# NEUROPROGNOSTICATION IN AN ICU SETTING

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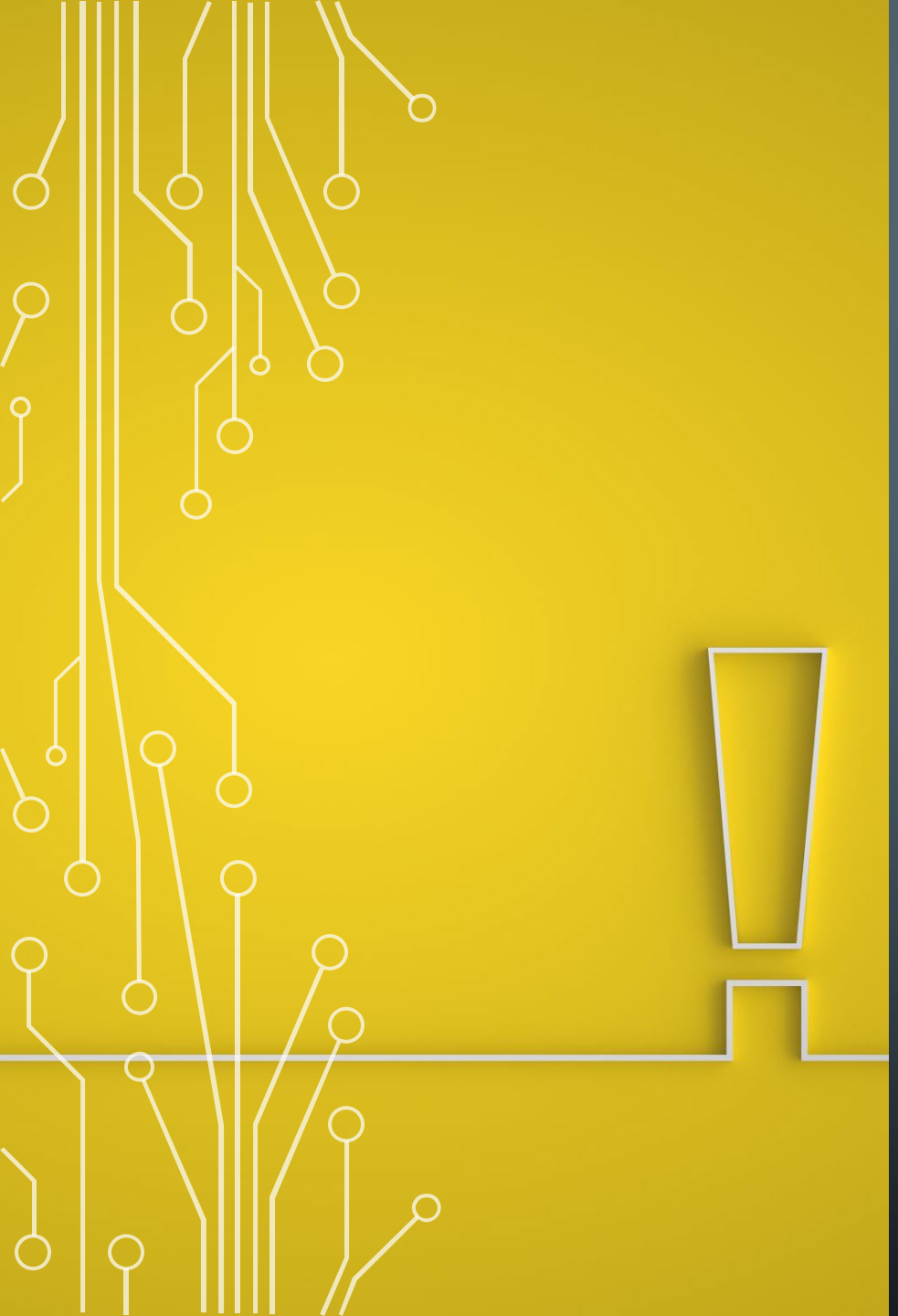
**OCHSNER NEUROSCIENCES SYMPOSIUM**

# DISCLOSURES

- I have no financial disclosures related to this topic or any related vendor.

# NEUROPROGNOSTICATION

- That first question – “Will ____ be ok?”
- Complicated topic with no clear consensus
- Rapidly evolving
- Profound impact



# WHY IS THIS IMPORTANT

- Accurate neuroprognostication allows patients with good prognoses to be supported aggressively, survive, and recover; conversely, it avoids inappropriate prolonged care that may not be aligned with the goals of care in those with devastating injuries.
- Neuroprognostication also guides termination of efforts in cardiac arrest and resuscitation and helps provide closure for families.

