



Duke Anesthesiology

Postoperative Neurocognitive Disorders- a common language, and biomarker studies

Miles Berger, MD, PhD

Assistant Professor, Neuroanesthesia Division

Senior Fellow, Duke Center for Aging

Adjunct Faculty, Duke Center for Cognitive
Neuroscience



Outline:

I. Postoperative Delirium and Cognitive Dysfunction (POCD): Differences, Similarities, Nomenclature

II. Is POCD (or delirium) associated with accelerated Alzheimer's disease pathogenesis? (MADCO-PC study results)



Postop Delirium & POCD: Differences

Delirium- (DSM-V definition)

- fluctuating disturbance in attention/awareness,
- an acute change from baseline,
- with disturbed cognition/perception,
- not due to a pre-existing neurocognitive disorder,
- not in context of severely reduced arousal (i.e. coma)

POCD- Postoperative Cognitive Dysfunction

- a postoperative decline in cognitive function,
- measured with cognitive tests before & after anesthesia/surgery



Postop Delirium & POCD: Timeframe

Time Frame of Delirium and POCD

**Emergence
Delirium**

**Post-Op
Delirium**

**Post-Op Cognitive
Dysfunction**

Pre-Op

OR PACU

24-72 hours Post-Op

Weeks-Months

Silverstein J et al, *Anesthesiology*, 2007



A Unified Nomenclature for Postoperative Neurocognitive Disorders (PND)

Postoperative Delirium- based on DSM-V delirium criteria, occurs in hospital up to 1 wk postop or hospital discharge (whichever occurs first).

Delayed Neurocognitive Recovery- DSM-V criteria for major or mild neurocognitive disorder, from 1-30 days postop

Postoperative Neurocognitive Disorder (POCD)- DSM-V criteria for mild or major neurocognitive disorder, from 1-12 months postop

