

Vicenza

CONGRESSO NAZIONALE IRC 2023



20 • 21 OTTOBRE

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LA RIVOLUZIONE DEI SISTEMI



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Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Misurare l'outcome: quando è buono e quando è cattivo



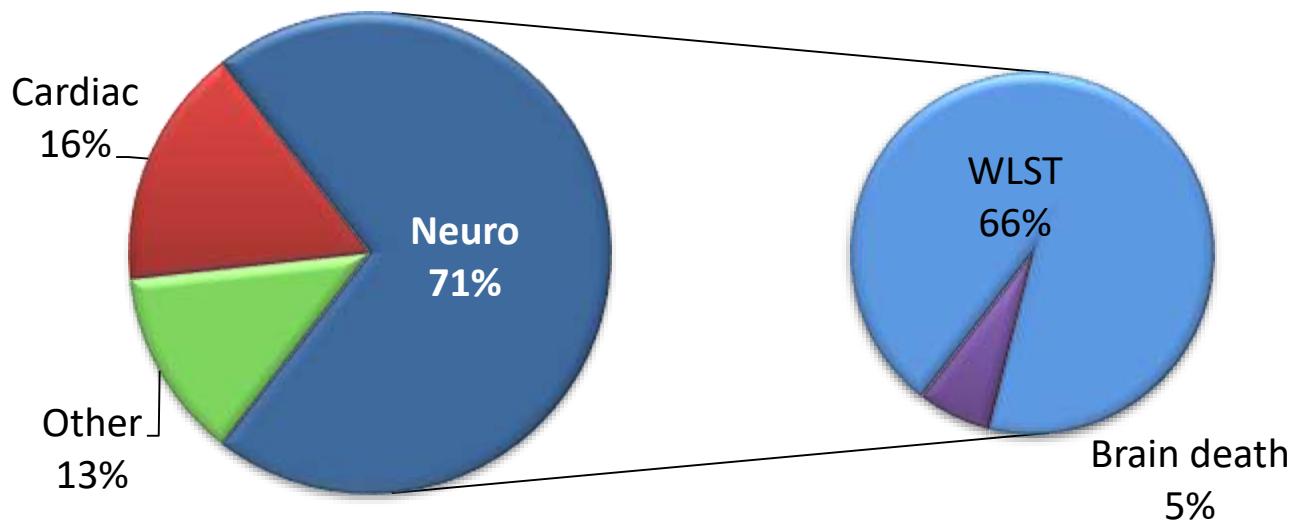
Sonia D'Arrigo

UOC Rianimazione, Terapia Intensiva e Tossicologia Clinica
Fondazione Policlinico Universitario A. Gemelli IRCCS
Roma

Causes of death after resuscitation

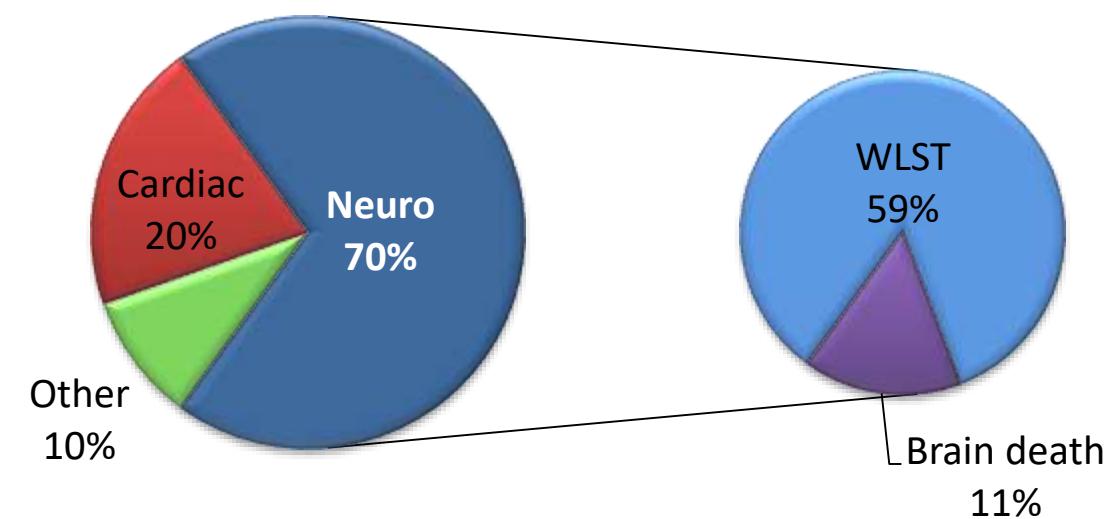
Dragancea 2013, Sweden

n= 86



Elmer 2016, USA

n= 2760



WLST = Withdrawal of Life-Sustaining Treatment

Perché formulare una prognosi ?



Per fornire
informazioni corrette



Per fornire cure
appropriate e proporzionate

Cure appropriate e proporzionate

Evitare
trattamenti futili

**Il paziente
'cristallizza'**



Evitare una
inappropriata
limitazione
dei trattamenti



Strategia multimodale

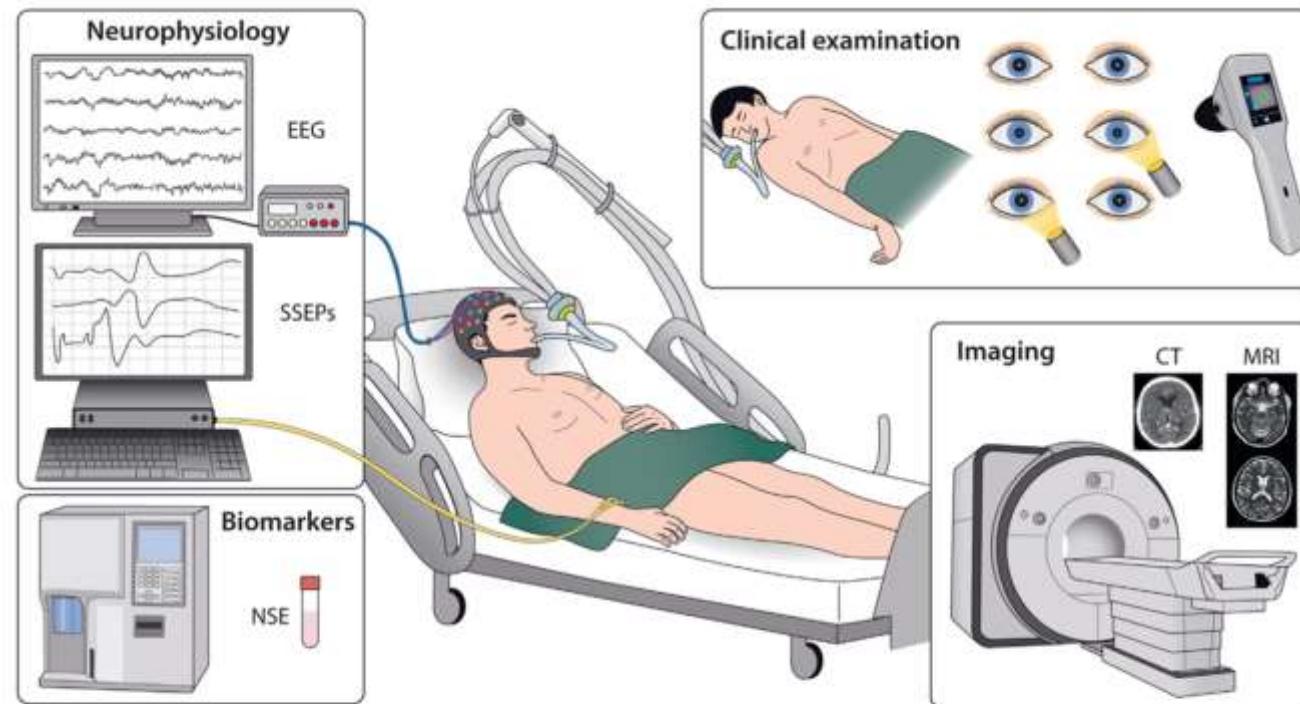
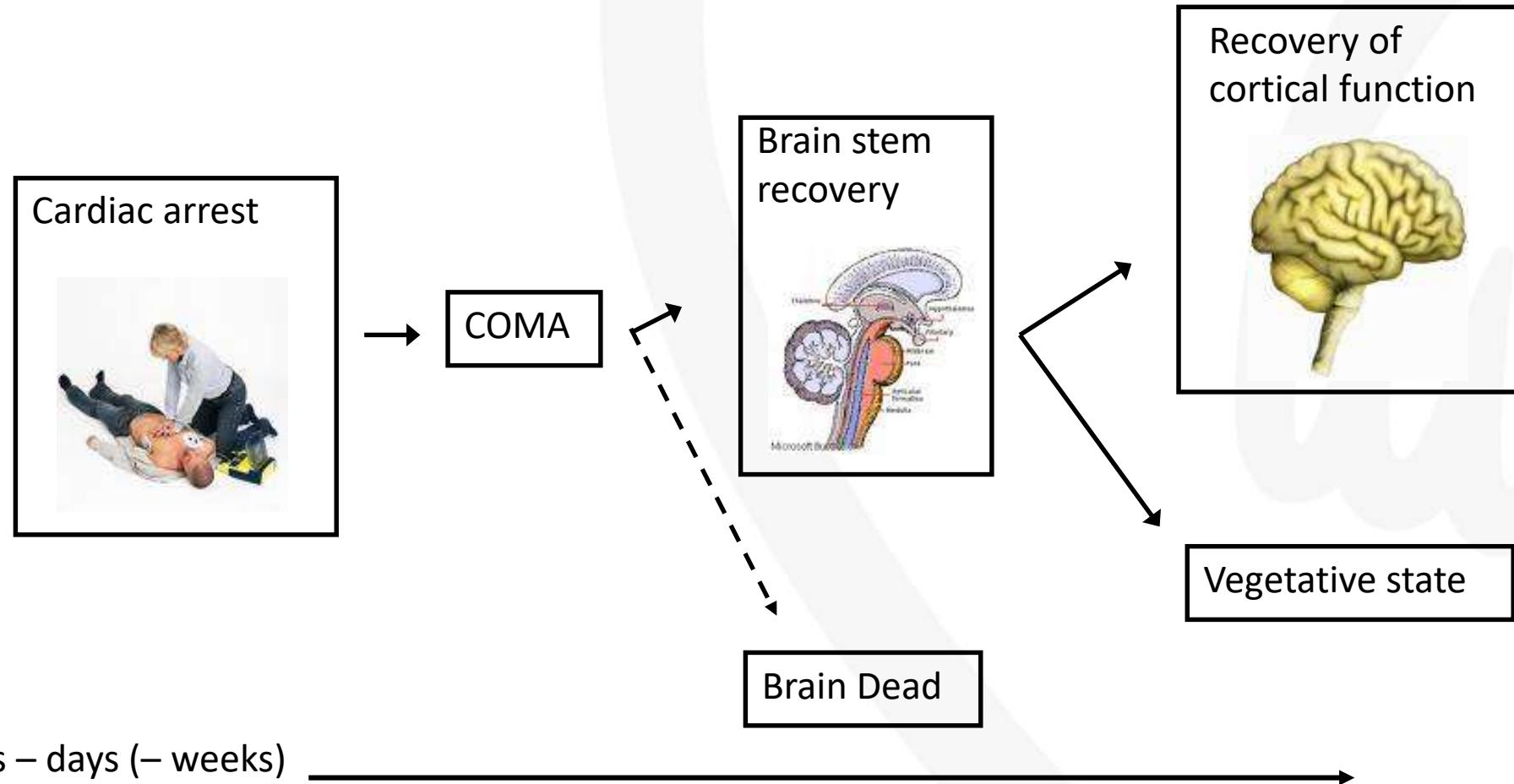


Fig. 4 – Prognostication modes. EEG electroencephalography; NSE neuron specific enolase; SSEP somatosensory evoked potential.

Nessun preditore è accurato al 100%

Natural course of neurological recovery following cardiac arrest

Patil KD et al. Circ Res. 2015 Jun 5;116(12):2041-9



No early predictors

3 main scenarios

1.The Good



2.The Ugly



3.The Bad



Prognosi dell'arresto

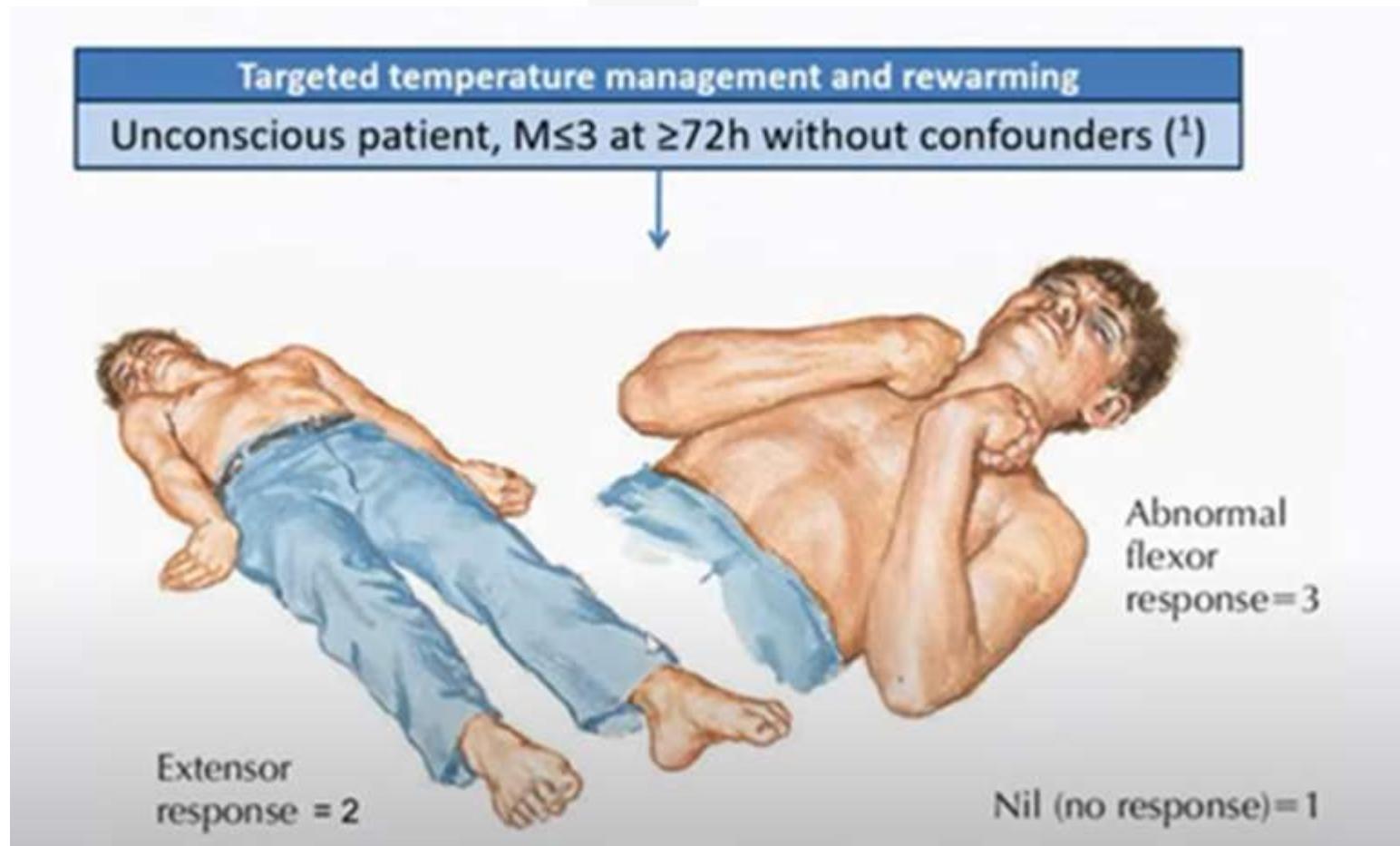
- >2/3 delle morti dopo arresto cardiaco sono neurologiche
 - e basate sulla prognosi attesa
- Prognostication = predizione di esito neurologico *sfavorevole*

