Delirium and Neuroimaging: Structural, Functional, Amyloid

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Structural Imaging

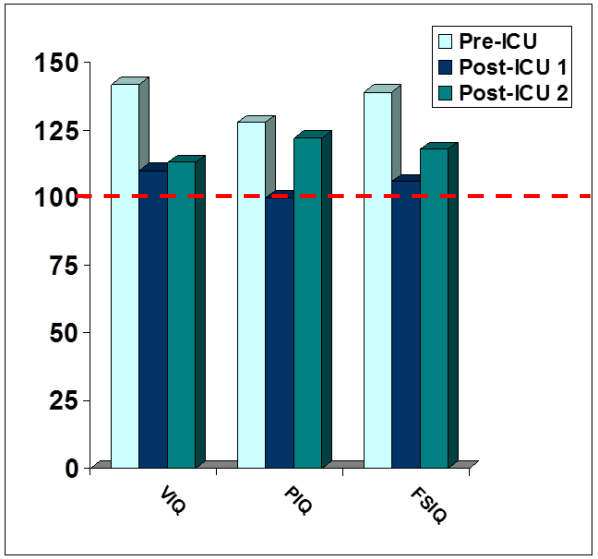
49 year Female – 16 yrs education

Severe community acquired pneumonia

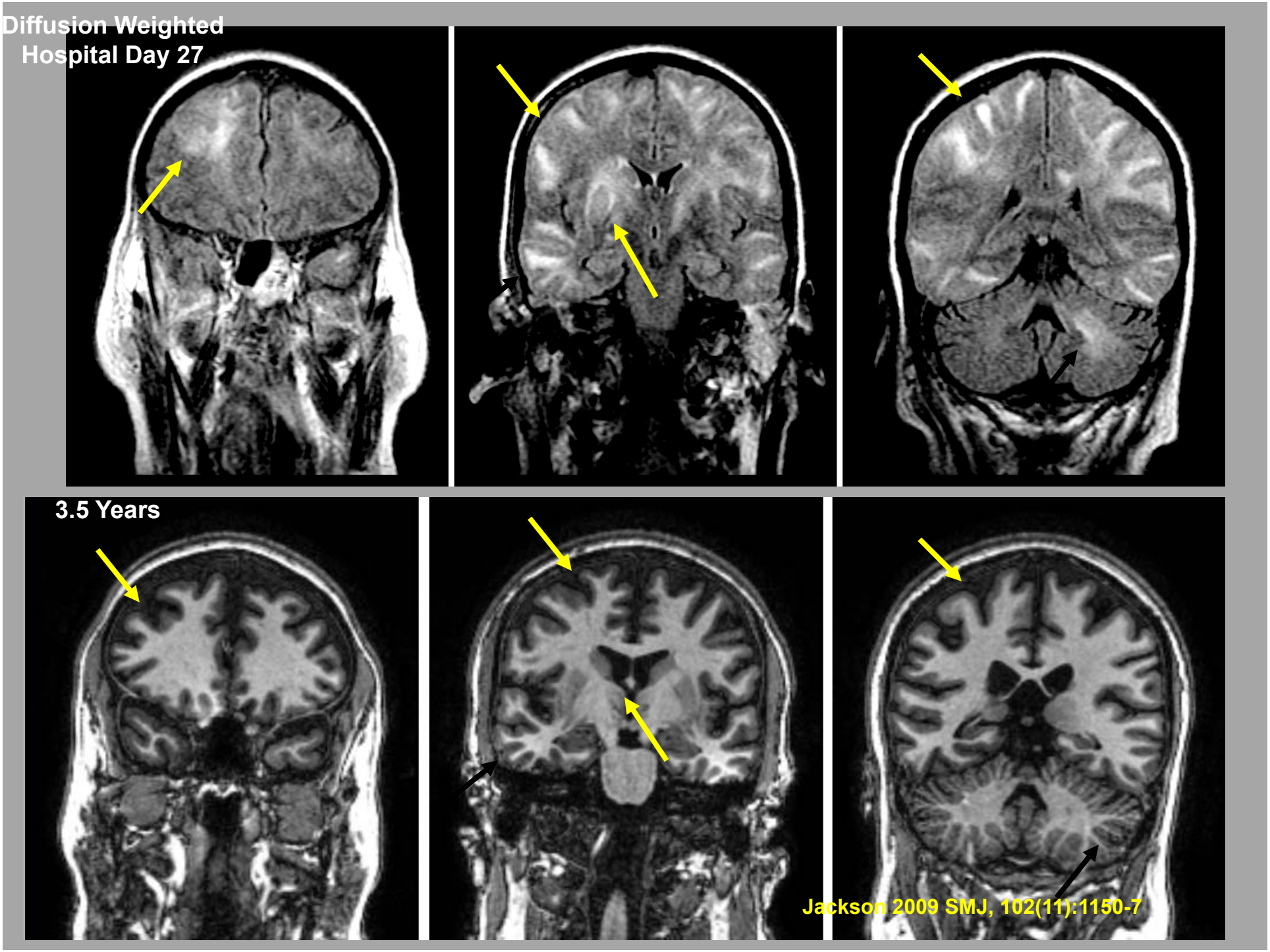
Hypoxia and hypotension → intubation and mechanical ventilation

48 hours → renal failure, septic shock → ARDS

- 31 days - MV
- 37 days ICU LOS
- 43 days hospital LOS
- 11 days delirium duration



Jackson 2009 SMJ, 102(11):1150-7

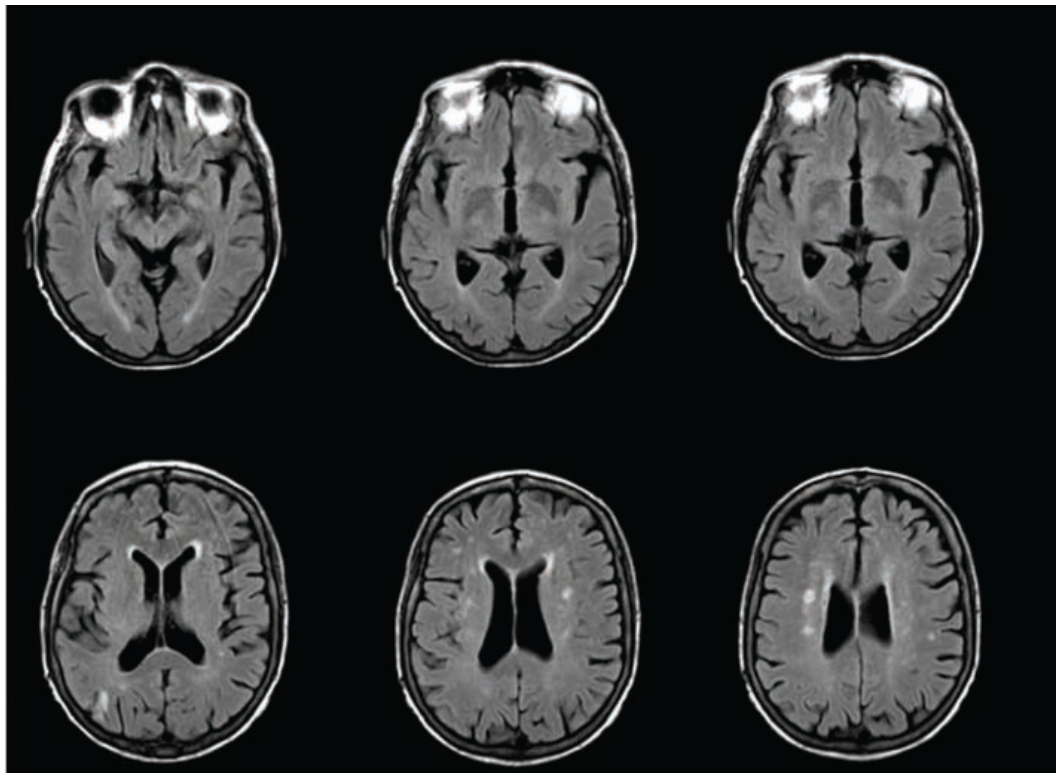

Diffusion Weighted
Hospital Day 27
3.5 Years
Jackson 2009 SMJ, 102(11):1150-7

MRI, Critical illness and Delirium

- 43 year old
- All with delirium
- 7 normal CT scans

- 6 of 8 had WMH
  - 2 pts. Fazekas grade 1
  - 2 pts. grade 2
  - 2 pts. grade 3

