

The Neurological and Neuropsychological Consequences of Occupational Exposure to PCBs and Lead

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Objectives and Rationale

- Objective
 - Assess Effects of Occupational Exposure to PCBs and Lead on Nervous System Function in Former Capacitor Workers in Fort Edward and Hudson Falls, NY
- Rationale
 - Declines in Nervous System Function with Age May Be Exacerbated by Environmental Contaminants

Identification and Recruitment Plan

6,798 Workers Identified
from Records



2,844 Randomly Selected



1,124 Lived Within
100 miles of Albany



484 Agreed to Be Screened and
Found to Be Eligible



241 Eligible and Agreed
to Participate

WORKER DESCRIPTION

- ◆ Subject population consists of 6,700 former capacitor workers who were employed at Ft. Edward or Hudson Falls, New York capacitor plants for at least three months.
- ◆ Average duration of employment was 17.8 years; median age is 65 years; women constitute 44.4 % of the work force.

WHY STUDY CAPACITOR WORKERS?

- ◆ Workers were exposed to extraordinarily high levels of PCBs (geometric mean of serum PCB concentrations \approx 300 ppb; maximum $>$ 2 ppm); levels in unexposed individuals are 2-4 ppb.
- ◆ Workers were also exposed to lead (soldering)
- ◆ They are an aging population

WHAT DID WE MEASURE?

Current and Archived Serum PCB Concentrations (Wolff)

[¹²³I]β-CIT SPECT Imaging of Dopamine Transporter (Marek and Seibyl)

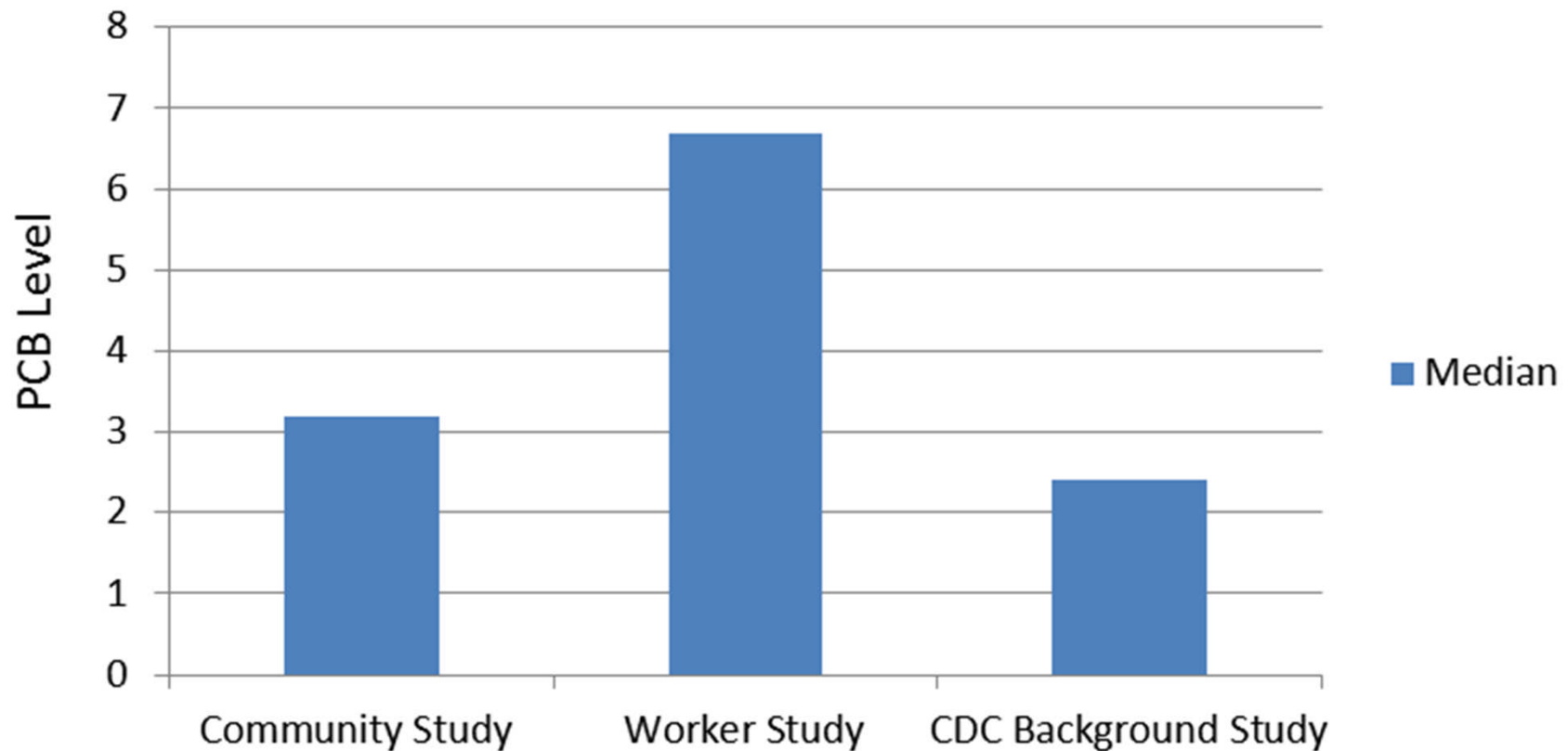
X-Ray Fluorescence Bone Lead Concentrations
(Todd, Parsons)

Neuropsychological [Motor Function, Memory and Executive Function] (McCaffrey)