Timing della valutazione prognostica

- La valutazione deve iniziare con un esame clinico
- In assenza di sedazione residua, l'esame è attendibile $\geq 72\text{h}$ dopo ROSC
- L'attendibilità dell'esame clinico è ridotta se sono stati somministrati sedativi $\leq 12\text{h}$ prima
- L'ipotermia prolunga gli effetti dei sedativi



Paziente incosciente



NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST



Targeted temperature management and rewarming

Unconscious patient,
 $M \leq 3$ at $\geq 72\text{h}$ without confounders ⁽¹⁾

YES

At least TWO of:

- No pupillary ⁽²⁾ and corneal reflexes at $\geq 72\text{h}$
- Bilaterally absent N20 SSEP wave
- Highly malignant ⁽³⁾ EEG at $> 24\text{h}$
- NSE $> 60 \mu\text{g/L}$ ⁽⁴⁾ at 48h and/or 72h
- Status myoclonus ⁽⁵⁾ $\leq 72\text{h}$
- Diffuse and extensive anoxic injury on brain CT/MRI

NO

Observe and re-evaluate

¹ Major confounders may include analgo-sedation, neu

severe hypotension, hypoglycaemia, sepsis, and met

able, to a

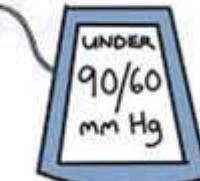
ges or bu

24/48 and 72h further support a likely poor outcome

yoctonus persisting for 30 min

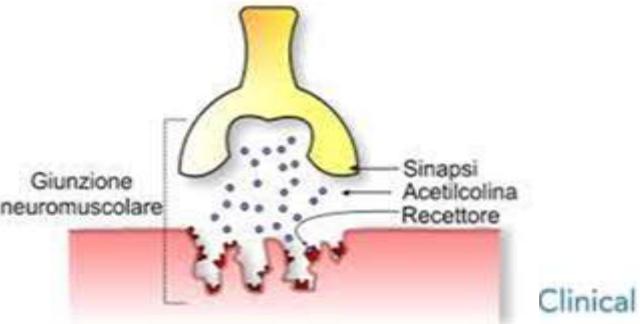
19

Hypotension

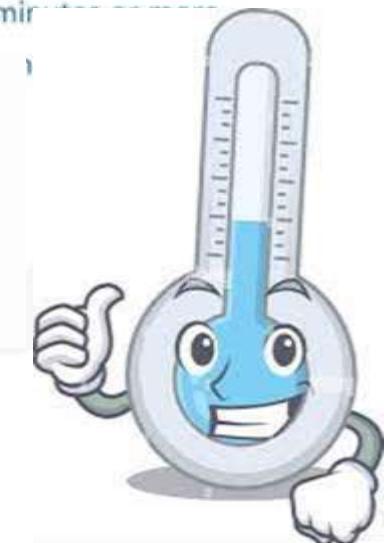
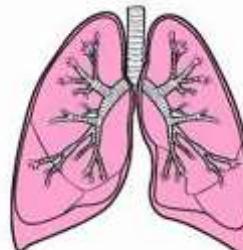


YES

Poor
outcome
likely (*)



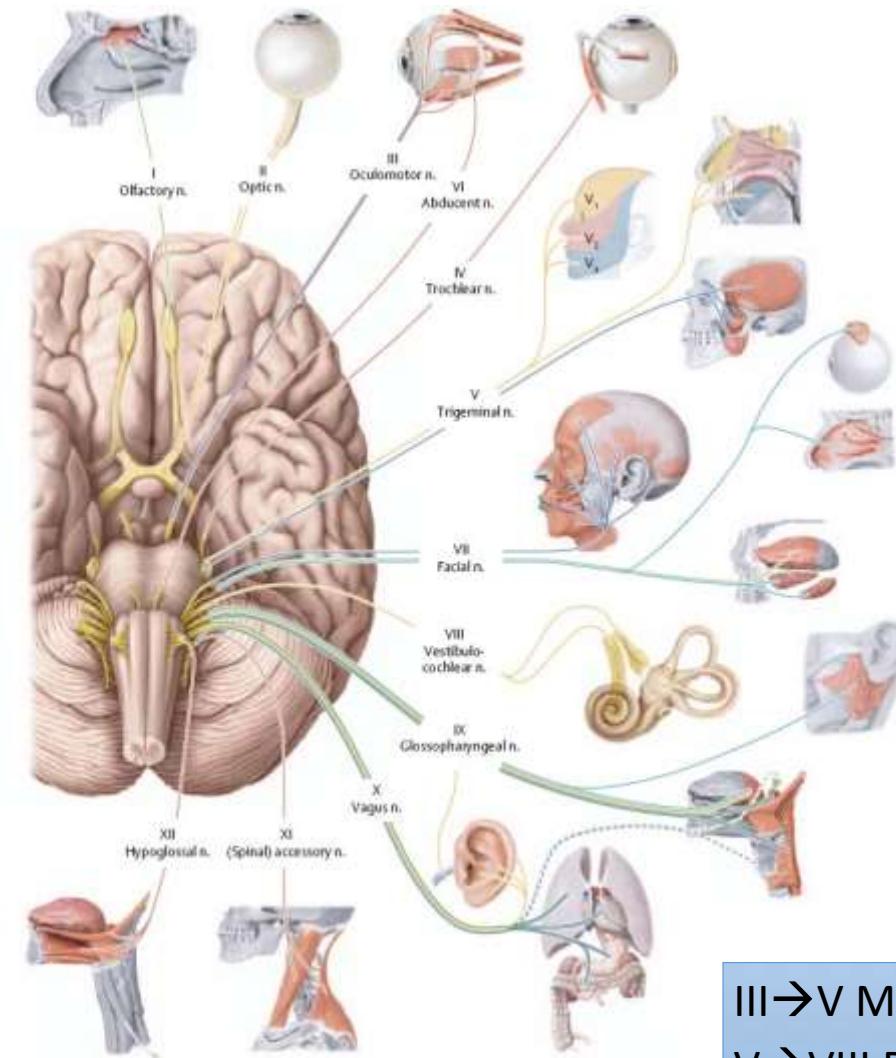
Clinical



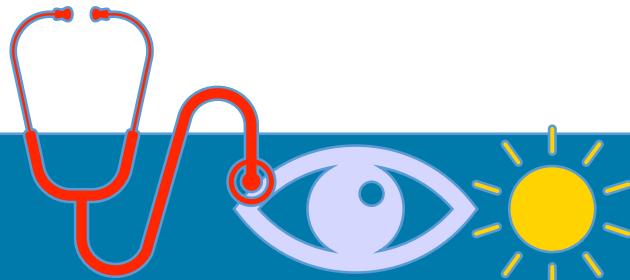
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LA RIVOLUZIONE DEI SISTEMI

Standard vs Automated



III→V Midbrain
V→VIII Pons
V, VII→XII Medulla



Pros easy and inexpensive

Cons qualitative, Inter examiner variability (>39%) and lack of reliability

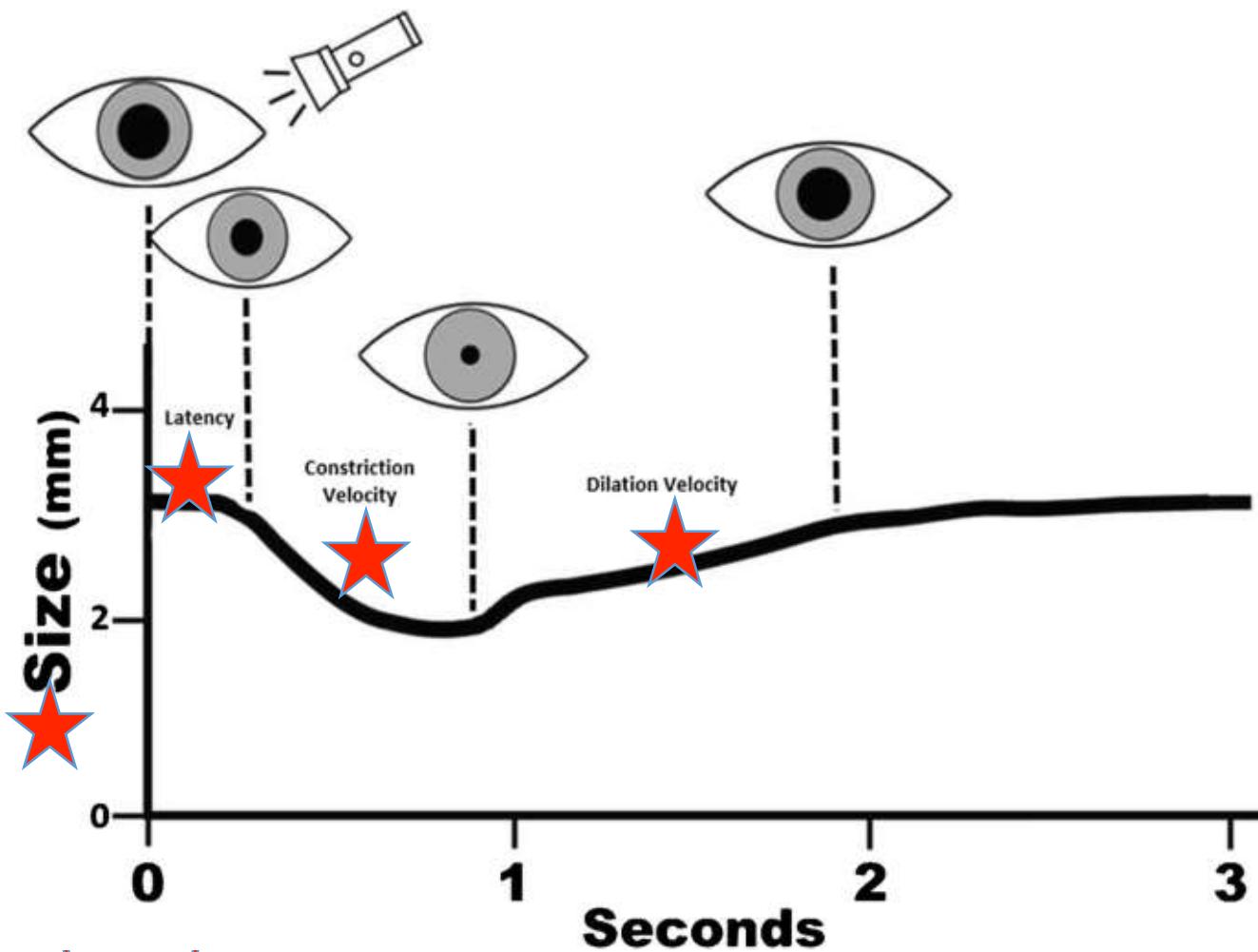


Pros standardise the intensity, distance from the eye and duration of stimulus. Displays a quantitative and reproducible measures.

Cons cost



Automated pupillometry technique



Infrared & visible light source coupled with a camera

A infrared light measure the pupil baseline

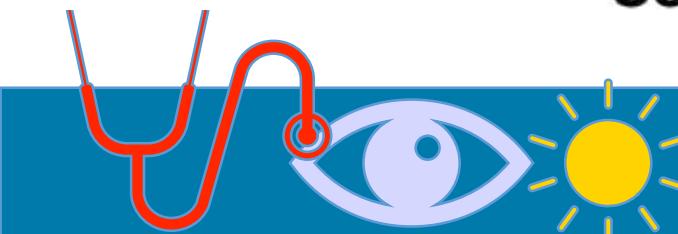
After 3" a visible light delivered

The pupillary response recorded with camera

Other parameters

- pupillogram
- data trending

Non invasive
neuromonitoring
bedside tool





No comparable data on available devices
Possible that information with both devices is not the same

No comparable studies that examine accuracy

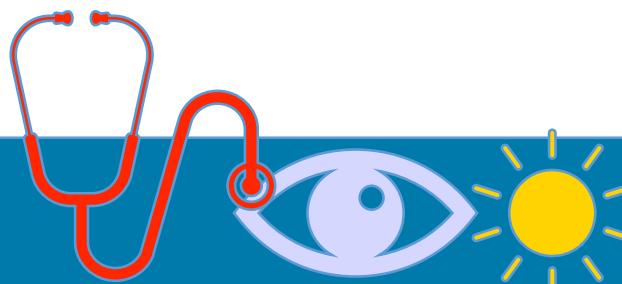
cubical nerve stimulator (10-60 mA)