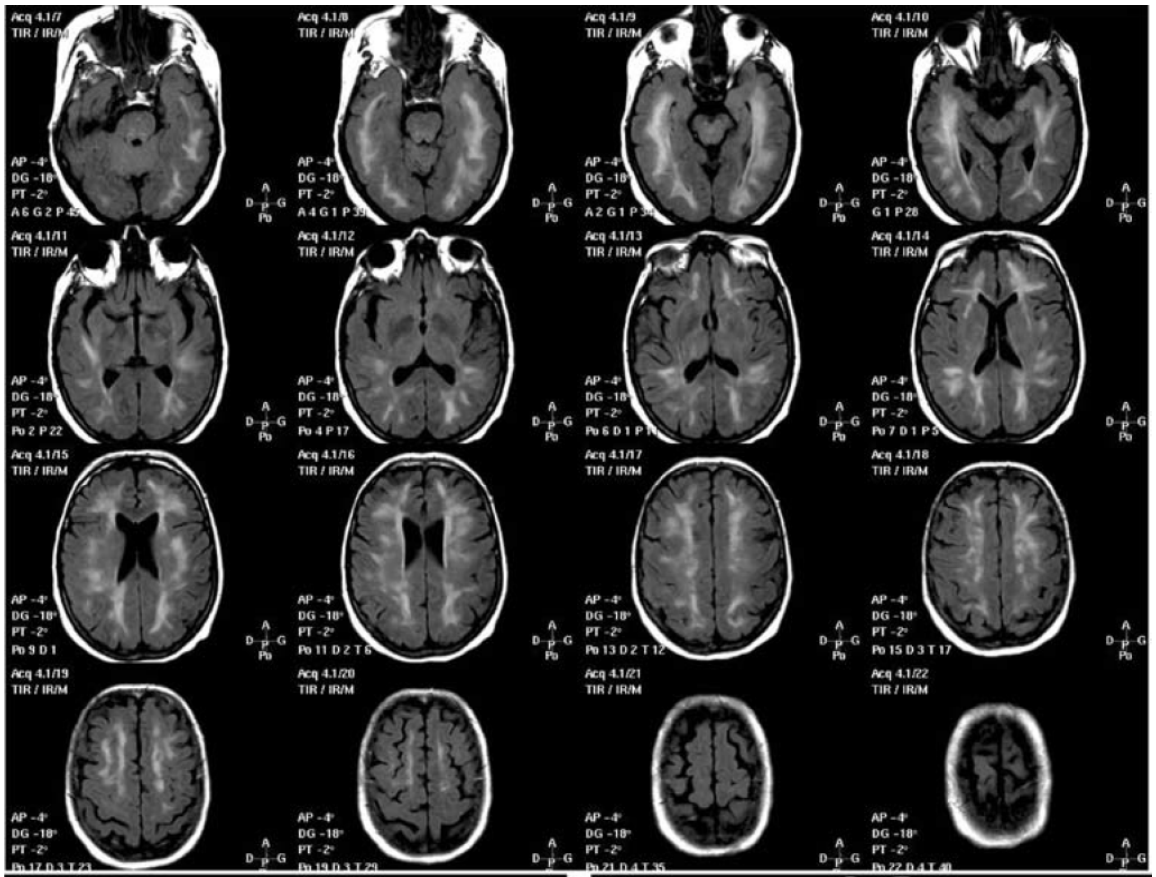
- No
  - Atrophy
  - Ischemic lesions
  - Hemorrhagic lesions



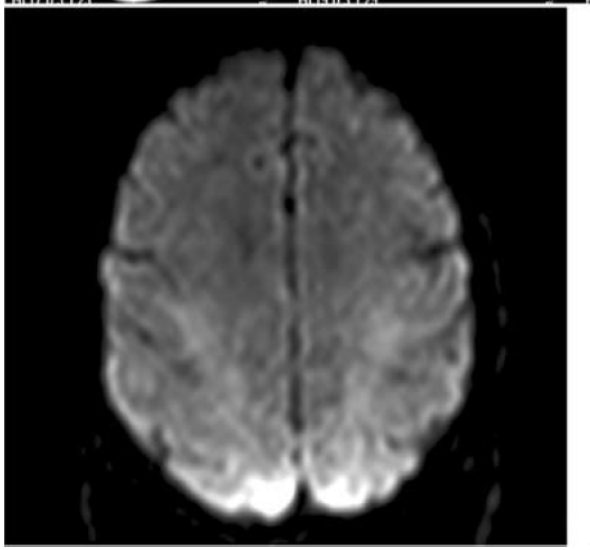
Morandi et al., 2010, Psychiatry 7(9):28-33

67 year old female

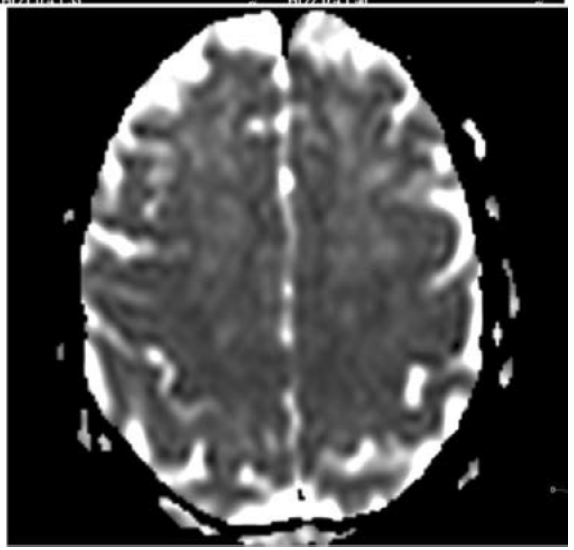
Axial Flair
WMHs Grade 3



Left – DWI map
Anterior white matter hypointense



Right – ADC map
Diffuse ADC increase: vasogenic edema



Sharshar et al., 2007 ICM, 33:798-806

Post-Cardiac Surgery

- 130 patients – 18 (13.8%) delirium
- Prevalence of severe WMH higher patients with delirium
  - Fazekas score = 3
  - OR: 3.9; 95% [CI] 1.2-12.5
- WMH risk factor for development of delirium

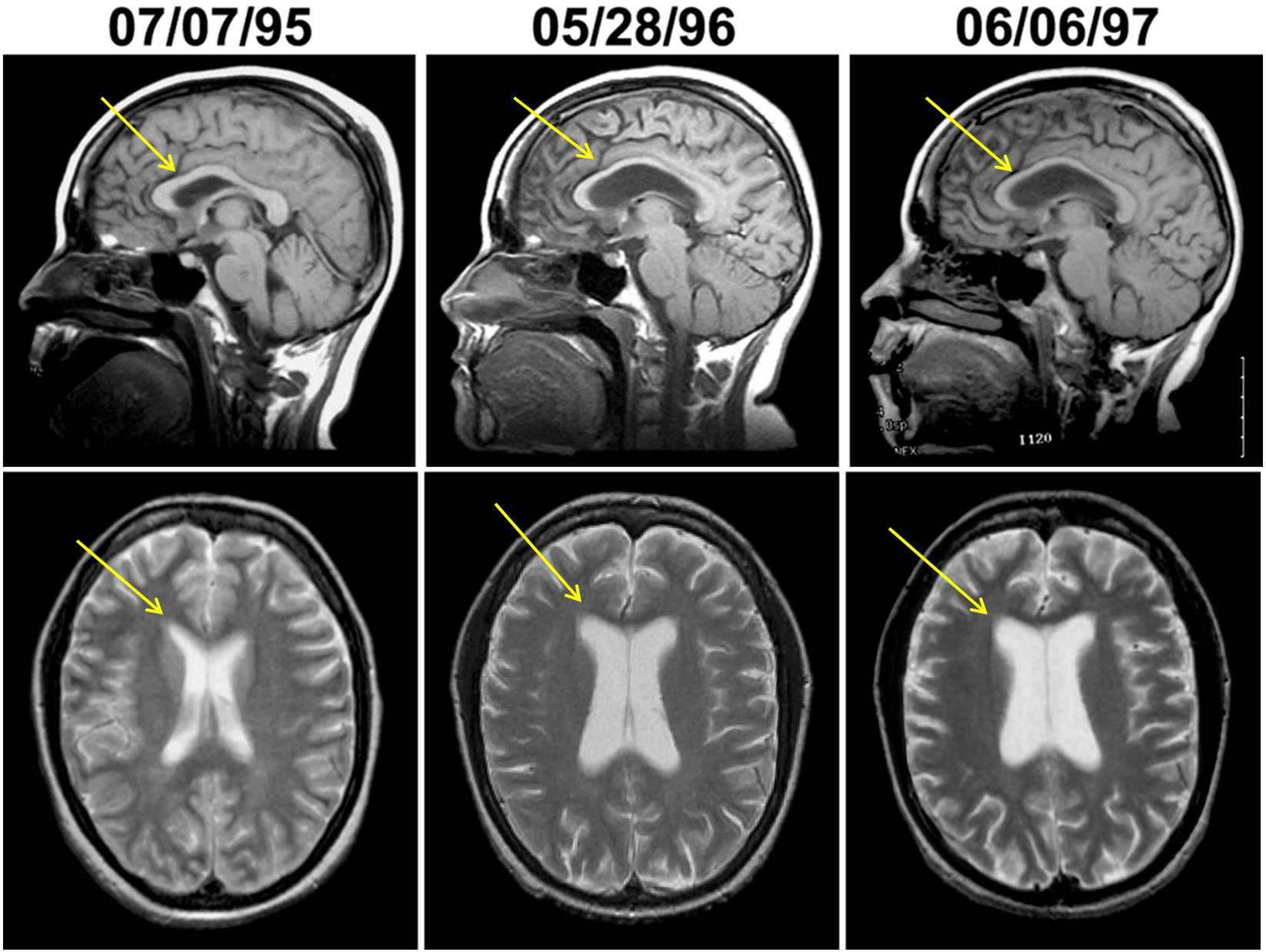
Hantano et al.k, 2013, Am J Geriatr Psychiatry; 21(10);938-45)

Study	Imaging Modality	N Pts./controls	Cause of delirium	Imaging Findings
Koponen et al., 1989	CT	69 / 31	Heterogeneous	**Atrophy** **R side focal infarcts**
Figiel et al., 1989	MRI	5 / 55	Antidepressant	**Basal ganglia lesions** **WMHs** **Cortical Atrophy** **↑ VBRs**
Figiel et al., 1990	MRI	10	ECT	**Basal ganglia lesions** **WMHs**
Figiel et al., 1990	CT / MRI	6	ECT	**Basal ganglia lesions** **WMHs**
Martin et al., 1992	CT / MRI	4 / 10	ECT in Stroke pts.	**Caudate Nucleus lesions**
Nargaratnam et al., 1995	CT	5	Stroke	**R subcortical infarcts**
Kishi et al., 1995	CT / MRI	38 / 197	Critical illness (medial and trauma)	**SAH / SDH** **R & L Ischemic lesions**
	CT / MRI	49 / 153	Stroke	**Cerebral Atrophy** **WM lesions**
Yokota et al., 2003	**Xenon CT**	10	Trauma / Medial	**↓ CBF frontal, temporal, occipital lobes, caudate, thalamus, lenticular nucleus**
Caeiro et al., 2004	CT / MRI	29 / 189	Stroke	**Ischemic lesions**
Samton et al., 2005	CT	22 / 11	Hypoxia, medical, drug intoxication	**WMHs** **Subcortical atrophy**
Fong et al., 2006	**SPECT**	22 / 11	Heterogeneous	**↓ CBF frontal, parietal, occipital** **L temporal lobe, pons**