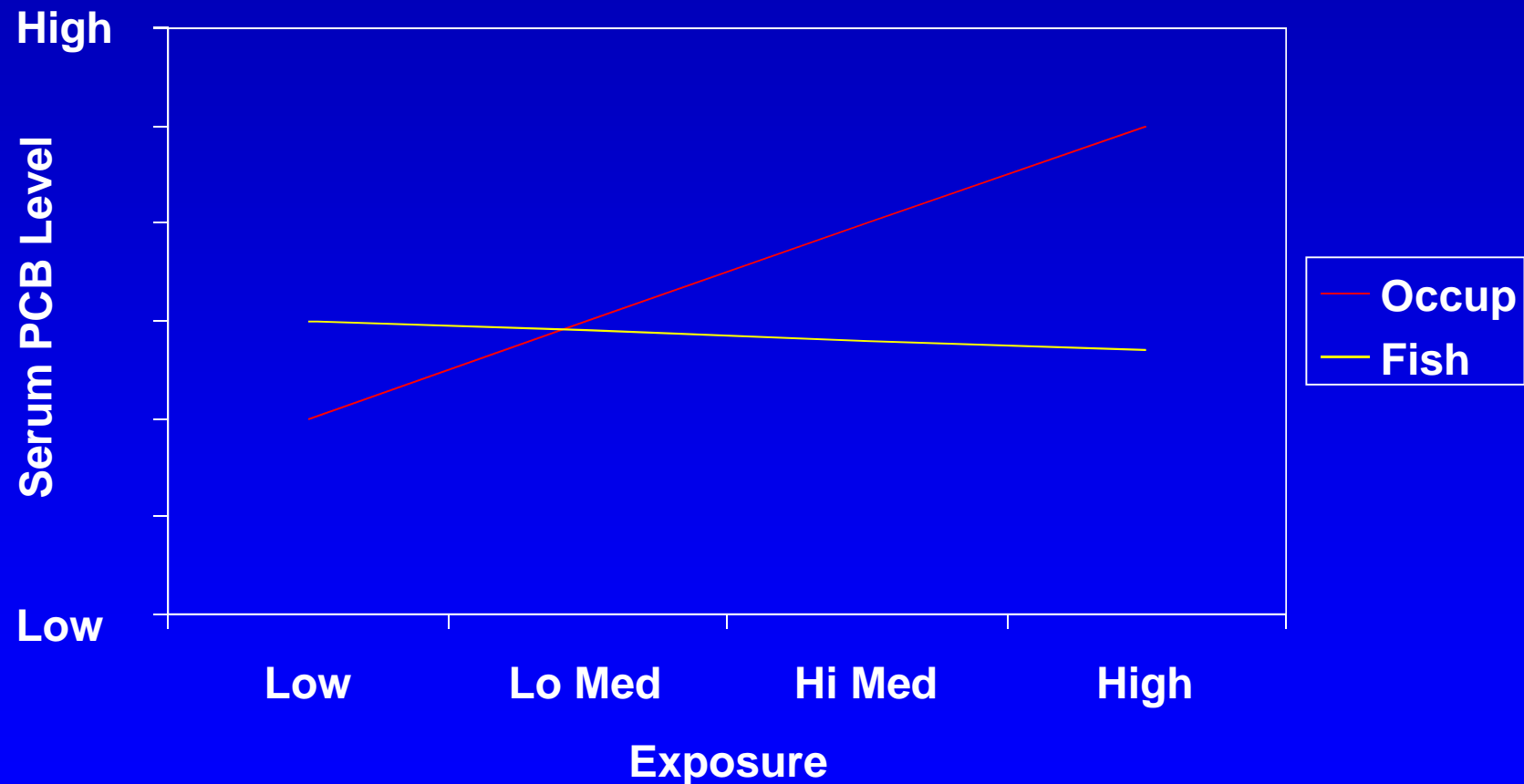
Neurological (Factor, Molho and Higgins)

Current PCB Levels in Blood Comparison

Median PCB Levels in Blood (wet weight, ppb)



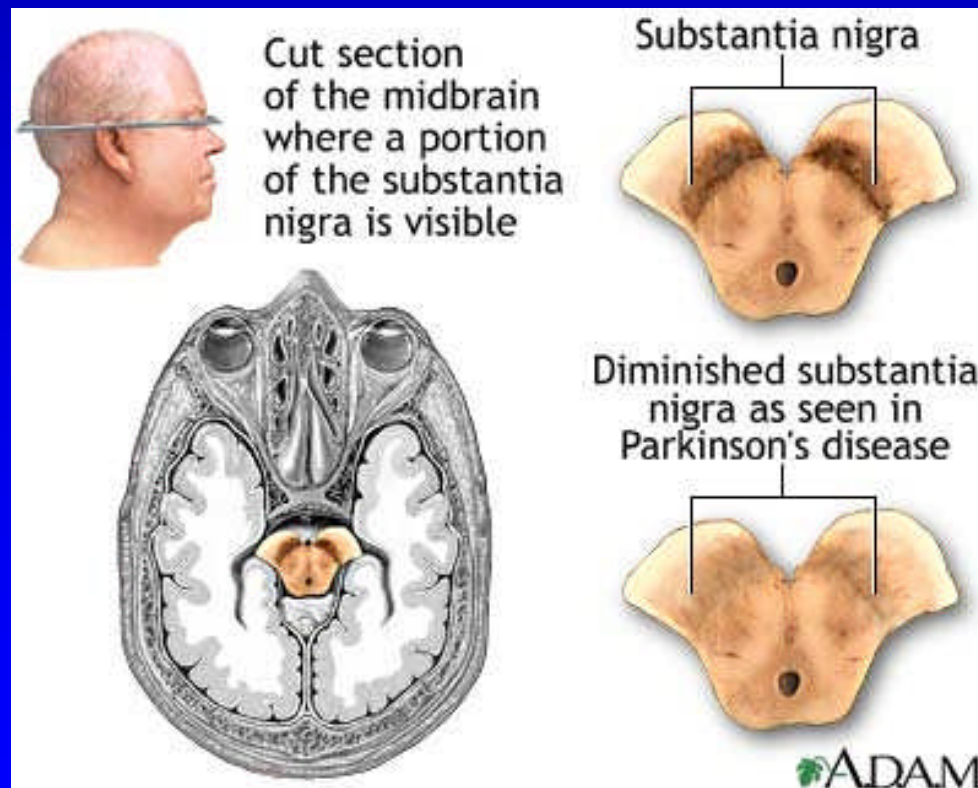
Relationship of Serum PCB Concentration on Exposure from Occupation and Fish Consumption