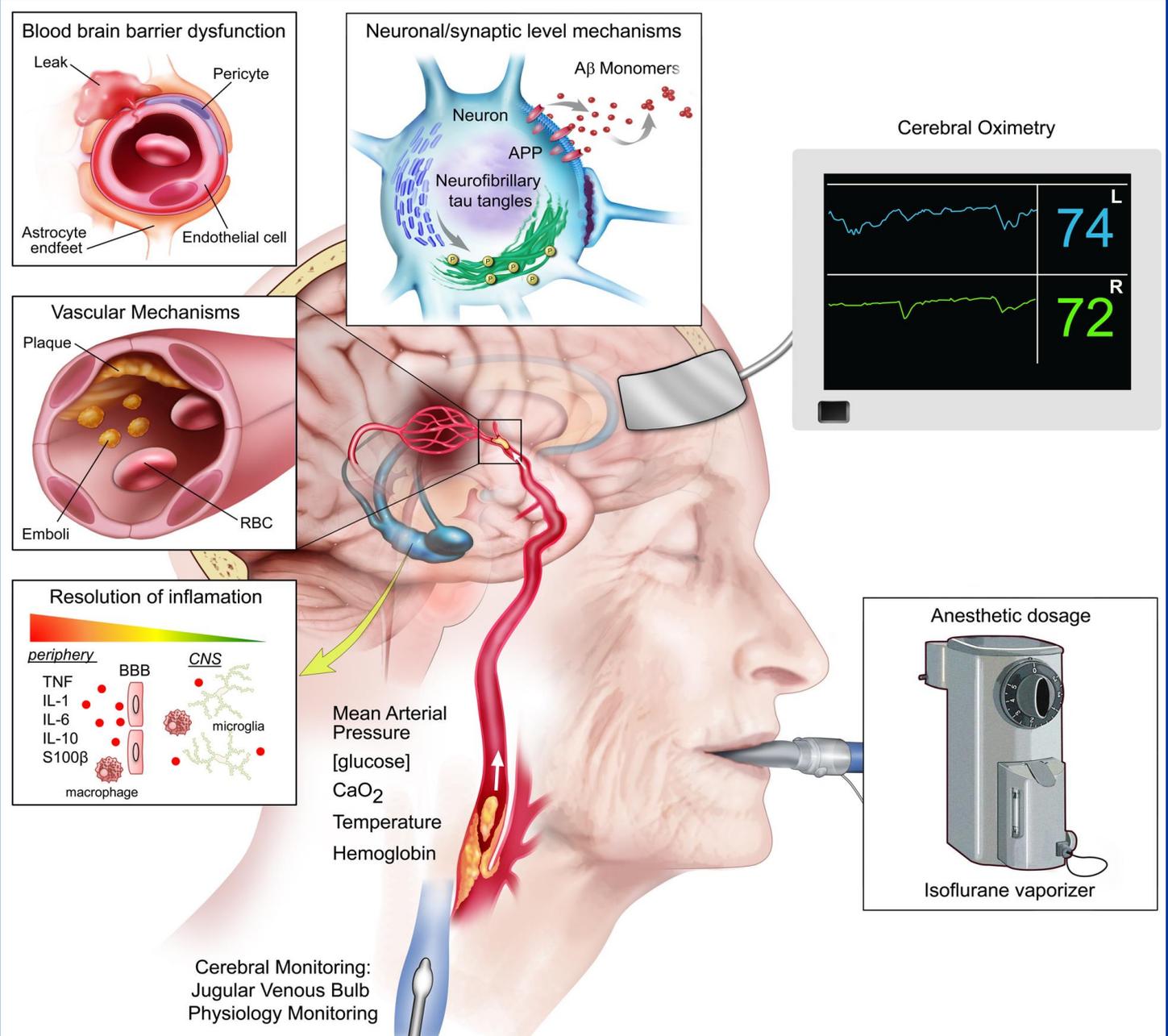


Postop Delirium & POCD: Similarities

	Postop Delirium	POCD
Risk Factors	Age, depression, pre-op cognitive dysfunction, pre-clinical AD pathology	Age, depression, pre-op cognitive dysfunction, pre-clinical AD pathology
Proposed Mechanisms	Neuro-inflammation, Blood-brain-barrier dysfunction,	Neuro-inflammation, Blood-brain-barrier dysfunction
Sequelae	↓Quality of Life, ↑1 yr mortality, Long term cognitive decline	↓Quality of Life, ↑1 yr mortality, Long term cognitive decline