# ACCURACY

- Zero false- positive rate when predicting a poor outcome
- Highly sensitive to avoid missing individuals destined to a poor outcome
- The burden of disabling neurologic injury on patients, their families, and communities can be profound

“Treatments should be defined as futile only when they will not accomplish their intended goal. Treatments that are extremely unlikely to be beneficial, are extremely costly, or are of uncertain benefit may be considered inappropriate and hence inadvisable but should not be labeled futile.”

Consensus statement of the Society of Critical Care Medicine's Ethics Committee regarding futile and other possibly inadvisable treatments

# DEVASTATING BRAIN INJURY

- Neurological injury where there is an immediate threat to life from a neurologic cause OR
- Severe neurological insult where early limitation of therapy (defined as treatment of disease) is being considered in favor of an emphasis on care (the provision of comfort measures)
  - Neurocritical Care Society

# NEUROPROGNOSTICATION

- Determine prognosis from repeated examinations over time to establish greater confidence and accuracy.
- Use a 72-hour observation period to determine clinical response and delay decisions regarding withdrawal of life-sustaining treatment in the interim.
- Consider all known prognostic variables in determining risk of death.
- Prognostication should be based on individualized assessment of risk factors, rather than on clinical scoring systems.

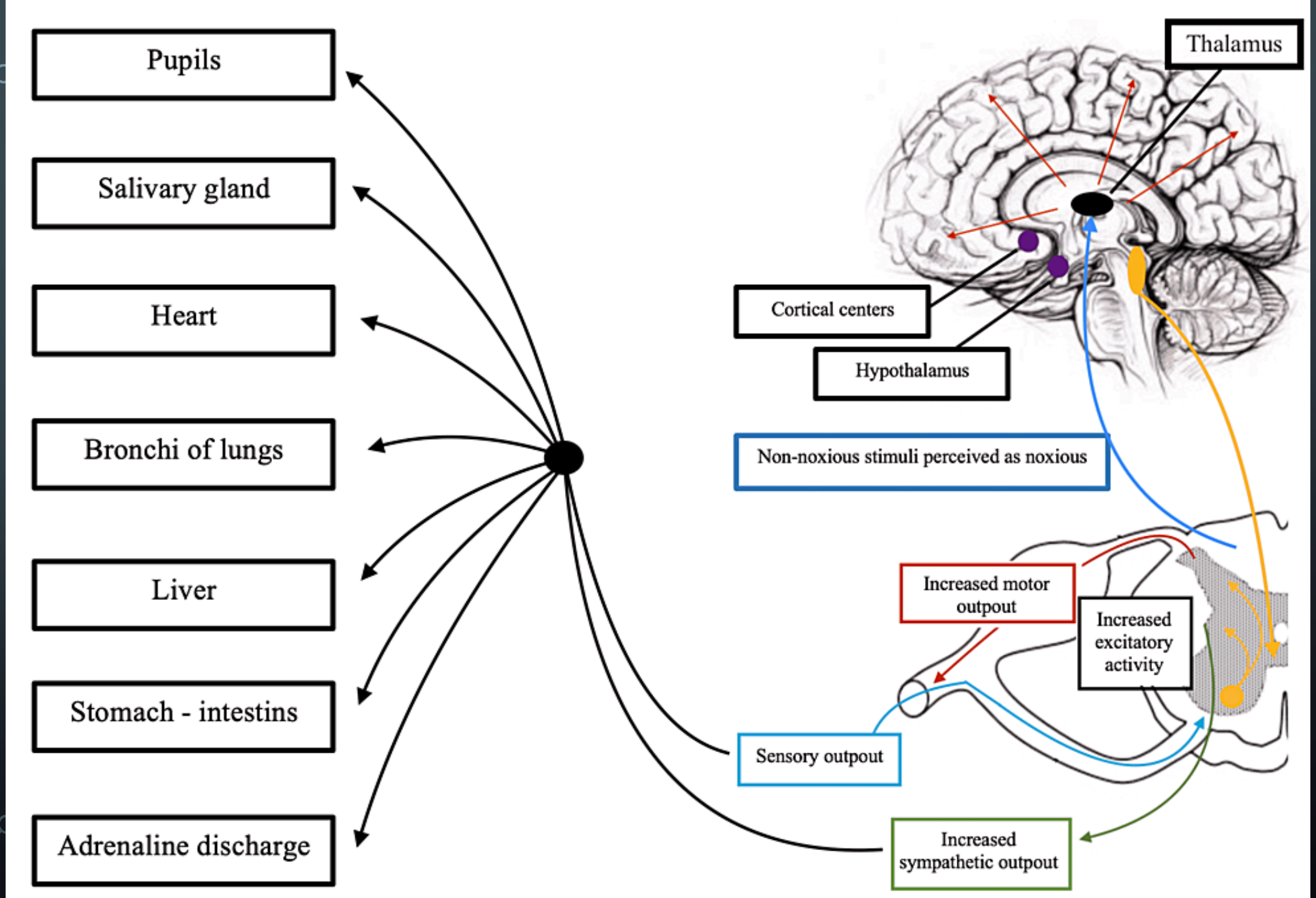
# NEUROPROGNOSTICATION

- Information pertaining to the burden of accrued neurologic injury (both primary and secondary) should be assessed in the context of individual factors pertaining to the potential for recovery and accepted level of disability
- Patient specific
- Overall volume and anatomic location of injured tissue

# EXAM, EXAM, EXAM…..

# NEUROLOGIC EXAM

- Brainstem reflexes and motor responses (ensure no confounders)
- Paroxysmal sympathetic hyperactivity
  - 10% of patients with severe acute brain injuries
  - Patients with paroxysmal sympathetic hyperactivity frequently require high doses of sedating medications and prolonged hospitalizations with worse morbidity and mortality

