Neuropronostication après ACR

Pr Nicolas WEISS

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Institut de Neurologie - DMU Neurosciences
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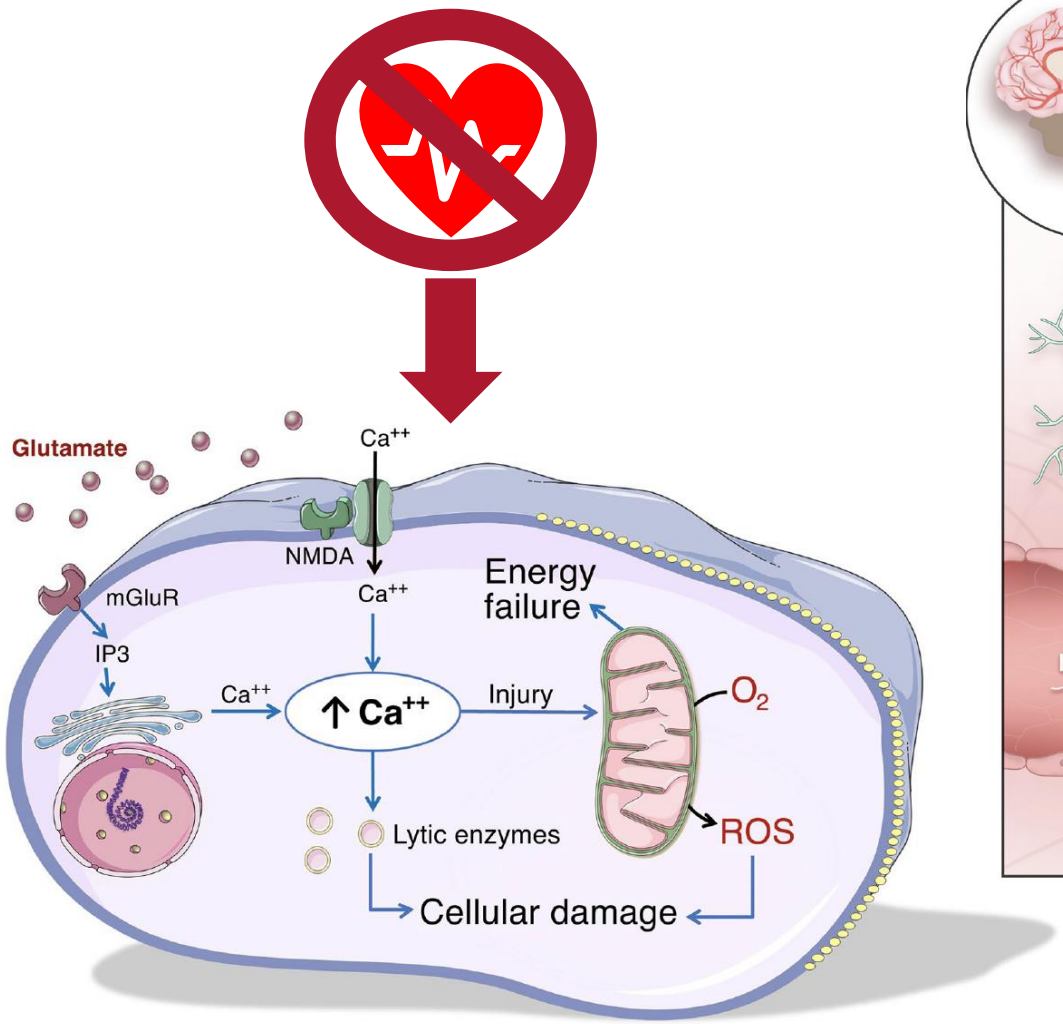
Liens d'intérêts

Financement de la recherche:	AP-HP (CRC-Innovation: EyeMTrackingHE) Sorbonne Université (bourse ISIR) DGOS (PHRC-N: CaccatoHEs, PENALTY)
Cours/symposium:	-
Activité de consultant:	Lucane Alexion
Autre:	Membre de la commission d'intégrité scientifique de la faculté de Santé Sorbonne U Mission égalité entre les femmes et les hommes Sorbonne U

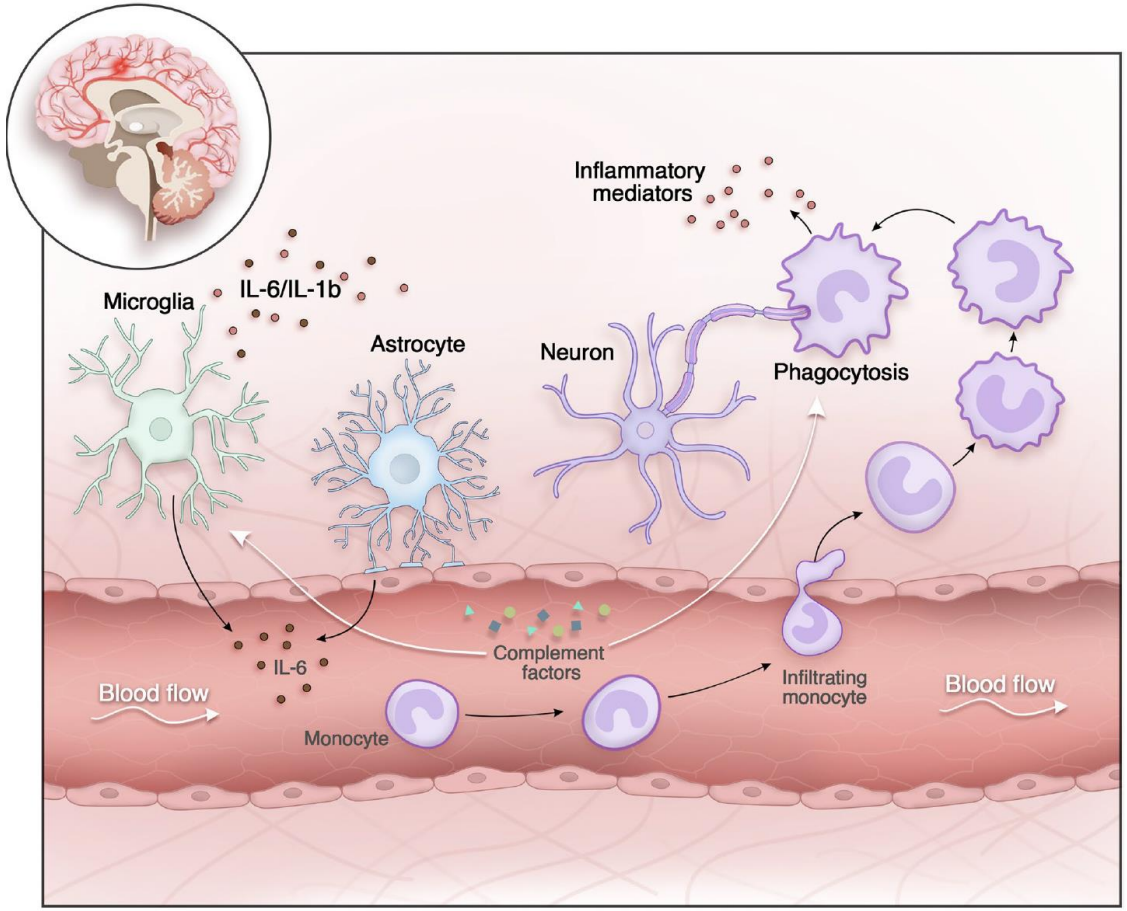
Base Transparence Santé:

https://www.transparence.sante.gouv.fr/flow/rechercheBeneficiaires?execution=e2s6

Introduction



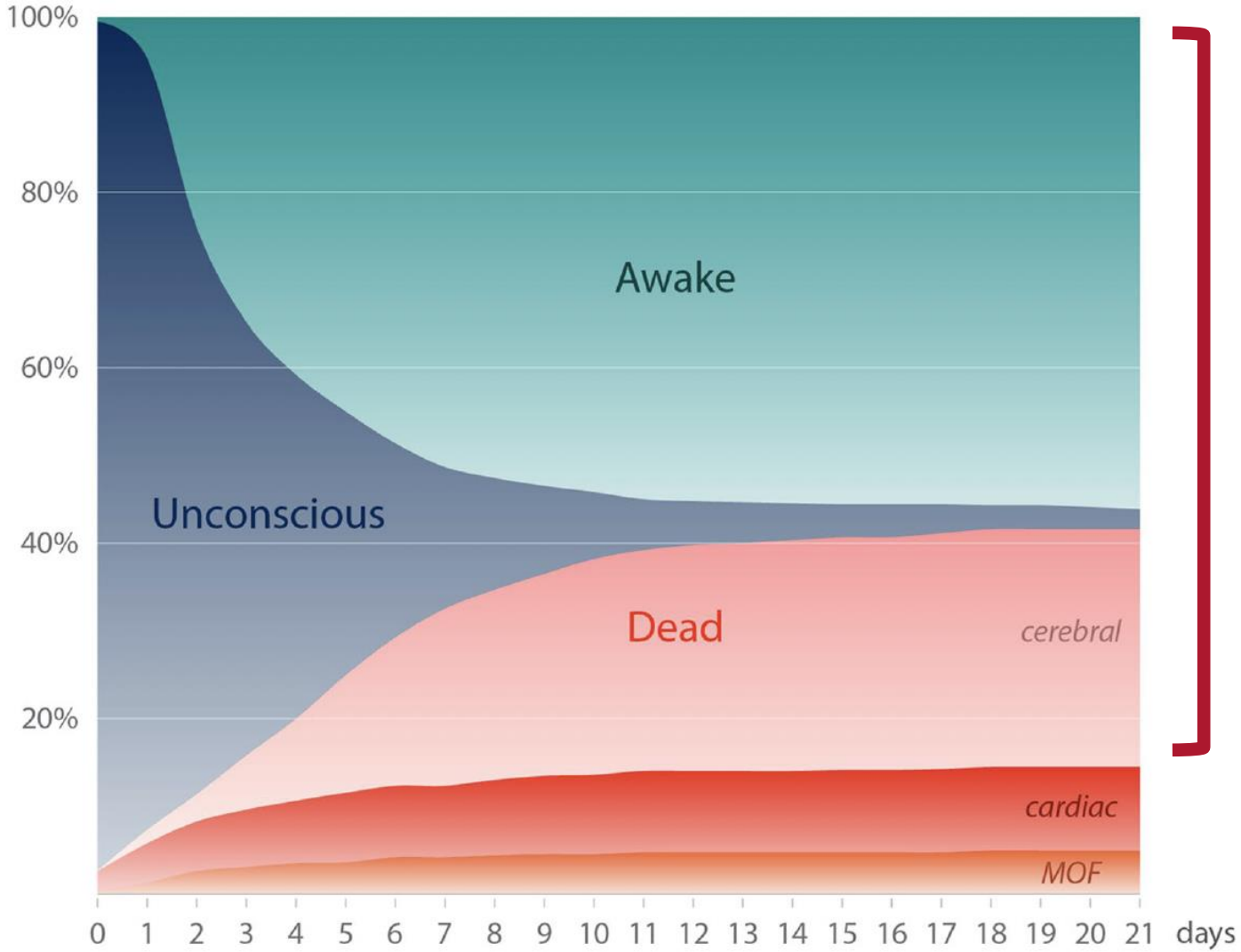
Lésions directes



Lésions indirectes (ischémie reperfusion)

Sandroni, Cronberg et Sekhon. Int Care Med 2021

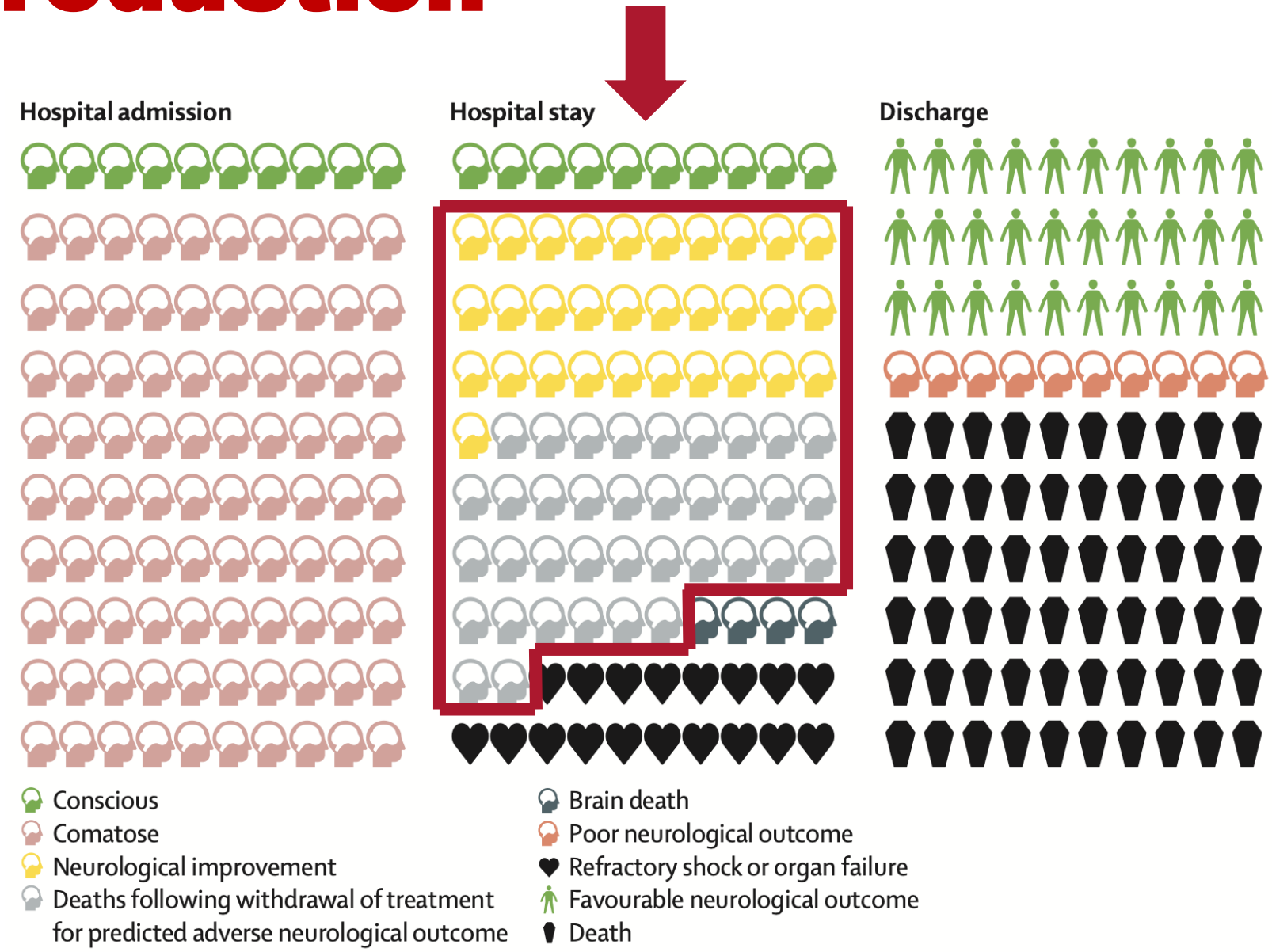
Introduction



Sandroni, Cronberg et Sekhon. Int Care Med 2021

Paul et al. Int Care Med 2016

Introduction



Perkins GD, …, Nolan JP. Lancet 2021

Plan

1 L'algorithme à connaître !!!

Resuscitation from cardiac arrest

Targeted temperature management and rewarming

Unconscious patient, M≤3 at ≥72h without confounders[1]

