

---

# **Metabolic Syndrome, Inflammation and Cognitive Impairment**

**Kristine Yaffe, MD**

**Univ. of California, San Francisco**

# The 'Metabolic Syndrome'

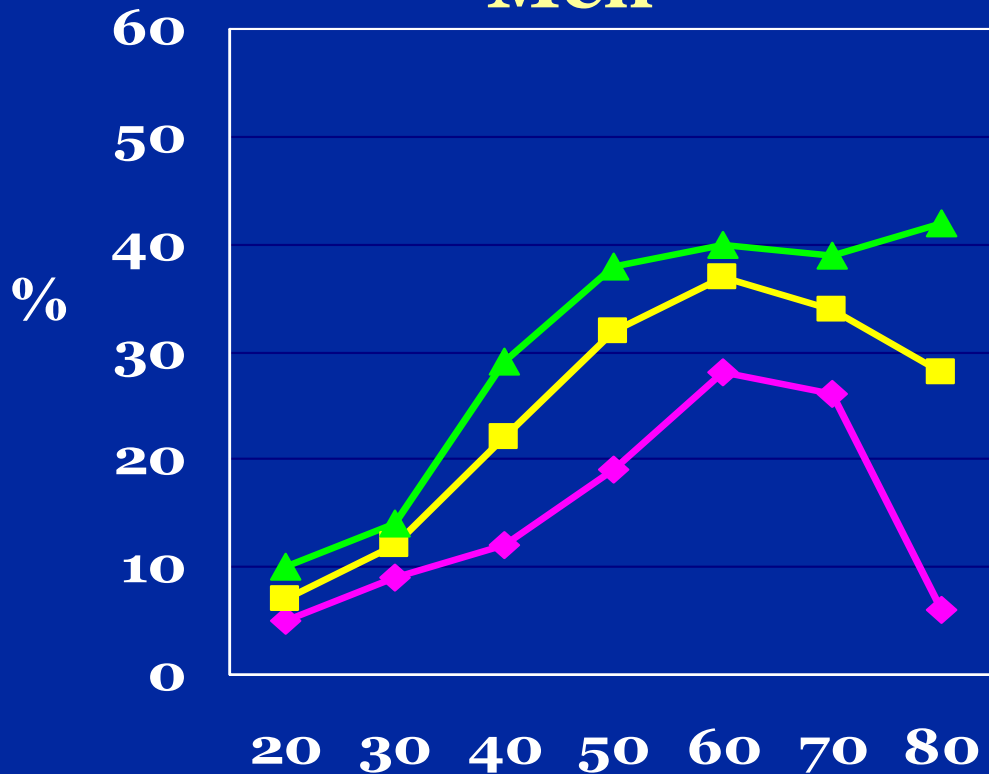
Also known as:

- **Syndrome X**
- **Insulin Resistance Syndrome**
- **The Deadly Quartet**
- **The Dysmetabolic Syndrome**

