GIGA-Consciousness Seminar

Language and consciousness recovery after coma

28/11/2023

Charlène AUBINET
FNRS postdoctoral researcher

Introduction

Consciousness disorders in post-comatose recovery

Trauma
Anoxia
Hemorrhage
Metabolic
Infection
Inflammation

Coma

Consciousness disorders in post-comatose recovery

Trauma
Anoxia
Hemorrhage
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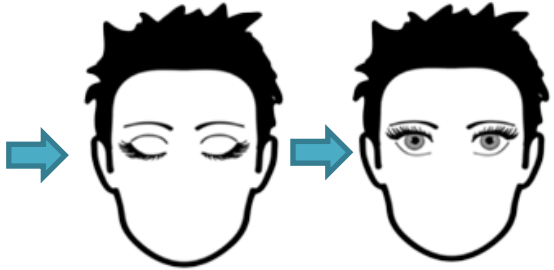
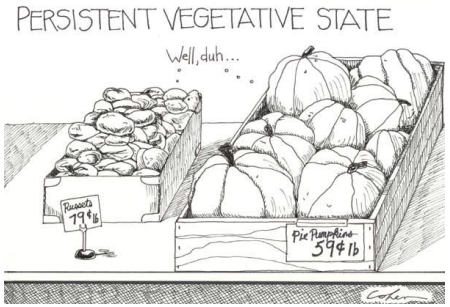
Infection
Inflammation



Coma

Unresponsive Wakefulness Syndrome (UWS)

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



Laureys et al., *BMC Med*, 2010

Consciousness disorders in post-comatose recovery

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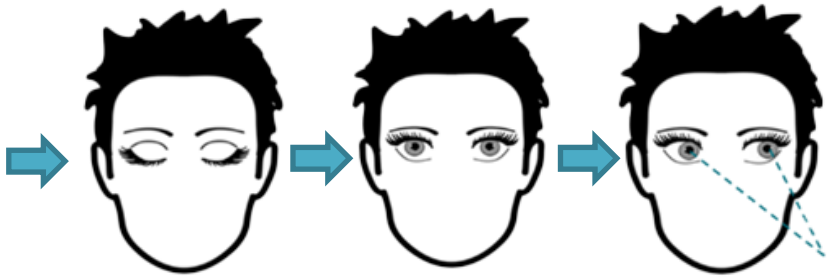

Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Reproducible signs of consciousness

Oriented behaviors
- **Visual**

Giacino et al., *Neurology*, 2002
Wannez et al., *Neuropsychol Rehabil*, 2017

Consciousness disorders in post-comatose recovery

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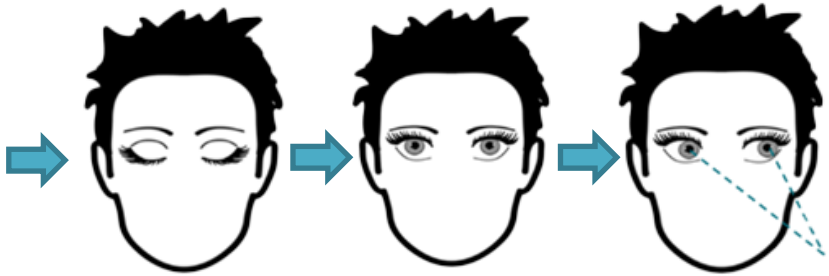

Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Oriented behaviors
- **Visual**
- **Motor**

Reproducible signs of consciousness

Giacino et al., *Neurology*, 2002
Wannez et al., *Neuropsychol Rehabil*, 2017

Consciousness disorders in post-comatose recovery

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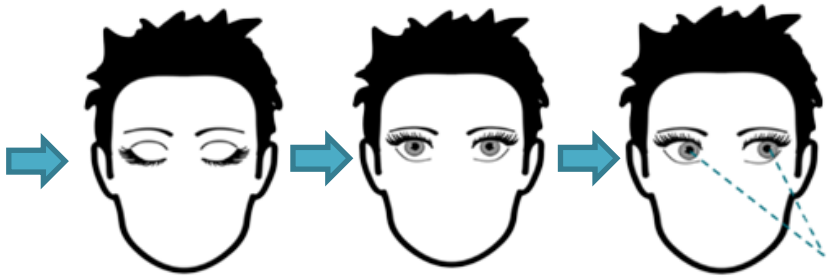

Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Reproducible signs of consciousness

Oriented behaviors
- **Visual**
- **Motor**
- **Auditory**

Carrière et al., *Brain Commun*, 2020
Mat et al., *Semin Neurol*, 2022

Consciousness disorders in post-comatose recovery

Trauma
Anoxia
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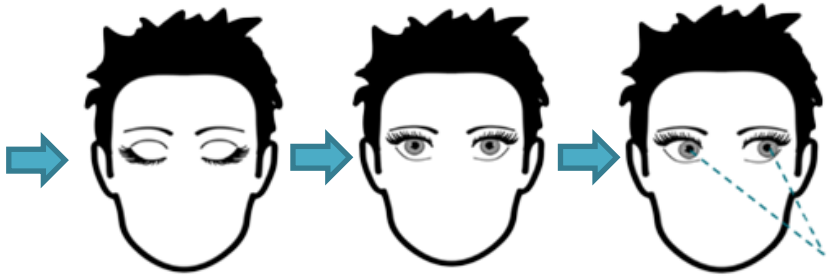
Inflammation



Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Oriented behaviors
- **Visual**
- **Motor**
- **Auditory**
- **Emotional**

Reproducible signs of consciousness

Giacino et al., *Neurology*, 2002
Wannez et al., *Neuropsychol Rehabil*, 2017

Consciousness disorders in post-comatose recovery

Reproducible language signs of consciousness

Trauma
Anoxia
Hemorrhage
Metabolic
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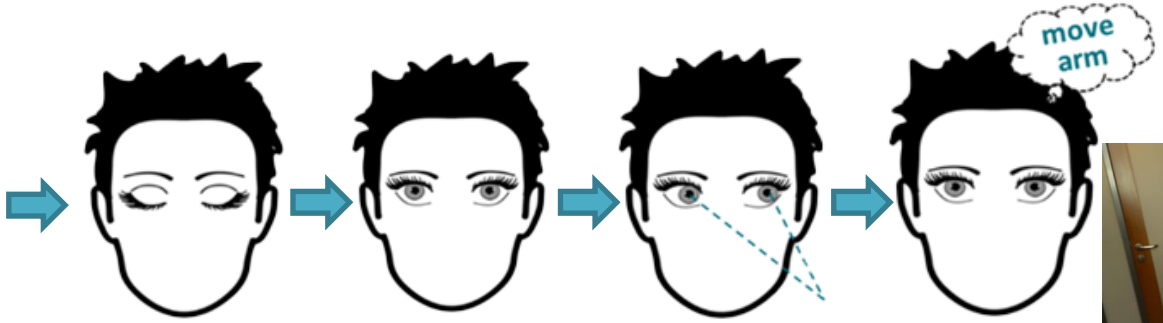

Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Minimally Conscious State (MCS+)

- **Command-following**

Bruno et al., *J Neurol*, 2011
Thibaut et al., *J Neurol*, 2020

Consciousness disorders in post-comatose recovery

Reproducible language signs of consciousness

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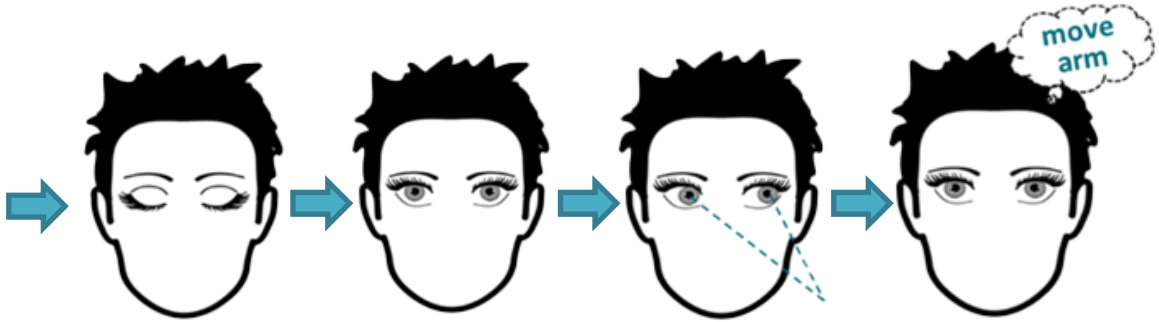
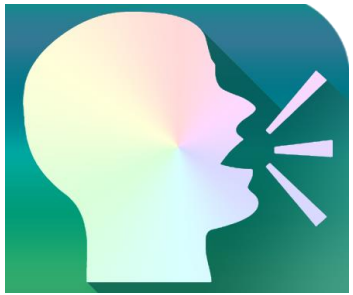


Coma

Unresponsive Wakefulness Syndrome (UWS)

Minimally Conscious State (MCS-)

Minimally Conscious State (MCS+)



- **Command-following**
- **Intelligible verbalization**

Bruno et al., *J Neurol*, 2011
Thibaut et al., *J Neurol*, 2020

Consciousness disorders in post-comatose recovery

Reproducible language signs of consciousness

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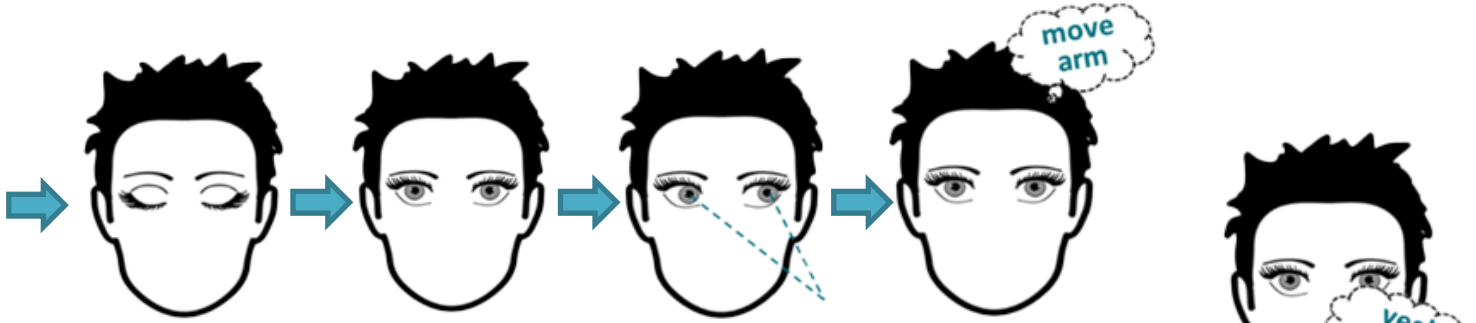


Coma

Unresponsive Wakefulness Syndrome (UWS)

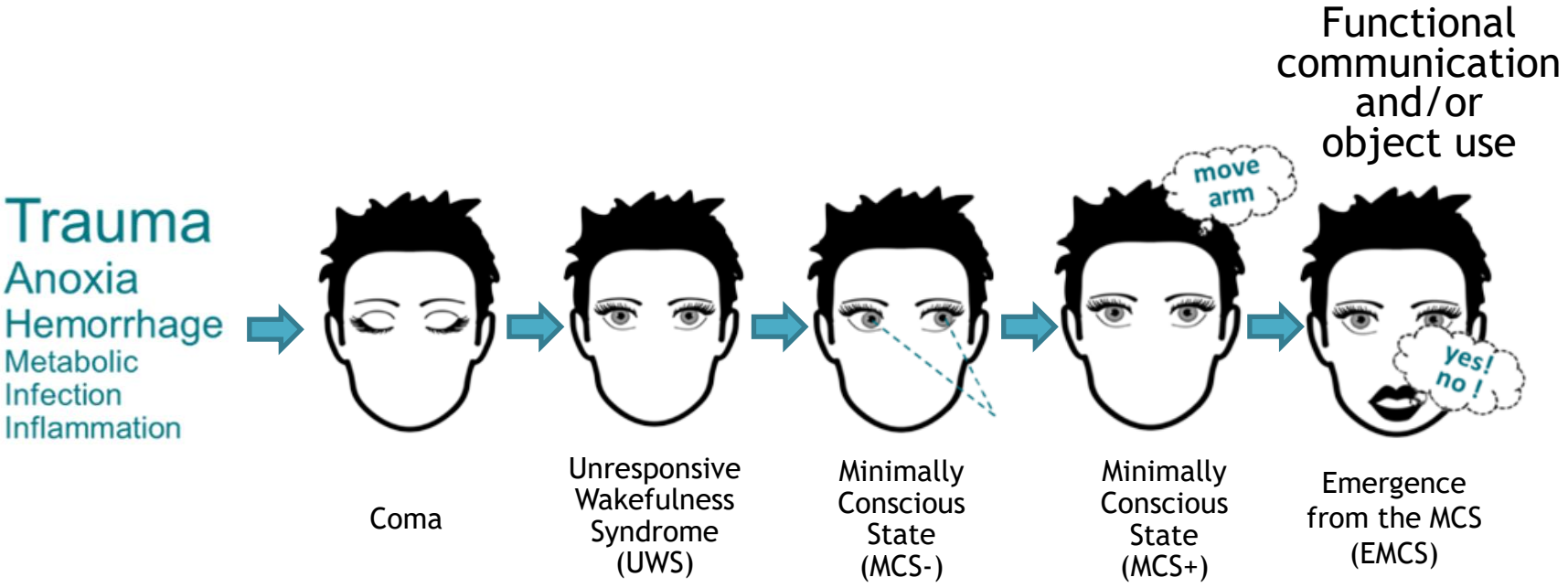
Minimally Conscious State (MCS-)

Minimally Conscious State (MCS+)

- **Command-following**
- **Intelligible verbalization**
- **Intentional communication**

Bruno et al., *J Neurol*, 2011
Thibaut et al., *J Neurol*, 2020

Consciousness disorders in post-comatose recovery

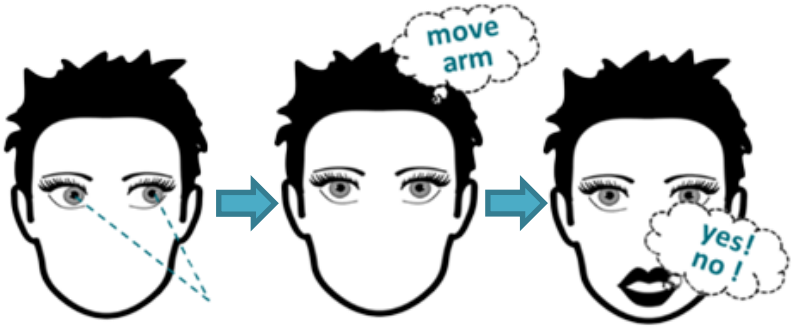


Giacino et al., *Neurology*, 2002
Wannez et al., *Neuropsychol Rehabil*, 2017

30-40% risk of DoC misdiagnosis

Deafness
Blindess
Motor impairment
Aphasia
…

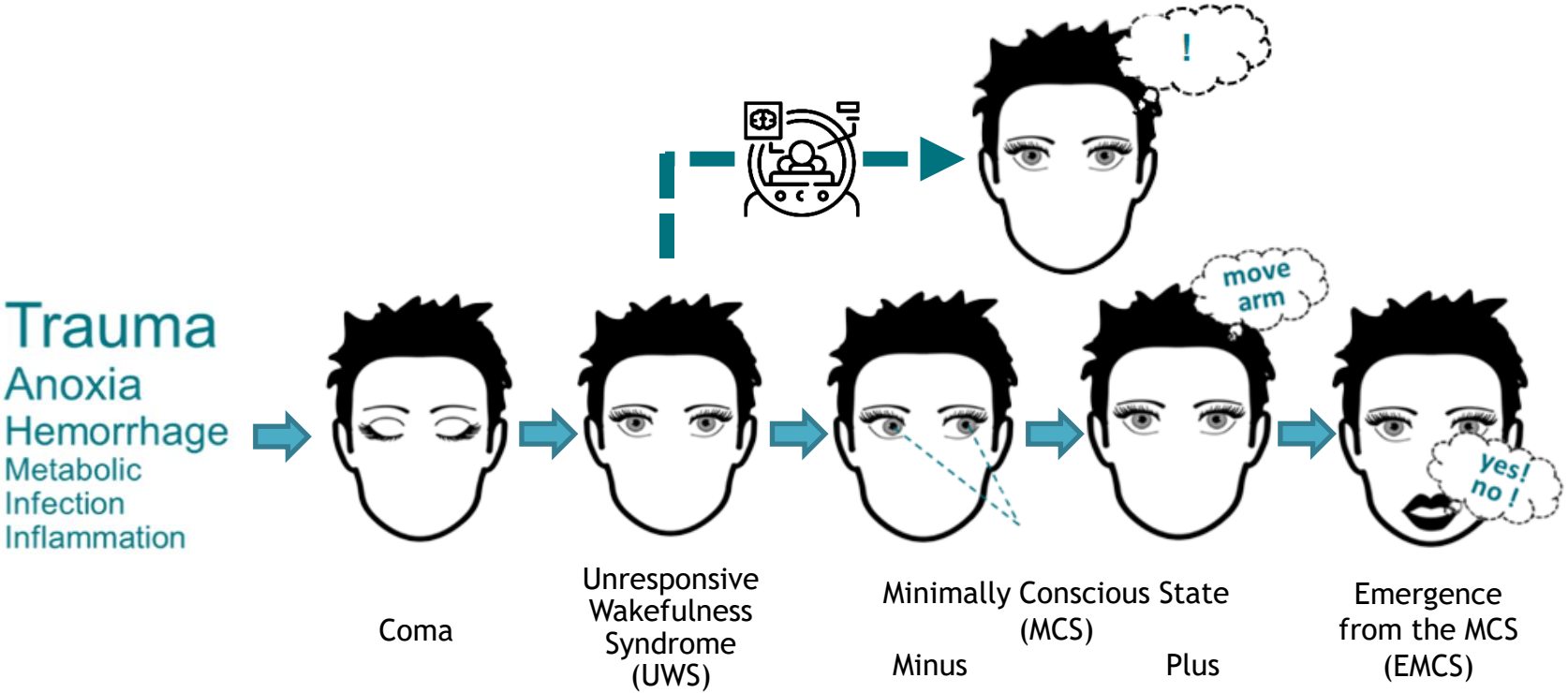
Underestimated consciousness!!!



