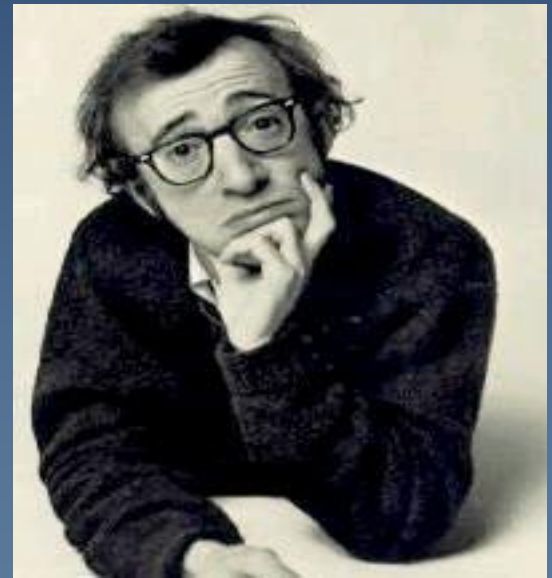


Preventing Postoperative Cognitive Decline in the Elderly



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"My brain, that's my second favorite organ"



Subtle Perioperative Brain Injury

- ◆ Emergence Delirium
- ◆ Postoperative Delirium
- ◆ Postoperative Cognitive Decline

Postoperative Delirium

An acute brain disorder that has a fluctuating course and characterized by disturbance of attention, memory, orientation, and perception

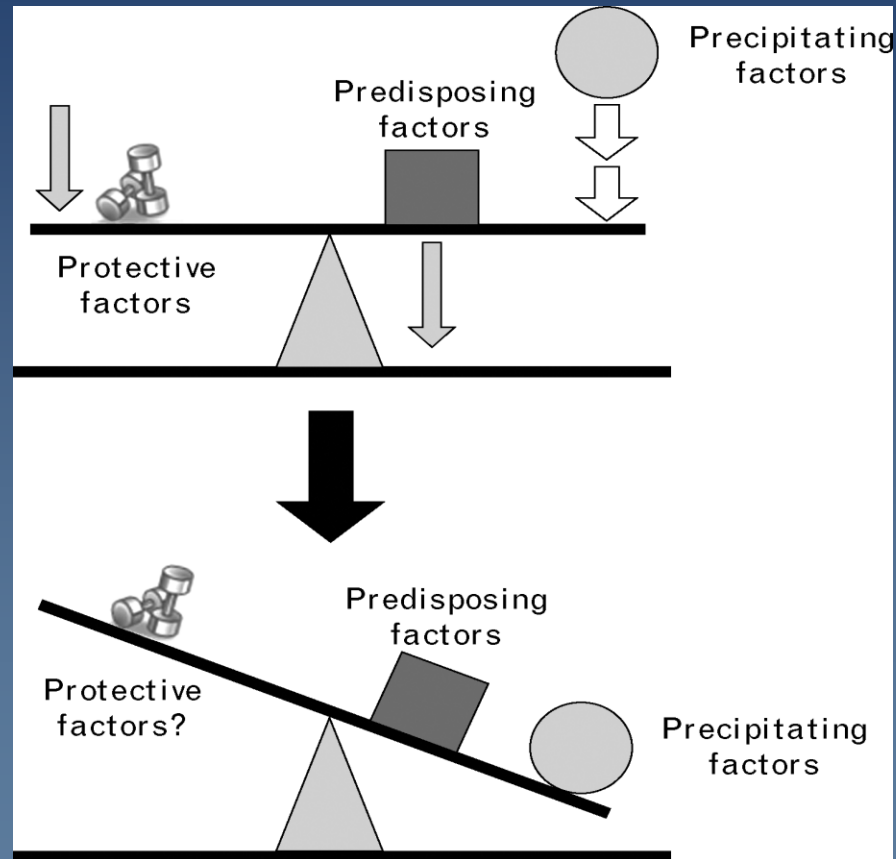
Incidence (in elderly)

**Noncardiac surgery:
10%-40%**

**Cardiac surgery: 20%-
70%**




Interplay of Factors Leading to Delirium



Predisposing Factors

- ◆ Age
- ◆ Functional impairment
- ◆ Cognitive impairment
- ◆ Medical co-morbidity
- ◆ Drugs
- ◆ Genetic factors (sigma 4 allele of apolipoprotein E4)

Precipitating Factors

- ◆ Admission to ICU
 - ◆ Drugs
 - ◆ Concomitant illness
 - ◆ Primary neurologic disease
 - ◆ Pain
 - ◆ Use of physical restraints
 - ◆ Prolonged sleep deprivation
- 

Can Delirium be Prevented in the Postoperative Period?