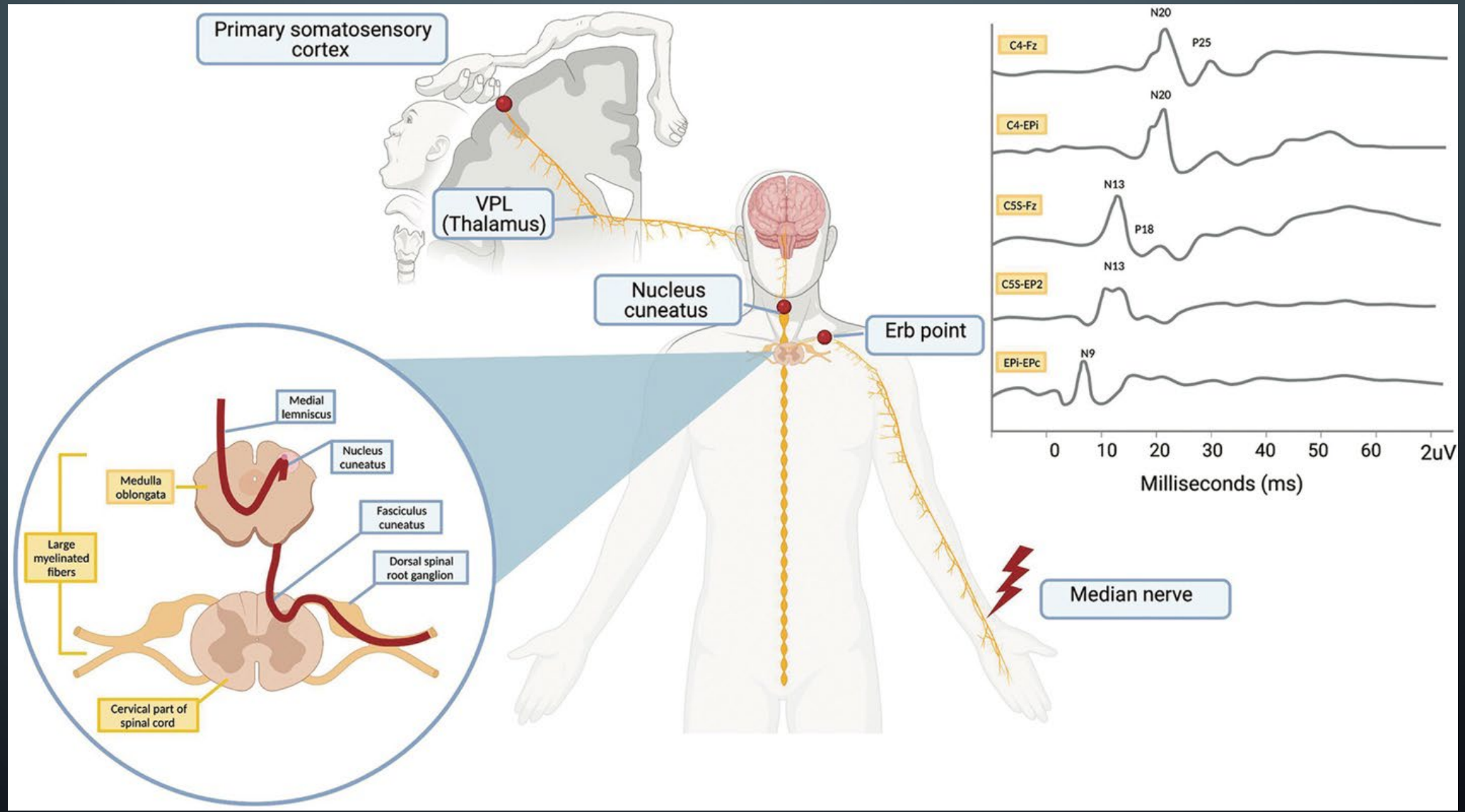

Pupils
Salivary gland
Heart
Bronchi of lungs
Liver
Stomach - intestins
Adrenaline discharge
Thalamus
Cortical centers
Hypothalamus
Non-noxious stimuli perceived as noxious
Increased motor outpout
Increased excitatory activity
Sensory outpout
Increased sympathetic outpout

# NEUROPHYSIOLOGIC TESTING

- EEG
  - Rhythmic and periodic patterns have prognostic utility, particularly in hypoxic-ischemic brain injury.
  - >50% suppression of background activity in the absence of sedation and loss of reactivity when a standardized approach

# NEUROPHYSIOLOGIC TESTING

- Sensory/Motor evoked potentials
  - Bilateral absence of cortical peaks (N20 potentials) following stimulation of median nerves is helpful in predicting poor outcome in hypoxic-ischemic brain injury
  - False-positive rates estimated to be around 25%.
  - Technical limitations also curb the potential for the widespread use of nerve conduction studies and EMG in the evaluation of patients who are critically ill


Primary somatosensory cortex
VPL (Thalamus)
Nucleus cuneatus
Erb point
Median nerve
Medial lemniscus
Nucleus cuneatus
Medulla oblongata
Fasciculus cuneatus
Large myelinated fibers
Dorsal spinal root ganglion
Cervical part of spinal cord
N20
P25
C4-Fz
N20
C4-EPi
N13
P18
C5S-Fz
N13
C5S-EP2
N9
EPi-EPc
0
10
20
30
40
50
60
2uV
Milliseconds (ms)

# NEUROIMAGING

- MRI can provide key information on factors that help estimate the individual's cerebral reserve
  - Burden of microvascular injury or white matter changes, degree of atrophy, and areas of encephalomalacia.

