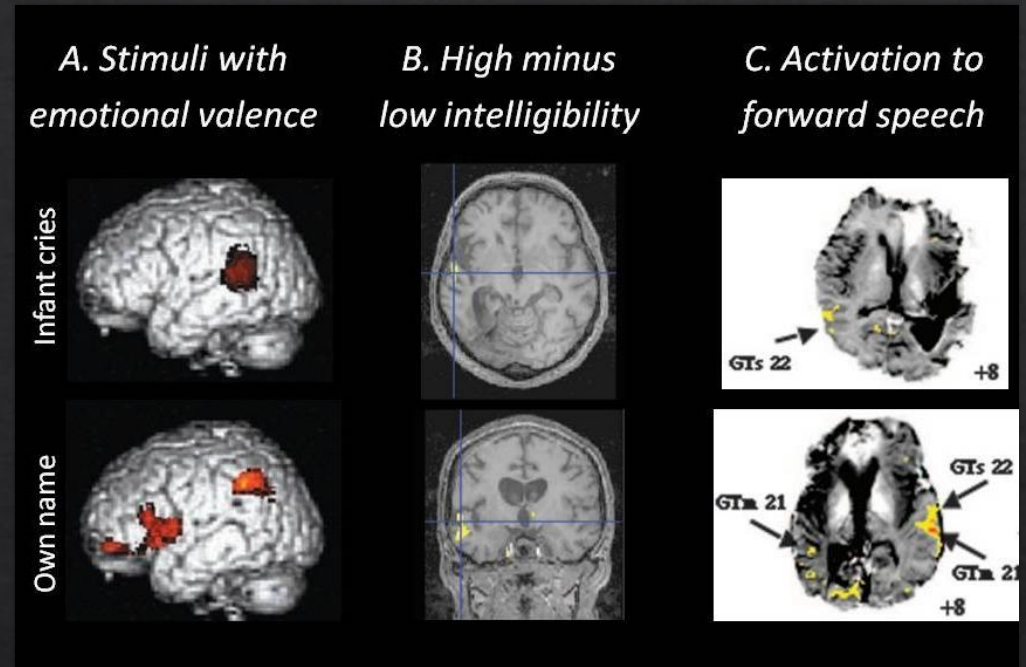
Brain metabolism

Brain functional connectivity



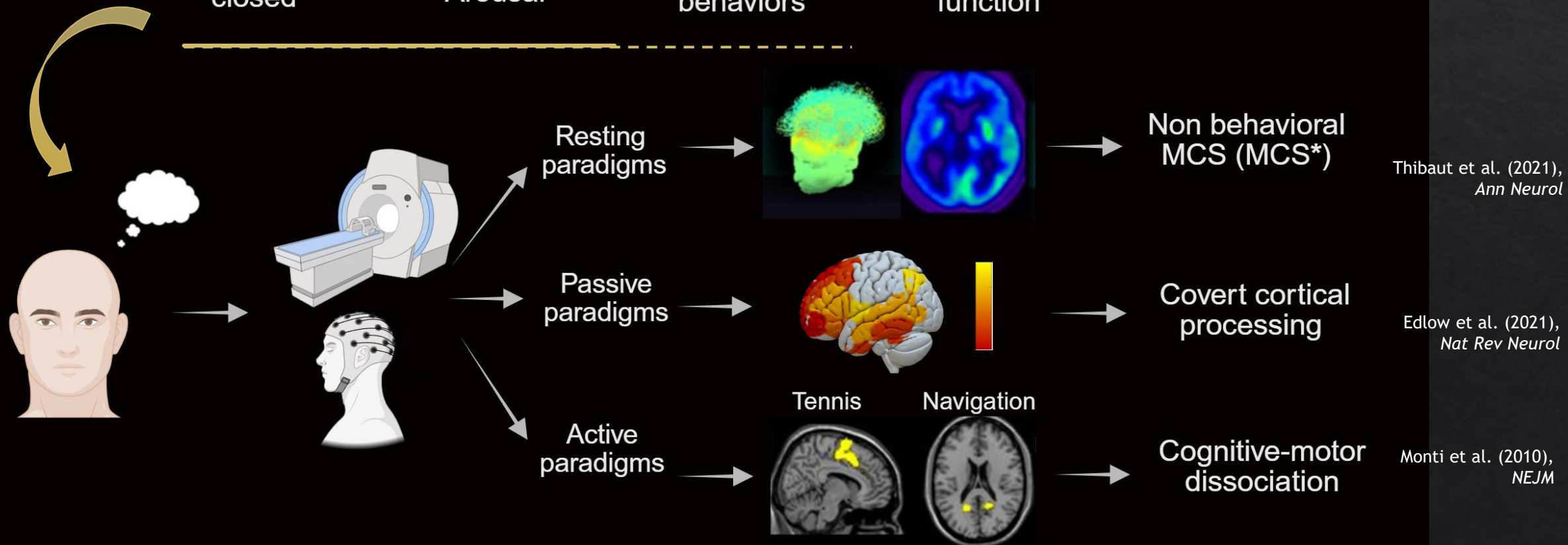
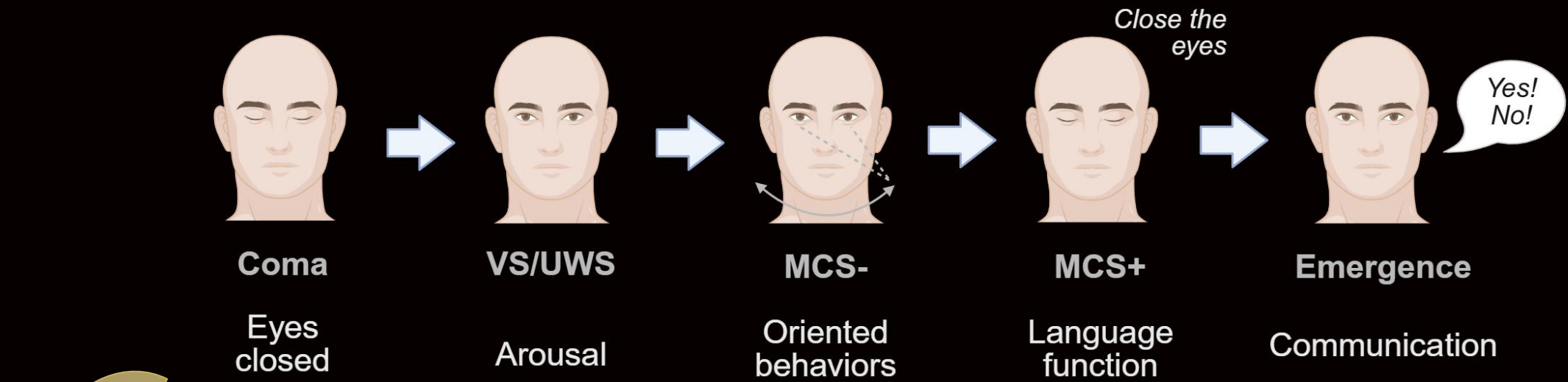


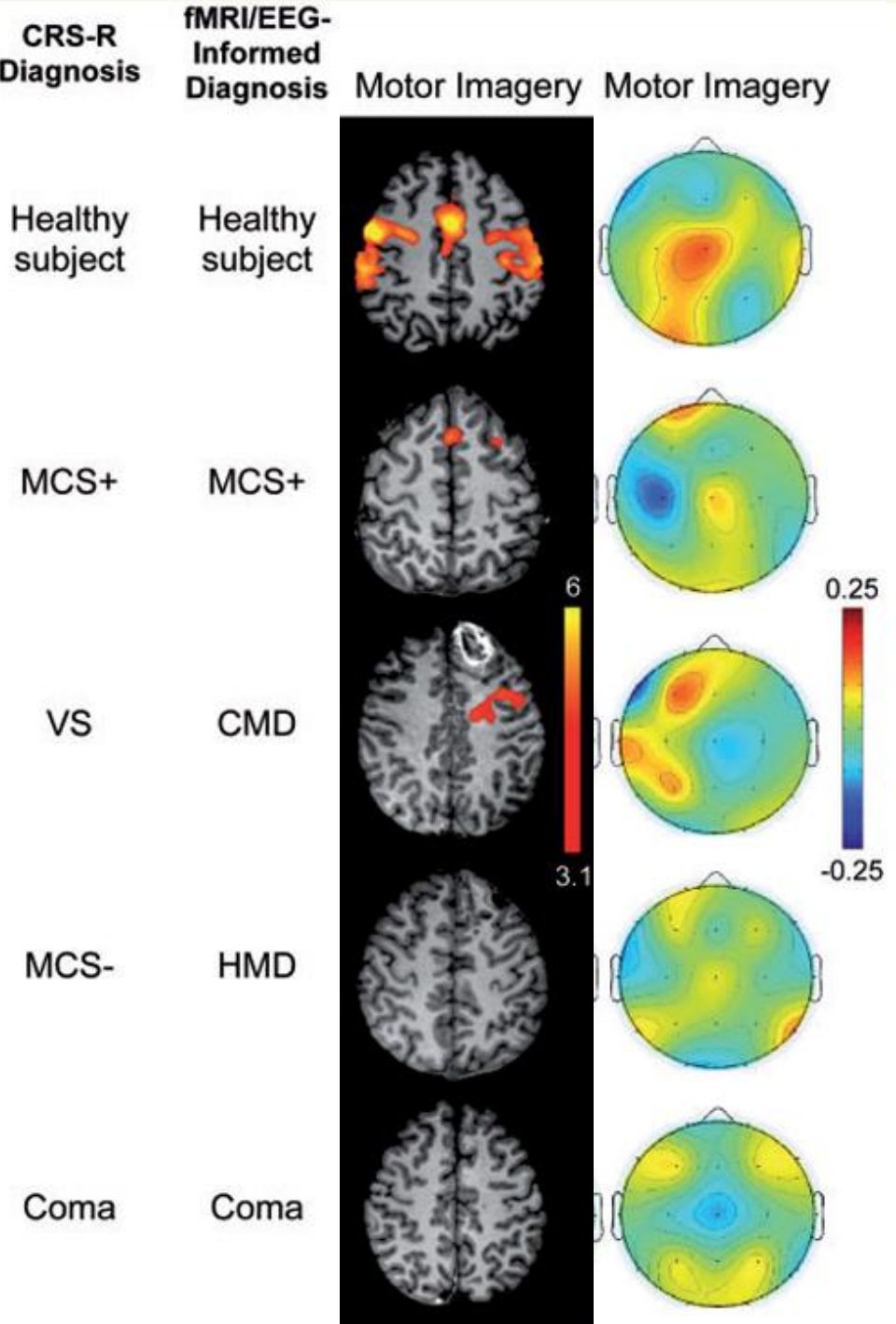
# Detection of residual cortical processing