- ◆ Pharmacological prevention
- ◆ Non-pharmacologic multicomponent strategies
 - Good nursing care
 - Regular orientation
 - Early mobilization
 - Reduce modifiable risk factors

Inouye S, JAMA, 1998

Pain Management and Postoperative Delirium

Table 6. Factors Associated with Postoperative Delirium by Multivariate Logistic Regression

Variable	OR	95% CI
Age \geq 70 years	2.50	1.47–4.24
Moderate pain at rest preoperatively (VAS 1–4 versus VAS = 0)	2.19	1.20–4.01
Severe pain at rest preoperatively (VAS \geq 5 versus VAS = 0)	3.72	1.54–8.96
Increase in pain at rest; baseline vs. postoperative Day 1	1.11	1.01–1.23
Neuraxial vs. patient-controlled analgesia for postoperative pain control ^a	0.83	0.39–1.74
Oral narcotics vs. patient-controlled IV analgesia for postoperative pain control	0.35	0.17–0.73

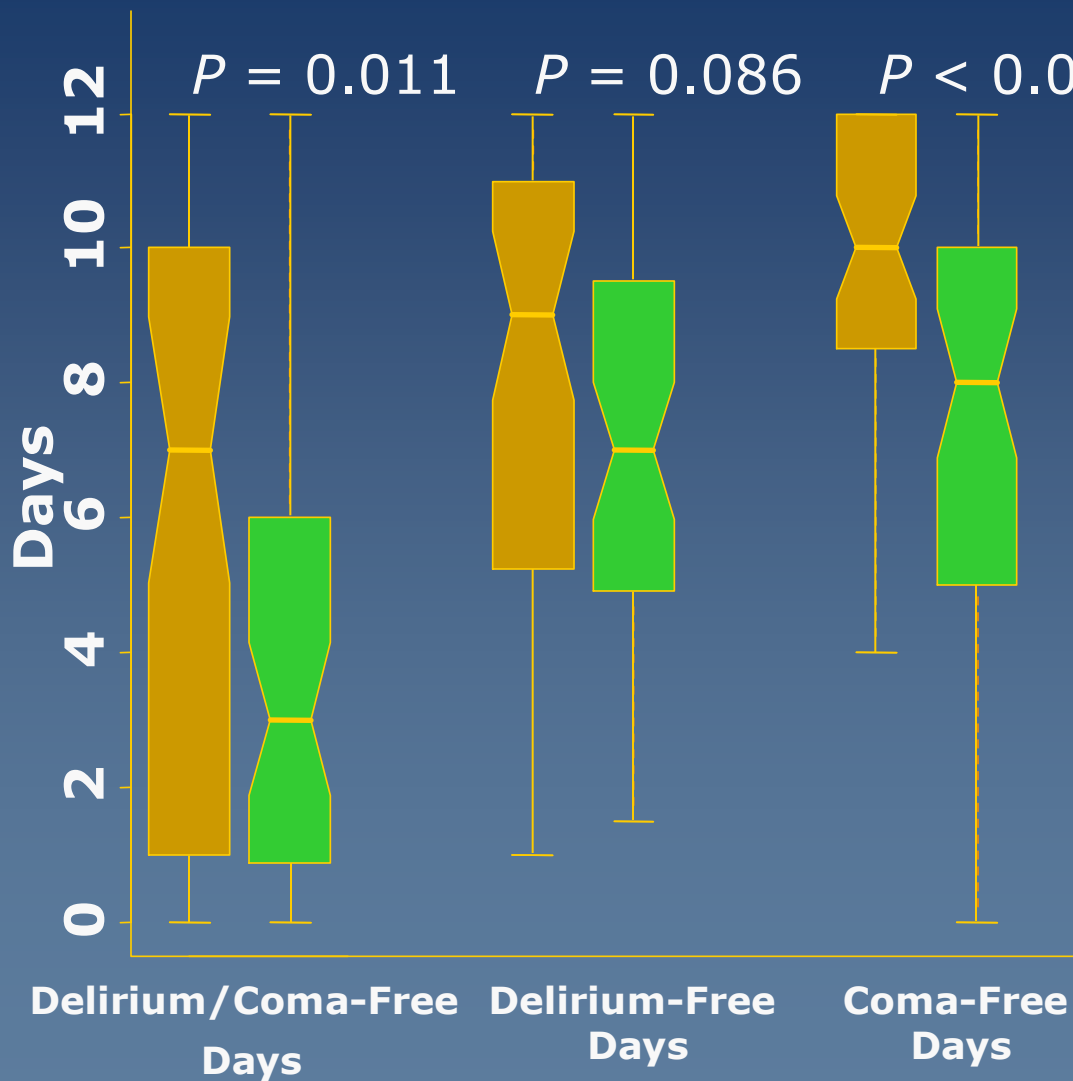
OR = odds ratio; CI, confidence interval; VAS = Verbal Version of Visual Analog Scale (0-10) [linear tool widely used to measure pain from none (0) to severe (10)].

^a Indicated by an increase in VAS self-reported pain by \geq 2 points.

