Functional cerebral monitoring in patients with critically illness

Anne-Marie Guerguerian MD PhD
Assistant Professor of Critical Care Medicine & Pediatrics
Scientist in Neurosciences & Mental Health, Research Institute
Hospital for Sick Children, University of Toronto
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Objectives

(1) Provide an overview of current & innovative approaches available for the assessment of the critically ill patient at risk of neurological injury

(2) Review some indications, potential complications, and expected results

(3) Highlight the exciting potential implementing neuromonitoring using an integrated interdisciplinary approach at the bedside.
How close are we to a brain global functioning positioning system?

Brain global FPS?
Outline

• Preclinical and clinical rationale for measuring cerebral function during critical illness
• What’s feasible with research vs. clinical resources?
• Why it’s important at an
  – Individual level: What does it mean for the patient now and later?
  – Collective level: What can it tell us about the care we deliver?
Preclinical experimental models of acquired brain injury

• Are important but have intrinsic limitations
  – Intended to examine very specific mechanisms & hypotheses, e.g., isolated pathway
  – Specific to species, insult paradigm, outcomes
  – Fail to reproduce duration of critical illness and management
Clinical rationale for integrated neuromonitoring = clinical reality

- Clinical reality = patient
  - Genotype
  - Phenotype
  - Exposure to disease(s) with underlying conditions
  - Exposure therapy(ies)
Preclinical to clinical translation

- Single
- Discrete in *time*
- Clear developmental or age stage
- Pharmacological & environmental exposure are systematic and consistent
- Genetically homogeneous

- Complex
- Continuous and/or repeated
- Age with maturation modifications
- Pharmacological & environmental exposure are variable
- Genetically ?
Cerebral function monitoring

Assumptions about measurement:

Physiologic brain activity = wellness
  - Communication
  - Sleep
  - Pressure regulation

Pathologic brain activity (or change) = badness
  - Coma
  - Delirium
  - Seizure
Functional Neuromonitoring

- Clinical Examination
- SBP, DBP, MBP, CVP
- SpO₂, SaO₂, SvO₂
- PaO₂, PaCO₂, ETCO₂
- Core Temperature
- ECG
- Blood/Serum chemistry
  - Glucose
  - Lactate
  - CPK, Troponin, LFTs
- Blood/Serum biomarkers
- VO₂, DO₂, ERO₂
- Echo
- Imaging

- Clinical Neurofunctional Examination
- ICP, CPP
- ETCO₂, cerebral rSO₂
- Brain tissue oxygenation PbtiO₂
- Core or Brain Temperature
- EEG
- Cerebral extracellular chemistry
  - Glucose
  - Lactate/Pyruvate
  - Glutamate & Glycerol
- Cerebral biomarkers
- Transcranial Doppler Ultrasonography
- Imaging CMRO₂
Computing set up

Main terminal server

Intellivue MP70

Lan

Recording data storage and analysis

Invos ForeSight NIRS RS 232

Analogue/digital convertor

ICU patient bedside area

sFv, cFv and Fv

Dong Joo Kim PhD
Domains & Devices integrated for critically ill patients

- Bedside Monitor
- Pulse Oxymeter
- Ventilator & ECLS
- Cerebral oximetry
- EEG
- Capnograph
- Transcranial Doppler ultrasonography
- ICP
- Extracellular chemistry
- Cerebral microdialysis
- RN
- Clinical Laboratory
- Patient & Family
- Metabolic cart

Judy VanHuyse, Vera Nenadovic & Karen Dryden Palmer
Going beyond the absolute values

CUMULATIVE EXPOSURE
ICP - responses to changes in intracranial compliance

• Absolute values - guide surgical evacuation of intracranial hemorrhages & space occupying lesions

• Repeated values - “ICP and CPP guided” management
Cumulative exposure to secondary injury
Pressure-time index: time x magnitude quantification of secondary CPP insults