- PRD
- PPI

NPi Index?
algorithm derived value
NPI >= 3 = normal reactivity



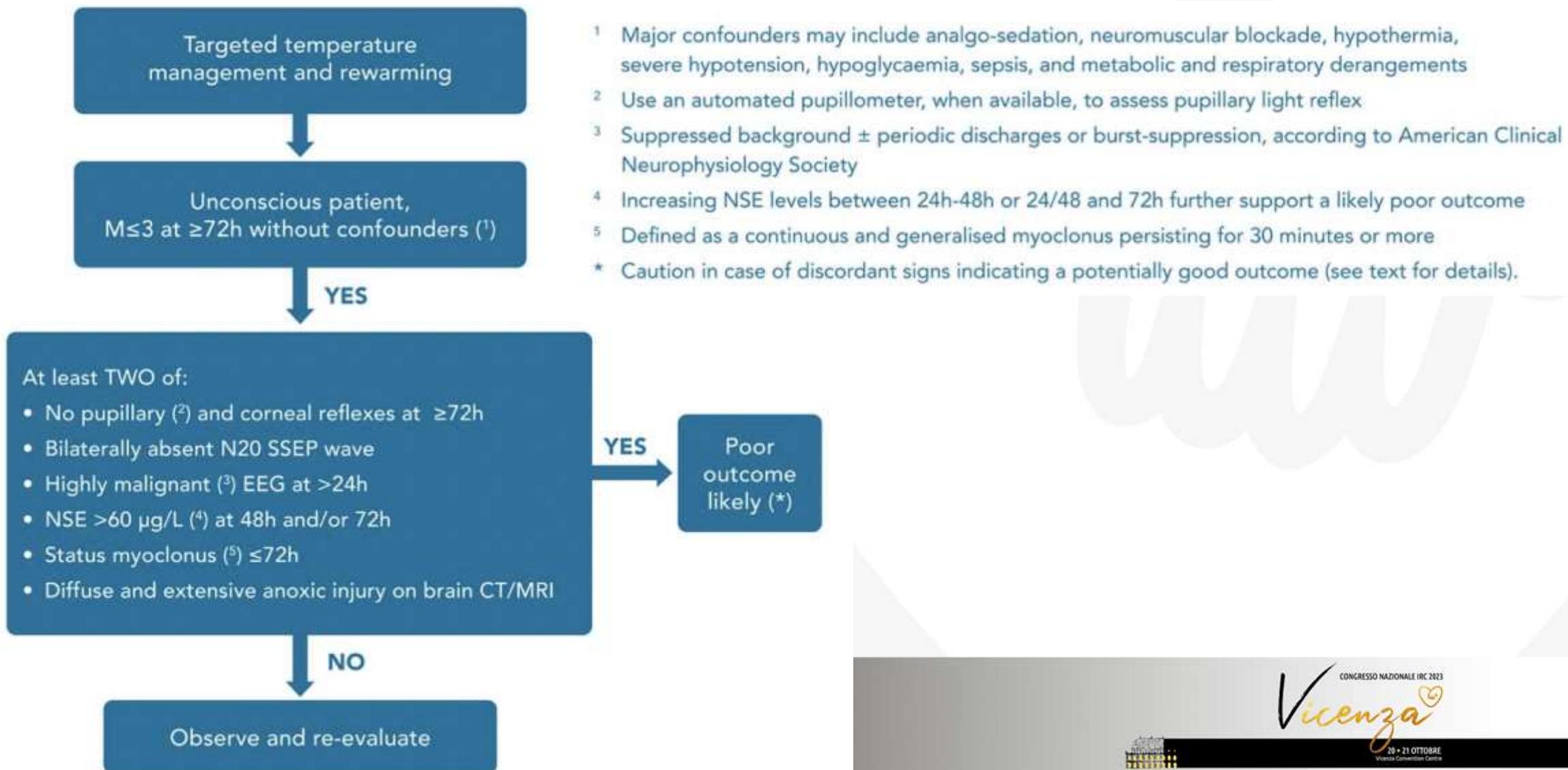
Neuroptics NPi



Confronto NPI vs. sPLR

Day after cardiac arrest (n)	Sample size n (%)	CPC 3–5 n (%)	Specificity % (95% CI)	Sensitivity % (95% CI)
Neurological pupil index (NPI) ≤ 2				
Day 1–3	456	269 (59)	100 (98–100)	32 (27–38)
Day 1	450	264 (59)	100 (98–100)	22 (17–27)
Day 2	361	213 (59)	100 (98–100)	19 (14–25)
Day 3	271	166 (61)	100 (97–100)	17 (12–24)
Bilaterally absent standard pupillary light reflex (sPLR)				
Day 1	392	225 (57)	90 (85–94)	35 (29–42)
Day 2	278	163 (59)	90 (84–95)	29 (22–36)
Day 3	206	128 (62)	94 (86–98)	18 (12–26)

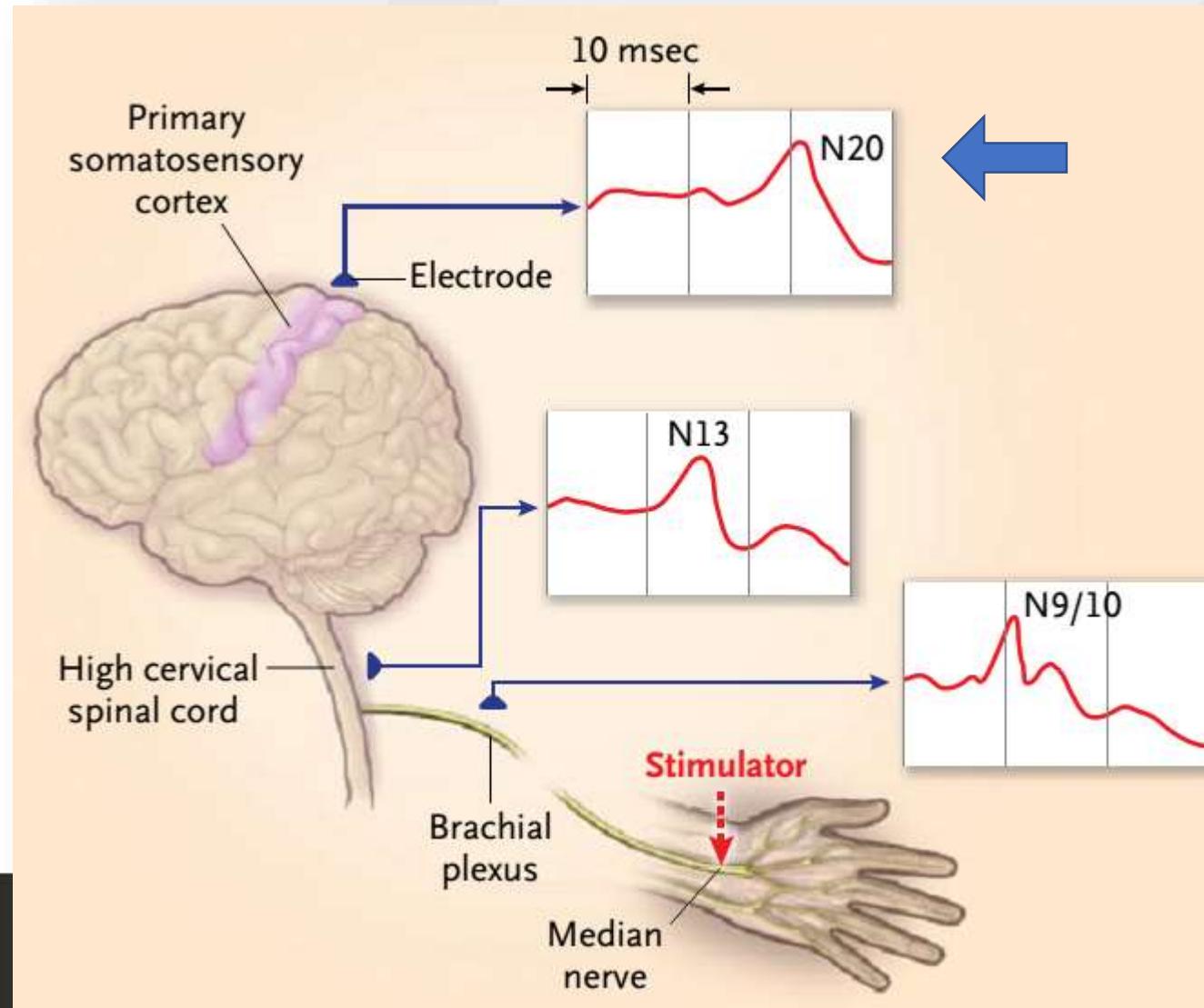
NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST

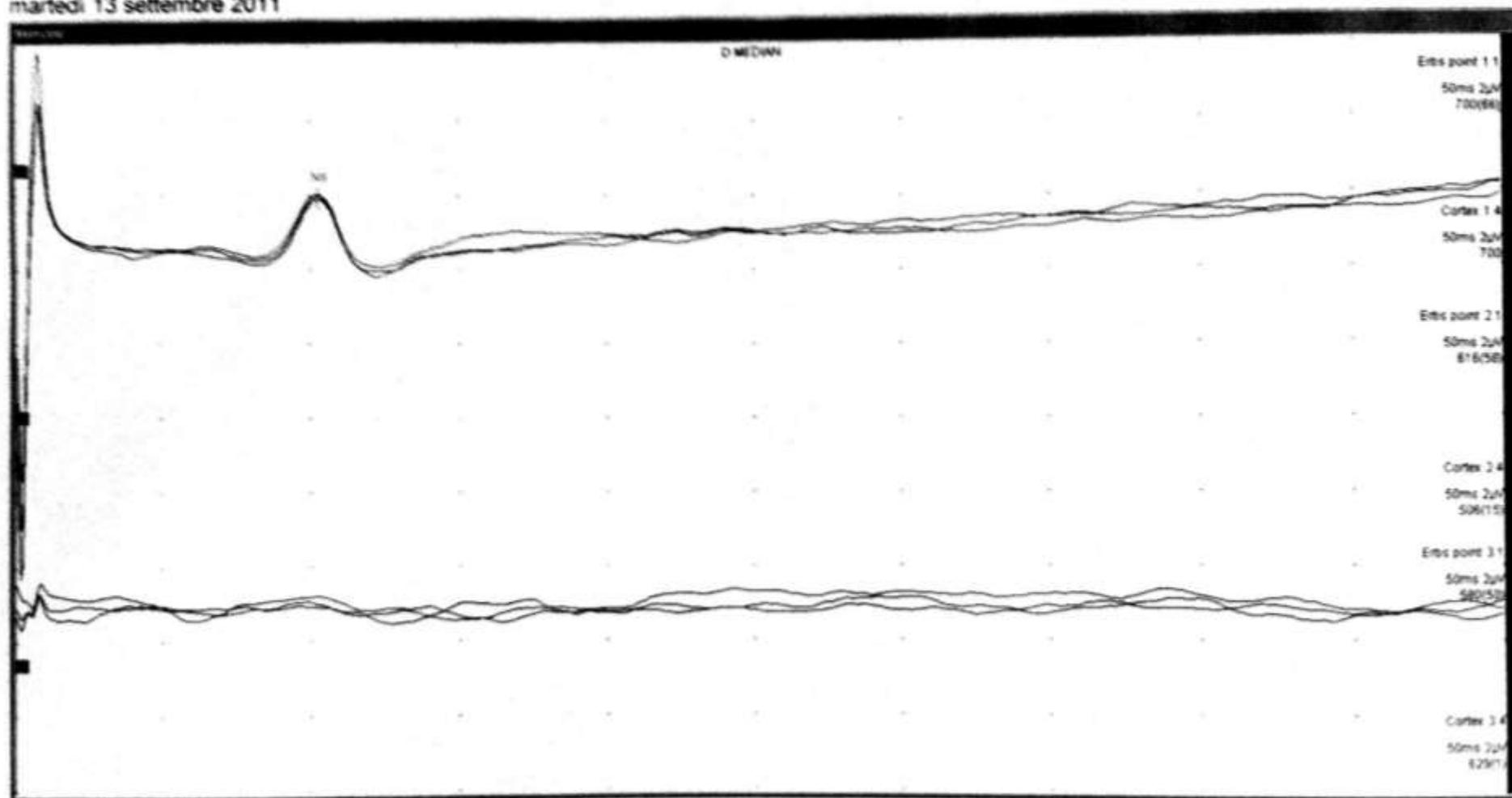


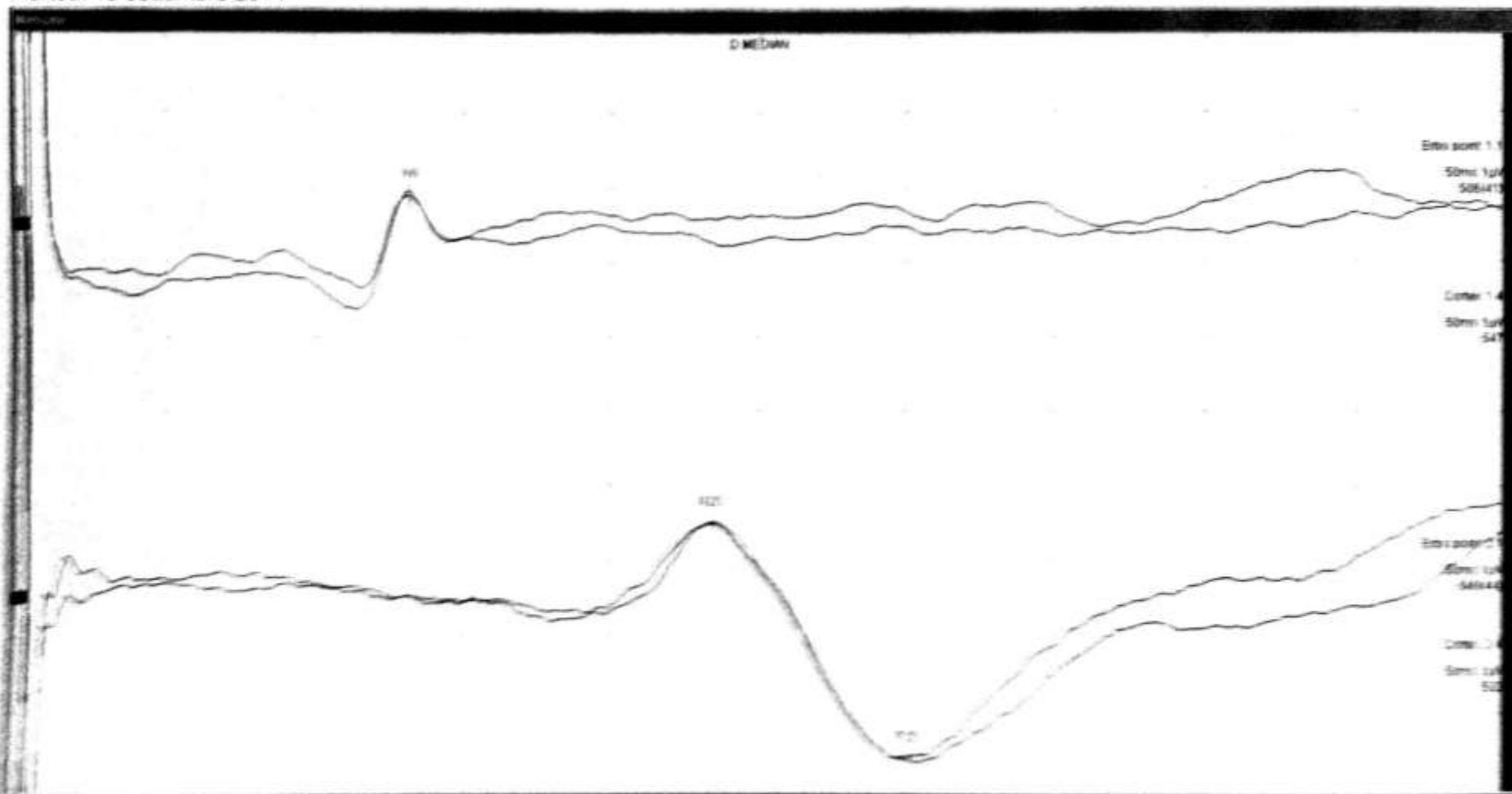
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Potenziali evocati somatosensoriali a breve latenza (SSEP)