Soiza et al., 2008, J Psychosomatic Res, 65:239-48

Female ARDS
22 years
12 years Education

Longitudinal Studies

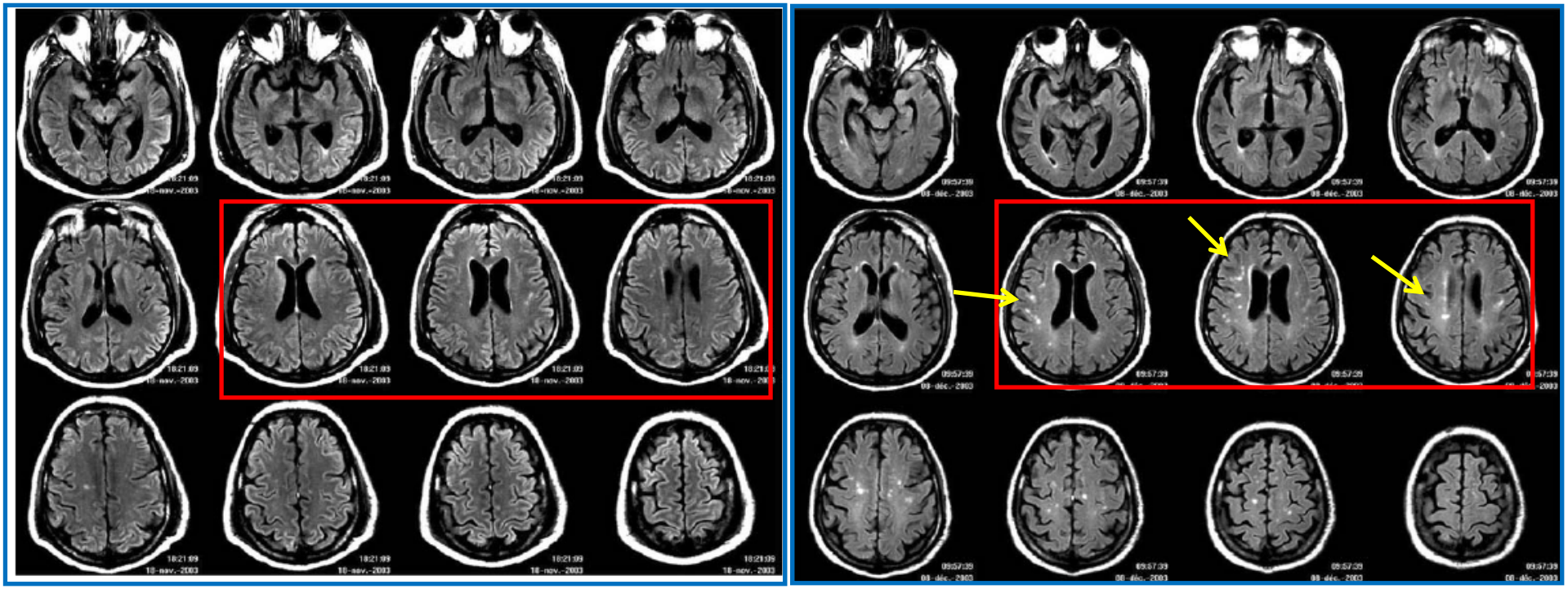


Hopkins 2012 NeuroRehabilitation 31:311-318

Sepsis

Before Sepsis

24 days after Sepsis onset

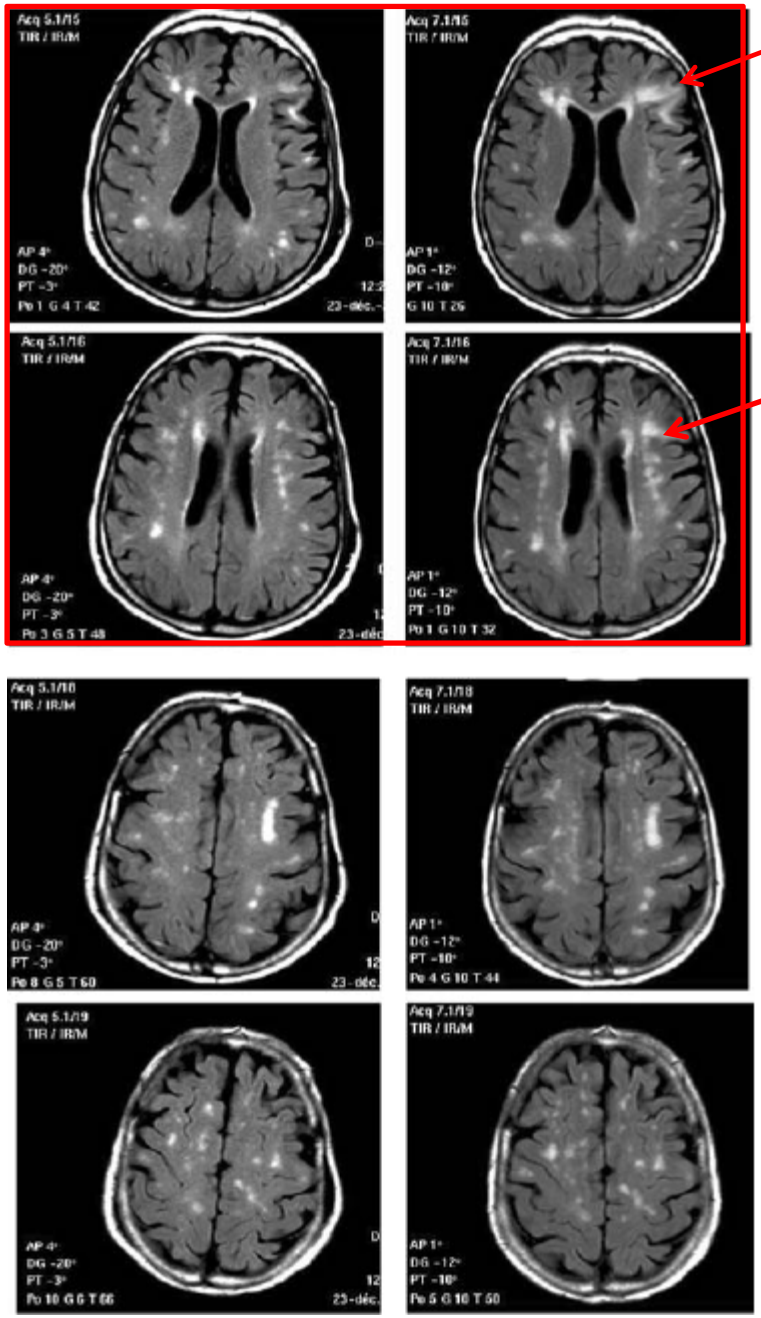


N = 9
4 delirium, 5 coma
2 with normal scans
2 ischemic stroke
5 WMHs
75% abnormal imaging

60 Year old Male
Increase in WMHs

Sharshar et al., 2007 ICM, 33:798-806

Before Sepsis 30 days after Sepsis



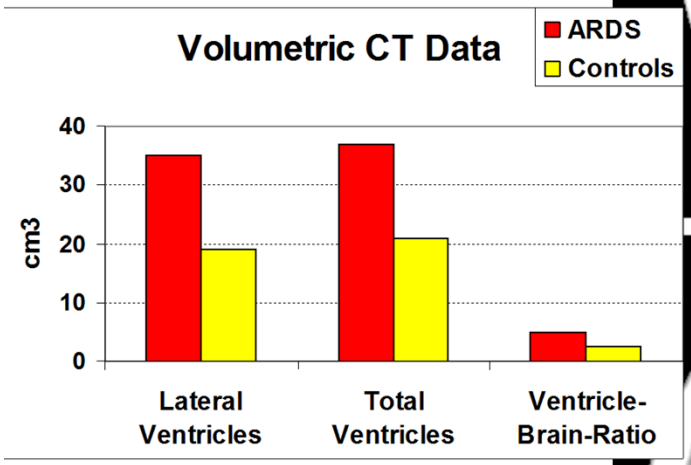
79 Year old Female
Increase in extent of WMHs