Pharmacologic Strategies

- ◆ Dopamine → Haloperidol
- ◆ Serotonin → Risperidone/Quetiapine
- ◆ Acetylcholine → Rivastigmine/Donazepil
- ◆ Norepinephrine → Dexmedetomidine
- ◆ **GABA** → **Benzodiazepines**

MENDS: Dexmedetomidine vs Lorazepam

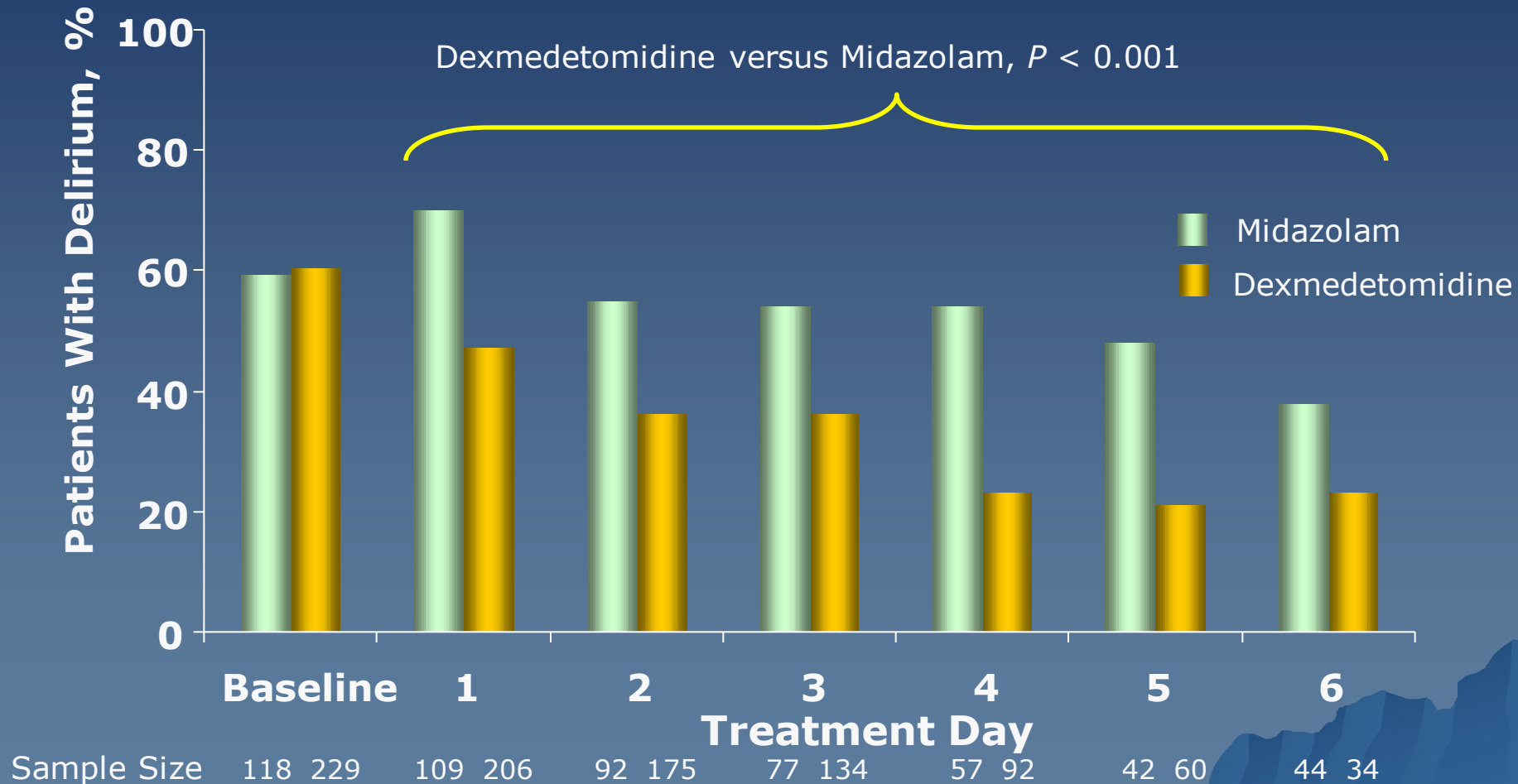


- Dexmedetomidine resulted in more days alive without delirium or coma ($P = 0.01$) and a lower prevalence of coma ($P < 0.001$) than lorazepam
- Dexmedetomidine resulted in more time spent within sedation goals than lorazepam ($P = 0.04$)
- Differences in 28-day mortality and delirium-free days were not significant

■ Dexmedetomidine n = 52
■ Lorazepam n = 51

Reduced Delirium Prevalence with Dexmedetomidine vs Midazolam

SEDCOM



Monitoring Depth of Anesthesia and Postoperative Delirium

Study	Routine Care	BIS-Guided	P-Value
Radtke F, Br J Anaesth, 2013	124/580 (21.4%)	95/575 (16.7%)	0.036
Chan M, J Neurosurg Anesth, 2013	109/452 (24.1%)	70/450 (15.6%)	0.01

Delirium Prevention

- ◆ Multicomponent targeted intervention strategy
- ◆ Optimizing medical condition
- ◆ Continue antidepressant treatment
- ◆ Postoperative pain control
- ◆ Avoid benzodiazepines
- ◆ Dexmedetomidine
- ◆ Use of brain function monitors (?)

Grandma Never Was The Same...

THE LANCET]

ORIGINAL ARTICLES

[AUGUST 6, 1955

ADVERSE CEREBRAL EFFECTS OF ANÆSTHESIA ON OLD PEOPLE*

P. D. BEDFORD

M.D. Leeds, M.R.C.P.