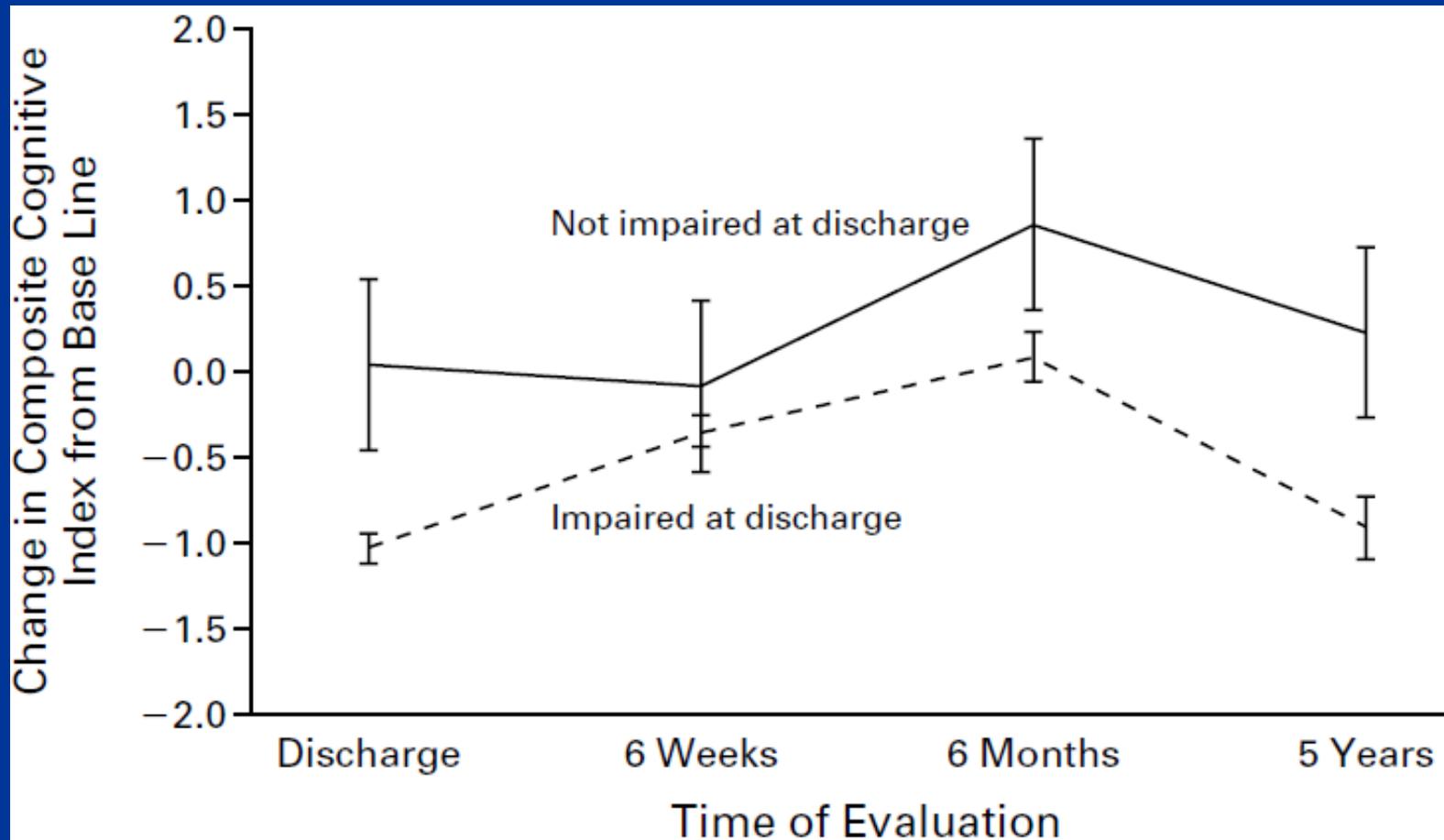
Potential Mechanisms of POCD, Delirium



Berger M et al,
Anesthesiol
 2018, *In Press*