Sharshar et al., 2007 ICM, 33:798-806

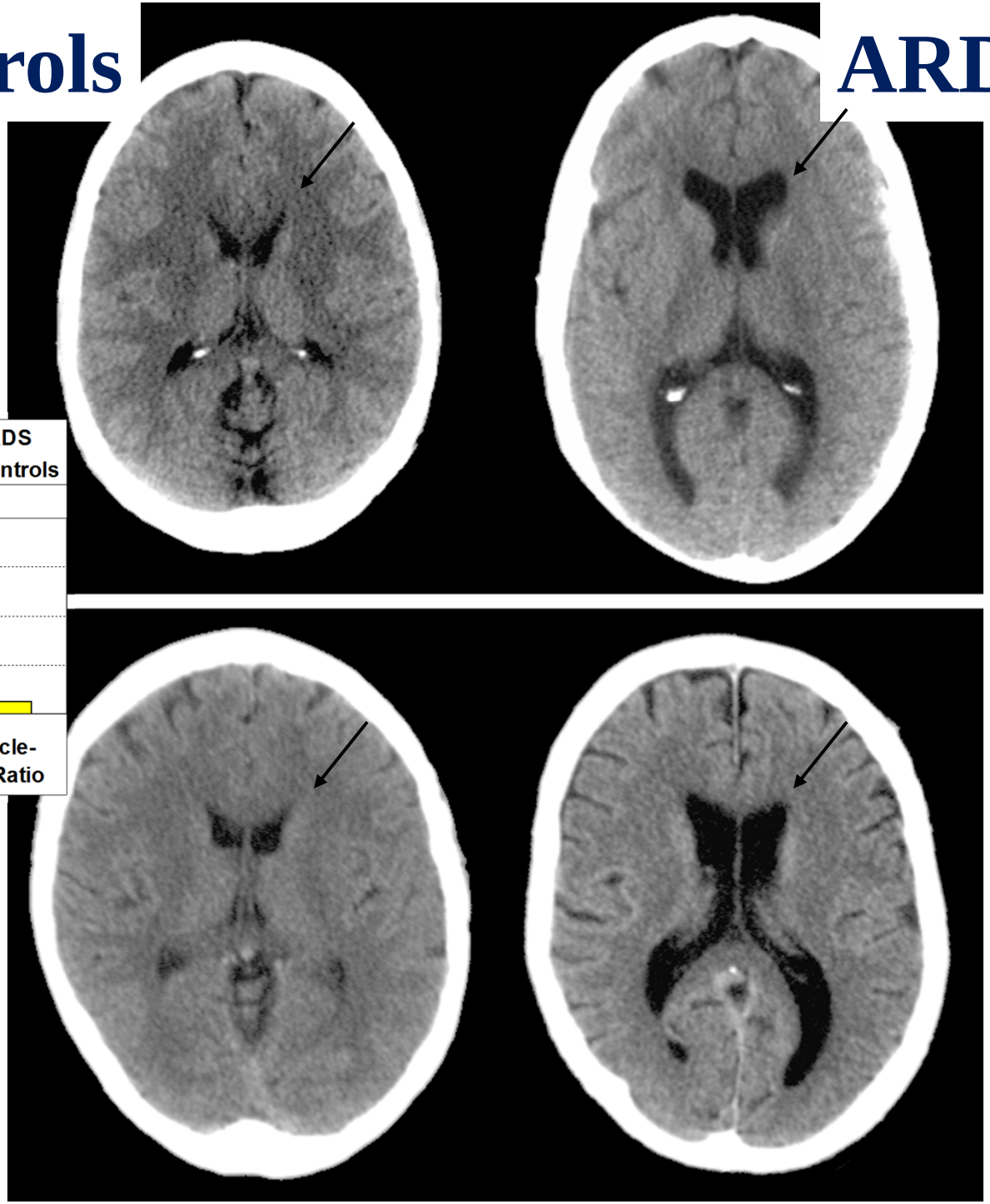
Controls

ARDS

36 Year Old Women



54 Year Old Men



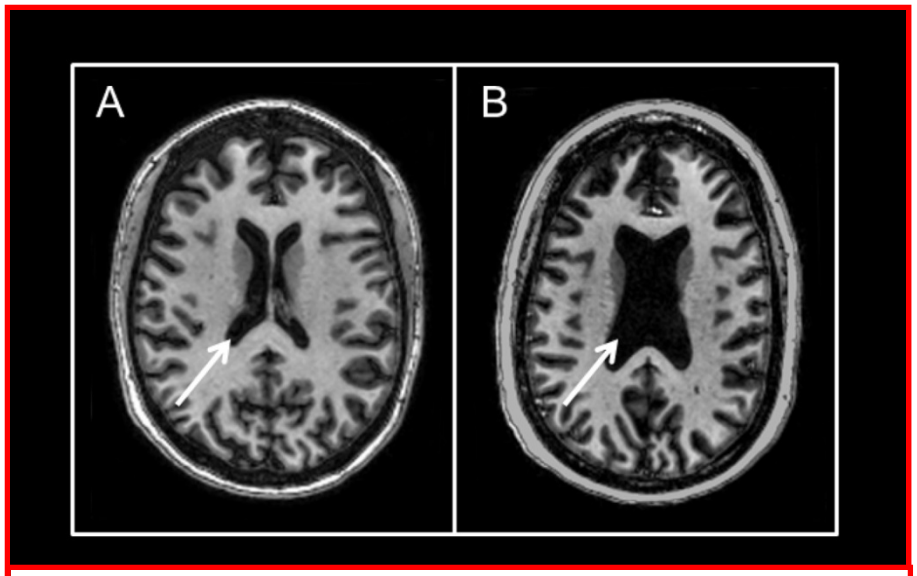
Hopkins 2006 Brain Injury 20;263-71

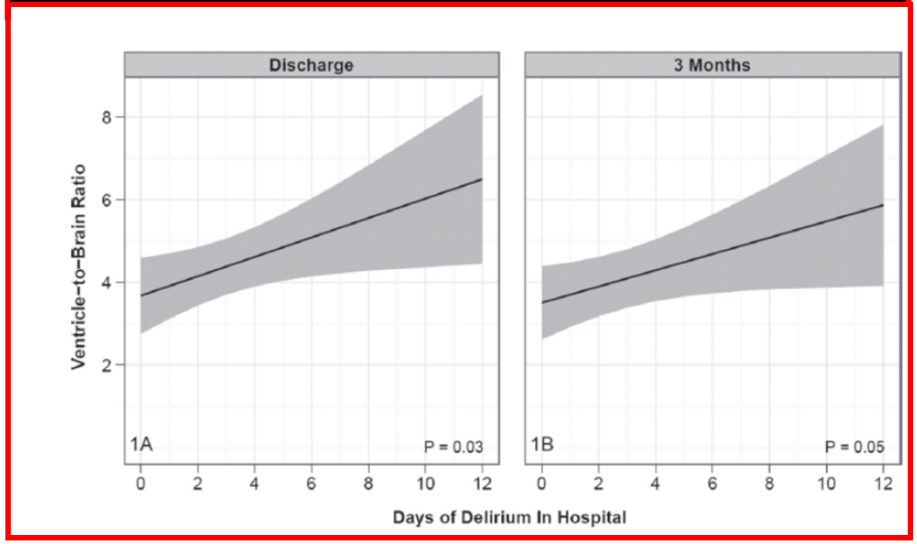
Delirium Duration and Atrophy

(all P values <0.001)

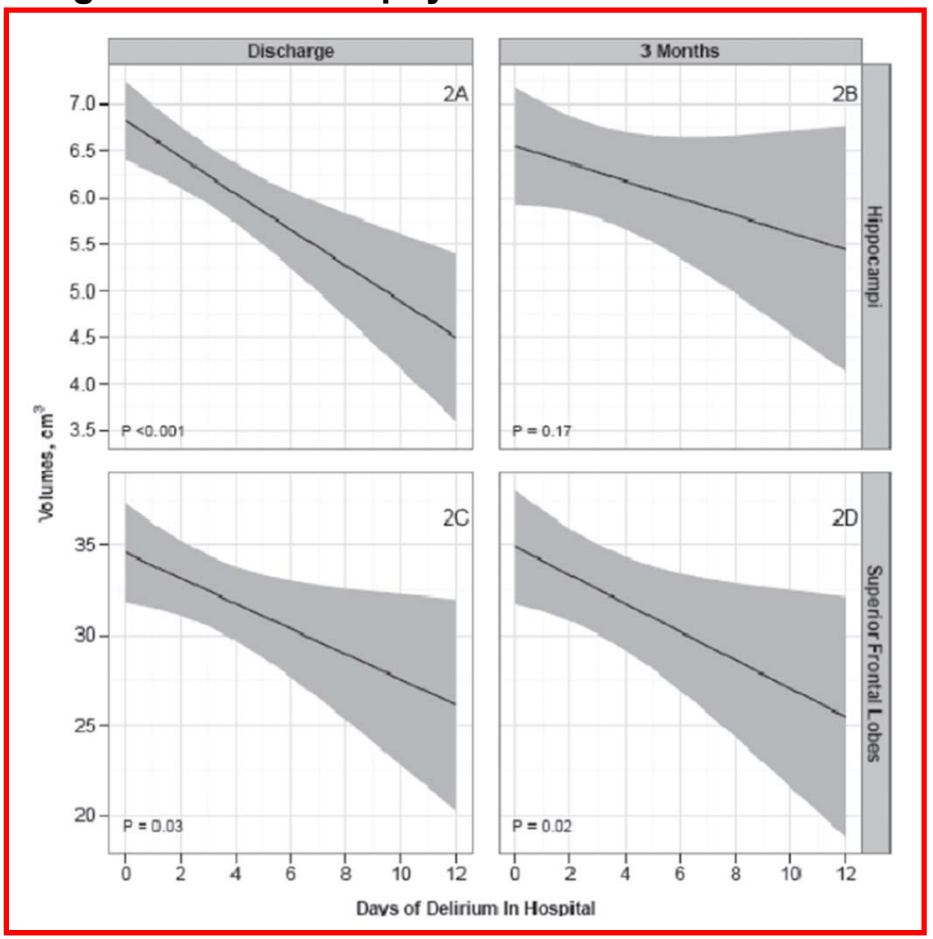
46 yr Female
No Delirium

42 yr Female
Delirium





- **47 Critical ill patients**
- **Longer duration of delirium associated with greater brain atrophy.**