CONSULTANT PHYSICIAN TO THE COWLEY ROAD HOSPITAL,
OXFORD

It is well established that the human brain is extremely vulnerable to short periods of vascular insufficiency (Courville 1939, Hoff et al. 1945, Corday et al. 1953). As the cerebral circulation of many elderly patients is

he is either quite unable to give an account of himself or gives a story upon whose accuracy no reliance can be placed. Secondly, relations and friends tend to blame any dramatic incident, such as an operation or an accident, for the dementia which has in fact been a slowly progressive intellectual degradation, antedating the operation or accident. This is a natural tendency. The old person had been suffering a mental decline so gradual as to have gone unnoticed by those with whom he lived. Defects which to an outsider would have been obvious signs of dementia had to his intimates been merely the old person's idiosyncrasies. The accident or

“He’s become so forgetful since...”

“He can’t concentrate on anything since...”

“She’s become childish and unreliable since...”

“He’s not just the same person since...”

CONCLUSION: Operations on elderly people should be confined to unequivocally necessary cases

Postoperative Cognitive Dysfunction (POCD):

An impairment of functioning in several cognitive domains: memory, executive functioning, attention, and comprehension



POCD Following Cardiac Surgery

Study	Follow-up	Incidence
Newman M, NEJM, 2001	6 months & 5 years	45% & 42%
Van Dijk D, Ann Thor Surg, 2008	5 years	34% versus 16 % in control
Selnes O, Ann Neurol, 2008	3 and 6 years	No difference
Wahrborg P, Circulation, 2004	1	No difference

POCD following Non-Cardiac Surgery

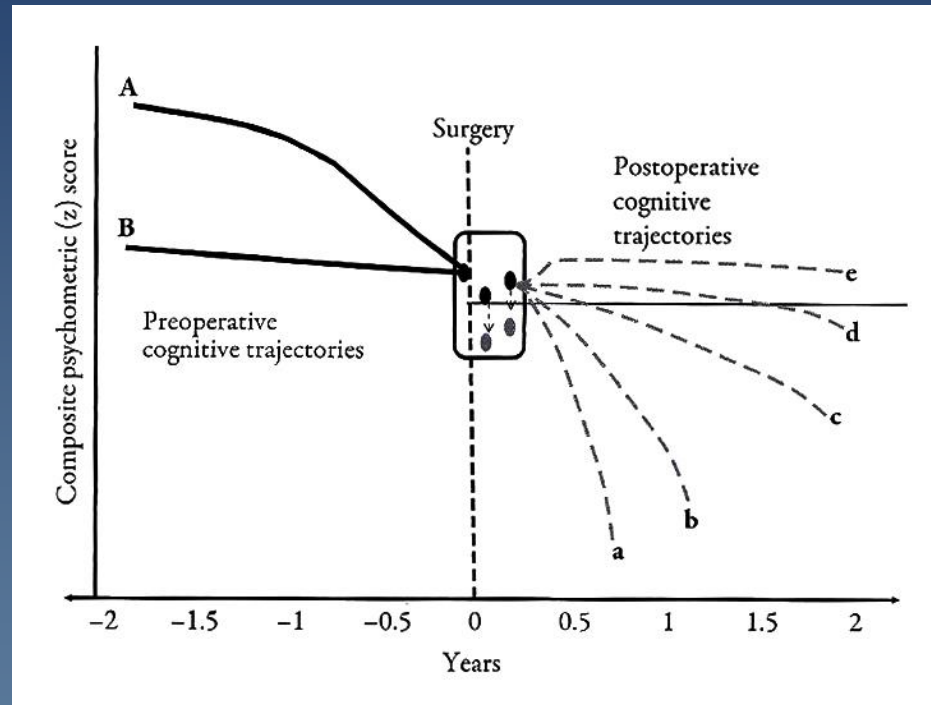
Study	Follow-up	Incidence
Molner J, Lancet, 1998	3 months	9.8%
Abidstrom H, Acta Anaest Scand, 2000	1-2 years	No difference
Avidan M, Anesthesiology, 2009	3.1 years(median)	No difference
McDonagh, Anesthesiology, 2010	1 year	46%
Kline R, Anesthesiology, 2012	9 month (median)	Only patients with MCI

Methodological Challenges

- ◆ Definition of POCD
- ◆ What tests should we use?
- ◆ Controls
- ◆ Learning effect
- ◆ Cognitive trajectory

There are no laboratory test or imaging study which can be used to predict or diagnose POCD