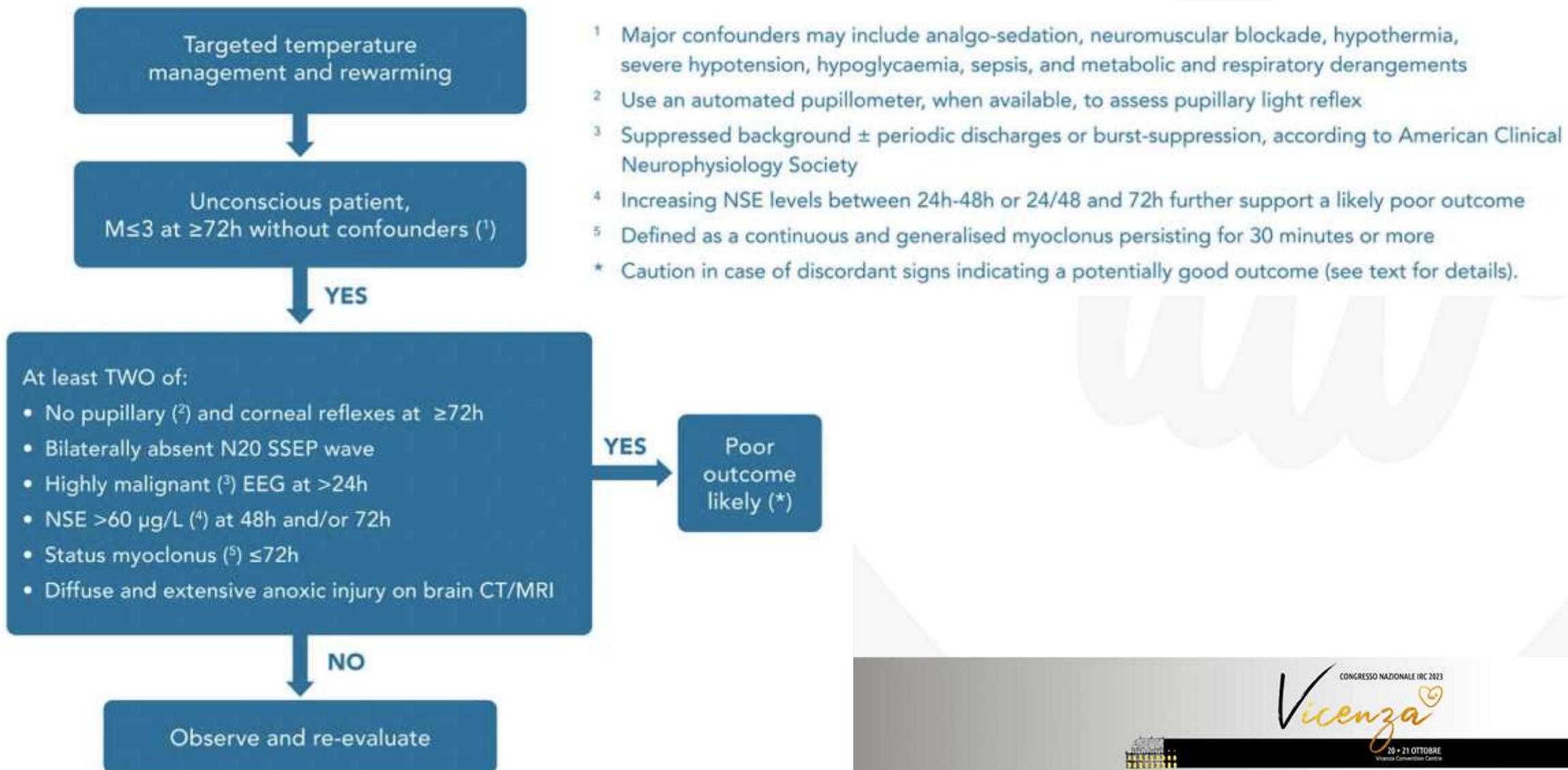








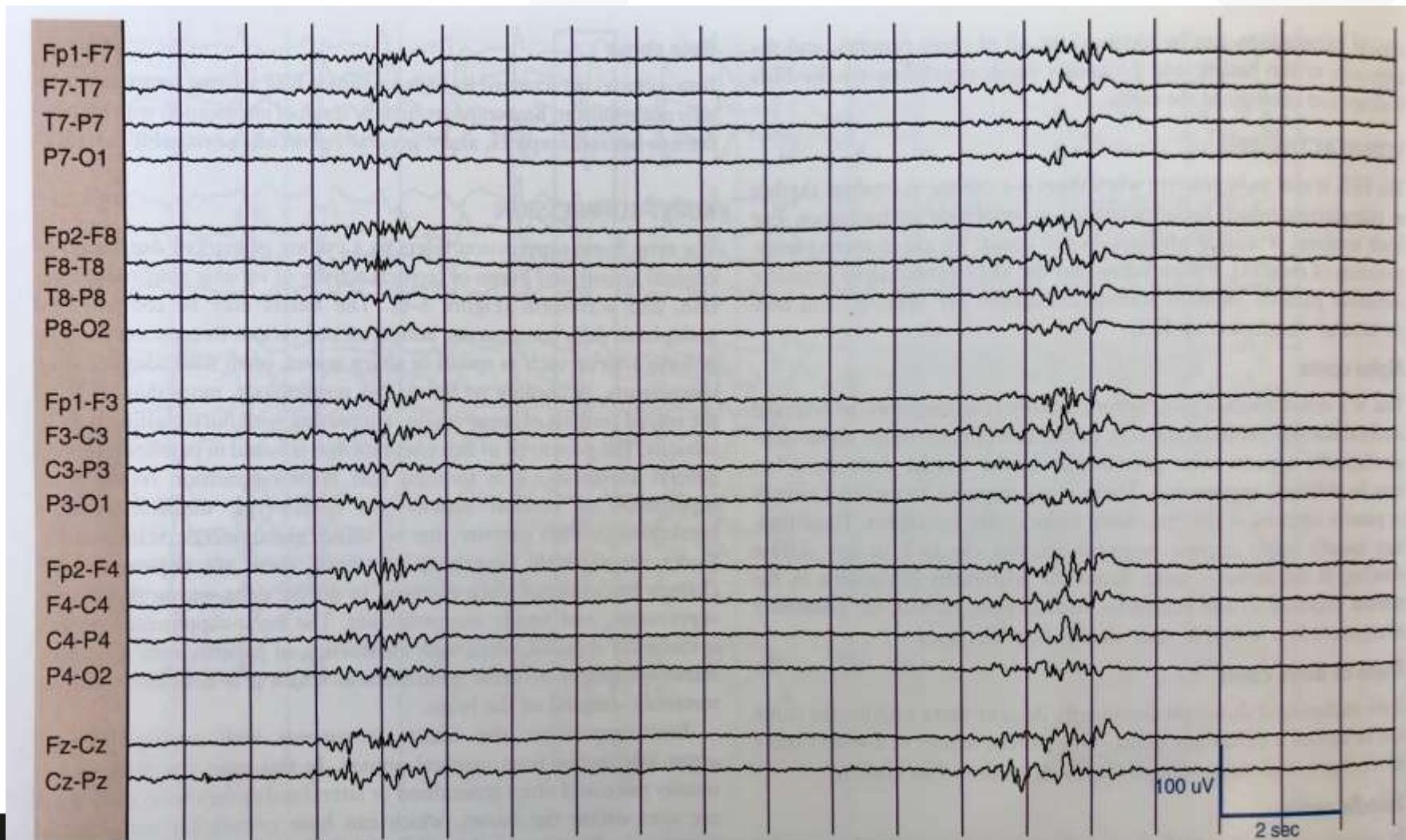
NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST



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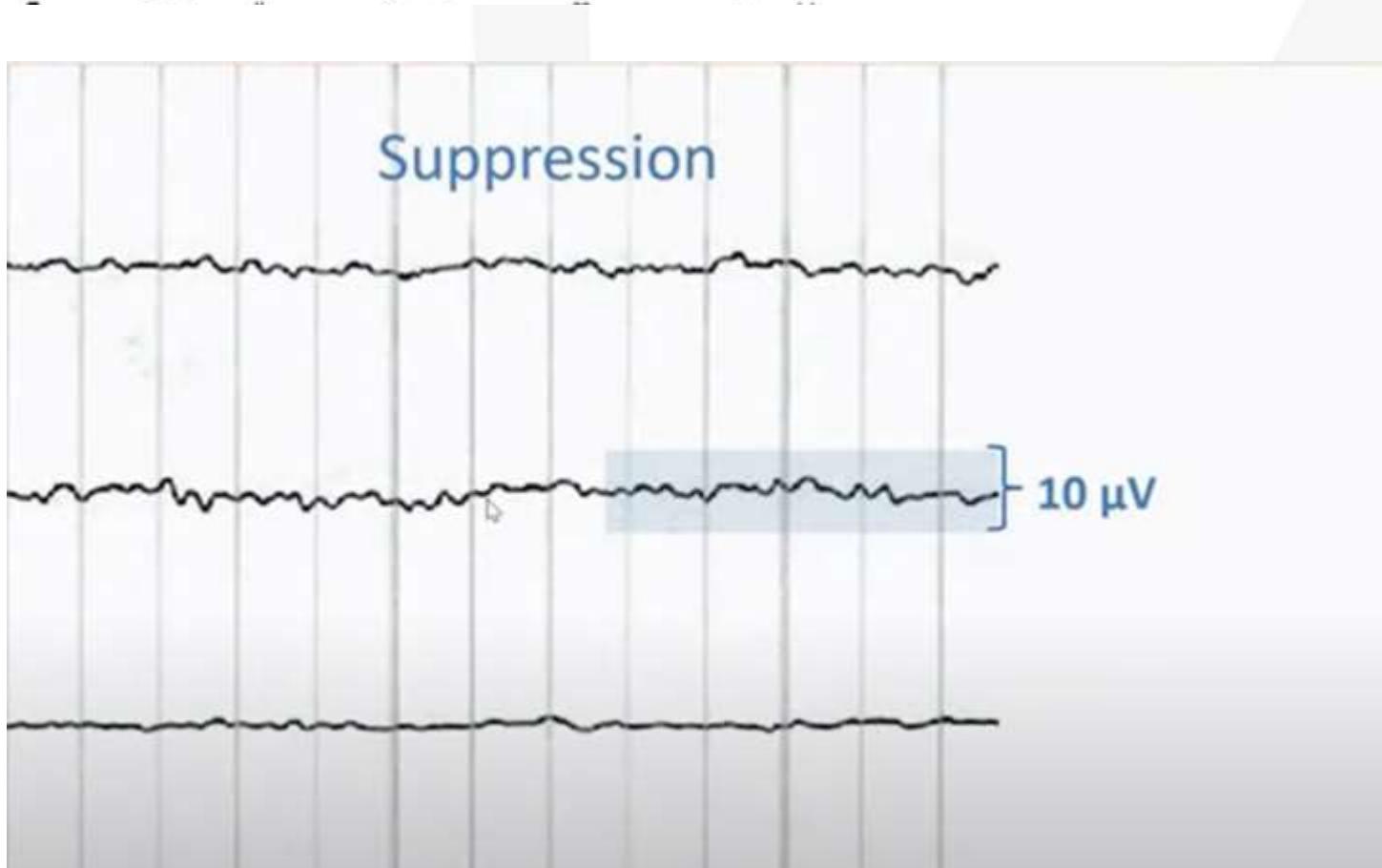
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Burst Suppression