Gunther et al., 2012 CCM, 40(7):2022-32

rCBF- Hypoactive Delirium

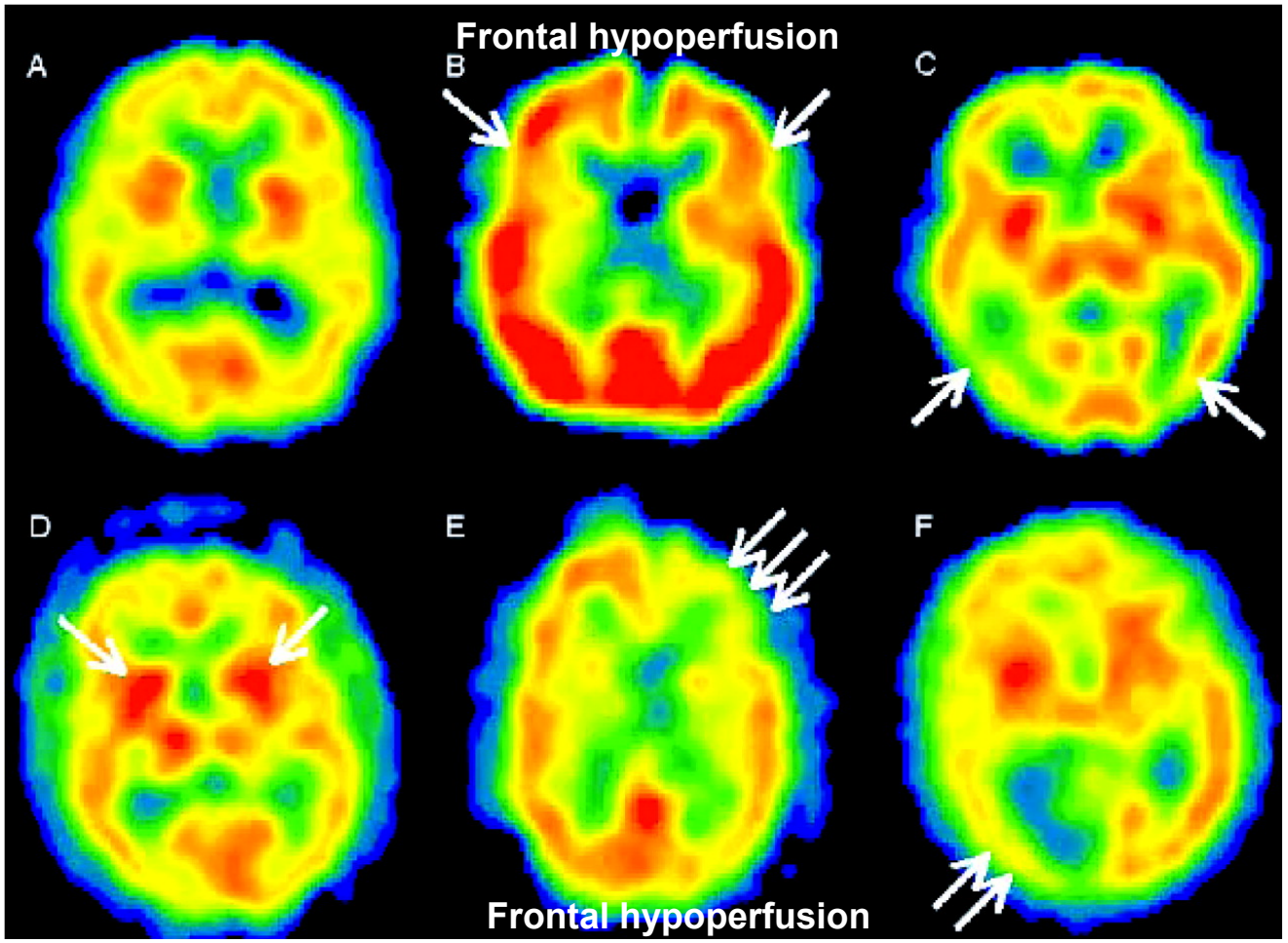
Critical ill patients
Age 47.5 ± 12.3
APACHE II 16.5 ± 5.8

Region	During Delirium: First measurement (mL/100 g per min)	After Recovery from Delirium: Second measurement (mL/100 g per min)	*P*
Whole brain	37.8 ± 7.8	65.4 ± 18.6	0.0056
Cortex			
Frontal (bilateral)	38.1 ± 10.6	58.7 ± 9.5	0.0010
Right frontal	38.8 ± 13.3	58.2 ± 8.4	0.0007
Left frontal	37.5 ± 8.4	59.2 ± 11.8	0.0030
Temporal (bilateral)	39.6 ± 7.2	70.5 ± 7.2	0.0041
Right temporal	40.7 ± 7.0	71.7 ± 17.1	0.0120
Left temporal	38.8 ± 7.7	69.3 ± 9.8	0.0013
Occipital (bilateral)	31.4 ± 7.3	60.4 ± 13.1	0.0047
Right occipital	31.6 ± 8.5	60.7 ± 13.2	0.0045
Left occipital	31.2 ± 6.3	60.1 ± 14.0	0.0067
Subcortex			
Caudate head (bilateral)	47.5 ± 16.4	88.0 ± 15.2	0.0220
Right caudate head	48.3 ± 18.4	88.0 ± 27.6	0.0473
Left caudate head	46.7 ± 17.2	85.3 ± 20.8	0.0273
Thalamus (bilateral)	52.4 ± 10.5	102.1 ± 21.7	0.0045
Right thalamus	54.4 ± 12.6	102.0 ± 25.7	0.0055
Left thalamus	50.2 ± 8.3	98.4 ± 23.4	0.0044
Lenticular nucleus (bilateral)	50.8 ± 17.4	92.3 ± 22.5	0.0053
Right lenticular nucleus	49.3 ± 17.8	90.1 ± 23.1	0.0080
Left lenticular nucleus	52.3 ± 18.1	92.3 ± 22.5	0.0038

Global and Regional Hypoperfusion **Hospital Day 35.3 ± 19.3** **Hospital Day 95.5 ± 13.5**

Yokota et al., 2003 Psychiatry Clin Neurosci 57:337-39

SPECT Perfusion Changes in Patients with Delirium.



Normal

Parietal hypoperfusion

Subcortical hyperperfusion

Parietal hypoperfusion

- Qualitative analysis: 50% changes in frontal & parietal perfusion
- Semi-quantitative analysis: change blood flow ratios L inferior frontal, R temporal, right occipital, and pons
- Inattention associated with perfusion abnormalities – L inferior frontal region
- Delirium vs. No Delirium: change blood flow ratio parietal lobe (n=6)

Fong T G et al. J Gerontol A Biol Sci Med Sci 2006;61:1294-1299

SPECT

Table 1. SPECT Cerebral Blood Flow Studies in Delirium and Related Conditions

Reference (Ref. No.)	No. of Patients/Controls	Cause of Onset	Location
Bogousslavshy et al. (10)	1/0	Right thalamic infarction	Right frontal hypoperfusion
Shih et al. (46)	1/0	Drug withdrawal	Left frontotemporal hypoperfusion
Kohira et al. (47)	1/0	Hepatic encephalopathy	Cerebellum, basal ganglia, cortical hyperperfusion
Doyle and Warden (48)	1/0	Cardiotomy	Right temporal-occipital hypoperfusion
Ohta et al. (49)	1/0	Portal-systemic encephalopathy	Bilateral parietal hypoperfusion Basal ganglia hyperperfusion
Kamijo et al. (50)	1/0	Barbiturate withdrawal	Diffuse bilateral decrease
Pittock et al. (51)	1/0	Transplant immunosuppression	Bilateral frontal, parietal, temporal hypoperfusion
Ikeda et al. (52)	6/0	Hepatic encephalopathy	Diffusely decreased cortical perfusion; in 4 participants recovery after liver transplant
Jalan et al. (53)	8/0	Oral amino acid loading in cirrhosis	Bilateral temporal lobe, left superior frontal gyrus, and right parietal and cingulate gyrus decrease
Trzepacz et al. (54)	6/6	Cirrhosis	Right basal ganglia and bilateral frontotemproal hypoperfusion
Strauss et al. (55)	10/9	Hepatic encephalopathy	Frontal and basal ganglia hypoperfusion
O'Carroll et al. (56)	10/10	Cirrhosis	Basal ganglia and occipital increase Anterior cingulate decrease
Yazgan et al. (57)	12/8	Hepatic encephalopathy	Bilateral thalamic hypoperfusion
Catafau et al. (58)	13/13	Hepatic encephalopathy	Prefrontal hypoperfusion. Striatal and medial temporal perfusion was higher in more impaired participants
Fong et al. (59)	22/6	Multiple etiologies in hospitalized medical patients	Parietal hypoperfusion in 6 Frontal hypoperfusion in 5 Reversible parietal hypoperfusion in 3 of 6
Ogasawara et al. (60)	5/36	Subdural hematoma	Hyperperfusion under surgical site
Gokgoz et al. (61)	6/44	Cardiac surgery	Reduced perfusion in bilateral temporoparietal and frontal and right occipital
Gunaydin et al. (62)	7/43	Cardiac surgery	Bilateral temporoparietal, frontal, and occipital

Note: SPECT = single photon emission computed tomography.