Minimally Conscious State (MCS)
Minus Plus

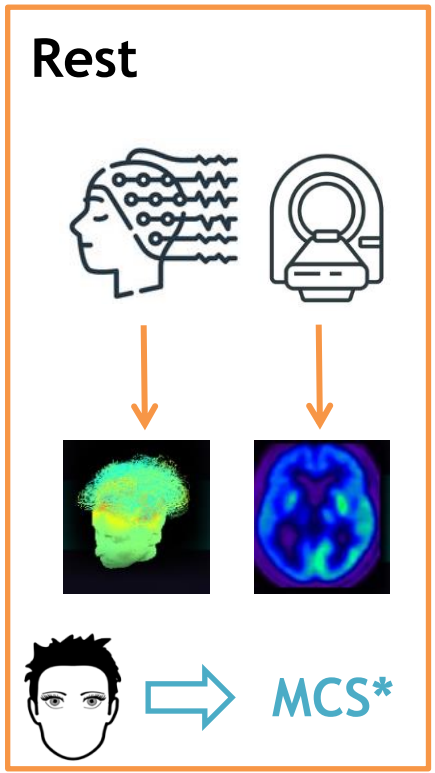
Emergence from the MCS (EMCS)

Schnakers et al., *BMC Neurol*, 2009
Schnakers et al., *NNR*, 2015



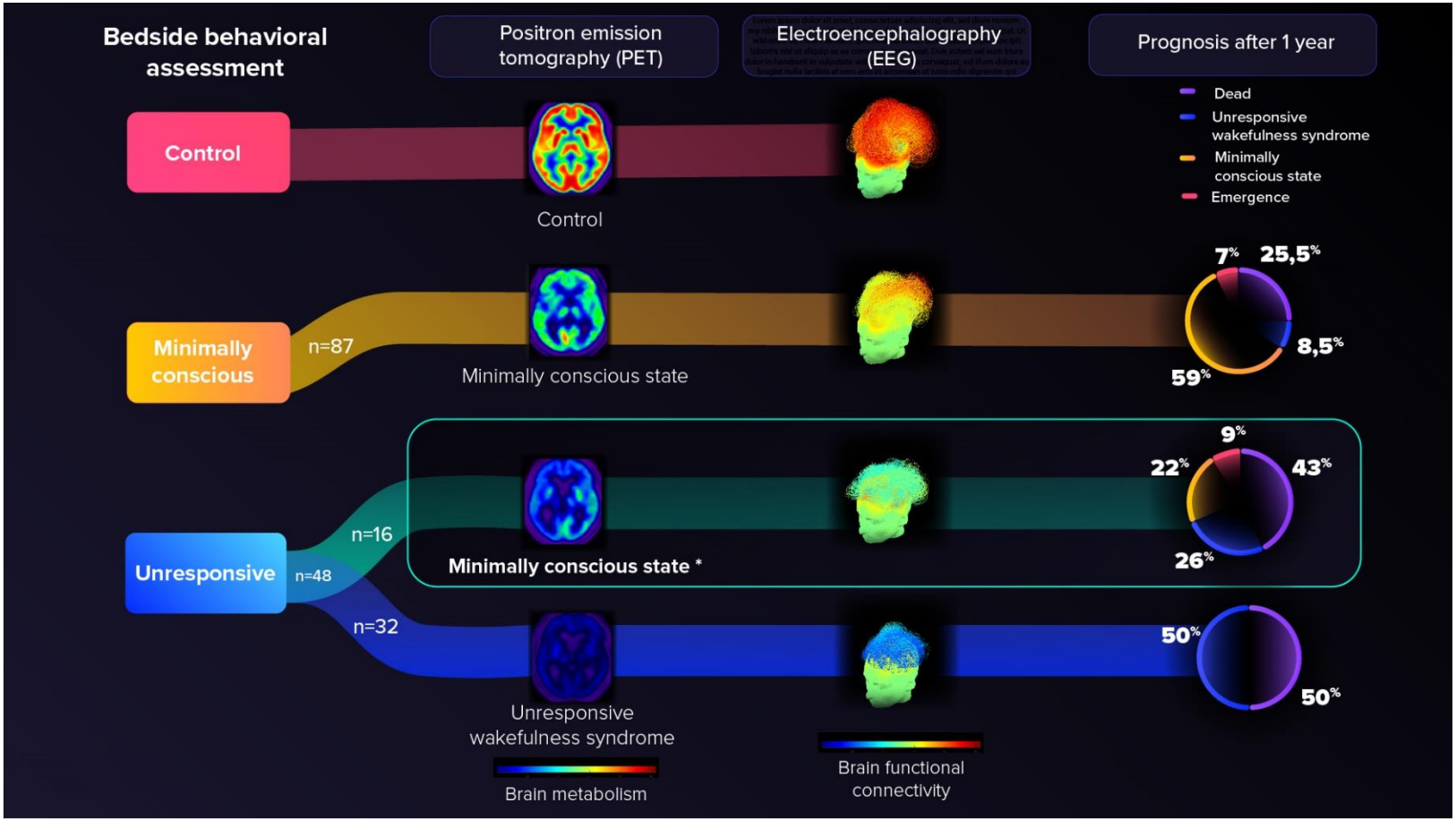
Thibaut et al. *Ann Neurol*, 2021

Detection of residual consciousness in post-comatose recovery



Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

DoC – Neuroimaging & electrophysiology – Behavioral tools – Theoretical implications



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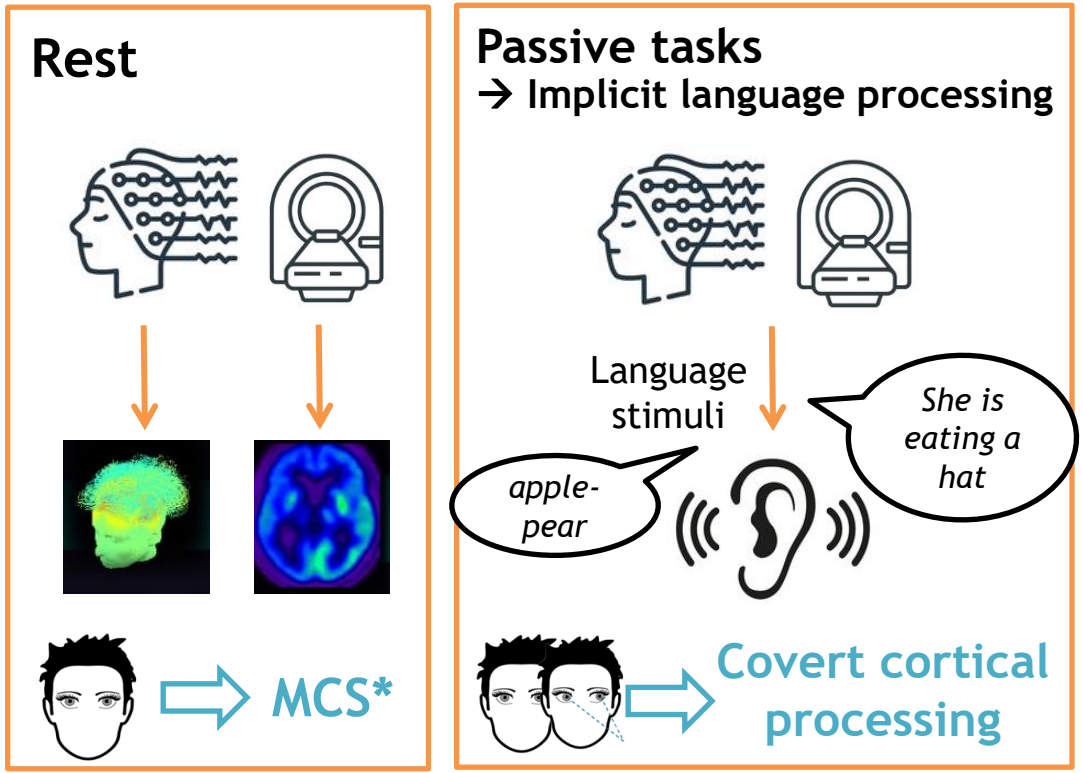
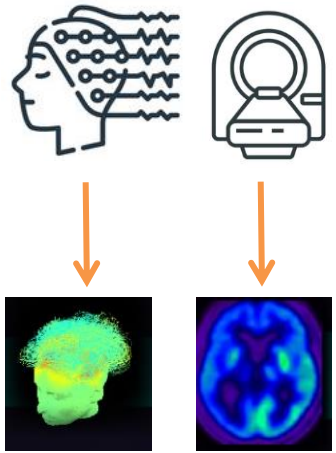


Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Detection of residual consciousness in post-comatose recovery

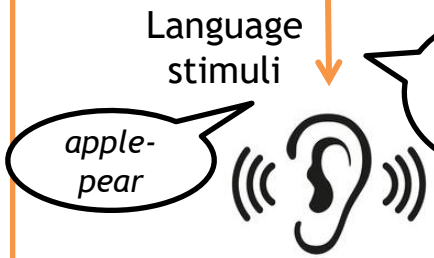
Rest

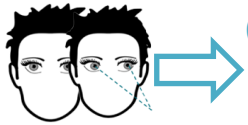


MCS*

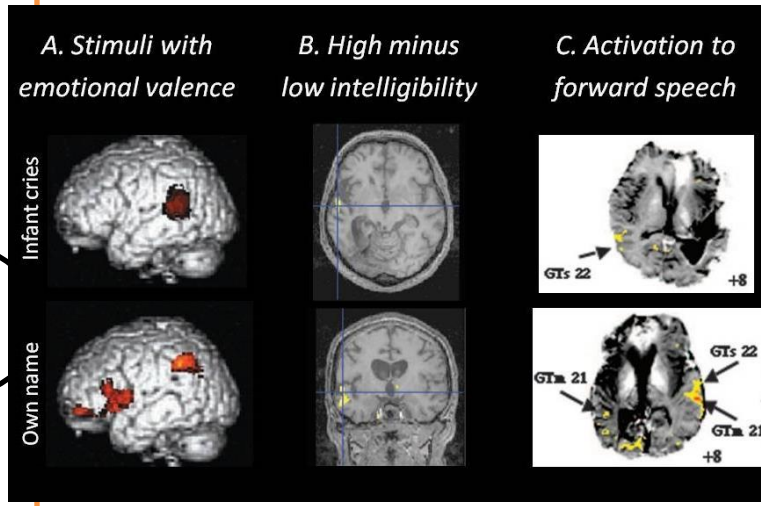
Passive tasks
→ Implicit language processing

Language stimuli





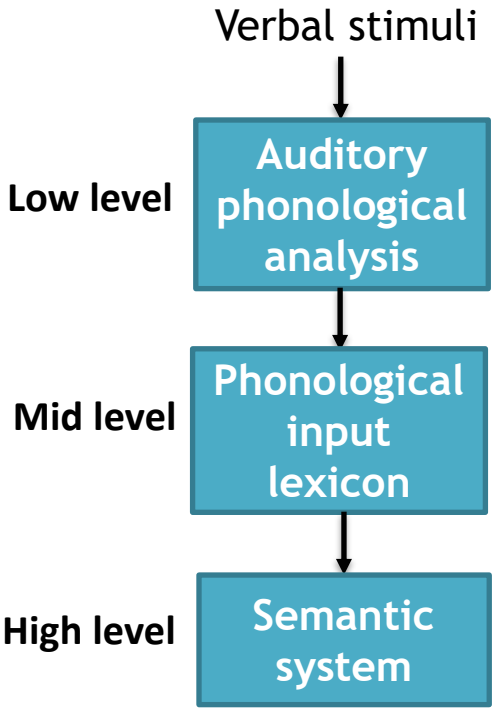
Covert cortical processing



Laureys et al., *Neurology*, 2004
Owen et al., *Neuropsychol. Rehabil.*, 2005
Schiff et al., *Neurology*, 2005
Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Passive tasks and implicit language processing

Distinction of various language components



Contrasting:

Speech vs. noise

Intelligible vs. unintelligible speech
Words vs. pseudowords

Semantically related vs. unrelated words
Sentences of low vs. high ambiguity
Congruous vs. incongruous sentences
Factually correct vs. incorrect sentences

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

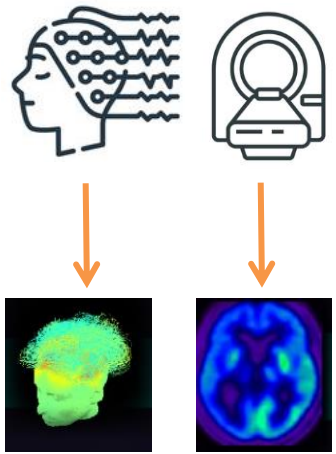
Brain response: UWS < MCS < EMCS

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; …

Patterson and Shewell (1987)

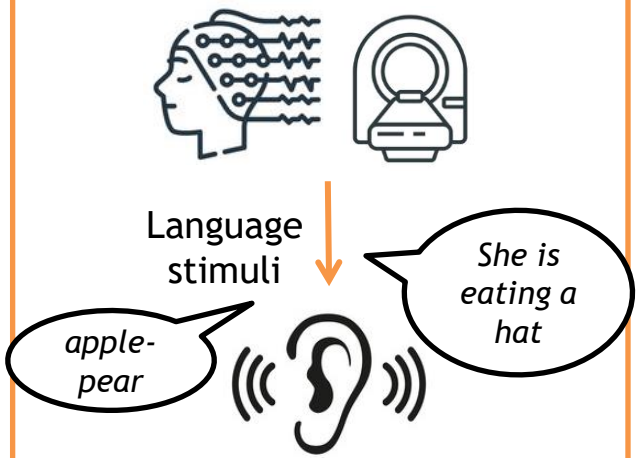
Detection of residual consciousness in post-comatose recovery

Rest



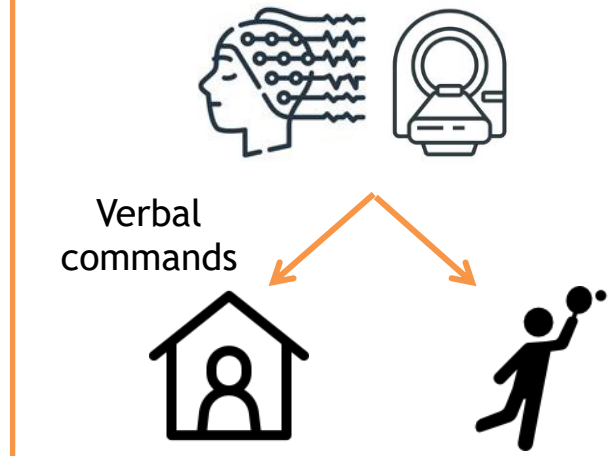
MCS*

Passive tasks
→ Implicit language processing



Covert cortical processing

Active tasks
→ Explicit language processing

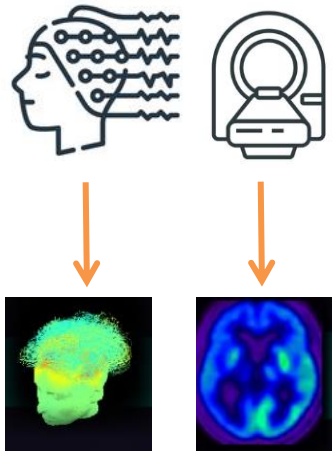


Cognitive-motor dissociation

Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

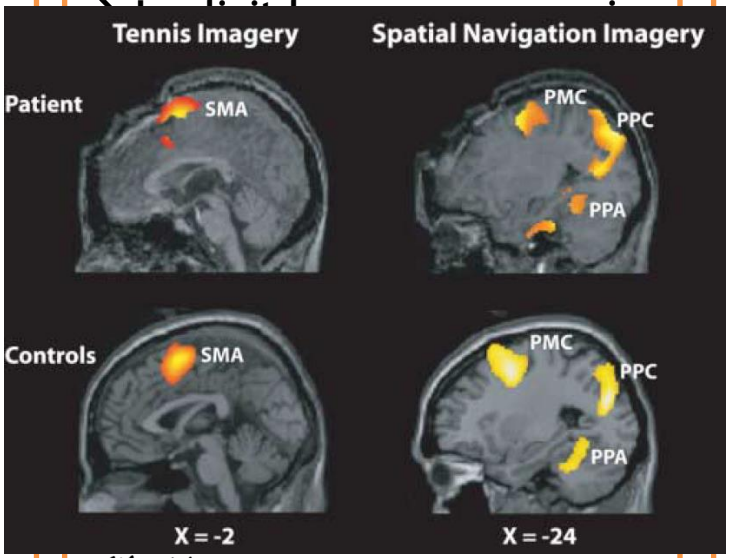
Detection of residual consciousness in post-comatose recovery

Rest



MCS*

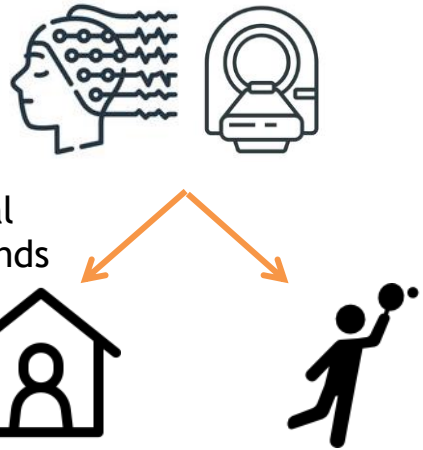
Passive tasks



Covert cortical processing

Active tasks

→ Explicit language processing



Cognitive-motor dissociation

Owen et al., *Neuropsychol. Rehabil.*, 2005
Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