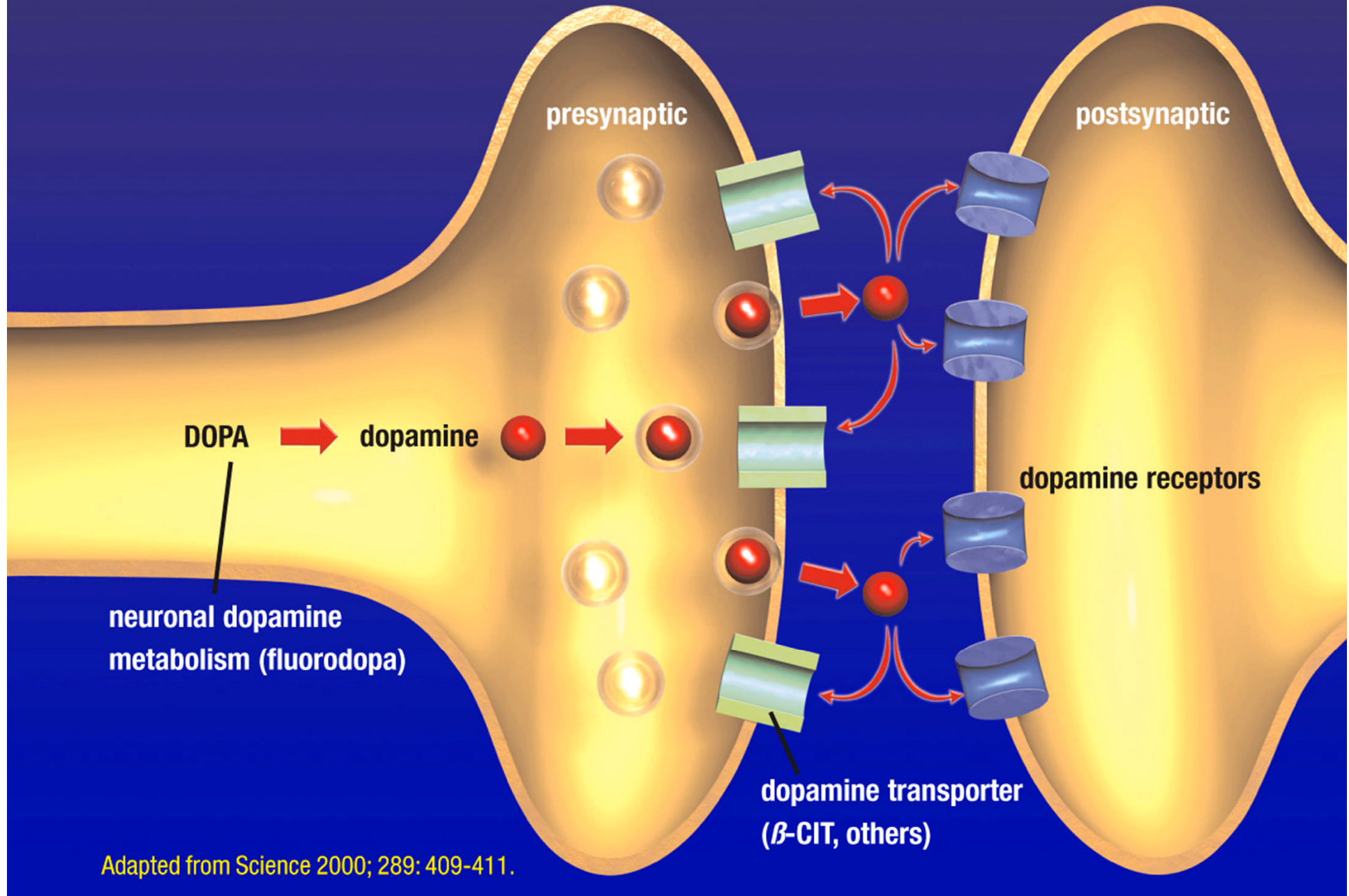
*Adjusted for Age, Sex, BMI, Education

Part I: PCBs and Brain Function

Parkinson's disease Neuropathology

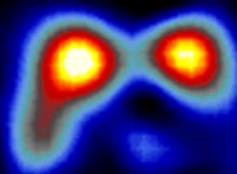


Imaging in the brain: Molecular targets of radioligands.⁷

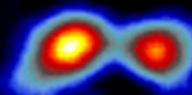


Adapted from Science 2000; 289: 409-411.