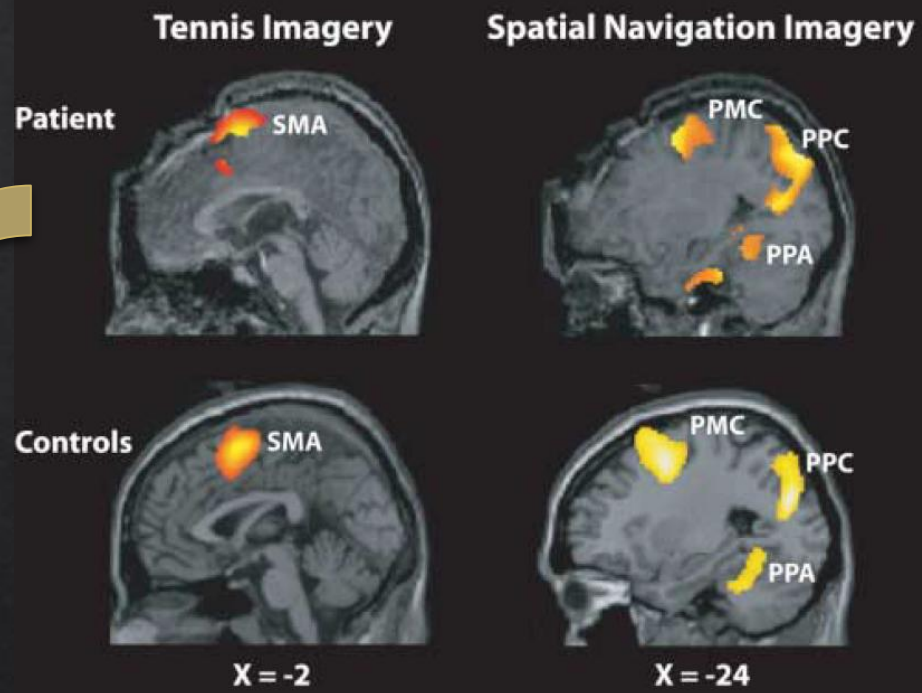
➔ Covert cortical processing

Laureys et al. (2004), *Neurology*  
 Owen et al. (2005), *Neuropsychol Rehabil*  
 Thibaut et al. (2005), *Neurology*  
 Edlow et al. (2017), *Brain*





# Detection of volitional cognitive processing



**Cognitive-motor dissociation  
~ 25% of unresponsive patients!**

Owen et al. (2005), *Neuropsychol Rehabil*  
 Edlow et al. (2017), *Brain*  
 Bodien et al. (2024), *NEJM*



Detection of residual language  
in disorders of consciousness

# Language is a crucial factor in consciousness recovery



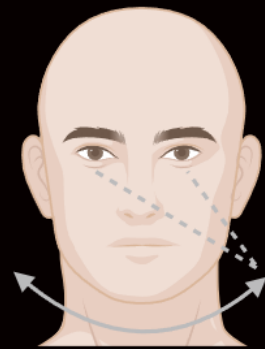
**Coma**

Eyes closed



**VS/UWS**

Arousal



**MCS-**

Oriented behaviors



*Close the eyes*

**MCS+**

Language function

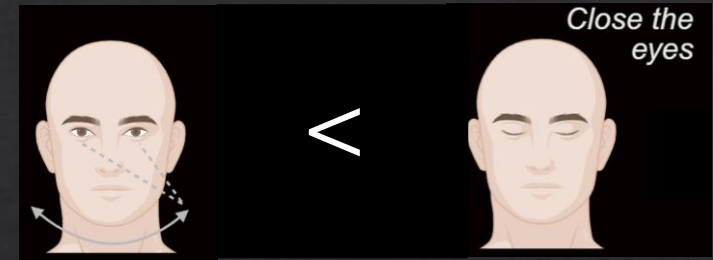


Yes!  
No!