Alsop et al., 2006, J of Gerontology, 61(12); 1287-93

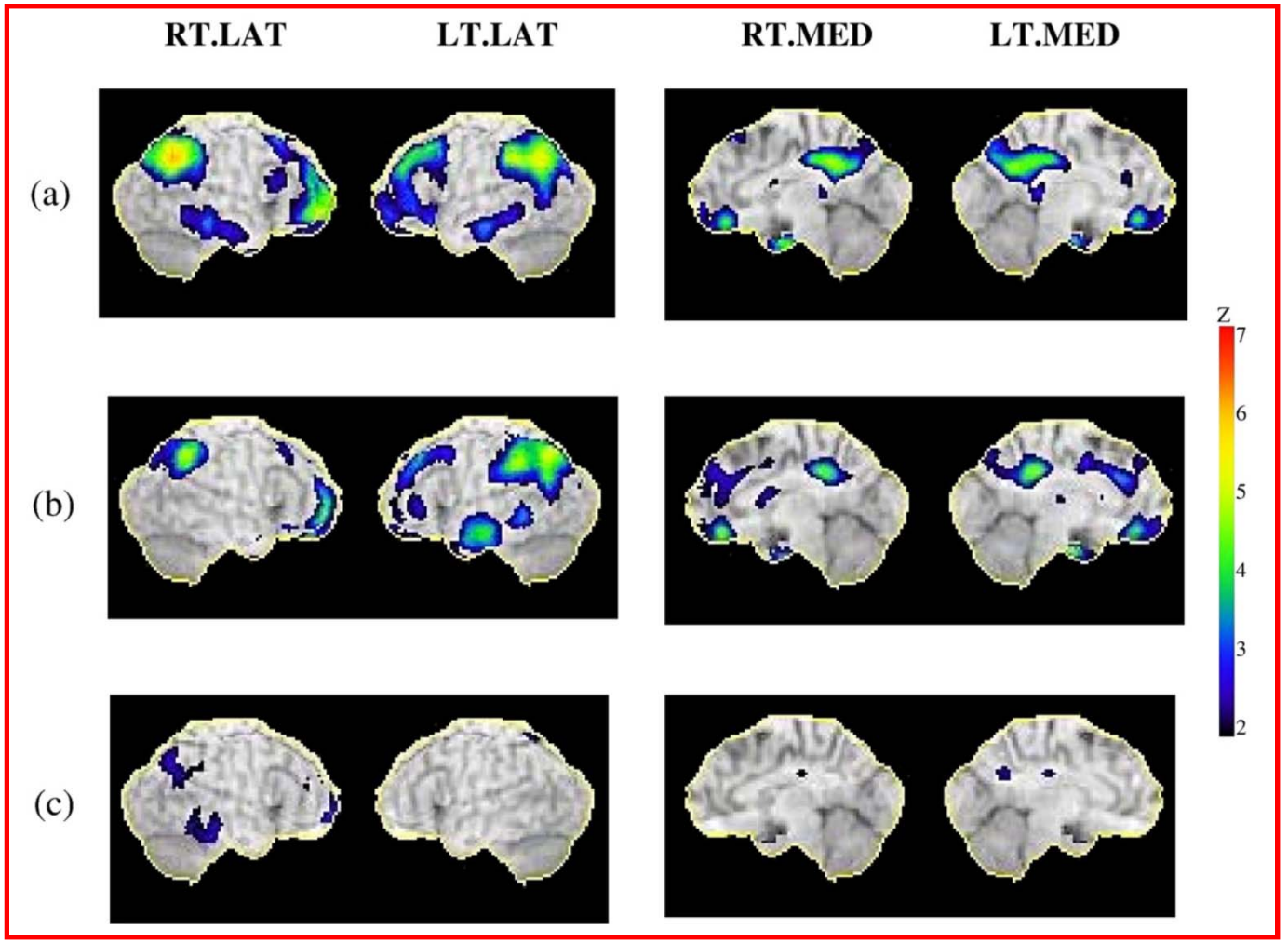
Longitudinal rCBF in AD

48 patients
Followed over 37 months
Grouped by MMSE scores

rCBF Rapidly Progressing vs. Controls

rCBF Slowly Progressing vs. Controls

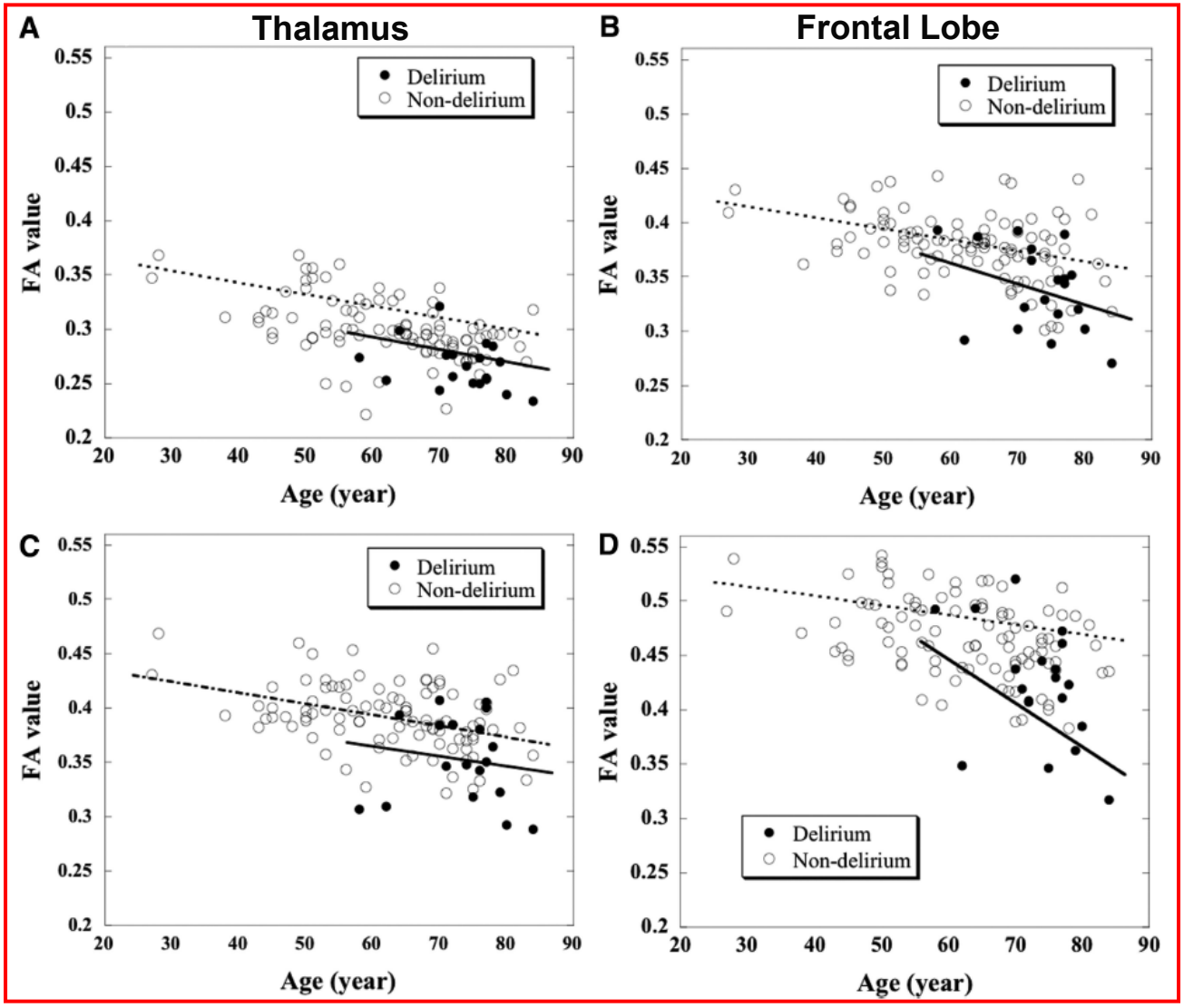
rCBF Rapidly vs. Slowly Progressing



Significant decrease in rCBF in frontal, temporal, parietal lobes, and posterior cingulate