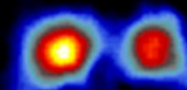
SPECT and B-CIT PROGRESSION



BASELINE

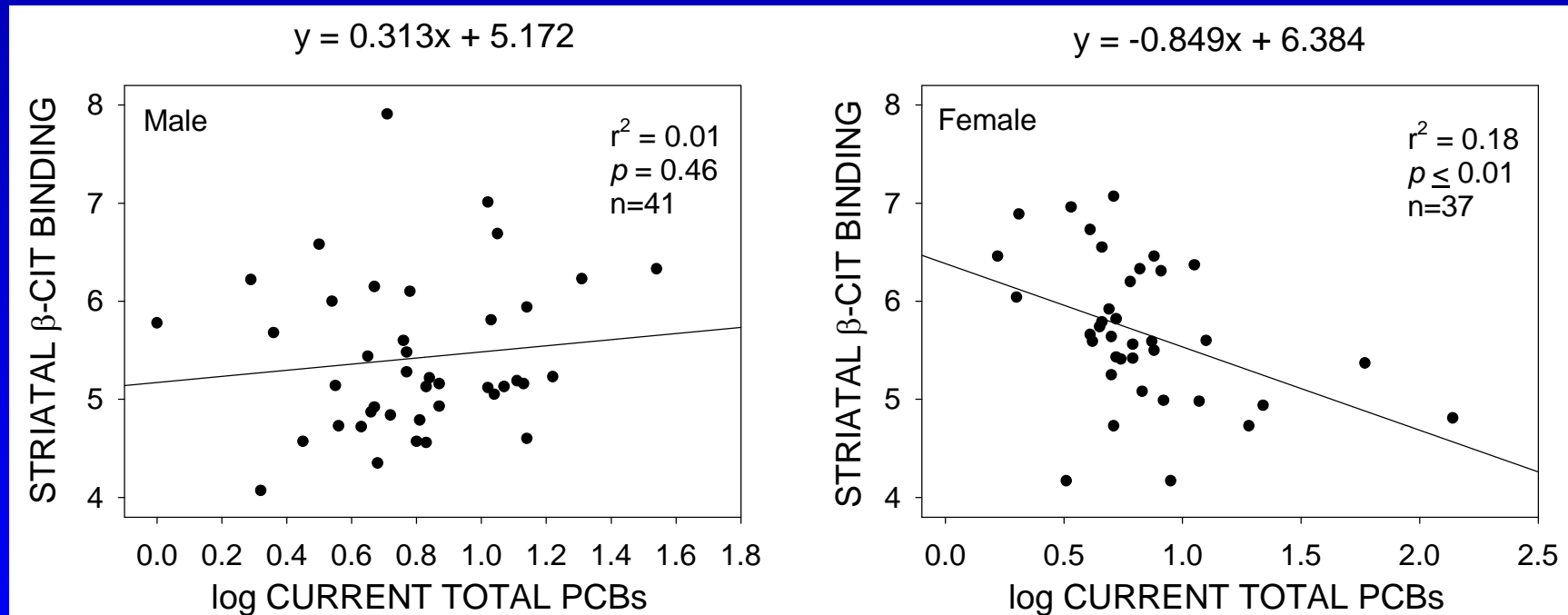


15 MONTHS



36 MONTHS

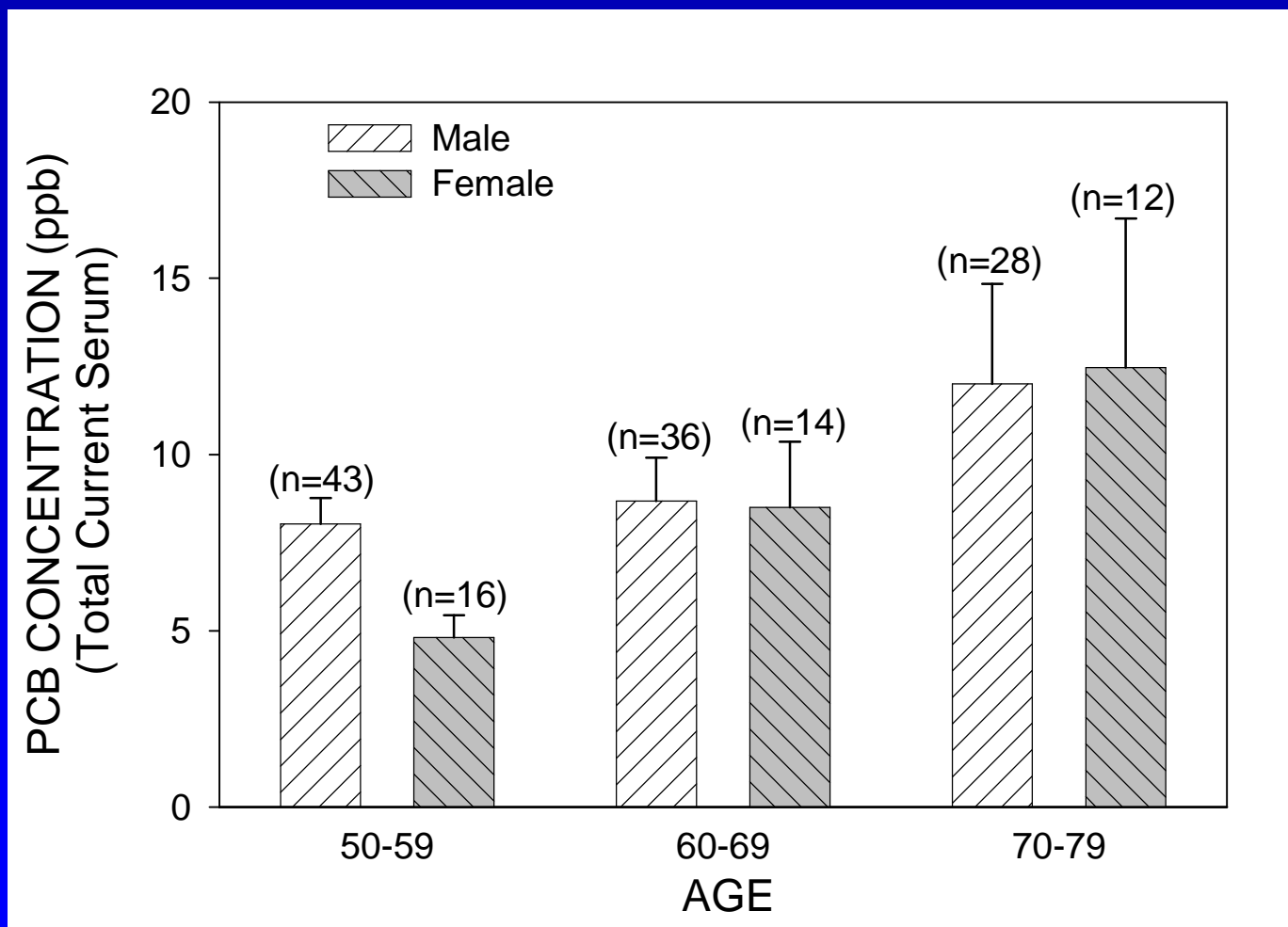
β -CIT SPECT Binding as a Function of Current Serum PCB Concentrations Adjusting for Potential Confounders*



* Age, BMI, Education, Bone Lead Body Burden, Income, Caffeine Consumption, Alcohol, Smoking, Cardiovascular Medication Use

Seegal *et al.*, *Neurobiol. Dis.*, **38**, 219, 2010

Total Current PCB Levels (mean \pm SEM)



Parkinson 's Disease Mortality is Seen Only in Women Occupationally Exposed to PCBs

GROUP	LOW EXPOSURE	HIGH EXPOSURE ^a	TOTAL
Men – PD Underlying Cause	1.34 (0.43 - 3.12) (5)	1.09 (0.13 - 3.93) (2)	1.25 (0.50 - 2.58) (7)
Women – PD Underlying Cause	0.42 (0.01 - 2.32) (1)	2.98 (1.09 - 6.49) (6)*	1.59 (0.64 - 3.27) (7)

^aHigh-exposure is defined as >500,000 cumulative exposure units, using a job-exposure matrix.

* $p \leq 0.05$

Steenland, *et al.*, *Epidemiology*, **17**, 8, 2006

CONCLUSIONS: I

PCB Effects on Dopamine/ Parkinson's Disease

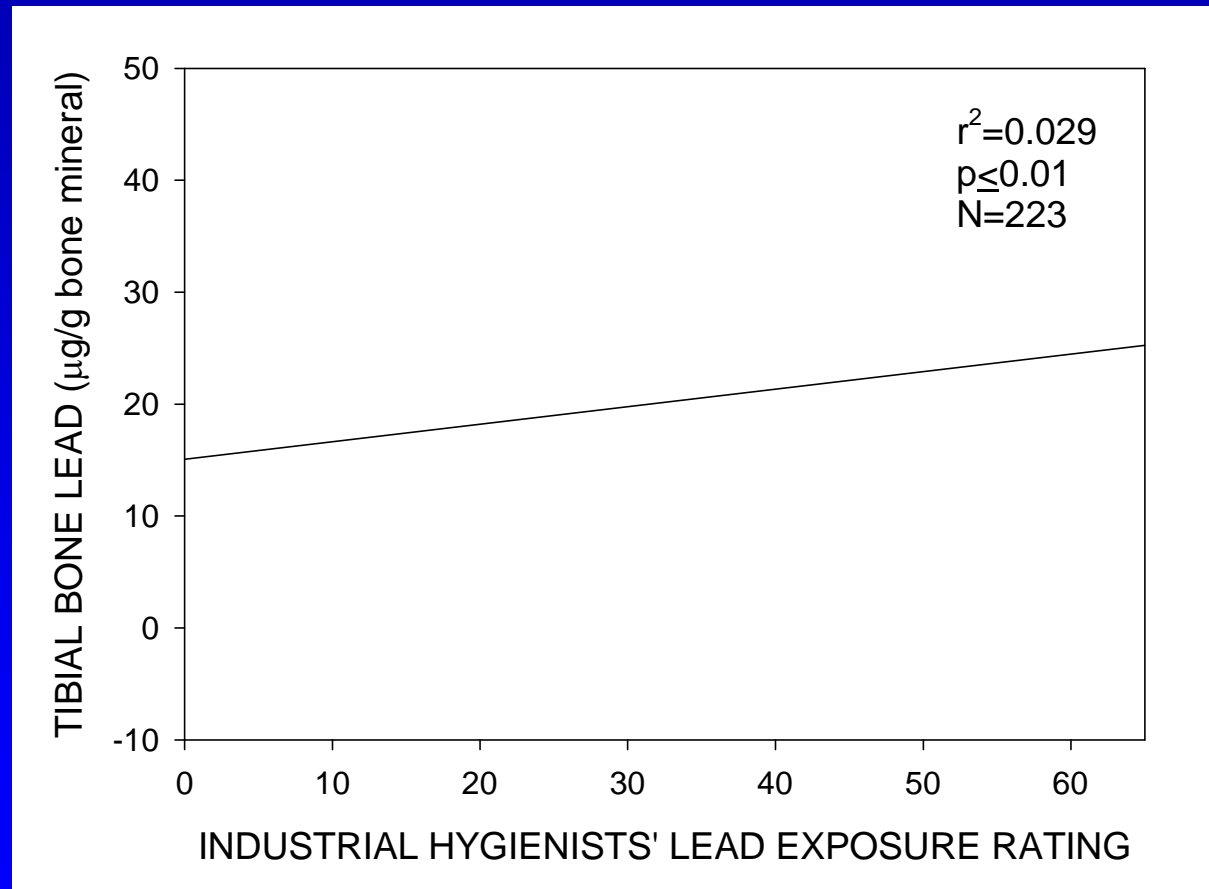
PCBs DIFFERENTIALLY AFFECT:

- DOPAMINE TRANSPORTER DENSITIES IN MEN AND WOMEN CAPACITOR WORKERS
 - POST MENOPAUSAL WOMEN SHOW GREATER PD-ASSOCIATED MORTALITY THAN DO MEN
- ESTROGEN WITHDRAWAL (MENOPAUSE) MAY CONTRIBUTE TO THIS GENDER DIFFERENCE

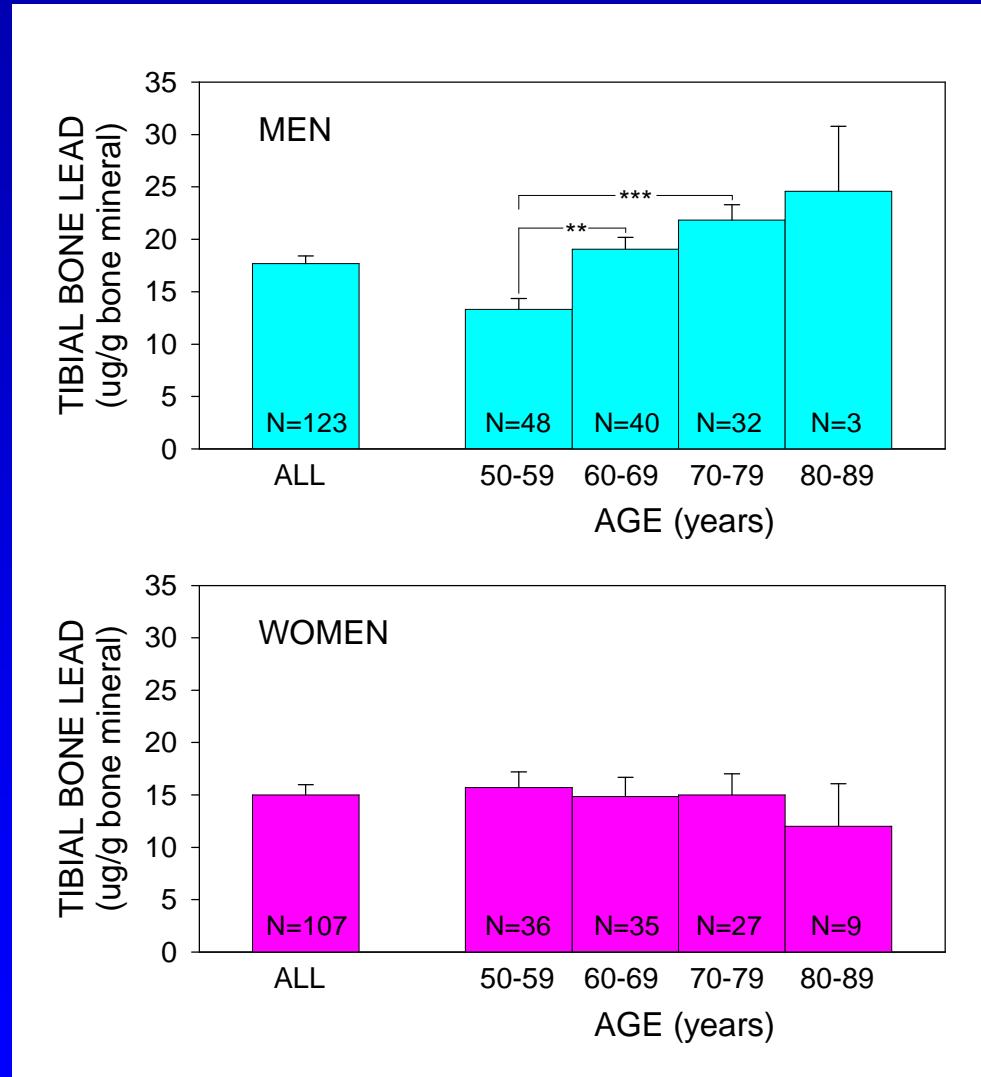
Part II: Effects of Bone Lead on Neuropsychological Performance

Manuscript in Preparation

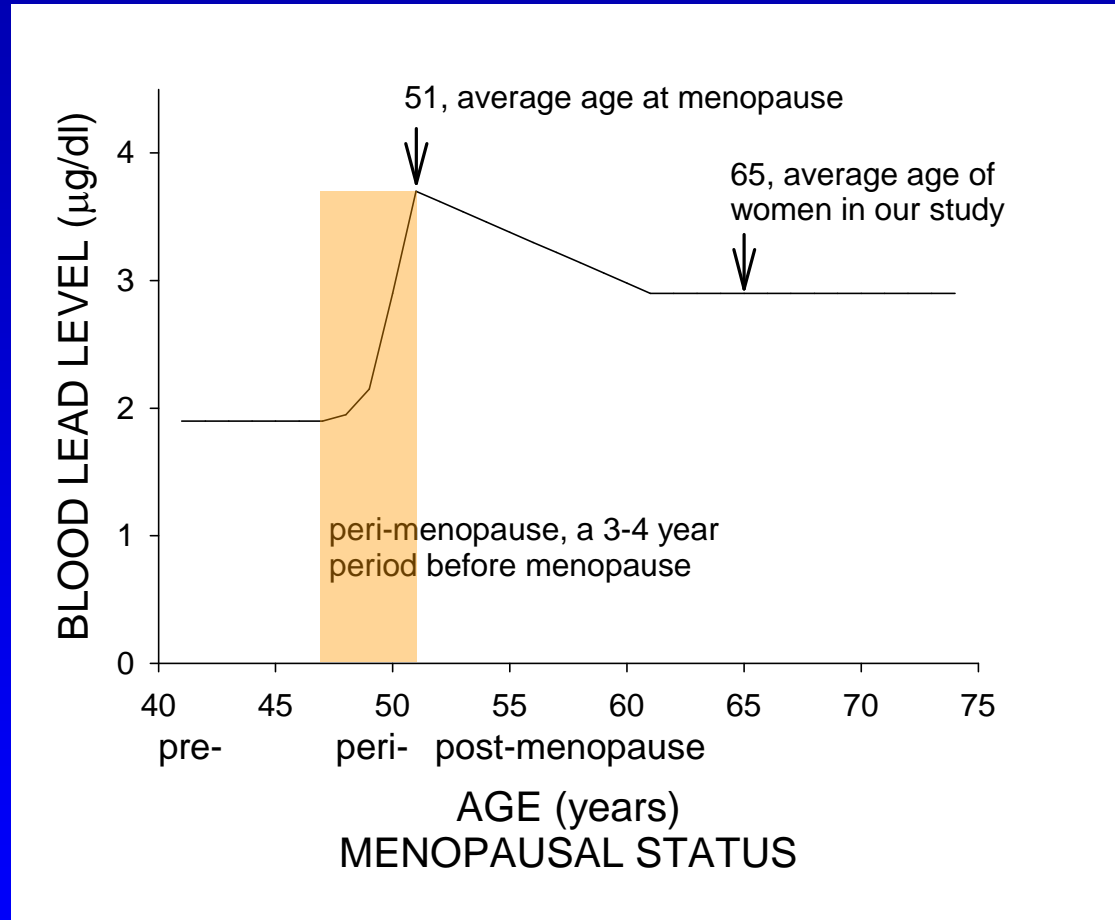
Tibial Bone Lead Levels Correlate with Industrial Hygienists' Rating of Lead Exposure