Preoperative and Postoperative Cognitive Trajectories



Sanders R, Neurologic outcomes of Surgery & Anesthesia, 2013

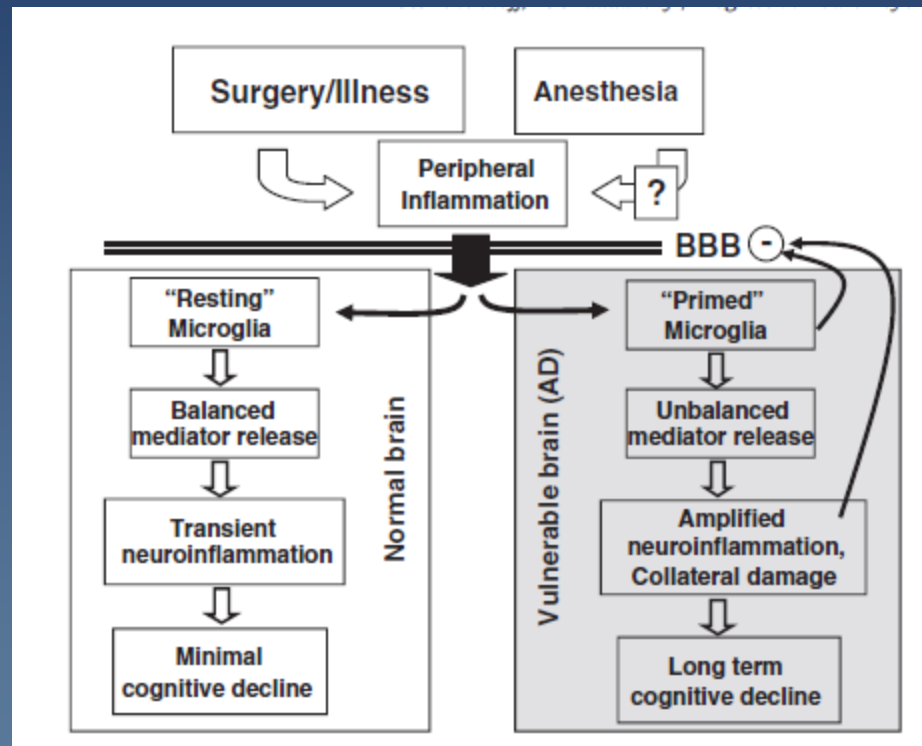
Predisposing Factors : POCD

- ◆ **Age**
- ◆ **Preoperative cognition**
- ◆ **Type of surgery**
- ◆ **Vascular risk factors**
- ◆ **Apolipoprotein E genotype (?)**

Possible causes of POCD Related to Surgery

- ◆ Altered cerebral perfusion
- ◆ Anesthetics
- ◆ Cerebral microemboli
- ◆ Inflammation
 - Surgery related
 - Patient related