Hanyu 2010 J Neurological Sciences, 290, 96-101

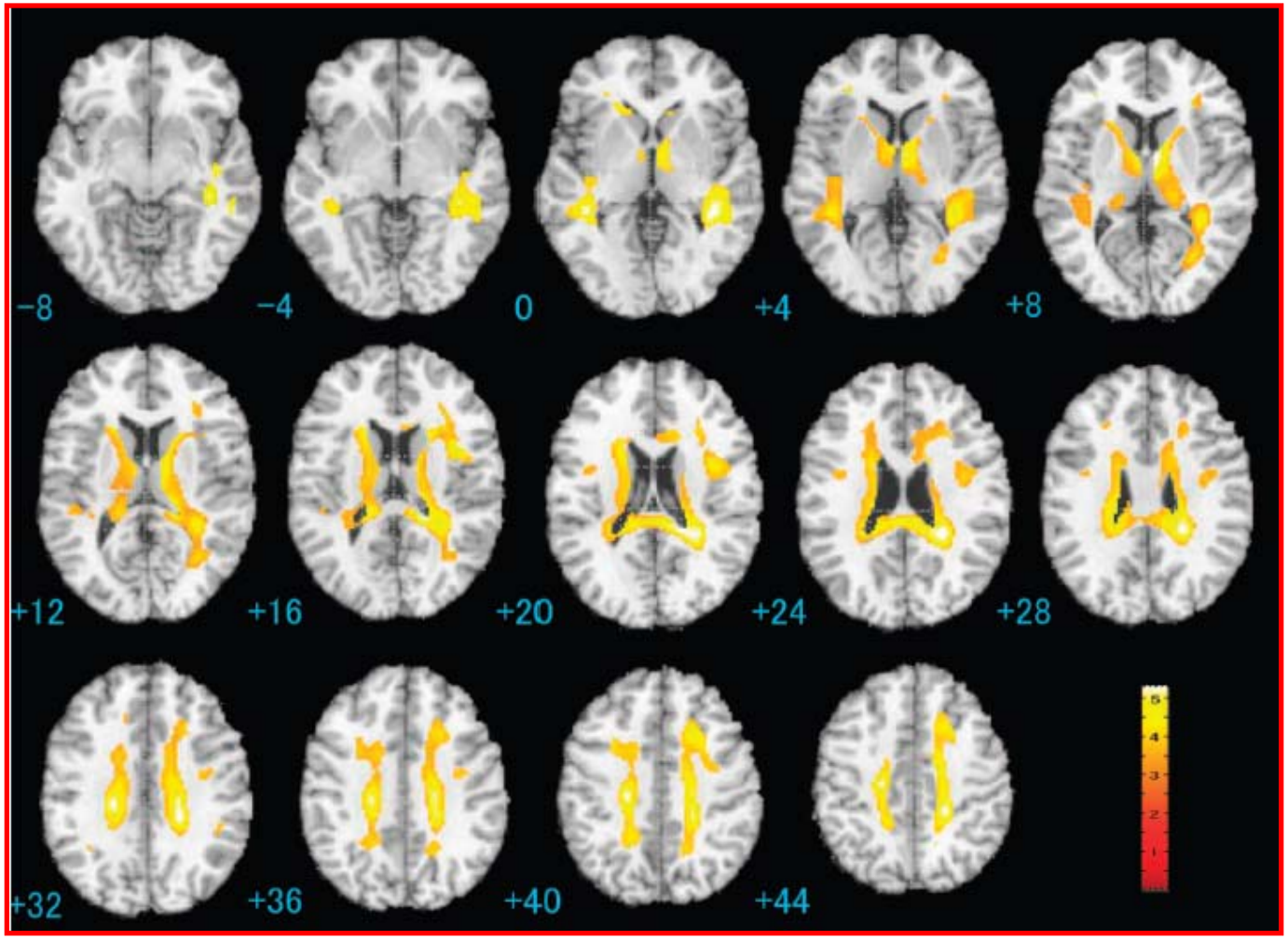
DTI – White Matter Integrity



Decreased FA values of the Delirium Group

Shioiri et al, Am J Geriatr Psychia, 2010

FA Values: Delirium vs. Non-delirium

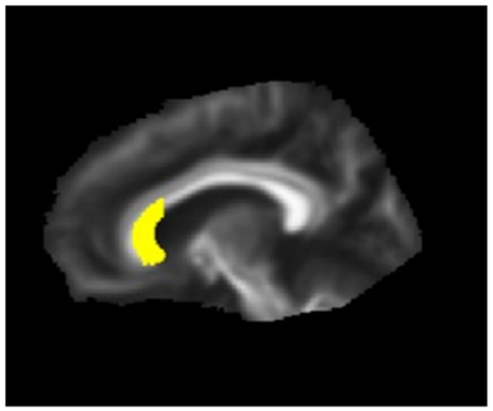


A significant decrease in the FA values for the delirium group in

- **Bilateral thalamus**
- **Bilateral deep white matter bilaterally**
- **Corpus callosum**

Shioiri et al, Am J Geriatr Psychia, 2010

Delirium Duration and Fractional Anisotropy in Corpus Callosum and Internal Capsule



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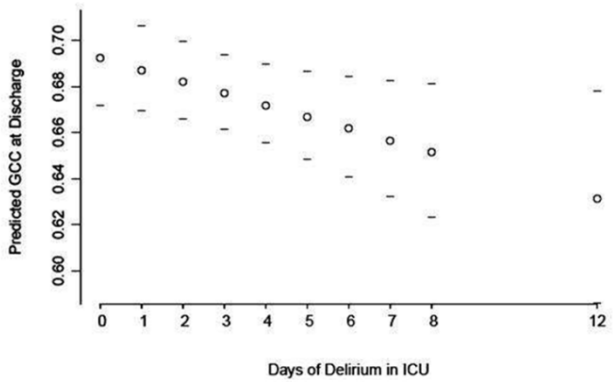

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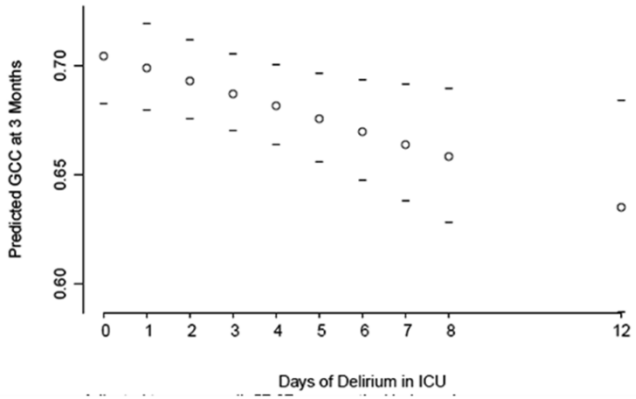

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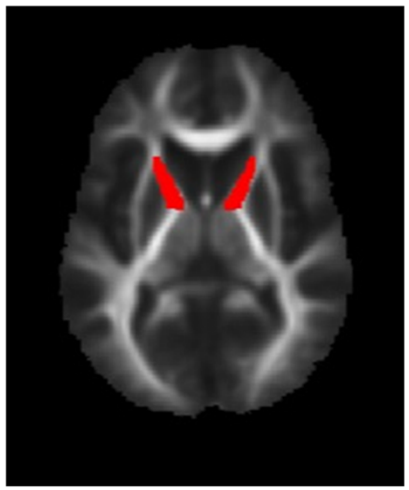

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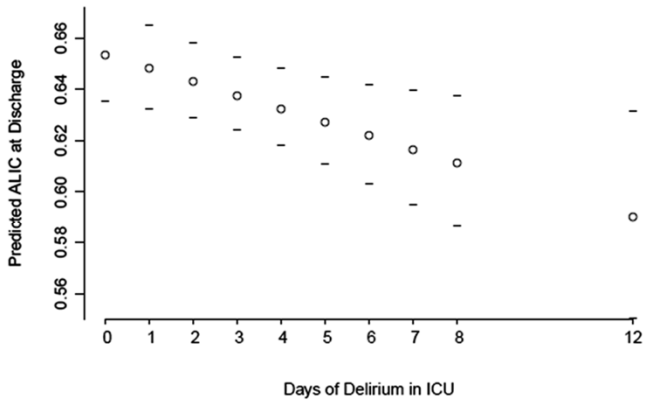

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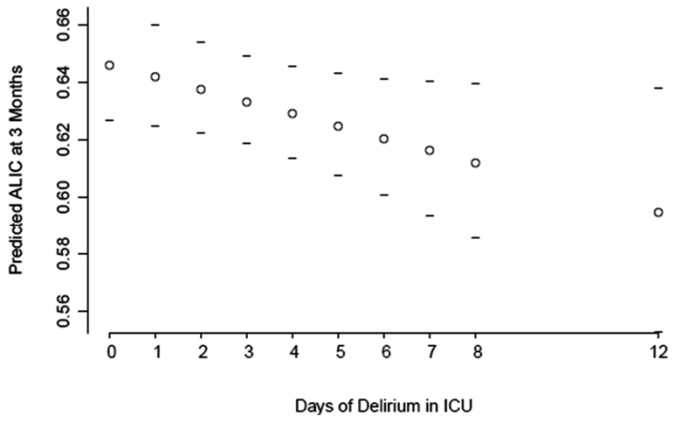
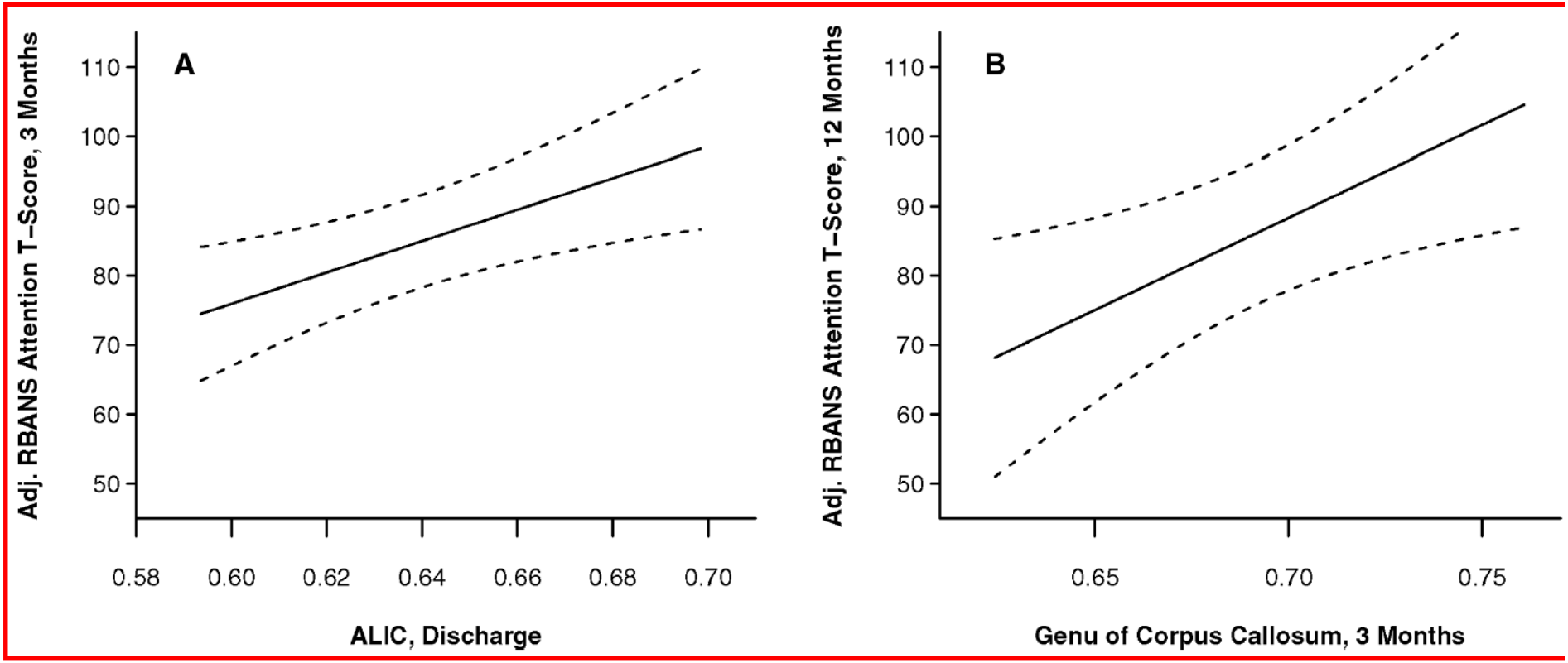