Long-term Cognitive Decline after POCD

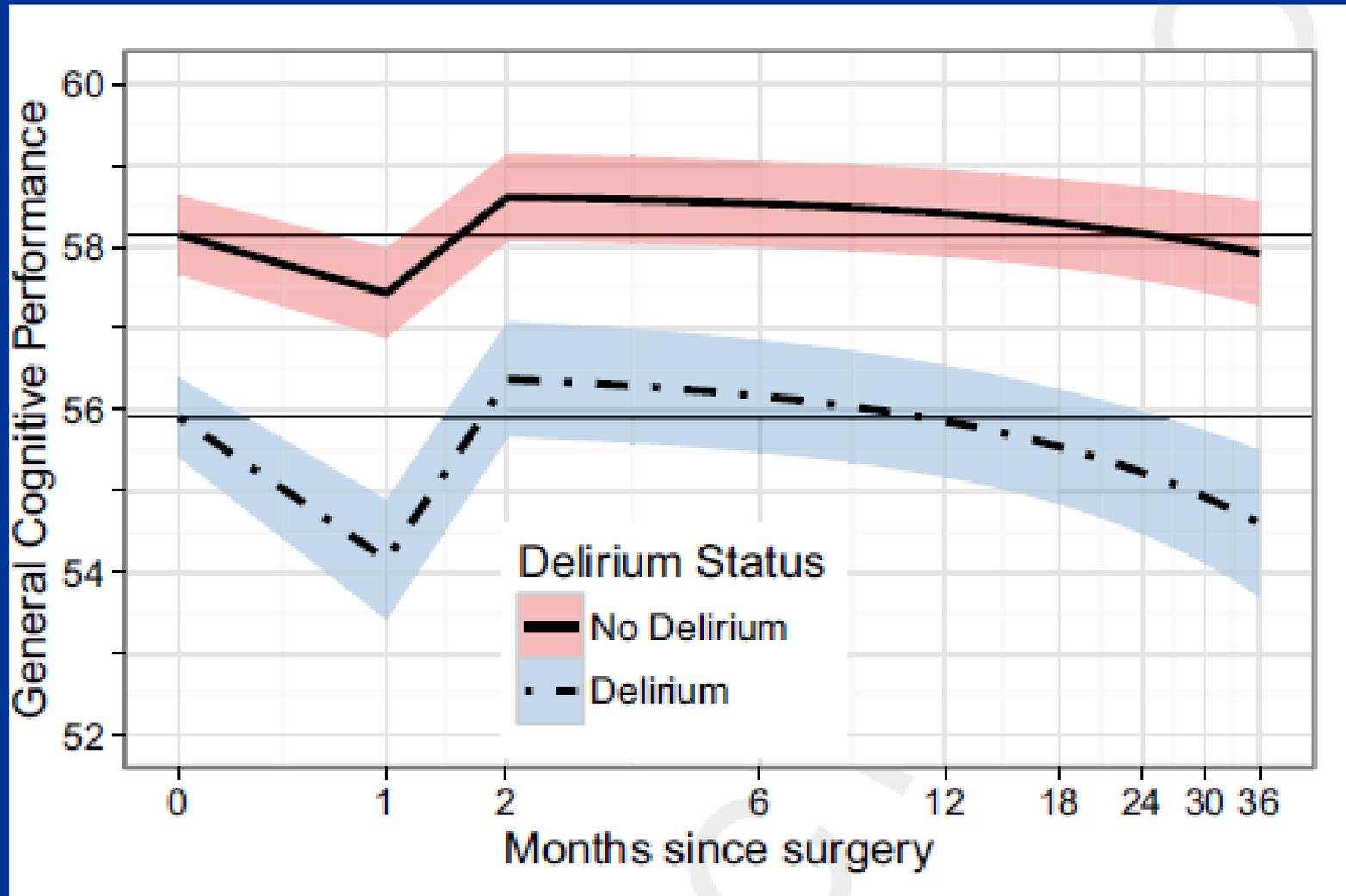


Composite Cognitive Index as a Function of Cognitive Impairment at Discharge.