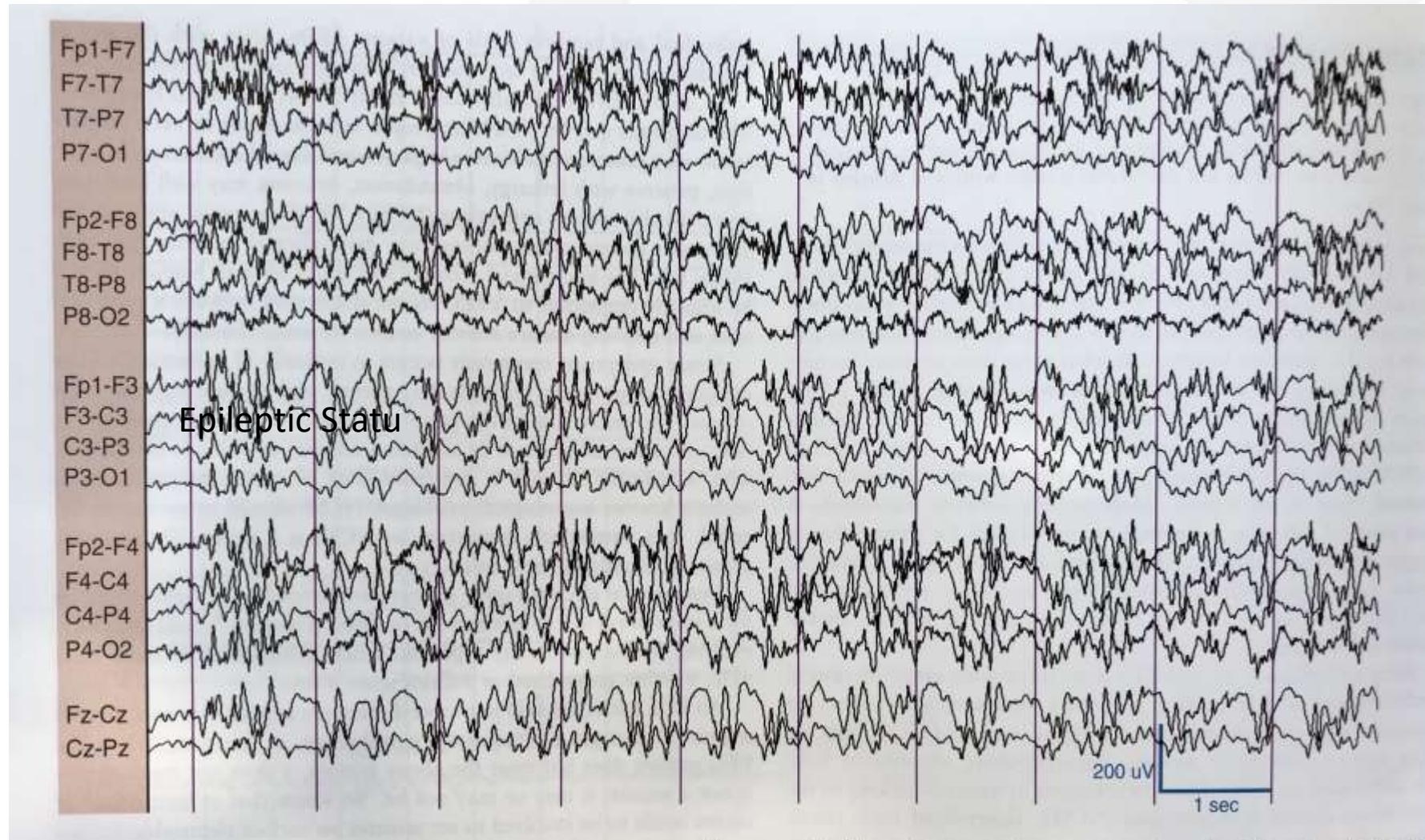


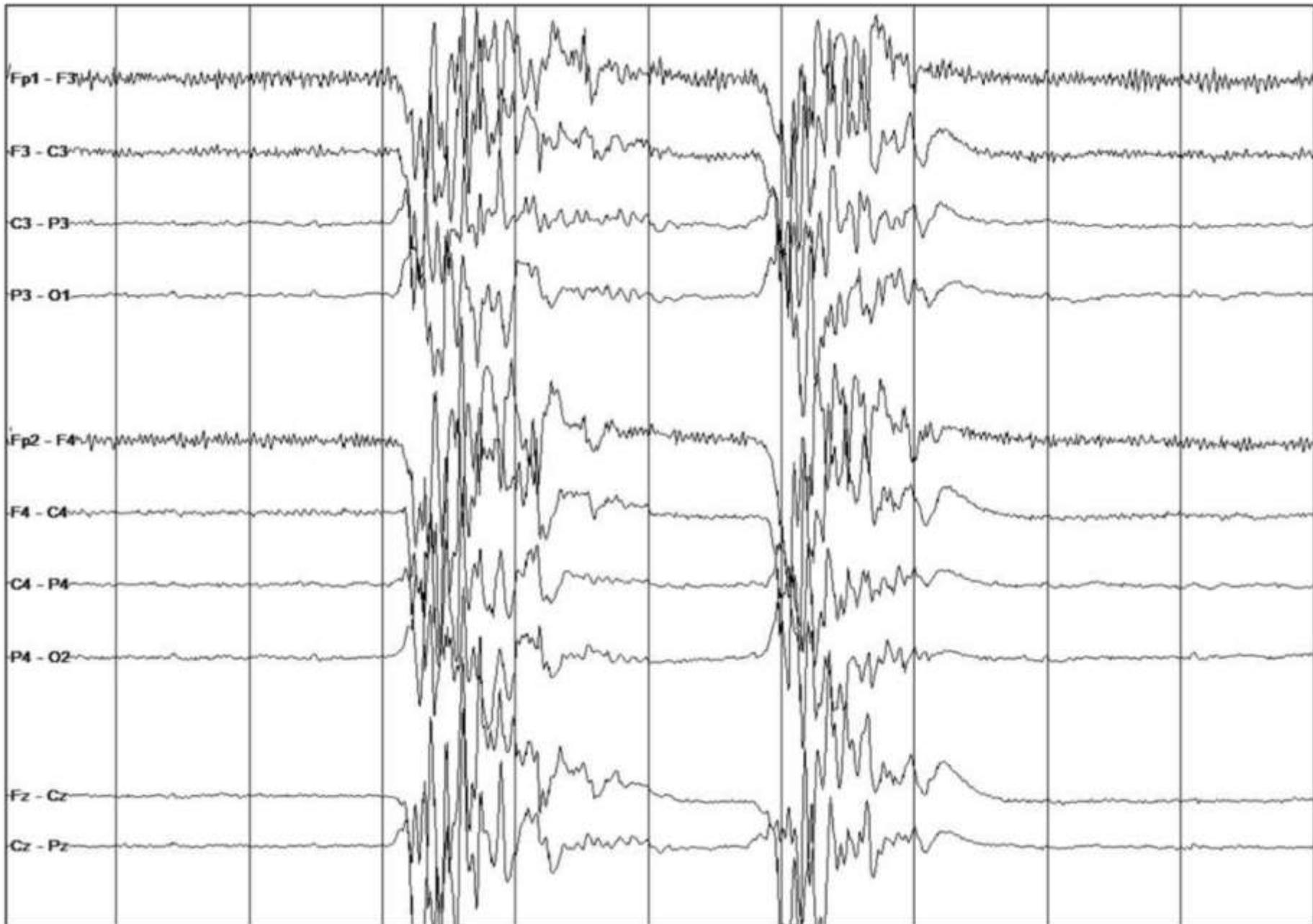
American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2021 Version

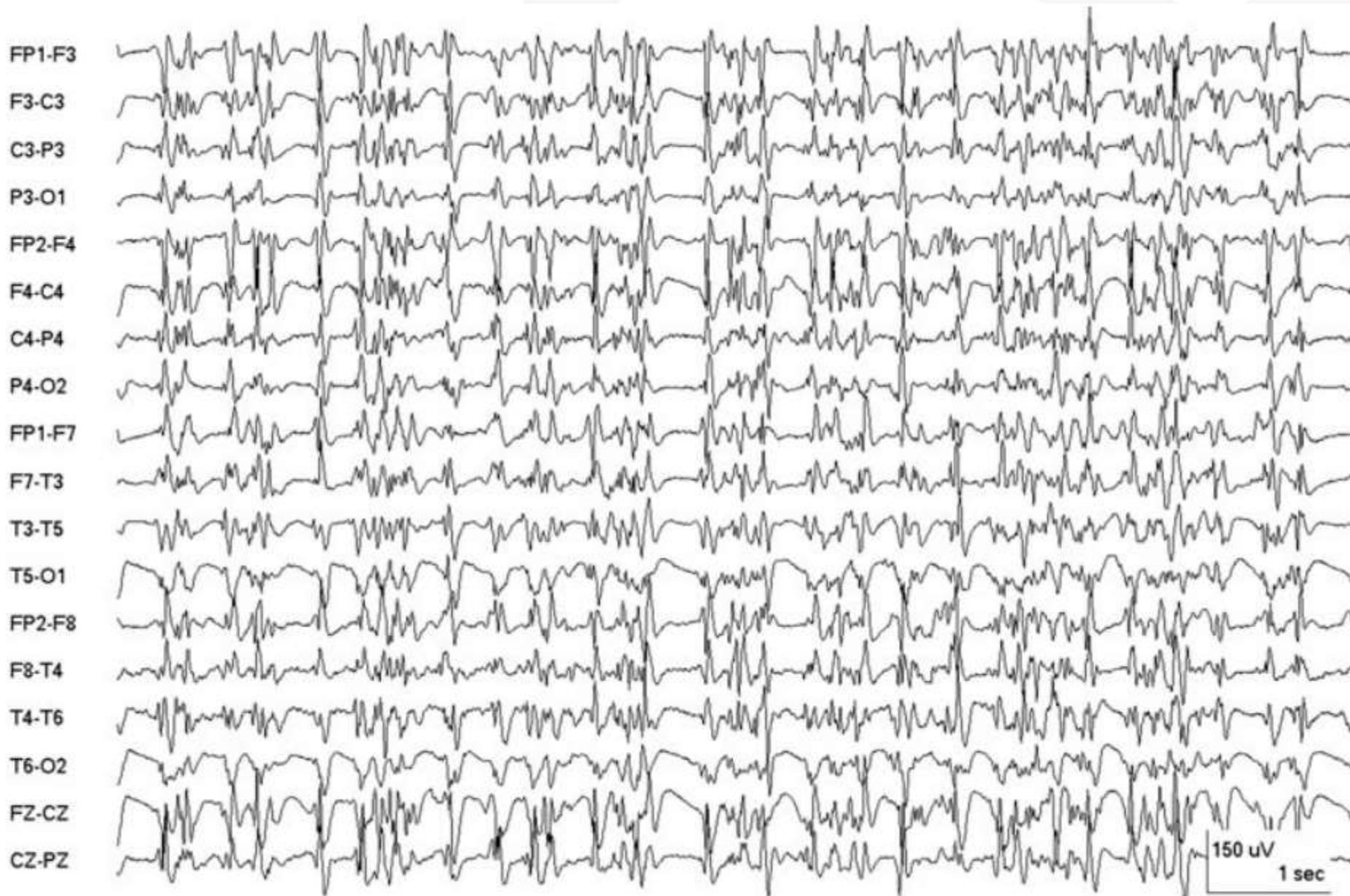
Lawrence J. Hirsch^{*}, Michael W.K. Fong[†], Markus Leitinger[‡], Suzette M. LaRoche[§], Sandor