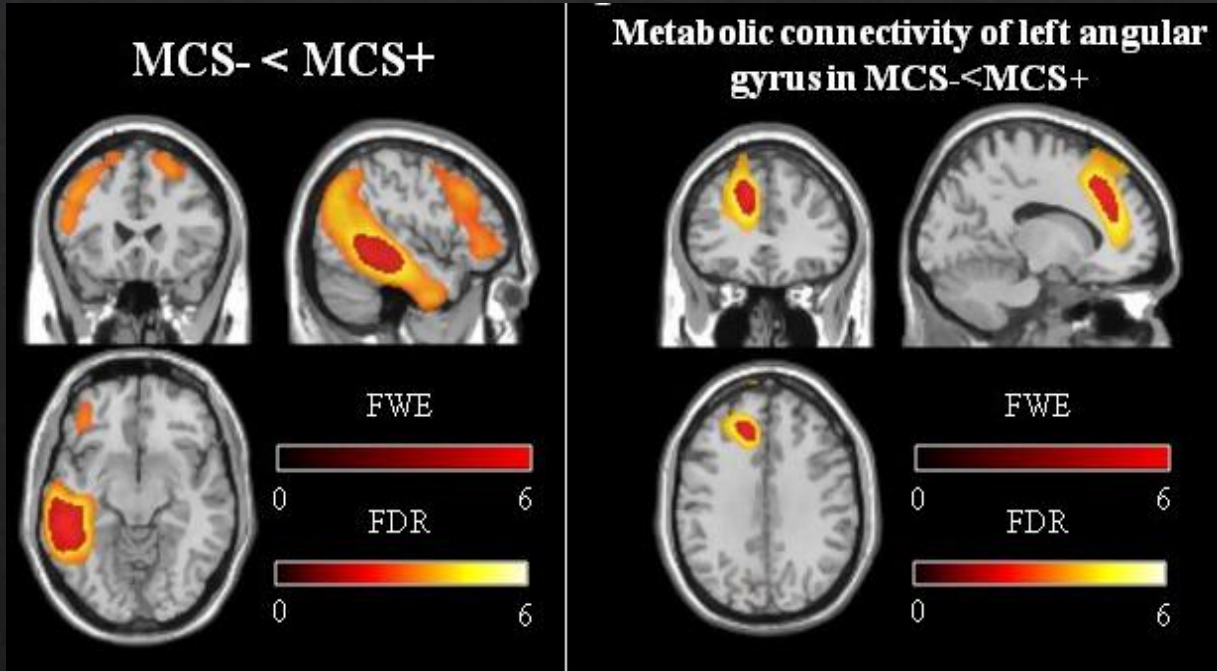
**Emergence**

Communication

# MCS+ as an example

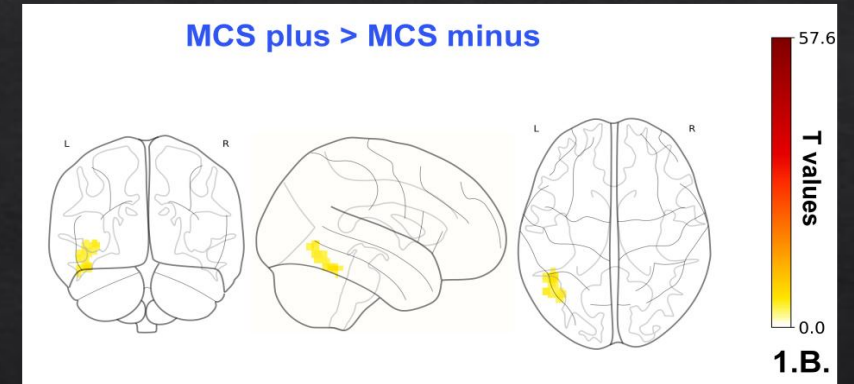


FDG-PET



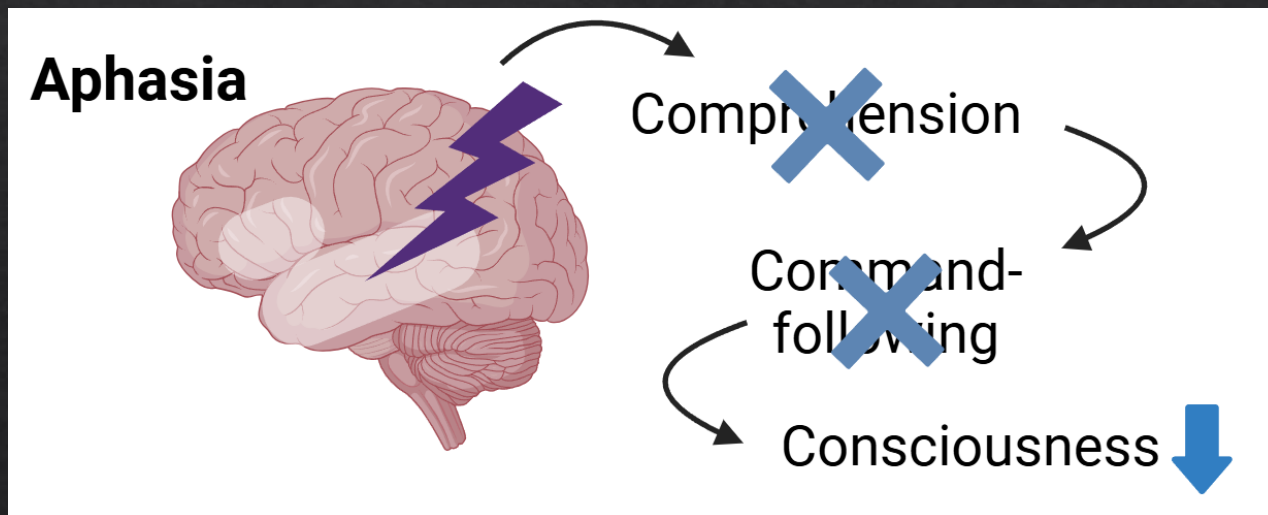
rsfMRI

Functional connectivity between the left DLPFC and left TOFC

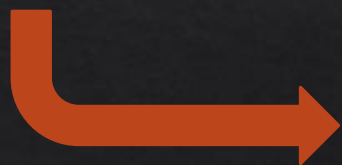


→ Recovery of language function more than consciousness

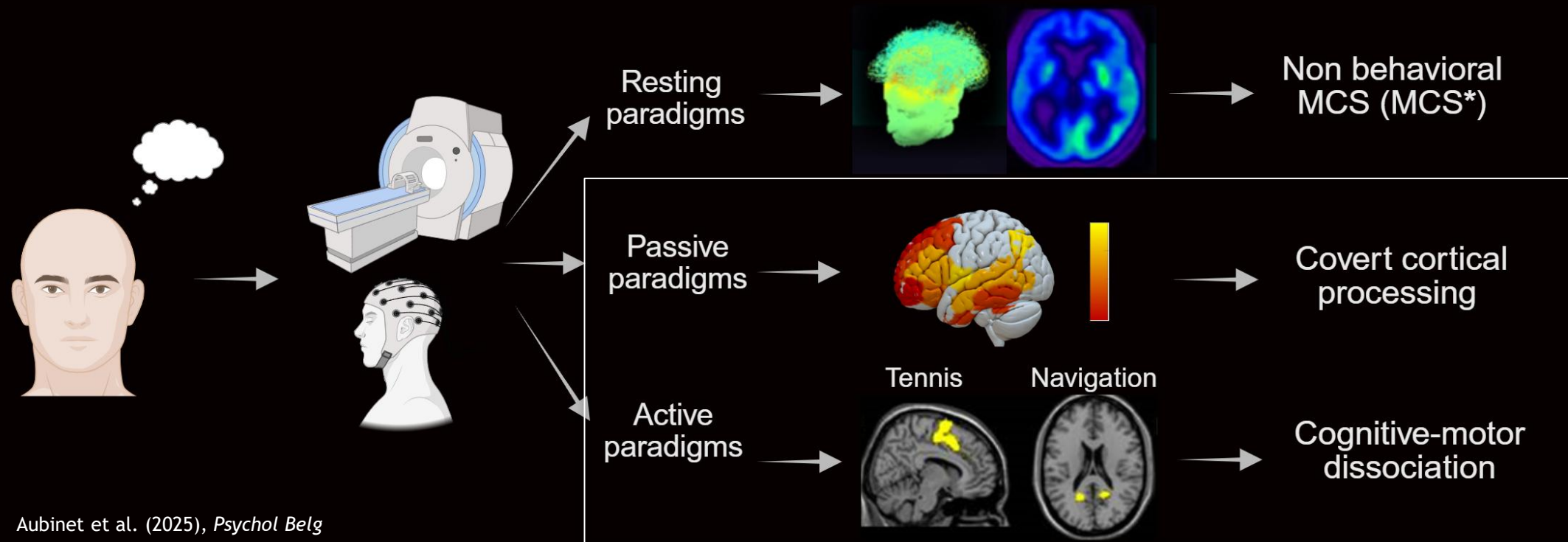
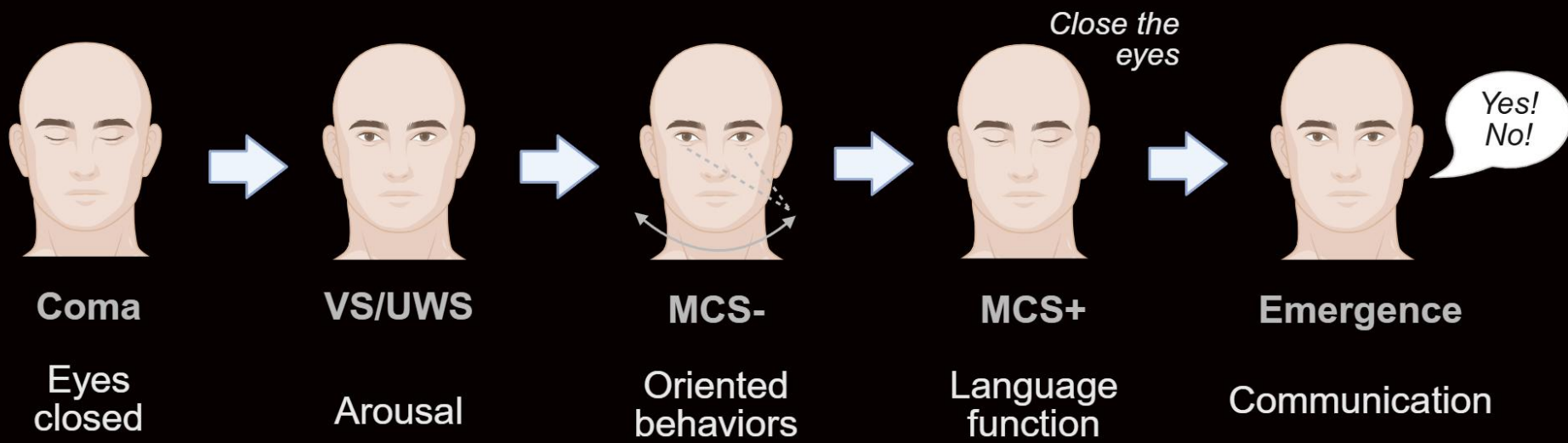
# Aphasia as a crucial factor of misdiagnosis



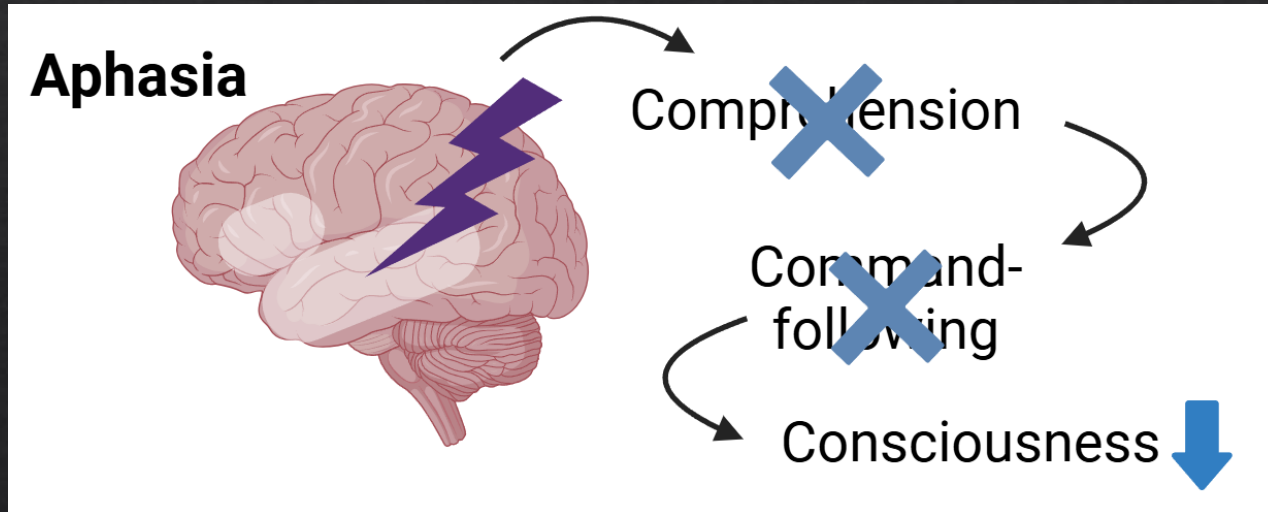
24 conscious aphasic patients  
→ CRS-R assessment  
→ 54% of patients with global aphasia: diagnosis = MCS!



