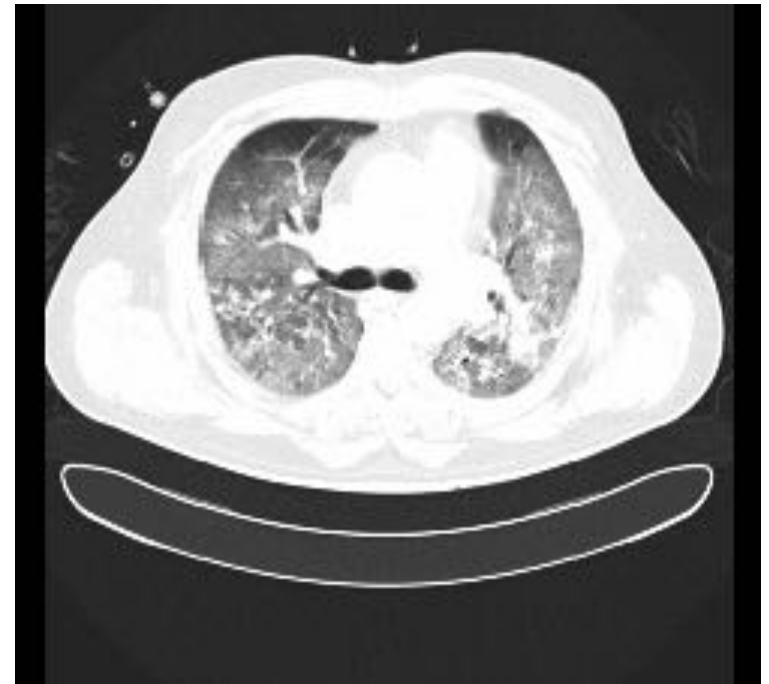
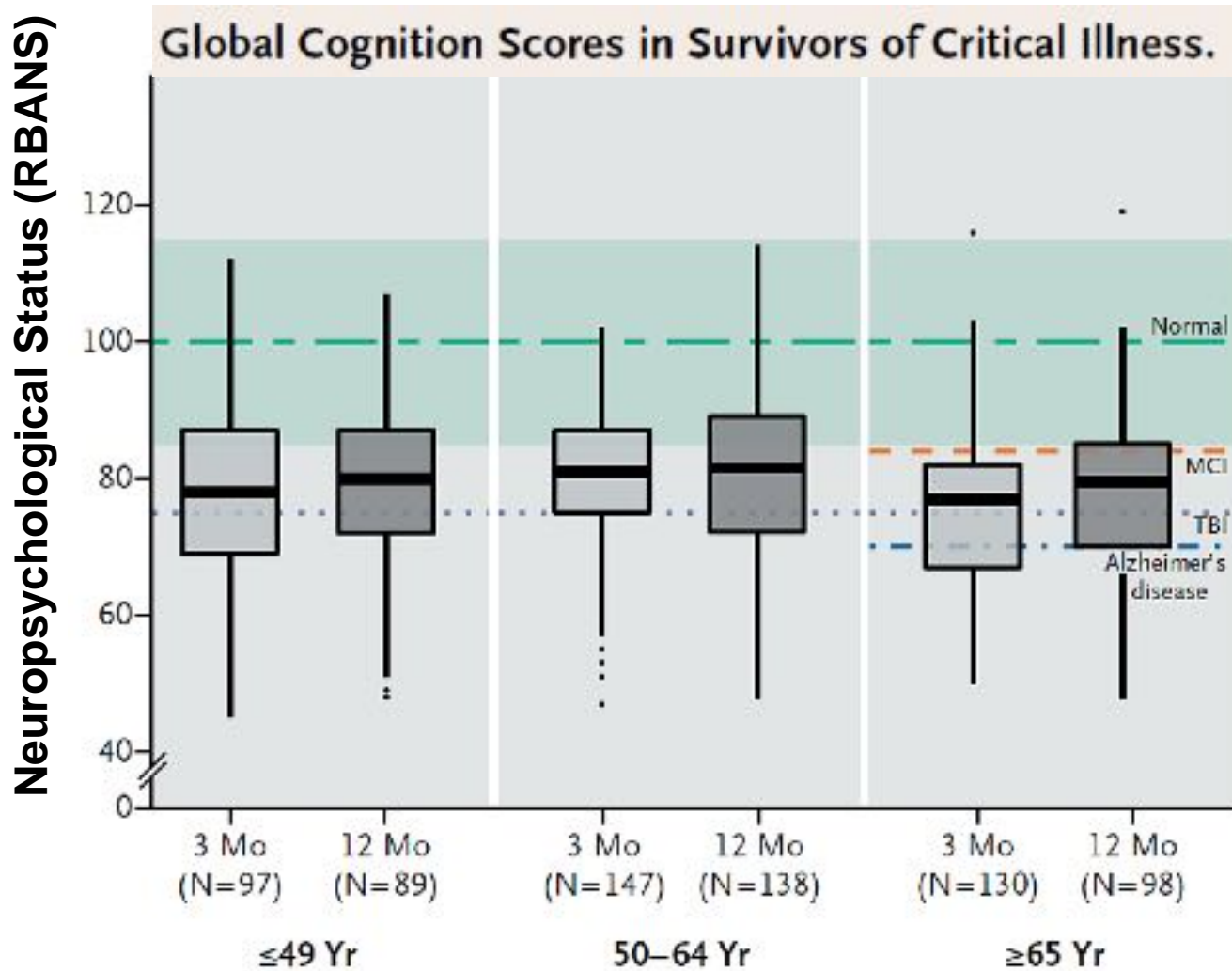