# CHEMICAL BIOMARKERS

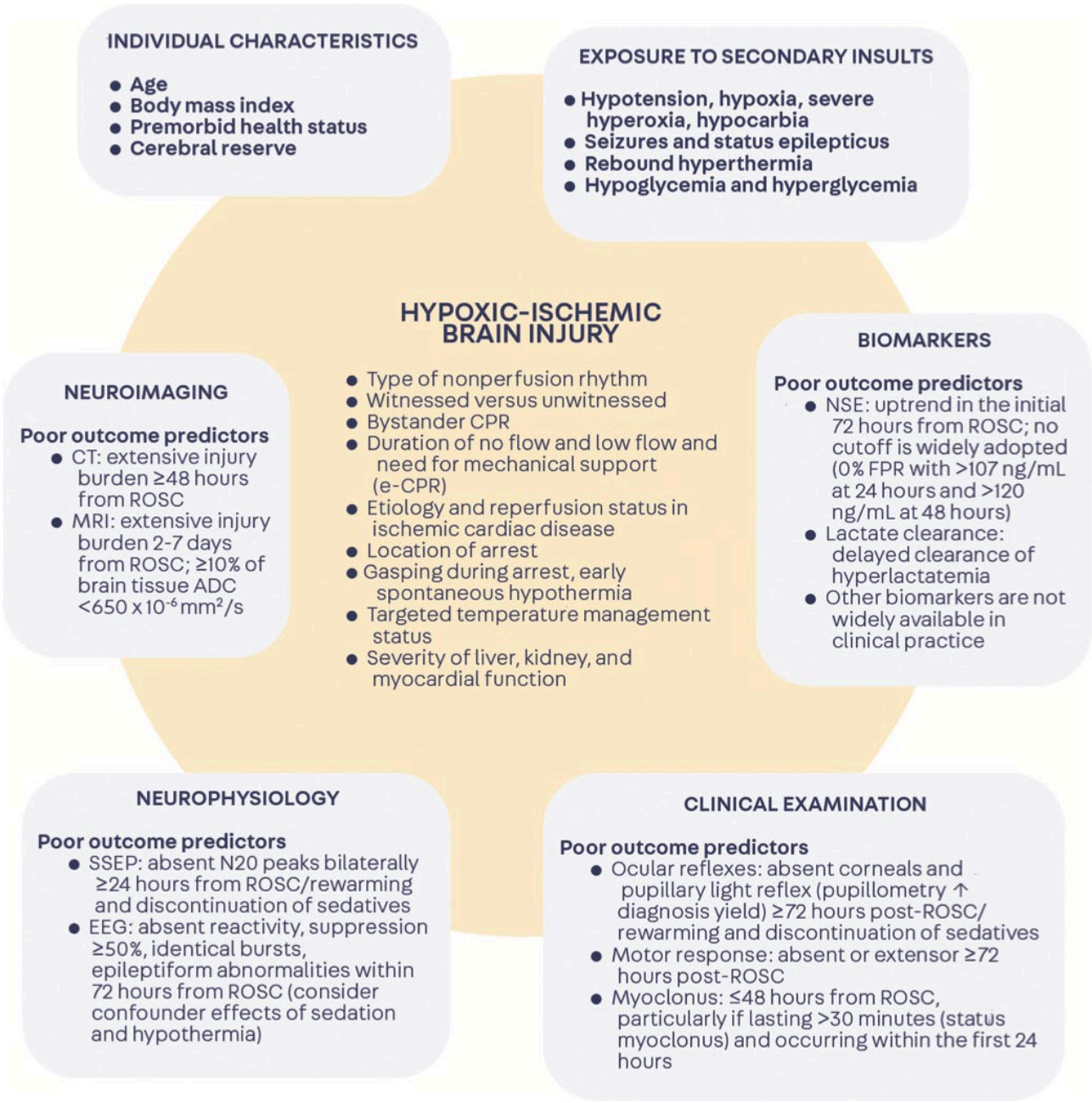
- CSF vs Blood
- Neuron-specific enolase
- Glial fibrillary acidic protein (GFAP)
- Neurofilament light chain
- S100B

# HYPOXIC-ISCHEMIC BRAIN INJURY

- Post cardiac arrest, better outcomes are generally seen in shockable versus nonshockable rhythms, cardiac versus noncardiac etiology, in-hospital cardiac arrest versus out-of-hospital cardiac arrest, witnessed versus unwitnessed events, and when bystander cardiopulmonary resuscitation (CPR) is performed.
- Prompt reperfusion therapies (if ischemic etiology) and targeted temperature management also have higher odds of achieving a favorable outcome
  - Shivering during TTM and early rebound hyperthermia reflect relative sparing of hypothalamic injuries

