Monitoring the Brain

Michael Ramsay MD FRCA
Chairman Department of Anesthesia
Baylor University Medical Center
President Baylor Research Institute
Dallas Texas
Speaker Disclosure

I have received research grants and honoraria from Masimo Inc.
Cognition
The Biological Cost of the Depression of Consciousness
Long-Term Cognitive Impairment after Critical Illness


- Patients in medical and surgical ICUs are at a high risk for long-term cognitive impairment. A longer duration of delirium in the hospital was associated with worse global cognition and executive function scores at 3 months (40%)(P=0.001) and 12 months (34%)(P=0.004)

- 40% equivalent to TBI

- 26% equivalent to mild Alzheimer’s
Manifestations of CNS Failure in ICU

- Delirium
- Agitation
- Coma
  - Linked to increased short-term morbidity and mortality and long-term functional disability
Causes of Neurologic Failure

- Trauma
- Circulatory shock
- Hypoxemia
- Infection
- Systemic inflammation
- Metabolic and endocrine imbalances
- Pharmacologic agents
- Trauma
Traumatic Brain Injury

- Evacuate hematoma
- Maintain cerebral perfusion
- Control Intracranial pressure
Study of therapeutic hypothermia (32 to 35°C) for intracranial pressure reduction after traumatic brain injury (the Eurotherm3235Trial): outcome of the pilot phase of the trial

Peter J D Andrews¹*, Louise H Sinclair¹, Bridget Harris¹, Melissa J Baldwin², Claire G Battison¹, Jonathan K J Rhodes¹, Gordon Murray³, Daniel De Backer⁴ and On behalf of the Eurotherm3235Trial collaborators
Acute Brain Dysfunction During Critical Illness – Result of Inflammation Causing Endothelial Dysfunction
Hughes et al.
Major Surgery Promotes an Inflammatory Response

- Increased levels of IL6 are associated with:
  - Postoperative left ventricular wall motion abnormalities
  - Myocardial ischemic episodes
  - The severity of adult respiratory distress syndrome postoperatively
  - Postoperative morbidity and mortality in children after open-heart surgery,
Surgery and POCD

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Peripheral systemic response</th>
<th>CNS response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>Cellular damage</td>
<td>Neuroinflammation</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Endogenous DAMPs</td>
<td>Proteinopathies</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>Cytokines</td>
<td>Neurotoxicity</td>
</tr>
<tr>
<td>Drugs</td>
<td>Innate immunity</td>
<td></td>
</tr>
</tbody>
</table>

DAMPs: Damage-Associated Molecular Patterns
Role of Interleukin-1β in Postoperative Cognitive Dysfunction

Mario Cibelli, MD, PhD,1,2 Antonio Rei Fidalgo, MSc,1 Niccolò Terrando, PhD,1,3 Daqing Ma, MD, PhD,1 Claudia Monaco, MD, PhD,4 Marc Feldmann, MD, PhD,4 Masao Takata, MD, PhD,1 Isobel J. Lever, PhD,1 Jagdeep Nanchahal, MBBS, PhD,4 Michael S. Fanselow, PhD,5 and Mervyn Maze, MB, ChB1,3

Objective: Although postoperative cognitive dysfunction (POCD) often complicates recovery from major surgery, the pathogenic mechanisms remain unknown. We explored whether systemic inflammation, in response to surgical trauma, triggers hippocampal inflammation and subsequent memory impairment, in a mouse model of orthopedic surgery.

Methods: C57BL/6J, knock out (lacking interleukin [IL]-1 receptor, IL-1R−/−) and wild type mice underwent surgery of the tibia under general anesthesia. Separate cohorts of animals were tested for memory function with fear conditioning tests, or euthanized at different times to assess levels of systemic and hippocampal cytokines and microglial activation; the effects of interventions, designed to interrupt inflammation (specifically and nonspecifically), were also assessed.

Results: Surgery caused hippocampal-dependent memory impairment that was associated with increased plasma cytokines, as well as reactive microgliosis and IL-1β transcription and expression in the hippocampus. Nonspecific attenuation of innate immunity with minocycline prevented surgery-induced changes. Functional inhibition of IL-1β, both in mice pretreated with IL-1 receptor antagonist and in IL-1R−/− mice, mitigated the neuroinflammatory effects of surgery and memory dysfunction.

Interpretation: A peripheral surgery-induced innate immune response triggers an IL-1β-mediated inflammatory process in the hippocampus that underlies memory impairment. This may represent a viable target to interrupt the pathogenesis of postoperative cognitive dysfunction.