YES

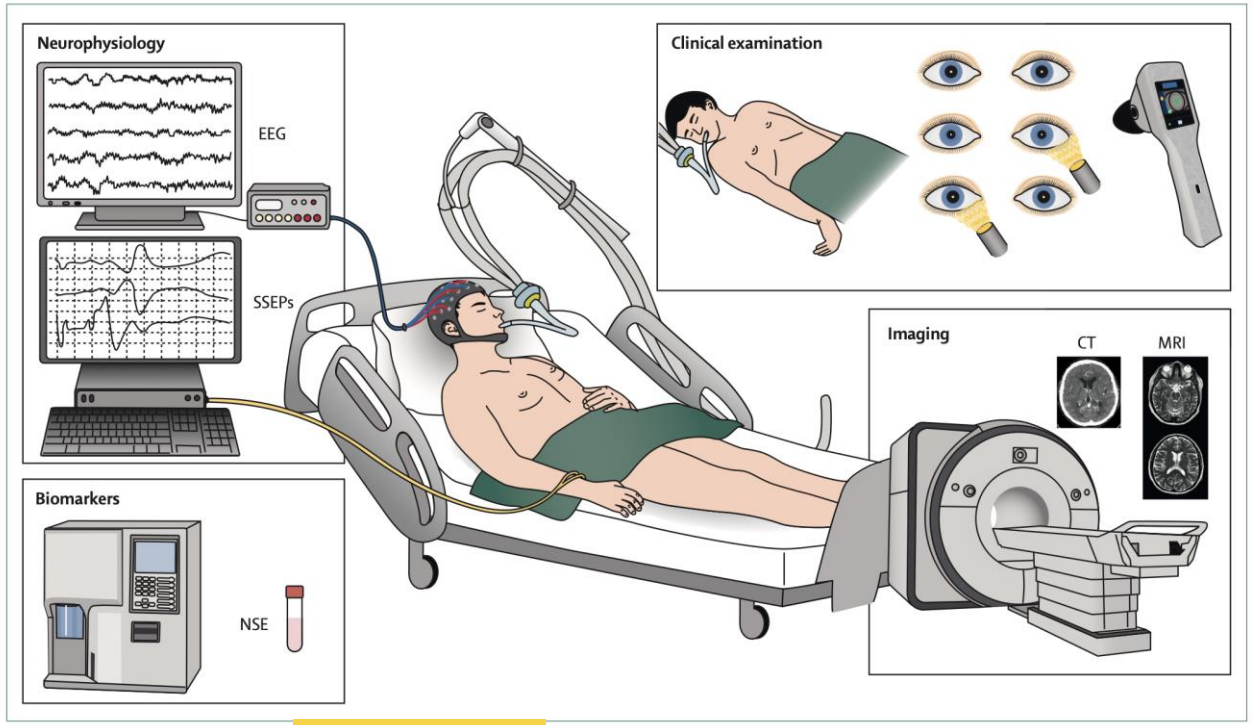
At least TWO of:

- No pupillary[2] and corneal reflexes at ≥72h
- Bilaterally absent N20 SSEP wave
- Highly malignant[3] EEG at >24h
- NSE >60 µg/L[4] at 48h and/or 72h
- Status myoclonus[5] ≤72h
- Diffuse and extensive anoxic injury on brain CT/MRI

YES → Poor outcome likely[*]

NO → Observe and re-evaluate

2 Les outils



3 Les biais cognitifs

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

Perkins GD, …, Nolan JP. Lancet 2021

L'algorithme indispensable !!!

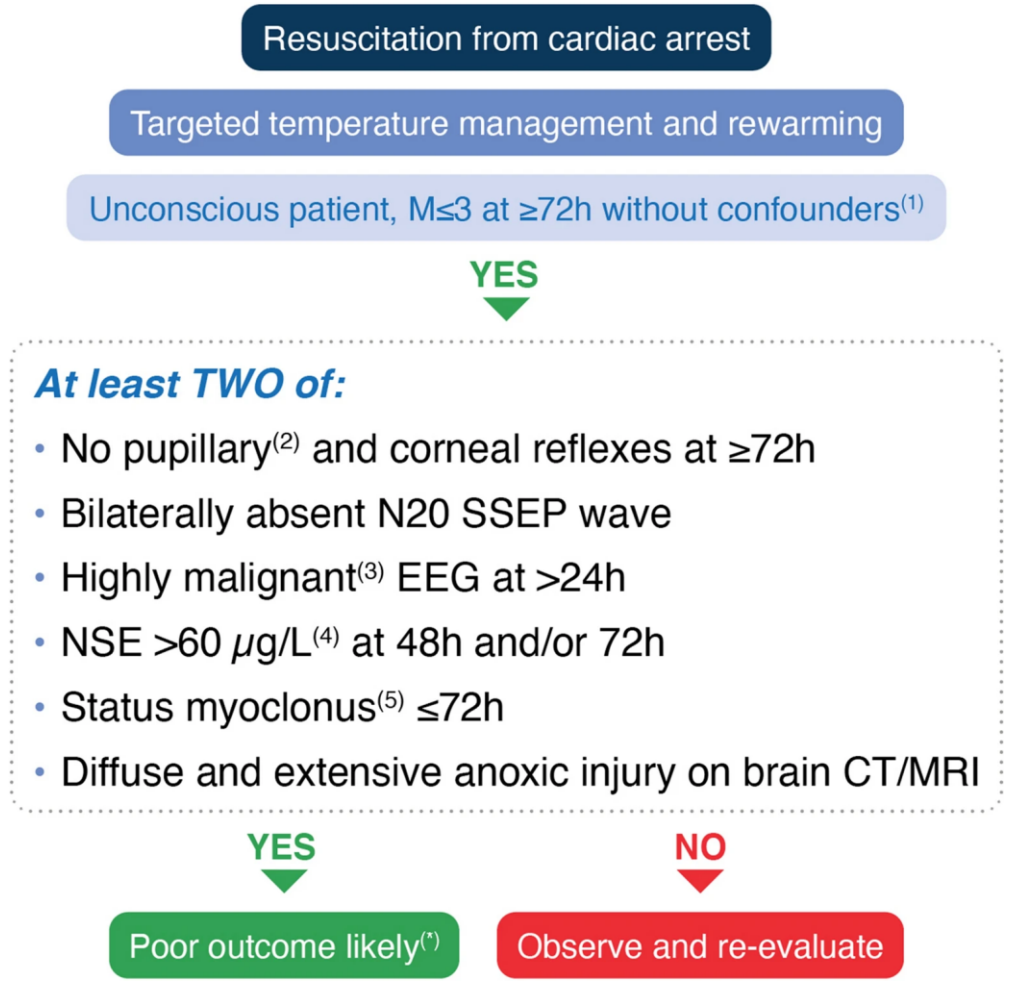


Table 6 Accuracy of clinical examination. Absent corneal reflex (CR)

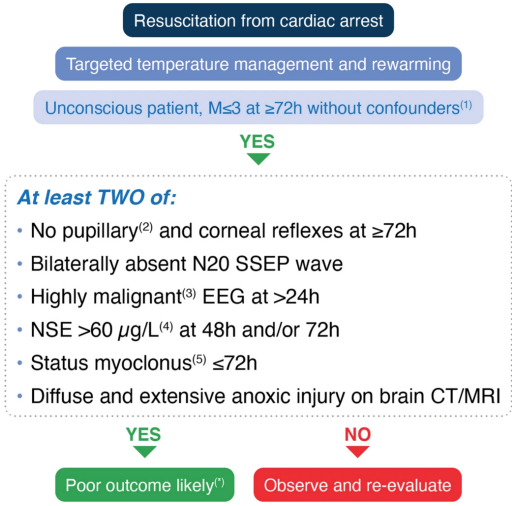
Author, year	Sample size, *n*	Timing	Timing outcome	TP	FP	FN	TN	Sensitivity % [95% CI]	FPR % [95% CI]
At ROSC									
Choi, 2017 [91]	115	At ROSC	HD	81	23	3	8	96.4 [89.9–99.3]	74.2 [55.4–88.1]
Ryoo, 2015 [108]	172	At ROSC	HD	110	27	8	27	93.2 [87.1–97.0]	50 [36.1–63.9]
≤ 24 h									
Matthews, 2018 [29]	137	≤ 24 h	12 mo	52	12	50	23	51.0 [40.9–61]	34.3 [19.1–52.2]
Sivaraju, 2015 [111]	97	≤ 24 h	HD	54	12	14	17	79.4 [67.9–88.3]	41.4 [23.5–61.1]
36–72 h									
Maia, 2013 [104][a]	26	< 72 h	6 mo	8	0	10	8	44.4 [21.5–69.2]	0 [0–31.2]
Dragancea, 2015 [95]	33	< 72 h	6 mo	18	0	11	4	62.1 [42.3–79.3]	0 [0–52.7]
Fatuzzo, 2018 [96]	490	36-48 h	3 mo	117	14	146	213	44.5 [38.4–50.7]	6.2 [3.4–10.1]
Kongpolprom, 2018 [26]	51	48-72 h	HD	14	1	28	8	33.3 [19.6–49.5]	11.1 [0.3–48.2]
Sivaraju, 2015 [111]	83	48-72 h	HD	37	0	18	28	67.3 [53.3–79.3]	0 [0–10.1]
72 h									
Chung-Esaki, 2018 [92]	85	72 h	6 mo	22	0	39	24	36.1 [24.2–49.4]	0 [0–11.7]
Greer, 2013 [22]	104	72 h	6 mo	41	0	43	20	48.8 [37.7–60]	0 [0–13.9]
Matthews, 2018 [29]	137	72 h	12 mo	33	2	69	33	32.4 [23.4–42.3]	5.7 [0.7–19.2]
72–107 h									
Dragancea, 2015 [95]	77	72-107 h	6 mo	26	1	38	12	40.6 [28.5–53.6]	7.7 [0.2–36]
72 h-Day 7									
Kim, 2018 [101]	173	≥ 72 h	1 mo	59	1	33	80	64.1 [53.5–73.9]	1.2 [0–6.7]
Day 4–6									
Dragancea, 2015 [95]	127	Day 5–6	6 mo	32	0	73	22	30.5 [21.9–40.2]	0 [0–12.7]
Matthews, 2018 [29]	137	Day 5	12 mo	28	0	74	35	27.5 [19.1–37.2]	0 [0–8.2]
Day 7									
Greer, 2013 [22]	59	Day 7	6 mo	9	0	30	20	23.1 [11.1–39.3]	0 [0–13.9]
Kongpolprom, 2018 [26]	51	Day 7	HD	17	0	25	9	40.5 [25.6–56.7]	0 [0–28.3]
Matthews, 2018 [29]	137	Day 7	12 mo	26	0	76	35	25.5 [17.4–35.1]	0 [0–8.2]

Répond à bcp de situations !

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

L'examen clinique



BRITISH MEDICAL JOURNAL 17 AUGUST 1974

Relation of Neurological Findings after Cardiac Arrest to Outcome

JOHN O. WILLOUGHBY, BRIAN G. LEACH

British Medical Journal, 1974, 3, 437-439

diac arrest and to relate these to outcome. The results sug-
gest that early neurological assessment is of great predictive

Summary

Routine neurolog
cardiac arrest se
nosis for life an
In 48 patients
by serial neurol
into two groups
after cardiac arr
or at most respo
at one hour; thes
damage. Patients
hour and survi
patients common
a variety of oth
were seen occasi

Predicting Outcome From Hypoxic-Ischemic Coma

David E. Levy, MD; John J. Caronna, MD; Burton H. Singer, PhD;
Robert H. Lapinski, PhD; Halina Frydman, PhD; Fred Plum, MD

• **Outcome from coma caused by cerebral hypoxia-ischemia (eg, cardiac arrest) was compared with serial neurological findings in 210 patients. Thirteen percent of patients regained independent function at some point during the first postarrest year. Computer application of new multivariate techniques to the prospectively observed findings generated easily utilized rules that classified patients by likely outcome. At the time of initial examination, 52 patients (one fourth of the total population) had absent pupillary light reflexes, and none of these patients ever regained independent daily function. By contrast, the initial presence of pupillary light reflexes, the development of spontaneous eye movements that were roving conjugate or better, and the findings of extensor, flexor, or withdrawal responses to pain identified a smaller group of 27 patients, 11 (41%) of whom regained independence in their daily lives. By 24 hours after onset, 93 poor-outcome patients were identified by motor responses that were absent, extensor, or flexor and by spontaneous eye movements that were neither orienting nor roving conjugate; only one regained independent function. This contrasts with recovery in 19 (63%) of 30 patients who at that time showed improvement in their eye-opening responses and obeyed commands or had motor responses that were withdrawal or localizing. Similarly simple rules distinguished between good- and poor-prognosis patients on postarrest days 3, 7, and 14.**

(*JAMA* 1985;253:1420-1426)

METHODS

Patient Evaluation

The analysis was performed on 210 patients with cerebral hypoxia-ischemia, drawn from a larger group of 500 subjects with nontraumatic coma.[1,2] The operational definition of coma was that patients failed to open their eyes either spontaneously or in response to noise, that they expressed no comprehensible words, and that they neither obeyed commands nor moved their extremities appropriately to localize or resist painful stimuli. At predetermined intervals (the initial examination and 0 to 1, 2 to 3, 4 to 7, and 8 to 14 days after the onset of coma), patients underwent focused neurological examinations.[1,3] More than half (115, or 55%) were first examined by the investigators within six hours, 176 (84%) within 12 hours, and 200 (95%) within the first day. When information was available from several examinations, the best response in a given interval was used for analysis. To concentrate on patients in whom prognosis was

Resuscitation xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Commentary and concepts

From clinical judgment to odds: A history of prognostication in anoxic coma☆

Eelco F.M. Wijdicks*

Division of Critical Care Neurology, Mayo Clinic, Rochester, MN 55905, United States

