Lung-Brain interactions in critically ill patients receiving Mechanical Ventilation

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Seoul, 30 August 2015
Organ crosstalk during ALI, ARDS, and MV

Lopez-Aguilar J et al. Med Intensiva 2013
Pathophysiology of neurocognitive alterations in the critically ill

Turon M et al (submitted)

Mechanical Ventilation

Critical illness-related risk factors
- Hypoxemia/hypoxia
- Hypotension
- Blood glucose dysregulation
- Sepsis

Management-related risk factors
- Drug exposure
- Mechanical ventilation
- Sleep deprivation

SAA: Serum Anticholinergic Activity

DELIRIUM

↑ SAA

LONG-TERM NEUROCOGNITIVE IMPAIRMENTS

Turon M et al (submitted)
At 5 yr ARDS patients have:

Exercise limitation
Physical sequelae
Psychological sequelae
Decreased QOL
Problems in caregivers
Increase health costs

Figure 3. Cumulative Costs to 5 Years after Discharge from the Intensive Care Unit (ICU), Stratified According to Number of Coexisting Illnesses at Time of ICU Admission. Costs are in 2009 Canadian dollars.

Long-Term Cognitive Impairment after Critical Illness

Global Cognition Scores in Survivors

448 adults with acute respiratory failure or shock

Lung & Brain Cross-Talk during Mechanical Ventilation

Promising Theories
Wiring of the Neuro-Inflammatory Reflex

Tracey KJ. Nature 2002;420:853-9
Effect of vagotomy on high VT ventilation-induced ALI in mice

BALF

Lung Tissue
In experimental VILI, vagotomoy exacerbated while vagus stimulation attenuates lung injury in rats ventilated with either high or low volume strategies. Treatment of both mice and rats with the vagus mimetic drug, semapimod, resulted in decreased lung injury.
Objective:
To identify the mechanisms that lead to brain dysfunction during mechanical ventilation brains from mechanically ventilated mice were studied

Results:
1) Lung stretch–induced a hyperdopaminergic state in the hippocampus causing apoptosis
2) Vagotomy, systemic haloperidol, or intracerebroventricular raclopride (a type 2 dopamine receptor blocker) ameliorated this effect

Am J Respir Crit Care Med 2013;188:693–702
Male Sprague Dawley rats were randomized to 3 groups:

1) Anesthetized not ventilated

2) Low Vt (8 ml(kg), zero PEEP and 3 h of MV.

3) High Vt (30 ml/kg), zero PEEP and 3 h of MV

Measurement: **cFos**

- **RtsCX:** Retrosplenial Cortex, **CeA:** Central Amygdala
- **Cortex, Hippocampus, PVP:** Paraventricular Thalamic nucleus, **PVN:** Paraventricular Hypothalamic Nucleus
Central Amygdala


Functions:
- motivated behaviours
- emotional states
- housekeeping activities

Injury:
- cognitive impairments

Basal

Spontaneous Breathing

Low VT

High VT
Retrospenial Cortex

Functions:
- spatial memory
- learning

Injury:
- memory deficits

Basal
Spontaneous Breathing

Low VT
High VT
Thalamus

Functions:
- Interpretation of sensory information

Basal
Spontaneous Breathing
Low VT
High VT
Sprague-Dawley rats 3 h MV with VT 7 ml/kg at PEEP 2 or 7 cmH2O with intratracheal instillation of LPS or saline.
Shock: Injury, Inflammation, and Sepsis: Laboratory and Clinical Approaches

Moderate PEEP after tracheal lipopolysaccharide instillation prevents inflammation and modifies the pattern of brain neuronal activation.