ANN NEUROL 2010;68:360–368
Alarming knowledge of football concussions grows

by Thomas C. Fox | Nov. 9, 2013

Several days ago I received the following article from NCR reader Jim Ewens, a graduate of Marquette High School in Milwaukee, Wisconsin from where I also graduated. He writes of the growing – and alarming – understanding we are gaining of football related brain injuries from repeated concussions. We now know these concussions can lead to long-term disabilities and even death.
Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

Juliana Barr, MD, FCCM; Gilles L. Fraser, PharmD, FCCM; Kathleen Puntillo, RN, PhD, FAAN, FCCM; E. Wesley Ely, MD, MPH, FACP, FCCM; Céline Gélinas, RN, PhD; Joseph F. Dasta, MSc, FCCM, FCCP; Judy E. Davidson, DNP, RN; John W. Devlin, PharmD, FCCM, FCCP; John P. Kress, MD; Aaron M. Joffe, DO; Douglas B. Coursin, MD; Daniel L. Herr, MD, MS, FCCM; Avery Tung, MD; Bryce R. H. Robinson, MD, FACS; Dorrie K. Fontaine, PhD, RN, FAAN; Michael A. Ramsay, MD; Richard R. Riker, MD, FCCM; Curtis N. Sessler, MD, FCCP, FCCM; Brenda Pun, MSN, RN, ACNP; Yoanna Skrobik, MD, FRCP; Roman Jaeschke, MD
SCCM 2013 PAD Guidelines

• Routinely monitor for delirium

• Confusion Assessment Method in the ICU (CAM-ICU)

• Intensive Care Delirium Screening Checklist (ICDSC)
  • most valid & reliable delirium monitoring tools

• Quick & reliable
Sequelae of Delirium

During the ICU/Hospital Stay
- Increased mortality
- Longer intubation time
- Average 10 additional days in hospital
- Higher costs of care

After Hospital Discharge
- Increased mortality
- Development of dementia
- Long-term cognitive impairment
- Requirement for care in chronic care facility
- Decreased functional status at 6 months

Over Sedation in ICU

- Excessive sustained alteration in consciousness
- Prolonged time on mechanical ventilation
- Increased ventilator associated pneumonia
- Increased prolonged muscular weakness
  - Annals of Intensive Care 2013, 3:24
“But what I see these days are sedated patients, lying without motion, appearing to be dead, except for the monitors that tell me otherwise..... By being awake and alert...they could interact with family.....feel human...sustain the zest for living which is a requirement for survival”
One Year Outcomes in Survivors of ARDS  
Herridge et al. NEMJ 2003;348:683-93

- Functional limitations 1 year later
- Most patients have muscle wasting and weakness.
- **Neurocognitive impairments.**  
- Depression and memory dysfunction increased in ARDS survivors.  
  Chest 2009;135:678
Ramsay Sedation Scale

1. Anxious and agitated or restless or both
2. Cooperative, oriented, and tranquil
3. Responding to commands only
4. Asleep, brisk response to stimuli*
5. Asleep, sluggish response to stimuli*
6. Asleep, no response to stimuli*

* light glabellar tap

## Sedation-Agitation Scale (SAS)

<table>
<thead>
<tr>
<th>Score</th>
<th>State</th>
<th>Behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Dangerous Agitation</td>
<td>Pulling at ET tube, climbing over bedrail, striking at staff, thrashing side-to-side</td>
</tr>
<tr>
<td>6</td>
<td>Very Agitated</td>
<td>Does not calm despite frequent verbal reminding, requires physical restraints</td>
</tr>
<tr>
<td>5</td>
<td>Agitated</td>
<td>Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions</td>
</tr>
<tr>
<td>4</td>
<td>Calm and Cooperative</td>
<td>Calm, awakens easily, follows commands</td>
</tr>
<tr>
<td>3</td>
<td>Sedated</td>
<td>Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off</td>
</tr>
<tr>
<td>2</td>
<td>Very Sedated</td>
<td>Arouses to physical stimuli but does not communicate or follow commands</td>
</tr>
<tr>
<td>1</td>
<td>Unarousable</td>
<td>Minimal or no response to noxious stimuli, does not communicate or follow commands</td>
</tr>
</tbody>
</table>

# Richmond Agitation Sedation Scale (RASS)

<table>
<thead>
<tr>
<th>Score</th>
<th>State</th>
<th>Verbal Stimulus</th>
<th>Physical Stimulus</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 4</td>
<td>Combative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ 3</td>
<td>Very agitated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ 2</td>
<td>Agitated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ 1</td>
<td>Restless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>eye contact &gt; 10 sec</td>
<td></td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>eye contact &lt; 10 sec</td>
<td></td>
</tr>
<tr>
<td>-3</td>
<td>Moderate sedation</td>
<td>no eye contact</td>
<td></td>
</tr>
<tr>
<td>-4</td>
<td>Deep sedation</td>
<td>physical stimulation</td>
<td></td>
</tr>
<tr>
<td>-5</td>
<td>Unarousable</td>
<td>no response even with physical</td>
<td></td>
</tr>
</tbody>
</table>