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

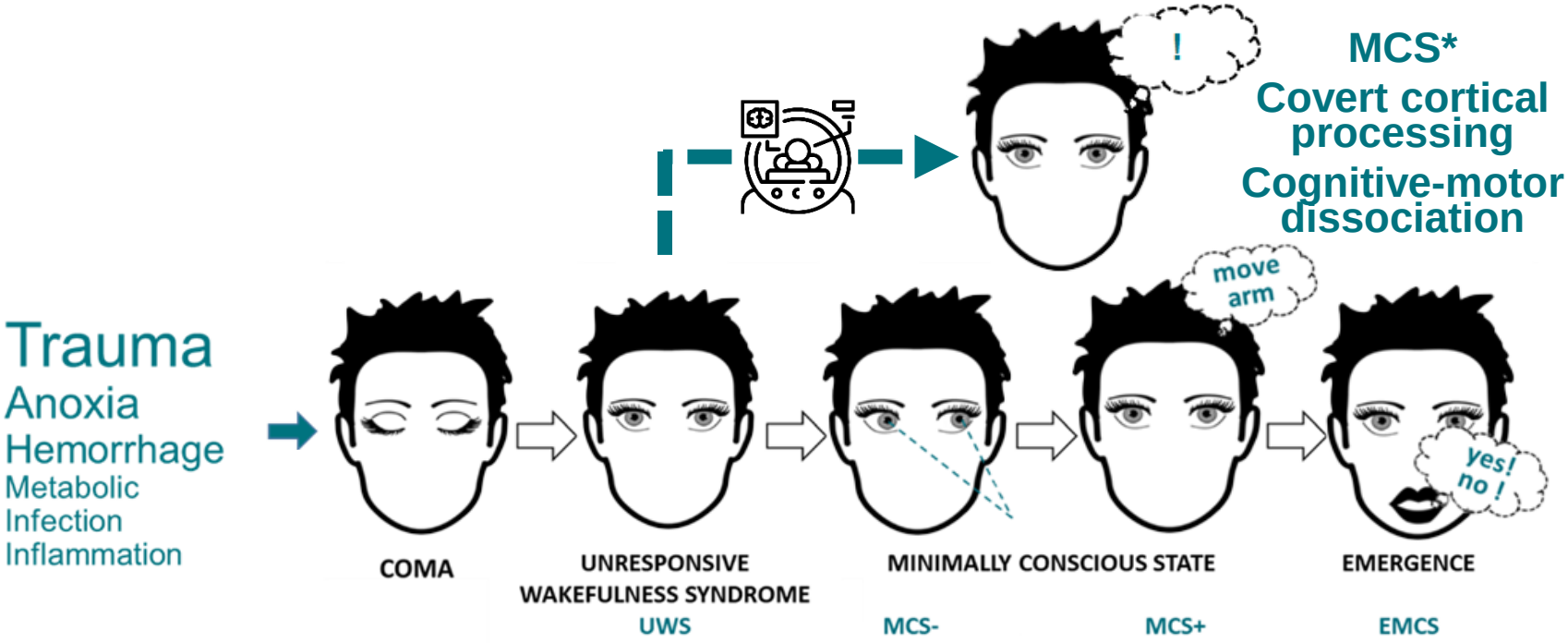
Silent picture naming

Rodriguez-Moreno et al., 2010

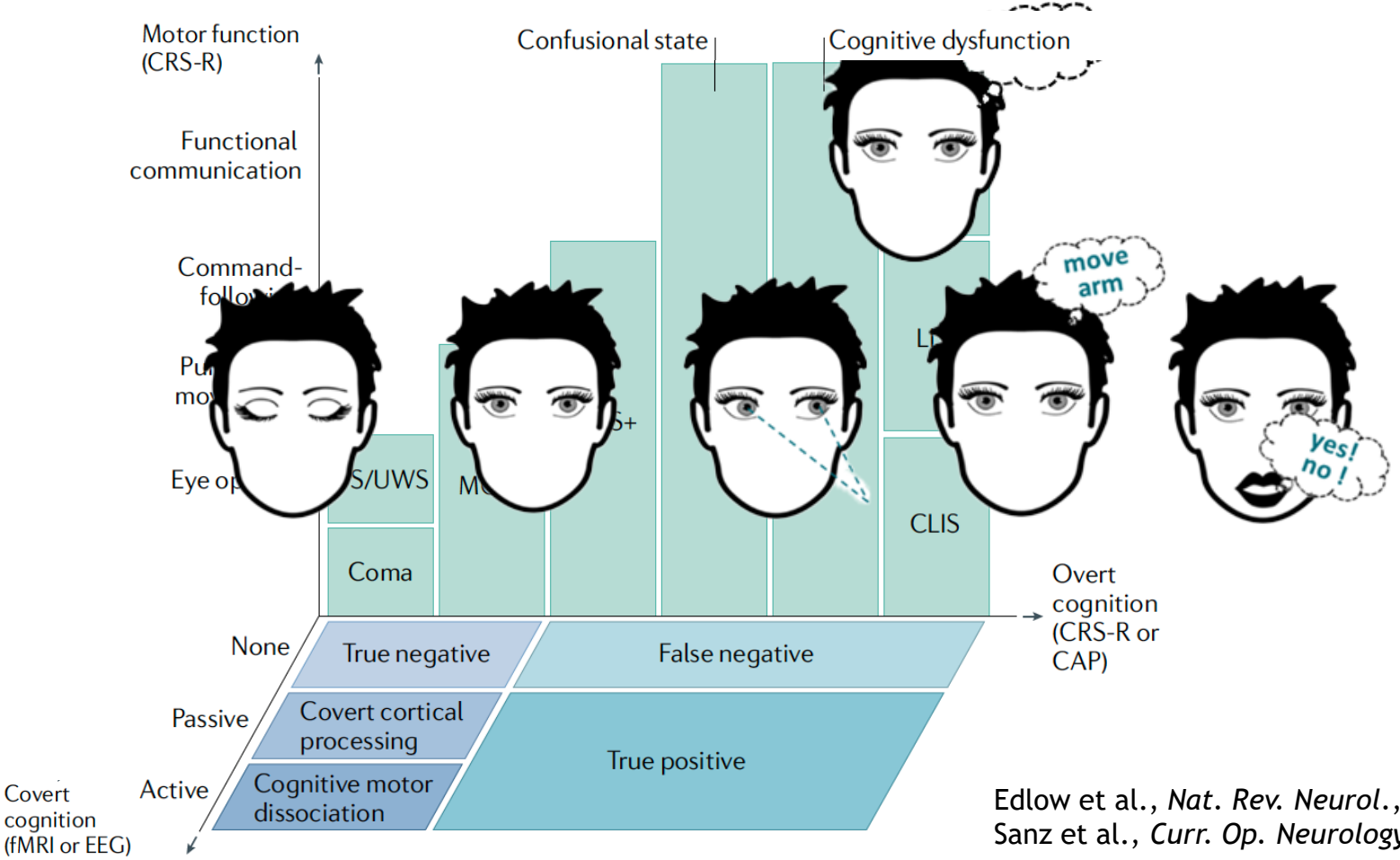
Potential residual brain response in all DoC categories

→ ~20% UWS and ~33% MCS-

= CMD!


Trauma
Anoxia
Hemorrhage
Metabolic
Infection
Inflammation
!
MCS*
Covert cortical processing
Cognitive-motor dissociation
move arm
yes!
no !
COMA
UNRESPONSIVE WAKEFULNESS SYNDROME
UWS
MINIMALLY CONSCIOUS STATE
MCS-
MCS+
EMERGENCE
EMCS

Multi-dimensional model



Edlow et al., *Nat. Rev. Neurol.*, 2020
Sanz et al., *Curr. Op. Neurology*, 2021

Behavioral scales including command-following items

Coma Recovery Scale-Revised
(CRS-R)

Simplified Evaluation of CONsciousness Disorders
(SECONDs)

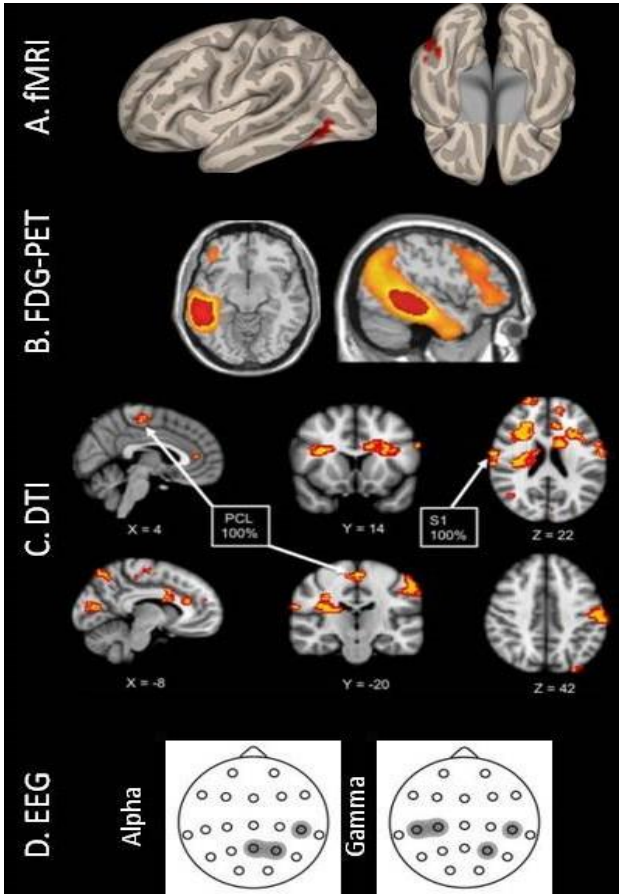
…

Aubinet et al., *Brain Inj.*, 2021

Command-following

Neural correlates

MCS- < MCS+



Aubinet et al., *HBM*, 2018

Aubinet et al., *NNR*, 2020

Zheng et al., *HBM*, 2017

Claassen et al., *Ann Neurol*, 2016

Behavioral scales including command-following items

DoC diagnosis

BUT no language assessment…

→ Language components?
→ Psycholinguistic variables?

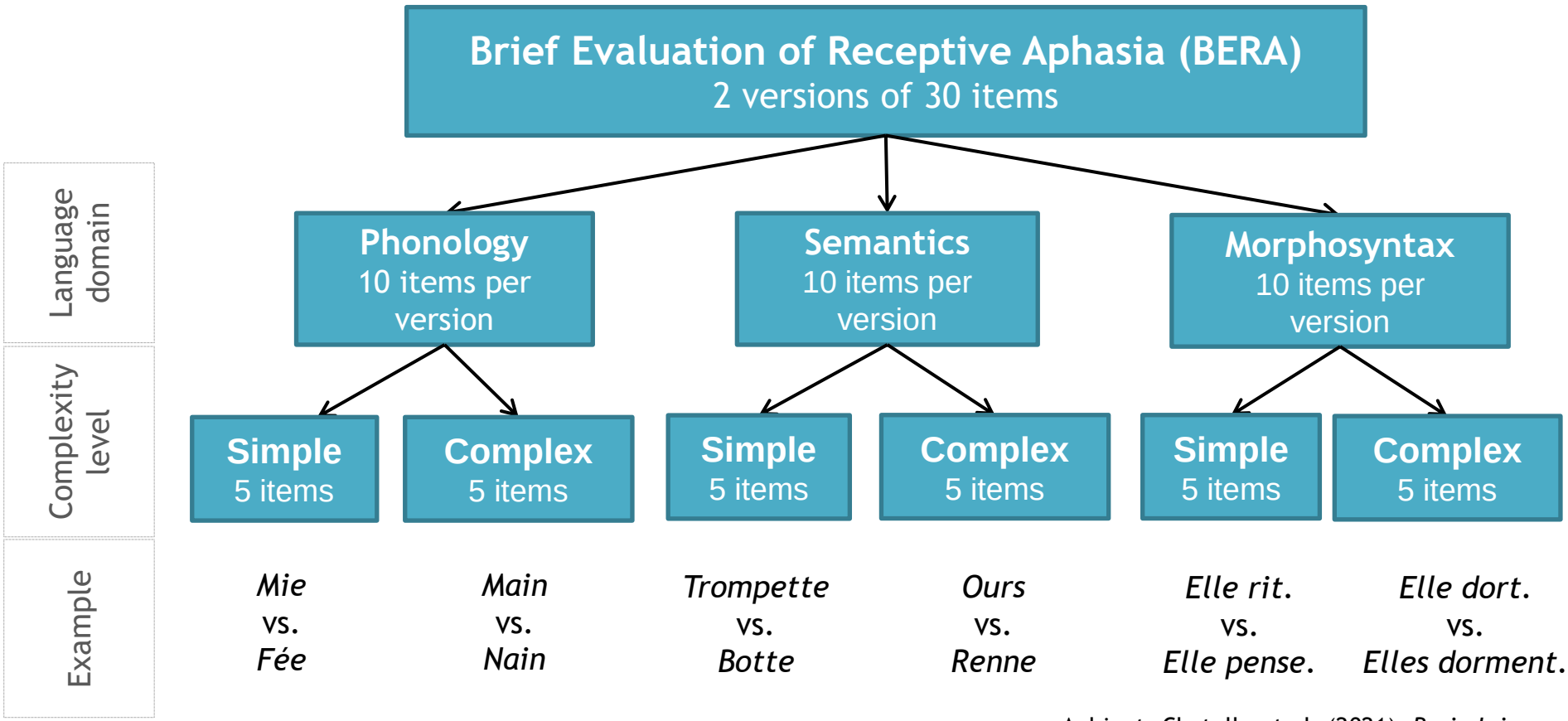
Aubinet et al., *Brain Inj.*, 2021

Towards a language-specific assessment…

Brief Evaluation of Receptive Aphasia
(BERA)

→ *Poster session (Pauls et al.)*

Aubinet et al., *Brain Inj.*, 2021



Aubinet, Chatelle et al. (2021), *Brain Injury*

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

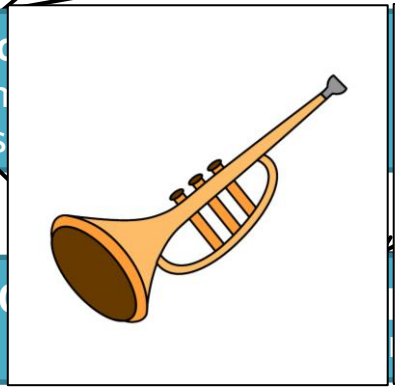
Language domain

Phonc
10 iten
vers

Morphosyntax
10 items per version

Complexity level

Simple
5 items



Simple
5 items

Complex
5 items

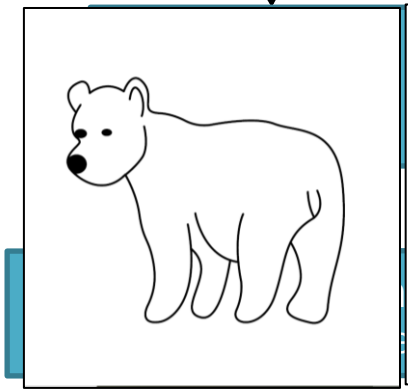
Example

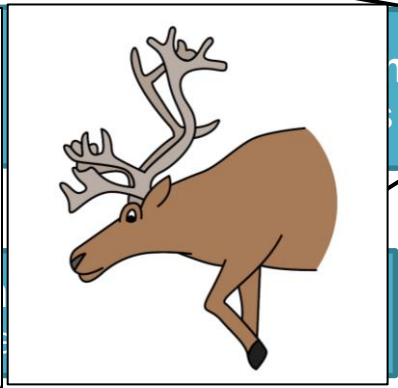
Mie vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*

Aubinet, Chatelle et al. (2021), *Brain Injury*

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

Language domain	**Phonology** 10 items per version			**nosyntax** per version	
Complexity level	**Simple** 5 items	**Complex** 5 items			**Complex** 5 items
Example	*Mie* vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*





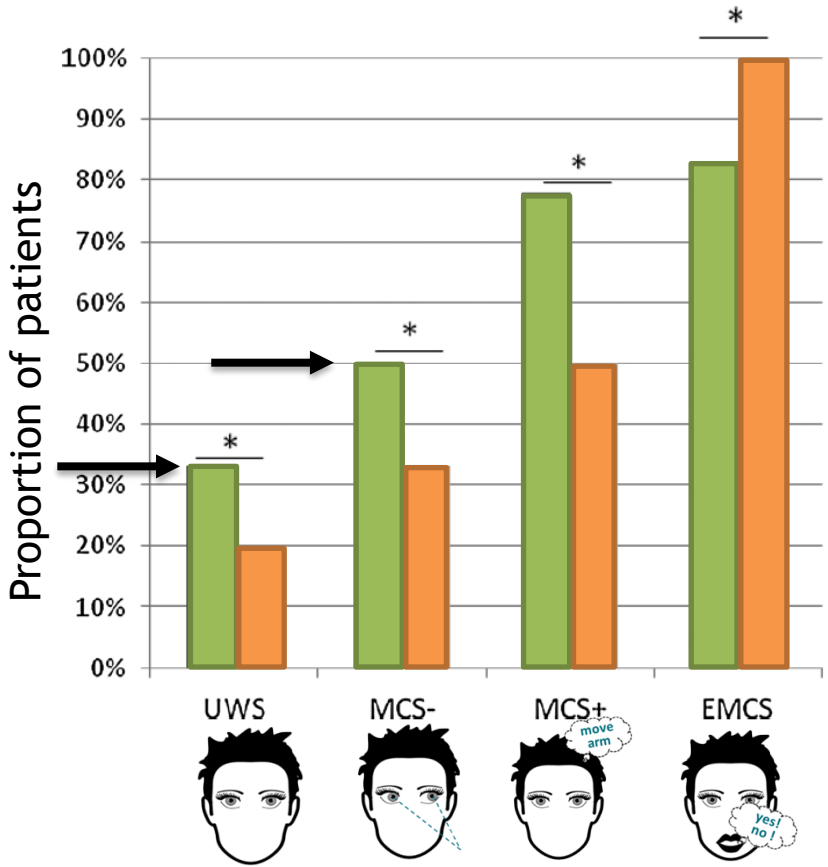
Aubinet, Chatelle et al. (2021), *Brain Injury*