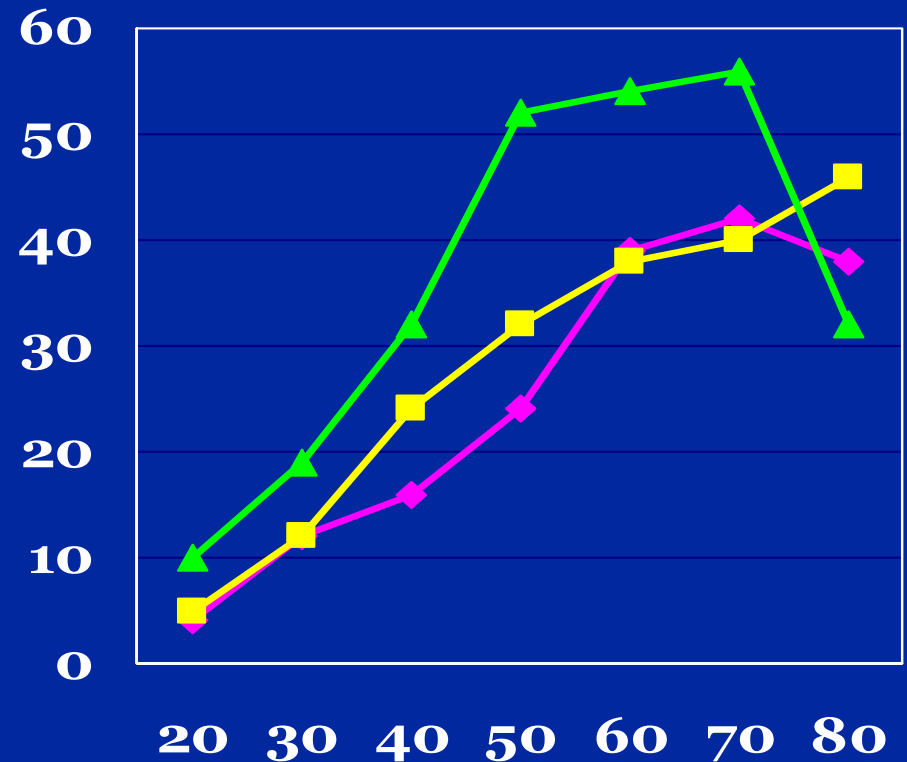


# Metabolic Syndrome Prevalence

## Men



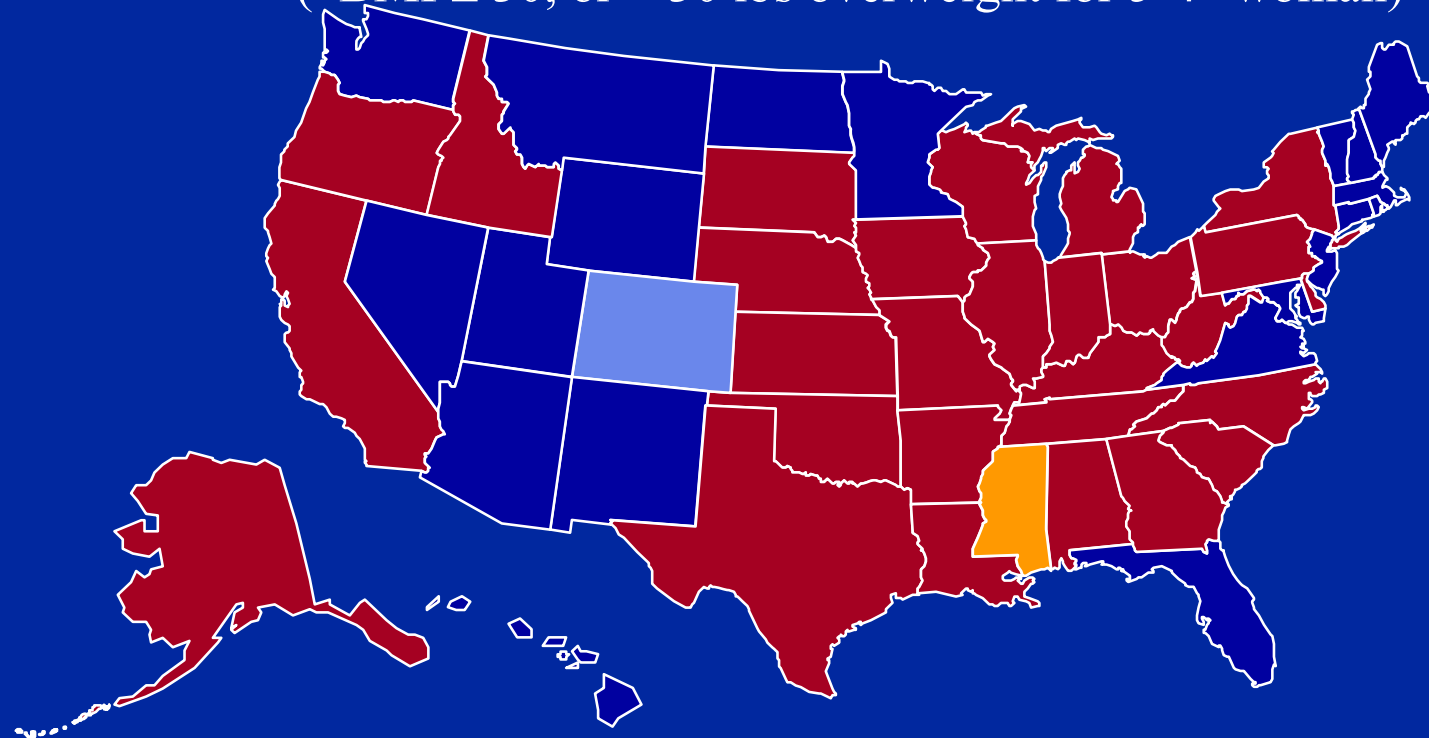
## Women



◆ Black    ■ White    ▲ Mex. Am

# Obesity trends\* among U.S. adults BRFSS, 2001

(\*BMI  $\geq 30$ , or  $\sim 30$  lbs overweight for 5'4" woman)



□ No Data   □ <10%   □ 10%-14%   □ 15%-19%   □ 20%-24%   □  $\geq 25\%$

Source: Mokdad A H, et al. *J Am Med Assoc* 1999 and 2001

# Metabolic Syndrome: Background

- **The metabolic syndrome is associated with CV disease, mortality and other poor health outcomes**
- **Individual components of the metabolic syndrome such as hypertension & diabetes are associated with cognitive decline**
- **Few have investigated the association between the metabolic syndrome and cognitive decline**
- **Inflammation may mediate some of the effects of metabolic syndrome on adverse outcomes, ?also in cognition?**