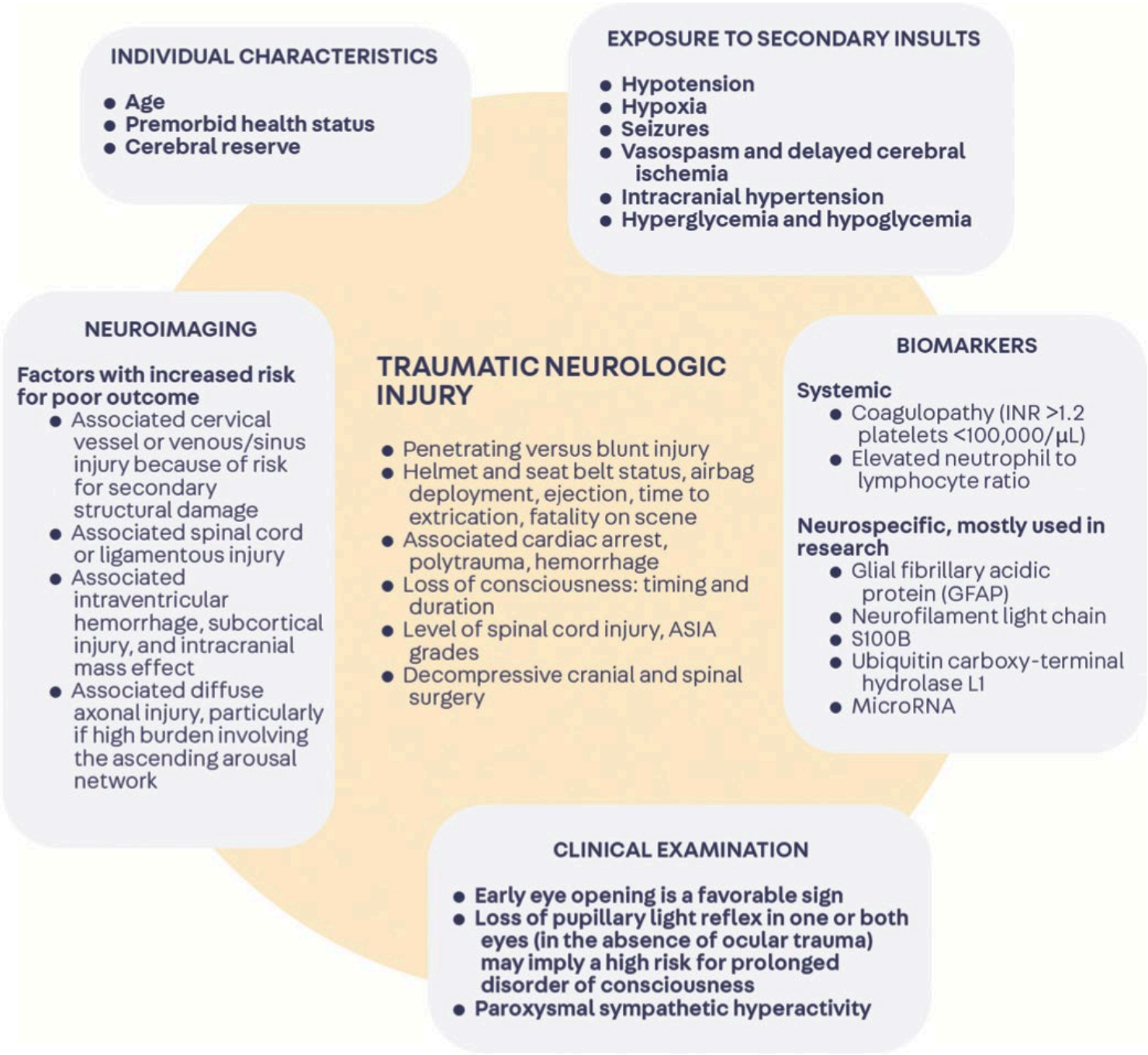
# HYPOXIC-ISCHEMIC BRAIN INJURY

- Exposure to secondary insults
- Poor clinical exam – Brainstem reflexes, absent motor response or myoclonus
- Imaging – Extensive brain injury (location specific)
- Biomarkers – NSE uptrends, persistent hyperlactatemia
- Neurophysiology
  - SSEP w/ absent N20 peaks bilaterally >24 hours post insult
  - EEG w/ absent reactivity, burst suppression or epileptiform abnormalities


INDIVIDUAL CHARACTERISTICS
Age
Body mass index
Premorbid health status
Cerebral reserve
EXPOSURE TO SECONDARY INSULTS
Hypotension, hypoxia, severe hyperoxia, hypocarbia
Seizures and status epilepticus
Rebound hyperthermia
Hypoglycemia and hyperglycemia
HYPOXIC-ISCHEMIC BRAIN INJURY
Type of nonperfusion rhythm
Witnessed versus unwitnessed
Bystander CPR
Duration of no flow and low flow and need for mechanical support (e-CPR)
Etiology and reperfusion status in ischemic cardiac disease
Location of arrest
Gasping during arrest, early spontaneous hypothermia
Targeted temperature management status
Severity of liver, kidney, and myocardial function
NEUROIMAGING
Poor outcome predictors