TIBIAL BONE LEAD VARIES BY SEX AND AGE



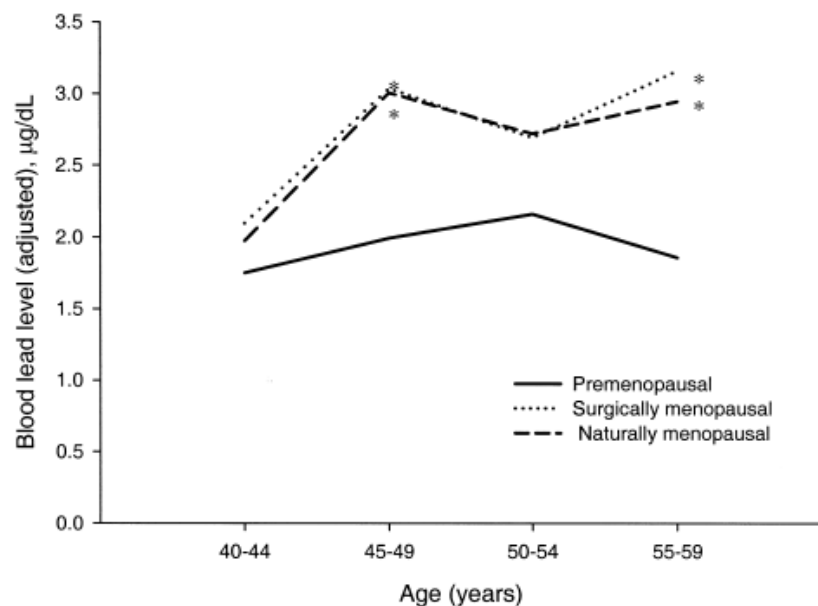
Blood Lead Levels in Women Vary Across Menopausal Status



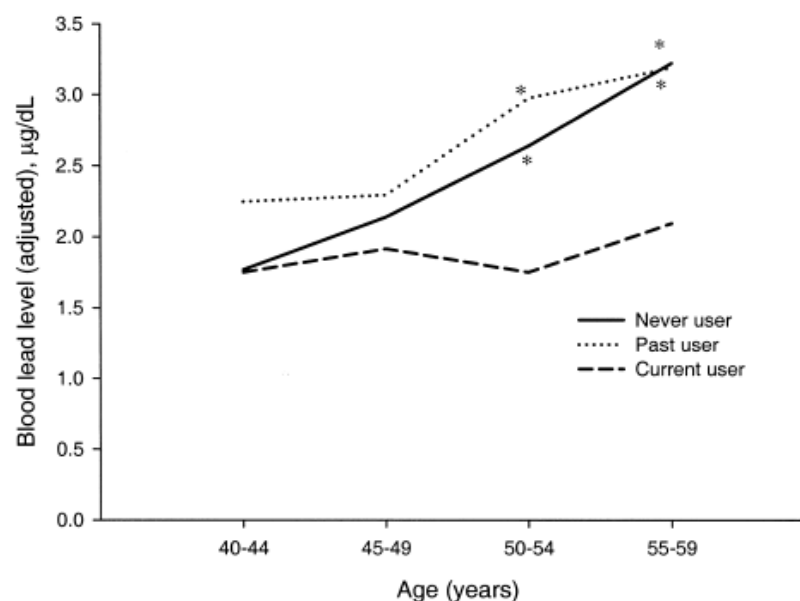
Model based on data from Nash *et al.*, *Am. J. Epidemiol.*, **160**, 901, 2004

Blood Lead Levels in Women Based on Age, Menopausal Status and the Use of Hormone Replacement Therapy (HRT)