*Crucial need to better characterize language impairments in post-comatose DoC patients*



# Aphasia as a crucial factor of misdiagnosis



50 conscious aphasic patients

- Comprehensive aphasia assessment
- EEG-based motor command task

→ Appropriate EEG responses 4x less likely in patients with receptive or global aphasia



*Crucial need to better characterize language impairments in post-comatose DoC patients*

# Behavioral scales including command-following

DoC diagnosis

BUT no language assessment...

→ Language domains?

→ Psycholinguistic variables?

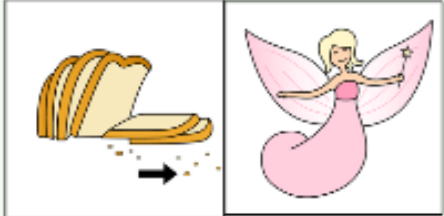


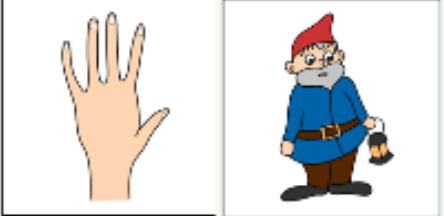
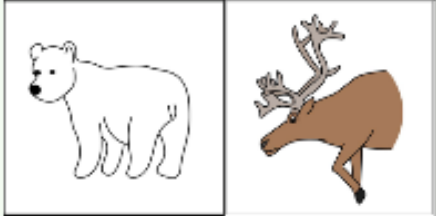

Towards a language-specific assessment



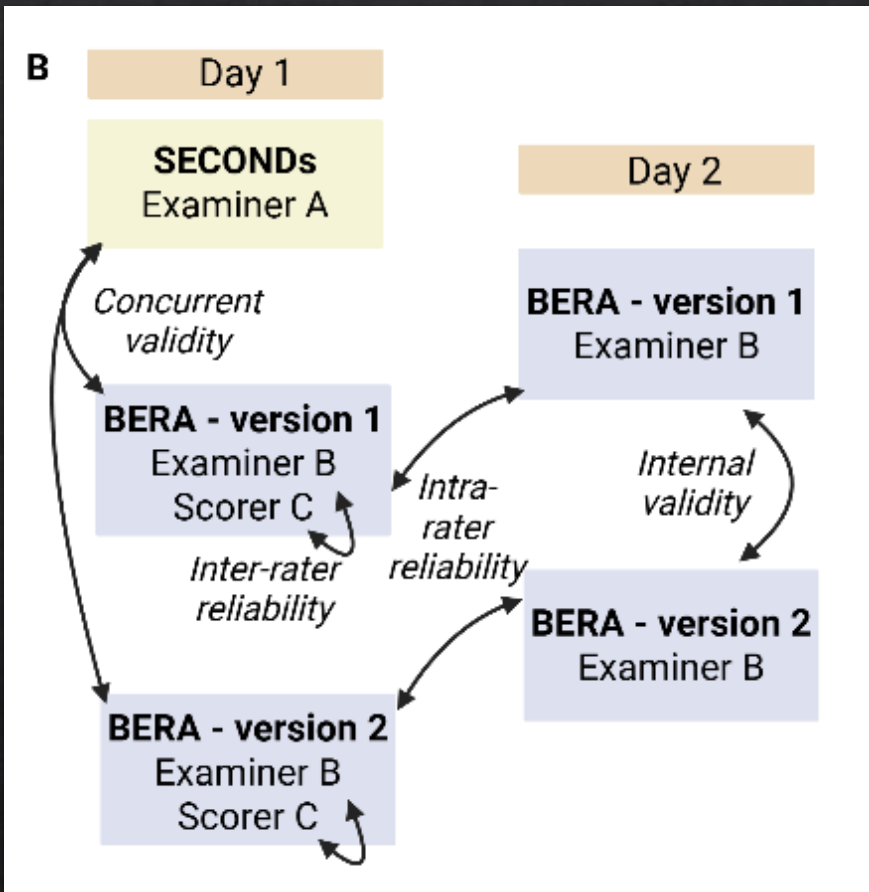
Elaboration of the  
*Brief Evaluation of Receptive Aphasia*



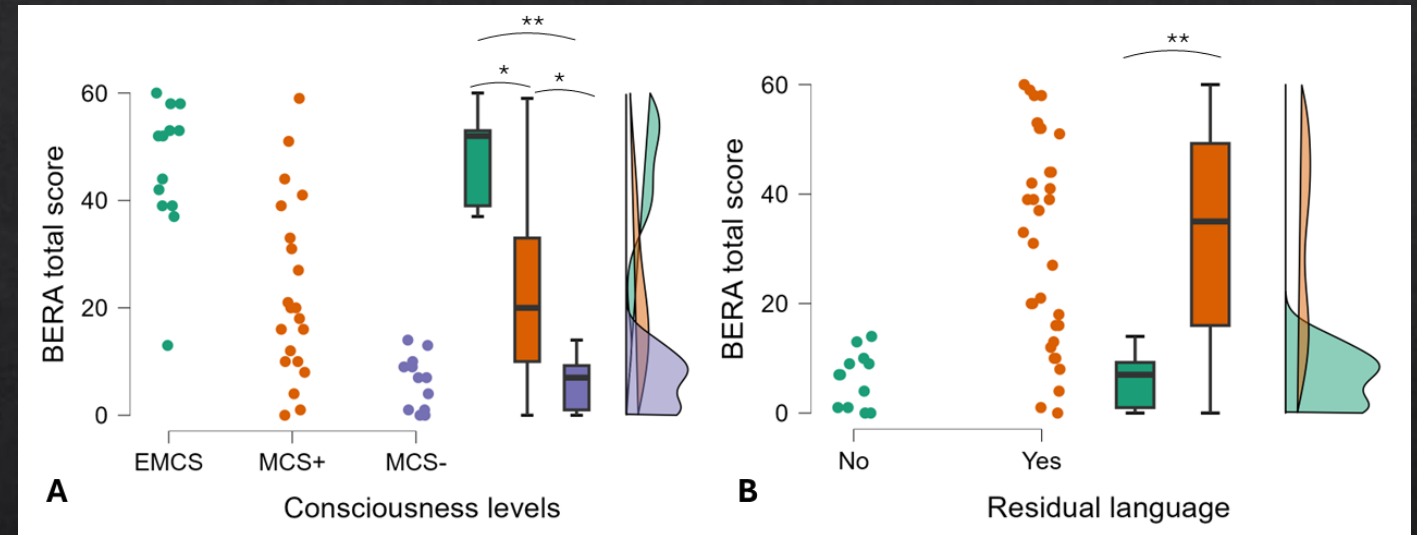
# 2 different versions of 30 items

Subscales	Phonology 10 items	Semantics 10 items	Morphosyntax 10 items
Unrelated items			
Related items			
Controlled psycholinguistic variables	Phonological similarity effect	Semantic category and word frequency effects	Length and complexity effects

# Validation of the BERA tool



- BERA total scores vs. SECONDS index:  $\rho = 0.816^{**}$
- BERA total scores vs. SECONDS language subindex:  $\rho = 0.776^{**}$



- Intra-rater reliability:  $ICC = 0.890$
- Inter-rater reliability:  $ICC = 0.997$
- Internal consistency between versions:  $ICC = 0.904$