**Plasma**

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**Lung tissue**

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Quilez M et al, in press
These 2 studies suggest that MV and PEEP level could modulate neuronal activity in some areas in the brain that are related to memory impairment and responses to stress.
Lung & Brain Cross-Talk during Mechanical Ventilation

Confort & Asynchronies
Asynchronies in VCV

Ineffective effort
Dyspnea

Flow Starvation
Air hunger, WOB
Double Triggering (VCV)

Patient effort

Double VT & Overinflation

EAdi
Flow
Paw
Mechanical Ventilation-Induced Reverse-Triggered Breaths

Reverse triggering & Respiratory Entrainment

Stretch receptors & vagal C fibers are responsible for the Hering-Breuer reflexes

Reverse Triggering (VCV)

No patient’s effort

- EAdi
- Flow
- Paw
Reverse Triggering (PCV)

No patient’s effort

- EAdi
- Flow
- Paw
Asynchrony Index (AI) for all patients in 24h periods over 25 consecutive days of MV
Asynchrony index (AI), percentage (%) per hour, continuously recorded over several days in 4 patients.

Neurophysiologic Model of Respiratory Discomfort:

Air Hunger
Dyspnea
Work/Effort
Tightness
Overinflation

O’Donnell DE et al
Resp Physiol Neurobiol 2009
Air Hunger Increases MRI Signal in Insula (Limbic System)

Insula (Limbic System):
- Perception of dyspnea, hunger, thirst
- Afferents of resp. chemoreceptors
- Stretch receptors project to insula
- Seat of emotions
- Large role in memory

Air hunger may cause severe psychological trauma
45 patients (47%) reported dyspnea (respiratory effort in seven cases, air hunger in 15, both in 16.

Dyspneic and nondyspneic patients did not differ in terms of age, SAPS II or indication for MV.

Dyspnea was significantly associated with anxiety (OR, 8.84; 95% CI, 3.26–24.0), assistcontrol ventilation (OR, 4.77; 95% CI, 1.60–4.3), and heart rate (OR, 1.33 per 10 beats/min; 95% CI, 1.02–1.75).
Dyspnea in mechanically ventilated critically ill patients

Matthieu Schmidt, MD; Alexandre Demoule, MD, PhD; Andrea Polito, MD; Raphaël Porchet, MD; Jerome Aboab, MD; Shidasp Siami, MD; Capucine Morelot-Panzini, MD, PhD; Thomas Similowski, MD, PhD*; Tarek Sharshar, MD, PhD*

**Effects of adjusting ventilator settings in the patients reporting dyspnea**

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<th>Parameter</th>
<th>Mean Variation, cm (95% Confidence Interval)</th>
<th>p</th>
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<td>Dyspnea VAS</td>
<td>$-4.6 \ (-6.1 \text{ to } -3.2)$</td>
<td>.0005</td>
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<tr>
<td>Anxiety VAS</td>
<td>$-1.7 \ (-3.3 \text{ to } -0.2)$</td>
<td>.041</td>
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<tr>
<td>Pain VAS</td>
<td>$+0.3 \ (-0.7 \text{ to } +1.2)$</td>
<td>.79</td>
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VAS, visual analogic scale.
Assessment of Physiologic Variables and Subjective Comfort Under Different Levels of Pressure Support Ventilation*

Michele Vitacca, MD; Luca Bianchi, MD; Ercole Zanotti, MD; Andrea Vianello, MD; Luca Barbano, MD; Roberto Porta, MD; and Enrico Clini, MD, FCCP

Comfort Borg Scale

36 pts Different PSV & PEEP levels

CHEST 2004; 126:851–859
Dyspnea and surface inspiratory electromyograms in mechanically ventilated patients

10 patients in High & Low PSV at High & Low Expiratory Trigger

Ineffective Efforts only found during High PSV

Low PSV increase dyspnea
Discomfort
Dyspnea
- Air Hunger
- Work/Effort
- Tightness
Agitation
VILI
Risk of Extubation

Physiologic Events & Asynchronies
24 h Report
Conclusions:

• Cross-Talk always exists between lung and brain during critical illness.
• Cyclic overinflation and asynchronies occur frequently and may influence outcome
• Patients receiving MV need protection and support of lung and brain
• Research on this area is in its infancy but this knowledge can benefit patients, their families and care providers.
Thank You! lblanch@tauli.cat