# Cognitive disorders and ARDS



- pathophysiology/inflammation
- crosstalk ?
- management consequences?

# Cognitive impairment is common after critical illness !



# Risk factors for cognitive disorders

- pre-existing psychiatric disease
- hypoxia and hypotension
- sepsis – inflammation
- sleep deficiency
- sedation
- dysglycemia
- metabolic derangement
- delirium



## Cognitive dysfunction after critical illness/ARDS

- general cognitive decline
  - attention and concentration
  - memory
  - executive function
  - mental processing speed
  - visuospatial competence
- 
- depression
  - post-traumatic stress disorder

### prevalence:

} hospital discharge: 70 - 100 %  
1 year follow up: 46 - 78 %  
2 year follow up: 25 - 47 %

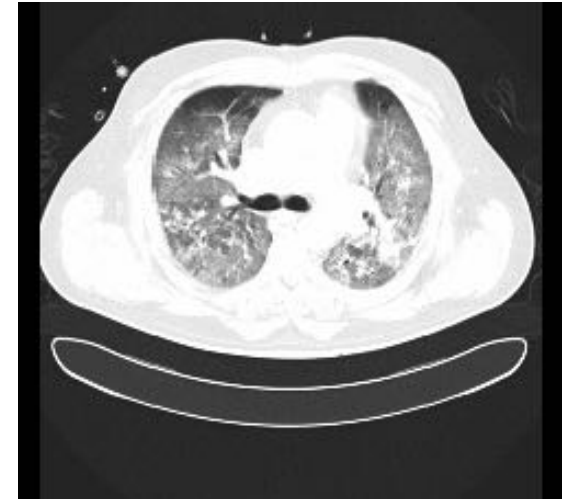
# ARDS and the brain – a special crosstalk



**hypoxia**  
**inflammation**  
**(injurious) ventilation**

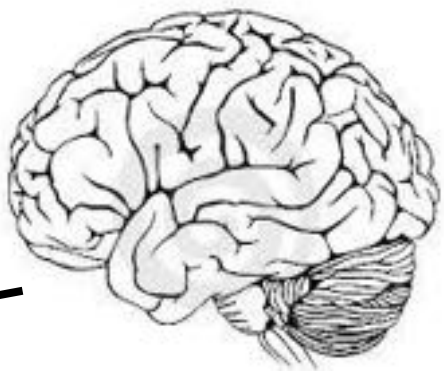
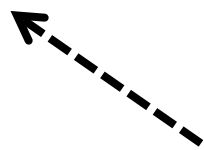