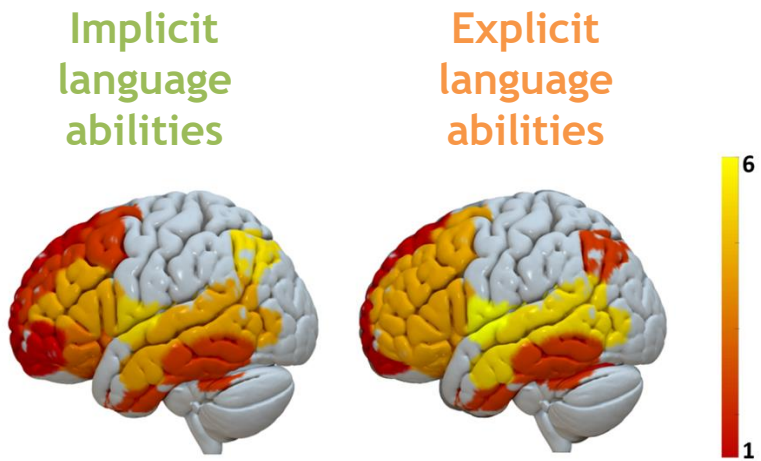
Towards a language-specific assessment…

***Brief Evaluation of Receptive Aphasia* (BERA)**

Aubinet et al., *Brain Inj.*, 2021; Aubinet et al., *in prep*

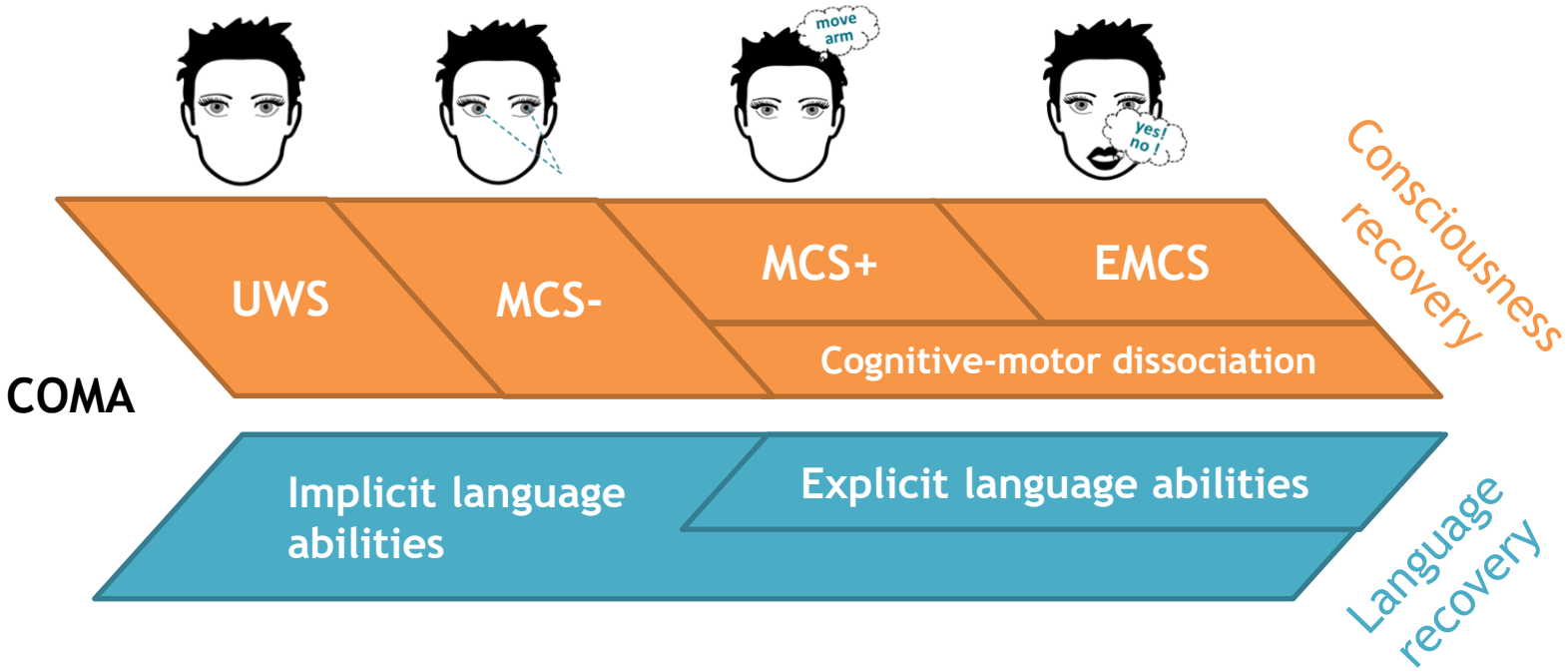
Comparing both implicit and explicit language recovery





Aubinet et al., *Neurosci. Biobeh. Rev.*, 2022

Language recovery // consciousness recovery



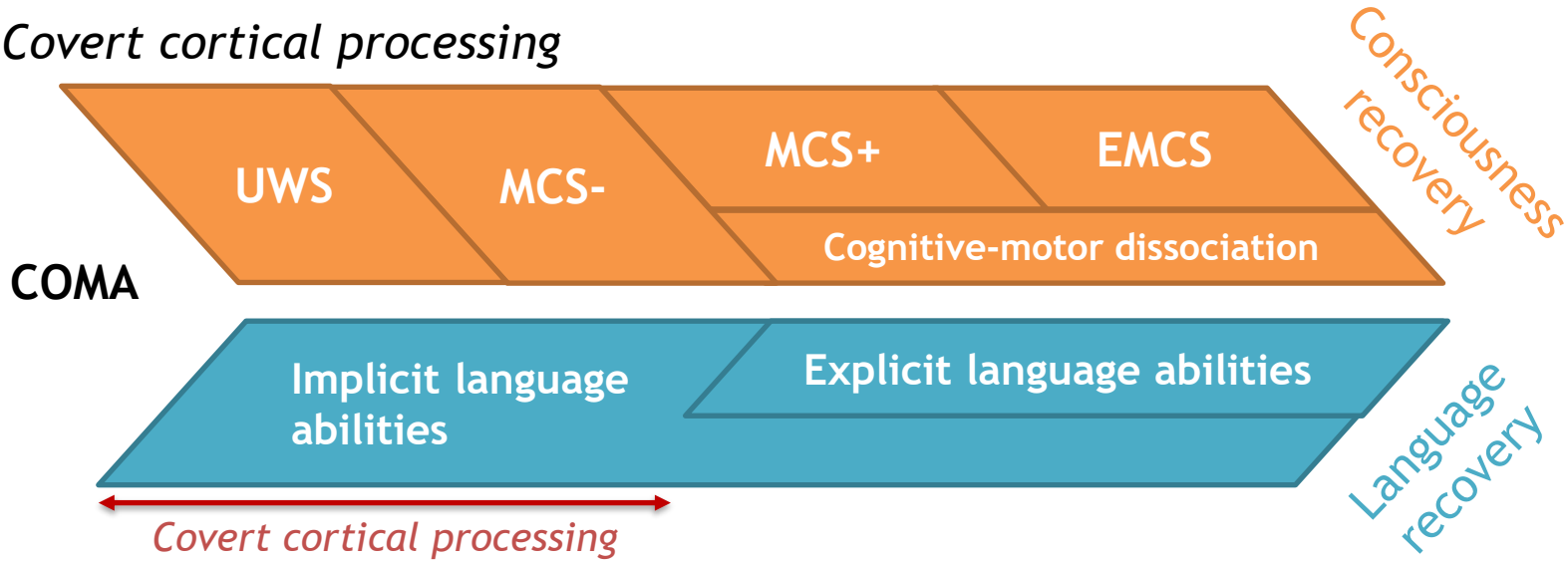
Aubinet et al., *Neurosci. Biobeh. Rev.*, 2022

Complex language processing in the absence of 'consciousness'?

DoC taxonomy?

Cognitive-motor dissociation

Covert cortical processing



UWS patients with residual brain activity reflecting semantic processing

Aubinet et al., *Neurosci. Biobeh. Rev.*, 2022
Edlow et al., *Brain*, 2017

Complex language processing in the absence of 'consciousness'?

Explicit language assessment

→ Detect **cognitive-motor dissociation** and reduce DoC misdiagnosis

Implicit language assessment

- **Covert cortical processing:** not considered in the current DoC taxonomy!
- Patients with the lowest level of consciousness can show residual brain activity reflecting complex semantic processing

→ *Is the presence of complex language processing in the absence of "consciousness" possible?*

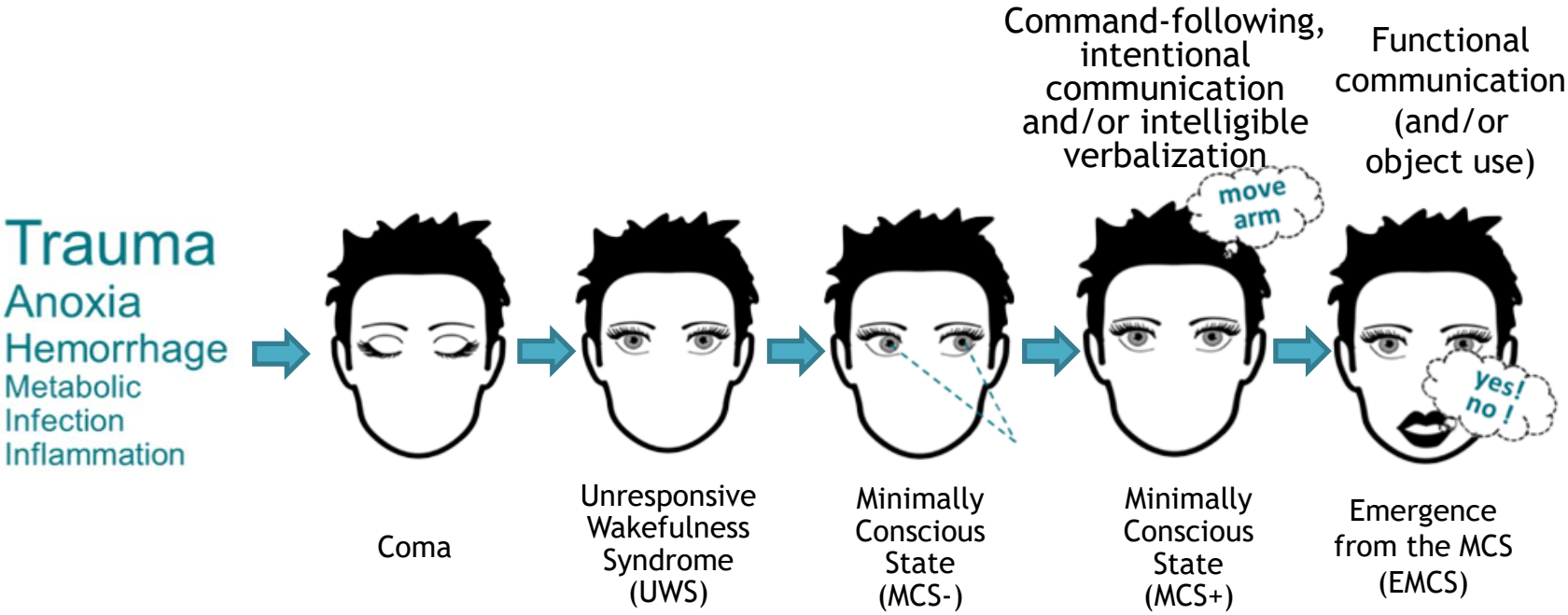
- First-order theories (activity in sensory areas → Consciousness) vs. higher-order theories (higher-order activity focusing on sensory activity → Consciousness) of consciousness

Melloni et al., *Science*, 2021
Edlow et al., *Brain*, 2017

Conclusion

- Language assessment is crucial to avoid misdiagnosis in post-comatose patients
  - MRI – EEG
  - Need for behavioral tools → BERA assessment
- Language recovery // consciousness recovery
- Theoretical implications
  - DoC taxonomy
  - Consciousness theories
  - Language ←→ Consciousness?

Consciousness disorders in post-comatose recovery

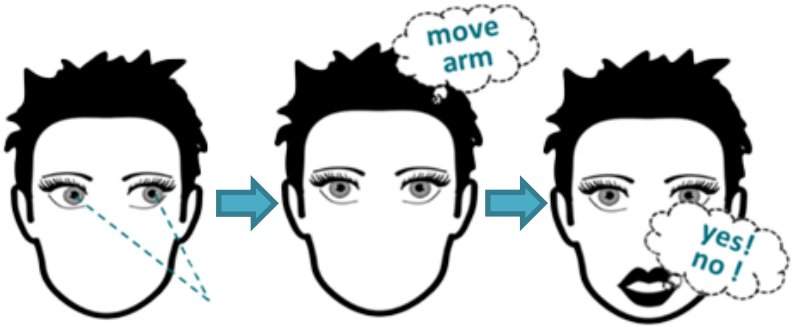


Giacino et al., *Neurology*, 2002
Wannez et al., *Neuropsychol Rehabil*, 2017

30-40% risk of DoC misdiagnosis

Deafness
Blindess
Motor impairment
Aphasia
…

Underestimated consciousness!!!

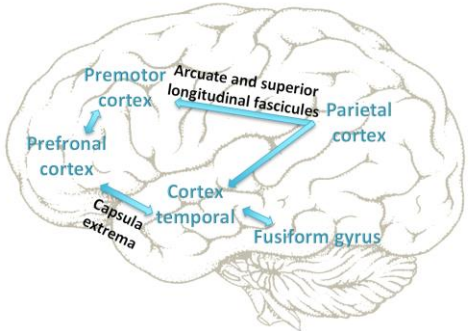


Minimally Conscious State (MCS)
Minus Plus

Emergence from the MCS (EMCS)

Schnakers et al., *BMC Neurol*, 2009
Schnakers et al., *NNR*, 2015

Aphasia in DoC diagnosis



Post-comatose language impairment → **Altered comprehension of verbal commands** → Underestimation of consciousness levels

24 conscious aphasic patients

→CRS-R assessment

→ 54% of patients with global aphasia: diagnosis = MCS!

Crucial need to detect the presence of language disorders in post-comatose DoC patients, despite their limited behavioral repertoire

Schnakers et al. (2015), *Neurorehabilitation and Neural Repair*
Majerus et al. (2009), *Progress in Brain Research*

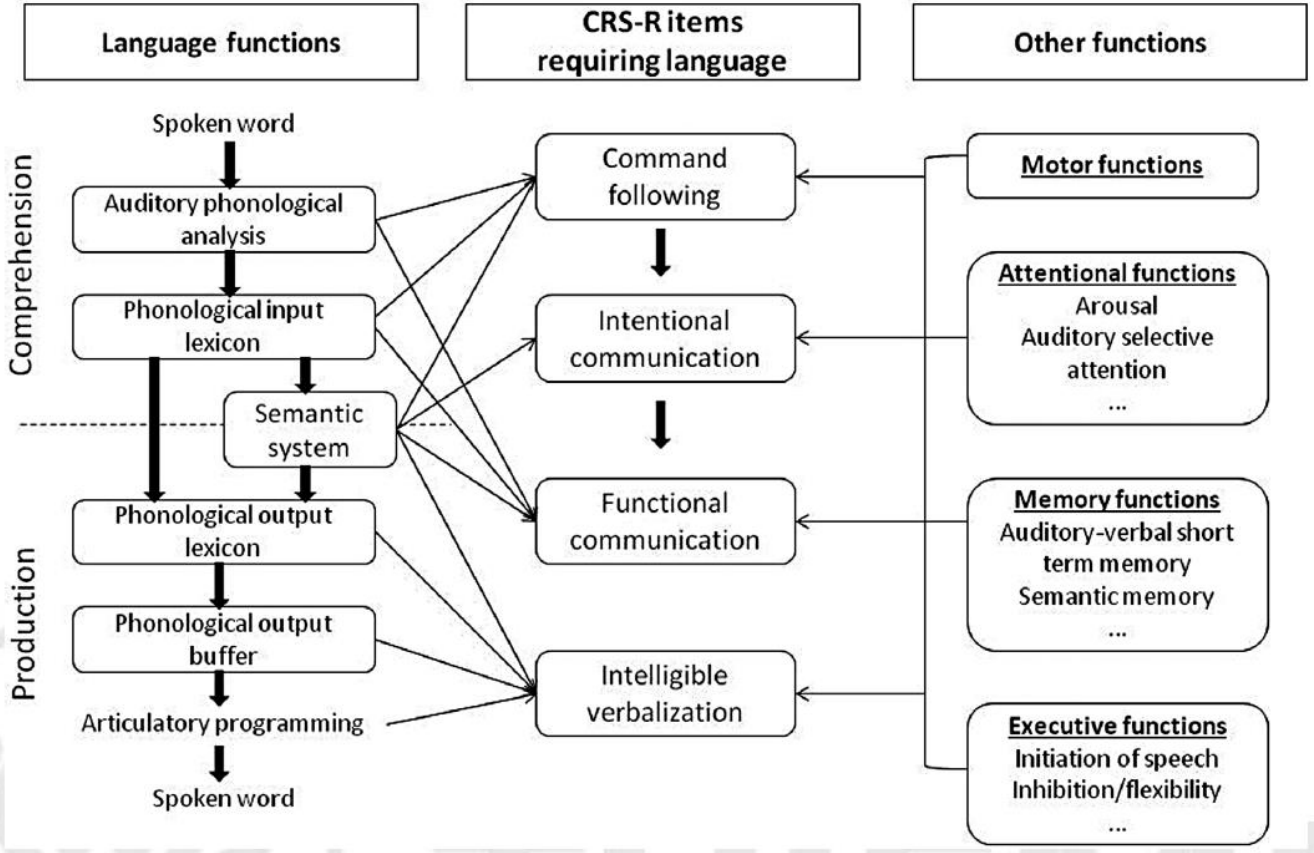
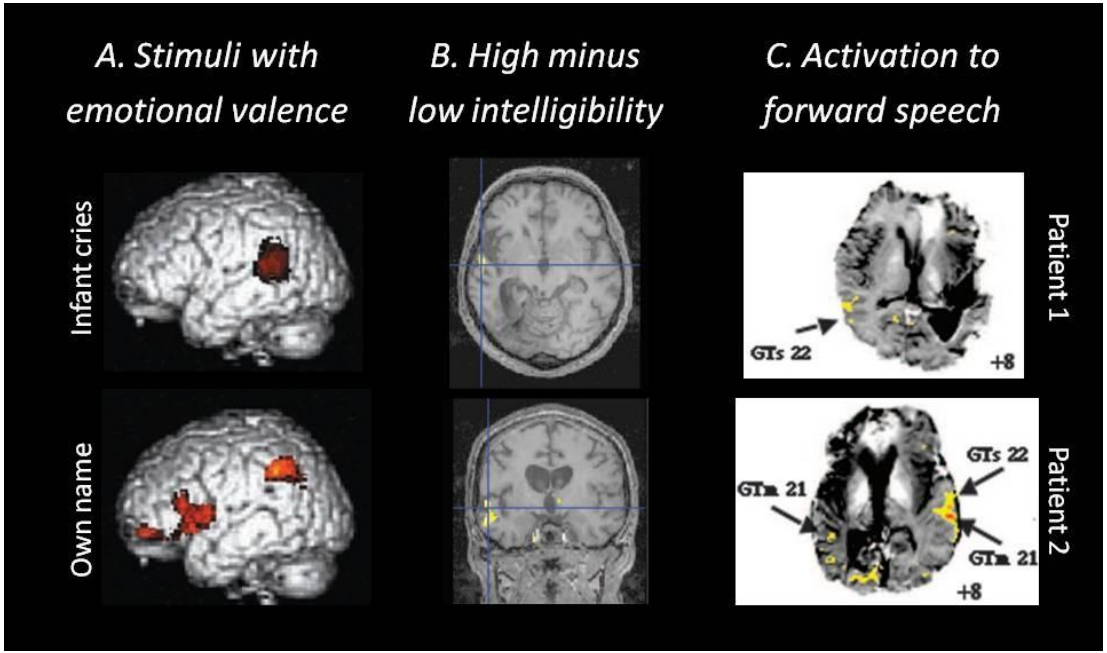


Fig. 1 Influence of specific language and motor/cognitive functions on CRS-R language-related items. **Left**: language model adapted from Patterson and Shewell (1987); **Center**: the four CRS-R items directly requiring language residual abilities; **Right**: motor and cognitive functions impacting patients' CRS-R performance.