# Computerized BERA using an eye-tracker

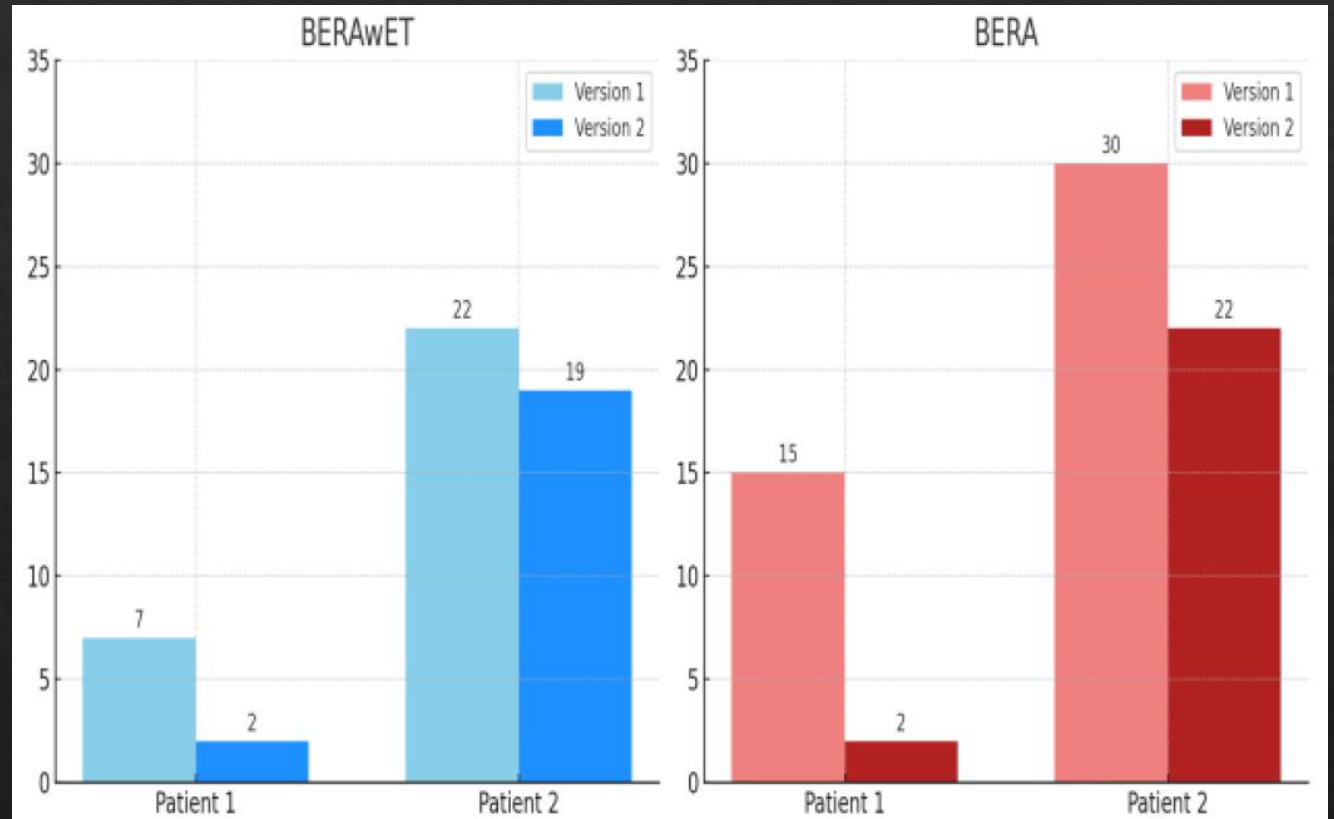
- Delphi study: opinion of 16 experts
  - 1st round → validation of **5 criteria**:
    - limitation of distractors
    - consideration of comorbidities
    - objectivity and consideration of the human factor
    - repeatability of measurements
    - consistency with the theoretical framework and characteristics of the target population
  - 2<sup>nd</sup> round → validation of **2 remaining criteria**:
    - temporal accessibility
    - ease of use and handling



# Computerized BERA using an eye-tracker

2 patients with a locked-in syndrome

→ Impact of oculomotor impairments



DoC → Calibration procedure



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Neuroscience and Biobehavioral Reviews

journal homepage: [www.elsevier.com/locate/neubiorev](https://www.elsevier.com/locate/neubiorev)



### Residual implicit and explicit language abilities in patients with disorders of consciousness: A systematic review

Charlène Aubinet<sup>a,b,\*</sup>, Camille Chatelle<sup>a,b</sup>, Olivia Gosseries<sup>a,b,c</sup>, Manon Carrière<sup>a,b</sup>, Steven Laureys<sup>a,b,c</sup>, Steve Majerus<sup>c,d</sup>

<sup>a</sup> Coma Science Group, GIGA Consciousness, University of Liège, Belgium

<sup>b</sup> Centre du Cerveau, University Hospital of Liège, Belgium

<sup>c</sup> Fund for Scientific Research, FNRS, Belgium

<sup>d</sup> Psychology and Neuroscience of Cognition Research Unit, University of Liège, Belgium

# Implicit vs. explicit language

- **Explicit:** controlled volitional processing in **command-following** during behavioral or brain-based active tasks
- **Implicit:** automatic brain processing in **response to stimuli**, involving reduced controllability or lack of intention

# Active tasks and explicit language processing

## Covert command-following

### Mental tasks

#### Motor imagery

- Tennis, navigation, swimming, hand moving,...

E.g.: Coleman et al., 2009; Braiman et al., 2018, Edlow et al., 2017; Bodien et al., 2017

#### Counting

- Subject's own name, targeted sound or word

E.g.: Hauger et al., 2015; Naci & Owen, 2013; Haug et al., 2018

#### Silent picture naming

Rodriguez-Moreno et al., 2010

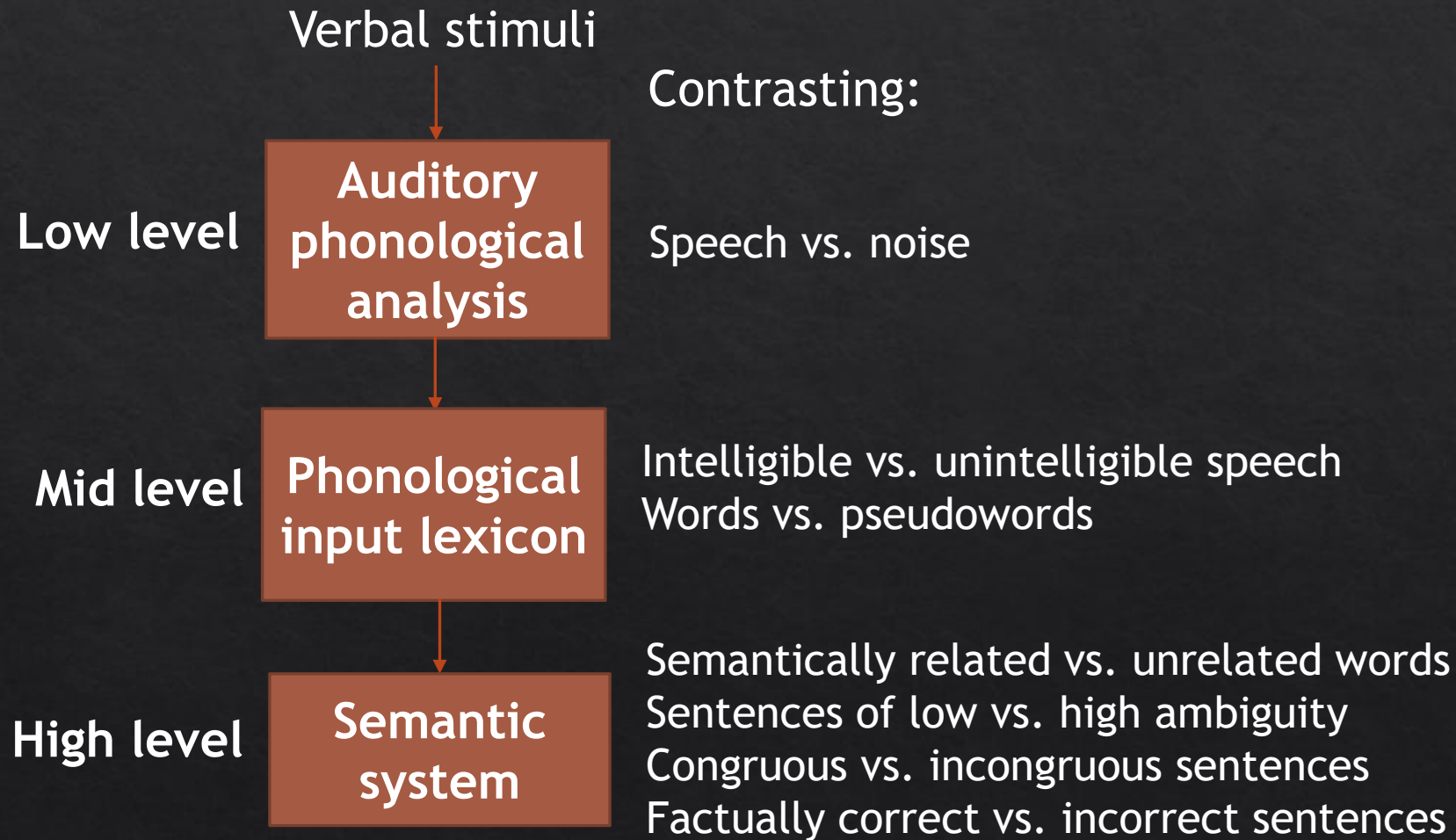
Potential residual brain response in all DoC categories

→ ~20% UWS and ~33% MCS-

= CMD!