Menopausal Status



Use of HRT

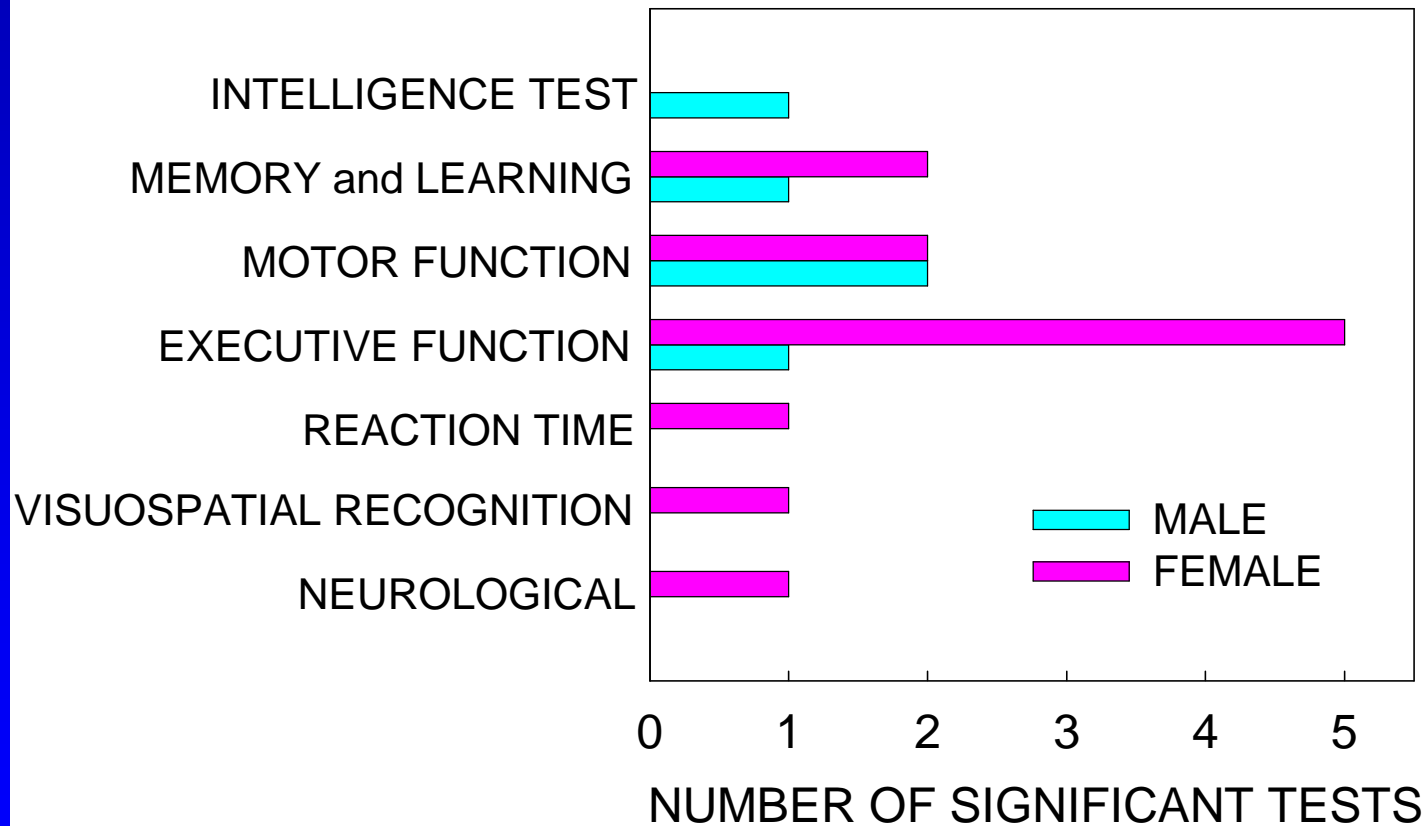


Nash *et al.*, *Am. J. Epidemiol.*, **160**, 901, 2004

ARE THESE BLOOD LEAD LEVELS OF CONCERN FOR ADULTS?

- THEY WOULD BE OF CONCERN ONLY FOR TODDLERS AND YOUNG CHILDREN
- WHAT ELSE HAPPENS DURING MENOPAUSE?
 - A LOSS OF OVARIAN HORMONES (ESTROGEN AND PROGESTERONE) - BOTH OF WHICH HAVE BEEN SHOWN TO BE NEUROPROTECTIVE

Significant Neuropsychological/ Neurological Tests with Bone Lead



Significant Neuropsychological/Neurological Tests with Bone Lead

Men

MEMORY and LEARNING

Wechsler Memory Scale
(logical memory delayed recall)

MOTOR FUNCTION

Static Motor Steadiness Test #6
(non-dominant hand)

Static Motor Steadiness Test #6
(non-dominant hand, contacts)

EXECUTIVE FUNCTION

Wisconsin Card Sorting Test
(number of trials)

INTELLIGENCE TEST

New Adult Reading Test-Revised

Women

MEMORY and LEARNING

California Verbal Learning Test
(list A short delay free recall)

Wechsler Memory Scale
(logical memory immediate recall)

MOTOR FUNCTION

Finger Tapping *(non-dominant hand)*

Grooved Pegboard *(non-dominant hand)*

EXECUTIVE FUNCTION

Trail Making Part A *(time to complete)*

Wisconsin Card Sorting Test
(number of correct responses)

Wisconsin Card Sorting Test
(number of errors)

Wisconsin Card Sorting Test
(percentage of conceptual responses)

Wisconsin Card Sorting Test
(number of categories completed)