**,neurogenic‘ lung edema**  
**inflammation**  
**ischemic preconditioning**



**Cross talk: brain → lung**

**microglia activation**

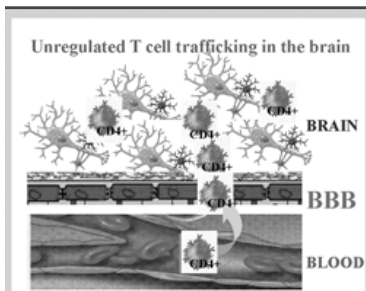


**inflammation ↑**

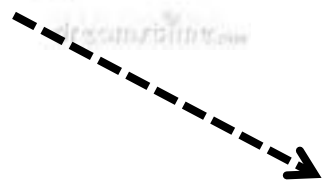


- S100
- NSE

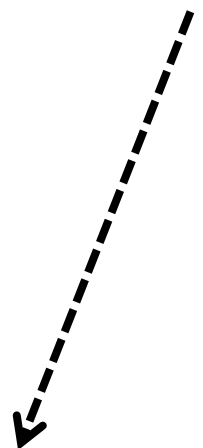
**blood-brain-barrier ↓**



**neurogenic edema**



**neuronal apoptosis**



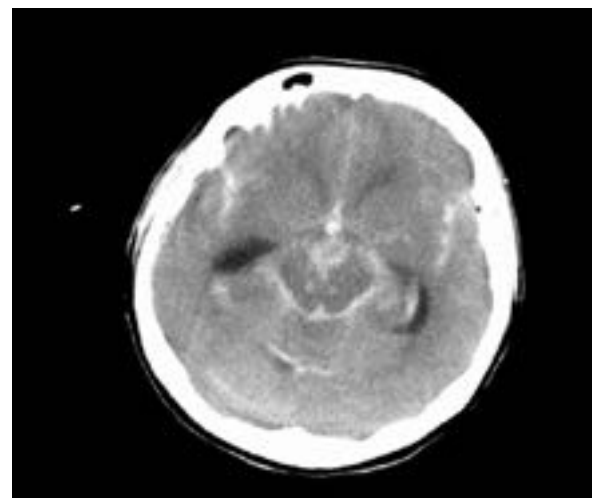


## Cardiac Troponin I and Acute Lung Injury After Subarachnoid Hemorrhage

Andrew M. Naidech · Sarice L. Bassin · Rajeev K. Garg ·  
Michael L. Ault · Bernard R. Bendok · H. Hunt Batjer ·  
Charles M. Watts · Thomas P. Bleck

**171 consecutive patients with SAH:**

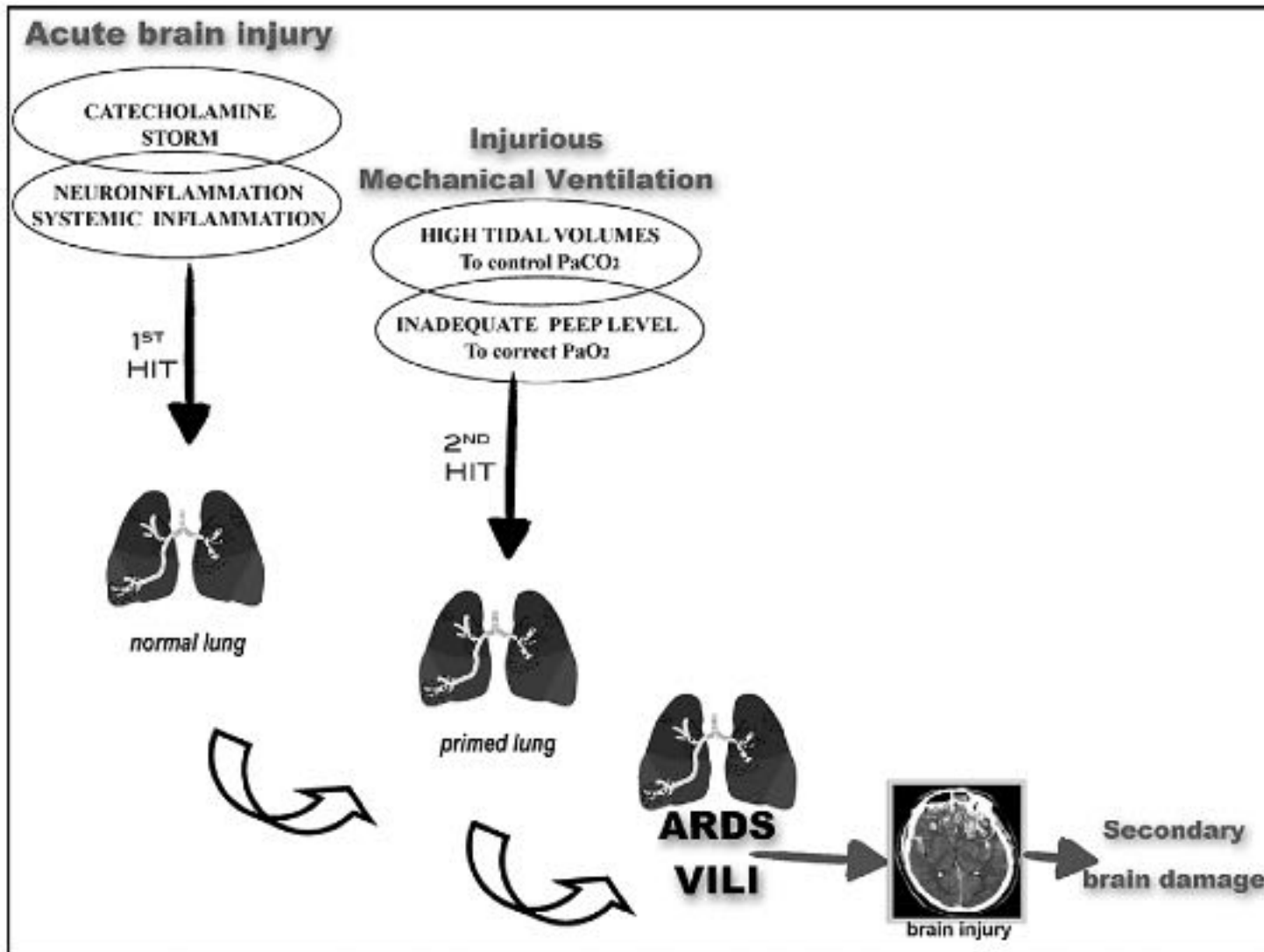
- acute lung injury 10 (6 %)
- ARDS 14 (8%)
- pulmonary edema 9 (5 %)