# Passive tasks and implicit language processing

## Distinction of various language components



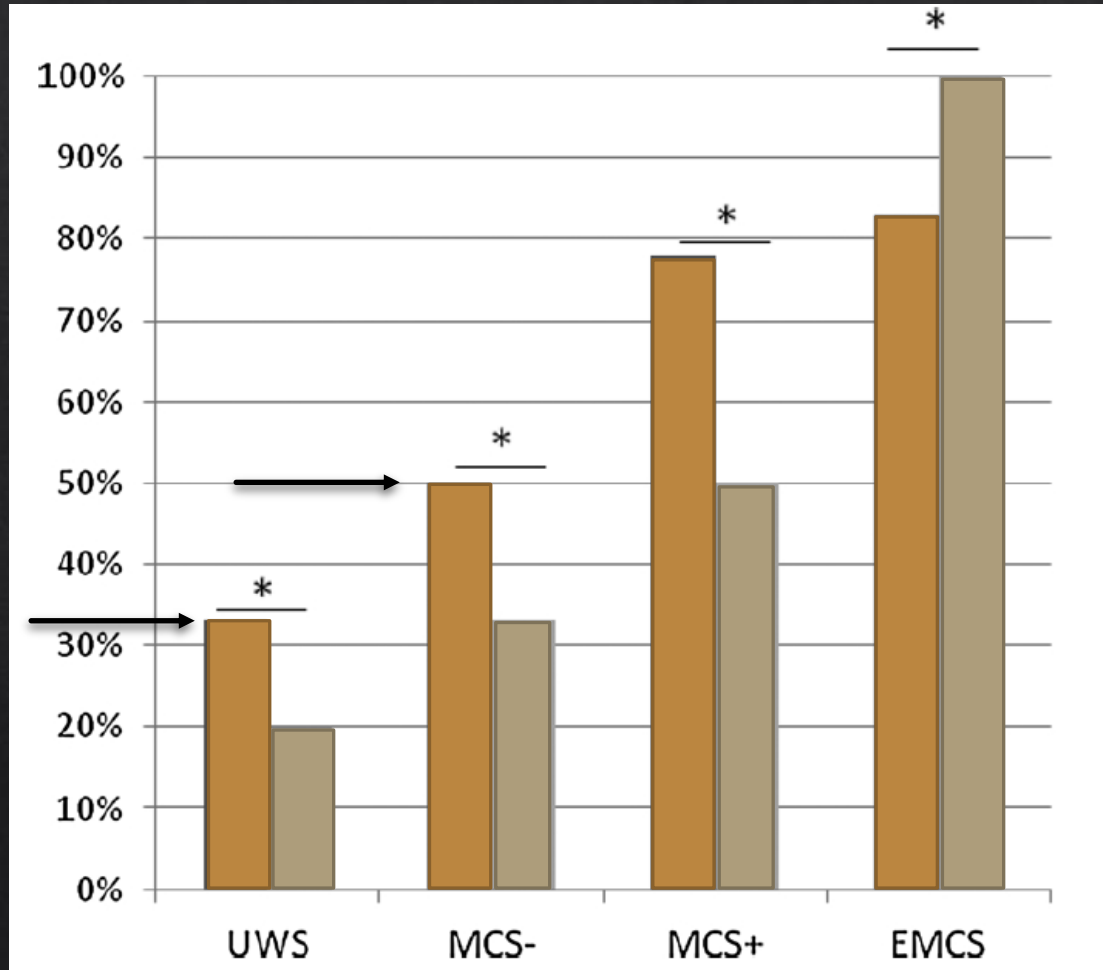
All language levels  
in all DoC  
→ High level also  
in UWS!

Brain response:  
UWS < MCS < EMCS

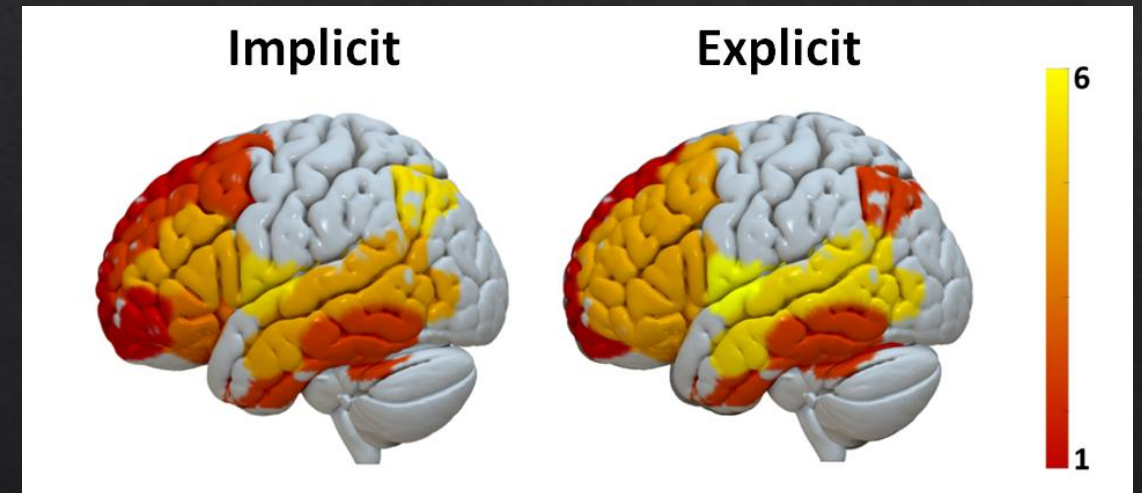
E.g.: Formisano et al., 2019;  
Kotchoubey et al., 2013; Balconi  
& Arangio, 2015; Kempny et al.,  
2018; Lechinger et al., 2016,  
Risetti et al., 2013, Rohaut et  
al., 2015; Tomaiuolo et al.,  
2016; ...