Jones 2005, Lo 2009
Cerebral Oxygenation
Direct Brain Tissue

• Tunneled probe inserted into the brain tissue by neurosurgeons
• Probe: thermocouple sensors for $O_2$ and Temperature that measures $O_2$ diffusing from tissue
• $P_{btiO_2} > 25-30$ mmHg
• Device: Monitor & Probes by Licox®
Hyperventilation associated with: decreased cerebral blood flow and brain tissue hypoxemia

Gopinath 1999
Survival & Duration of time below PbtiO$_2$

Survivors spend less time at a low PbtiO$_2$

Adults after Subarachnoid Hemorrhage

Ramakrishna & Leroux 2008
Going beyond the absolute values

NEUROVASCULAR UNIT FUNCTION?
Continuous monitoring of cerebrovascular pressure reactivity after traumatic brain injury

A

B

PRx = -0.54

C

D

PRx = 0.99

Brady 2009
Beyond the absolute values

BEDSIDE TCD & CEREBRAL OXIMETRY
Cerebral blood flow velocity and autoregulation index after pediatric traumatic brain injury

MCA flow velocity & ABP

- Autoregulation index testing & Cerebral hemodynamic predictors of poor 6-month Glasgow Outcome Score in severe pediatric traumatic brain injury

Aaslid
Vavilala 2006
+ Chawait 2009,
+ Udumphorn 2008,
(-) Figaji 2009
Impaired pressure regulation during CPB rewarming using MXa

Joshi 2010
Regional cerebral oxygenation saturation estimated by near infrared technology
Noninvasive infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters

Jobsis 1977
Cerebral oxygen saturation
rScO2
Methodology: NIRS
Near Infrared Spectroscopy
Device: INVOS®
Unit: %
Expected Normal: 50-90 %
Pressure regulation estimated with cerebral oxygenation measured by near-infrared spectroscopy

Lee 2009
Early efficacy endpoints? RCT surgical managements in neonatal congenital heart disease
Beyond the absolute values

CONTINUOUS EEG
Coma and seizures after hypoxic ischemic injury from cardiac arrest

Mueller 1968...Sherman 1999; Agnew 2003, Shahwan 2010
EEG monitoring during hypothermia after pediatric cardiac arrest

Abend 2009
Quantitative EEG correlates of low cerebral perfusion in severe stroke

Left stroke

Diedler 2009
Fluctuations in cortical synchronization in pediatric traumatic brain injury
Patient A (PCPC = 1)  Patient B (PCPC = 4)  Control Subject
Can extracellular milieu inform us on cerebral function?

- Cerebral tissue oxygen levels
- Brain tissue **extracellular space** chemistry with cerebral microdialysis
  - Glucose: energy substrate
  - Lactate/Pyruvate: indicator of anaerobic metabolism & ischemia
  - Glutamate: indicator of synaptic dysfunction or cell damage
  - Glycerol: indicator of cell membrane breakdown
- Bedside clinical applications was pioneered in Sweden
- 2004 FDA Workshop: role to enhance preclinical to clinical transition of therapy development?
- Pharmacology *Bullock*
- Biomarkers... cytokines *C. Roberston*
Cyclosporin A Preserves Mitochondrial Function after Traumatic Brain Injury in the Immature Rat and Piglet  

Kilbaugh et al 2011

Metabolism

Cerebral blood flow

Anatomical structure

Lactate/Pyruvate Ratio

Cerebral blood flow

Axonal Injury & Ischemic Volume
Remaining Limitations and Challenges

• Uncertainty
  – validity, reliability, assumptions, generalizability
  – risks, Hawthorn effects...

• Practical considerations:
  – Computing challenges
  – Complexity at the bedside
  – Costs
Quoi ? Ça coûte quelque chose ?
Exposure to disease & exposure to care

Clinical guideline for intervention and co-interventions

Acquired Brain Injury & Critical Illness Management

Protocol for intervention & co-interventions

Acquired Brain Injury & Critical Illness Management

Acquired brain injury
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