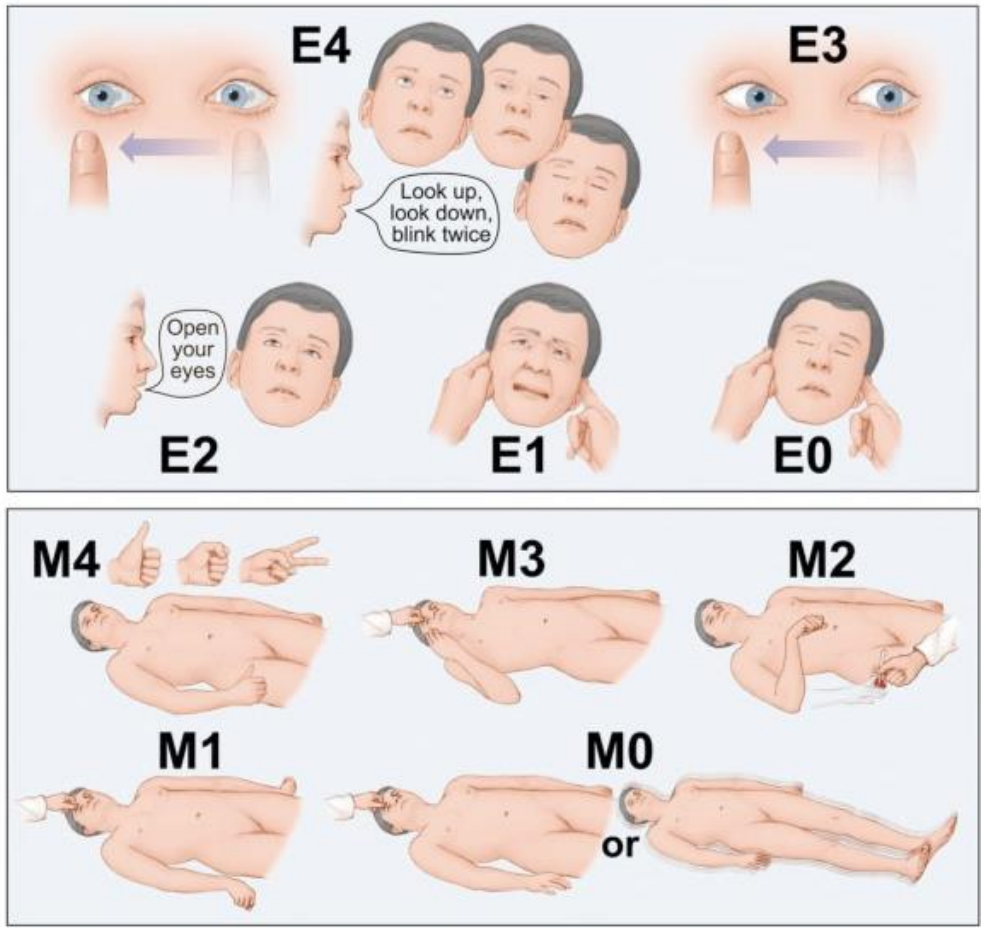
A 72h ou au-delà:

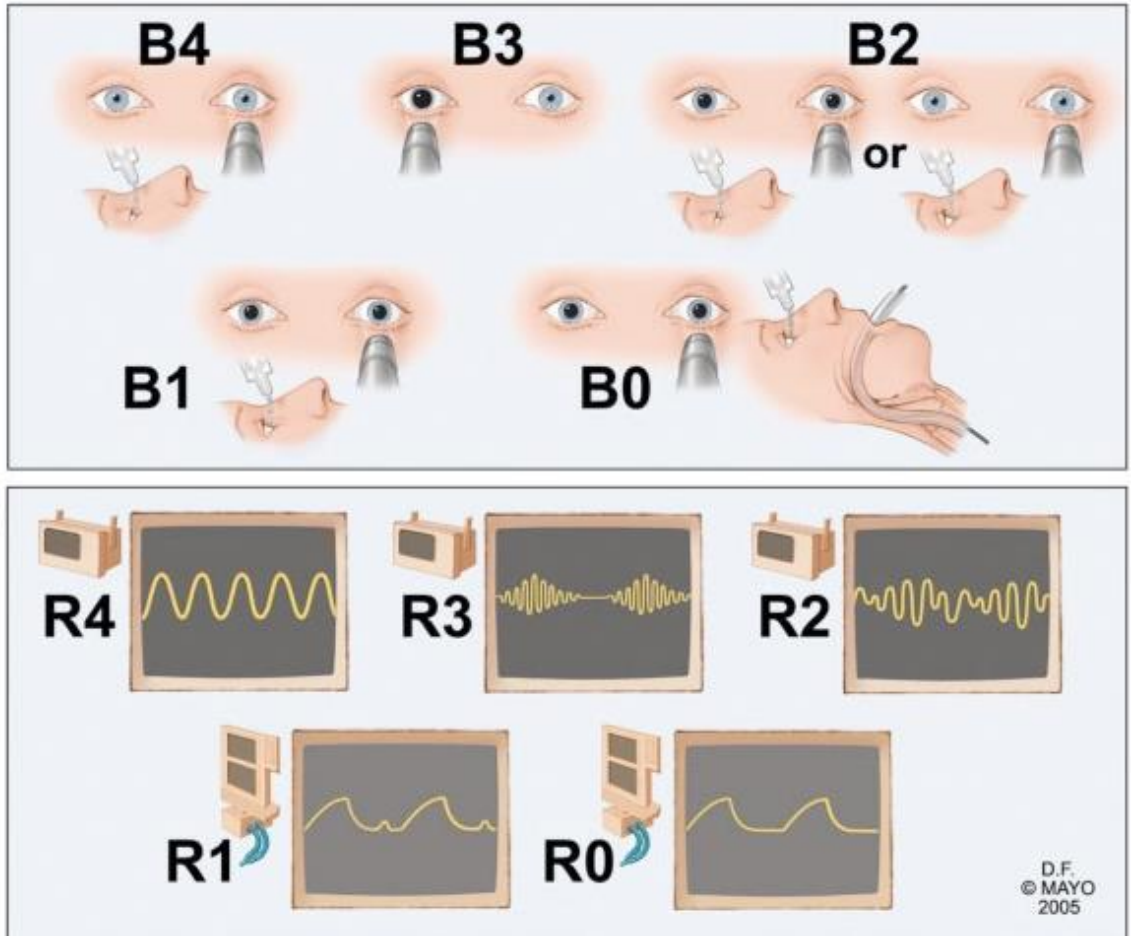
- **Absence de réflexe pupillaire**
- **Absence de réflexe cornéen**

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

The Full Outline of UnResponsiveness (FOUR) Score





Wijdick EFM et al. Annals of Neurology. 2005
Weiss N, et al. Revue Neurol. 2009 & 2015

L'électrophysiologie, EEG

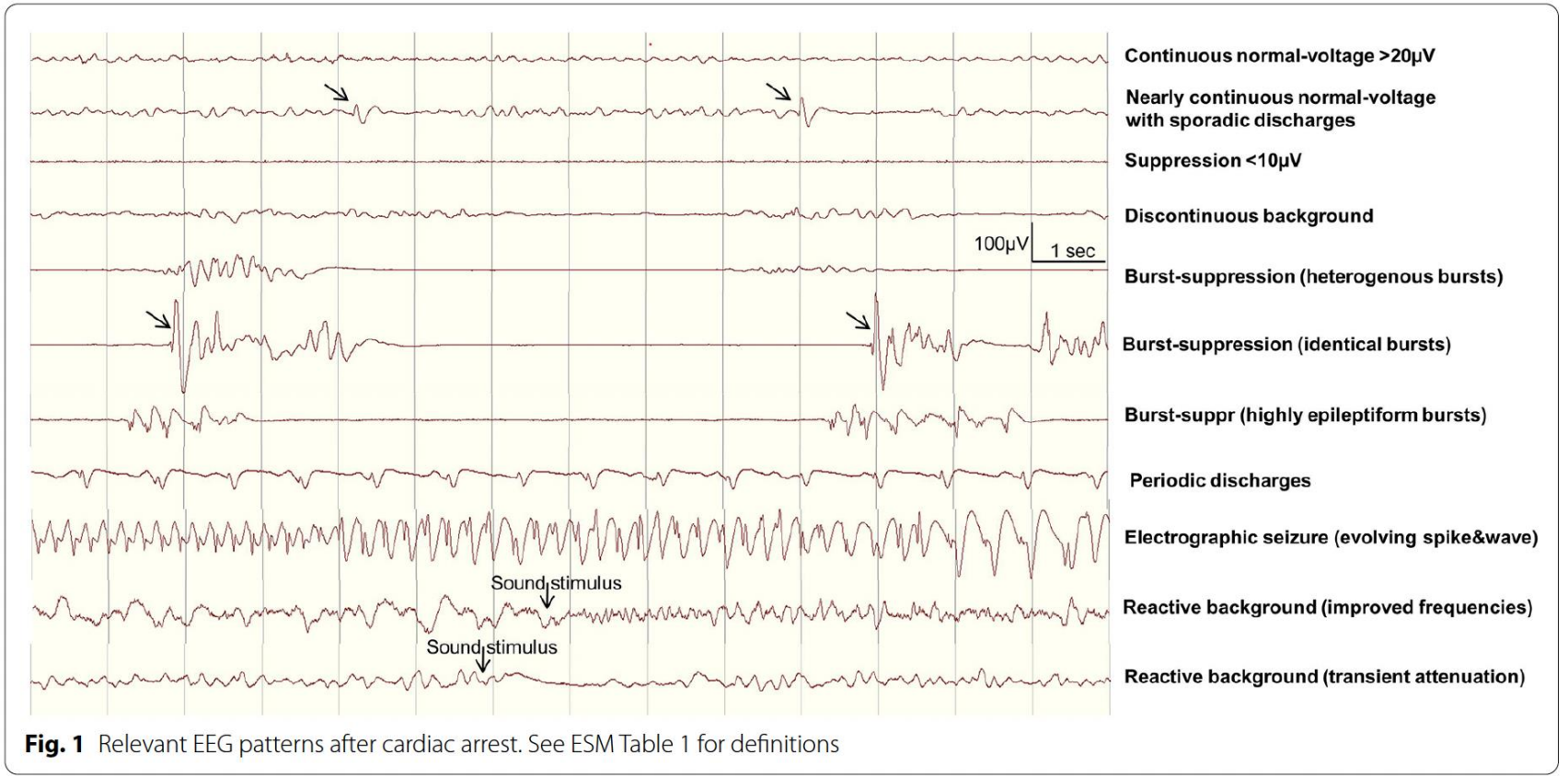
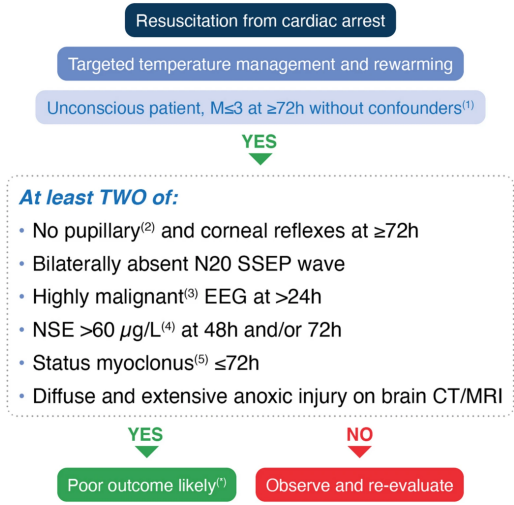


Fig. 1 Relevant EEG patterns after cardiac arrest. See ESM Table 1 for definitions



SANTÉ SORBONNE UNIVERSITÉ

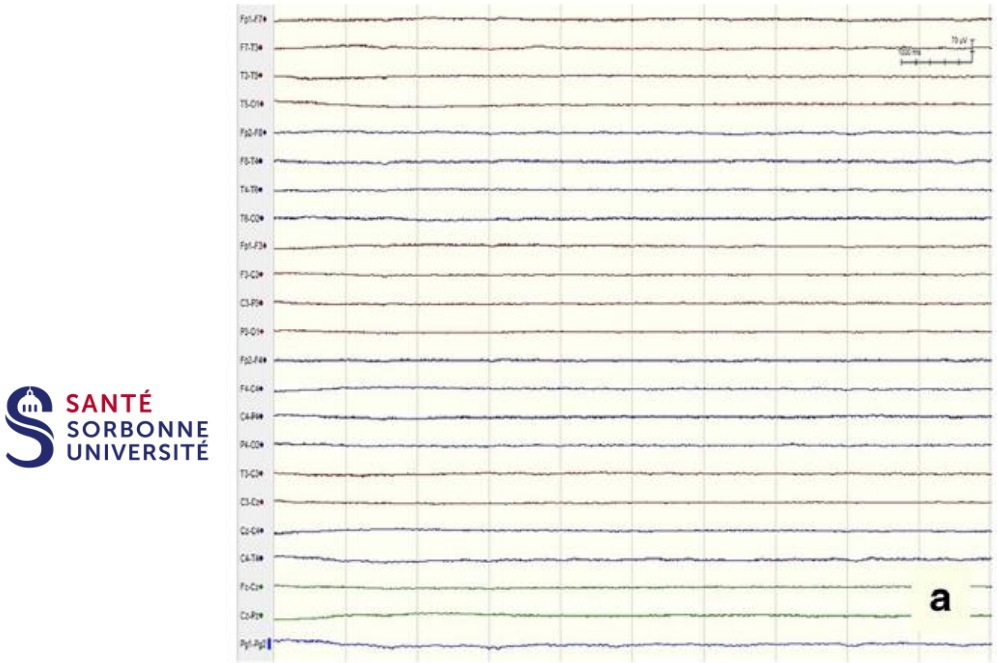
Sandroni, Cronberg et Sekhon. Int Care Med 2021

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

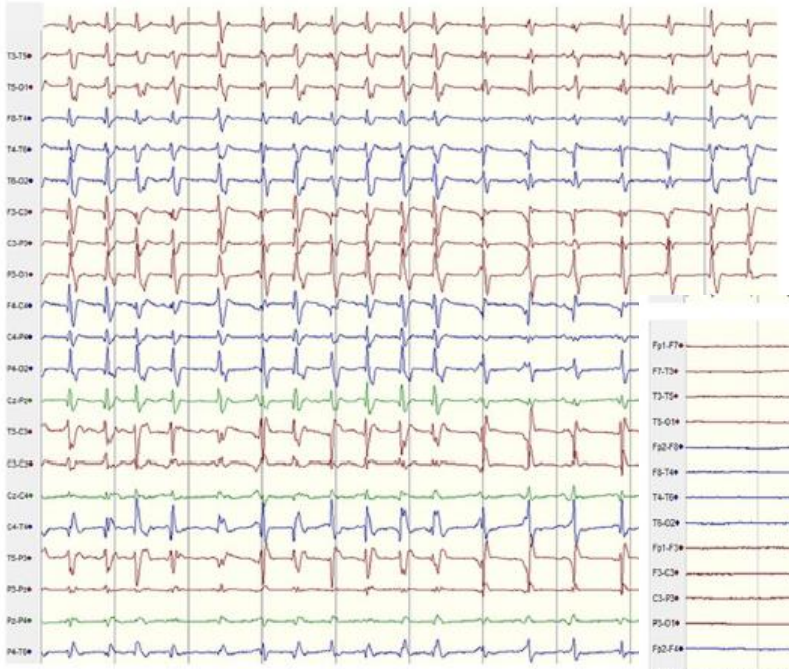
Sandroni, Cronberg et Sekhon. Int Care Med 2022