**Table 2** Multivariate model for ALI or ARDS

Variable	OR	95% CI	<i>P</i>
WFNS per grade	4.6	2.1–10.0	<0.001
Troponin I per quartile <sup>a</sup>	10.2	3.2–31.9	<0.001
WFNS by troponin I interaction	0.6	0.4–0.7	<0.001

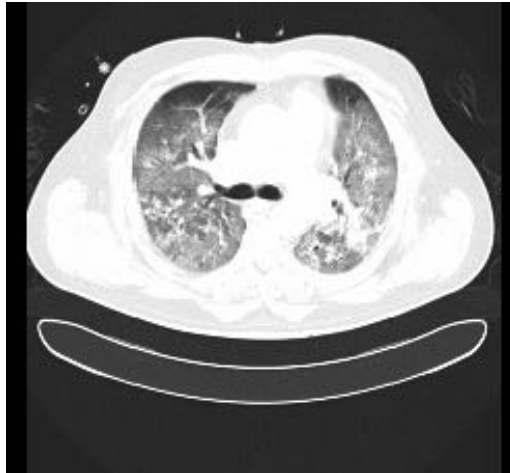
# A „two-hit“-model for brain-lung crosstalk





**Cross talk: lung → brain**

**blood-lung-barrier ↓**

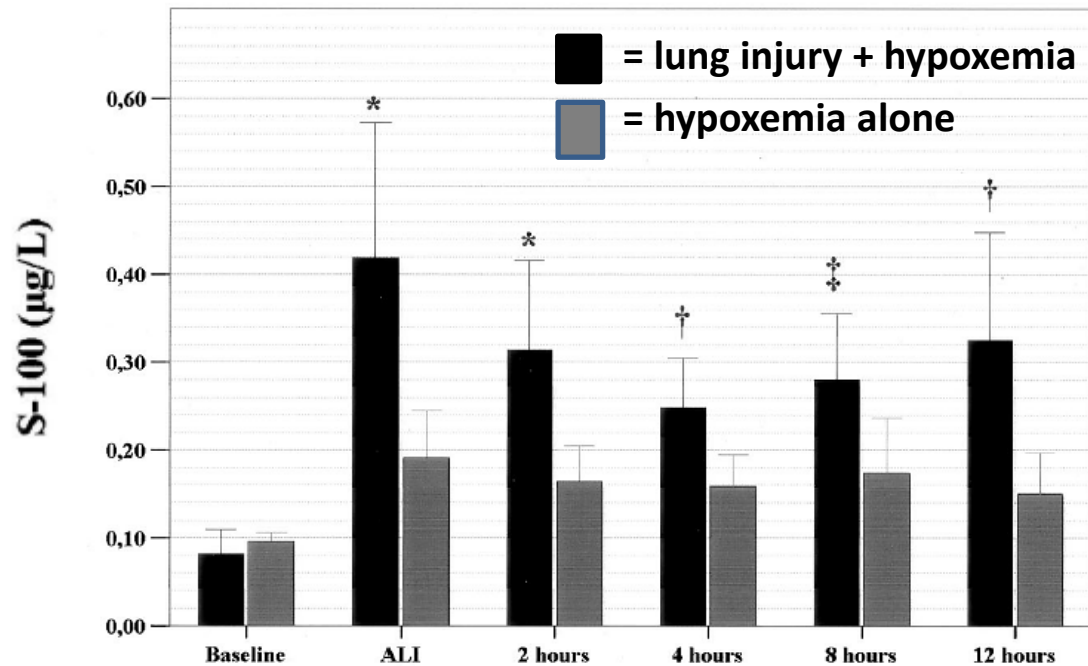


**hypoxia  
(injurious) ventilation**

**Inflammation ↑**  
- TNF  
- IL  
- .....

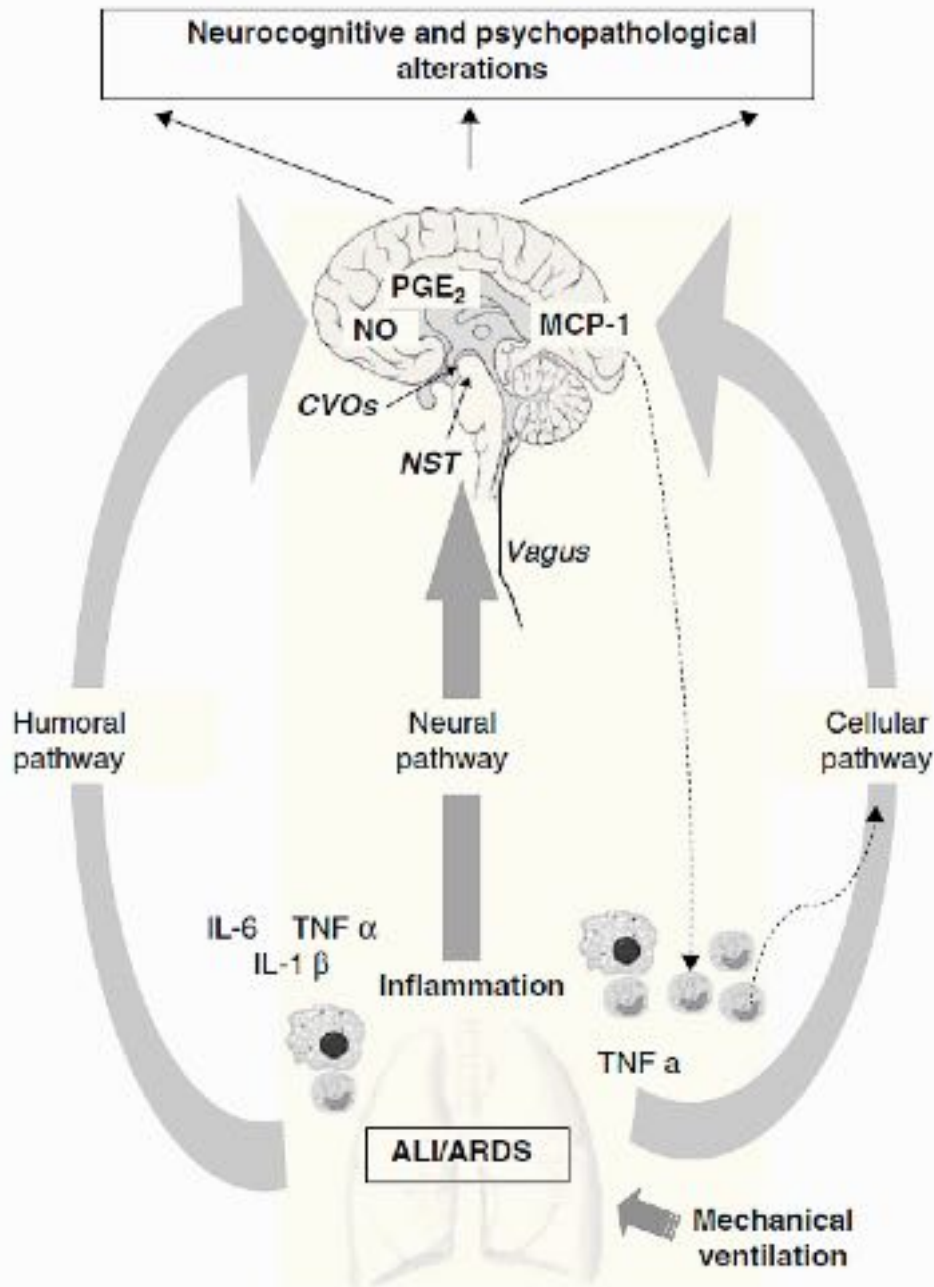
## *S-100 Protein and Neurohistopathologic Changes in a Porcine Model of Acute Lung Injury*

Michael Fries, M.D.,\* Johannes Bickenbach, M.D.,\* Dietrich Henzler, M.D.,\* Stefan Beckers, M.D.,\* Rolf Dembinski, M.D.,\* Bernd Sellhaus, M.D.,† Rolf Rossaint, M.D., Ph.D.,‡ Ralf Kuhlen, M.D., Ph.D.§



„Hypoxemia + lung injury induced a greater brain damage (S-100/histopathology) compared to hypoxemia alone.“

## Communication pathways between the lungs and the central nervous system



J. López-Aguilar

Med Intensiva. 2013;37(7):485-492

**The Association between Acute Respiratory Distress Syndrome, Delirium, and In-Hospital Mortality in Intensive Care Unit Patients**

S. Jean Hsieh<sup>1,2</sup>, Graciela J. Soto<sup>1,2</sup>, Aluko A. Hope<sup>1,2</sup>, Ana Ponea<sup>2</sup>, and Michelle N. Gong<sup>1,2</sup>

<sup>1</sup>Albert Einstein College of Medicine and <sup>2</sup>Department of Medicine, Montefiore Medical Center, Bronx, New York