CT: extensive injury burden ≥48 hours from ROSC
MRI: extensive injury burden 2-7 days from ROSC; ≥10% of brain tissue ADC <650 x 10-6 mm2/s
BIOMARKERS
Poor outcome predictors
NSE: uptrend in the initial 72 hours from ROSC; no cutoff is widely adopted (0% FPR with >107 ng/mL at 24 hours and >120 ng/mL at 48 hours)
Lactate clearance: delayed clearance of hyperlactatemia
Other biomarkers are not widely available in clinical practice
NEUROPHYSIOLOGY
Poor outcome predictors
SSEP: absent N20 peaks bilaterally ≥24 hours from ROSC/rewarming and discontinuation of sedatives
EEG: absent reactivity, suppression ≥50%, identical bursts, epileptiform abnormalities within 72 hours from ROSC (consider confounder effects of sedation and hypothermia)
CLINICAL EXAMINATION
Poor outcome predictors
Ocular reflexes: absent corneals and pupillary light reflex (pupillometry ↑ diagnosis yield) ≥72 hours post-ROSC/ rewarming and discontinuation of sedatives
Motor response: absent or extensor ≥72 hours post-ROSC
Myoclonus: ≤48 hours from ROSC, particularly if lasting >30 minutes (status myoclonus) and occurring within the first 24 hours