# Study 1: Health ABC

- Participants were part of the Health, Aging, and Body Composition Study (Health ABC)
  - Prospective cohort study of 3,075 well-functioning community dwelling elders
  - Aged 70-79
  - Living in Memphis, TN and Pittsburgh, PA
  - 43% Black
  - 2949 subjects with all measurements for this study; 2498 with 4-year follow-up

# Metabolic Syndrome Definition

- Fulfill  $\geq 3$  criteria (NCEP guidelines):
  - Waist:  $> 102$  cm  $\text{♂}$ ,  $> 88$  cm  $\text{♀}$
  - HDL:  $< 40$  for men,  $< 50$  for women
  - Triglycerides:  $\geq 150$  mg/dL
  - BP:  $\geq 130/ \geq 85$  (or med use)
  - Fasting glucose:  $\geq 110$  mg/dL (or med use)

# Cognitive Outcomes in Health ABC

- Modified Mini-Mental (3MS) at baseline and biannually
- Cognitive Decline
  - $\geq 5$  point decline with logistic regression
  - 4-year change using Random Effects
- Interaction with Inflammation ( $>$ median IL-6 and CRP at baseline)

# Results

---

- **Metabolic syndrome associated with greater 4-year change in 3MS scores (P=0.03)**
- **Metabolic syndrome associated with higher risk of cognitive decline**
  - **26% vs 21%**
  - **OR=1.31; 95%CI 1.06-1.64**

# Metabolic Syndrome & Cognitive Decline

## Health ABC

	High Inflammation N=618	Low Inflammation N=1880
No Metabolic Syndrome N=1534	1.0	1.0
Metabolic Syndrome N=964	1.94 (1.25-3.00)	1.13 (0.87-1.47)

P for interaction = 0.04

Yaffe et al, *JAMA*, 2004

## Study 2 SALSA

- Participants were part of the Sacramento Area Latino Study of Aging (SALSA)
  - community-based cohort of elderly Latinos (aged  $\geq 60$  y) from Sacramento area
  - 1,624 participants followed over 5 years
- Cognition measured by the 3MS and the Delayed Word-List Recall (DelRec)
- Inflammation measured with CRP

# Baseline CRP and Cognitive Scores

	<b>Without Metabolic Syndrome (N=906)</b>	<b>With Metabolic Syndrome (N=718)</b>	<b>P-value</b>
<b>C-Reactive Protein (mg/L)</b>	4.8 ± 7.2	6.8 ± 9.4	<0.001
<b>3MS score</b>	84.8 ± 14.0	84.3 ± 14.2	0.39
<b>DelRec score</b>	8.4 ± 3.2	8.4 ± 3.1	0.89

# Metabolic Syndrome & Cognitive Decline

## SALSA

	3MS Score		DelRec Score	
	Beta	P-value	Beta	P-value
All	-0.40	0.04	-0.12	0.03
CRP $\geq$ Median	-0.65	0.03	-0.13	0.16
CRP < Median	-0.26	0.45	-0.06	0.45

Multivariate results led to similar results

Yaffe et al, JAGS, 2007

# Association between Individual Components of Metabolic Syndrome and Cognitive Decline

Components	3MS Score		DelRec Score	
	Beta	P-value	Beta	P-value
Abdominal Obesity	-0.32	0.11	-0.06	0.25
Hypertriglyceridemia	0.03	0.87	-0.05	0.34
Low HDL cholesterol	-0.33	0.11	-0.01	0.87
High blood pressure	<b>-0.37</b>	<b>0.05</b>	-0.03	0.54
Elevated fasting blood glucose	-0.31	0.10	<b>-0.12</b>	<b>0.02</b>

## Study 3

# Longitudinal Aging Study Amsterdam (LASA)

- 1,183 participants aged 65 to 88 years
- Metabolic syndrome defined by NCEP criteria
- Inflammation: CRP and  $\alpha$ -1-antichymotrypsin
- Cognitive tests: general cognition (MMSE), memory (AVLT), fluid intelligence (Raven's Coloured Progressive Matrices), and information processing speed (Coding Task)
- Cross-sectional analysis with linear regression models, and adjusted for age, sex, education, smoking, and alcohol