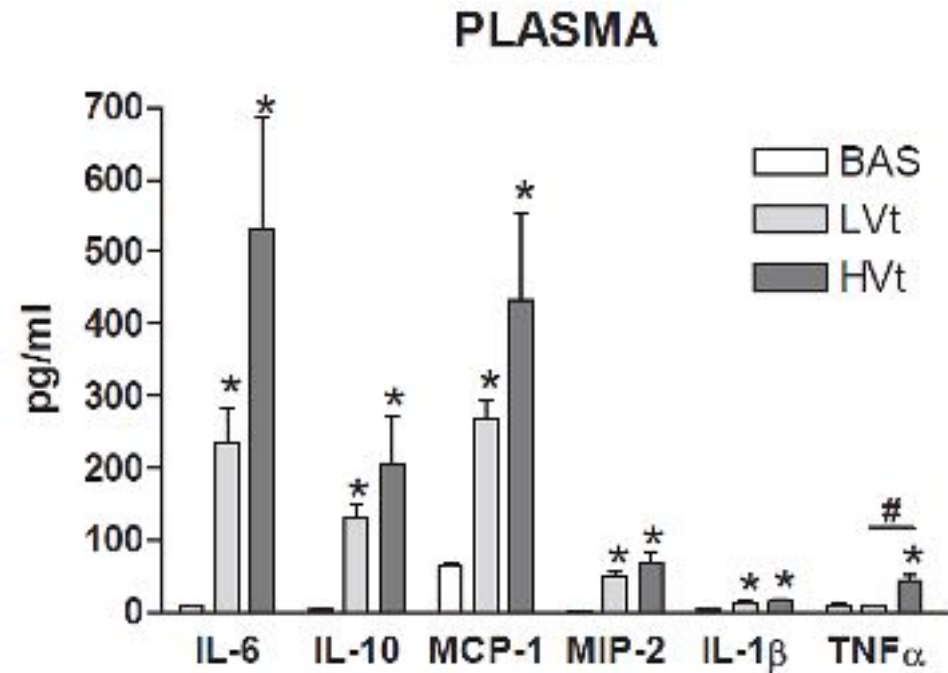
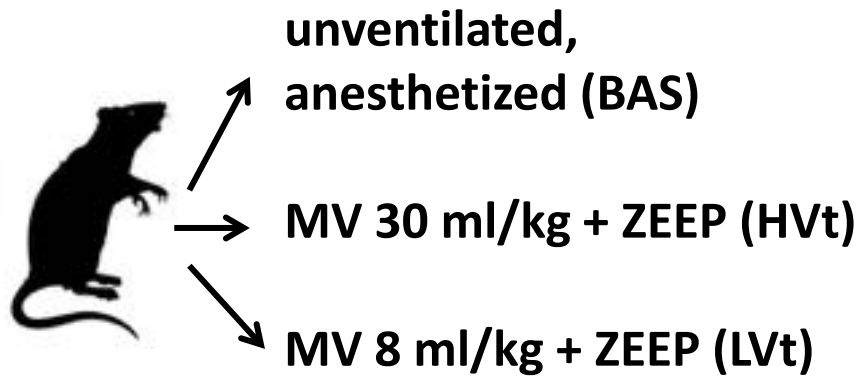
Am J Respir Crit Care Med Vol 191, Iss 1, pp 71–78, Jan 1, 2015

Outcome	Not Intubated (n = 198)	Intubated, No ARDS (n = 318)	Intubated with ARDS (n = 48)	P Value
Delirium and coma status, n (%)				<0.001
Never delirious	156 (79)	131 (41)	4 (8)	
Ever delirious	41 (21)	165 (52)	35 (73)	
Persistently comatose*	1 (0.5)	22 (7)	9 (19)	
Delirium days in ICU (max 14), median (IQR)	0 (0–0)	1 (0–2)	2 (0–4)	<0.001
Delirium and coma-free days (max 14), median (IQR) <sup>†</sup>	14 (13–14)	12 (3–14)	2 (0–9)	0.0001
% ICU days free of delirium and coma, median (IQR) <sup>‡</sup>	50 (33–75)	25 (0–56)	0 (0–14)	0.0001

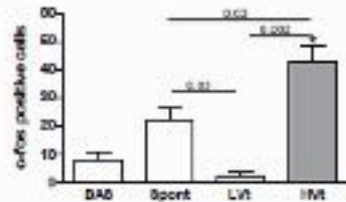
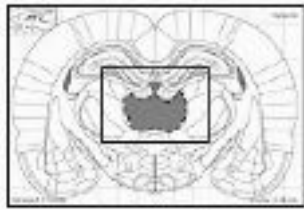
„ARDS is associated with a greater risk for ICU delirium than mechanical ventilation alone“.