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

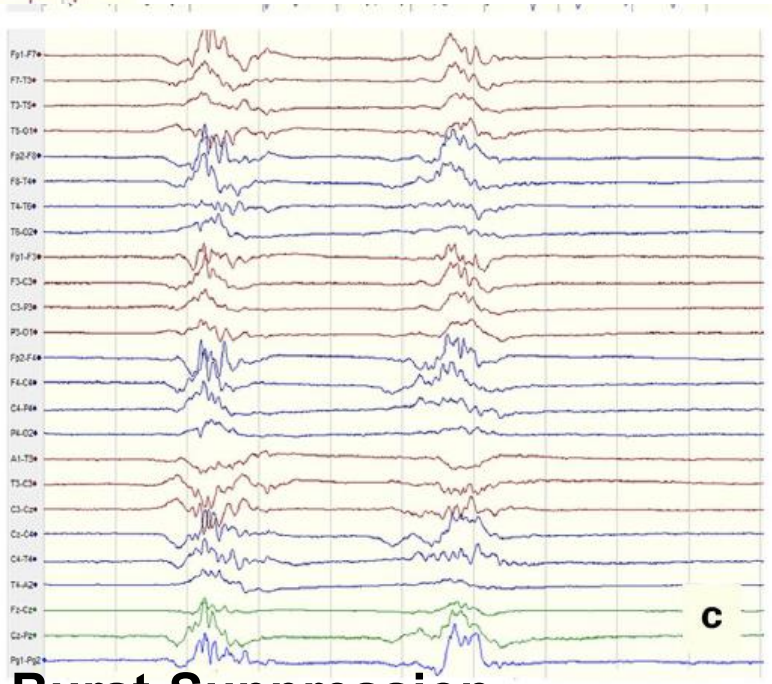
L'électrophysiologie, EEG



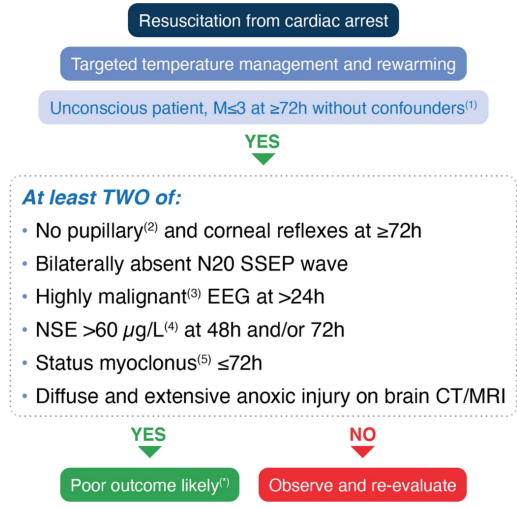
Suppression sans éléments critiques



Suppression avec décharges continues



Burst-Suppression



Tracés hautement malins

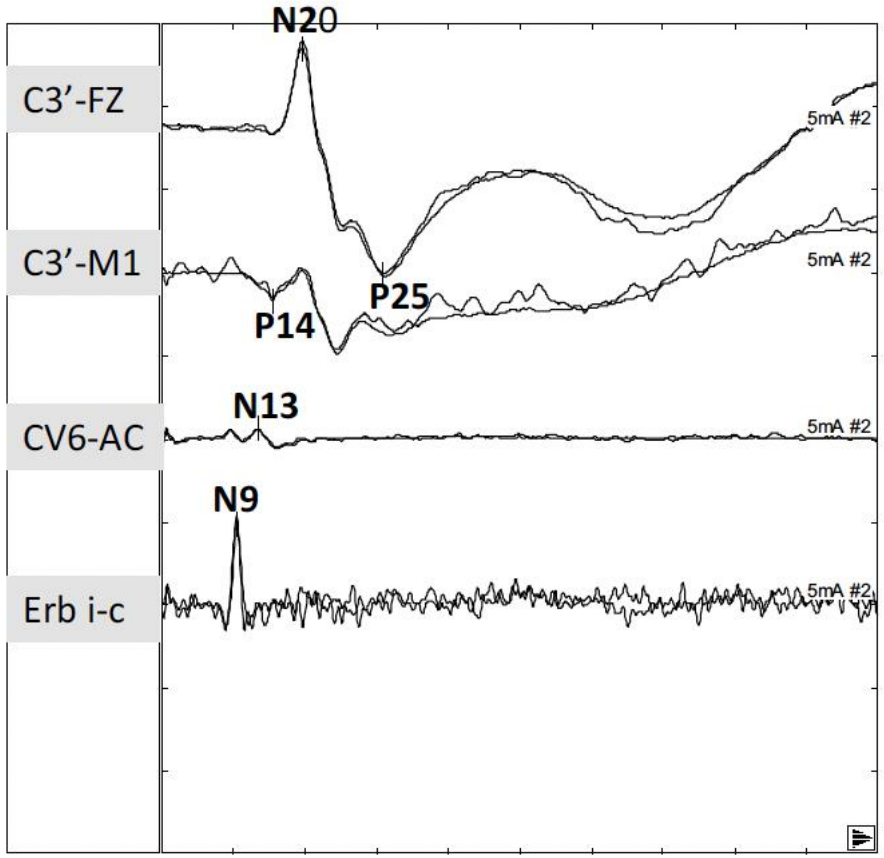
Sandroni, Cronberg et Sekhon. Int Care Med 2021

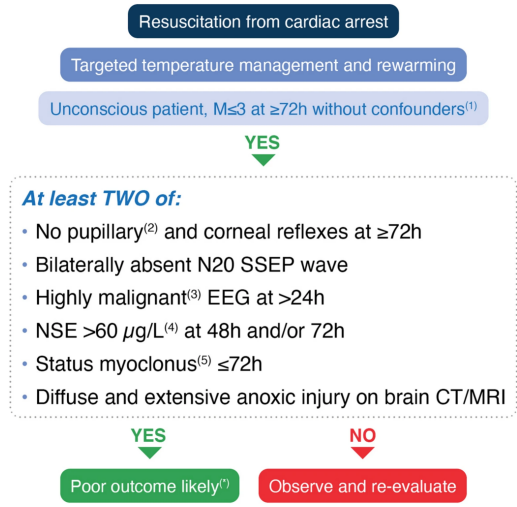
Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

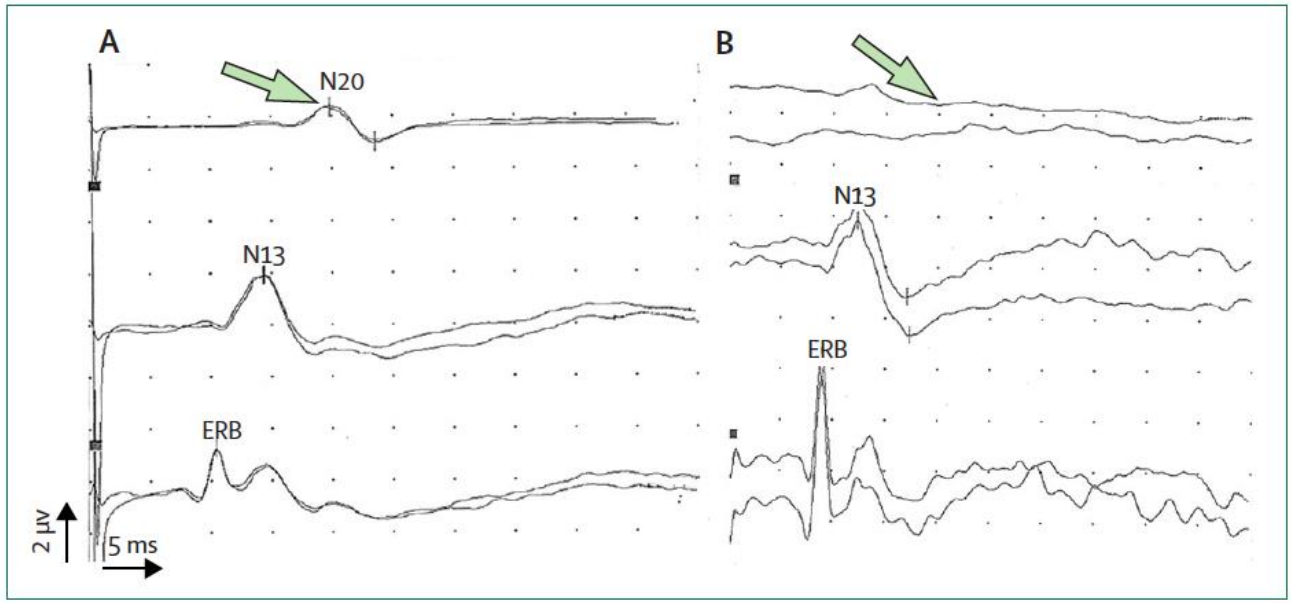
Sandroni, Cronberg et Sekhon. Int Care Med 2022

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

L'électrophysiologie, potentiels évoqués







Absence d'ondes N20

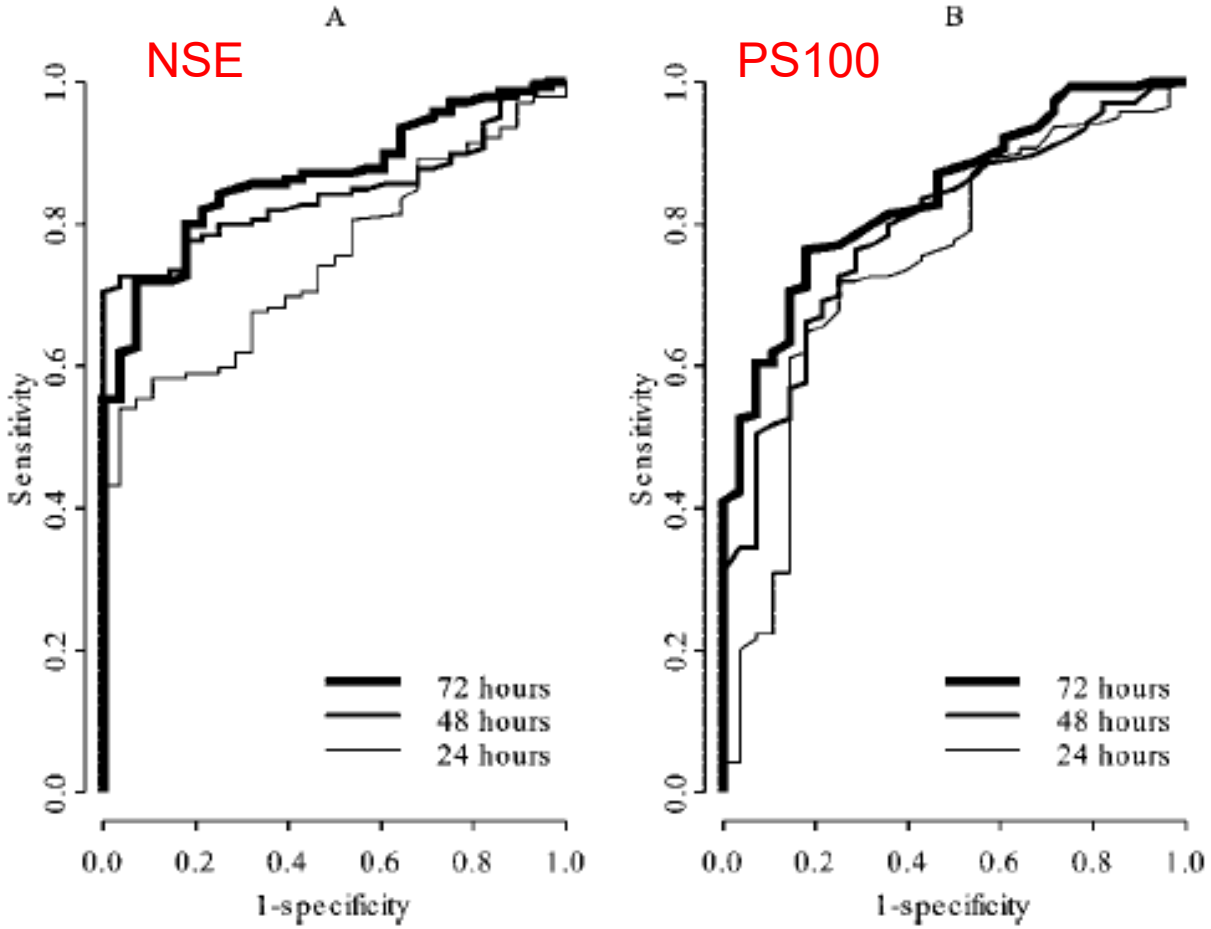
Sandroni, Cronberg et Sekhon. Int Care Med 2021

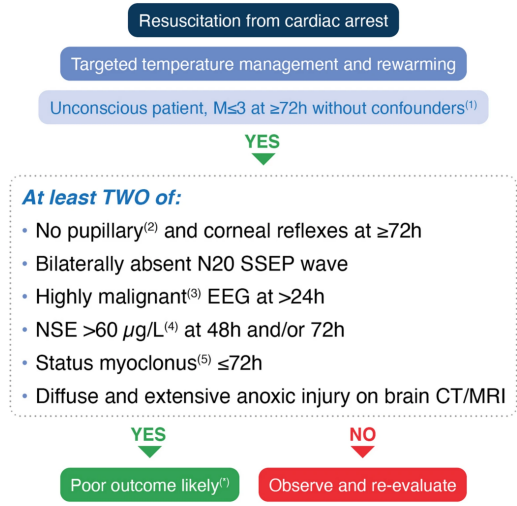
Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

Rossetti, Rabinstein and Oddo, Lancet Neurol 2016

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

Les biomarqueurs, NSE





NSE > 60µg/L à 48 et/ou 72h

Zandbergen at al, Neurology 2006;

Martens et al, Stroke 1998;

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

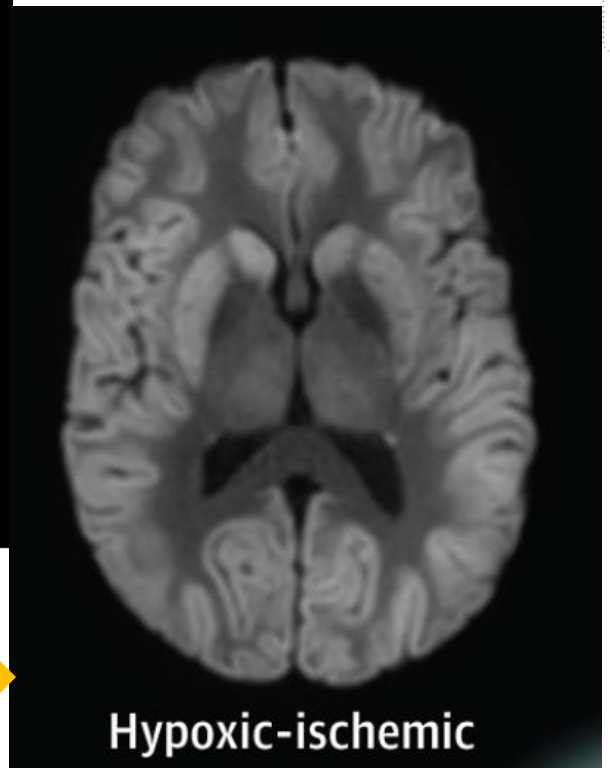
Hachimi-Idrissi et al, Resuscitation 2002;

Wijdicks et al, Neurology 2006

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

L’imagerie

Scanner cérébral



IRM cérébrale

Resuscitation from cardiac arrest

Targeted temperature management and rewarming

Unconscious patient, M≤3 at ≥72h without confounders[1]

YES

At least TWO of:

- No pupillary[2] and corneal reflexes at ≥72h
- Bilaterally absent N20 SSEP wave
- Highly malignant[3] EEG at >24h
- NSE >60 µg/L[4] at 48h and/or 72h
- Status myoclonus[5] ≤72h
- Diffuse and extensive anoxic injury on brain CT/MRI

YES → Poor outcome likely[*]

NO → Observe and re-evaluate

Sandroni, Cronberg et Sekhon. Int Care Med 2021

Nolan JP, et al. ERC and ESICM guidelines. ICM. 2021

Fischer D, Edlow B. JAMA Neurol 2024

Sandroni C, et al. ERC and ESICM guidelines ICM. 2020

Les nouveautés dans les outils !
Explorer la zone grise

Examen clinique

Biomarqueurs

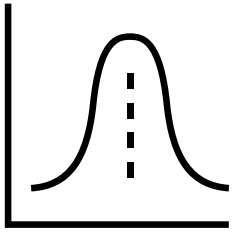
Electrophysiologie

Imagerie

Les outils cliniques

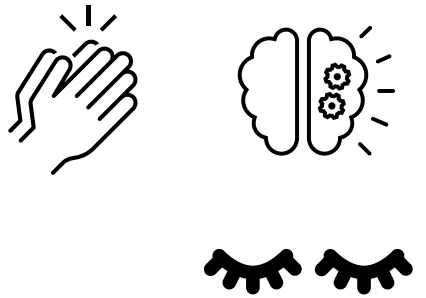
DOC feeling
= « EVA pronostique »