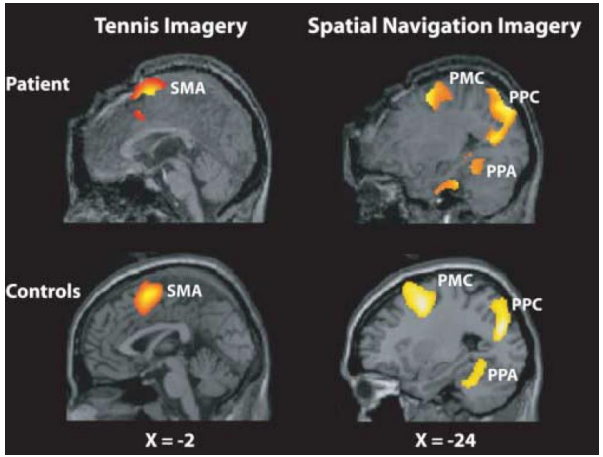
Aubinet et al., *SIN*, 2002

Insights of residual language abilities in DoC

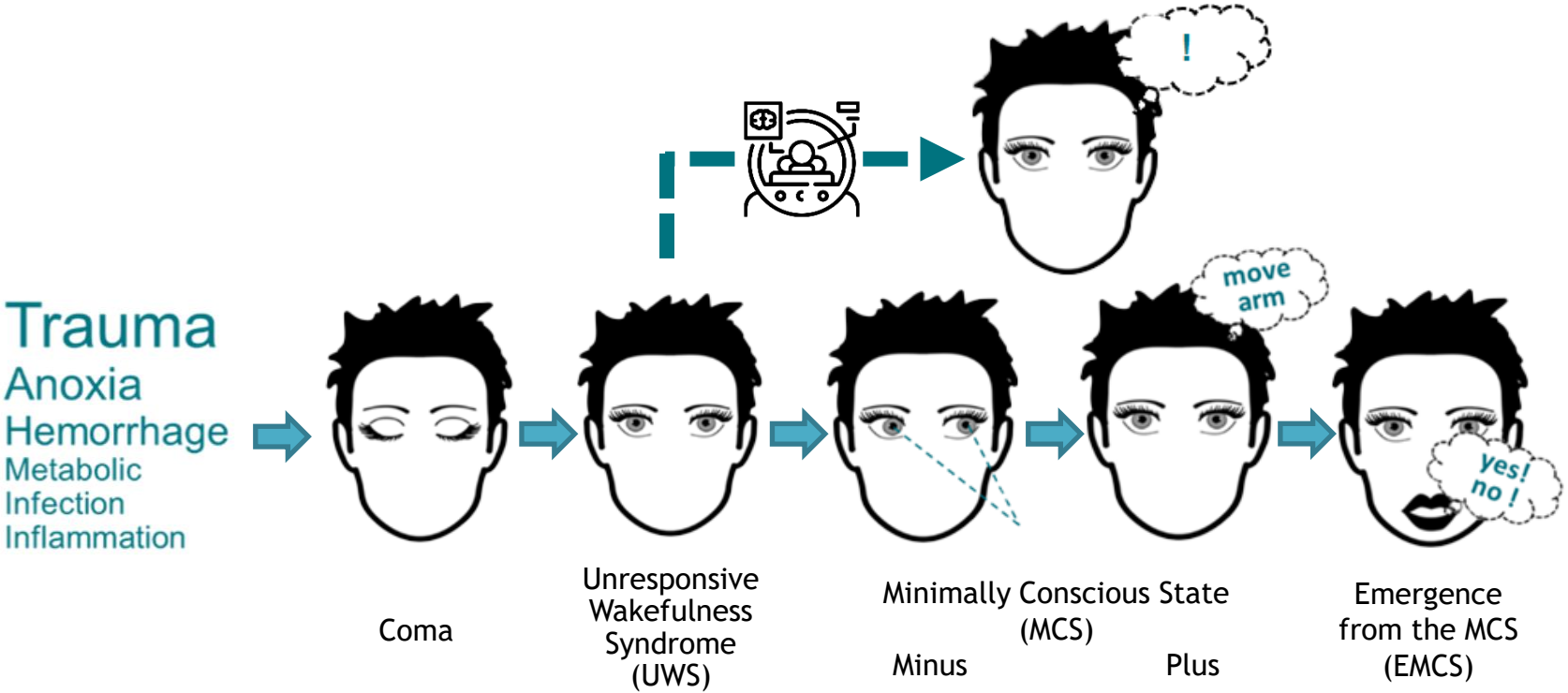
Passive tasks



Active tasks



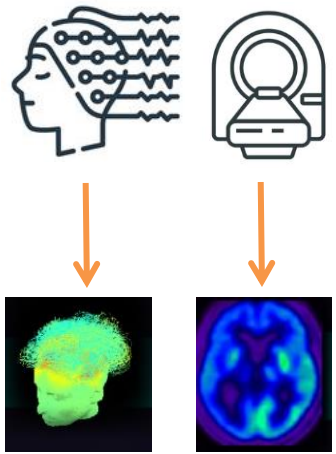
Laureys et al., *Neurology*, 2004
Owen et al., *Neuropsychol. Rehabil.*, 2005
Schiff et al., *Neurology*, 2005



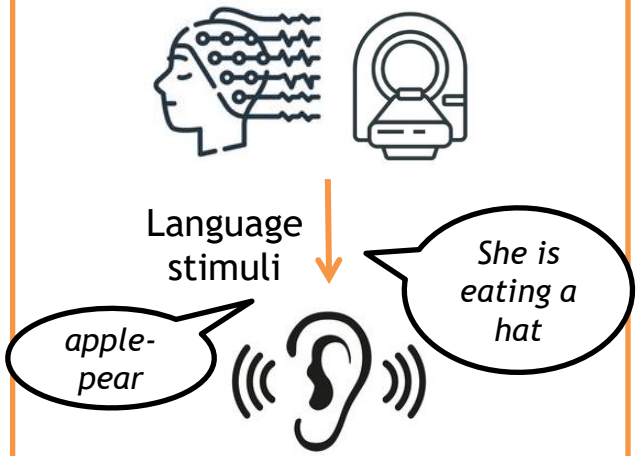
Thibaut et al. *Ann Neurol*, 2021

Implicit vs. explicit language processing in DoC patients

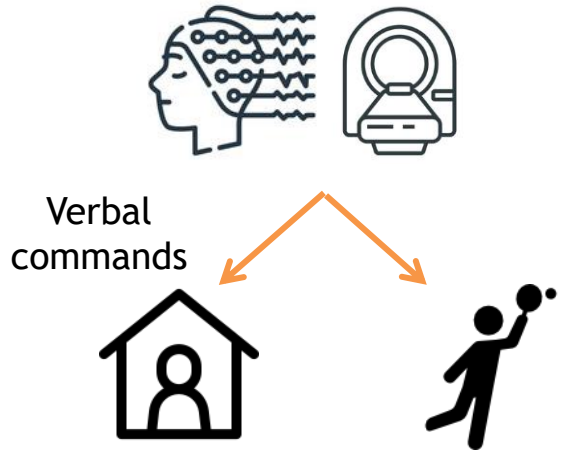
Rest



Passive tasks
→ Implicit language processing



Active tasks
→ Explicit language processing



Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Methods

Objectives

1) Identify the level and quality of language residual abilities as a function of DoC diagnosis
2) Examine *how*, *when* and *where* implicit and explicit language abilities reappear after severe brain injury associated with impaired consciousness

→ Review question:

Which residual language abilities were observed in patients with DoC following severe acquired brain injury using neuroimaging, electrophysiological and behavioral bedside assessment methods?

Preregistration on PROSPERO (CRD42020139361) database

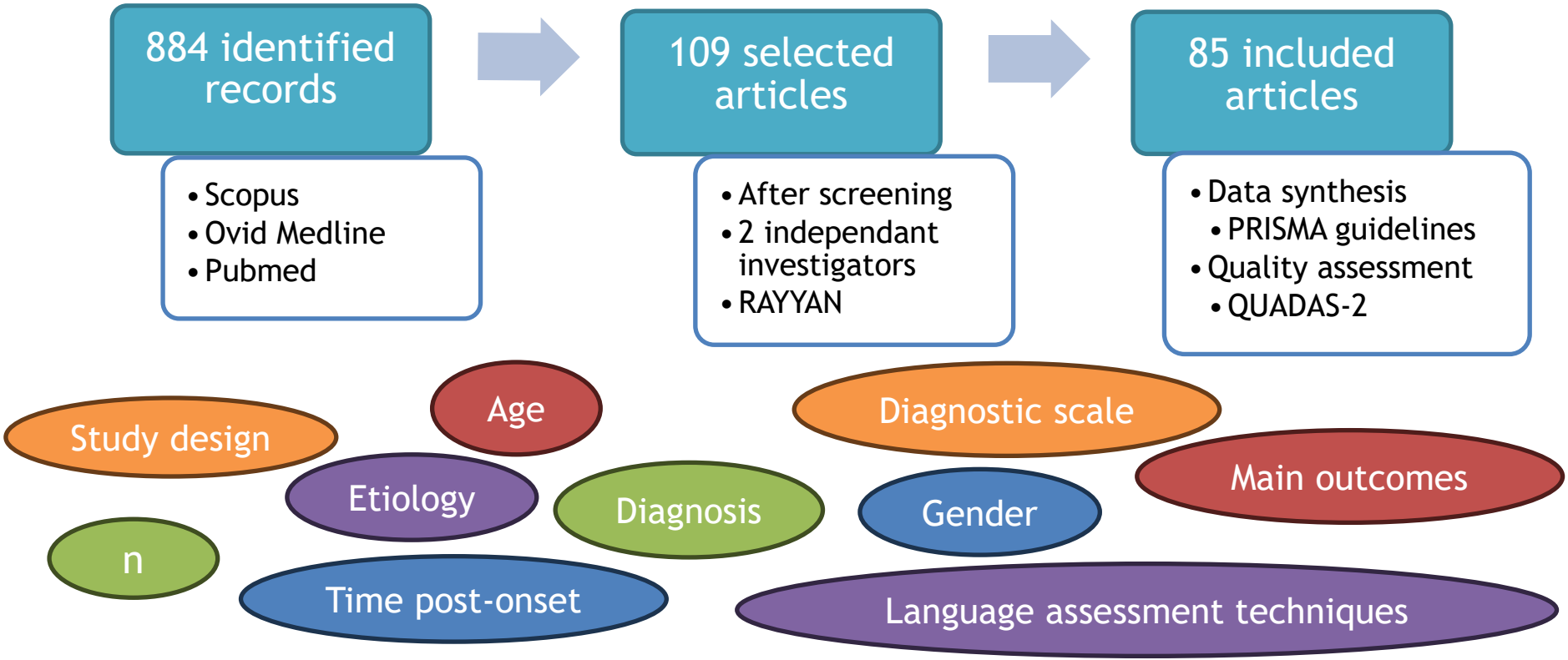
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Inclusion criteria

1) *Patients > 16 years old with DoC following severe acquired brain injury*
2) *Reporting of language-related neuroimaging, electrophysiological or behavioral measurements*
3) *Study targets the detection of residual language abilities (speech comprehension and/or production)*
4) *Empirical studies published in international peer-reviewed journals, in English*
5) *Use of the 2002 consensus-based criteria for diagnosing MCS*

Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Systematic review process



Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Results

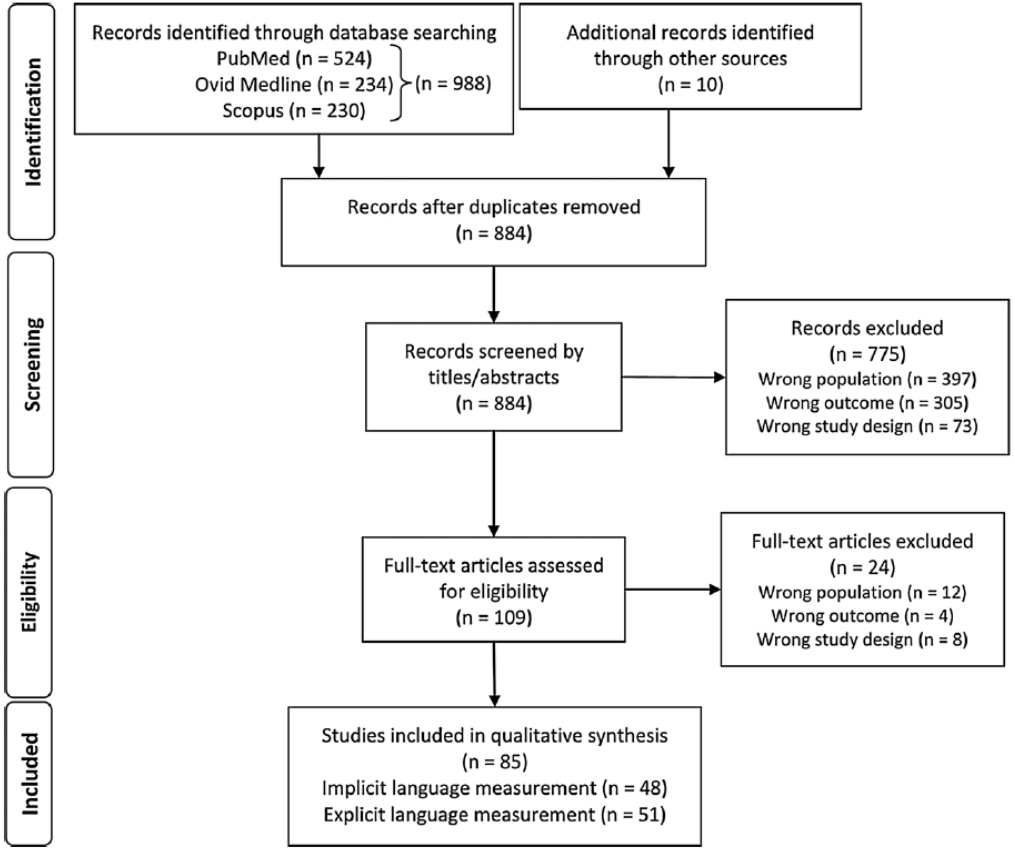


Fig. 1. Flowchart of the selection of articles. PRISMA 2009 flow diagram.

Aubinet et al., *Neurosci Biobehav Rev*, 2022

Table 1
Characteristics, main outcome and quality assessment of the included studies.