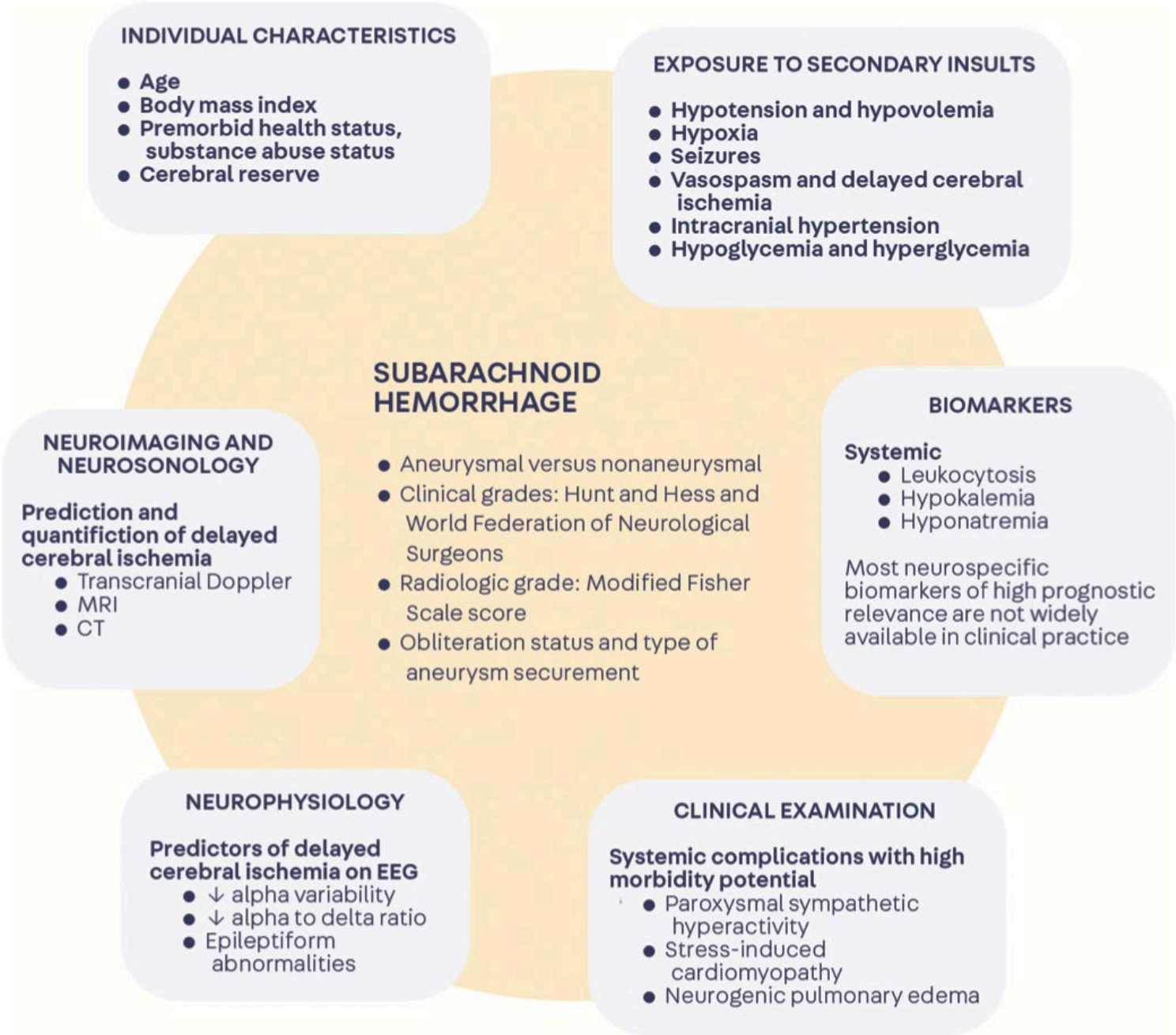
# TRAUMATIC BRAIN INJURY

- Details of the injury mechanism and offered therapies are very important
- Diffuse axonal injury is associated with poor outcomes (depends on grades of severity and predominant location of injury; high burden of injury in specific areas in the brainstem30 and in the corpus callosum appear to reflect the most severe end of this spectrum)
- The occurrence of hypotension and paroxysmal sympathetic hyperactivity, despite being treatable, carries a negative impact on prognosis.


INDIVIDUAL CHARACTERISTICS
Age
Premorbid health status
Cerebral reserve
EXPOSURE TO SECONDARY INSULTS
Hypotension
Hypoxia
Seizures
Vasospasm and delayed cerebral ischemia
Intracranial hypertension
Hyperglycemia and hypoglycemia
NEUROIMAGING
Factors with increased risk for poor outcome
Associated cervical vessel or venous/sinus injury because of risk for secondary structural damage
Associated spinal cord or ligamentous injury
Associated intraventricular hemorrhage, subcortical injury, and intracranial mass effect
Associated diffuse axonal injury, particularly if high burden involving the ascending arousal network
TRAUMATIC NEUROLOGIC INJURY
Penetrating versus blunt injury
Helmet and seat belt status, airbag deployment, ejection, time to extrication, fatality on scene
Associated cardiac arrest, polytrauma, hemorrhage
Loss of consciousness: timing and duration
Level of spinal cord injury, ASIA grades
Decompressive cranial and spinal surgery
BIOMARKERS
Systemic
Coagulopathy (INR >1.2 platelets <100,000/μL)
Elevated neutrophil to lymphocyte ratio
Neurospecific, mostly used in research
Glial fibrillary acidic protein (GFAP)
Neurofilament light chain
S100B
Ubiquitin carboxy-terminal hydrolase L1
MicroRNA
CLINICAL EXAMINATION
Early eye opening is a favorable sign