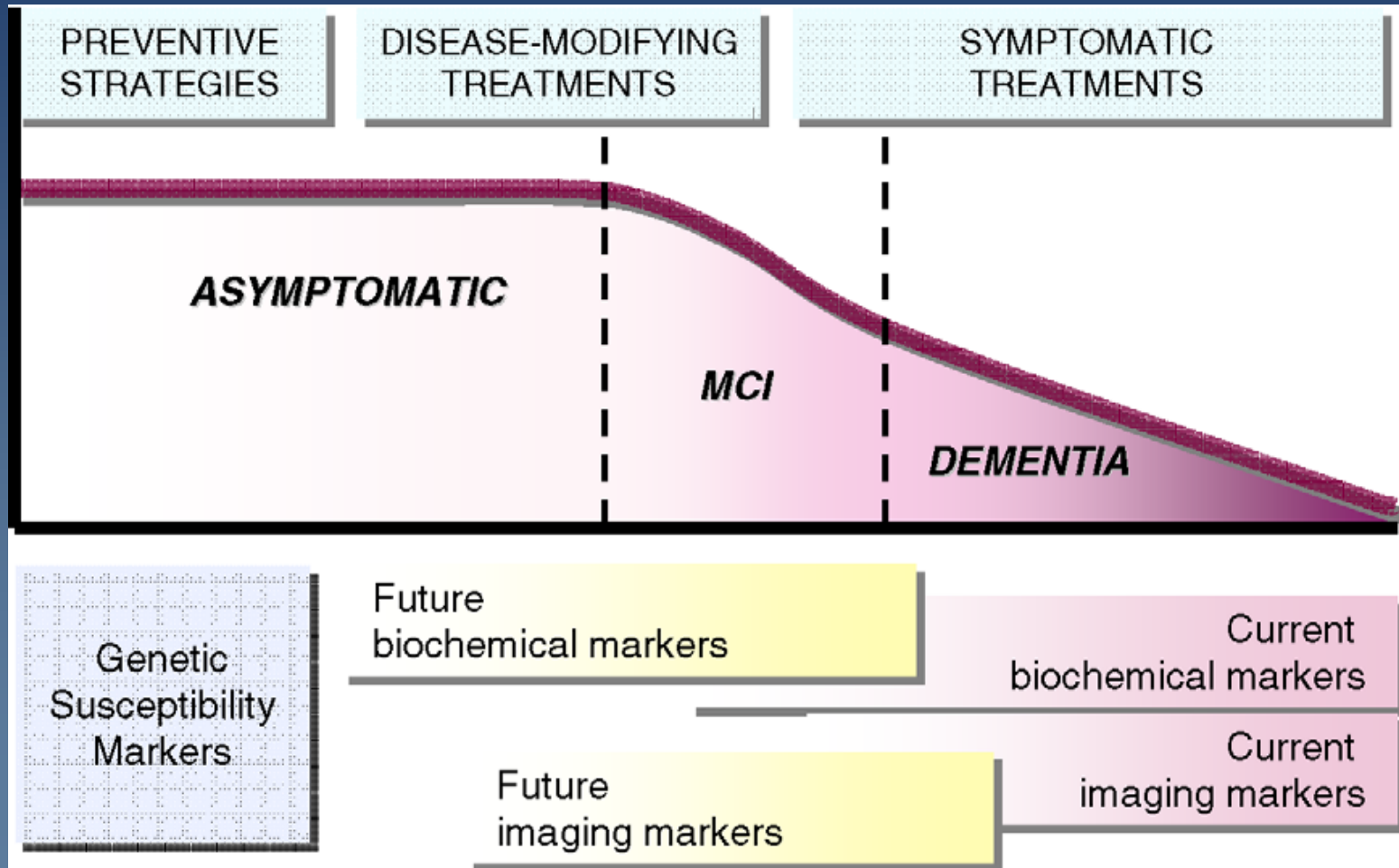
Conceptual Model of POCD



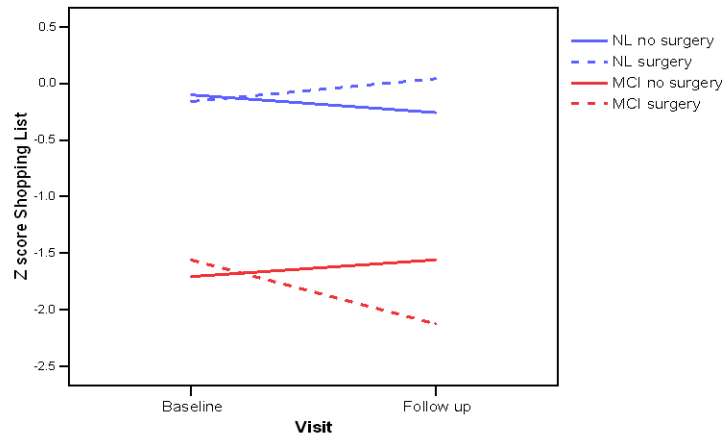
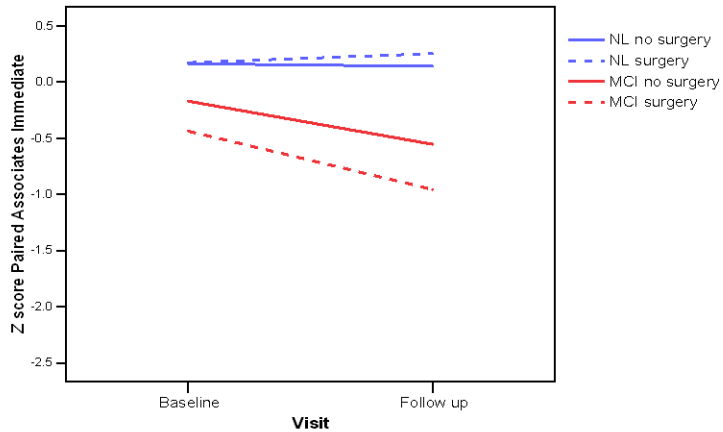
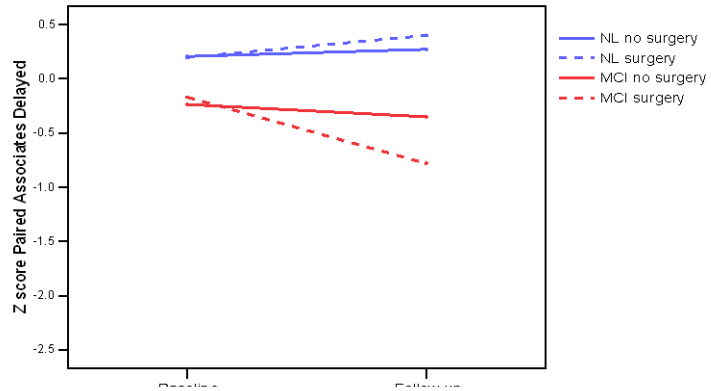
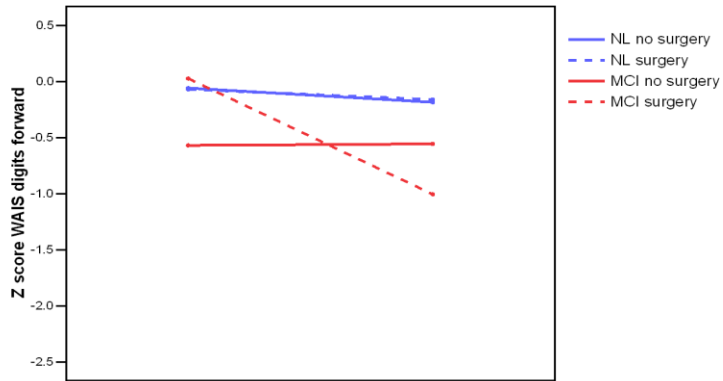
MCI: Diagnosis

- ◆ MCI is diagnosed when there is:
 - Evidence of memory impairment
 - Preservation of general cognitive and functional abilities
 - Absence of diagnosed dementia