*What is **your gut feeling** about the best level of consciousness of the patient **today;***
« Presence » or « is there anybody home? »

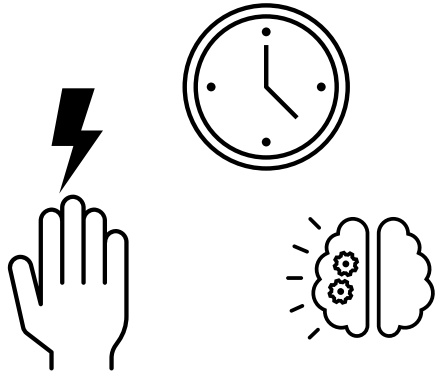


NB: en add-on de la CRS
Giacino et al. 2001

Hermann B*, Goudard G*, Courcoux K*, …
Rohaut B. BMJ Open 2019



Hermann B, et al. *Brain* 2020



Sangare A, et al. Brain Com 2025

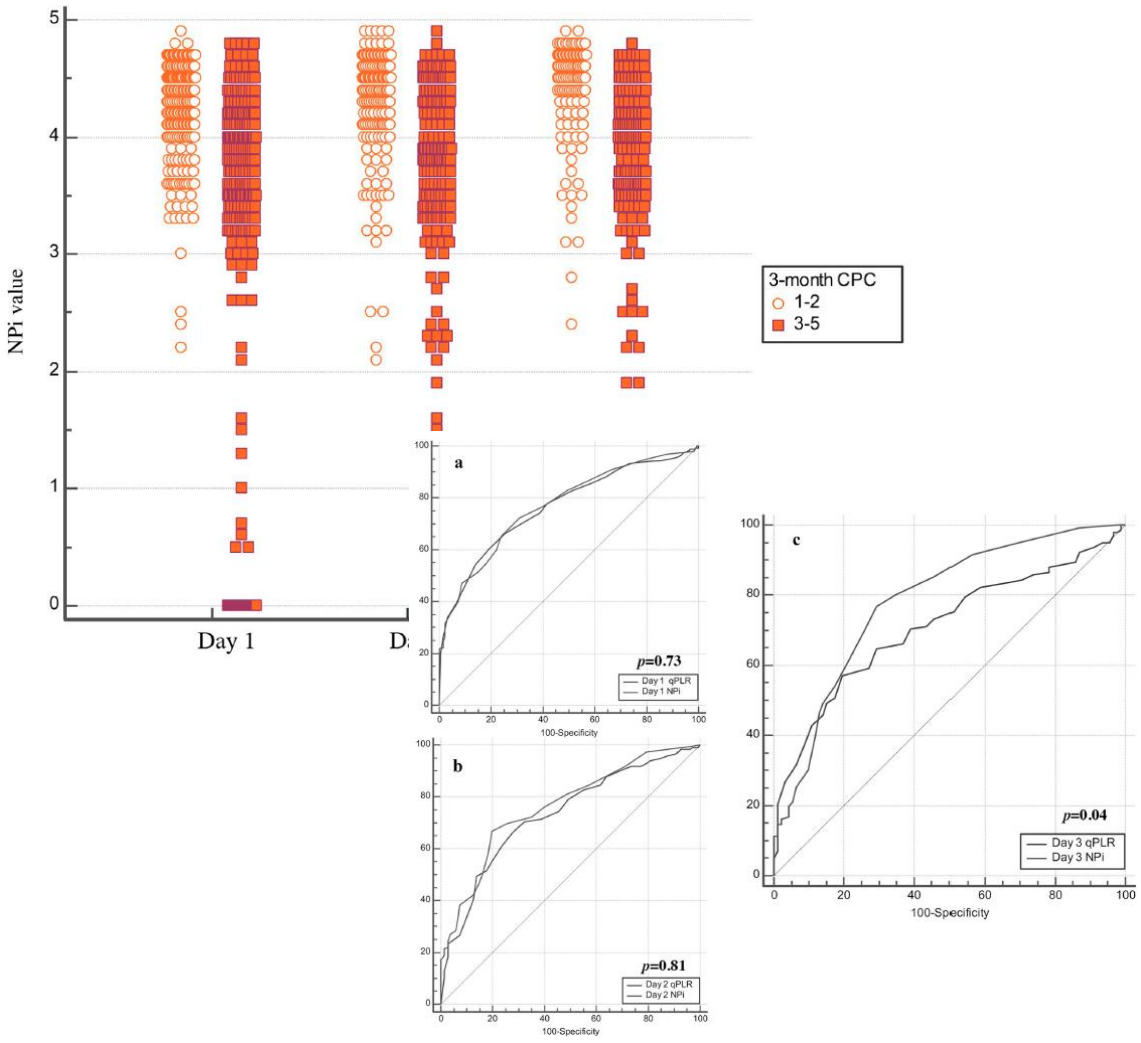
Poursuite oculaire = état de conscience minimale

Utilisez un miroir +++

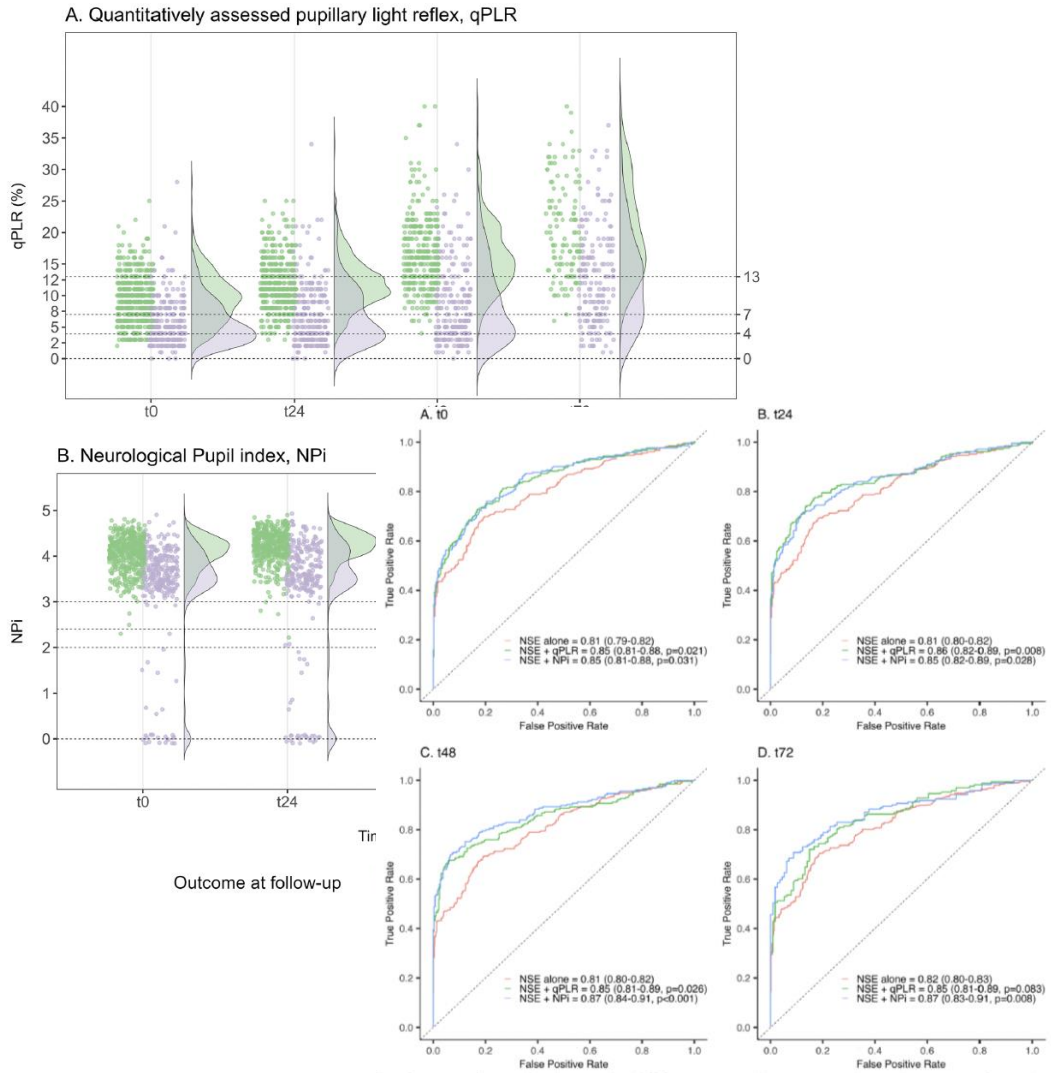
Wannez *et al. Brain Inj* 2017
Thonnard *et al. Brain Inj* 2014
Vanhaudenhuyse *et al. JNNP* 2008

Weiss et al. J Neurol 2012

La pupillométrie

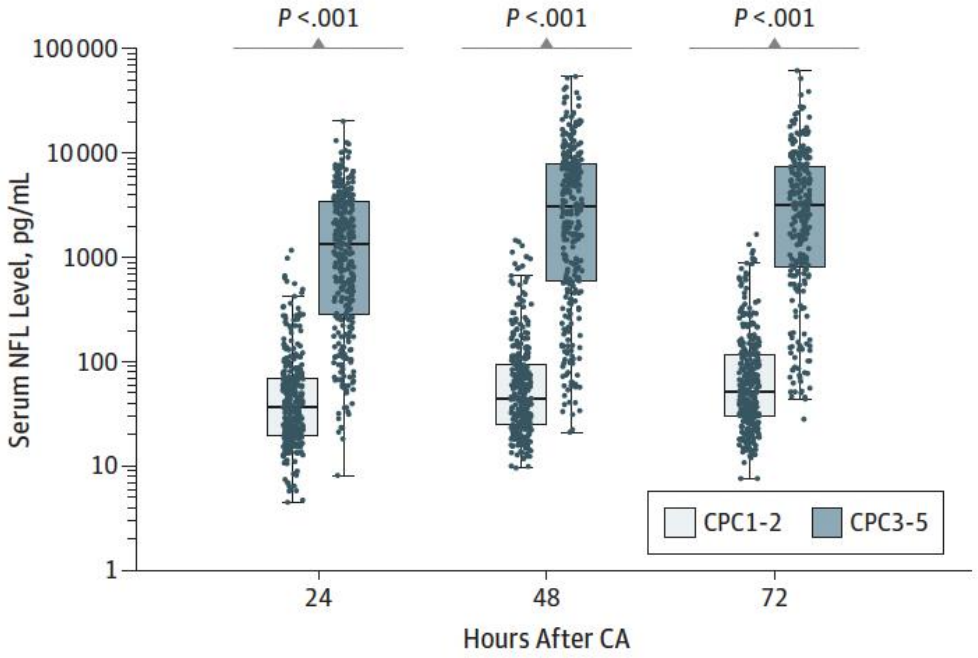


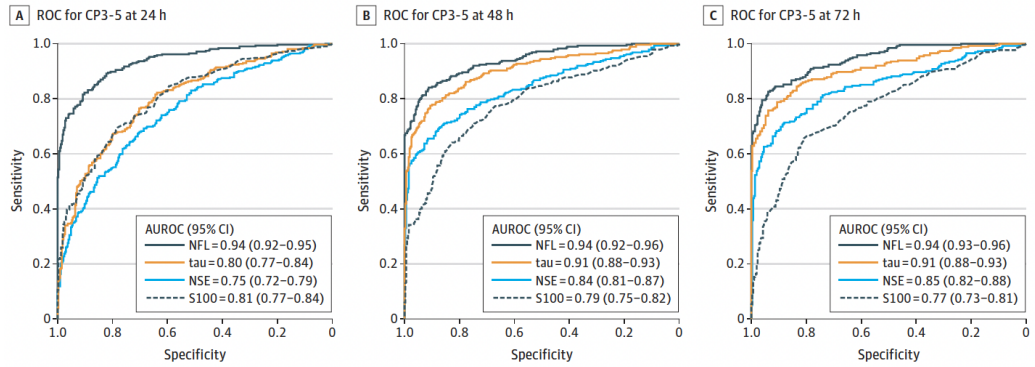
Oddo et al. Int Care Med 2018



Nyholm et al. Int Care Med 2024

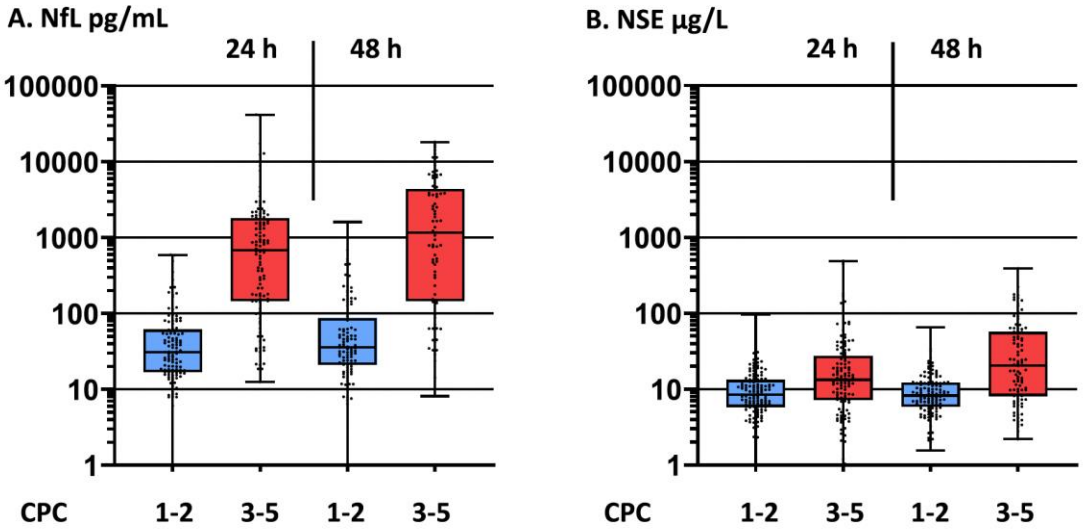
Les neurofilaments light-chain (NFL)