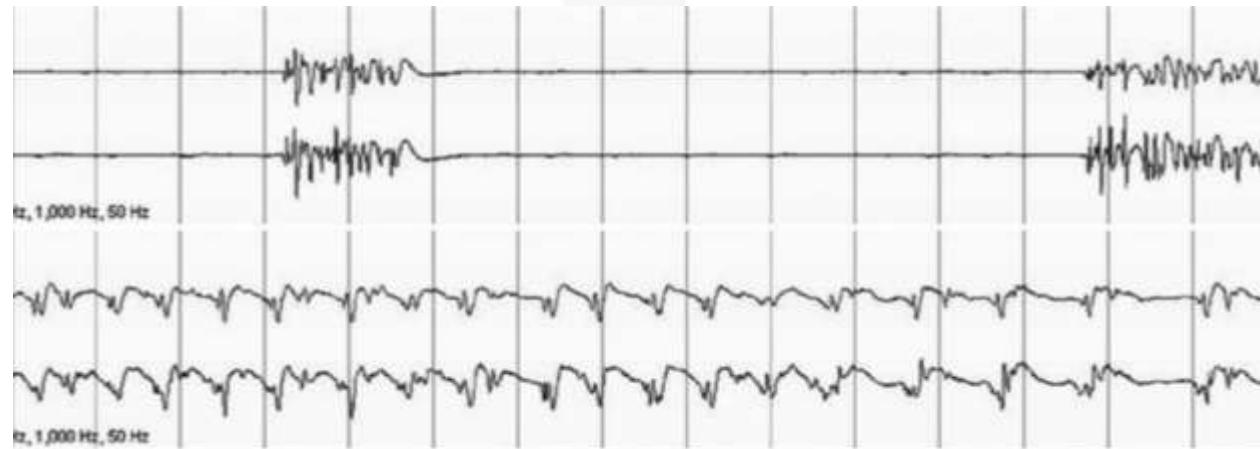
Epileptic Status







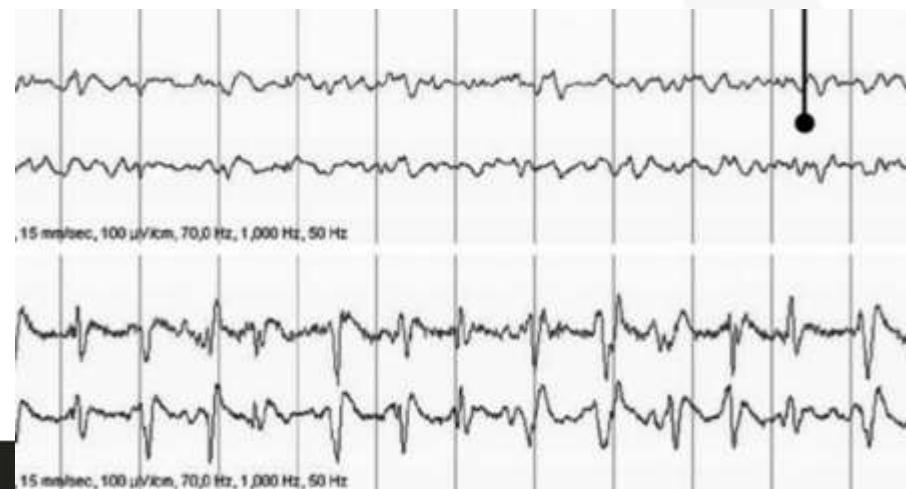
Importanza del background



SE da BS



0% risveglio



SE da EEG continuo



20% risveglio

Reattività EEG



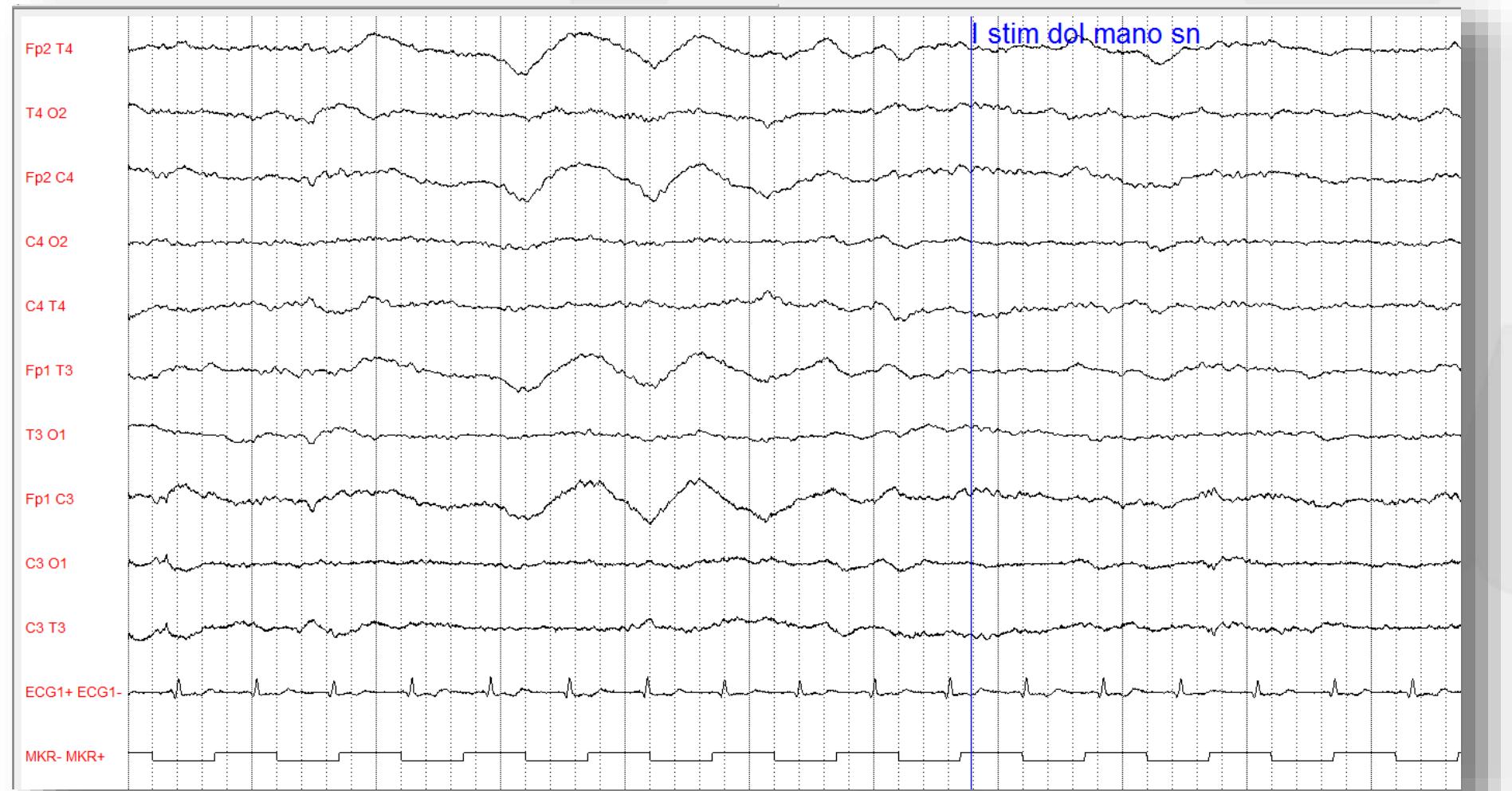
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Cambiamento di ampiezza e/o frequenza dopo stimolazione

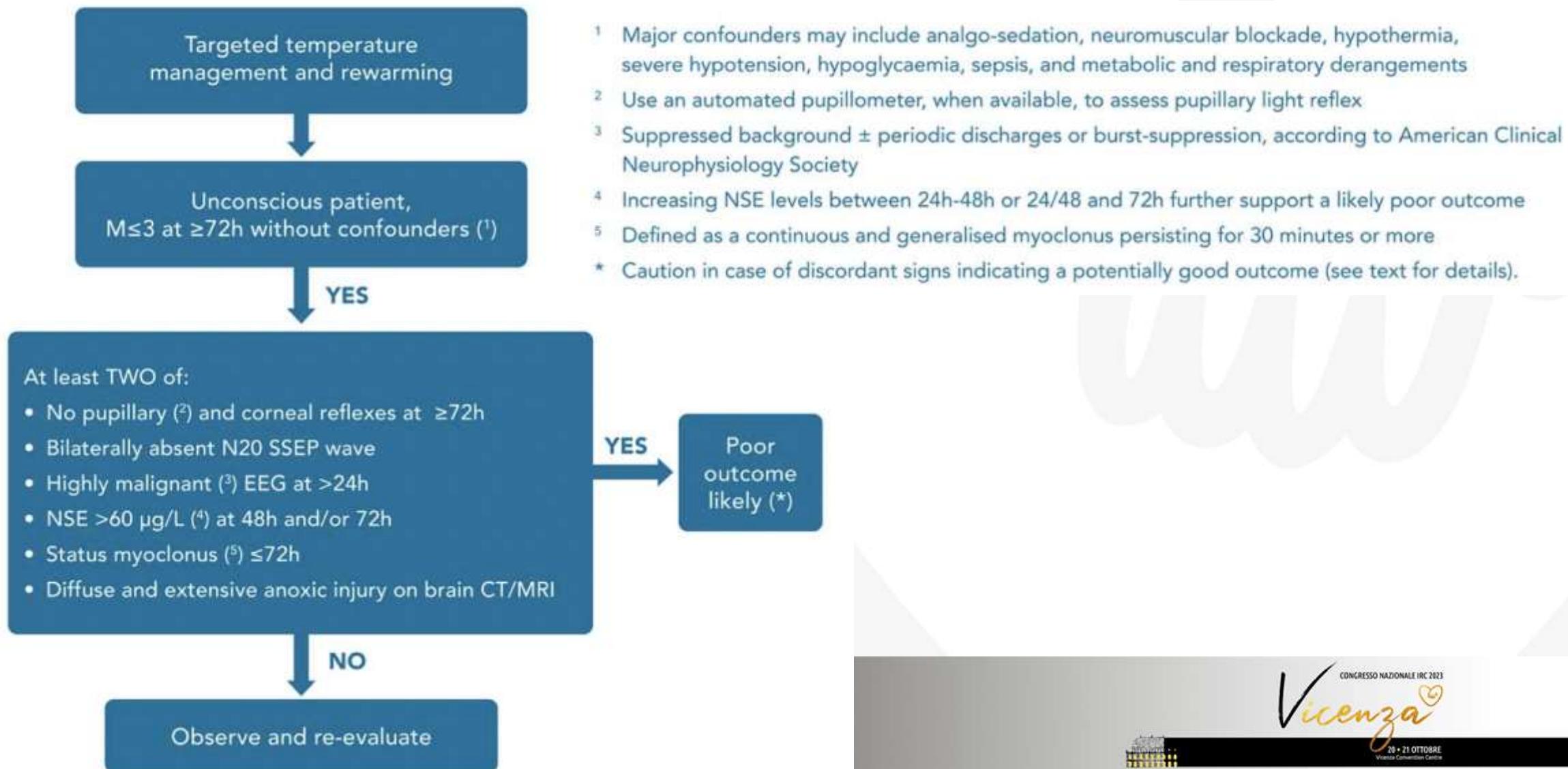


LA RIVOLUZIONE DEI SISTEMI

56h after CA

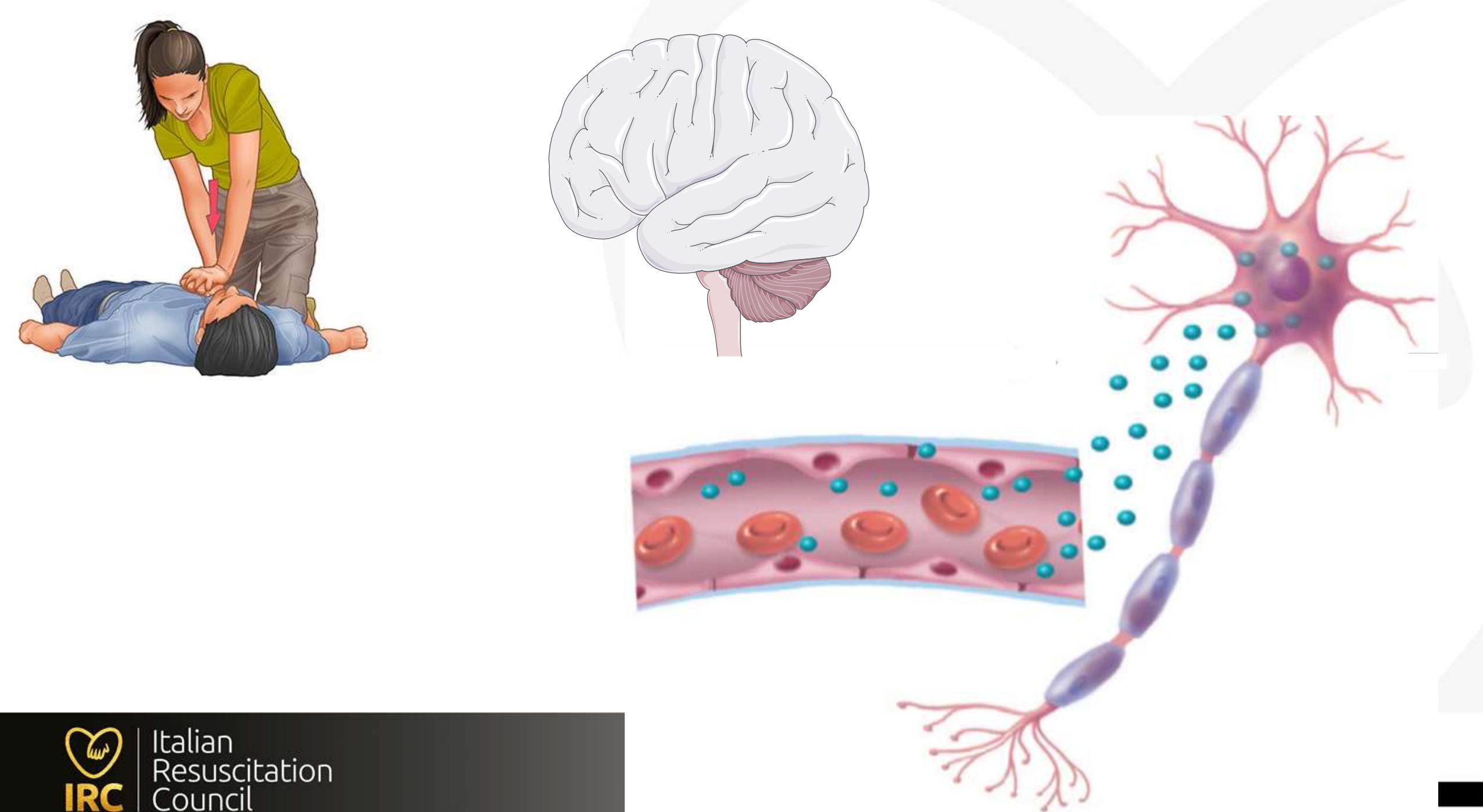


NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST



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LA RIVOLUZIONE DEI SISTEMI





Trend enolasi

24 48 72



Biomarkers



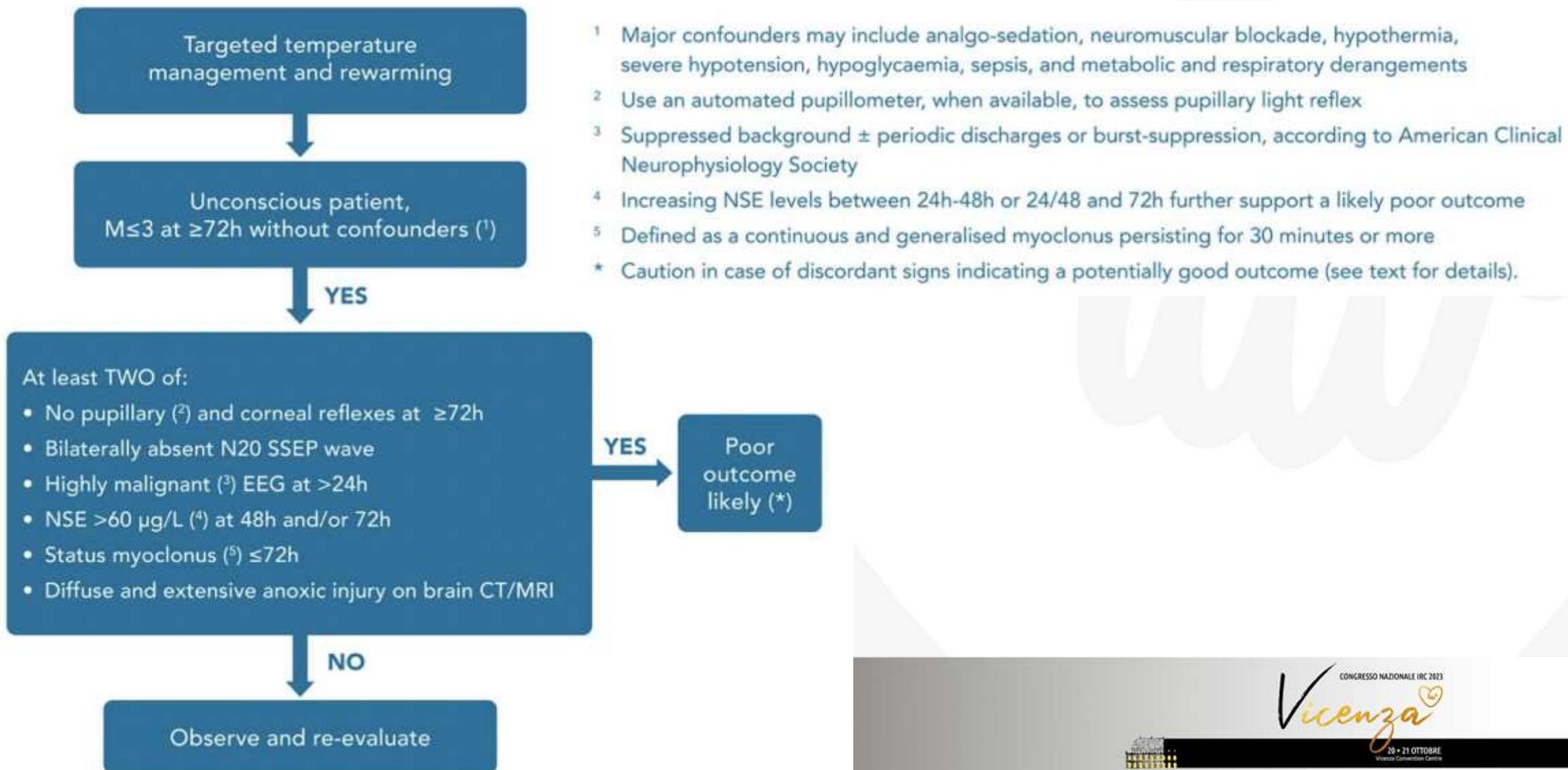
PLOS ONE

RESEARCH ARTICLE
Single versus Serial Measurements of
Neuron-Specific Enolase and Prediction of
Poor Neurological Outcome in Persistently
Unconscious Patients after Out-Of-Hospital
Cardiac Arrest – A TTM-Trial Substudy

Sebastian Wiberg^{1*}, Christian Hassager¹, Pascal Stammert², Matilde Winther-Jensen¹,
Jakob Hartvig Thomsen¹, David Erlinge³, Michael Wanscher¹, Niklas Nielsen⁴,
Tommaso Pellis⁵, Anders Aneman⁶, Hans Friberg⁷, Jan Hovdenes⁸, Janneke Horn⁹,
Jørn Wetterslev¹⁰, John Bro-Jeppesen¹, Matthew P. Wise¹¹, Michael Kuiper¹²,
Tobias Cronberg¹³, Yvan Gasche¹⁴, Yvan Devaux¹⁵, Jesper Kjaergaard¹



NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST



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LA RIVOLUZIONE DEI SISTEMI

Mioclono

- Contrazioni muscolari brevi, improvvise, involontarie (twitch o shock like contractions)
- Sono la manifestazione motoria più frequente in TI
- Spesso generalizzate ma possono essere focali o multifocali
 - Apertura occhi periodica
 - Deglutizione
 - Contrazioni diaframmatiche
- Da ‘subtle’ a intense e generalizzate
- Inducibili



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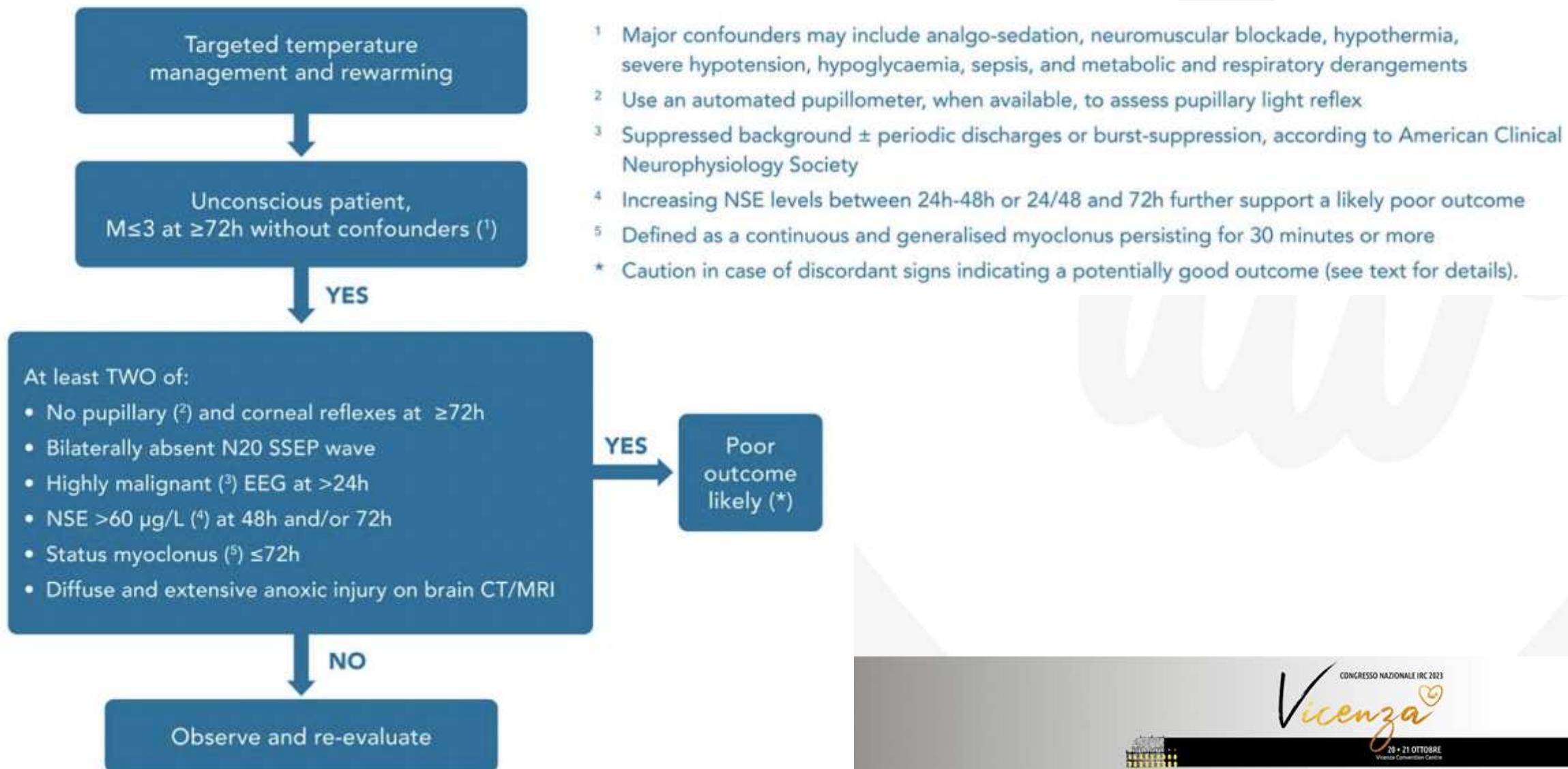
LA RIVOLUZIONE DEI SISTEMI



Mioclono

- La comparsa precoce è indicativa di prognosi infausta
- Possono avere una corrispondenza EEG corticale
- S. di Lance-Adams in chi riprende coscienza
 - Più comune dopo arresto asfittico
 - Interessa soprattutto gli arti
 - Indotto da movimento volontario o stimolazione

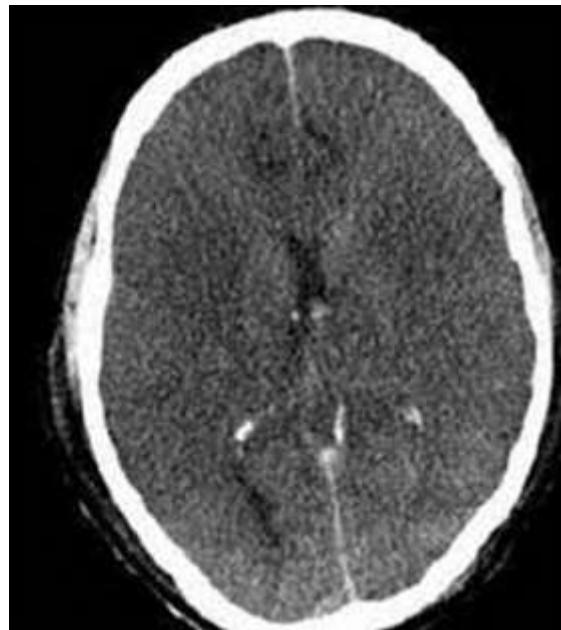
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LA RIVOLUZIONE DEI SISTEMI

Danno anossico diffuso ed esteso alla TC/RMN encefalo

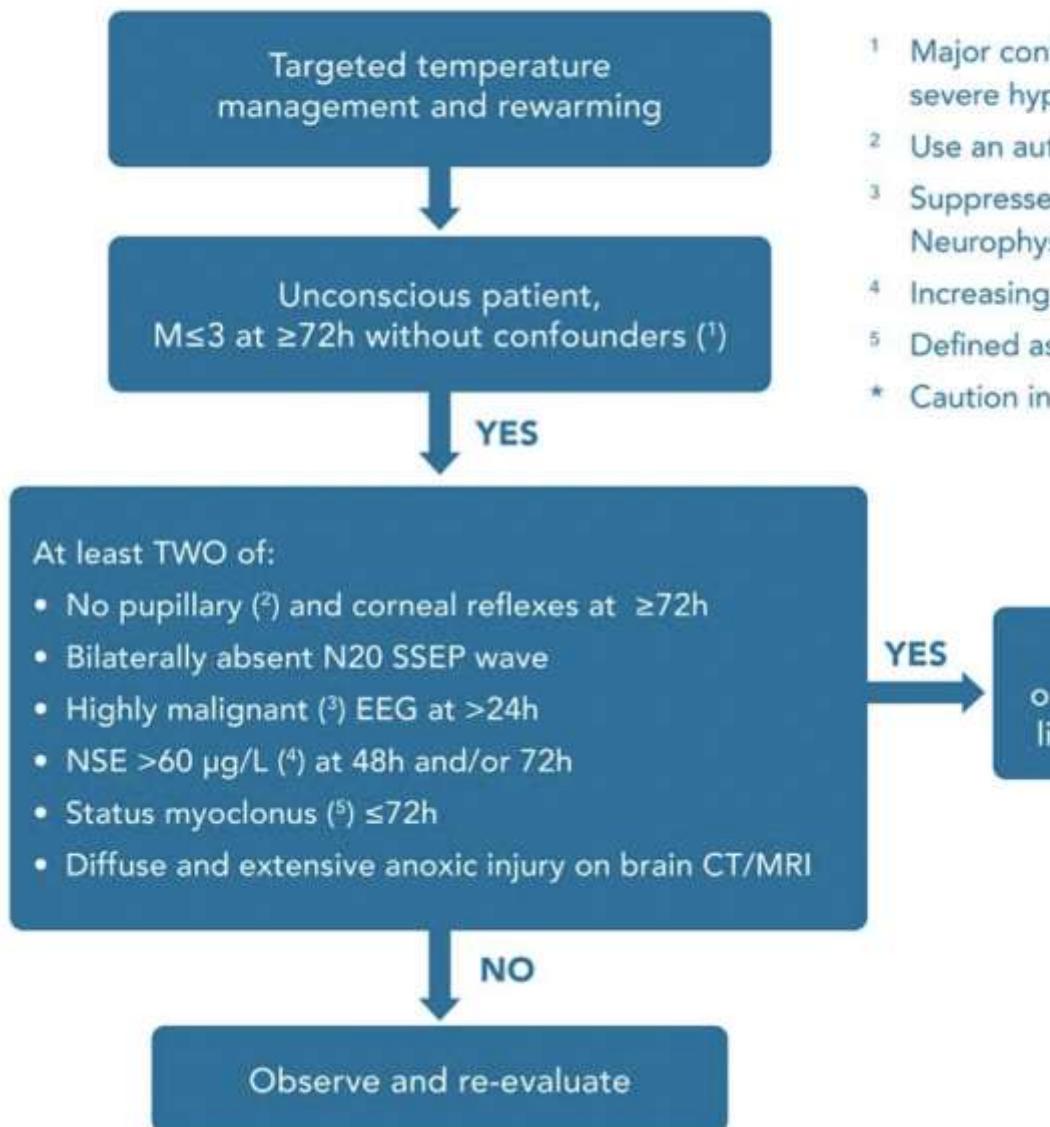


Riduzione del rapporto GM/WM
entro 72 ore dal ROSC



Alterazioni diffuse (DWI o ADC)
entro 7 giorni dal ROSC

NEUROPROGNOSTICATION FOR THE COMATOSE PATIENT AFTER RESUSCITATION FROM CARDIAC ARREST



- ¹ Major confounders may include analgo-sedation, neuromuscular blockade, hypothermia, severe hypotension, hypoglycaemia, sepsis, and metabolic and respiratory derangements
- ² Use an automated pupillometer, when available, to assess pupillary light reflex
- ³ Suppressed background ± periodic discharges or burst-suppression, according to American Clinical Neurophysiology Society
- ⁴ Increasing NSE levels between 24h-48h or 24/48 and 72h further support a likely poor outcome
- ⁵ Defined as a continuous and generalised myoclonus persisting for 10 minutes or more
- * Caution in case of discordant signs indicating a potentially good outcome (see text for details).

Attenzione a
test discordanti

Prognosi favorevole

SYSTEMATIC REVIEW

Prediction of good neurological outcome in comatose survivors of cardiac arrest: a systematic review



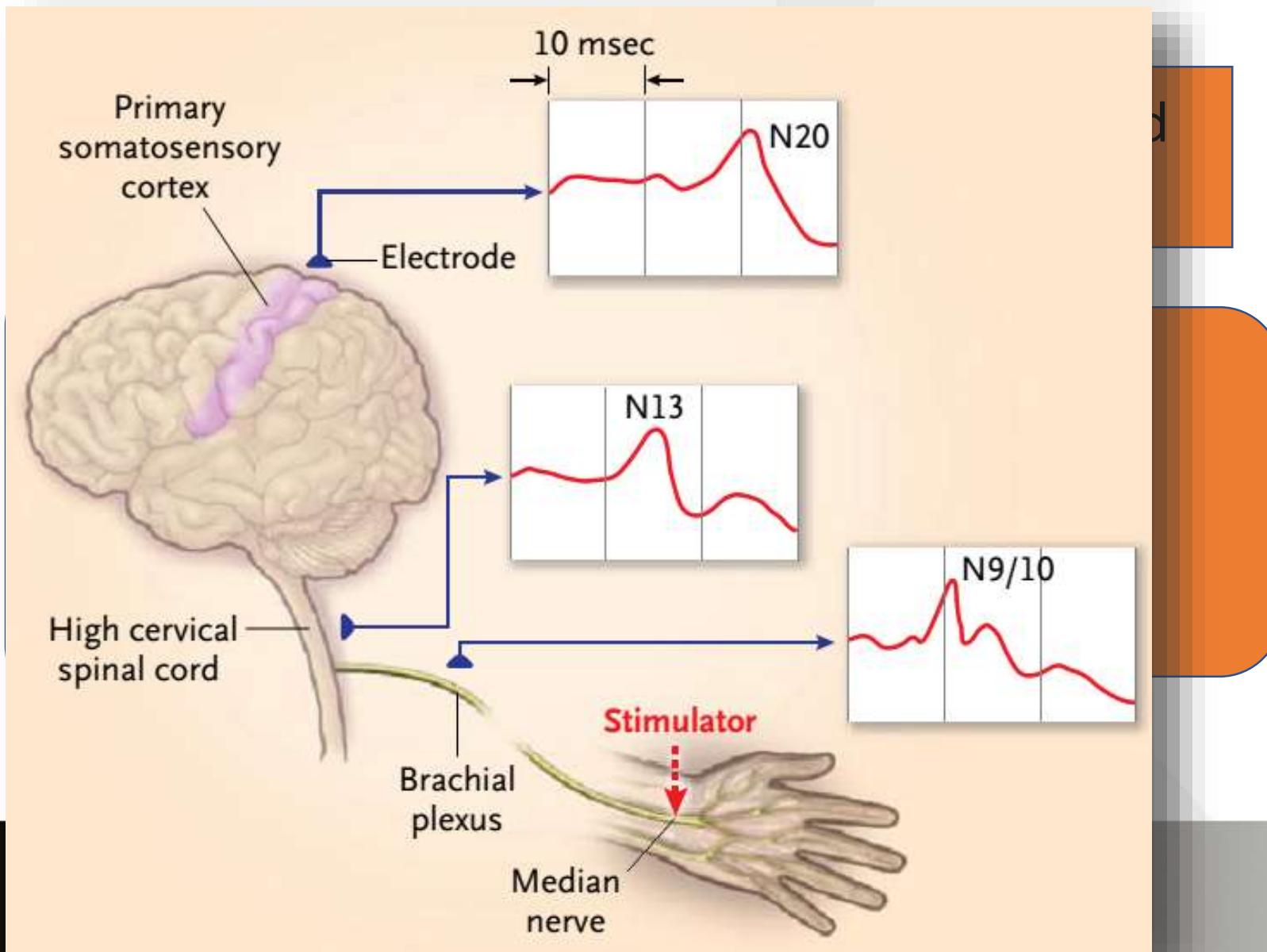
Claudio Sandroni^{1,2}, Sonja D'Arrigo^{1*}, Sofia Cacciola¹, Cornelia W. E. Hoedemaekers³, Erik Westhäll⁴, Marlijn J. A. Kamps⁵, Fabio S. Taccone⁶, Daniele Poole⁷, Frederick J. A. Meijer⁸, Massimo Antonelli^{1,2}, Karen G. Hirsch⁹, Jasmeet Soar¹⁰, Jerry P. Nolan¹¹ and Tobias Cronberg^{1,2}