# GLASCOW COMA SCALE

## Glasgow Coma Score

<table>
<thead>
<tr>
<th>Eye Opening (E)</th>
<th>Verbal Response (V)</th>
<th>Motor Response (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4=Spontaneous</td>
<td>5=Normal conversation</td>
<td>6=Normal</td>
</tr>
<tr>
<td>3=To voice</td>
<td>4=Disoriented conversation</td>
<td>5=Localizes to pain</td>
</tr>
<tr>
<td>2=To pain</td>
<td>3=Words, but not coherent</td>
<td>4=Withdraws to pain</td>
</tr>
<tr>
<td>1=None</td>
<td>2=No words......only sounds</td>
<td>3=Decorticate posture</td>
</tr>
<tr>
<td></td>
<td>1=None</td>
<td>2=Decerebrate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1=None</td>
</tr>
</tbody>
</table>

**Total = E+V+M**

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11/21/2013 11:30 AM

Teasdale & Jennett 1974
Sedation Scales

Courtesy of R. Riker, MD
Sedation

• Controlled **lighter sedation** better than deeper sedation

• Maintain **cognitive function**
  • Shorter length mechanical ventilation, LOS in ICU and hospital
SCCM Guidelines

- Monitor for depth of sedation
  - Use protocols for monitoring, reassess regularly

- Richmond agitation sedation scale (RASS) & Sedation-Agitation Scale (SAS) most valid & reliable scales for assessing quality & Depth of Sedation: (Ramsay Sedation Scale most simple and most used)

- Recommend objective measures of brain function (BIS, Sedline (PSI), SE, AEP, & NI) as 1st method to monitor Depth of Sedation in comatose and/or paralyzed patients. Monitor EEG for non-convulsive seizure activity
iv. We recommend that EEG monitoring be used to monitor nonconvulsive seizure activity in adult ICU patients with either known or suspected seizures, or to titrate electroencephalographic suppression to achieve burst suppression in adult ICU patients with elevated intracranial pressure (+1A).
EEG: Typical Absence Seizure
Scientific Basis for Monitoring EEG

- EEG is tightly linked to cerebral metabolism
- EEG is sensitive to common causes of cerebral injury: ischemia and hypoxia
- EEG detects neuronal dysfunction at a reversible stage
- EEG detects neuronal recovery before clinical signs
- EEG best technology for detecting epileptic activity
- Continuous EEG provides dynamic information not just a snapshot
Brain Monitoring

- The EEG has a long history of use in the ICU
- A routine EEG recording lasts around 30 minutes
- Electrode failure and artifact impede the quality
- Pathological events are missed because record is short
- New resilient brain function monitors allow continual monitoring
- Enhanced signal extraction allows diagnostic and prognostic value
Fig. 4. (A) In the 10/20 convention, odd numbers refer to placements over the left hemisphere, even numbers refer to placements over to the right hemisphere, and Z refers to midline locations. Uppercase letters indicate underlying brain regions; C = central; F = frontal; Fp = frontopolar; O = occipital; P = parietal; T = temporal. (B) Sample of electroencephalographic recording. Each tracing comes from 1 of the 19 electrodes in the 10/20 array, positioned according to the labels at the left side of each trace. An artifact-free segment lies in the region above the two arrowheads on the bottom line.
BIS VISTA

Connect SRS Electrodes to Patient

Continue

60
Electrodes on the forehead cover the frontalis muscle
EEG Artifact Problem - EMG

Fig 1 Schematic representation of possible mechanisms through which muscle relaxation may influence depth of anesthesia (DOA), or what is measured as depth of anesthesia (DOA index). (1): muscle relaxation...
Pattern Recognition

The Brain is NOT a number
Representative electroencephalogram (EEG) patterns at different stages of anesthesia

4 Simultaneous Channels of EEG
EEG is mostly Beta
Typical EEG prior to Induction
At 69 it’s becoming easier to really see how the waves are changing.
The EEG slows to more Delta Waves
General anesthesia, slow big waves (mostly Delta)
Deeper Anesthesia – Slower larger waves
Deeper with slower bigger waves
“Burst Suppression”
More “Burst Suppression”
Isoelectric: COMA
Electroencephalogram signatures of loss and recovery of consciousness from propofol