Moseby-Knappe et al. JAMA Neurol 2019

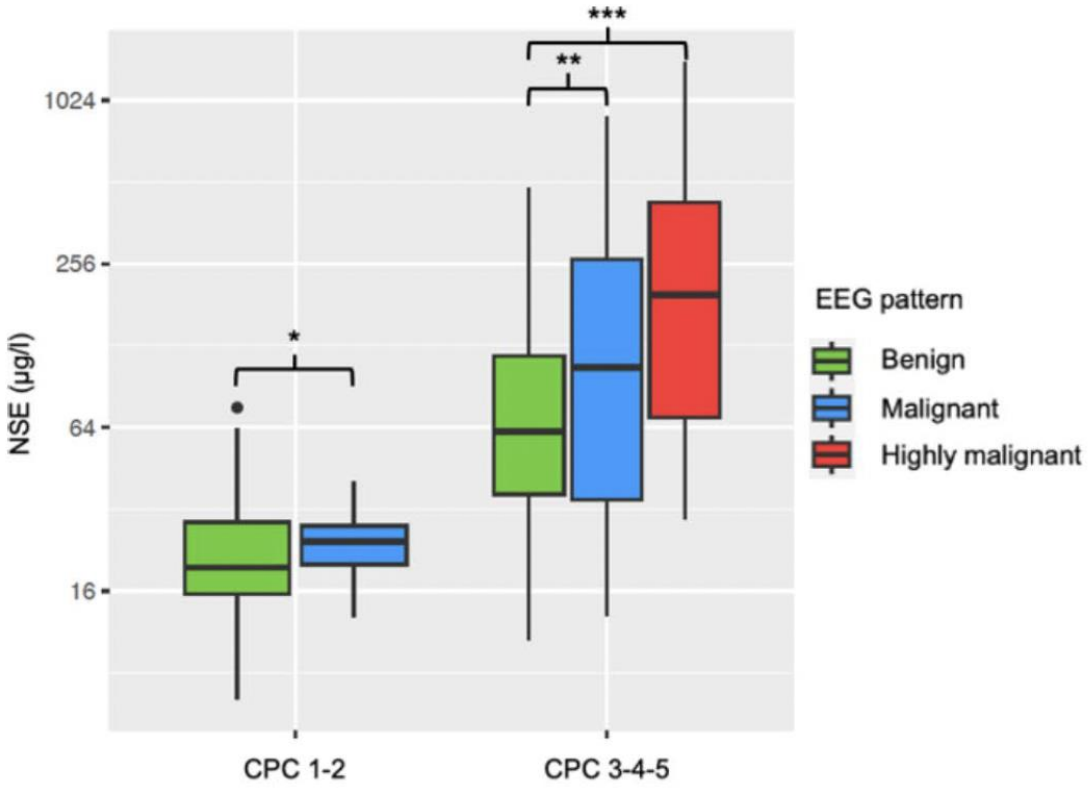
- ✓ **Possiblement > NSE**
- ✓ **Les valeurs se recoupent peu**
- ✓ **De plus en plus de données …**



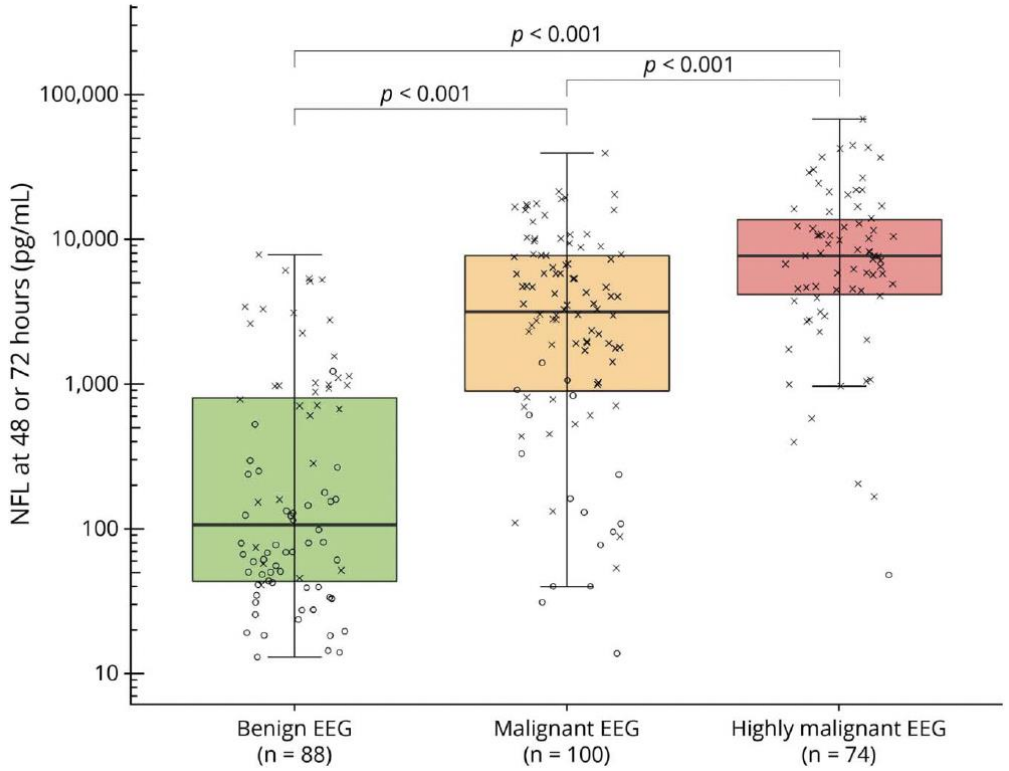
Wihersaari et al. Resuscitation 2022

Les biomarqueurs pondérés par l'EEG

NSE



NFL



Pelle et al. Ann Int Care 2025

Grindegard et al. Neurol 2022

Analyse quantitative des potentiels évoqués somesthésiques

Benghanem et al. Annals of Intensive Care (2022) 12:25
https://doi.org/10.1186/s13613-022-00999-6

Annals of Intensive Care

RESEARCH Open Access

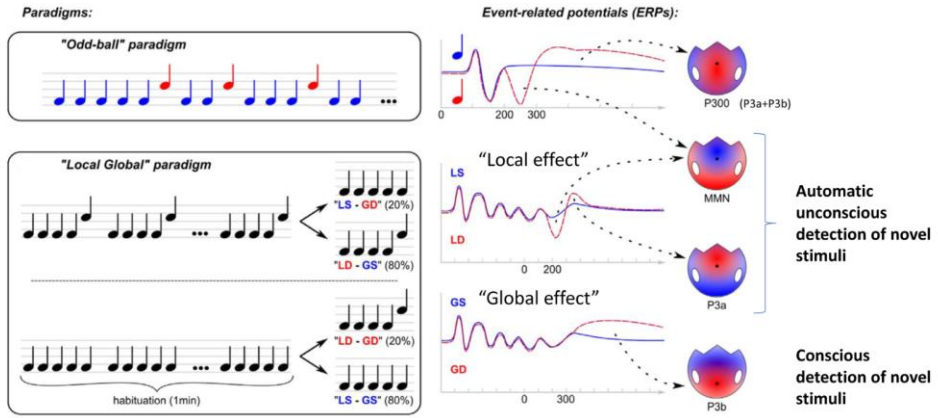
SSEP N20 and P25 amplitudes predict poor and good neurologic outcomes after cardiac arrest

Sarah Benghanem[1,2,5,7*], Lee S. Nguyen[3], Martine Gavaret[2,4,7], Jean-Paul Mira[1,2], Frédéric Pène[1,2], Julien Charpentier[1], Angela Marchi[2,4,7] and Alain Cariou[1,2,5,6]

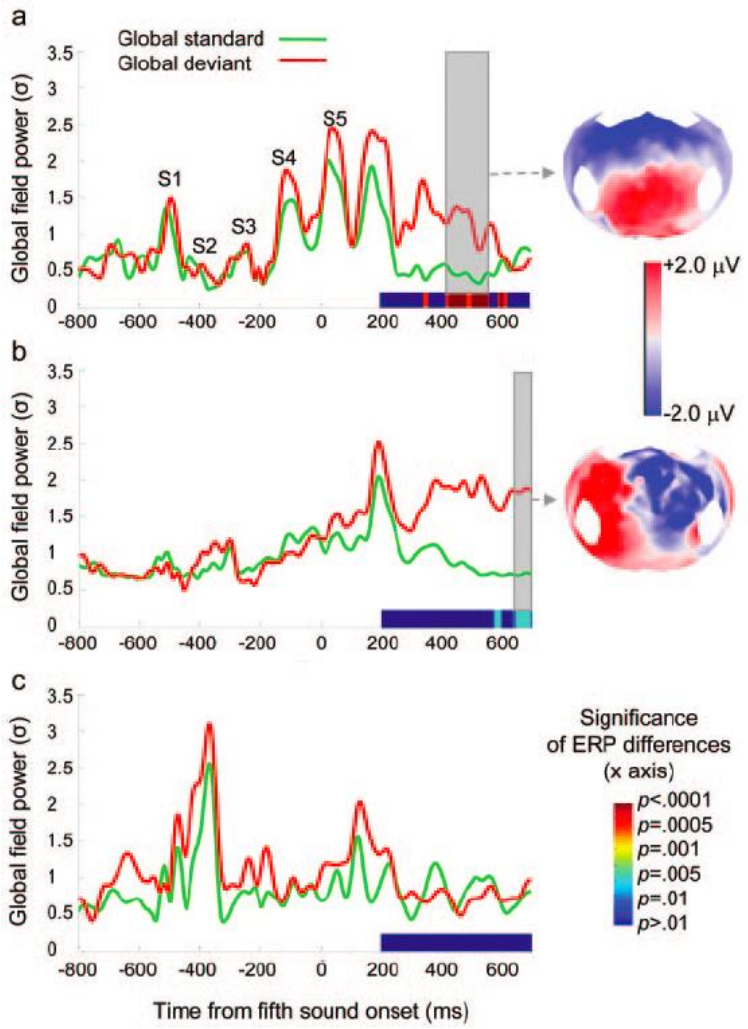
	Se(%)	Sp(%)	FPR(%)
N20-baseline > 2 µV	39 (33–44)	73 (68–78)	27 (22–32)
N20-baseline > 2.7 µV	28 (23–33)	87 (83–91)	13 (9–17)
N20–P25 > 3,2 µV	29 (23–34)	93 (90–96)	7 (4–10)
N20–P25 > 4 µV	14 (10–18)	95 (92–97)	5.4 (3–8)
No status myoclonus	94 (92–97)	56 (51–62)	44 (38–49)
Day 3 NSE peak < 60 µg/ml	93 (90–96)	74.5 (69–80)	25.5 (20–31)
Benign EEG	89 (85–92)	86 (82–90)	14 (10–18)
N20-baseline > 2 µV + benign EEG	33.3 (28–39)	96.9 (95–99)	3.1 (1–5)
N20-baseline > 2 µV + NSE < 60 ng/ml	28 (23–33)	90.6 (87–94)	9.4 (6–13)
N20-baseline > 2 µV + no status myoclonus	33.3 (28–39)	86 (82–90)	14 (10–18)
N20–P25 > 3.2 µV + benign EEG	17 (13–21)	97 (93–98)	3 (2–7)
N20–P25 > 3.2 µV + day 3 NSE < 60 µg/ml	17 (13–21)	98.4 (97–100)	1.6 (0–3)
N20–P25 > 3.2 µV + No status myoclonus	17 (13–21)	95.3 (93–98)	4.7 (2–7)

Benghanem et al. Ann Int Care 2022

Potentiels évoqués cognitifs



Bekinschtein TA, et al. PNAS 2009



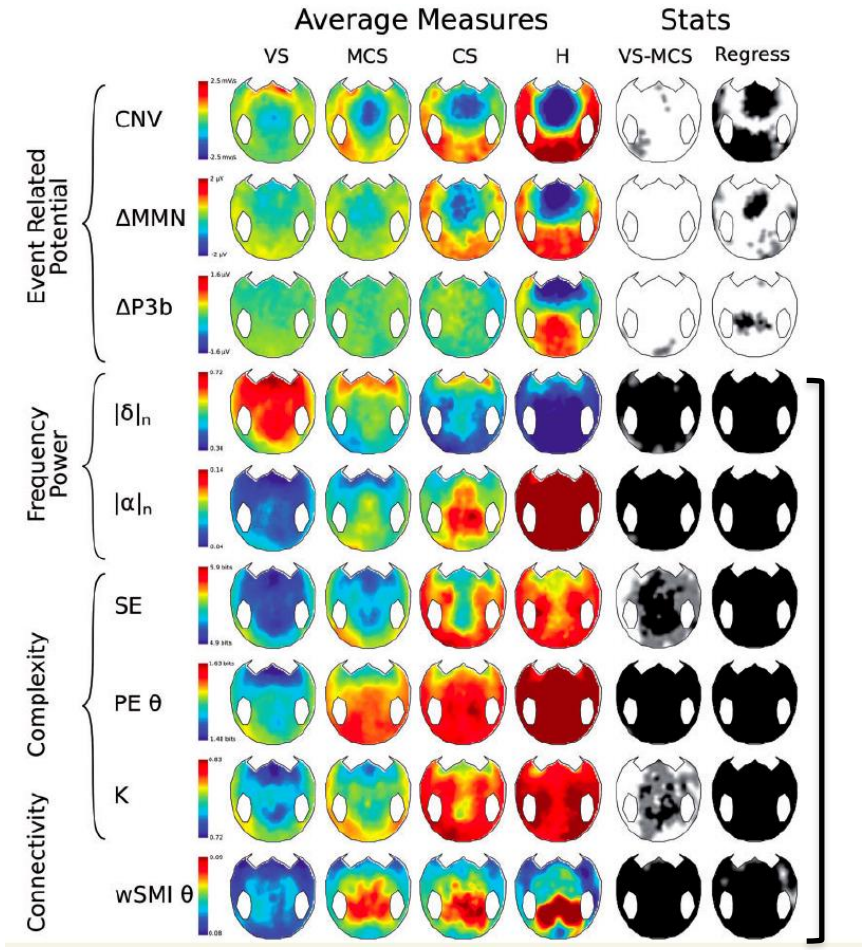
Sujet contrôle

Patient ayant un traitement conscient de l'information (=MCS)

Patient n'ayant pas de traitement conscient de l'information (=VS)

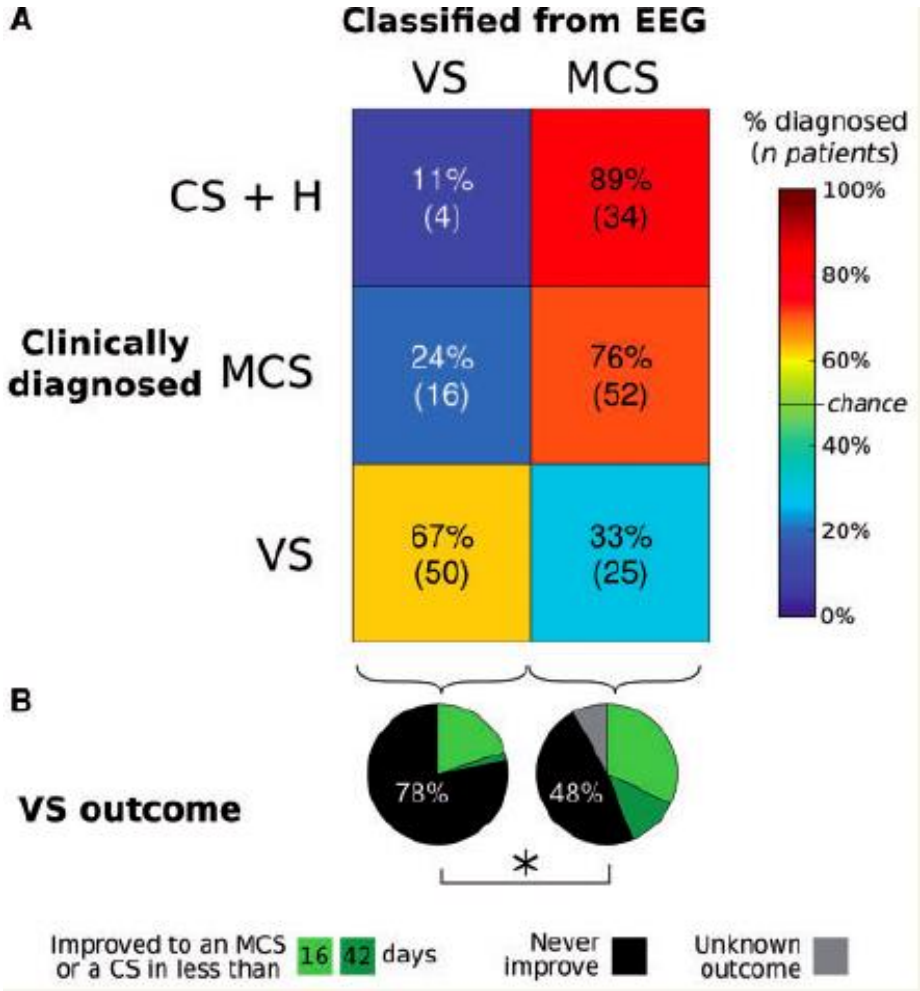
Faugeras, Rohaut et al., Neurology 2011
Faugeras, Rohaut et al., Neuropsychologica 2012
Rohaut, Faugeras et al., Neuropsychologogica 2015