Specificità > 80%
Sensibilità > 40%

- GCS Motor score 4 o 5 allo stimolo doloroso
- Pattern EEG continuo, con normale voltaggio e reattivo
- N20 presenti con un'ampiezza $\geq 4 \mu\text{V}$
- Bassi livelli o livelli decrementali di enolsi (NSE)
- RMN encefalo normale



Valutazione Neurofisiologiche



Reactivity

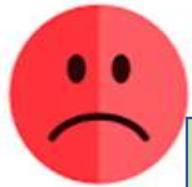
Changes in amplitude or frequency upon external stimulation



THANK YOU

TTM and rewarming

Unconscious, M≤3 at ≥ 72 h without confounders



Almeno DUE di:

- Riflessi pupillare e corneale assente a ≥ 72 ore
- Onda N20 assente bilateralmente ai SSEP a ≥ 24 ore
- Pattern EEG altamente maligno a ≥ 24 ore
- Enolasi $>60 \mu\text{g/L}$ a 48-72 ore
- Stato mioclonico entro le 72 ore
- Danno anossico diffuso ed esteso alla TC/RMN encefalo entro 7 giorni

→ **Si**

Prognosi sfavorevole
altamente probabile
(FPR 5%)

no

Osserva e
rivaluta

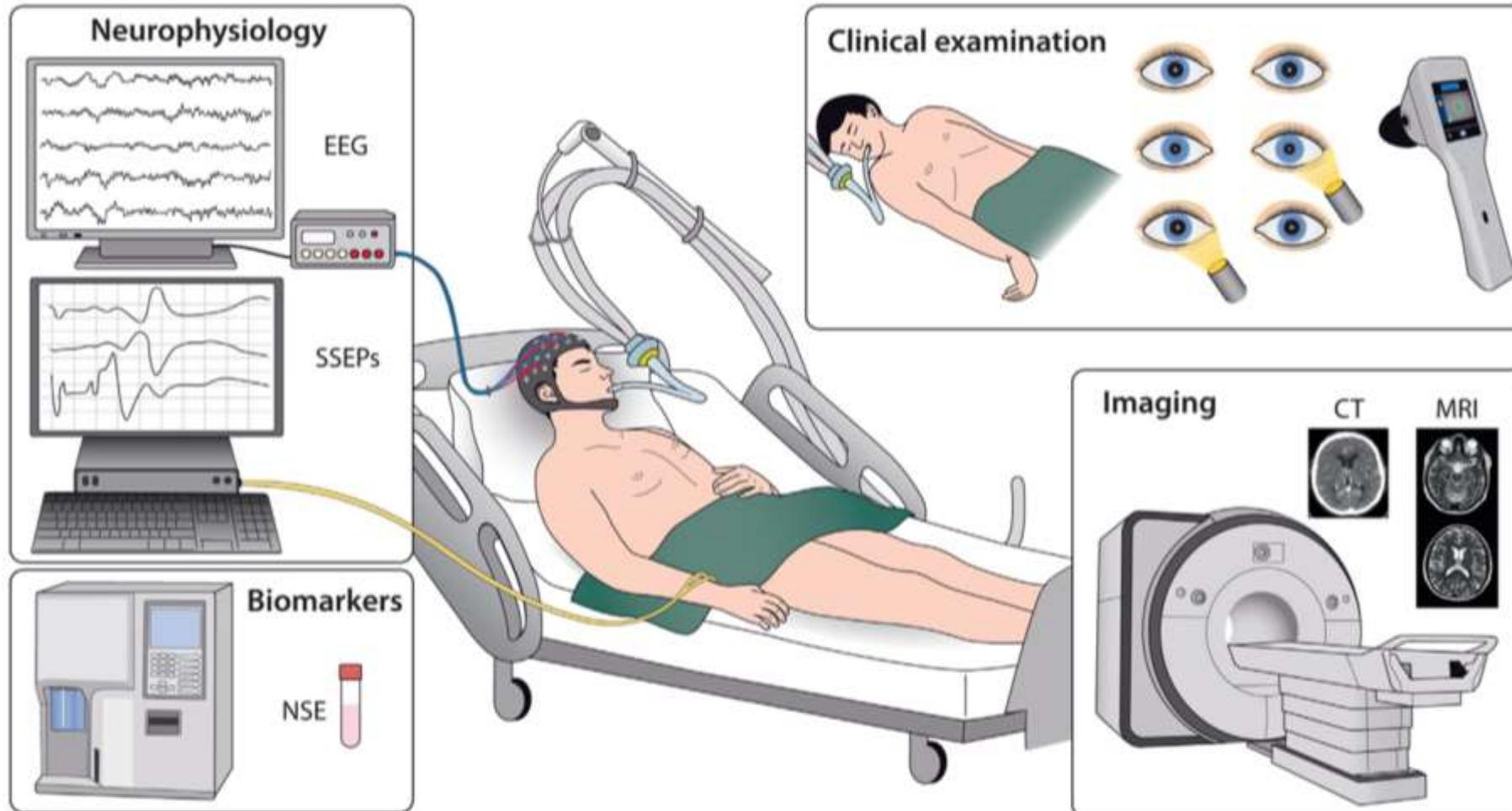
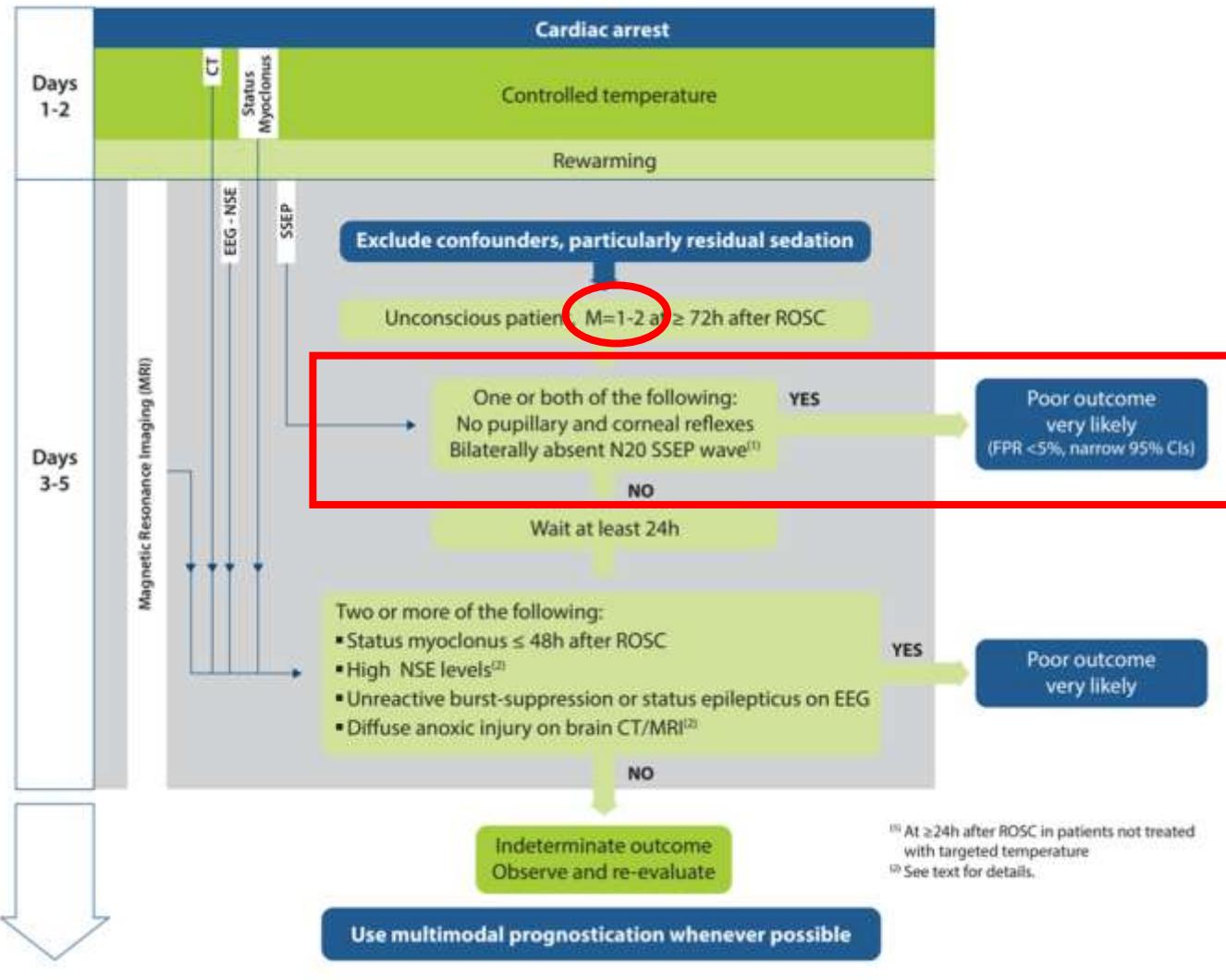


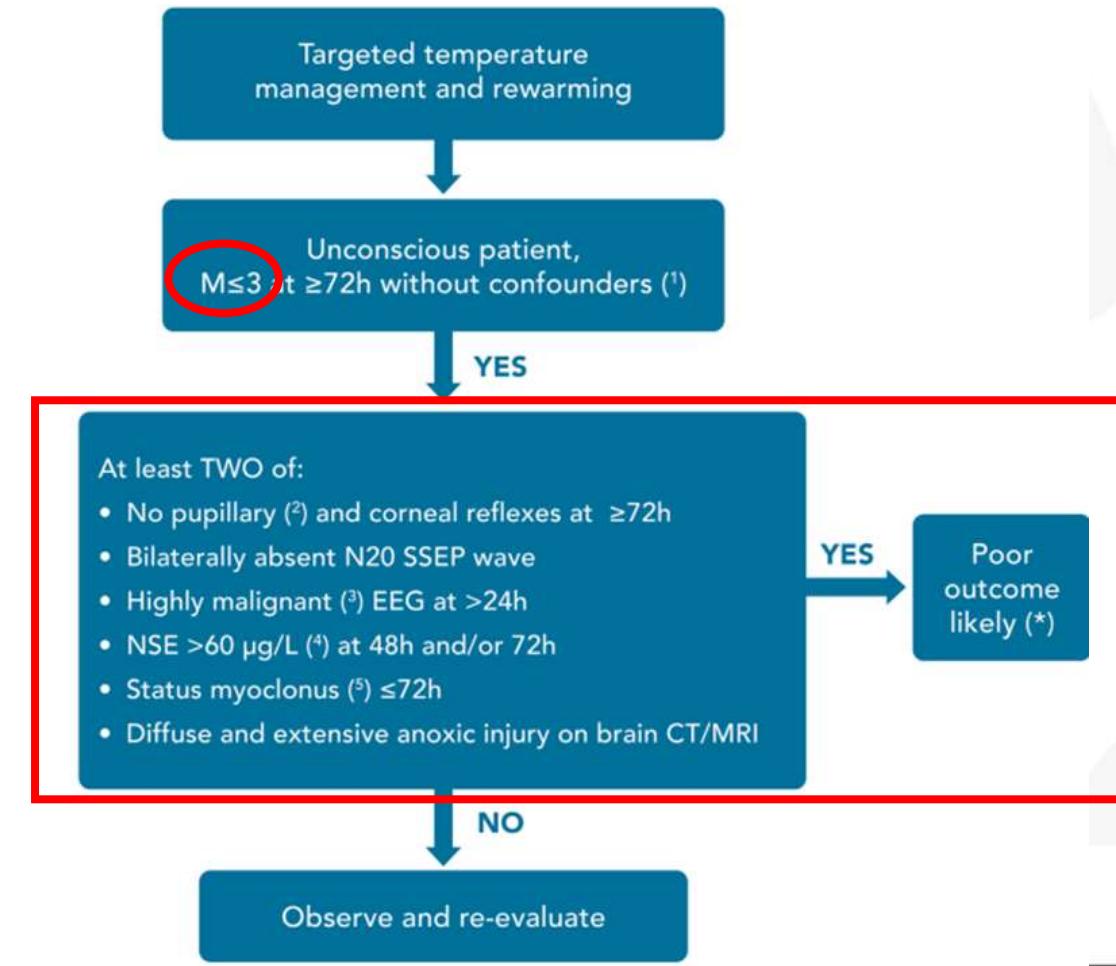
Fig. 4 – Prognostication modes. EEG electroencephalography; NSE neuron specific enolase; SSEP somatosensory evoked potential.



2015 Guidelines



2021 Guidelines



Prognosi favorevole

Intensive Care Med (2022) 48:389–413
<https://doi.org/10.1007/s00134-022-06618-z>

2022



SYSTEMATIC REVIEW

Prediction of good neurological outcome in comatose survivors of cardiac arrest: a systematic review



Claudio Sandroni^{1,2}, Sonia D'Arrigo^{1*} , Sofia Cacciola¹, Cornelia W. E. Hoedemaekers³, Erik Westhall⁴, Marlijn J. A. Kamps⁵, Fabio S. Taccone⁶, Daniele Poole⁷, Frederick J. A. Meijer⁸, Massimo Antonelli^{1,2}, Karen G. Hirsch⁹, Jasmeet Soar¹⁰, Jerry P. Nolan¹¹ and Tobias Cronberg¹²

Prognosi favorevole

SYSTEMATIC REVIEW

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- RMN encefalo normale



Conclusioni

Massimizzare la sicurezza nella prognostication

- Scegliere il predittore più specifico (con basso FPR)
- Strategia multimodale (combinazione di più predittori)
- Non precoce, ma dopo 72-96 ore dall'arresto cardiaco
- Solo dopo aver eliminato tutti i fattori di confondimento
- Con cautela se sono presenti segni discordanti

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