# LASA Results

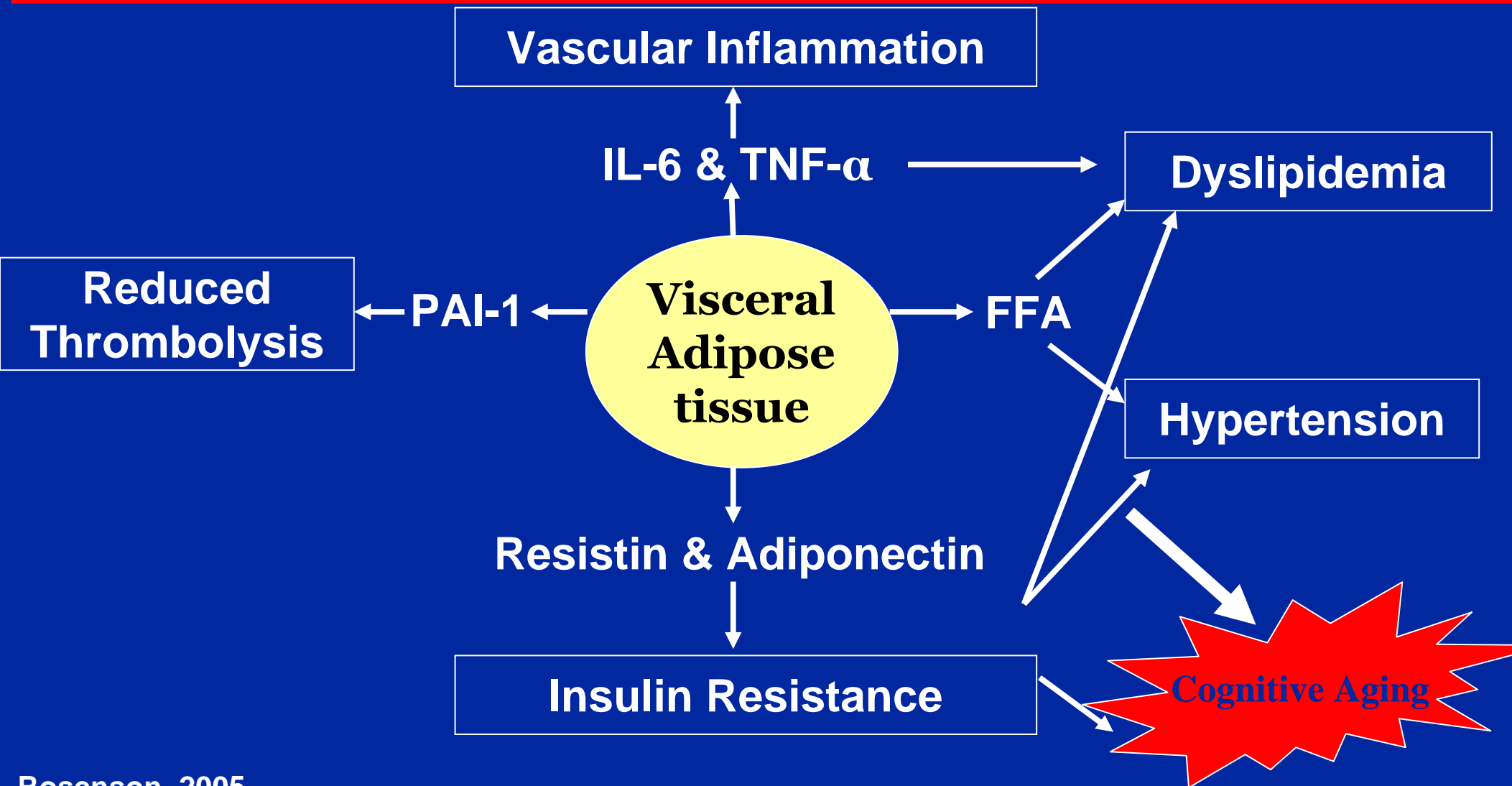
- **Metabolic syndrome associated with worse cognitive scores on All tests ( $p < 0.05$  for all)**
- **Interaction with inflammation with metabolic syndrome on All tests**
- **All components in one model revealed only high glucose had an assoc. with cognitive scores but less than metabolic syndrome as a whole**
- **# components of metabolic syndrome assoc with worse scores**

# Conclusions: Metabolic Syndrome

---

- In all 3 studies, elders with metabolic syndrome had an increased risk of developing cognitive impairment and decline over time
- Especially for those with high inflammation
- Results in Latino elders as well as in Black and White elders
- Results across different cognitive tests

# Proposed Mechanisms for Metabolic Syndrome and Dementia



# So, is the sum greater than its parts or does it matter?

---

- Seems greater than components but driven mostly by hyperglycemia
- Identifies elders at risk
- Need to determine if reducing metabolic syndrome or inflammation could prevent cognitive decline
- Most likely central obesity plays a big role

# Acknowledgement



- Dr. Yaffe is supported NIDDK DK070713 and NIA K24AG031155.
- Health ABC supported by NIA AG-6-2101, AG-2103, & AG-2106.
- SALSA supported by NIA AG12975 & NIDDK DK60753