EEG 256 électrodes



EEG 256 électrodes
Analyse de la:

- Fréq. spectrale
- Complexité
- Connectivité

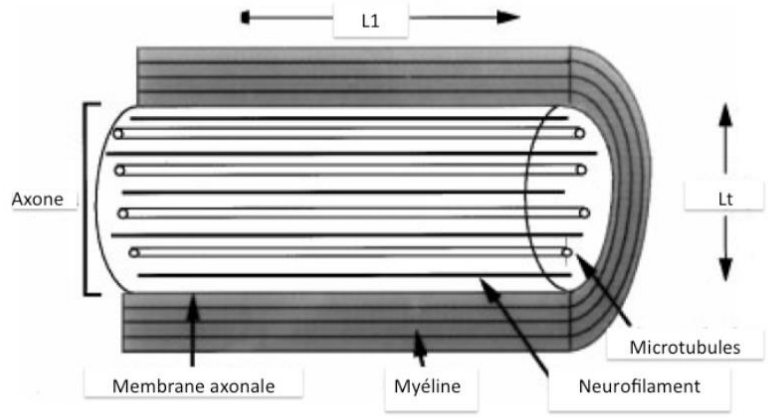


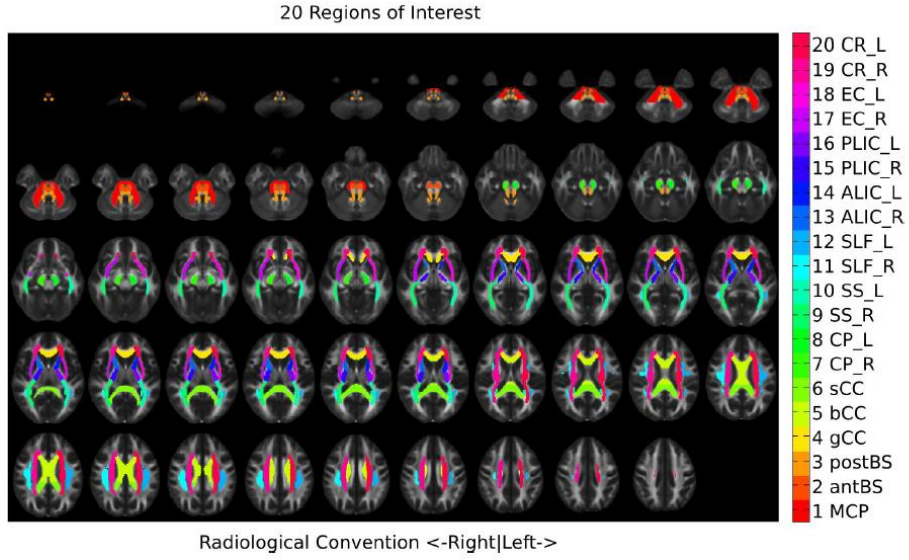
Sitt et al, Brain 2014

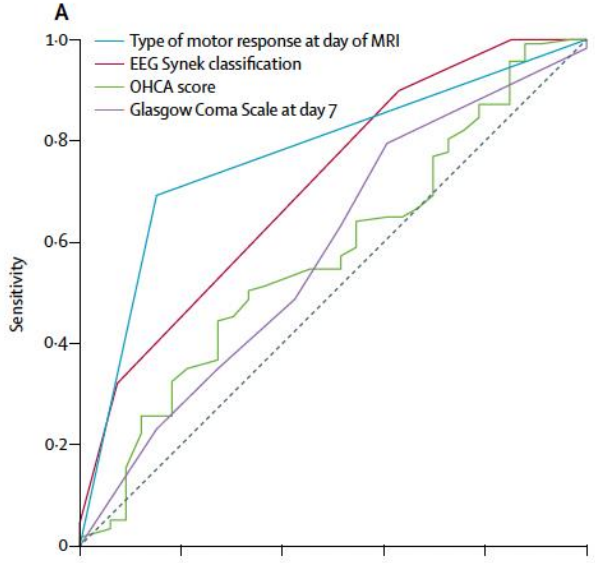
Algorithme de classement automatique par l'EEG

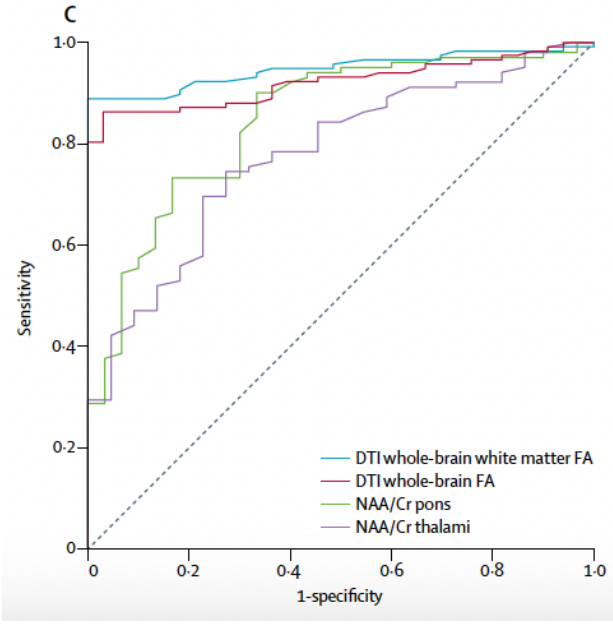
- Bonne corrélation à la clinique
- Excellente corrélation avec le devenir

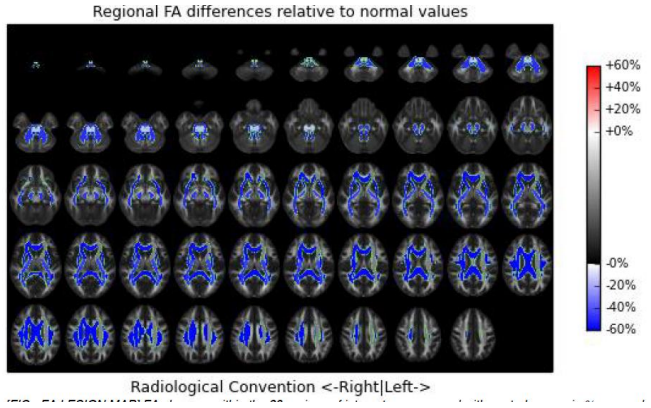
Imagerie IRM avec tenseur de diffusion (DTI)

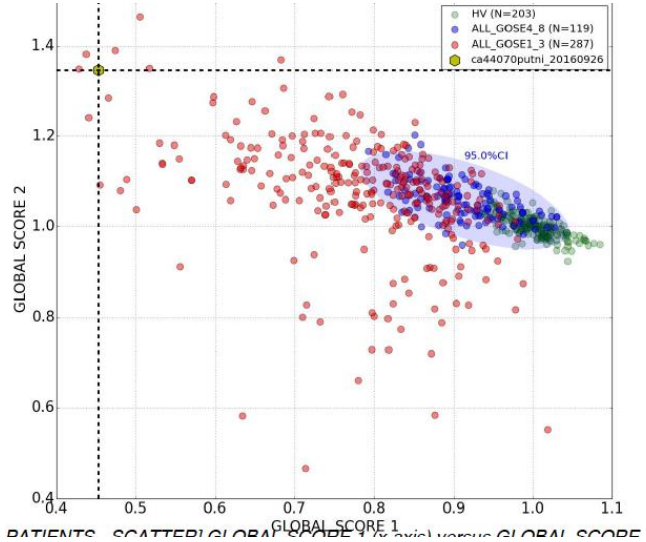




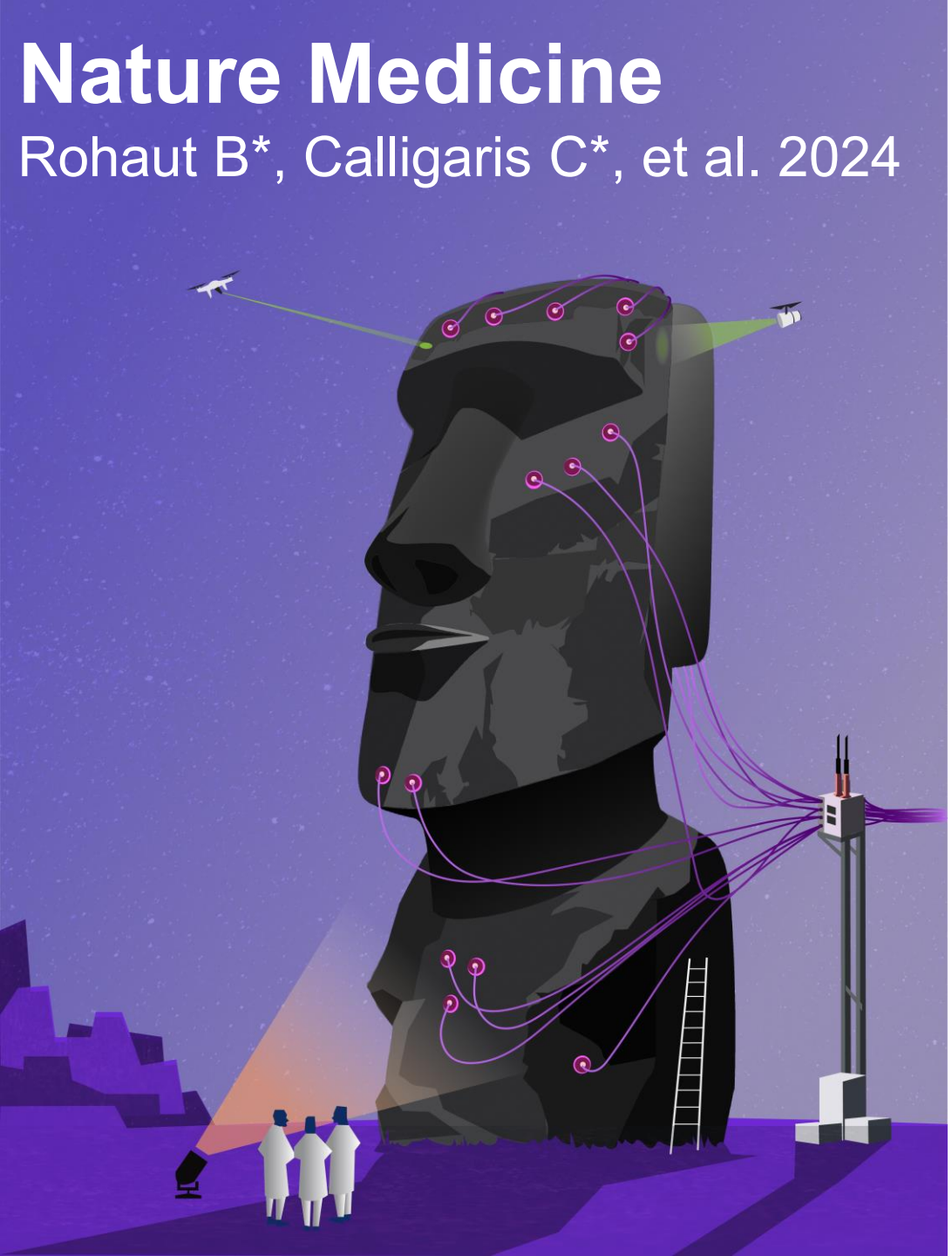








Luyt et al., Anesthesiology 2012
Velly et al. Lancet Neurol 2018
Pr D Galanaud, Pr L Puybasset