C

Adjusted for age and sepsis, longer duration of delirium

Gunther et al., 2010 CCM , 40:2022-32

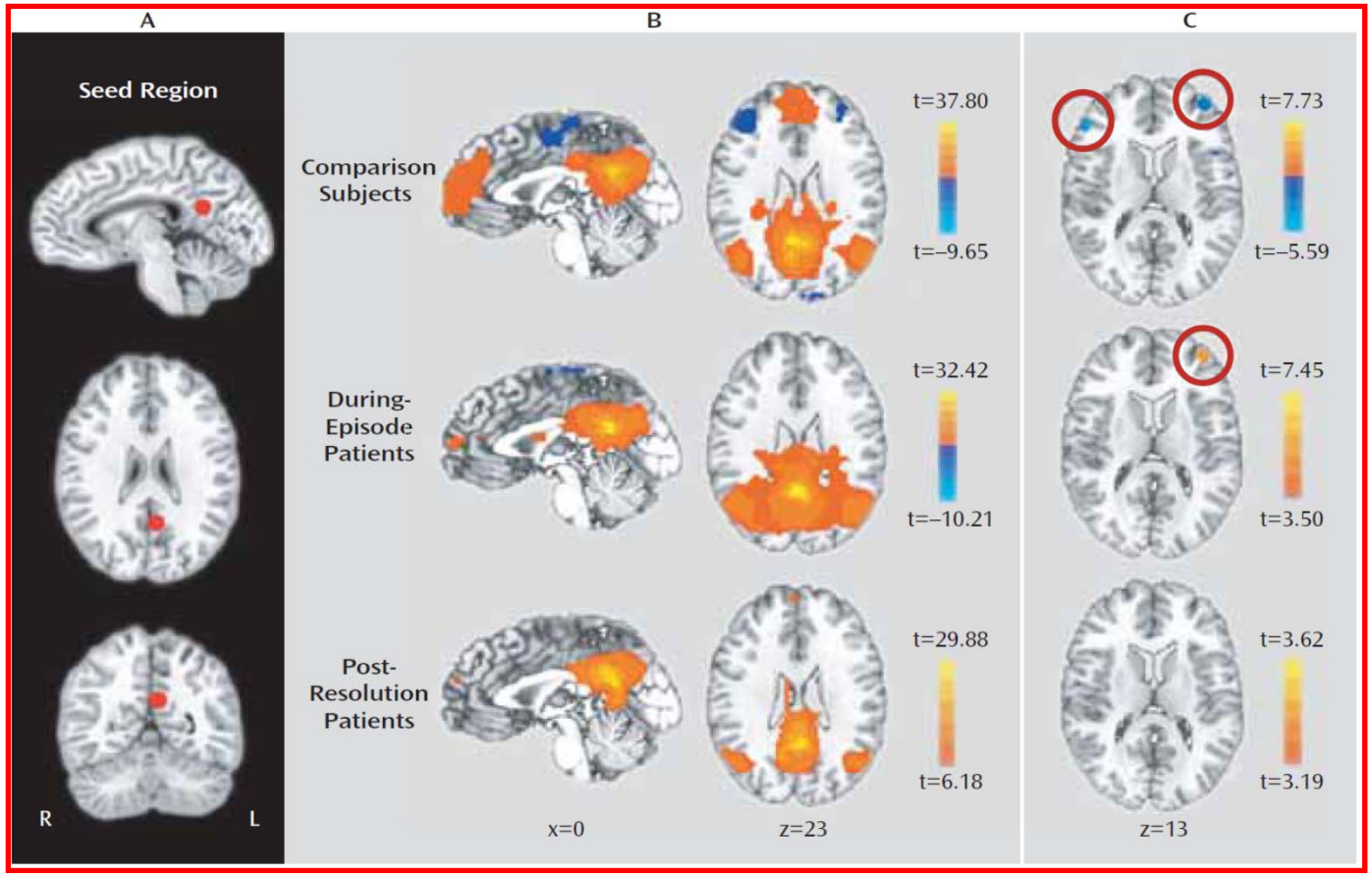
White Matter (FA) and Cognitive Function



Lower FA in ALIC associated with worse attention scores at 3 months
Lower FA in genu CC associated with worse attention scores at 12 months

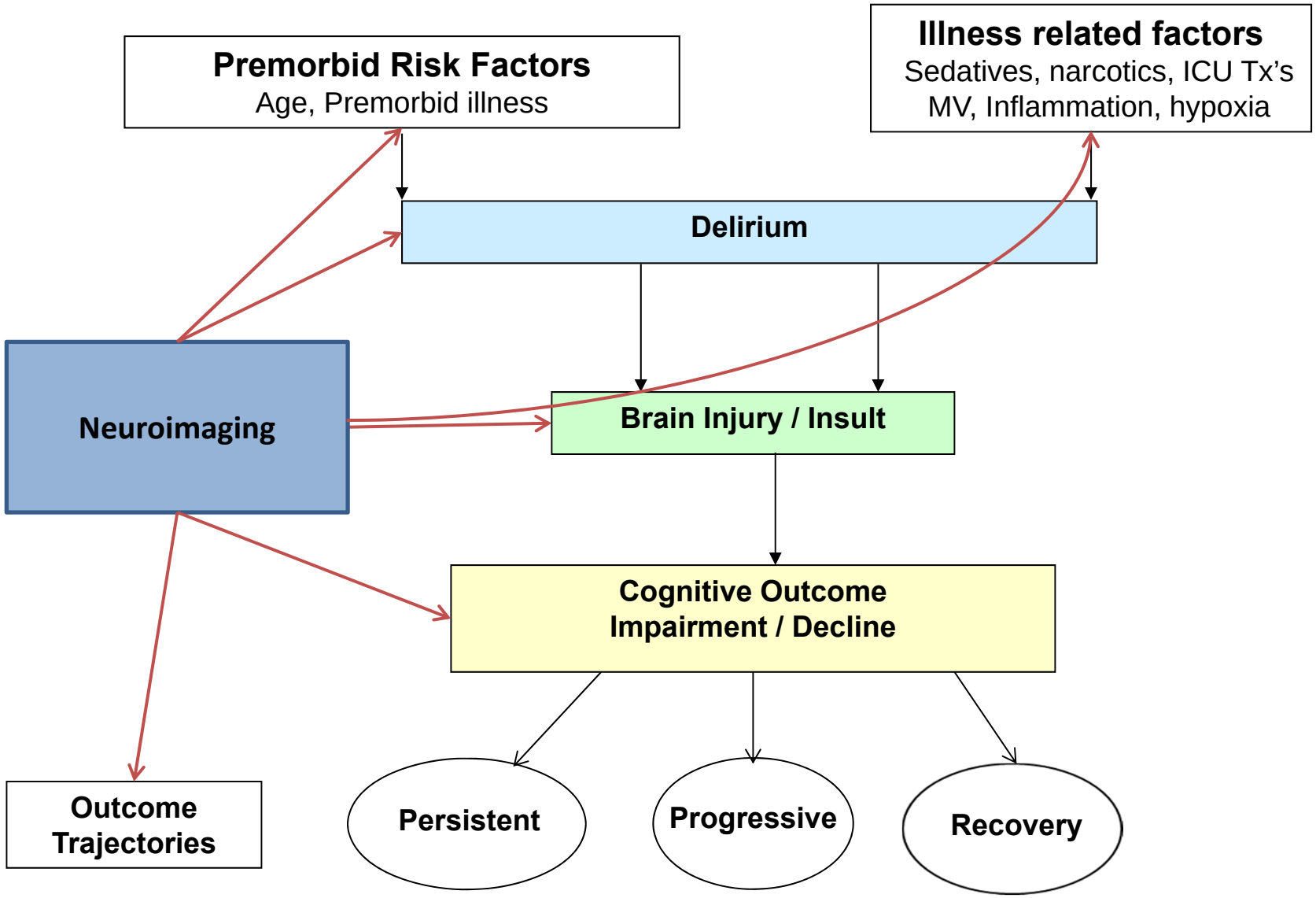
Morandi et al., 2010 CCM , 40:2182-89

fMRI: Resting State and Delirium



- Dorsolateral prefrontal and posterior cingulate activity were inversely correlated in controls, and were strongly correlated during delirium
- Functional connectivity of thalamic and caudate nuclei with subcortical regions were reduced during delirium, recovered after delirium resolution
- Abnormal resting-state functional networks may underlie the pathophysiology of delirium

Choi 2012 Am J psychiatry, 169:498-507


Premorbid Risk Factors
Age, Premorbid illness
Illness related factors
Sedatives, narcotics, ICU Tx's
MV, Inflammation, hypoxia
Delirium
Neuroimaging
Brain Injury / Insult
Cognitive Outcome
Impairment / Decline
Outcome
Trajectories
Persistent
Progressive
Recovery

Potential Areas for Investigation

- Limited studies – even in structural imaging
- Small sample sizes
- Lack of control groups
- Pathophysiology
- Risk factors
- Longitudinal studies
- Beyond clinical imaging- New analysis and modeling methods
- Other Imaging Modalities
  - Amyloid Imaging – amyloid deposition post-delirium
  - Arterial Spin Labeling – blood flow and resting blood flow
  - Blood Brain Barrier imaging – disruption
  - DTI – white matter integrity and connectivity
  - Functional MRI – resting state, stimuli or task responses
  - PET and SPECT neurotransmitter tracers (Ach, DA)
- Does etiology matter?