Loss of pupillary light reflex in one or both eyes (in the absence of ocular trauma) may imply a high risk for prolonged disorder of consciousness
Paroxysmal sympathetic hyperactivity

# SUBARACHNOID HEMORRHAGE

- Many prognostic tools center on the prediction of vasospasm and delayed cerebral ischemia because of their role in secondary brain injury development
  - TCDs, Perfusion scans, Vascular imaging
  - Leukocytosis, Hypokalemia, and Hyponatremia
- Paroxysmal sympathetic hyperactivity
- Stress-induced cardiomyopathy


INDIVIDUAL CHARACTERISTICS
Age
Body mass index
Premorbid health status, substance abuse status
Cerebral reserve
EXPOSURE TO SECONDARY INSULTS
Hypotension and hypovolemia
Hypoxia
Seizures
Vasospasm and delayed cerebral ischemia
Intracranial hypertension
Hypoglycemia and hyperglycemia
SUBARACHNOID HEMORRHAGE
Aneurysmal versus nonaneurysmal
Clinical grades: Hunt and Hess and World Federation of Neurological Surgeons
Radiologic grade: Modified Fisher Scale score
Obliteration status and type of aneurysm securement
NEUROIMAGING AND NEUROSONOLOGY
Prediction and quantifiction of delayed cerebral ischemia
Transcranial Doppler
MRI
CT
BIOMARKERS
Systemic
Leukocytosis
Hypokalemia
Hyponatremia
Most neurospecific biomarkers of high prognostic relevance are not widely available in clinical practice
NEUROPHYSIOLOGY
Predictors of delayed cerebral ischemia on EEG
↓ alpha variability
↓ alpha to delta ratio
Epileptiform abnormalities
CLINICAL EXAMINATION
Systemic complications with high morbidity potential
Paroxysmal sympathetic hyperactivity
Stress-induced cardiomyopathy
Neurogenic pulmonary edema

# FINAL THOUGHTS

- The pillars of modern neuroprognostication include a comprehensive characterization of injury burden, estimation of cerebral resilience and reserve, and the patient's perception of acceptable degree of disability and attitude toward an arduous convalescence journey.
- Ethics, Autonomy and Justice

# THANK YOU.