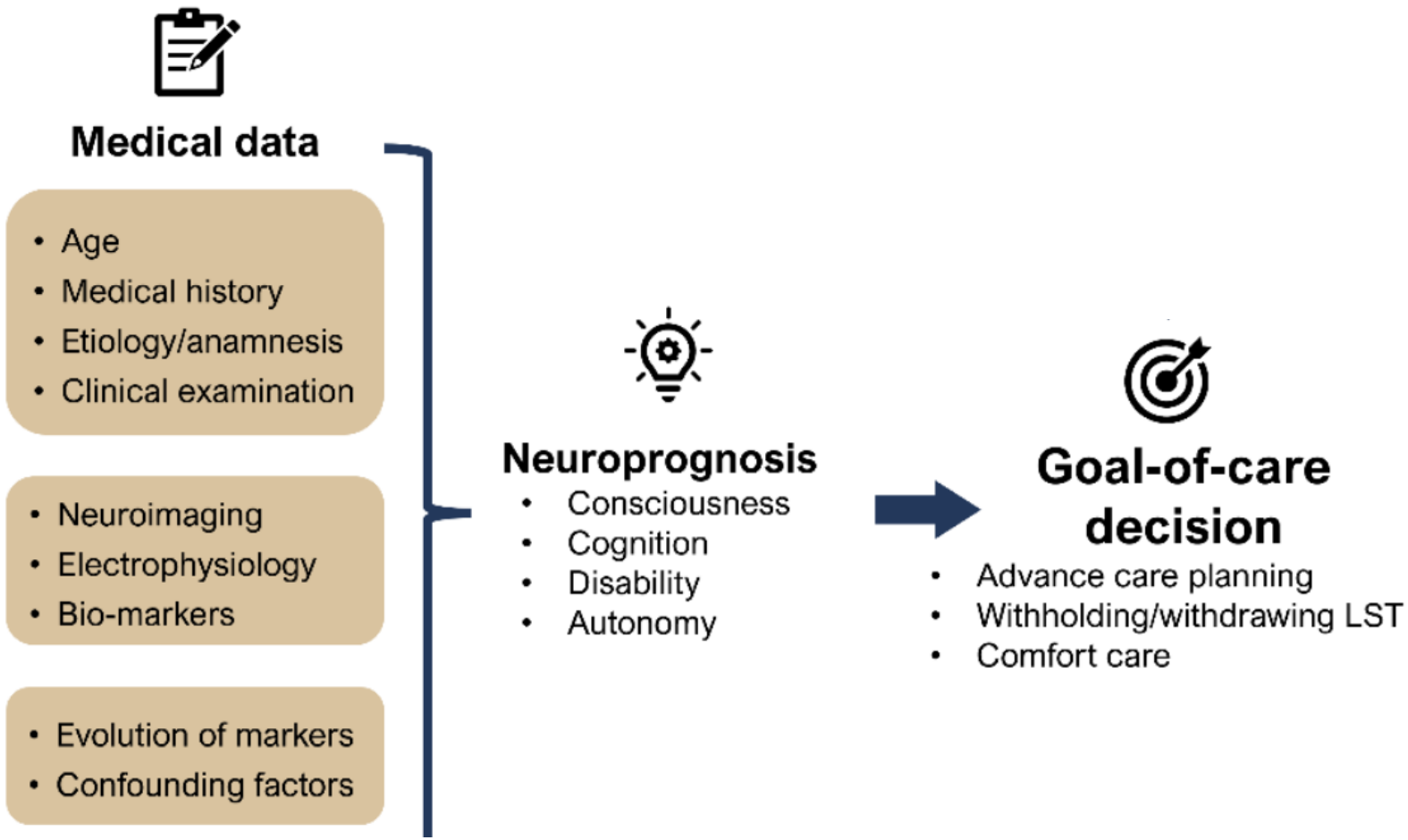
M-Neuro-DoC study

Clinical markers

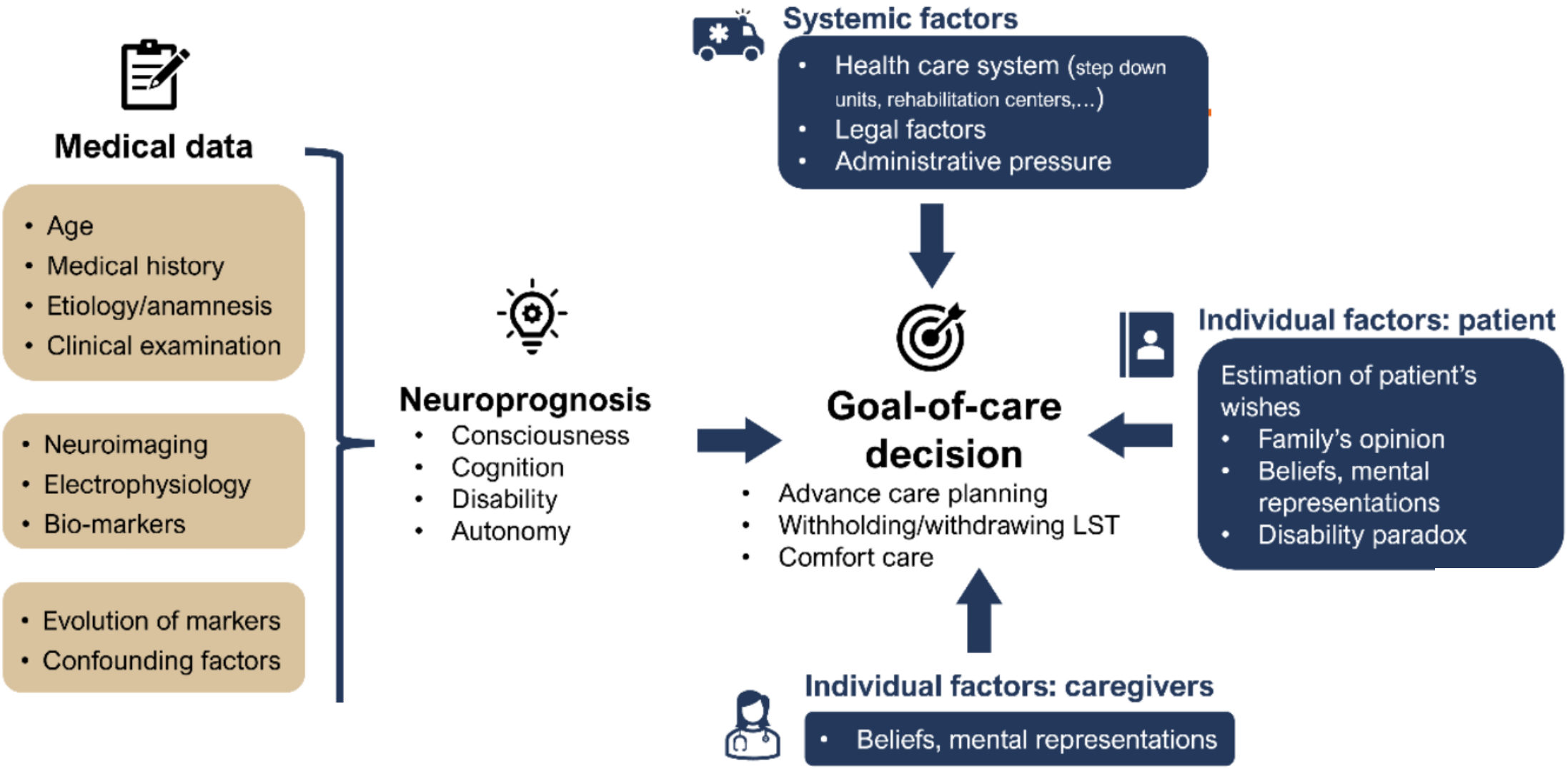
- FOUR-score
- CRS-R (Coma Recovery Scale- Revised)
- DoC-Feeling
- Habituation of auditory startle reflex

Neurophysiology & Neuroimagery markers

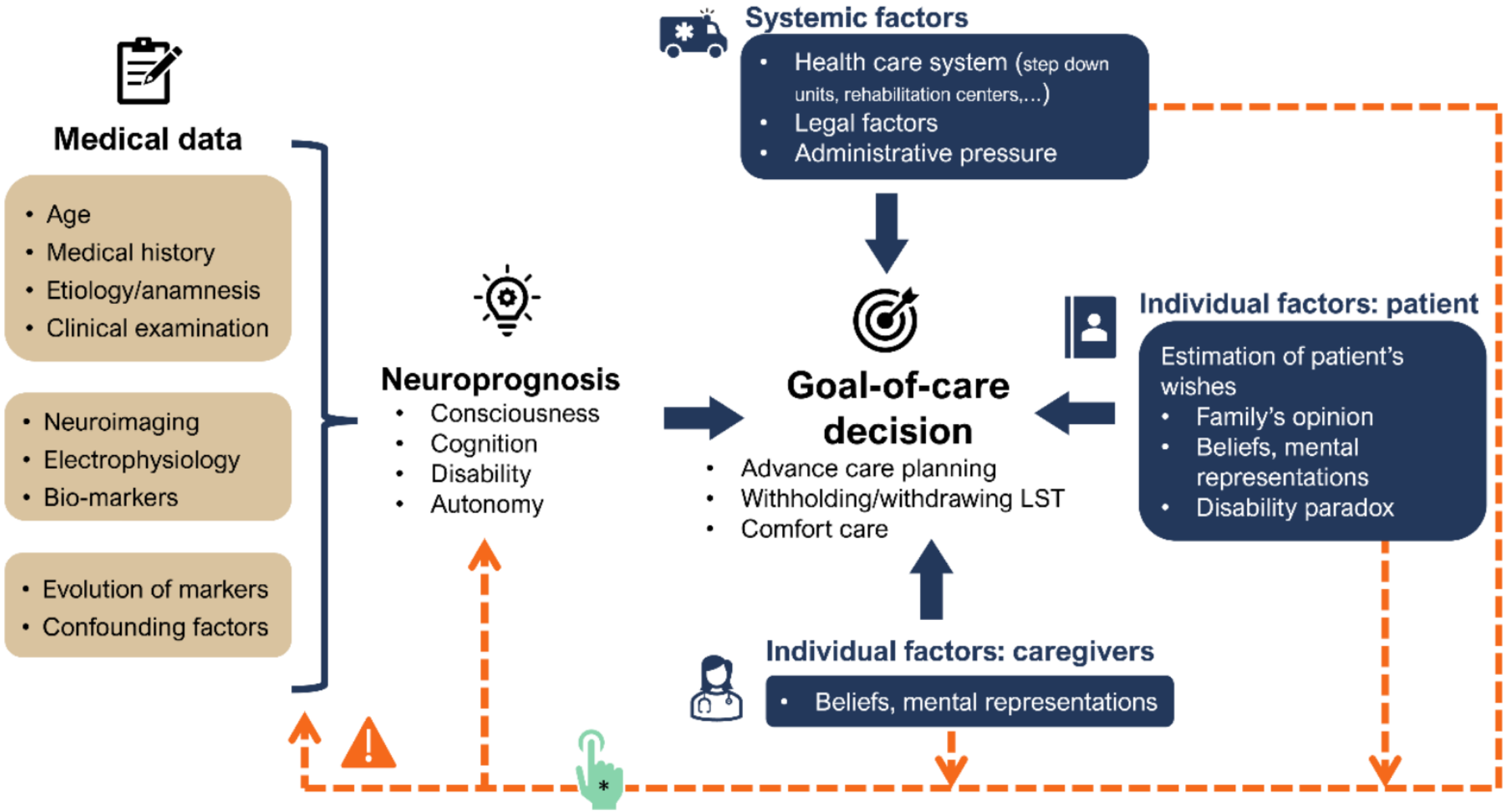
- Structural: TDM, quantitative MRI (WWM-FA/ DTI)
- Functional « at rest»: EEG standard, EEGq, fMRI, PET-FDG
- Functional « in action»: EEG / fMRI, ERPs, Motor command protocol (CMD)



Lakhlifi C, Rohaut B. Presse Med. 2023



Lakhlifi C, Rohaut B. Presse Med. 2023



Lakhlifi C, Rohaut B. Presse Med. 2023

Biais cognitifs

British Journal of Anaesthesia, 120 (1): 5–9 (2018)
doi: 10.1016/j.bja.2017.11.007
Advance Access Publication Date: 23 November 2017

Decision making in perceived devastating brain injury: a call to explore the impact of cognitive biases

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Cognitive bias	Description	Example
Confirmation bias	To look for or to interpret evidence to support prior hypothesis rather than look for disconfirming evidence.	Looking for evidence to support the presumed prognosis rather than contradictory elements.
Availability bias	Judgments of likelihood or percentages based on ease of recall (greater 'availability' in memory) rather than on actual probabilities.	Overestimate the likelihood of a prognosis based on a recent experience with a similar case.
Anchoring effect	To rely heavily on one piece of information when making decisions (usually the first piece of information acquired: the 'anchor').	Focusing on salient features in the patient's presentation too early in the prognosis process and failing to adjust this initial impression in the light of new information.
Framing effect	To draw different conclusions from the same information, depending on how that information is presented.	Allowing the way evidence is framed or whom the information came from to influence prognosis making.
Loss aversion	To view losses as looming larger than corresponding gains.	Continue with a given prognosis, even though it may not fit the new evidence (avoiding the loss of 'being right').
Attribute substitution	Answering a complex, difficult question by substituting it by a related but simpler one.	Translate a legitimate high confidence in diagnosis elements into overconfidence on prognosis issue.
Sunk-cost effect	To allow previously spent time, money, or effort to influence present or future decisions.	Overestimation of a good prognosis if a lot of resources (typically surgery or organ supply) have been successful (in terms of short outcome).
Dunning–Krúger effect	Tendency for unskilled individuals to overestimate their own ability ('illusory superiority') and the tendency for experts to underestimate their own ability.	Being overconfident in a prognosis in case of a lack of knowledge in this specific field (in comparison to an expert).
Bandwagon effect	To do (or believe) things because many other people do (or believe) the same.	Rely too much on apparent consensus and/or common practices.
Commission bias	To favour action rather than inaction.	Jumping to a withdrawal of care procedure (with/without organ donation) rather than giving more time to get more information.
Blind obedience	To show undue deference to authority or technology.	Relying too much on a unique expert opinion or test results.

Rohaut & Claassen Br J Anesth 2018

Conclusion

Avoir quelques repères solides (recos ESICM/ERC) qui permettent, le plus souvent, de répondre à la question

Savoir raisonner à plusieurs (approche multidisciplinaire) et avec différents outils (approche multimodale)

Se méfier de nos **biais cognitifs** (parfois favorisés par notre système de soins)

Favoriser une **discussion éclairée et honnête avec les familles et les proches**, les associer au projet de soin

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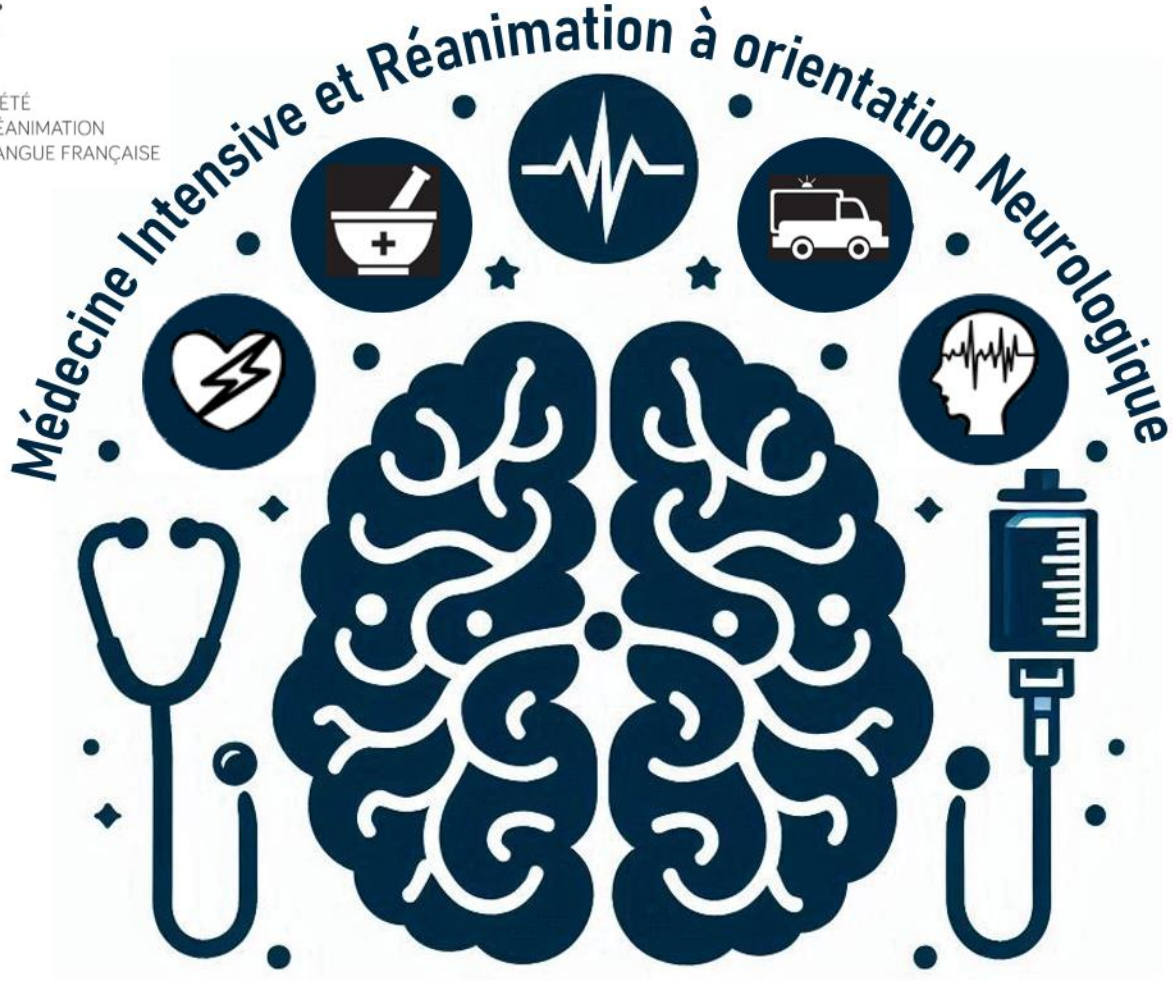

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