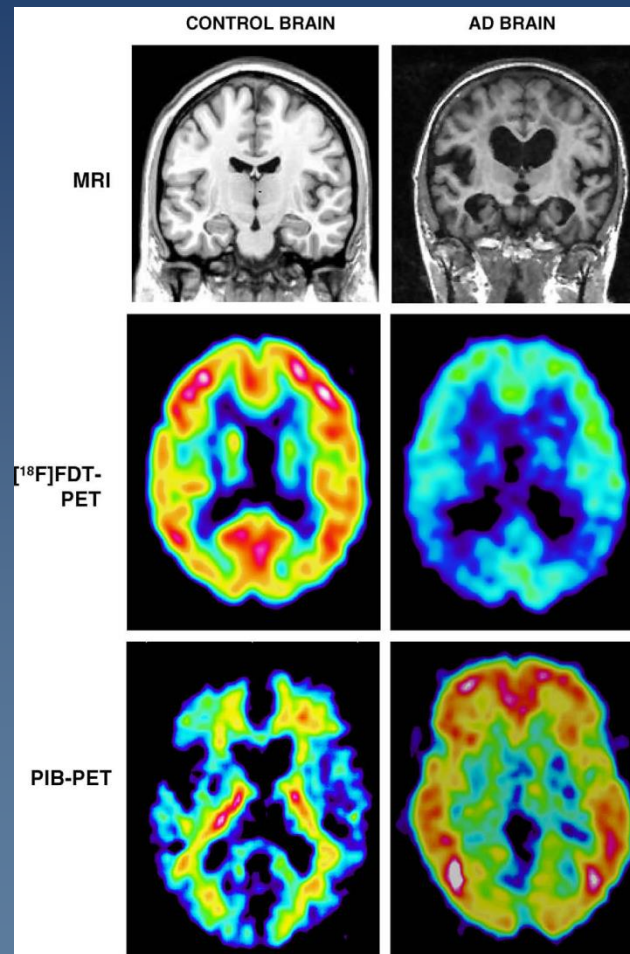
Diagnostic and Treatment Possibilities Along the Evolution of Dementia




Does MCI Increases the Risk of POCD?



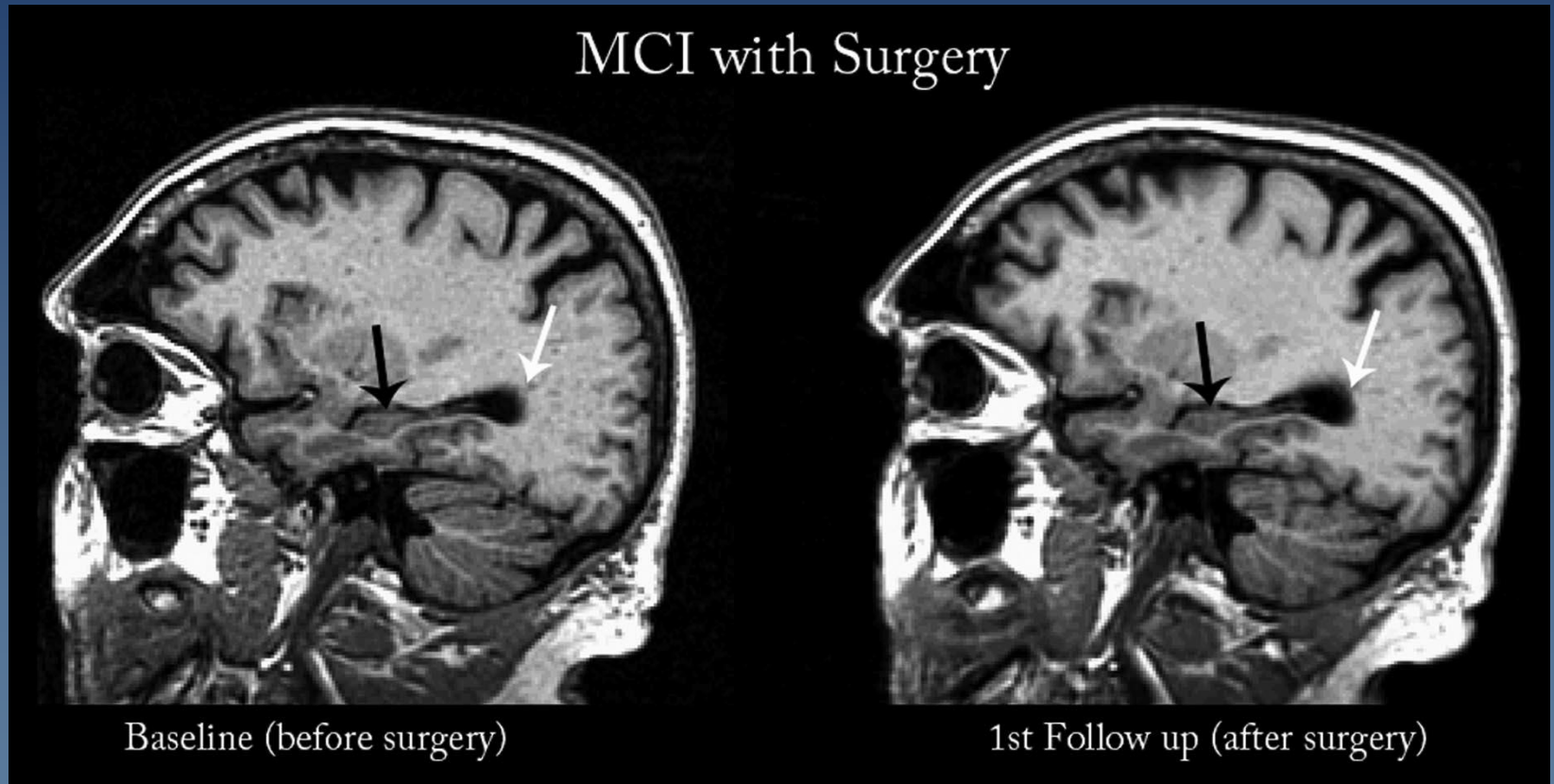
Brain Images from Age Matched Cognitively Intact Individuals and AD Patients