Patrick L. Purdon\textsuperscript{a,b,1}, Eric T. Pierce\textsuperscript{a}, Eran A. Mukamel\textsuperscript{c,d}, Michael J. Prerau\textsuperscript{a}, John L. Walsh\textsuperscript{a}, Kin Foon K. Wong\textsuperscript{a}, Andres F. Salazar-Gomez\textsuperscript{a}, Priscilla G. Harrell\textsuperscript{a}, Aaron L. Sampson\textsuperscript{a}, Aylin Cimenser\textsuperscript{a}, ShiNung Ching\textsuperscript{a,b}, Nancy J. Kopell\textsuperscript{a,1}, Casie Tavares-Stoeckel\textsuperscript{a}, Kathleen Habeeb\textsuperscript{a}, Rebecca Merhar\textsuperscript{a}, and Emery N. Brown\textsuperscript{a,b,g,h,1}

\textsuperscript{a}Department of Anesthesia, Critical Care, and Pain Medicine, and \textsuperscript{1}Clinical Research Center, Massachusetts General Hospital, Boston, MA 02114; \textsuperscript{b}Department of Brain and Cognitive Sciences, \textsuperscript{c}Division of Health Sciences and Technology, and \textsuperscript{h}Institute for Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, MA 02139; \textsuperscript{d}Center for Brain Science, Harvard University, Cambridge, MA 02139; \textsuperscript{e}Center for Theoretical Biological Physics, University of California at San Diego, La Jolla, CA 92093; and \textsuperscript{f}Department of Mathematics and Statistics, Boston University, Boston, MA 02215

Proceedings of the National Academy of Science 2013; Published ahead of print March 4\textsuperscript{th} 2013.
Trough Max = Transition
Peak Max = Deep
EEG: Partial Seizure

Right Frontal seizure
EEG: Partial Seizure

Continuation of the same seizure with change in amplitude and frequency
EEG: Partial Seizure

Continuation of the same seizure with spread to the other hemisphere
Prognosis after Cardiac Arrest

- Burst suppression or generalized epileptiform discharges are associated with poor outcomes.

## Classification of EEG Findings Post CPR

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Dominant, normal alpha activity</td>
</tr>
<tr>
<td></td>
<td>Dominant, normal alpha activity with theta-delta activities</td>
</tr>
<tr>
<td>Grade II</td>
<td>Dominant theta-delta activity with still detectable normal alpha activities</td>
</tr>
<tr>
<td>Grade III</td>
<td>Theta-delta activity without alpha activities</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Delta activity, low voltage, possibly with short isoelectric intervals</td>
</tr>
<tr>
<td></td>
<td>Dominant, monomorphic, nonreactive alpha activity (alpha coma)</td>
</tr>
<tr>
<td></td>
<td>Periodic generalized phenomena (spikes, sharp waves, slow waves) with very low-voltage background activity</td>
</tr>
<tr>
<td>Grade V</td>
<td>Very flat to isoelectric EEG (less than 10–20 mV)</td>
</tr>
</tbody>
</table>

Kaplan PW Sem Neuro 2006; 26:403-411
<table>
<thead>
<tr>
<th>Electroencephalogram category</th>
<th>Recovery (%)</th>
<th>Survival with permanent neurologic damage (%)</th>
<th>Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>79</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Grade II</td>
<td>51</td>
<td>13</td>
<td>36</td>
</tr>
<tr>
<td>Grade III</td>
<td>26</td>
<td>7</td>
<td>67</td>
</tr>
<tr>
<td>Grade IV</td>
<td>0</td>
<td>2</td>
<td>98</td>
</tr>
<tr>
<td>Grade V</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Prognosis with the five electroencephalogram grades given (408 cases from the literature)
Reactivity of EEG

J Crit Care 2010;25:300-4
EEG Changes with Altered Mental Function - Delirium

- Generalized decrease in fast frequency
- Prominent delta and theta waves
- Loss of reactivity to eye opening
Example of Asymmetrical DSA Post Severe Left-Side Trauma
Proof of concept evaluation of the electroencephalophone as a discriminator between wakefulness and general anaesthesia

J. Glen¹*, B. Porr², R. Hamilton¹ and L. Tait¹

¹ Southern General Hospital, Glasgow, UK
² School of Engineering, University of Glasgow, UK
* Corresponding author. E-mail: johnglen@doctors.org.uk

Fig 2 Example of amplitude spectra from a representative 20 s sample obtained from an awake (A) and an anaesthetized (B) patient.
Cerebral function monitors may provide another level of safety for our patients and, as this area of technology advances, improved care of the mental and cognitive functions of the critical care patient is likely to follow.

Critical Care 2008; 12(Supp3):S2