# Comparison in the various consciousness levels

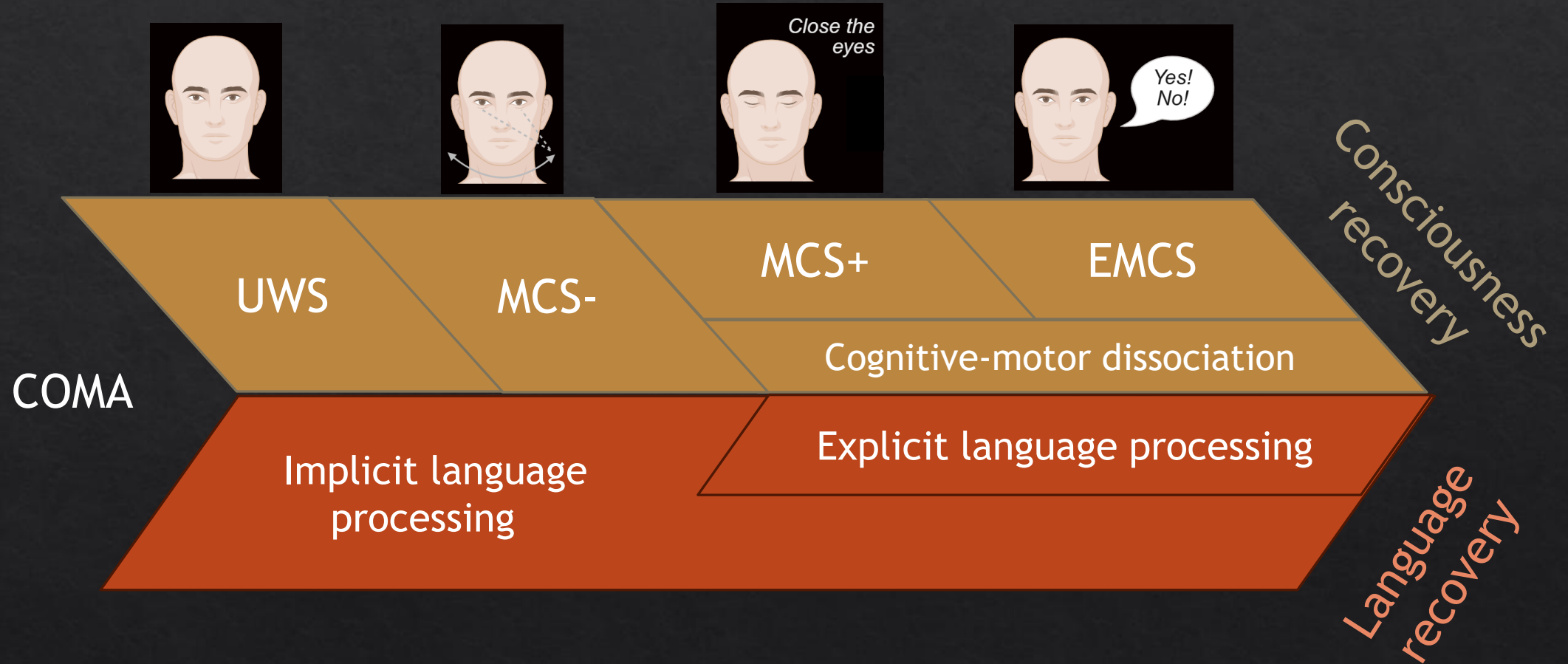
Proportion of patients



Brain location



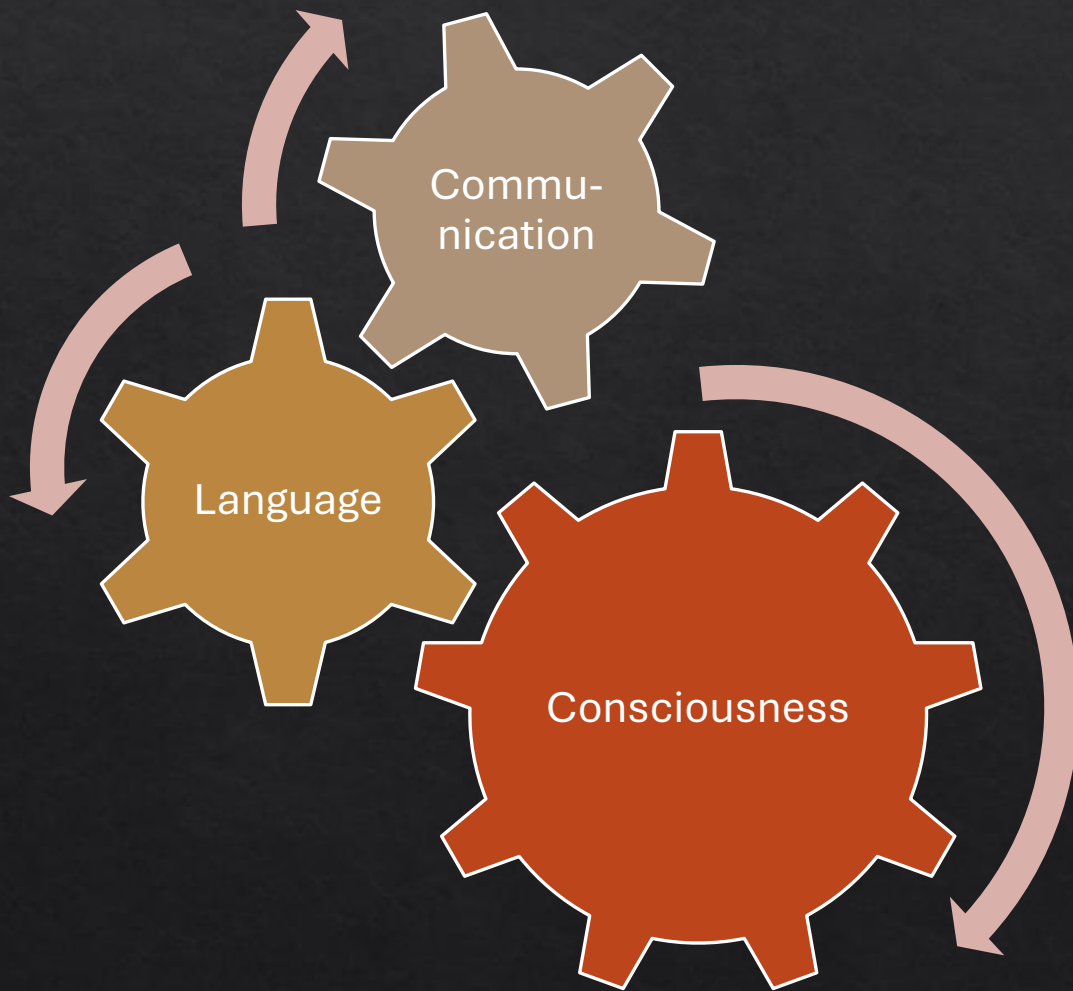
# Language recovery // consciousness recovery





# Interdependence of language and consciousness

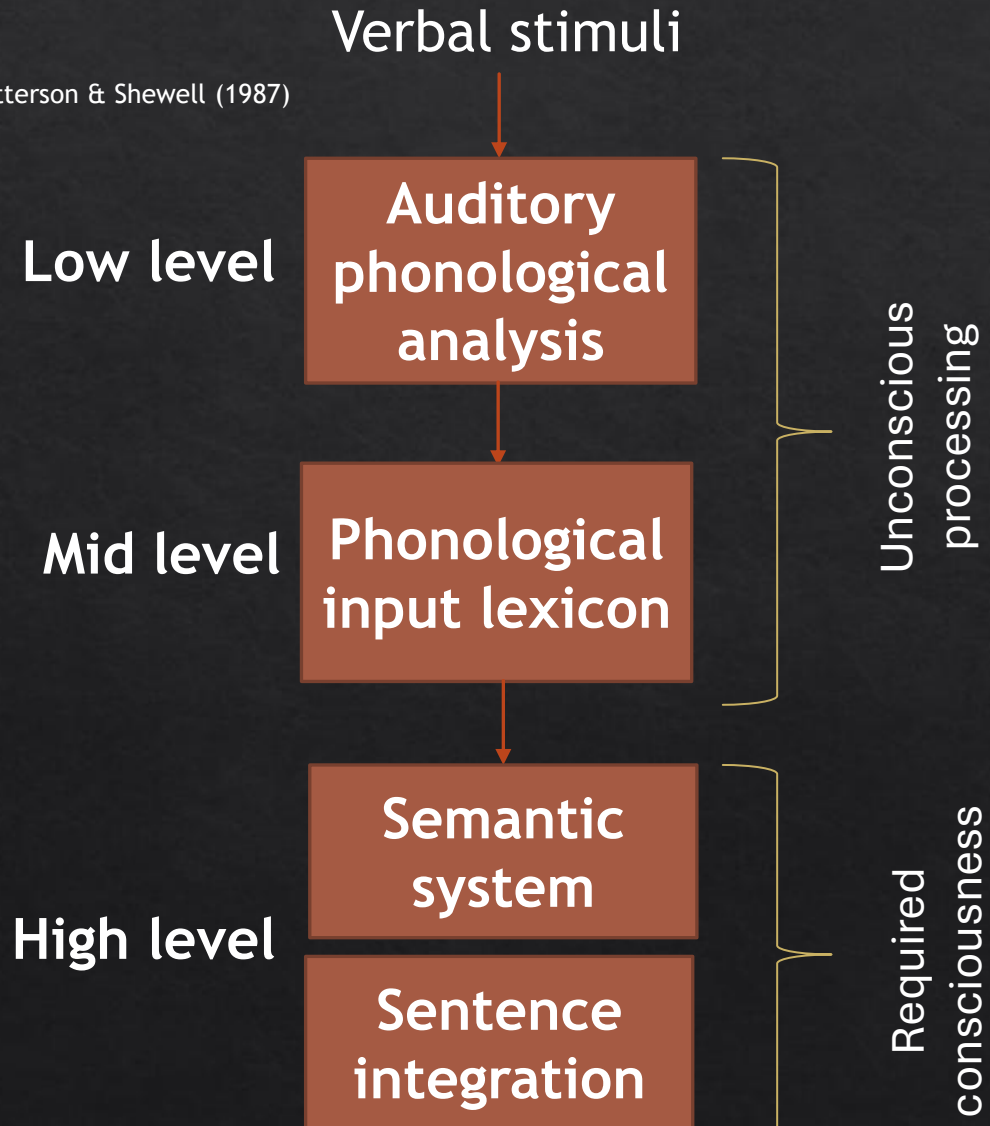
# Language vs. consciousness: the circularity issue



- How to disentangle language and consciousness processes?
- Bilateral functional interactions between them?