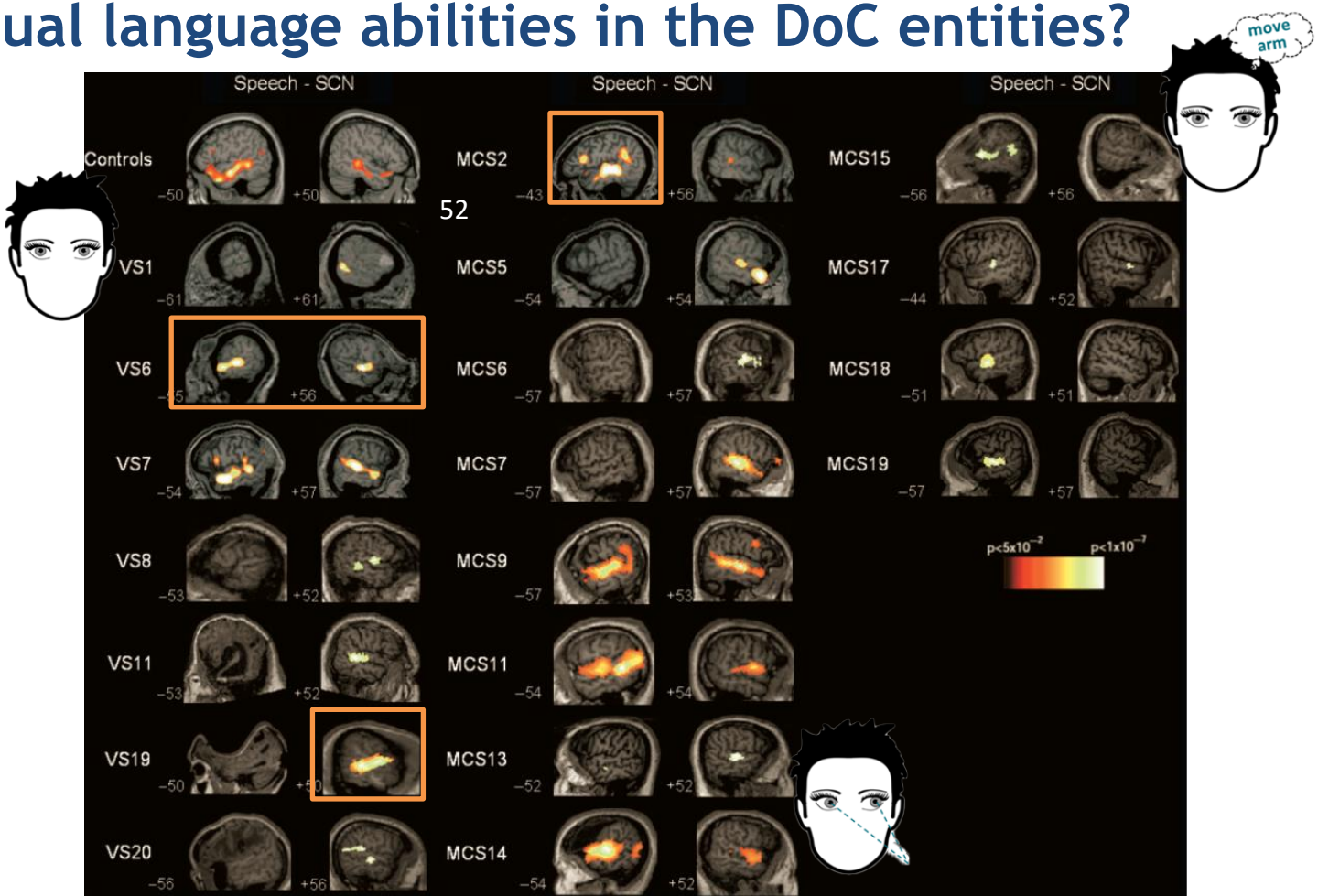
REFERENCE	N (and diagnoses)	ETIOLOGY	AGE (years)	GENDER	TIME POST-ONSET	SCALE	TECHNIQUE	MAIN OUTCOME	Risk of bias			
									POPULA-TION	INDEX TEST	REFERENCE STANDARD	FLOW & TIMING
Prospective cross-sectional studies												
Annen et al. (2018)	12 (8UWS, 4MCS-) HCS: 34 (PET)	5TBI, 6anoxia, 1hemorrhage	*Mdn* = 47.5, IQR = 20 MCS-: *M* = 47.5, *SD* = 20 UWS: *M* = 43.5, *SD* = 25.5	5F	*Mdn* = 7.5, IQR = 7.75 MCS-: *M* = 7.5, *SD* = 7.75 UWS: *M* = 50, *SD* = 30.5 months	CRS-R	Active EEG (counting), PET	Explicit: 0%UWS, 25%MCS	+	?	?	?
Balconi et al. (2013)	18 (10UWS, 8MCS) HCS: 20	5TBI, 10 anoxia, 3stroke	*M* = 50, *SD* = 10.11, R = 25–69	8F	*M* = 52, R = 6–70 months	CNC, DRS, GCS	Passive EEG (N400)	Implicit : 100% UWS, 100% MCS, 100%HCS (but delayed peaks in DoC)	+	?	+	?
Balconi and Arangio (2015)	18 (7UWS, 11MCS)	6TBI, 9anoxia, 3stroke	*M* = 49.5, *SD* = 11.7, R = 25–64	10F	*M* = 48, R = 6–63 months for initial sample of 22patients	CNC, DRS			+	+	+	?
Bekinschtein et al. (2011)	5 (UWS) HCS: 3	4TBI, 1mixed	*M* = 29.4, *SD* = 7.8, R = 20–40, Mdn = 30	?	*M* = 10.4, *SD* = 7.1, R = 5–20, *Mdn* = 6 months	CRS-R	Passive EEG (speech detection), active fMRI (moving hand)	Implicit : 100%UWS Explicit : 40%UWS	+	?	–	?
Beukema et al. (2016)	16 (8UWS, 8MCS) HCS: 17	8TBI, 8NTBI	*M* = 38.5, *SD* = 17.2, R = 16–69	4F	*M* = 42.8, *SD* = 50.8, R = 5–202 months	CRS-R	Passive EEG (N400)	Implicit : 37.5%UWS, 50% MCS	+	?	?	+
Bodien et al. (2017)	10 (1coma, 4UWS, 2MCS-, 3MCS+) HCS: 10	10TBI	*M* = 27.9, *SD* = 9.1, R = 18–51	4F	*M* = 242.9, *SD* = 586.9, R = 3–1900, Mdn = 10 days	CRS-R, CAP	Active fMRI (imagery)	Explicit : 0%coma, 25%UWS, 0%MCS-, 67%MCS + for hand squeezing, 0%coma, 25%UWS, 50%MCS-, 0% MCS + for tennis playing	+	+	+	–
Braiman et al. (2018)	21 (3UWS, 12MCS, 6EMCS) HCS: 13	18TBI, 3NTBI	*Mdn* = 27, IQR = 9	7F	*Mdn* = 64, IQR = 40 months	CRS-R	Passive EEG (narrative), fMRI (motor imagery)	Implicit: Progressive delay in natural speech envelope latencies across diagnostic categories Explicit: 0%UWS, 58%MCS (including MCS-)	+	?	?	?
Charland-Verville et al. (2014)	25 (11UWS, 14MCS)	15TBI, 10NTBI	*M* = 33, *SD* = 13	10F	*M* = 31, *SD* = 27 months	CRS-R	Breathing-based "sniff controller"	Explicit: 0%UWS, 7%MCS	+	?	?	?
Chatelle et al. (2018)	10 (4coma, 1UWS, 4MCS, 1LIS) HCS: 10	2TBI, 3anoxia, 4hemorrhage, 1stroke	*M* = 56.7, *SD* = 12.2, *Mdn* = 56, R = 37–72	2F	*M* = 15.7, *SD* = 11.4, *Mdn* = 15, R = 3–38 days	CRS-R	Active EEG (counting, motor imagery)	Explicit: 0%UWS, 0%MCS Implicit: 100%coma, 100%	+	?	–	–

Which residual language abilities in the DoC entities?

Implicit:

Low level

→ Speech vs. noise



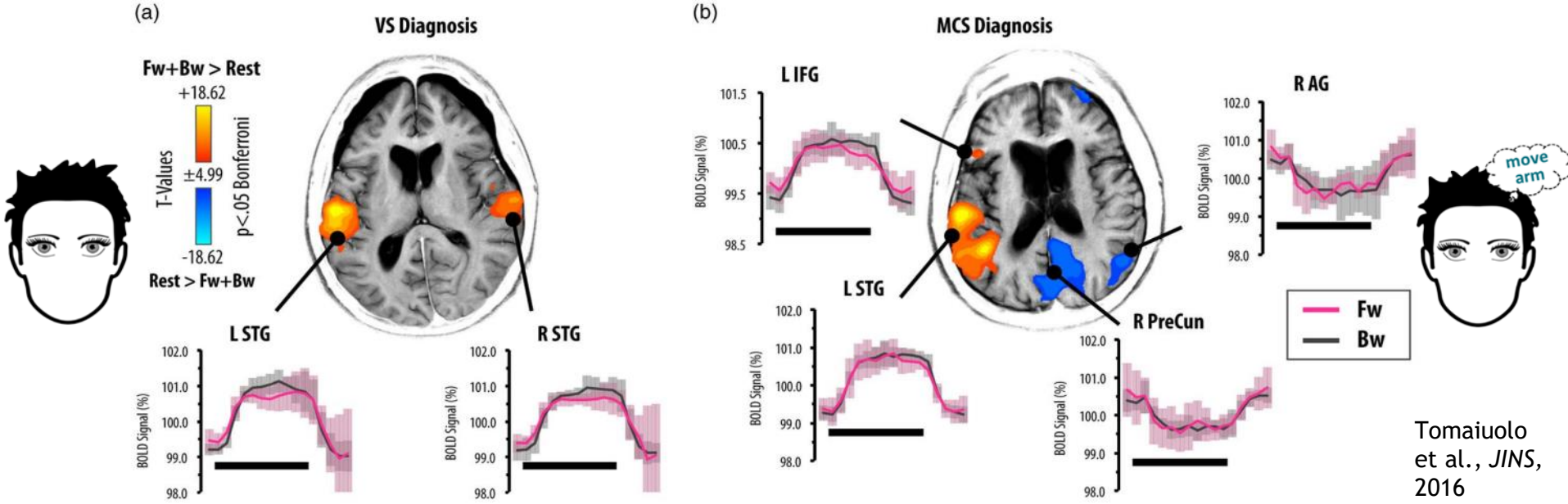
Coleman et al., *Brain*, 2009

Which residual language abilities in the DoC entities?

Implicit:

Low level

→ Forward vs. backward speech



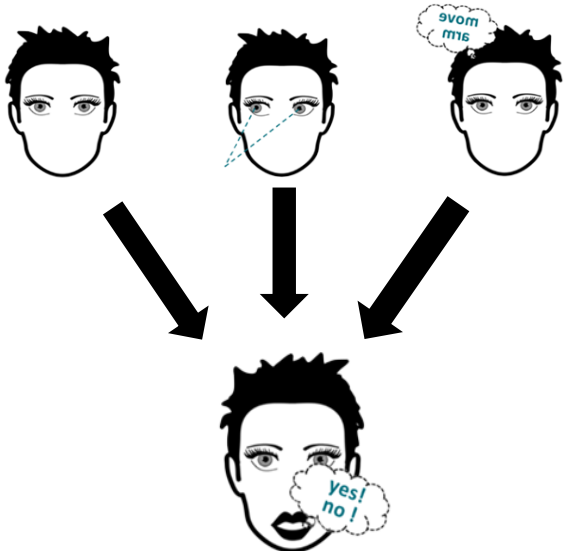
Tomaiuolo et al., *JINS*, 2016

Which residual language abilities in the DoC entities?

Implicit:

High level

→ Semantically congruent vs. incongruent sentences



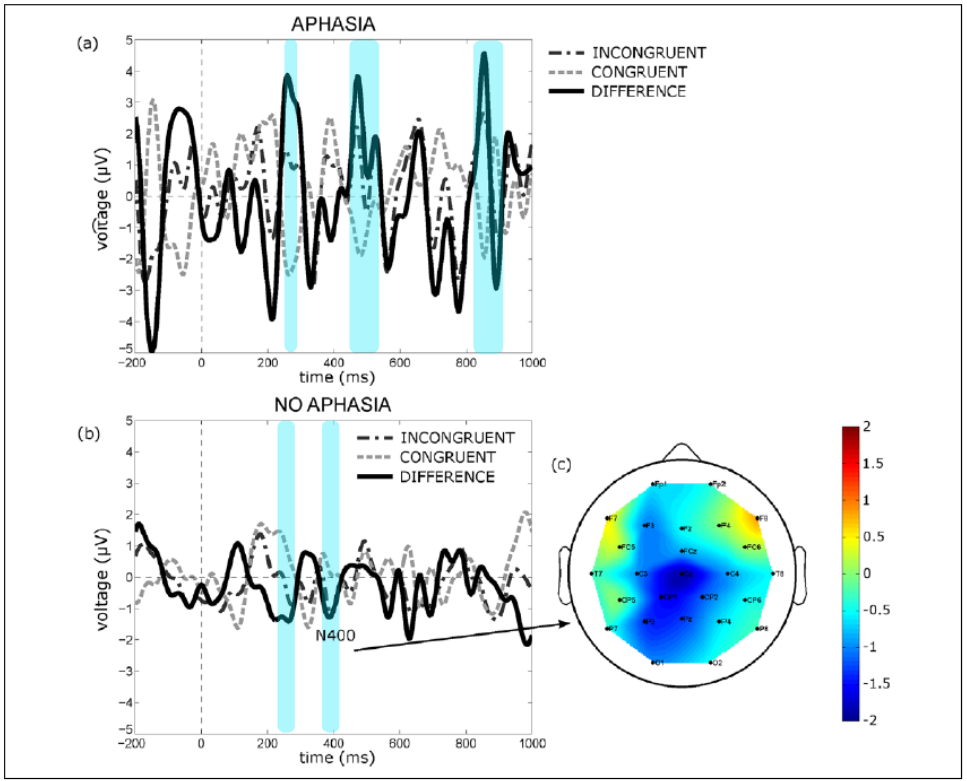


Figure 2. N400 in DoC patients. GA of the incongruent and congruent difference waves computed at Pz in DoC patients grouped according to the presence (panel A, Aphasia; n = 4) or not (panel B, No Aphasia; n = 4) of aphasia. Temporal windows in which we found a significant difference between incongruent and congruent conditions (nonparametric test, $P < .05$) are highlighted in light blue. Topographical map of averaged scalp potential at N400 latency in the No Aphasia patient group (panel C).

Formisano et al., *NNR*, 2019

Which residual language abilities in the DoC entities?

Implicit:

High level (even in some UWS patients)

→ Factually **correct** (e.g., *May follows April*) vs. **incorrect** sentences (e.g., *March follows April*)

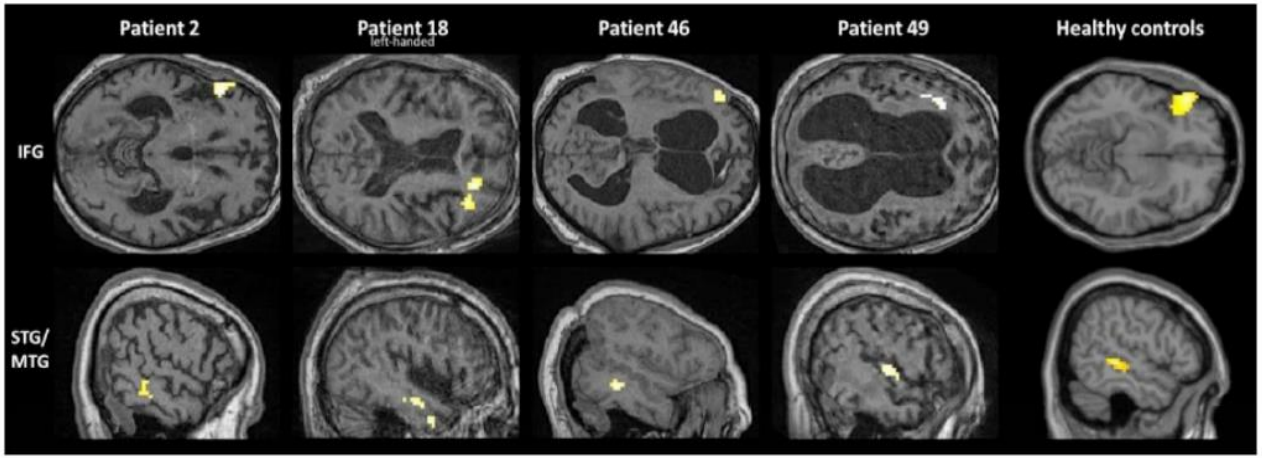
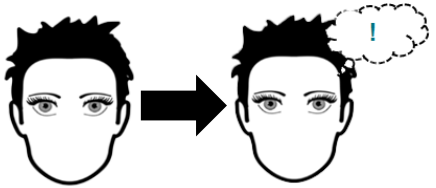


Fig. (1). Brain responses in the inferior frontal gyrus (IFG) and in the superior/middle temporal gyri (STG/MTG). These scans were obtained from a group of 21 age-matched healthy subjects and 4 patients who were regarded as "full responders". The statistical threshold employed was an uncorrected p value of 0.001 for illustrative purposes.

Kotchoubey et al., *Curr. Pharm. Des.*, 2013

Which residual language abilities in the DoC entities?

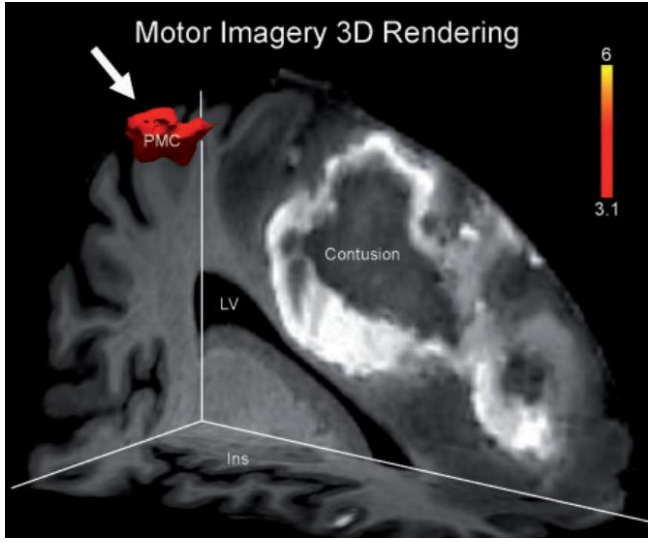


Explicit:

Command-following using brain-computer interfaces

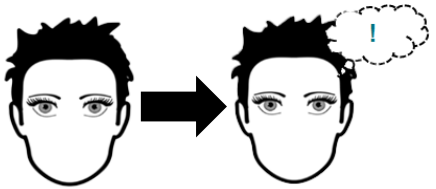
→ Detection of Cognitive-Motor Dissociation (CMD)

E.g.: Right hand squeeze imagery task → brain response in 3/3 UWS patients using fMRI, 0/3 UWS patients using EEG



Edlow et al., *Brain*, 2017

Which residual language abilities in the DoC entities?