-Newman MF et al, *NEJM*, 2001



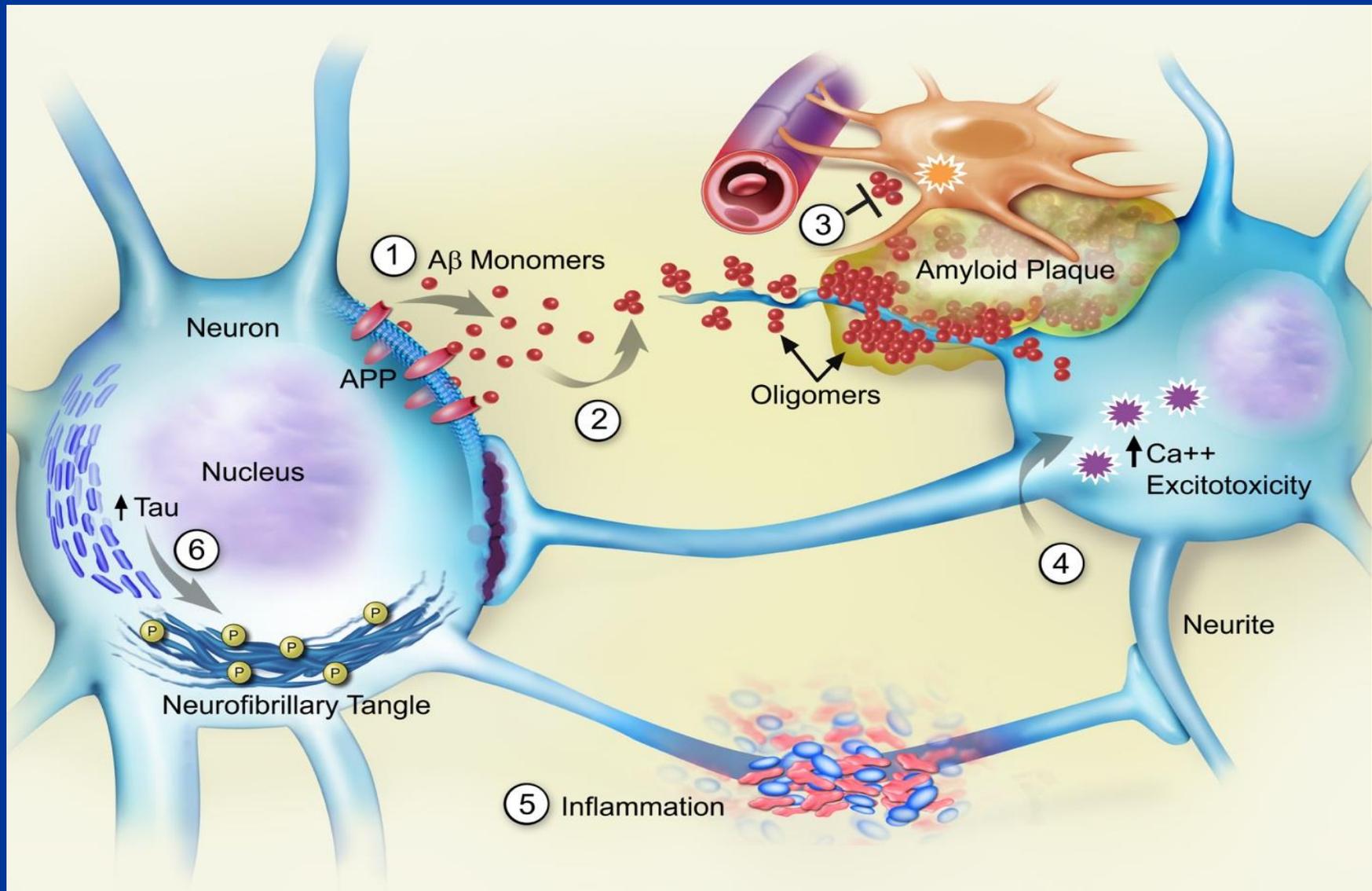
Long-term Cognitive Decline after Delirium