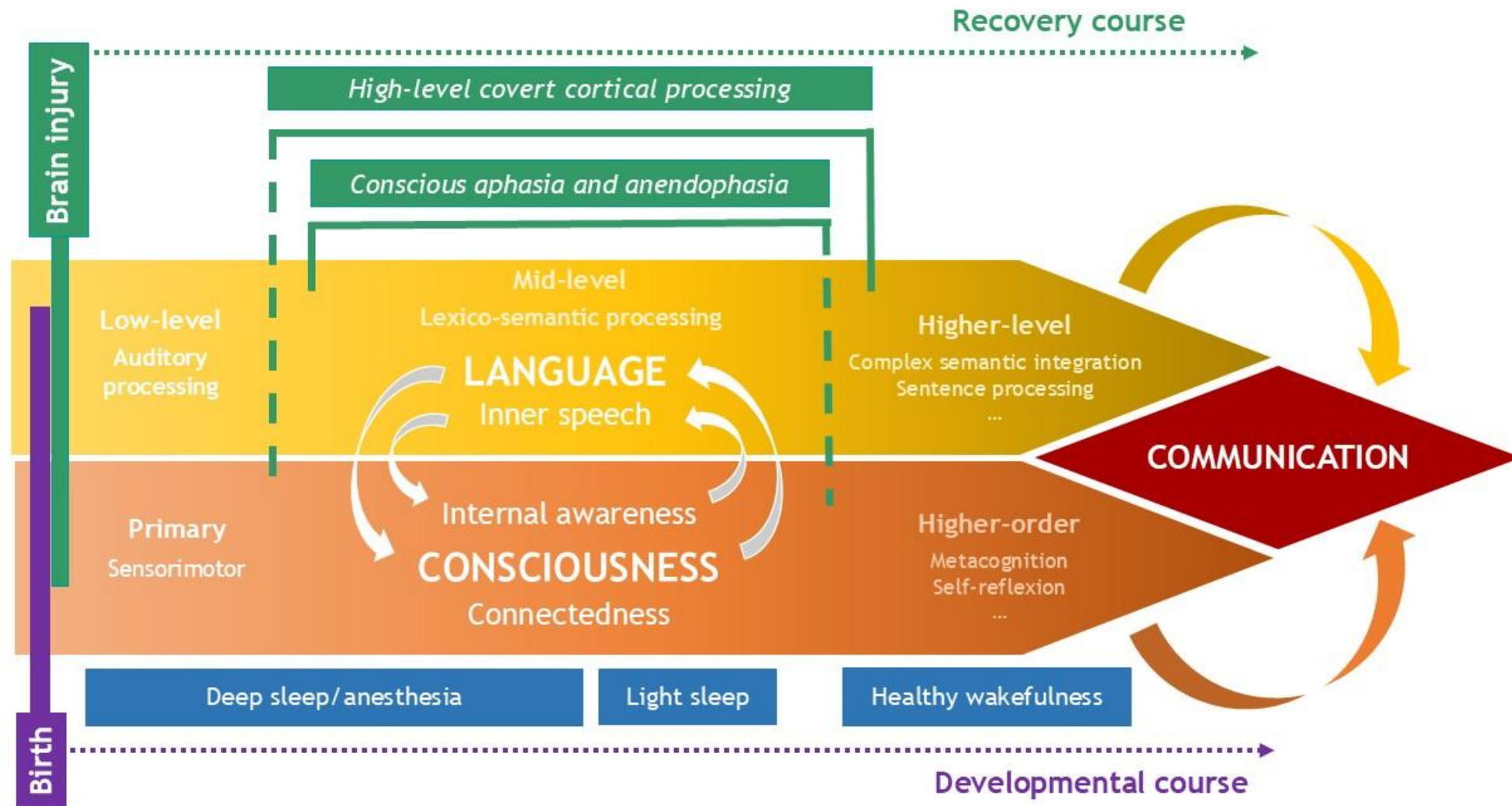
# Interactions between language and consciousness

Patterson & Shewell (1987)



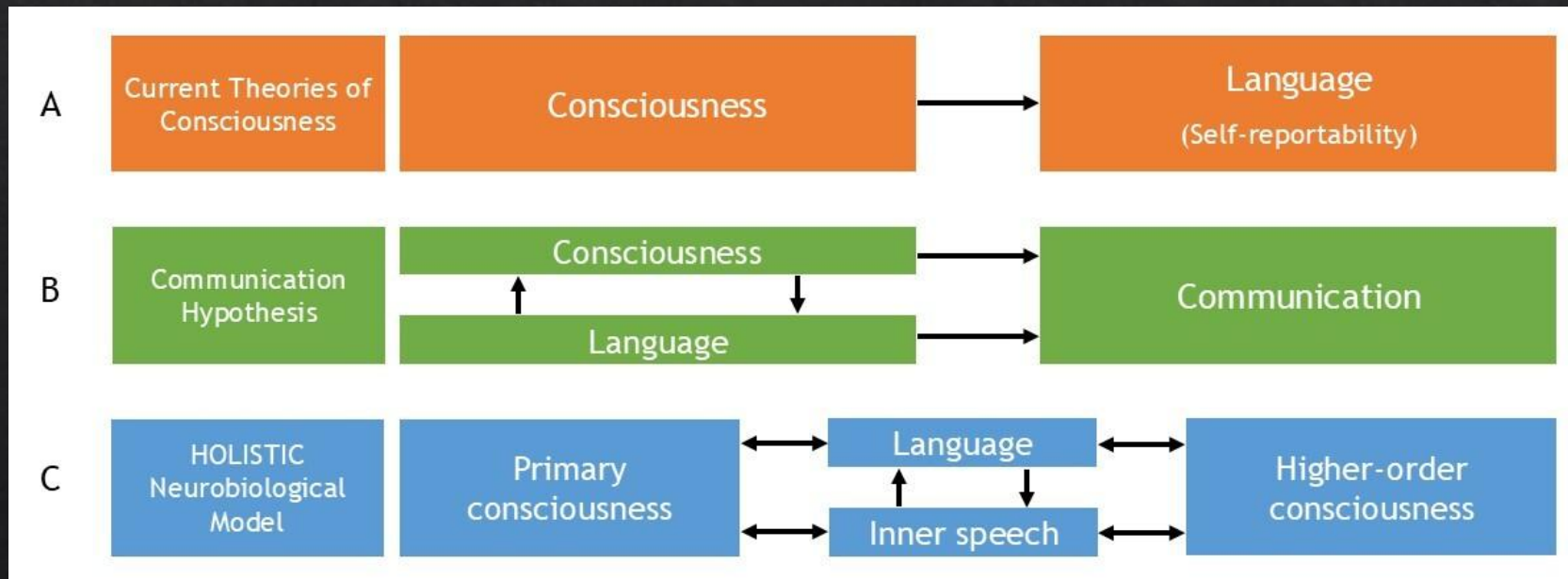
- **Developmental, neuroimaging, cognitive, and neuropsychological studies**
- Different **aspects** of language and **levels vs. contents** of consciousness
- Phonetic, phonological or lexico-semantic processing: in **absence** of **consciousness**
- **Semantic** and **sentence** integration: **consciousness** is needed
- Parallel **developmental** and **recovery** trajectories

# Associated and dissociated components of language and consciousness



# Interactions between language and consciousness

- Experimental and clinical evidence: language processing may **precede** consciousness
- **Language may not only report but also help structure conscious experience**
- Theoretical and methodological challenges



# Future research directions

- More precisely define the interacting aspects of language and dimensions of consciousness
  - Investigate the potential causality of these interactions
- Consciousness tests not requiring language / language tests not requiring consciousness:
  - ‘No report’ conditions in cognitive studies
  - Stimulus-free resting state paradigms or tasks based non-linguistic stimuli
  - Complexity-related measures of neural processing (perturbational complexity index)
  - Validated in healthy subjects and gradually extended to more challenging groups

# Conclusion

Language serves as a  
privileged window into residual  
(c)overt consciousness

Important methodological  
challenges

Emerging theoretical questions

Clinical and ethical  
consequences

COMA

SCIENCE GROUP



PsyNCog

Psychology & Neuroscience of Cognition

Thank you



# Future research directions

## Objectives

Characterize **language processing** impairments to better disentangle language and consciousness disorders

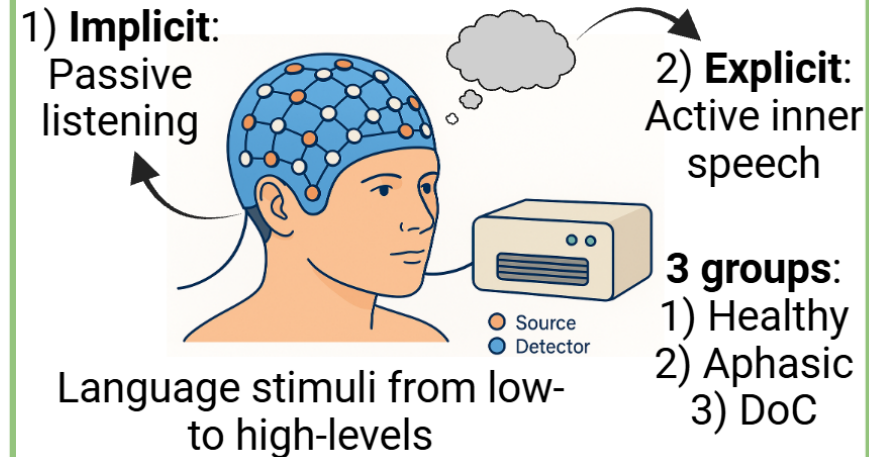


Develop and validate a novel fNIRS **assessment tool**:

- Examining a broad range of **language aspects**
- Detecting **covert consciousness** based on implicit vs. explicit language tasks

## Methods

**fNIRS dual paradigm:**



**Innovation:** for the 1st time

- Brain-based bedside language-assessment tool
- Contrasting implicit vs. explicit language processing in the same individual
- Assessing different language aspects in DoC patients