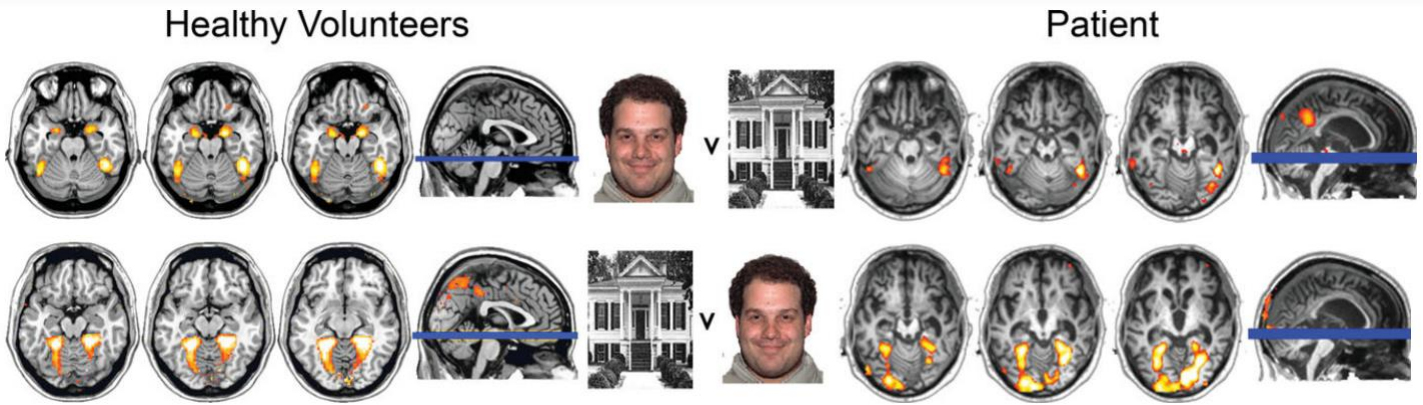


Explicit:

Command-following using brain-computer interfaces

→ Detection of Cognitive-Motor Dissociation (CMD)

E.g.: Visual recognition of faces vs. houses



Monti et al., *Brain*, 2017

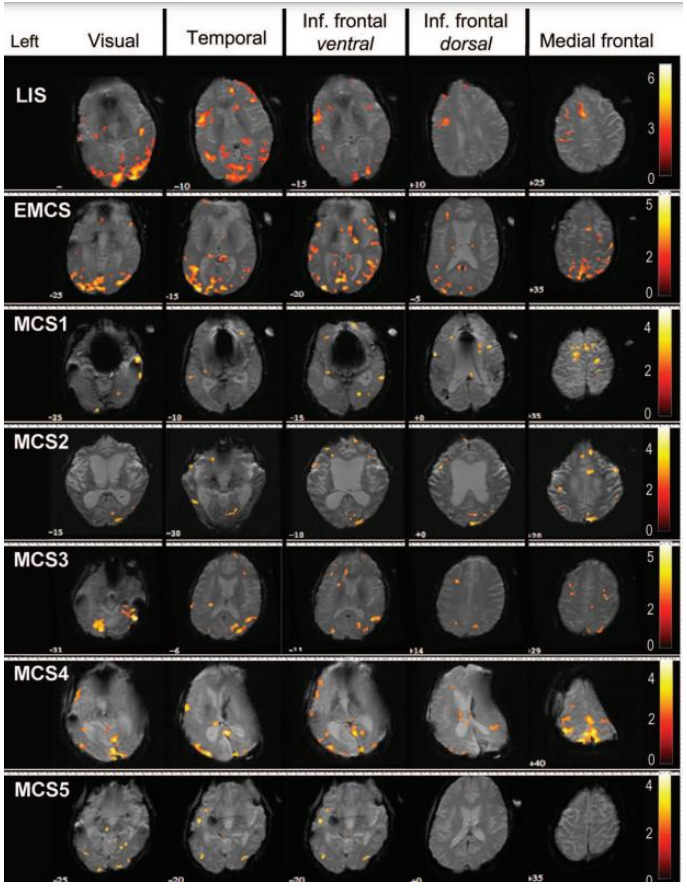
Which residual language abilities in the DoC entities?

Explicit:

Command-following using brain-computer interfaces

→ Detection of Cognitive-Motor Dissociation (CMD)

E.g.: silent picture-naming task



Rodriguez-Moreno et al., *Neurology*, 2010

Which residu

Explicit:

Behavioral command-following

Table 1 Behavioral tools allowing language assessment in post-comatose patients

Tool	Required level of consciousness	Advantages	Disadvantages
CRS-R (SECONDs, IQBA) language-related items	MCS+, EMCS	Included in validated scales allowing diagnosis of DoC	Multi-determinate, no distinction of language domains (►**Fig. 1**)
Chiba score[21]	MCS, EMCS	Distinction between language comprehension, expression, and communication, with reported level of severity	No available validation data, based on basic clinical observation
CAVE	MCS−, MCS+, EMCS	Assessment of item recognition, based on visual fixation (adapted to most MCS− patients), validated scale with high levels of inter-rater and test–retest reliability	Based on visual fixation (not adapted to patients with impaired vision and oculomotricity), no distinction of language domains and no assessment of psycholinguistic effects
BERA	MCS−, MCS+, EMCS	Assessment of item recognition, based on visual fixation (adapted to most MCS− patients), good psychometric properties in aphasic conscious patients, distinction of language domains, and assessment of some psycholinguistic effects	Based on visual fixation (not adapted to patients with impaired vision and oculomotricity), no validation group study on DoC patients
Loewenstein Communication Scale	EMCS	Validated scale to assess communication abilities with very good reliability and good inter-rater agreement	No characterization of residual language abilities per se, no concrete definition nor examples
Individual Nonverbal Communication Rating Scale	EMCS	Combination of patient observation, family interviews, and scores of the Glasgow Coma Scale to estimate patients' communication abilities	No characterization of residual language abilities per se, no concrete definition nor examples, no available validation data

Abbreviations: DoC, disorders of consciousness; EMCS, emergence of minimally conscious state; MCS, minimally conscious state.

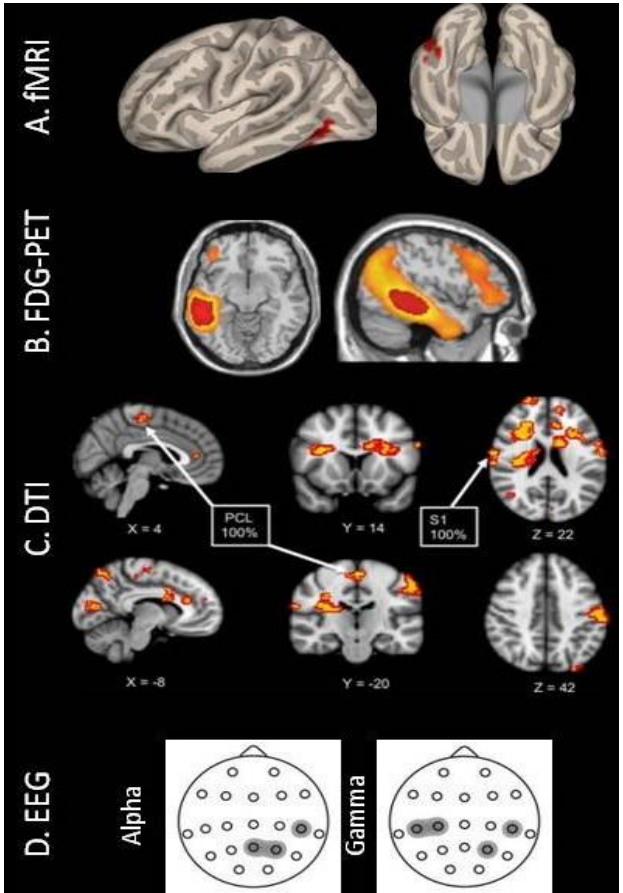
Aubinet et al., *SIN*, 2022

Which residual language abilities in the DoC entities?

Explicit:

Behavioral command-following

→ MCS- < MCS+



Aubinet et al., *HBM*, 2018
Aubinet et al., *NNR*, 2020
Zheng et al., *HBM*, 2017
Claassen et al., *Annals Neurol.*, 2016

Which residual language abilities in the DoC entities?

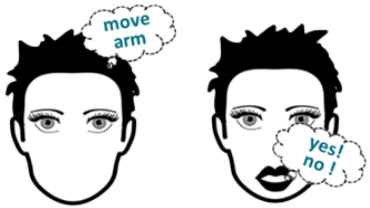
Explicit:

Behavioral command-following

→ *Brief Evaluation of Receptive Aphasia (BERA)*

Aubinet et al., *Brain Inj.*, 2021

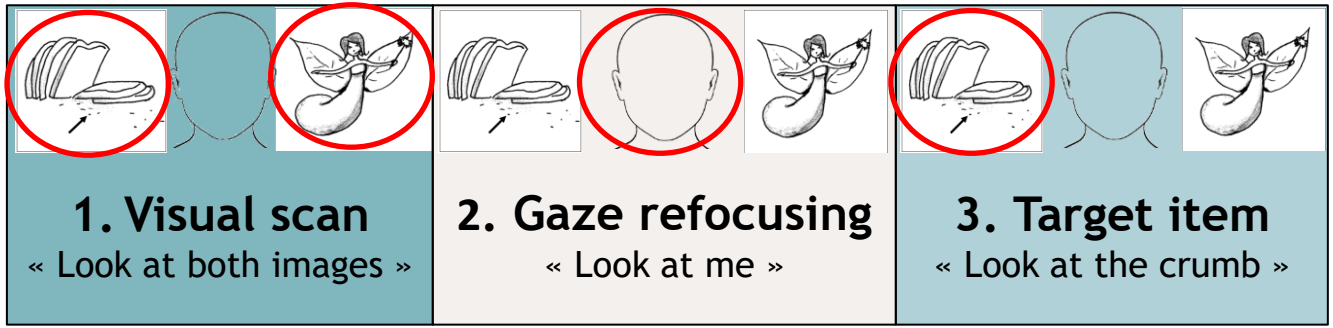
Which residual language abilities in the DoC entities?



Explicit:

Behavioral command-following

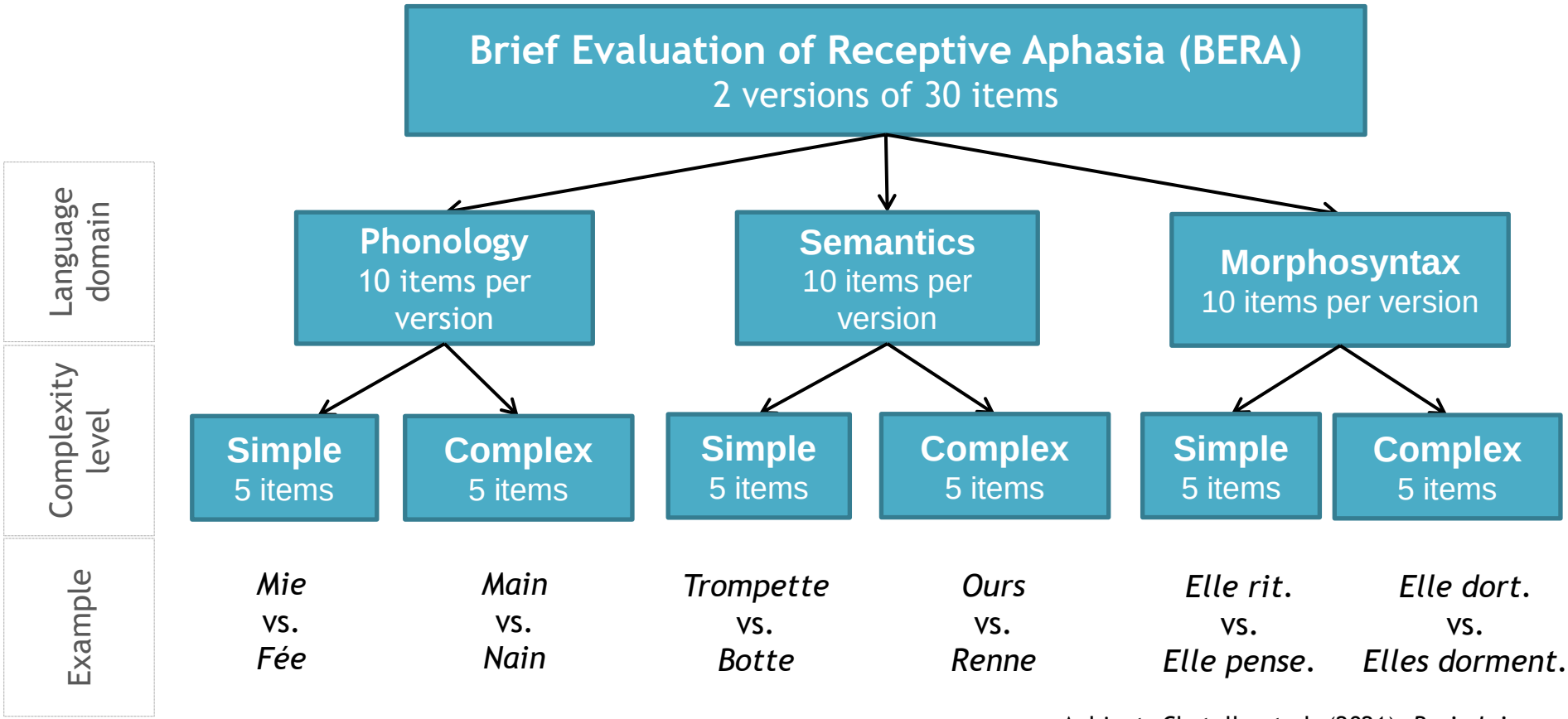
→ *Brief Evaluation of Receptive Aphasia (BERA)*



→ ≠ language domains (word phonological/semantic contrasts, sentences contrasting various morphosyntactic elements

Aubinet et al., *Brain Inj.*, 2021

Elaboration of the BERA language-specific tool

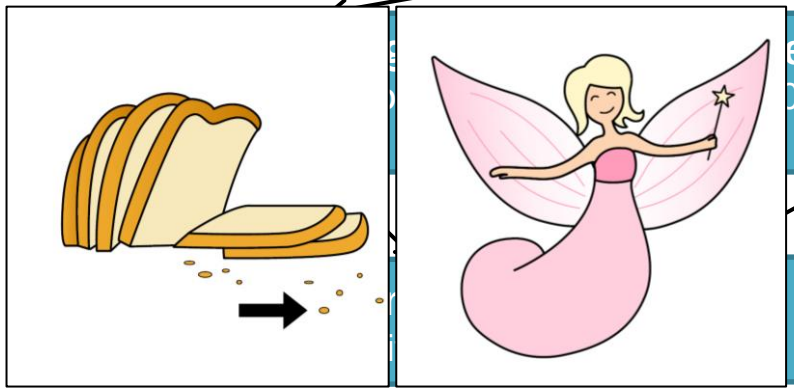


Aubinet, Chatelle et al. (2021), *Brain Injury*

Elaboration of the BERA language-specific tool

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

Language domain		**emantics** 0 items per version		**Morphosyntax** 10 items per version	
Complexity level			**Complex** 5 items	**Simple** 5 items	**Complex** 5 items
Example	*Mie* vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*



Aubinet, Chatelle et al. (2021), *Brain Injury*

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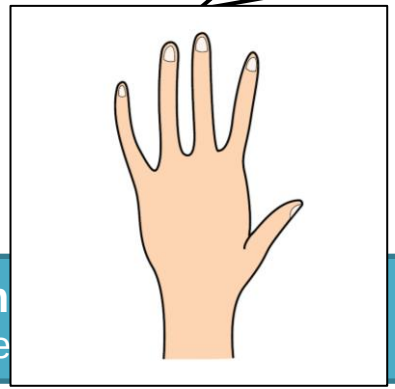
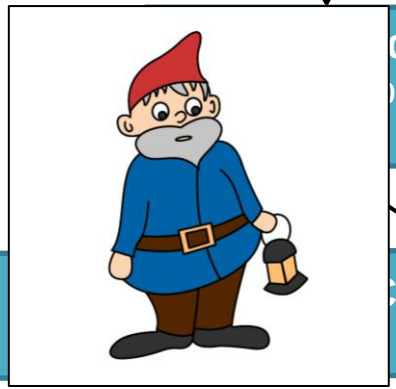
Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

Language domain				**Morphosyntax** 10 items per version	
Complexity level	**Sim** 5 ite		**Complex** 5 items	**Simple** 5 items	**Complex** 5 items
Example	*Mie* vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*



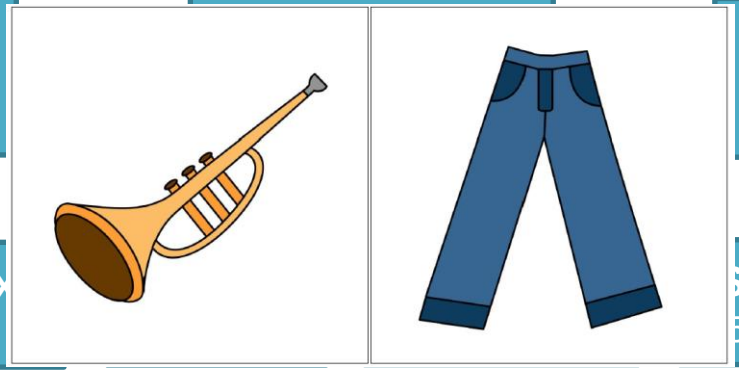


Aubinet, Chatelle et al. (2021), *Brain Injury*

Elaboration of the BERA language-specific tool

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

Language domain	Complexity level	Example					
Phonology 10 items per version	**Simple** 5 items	*Mie* vs. *Fée*	*Main* vs. *Nain*				
	Complex 5 items			*Trompette* vs. *Botte*			
					Ours vs. *Renne*		
Morphosyntax 10 items per version	**Simple** 5 items					*Elle rit.* vs. *Elle pense.*	
	Complex 5 items						*Elle dort.* vs. *Elles dorment.*



Aubinet, Chatelle et al. (2021), *Brain Injury*

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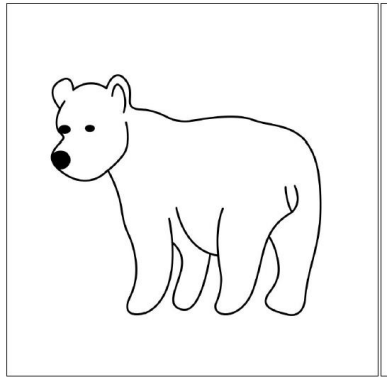
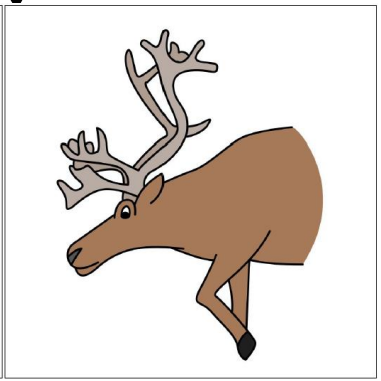
2 versions of 30 items

Language domain	Complexity level	Example					
Phonology 10 items per version	**Simple** 5 items	*Mie* vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*
	Complex 5 items						
Morphosyntax 10 items per version	**Simple** 5 items						
	Complex 5 items						





Aubinet, Chatelle et al. (2021), *Brain Injury*

Elaboration of the BERA language-specific tool

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

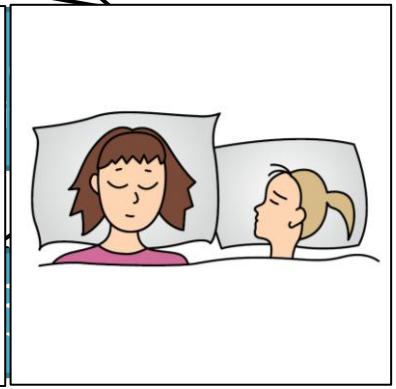
Language domain	Complexity level	Example
Phonology 10 items per version	Simple 5 items	*Mie* vs. *Fée*
	Complex 5 items	*Main* vs. *Nain*
Simp…	Simp… 5 item…	*Trompette* vs. *Botte*
		Ours vs. *Renne*
…ax …sion		*Elle rit.* vs. *Elle pense.*
	…mplex …items	*Elle dort.* vs. *Elles dorment.*