-Inouye S. et al, *Alz Dementia*, 2016



Anesthesia/Surgery → ↑ AD pathology



Alzheimer's Disease (AD) Pathology as a risk factor for Delirium, POCD

3 Phases of Alzheimer's disease

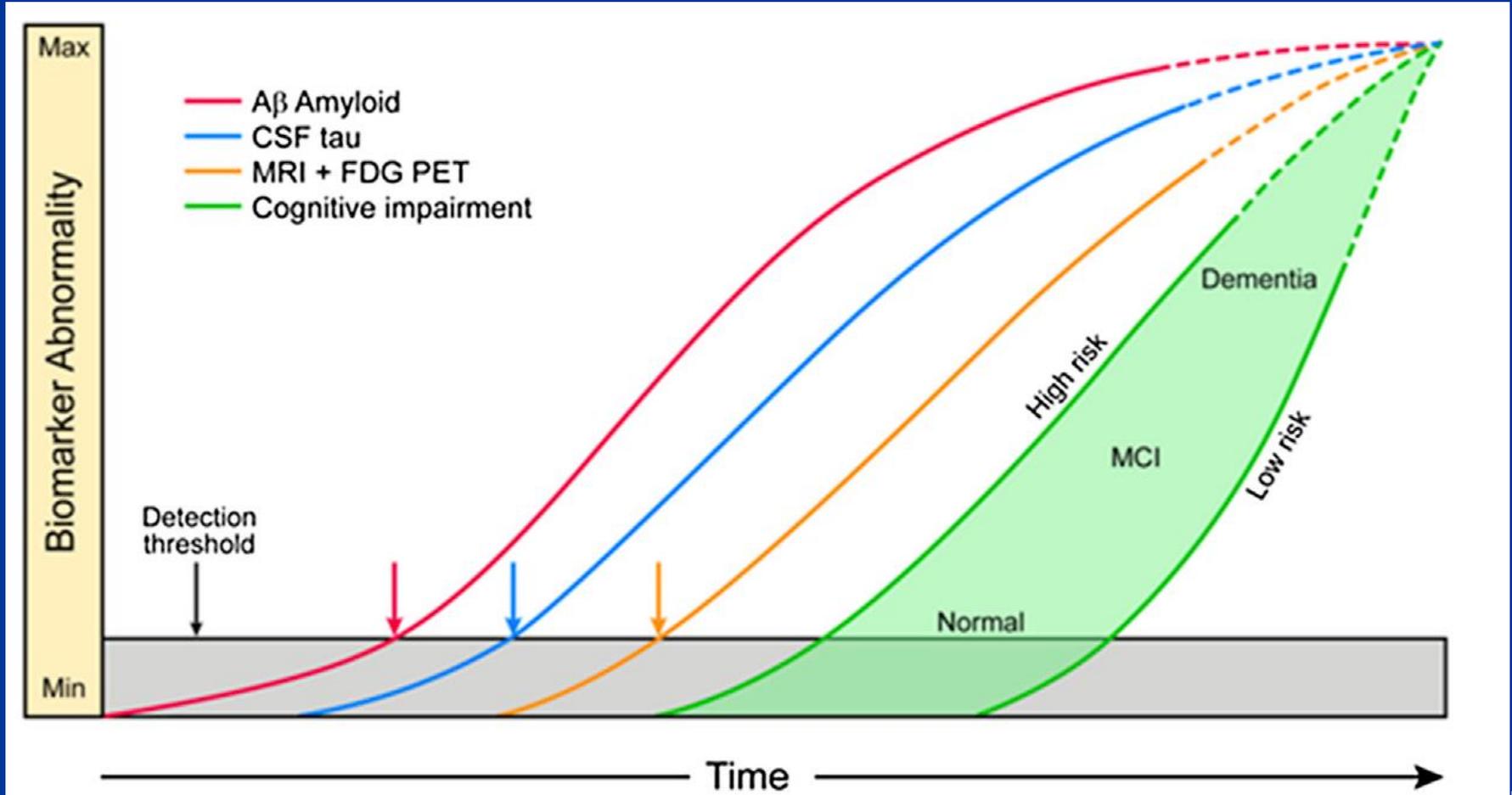
1. Preclinical AD (biomarker positive, asymptomatic)
2. MCI (Mild Cognitive Impairment)
3. Dementia due to Alzheimer's Disease

- McKhann G et al, *Alz & Dementia*, 2011
- Sperling RA et al, *Alz & Dementia*, 2011
- Albert MS et al, *Alz & Dementia*, 2011



Delirium & POCD, Alzheimer's Disease

Alzheimer's develops over a long time:



-Jack CR et al, *Neuron*, 2013



Preclinical AD → ↑ risk for Delirium, POCD

Elevated CSF tau/A β ratio → ↑ delirium risk

Low CSF A β levels → ↑ POCD risk

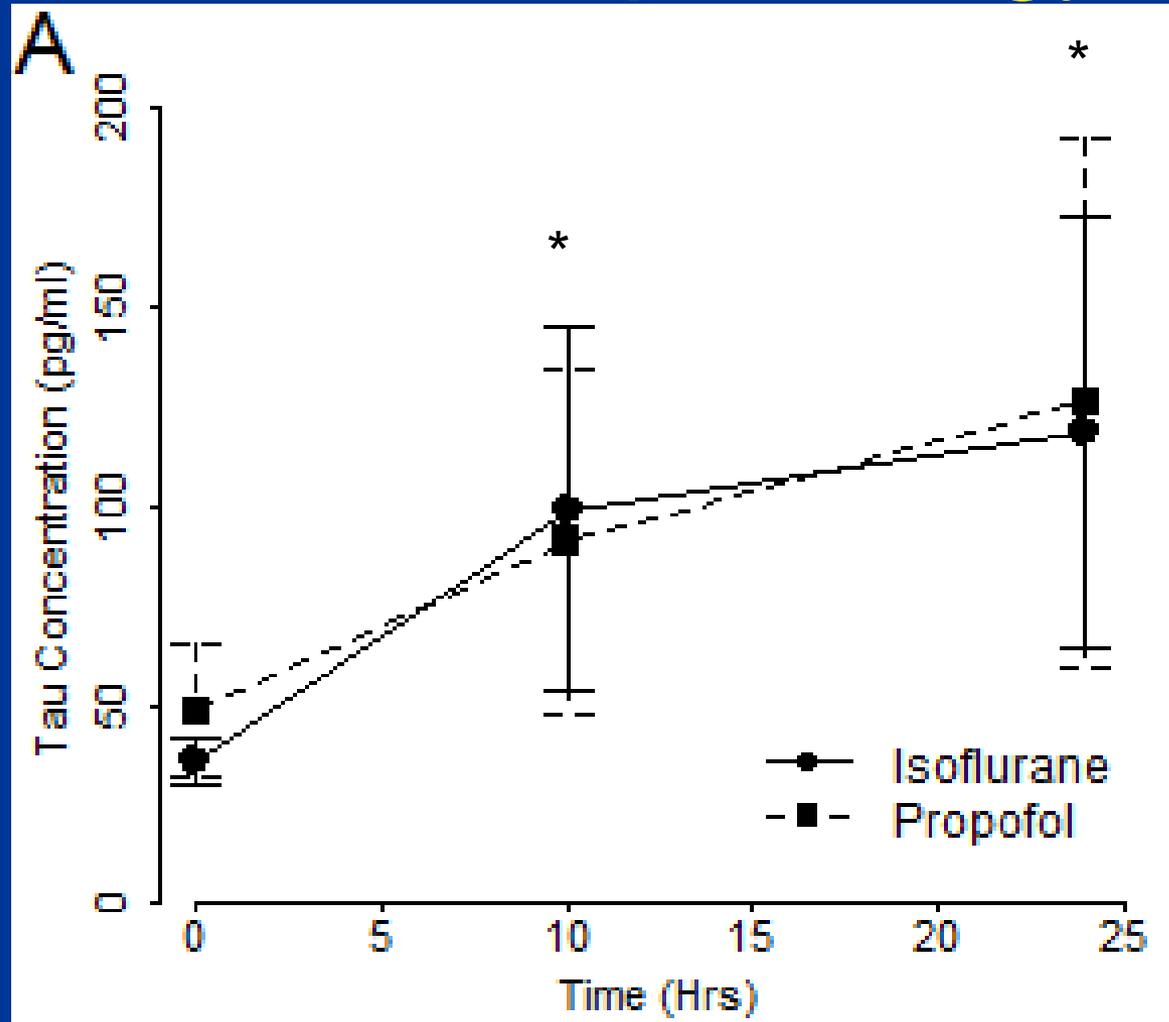
-Xie Z et al, *Ann Surgery*, 2013

-Xie Z et al, *Ann Clin Transl Neurol*, 2014

-Evered et al, *Anesthesiology*, 2016;



II. Is POCD associated with an acceleration of AD pathology?



-Berger M, Nadler J et al, *J Alz Dis*, 2016



II. Is POCD Associated with an Acceleration of AD Pathology?

MADCO-PC: Markers of Alzheimer's Disease and neuroCognitive Outcomes after Periooperative Care

Primary outcome- correlation between perioperative change in CSF AD biomarker (tau) and continuous cognitive change index (from preop to 6 weeks post-op)



II. The MADCO-PC study

Patients scheduled for surgery



Enrollment, baseline cognitive testing



Pre-Induction CSF + blood samples



24 hr post-op CSF + blood samples,
delirium screening POD 1-5



6 week post-op cognitive testing, CSF + blood samples



Correlate CSF AD biomarkers, cognitive findings

N=110 surgical patients



II. The MADCO-PC study

Inclusion Criteria:

- Age ≥ 60
- Having non-neurologic, non-cardiac surgery under general anesthesia, scheduled for >2 hours
- English Speaking

Exclusion Criteria:

- Pregnancy
- Prisoners
- Chronic Anticoagulant Use
- Severe Claustrophobia



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