# Injurious mechanical ventilation affects neuronal activation in ventilated rats

Quilez *et al. Critical Care* 2011, **15**:R124  
<http://ccforum.com/content/15/3/R124>



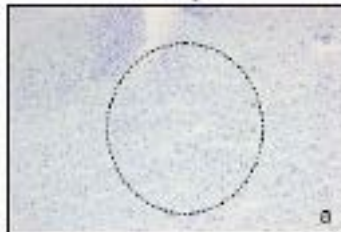
## Thalamus



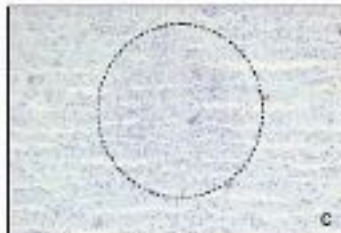
cresyl

c-fos

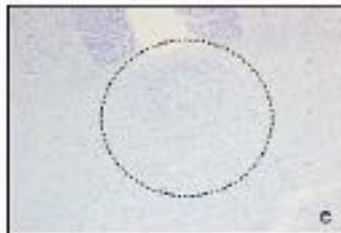
BAS



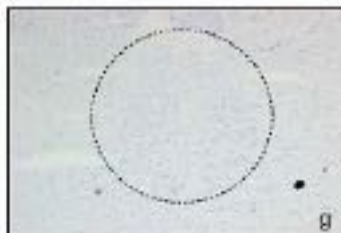
Spont



LVt



HVt



**C-fos proto-oncogene  
positive neurons**

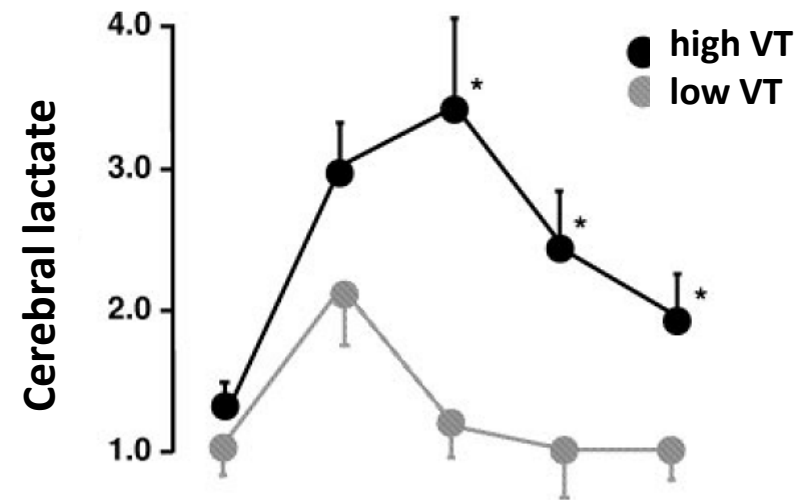
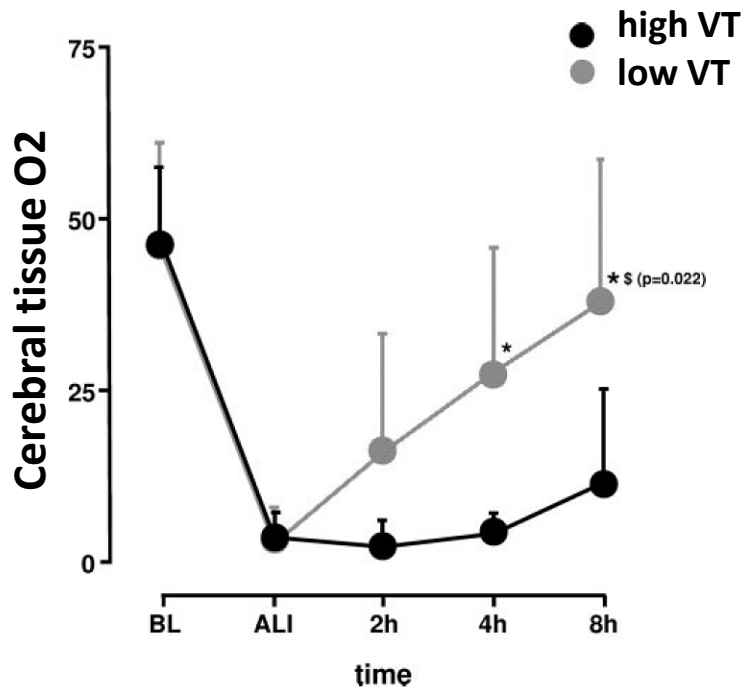
**„Mechanical ventilation promotes  
brain activation. The intensity is  
higher in high tidal volume, suggesting  
an iatrogenic effect on the brain“.**