Aubinet, Chatelle et al. (2021), *Brain Injury*

Elaboration of the BERA language-specific tool

Brief Evaluation of Receptive Aphasia (BERA)
2 versions of 30 items

Language domain	**Phonology** 10 items per version		**Semant** 10 items version			
Complexity level	**Simple** 5 items	**Complex** 5 items	**Simple** 5 items			
Example	*Mie* vs. *Fée*	*Main* vs. *Nain*	*Trompette* vs. *Botte*	*Ours* vs. *Renne*	*Elle rit.* vs. *Elle pense.*	*Elle dort.* vs. *Elles dorment.*



Aubinet, Chatelle et al. (2021), *Brain Injury*

Validity and feasibility of the BERA tool: preliminary results

1. Validation study on aphasic conscious patients (n=52)

- Concurrent validity with Language Screening Test (LAST)

  → Sensitive to language disorders
- Content validity (2 versions)
- Intra-/inter-rater reliability (α=0,919)

Aubinet, Chatelle et al. (2021), *Brain Injury*

2. BERA with eye-tracker: Delphi study (n=18)

- 100% highlight the need for such tools
- 100% consider that the use of an eye-tracker is appropriate in this context

Mazué, Aubinet et al. (2022), Master Thesis

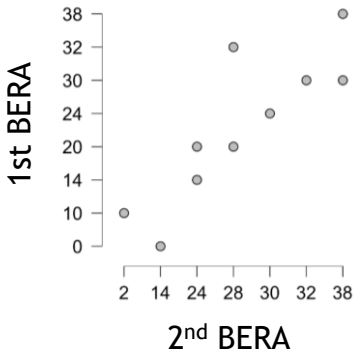
3. Ongoing BERA validation study on DoC patients (n=18)

Aubinet et al., *in prep*

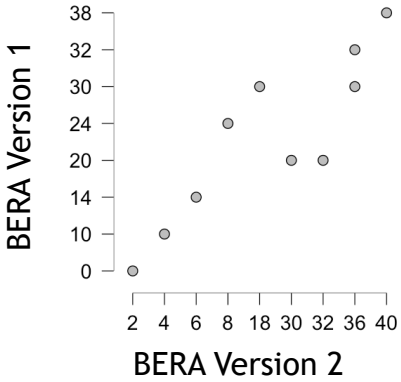
Validity and feasibility of the BERA tool: preliminary results

3. Ongoing validation study on DoC patients (n=10)

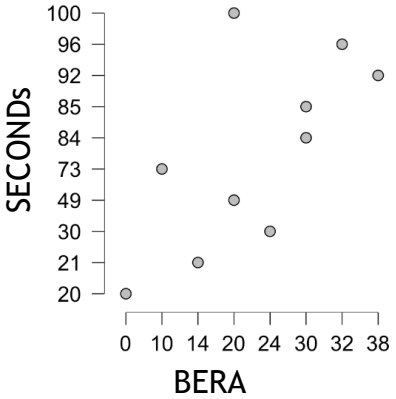
Intra-rater reliability



Content validity



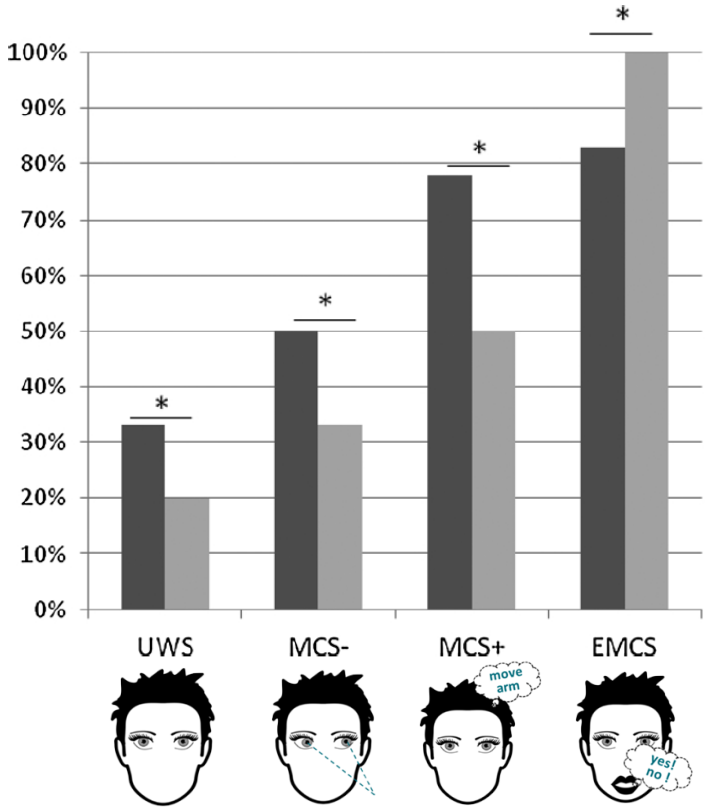
Concurrent validity

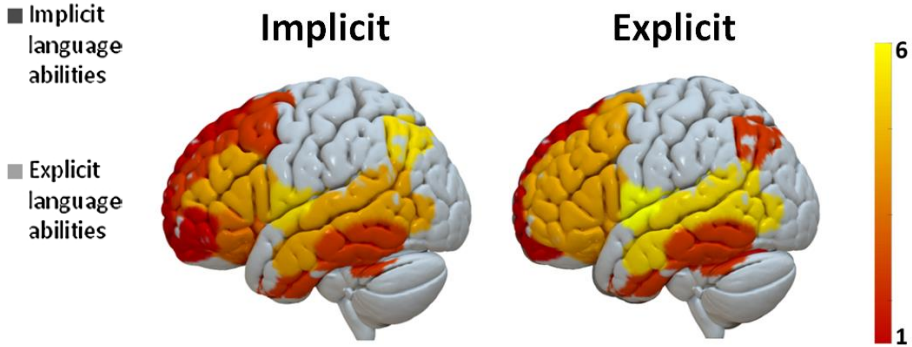


Inter-rater reliability: α = 0.989

Aubinet et al., *in prep*

Residual language abilities in the DoC entities





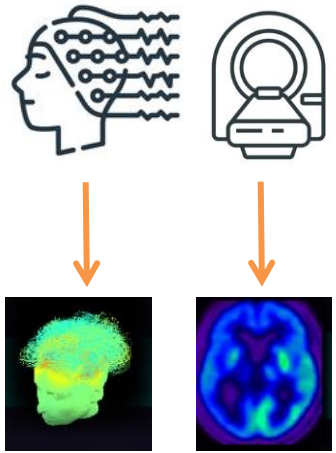
Aubinet et al., *Neurosci. Biobeh. Rev.*, 2022

LIÈGE université
GIGA

Discussion

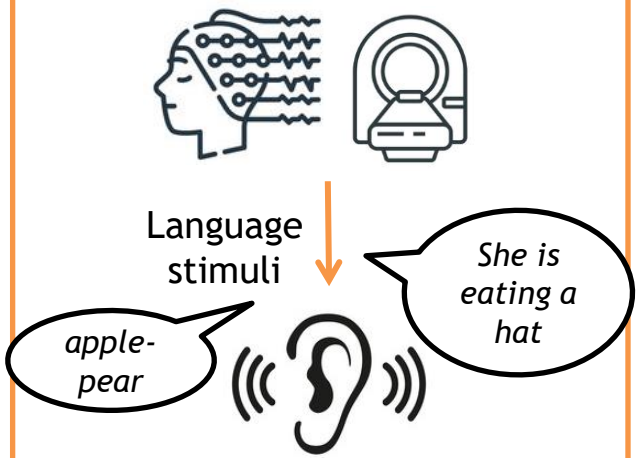
Implicit vs. explicit language processing in DoC patients

Rest



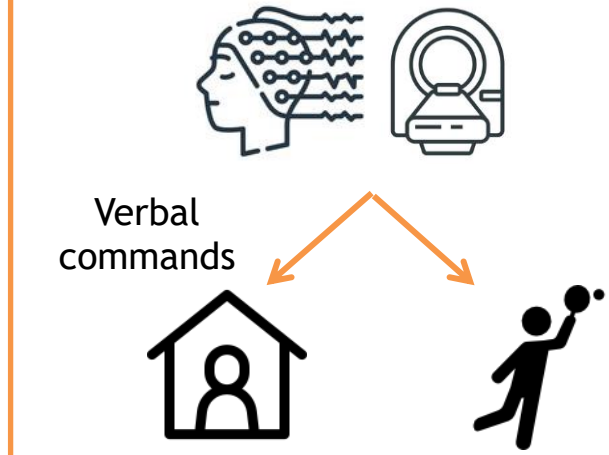
MCS*

Passive tasks
→ Implicit language processing



Covert cortical processing

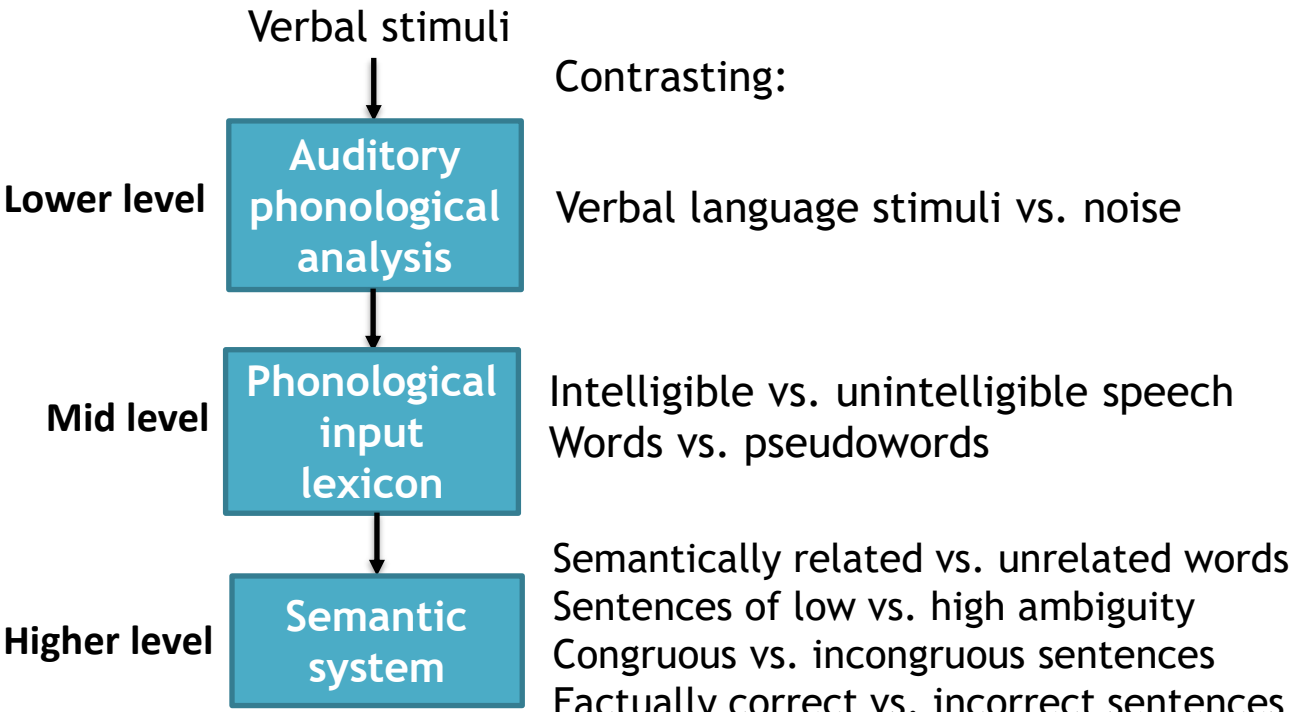
Active tasks
→ Explicit language processing



Cognitive-motor dissociation

Thibaut et al. *Ann Neurol*, 2021
Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Implicit language processing



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; …

Patterson and Shewell (1987)

Implicit language processing

- Not considered in the current DoC taxonomy
- Patients with the lowest level of consciousness can show residual brain activity reflecting complex semantic processing

→ *Is the presence of complex language processing in the absence of "consciousness" possible?*

  - First-order theories (activity in sensory areas → Consciousness) vs. higher-order theories (higher-order activity focusing on sensory activity → Consciousness) of consciousness
  - Priming paradigms: high-level semantic associations require conscious processing but not low-level categorical semantic associations

Melloni et al., *Science*, 2021
Edlow et al., *Brain*, 2017
Chien et al., *Current Psychol*, 2023

Explicit language processing

Command-following ability

- Overt → CRS-R, SECONDs, BERA
- Covert

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

Picture naming

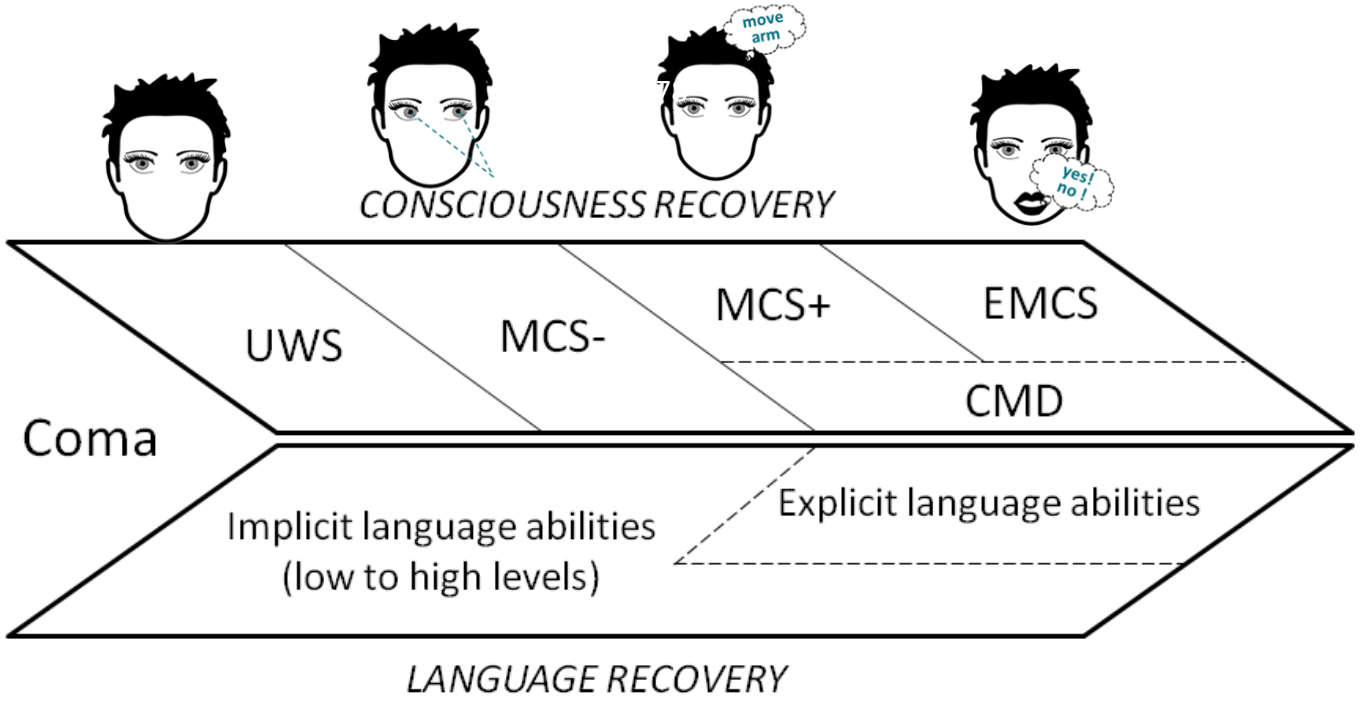
Rodriguez-Moreno et al., 2010

Potential residual brain response in all DoC categories

→ ~20% UWS and ~33% MCS-

= CMD!

Recovery trajectory of both language and consciousness



Aubinet et al., *Neurosci. Biobeh. Rev.*, 2022

Methodological issues

Use of language measures to assess consciousness

Heterogeneity regarding language measures

Large variability of:

- Dependent variables
- Techniques
- Verbal stimuli

QUADAS-2:

- Lack of blinding procedures and clarity regarding the timing of data acquisition in numerous studies
- High risk of bias regarding the population → difficult to apply to DoC patients

Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022

Perspectives

Clinical level:

- Longitudinal studies to assess the timing of recovery of both implicit and explicit language functions in a more systematic manner
- Neuroimaging studies to quantitatively assess the neural correlates of residual implicit language processing
- New taxonomy of DoC based on a multidimensional framework → residual language abilities should be included
- BERA validation + other scales to develop (e.g., non-sighted patients)

Theoretical level:

- Dissociation between both language and conscious processes
- Priming paradigms? Developmental studies?
- Language (inner speech) → higher-order consciousness?

Aubinet et al., *Neurosci Biobehav Rev*, 2022
Bayne et al., *Ann. Neurol.*, 2017
Skipper, *Neurosci Biobehav Rev*, 2022

In brief…

- Residual language abilities in DoC patients < neuroimaging, electrophysiological and behavioral assessments
- Implicit language abilities in 33% UWS, 50% MCS-, 78% MCS+ and 83% EMCS patients
  - → language recognition, detection of intelligibility, lexical and semantic processing of words and sentences
  - → theoretical and clinical issues
- Explicit language processing in 20% UWS and 33% MCS- (CMD), 50% MCS+ and 100% EMCS patients
- Language processing in consciousness research: clinical and theoretical implications

Questions?

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Aubinet C, Chatelle C, Gosseries O, Carrière M, Laureys S, Majerus S. Residual implicit and explicit language abilities in patients with disorders of consciousness: A systematic review. *Neurosci Biobehav Rev.* 2022 Jan;132:391-409.

Quality assessment

Patient selection

- E.g., single case or convenience sample?

Index test (language assessment)

- E.g., blinding?

Reference standard

- E.g., DoC diagnosis < consensus-based criteria?

Flow and timing

- E.g., interval between IS and RS?

https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/

Aubinet et al., *Neurosci. Biobehav. Rev.*, 2022