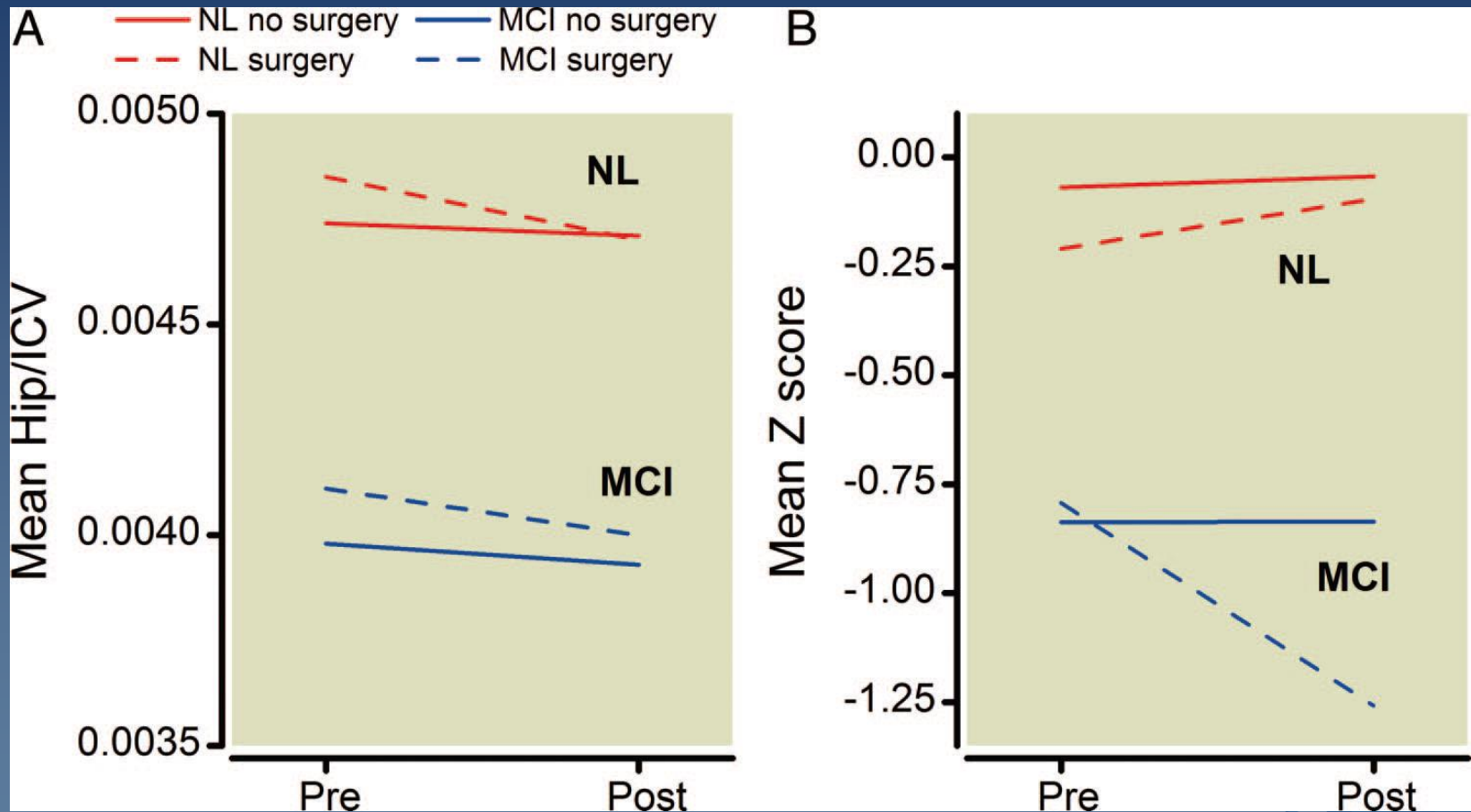
Study Design: Longitudinal Examination of Structural MRI From ADNI Database

- ◆ Apply MRI to study perioperative cortical volume change in surgical subjects
 - ◆ Examine hippocampus, gray matter, white matter and lateral ventricle.
 - ◆ Examine composite cognitive score
- 

LV Volume Changes in a Surgical Patient with MCI



Atrophy of Hippocampus in the Perioperative Period



POCD: Concluding Remarks

- ◆ Standardization of diagnostic criteria
- ◆ Neuroinflammation
- ◆ Low intraoperative cerebral oxygenation
- ◆ Patient-related factors:
 - Age
 - Pre-existing cognitive impairment
 - Cognitive reserve
 - Priming of the immune system

Low Tech Prescriptions for Longevity

“Swim, dance a little, go to Paris every August and live within walking distance of two hospitals”

Horatio Lure, at 80

“Stay busy, get plenty of exercise and don’t drink too much.

Then again, don’t drink too little”

Herman “Jack Rabbit” Smith-Johannsen, at 103

“The secret to longevity is to keep breathing”

My observation