# Low Tidal Volume Ventilation in a Porcine Model of Acute Lung Injury Improves Cerebral Tissue Oxygenation

Johannes Bickenbach, MD\*

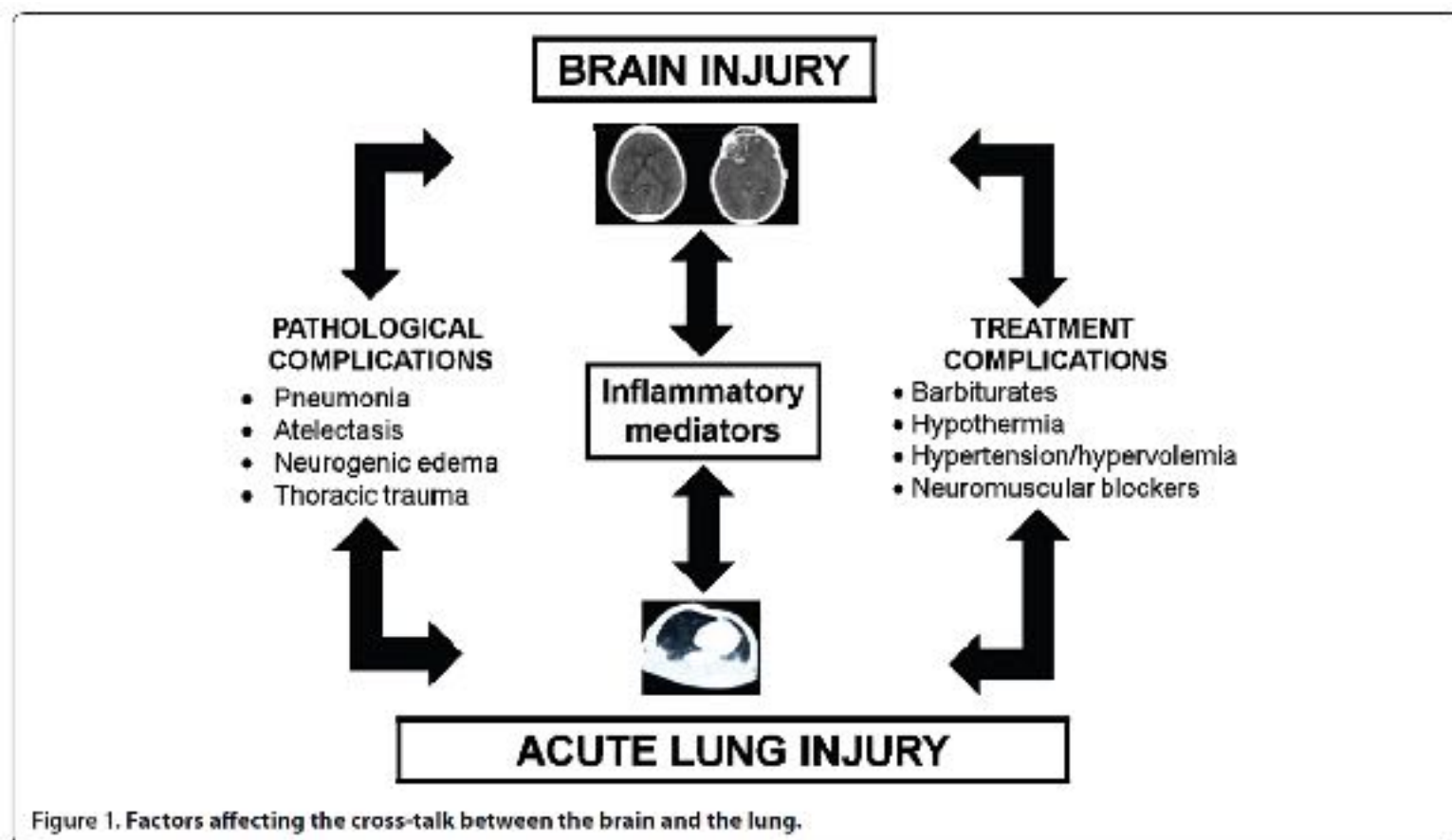
(Anesth Analg 2009;109:847-55)



„Protective ventilation with low tidal volume yielded a significant improvement in cerebral tissue oxygenation and metabolism...“

**COMMENTARY**

# The lung and the brain: a dangerous cross-talk

Paolo Pelosi<sup>1</sup> and Patricia RM Rocco<sup>2</sup>*Critical Care* 2011, **15**:168

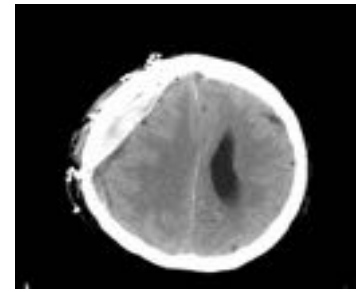


## Summary I

- **neuropsychological alterations in ARDS patients have an important adverse effect**
- **in critically ill patients a complex interaction between brain and lung is observed**
- **complex interactions include ,inflammation crosstalk‘, hypoxia, and impaired blood-organ-barrier**
- **the brain-lung crosstalk is inforced by injurious ventilation**



## Summary II



- **prevention of neurological complications in ARDS patients is important**
- **Management of brain disorders MUST consider crosstalk to other organs (the lung!)**
- **Management of ARDS MUST consider crosstalk to the brain**



- **Lung protection is brain protection!**