REACTION TIME

Mean Reaction Time *(dominant hand)*

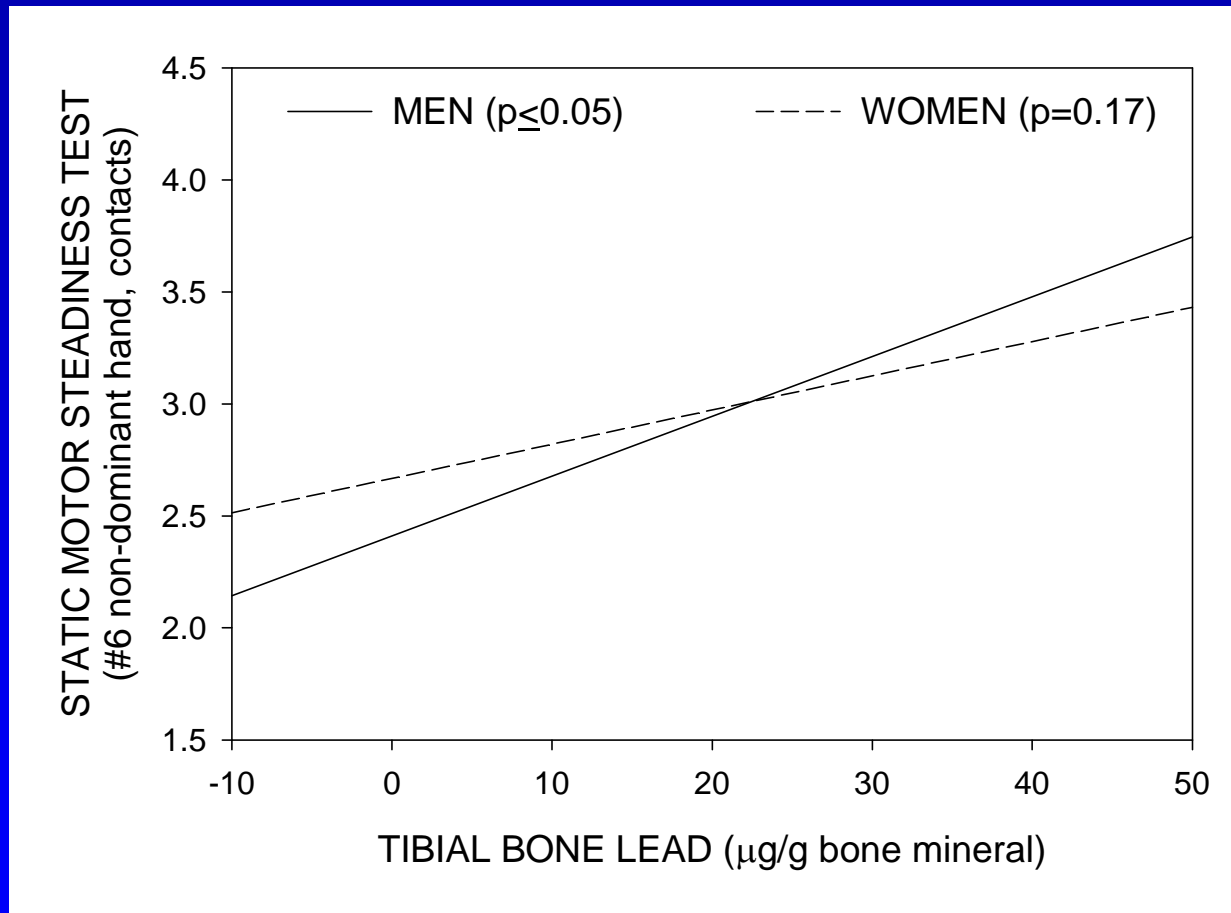
VISUOSPATIAL RECOGNITION

Block Design *(total score)*

NEUROLOGICAL

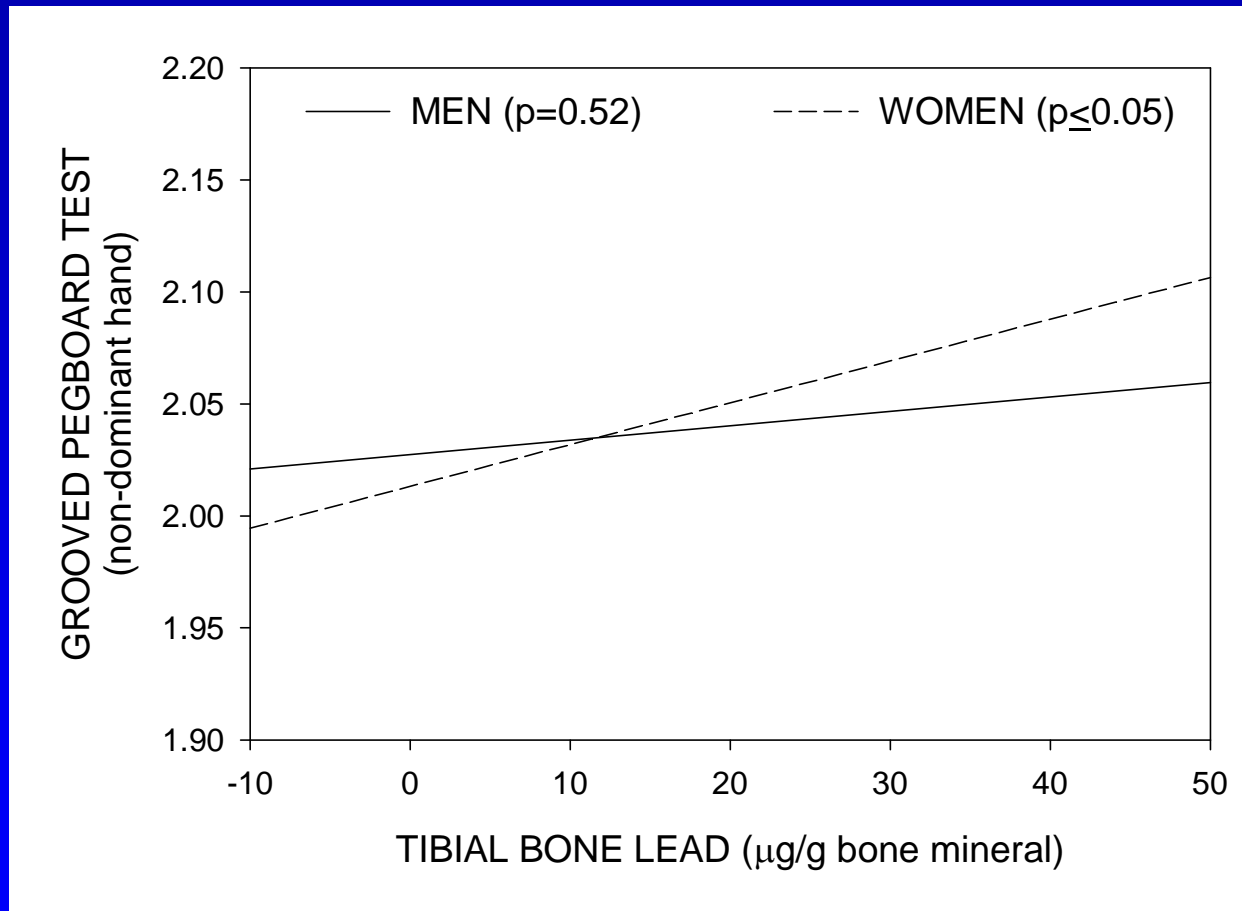
Tremor

STATIC MOTOR STEADINESS TEST



No covariates/confounders

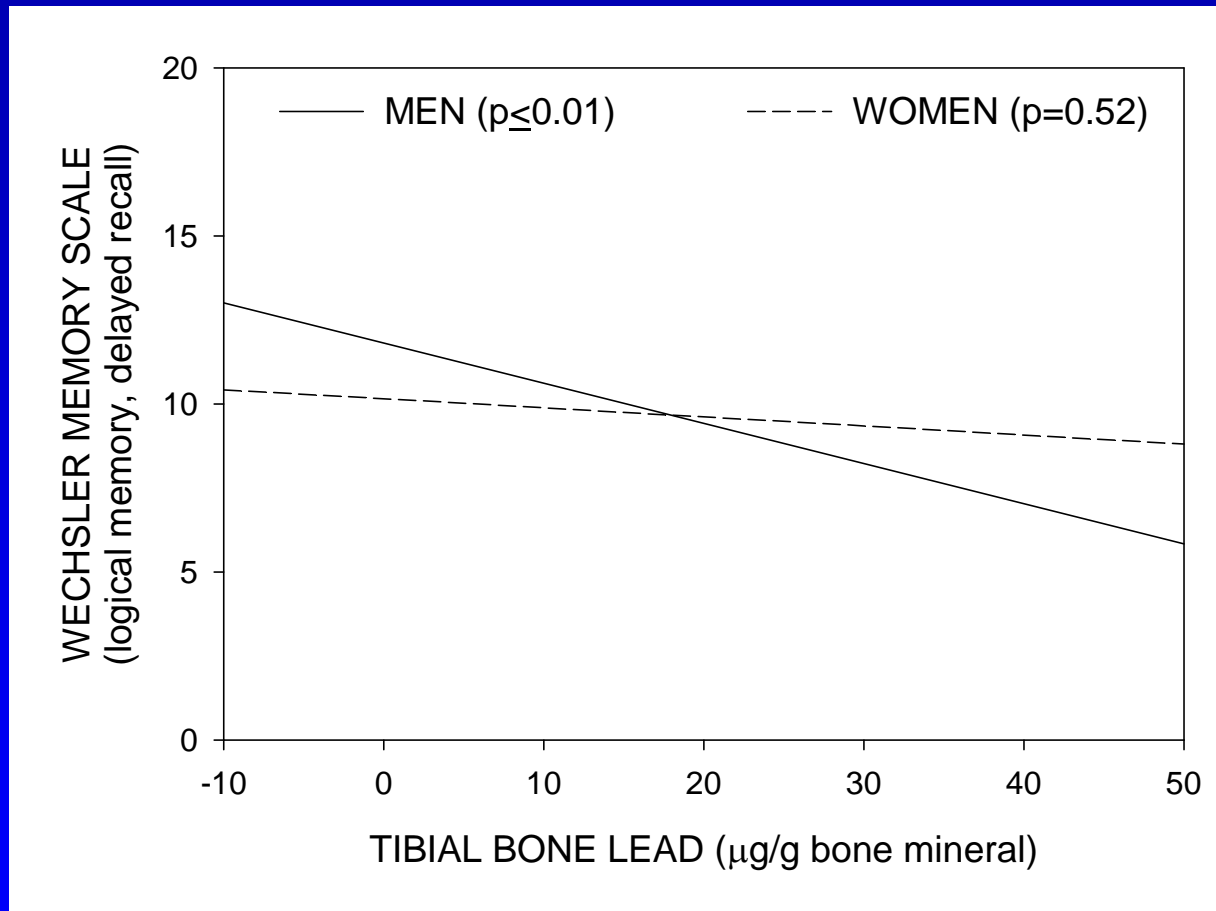
GROOVED PEGBOARD TEST



Adjusted for age, hypertension, state anxiety, diuretics, hypoglycemic agents

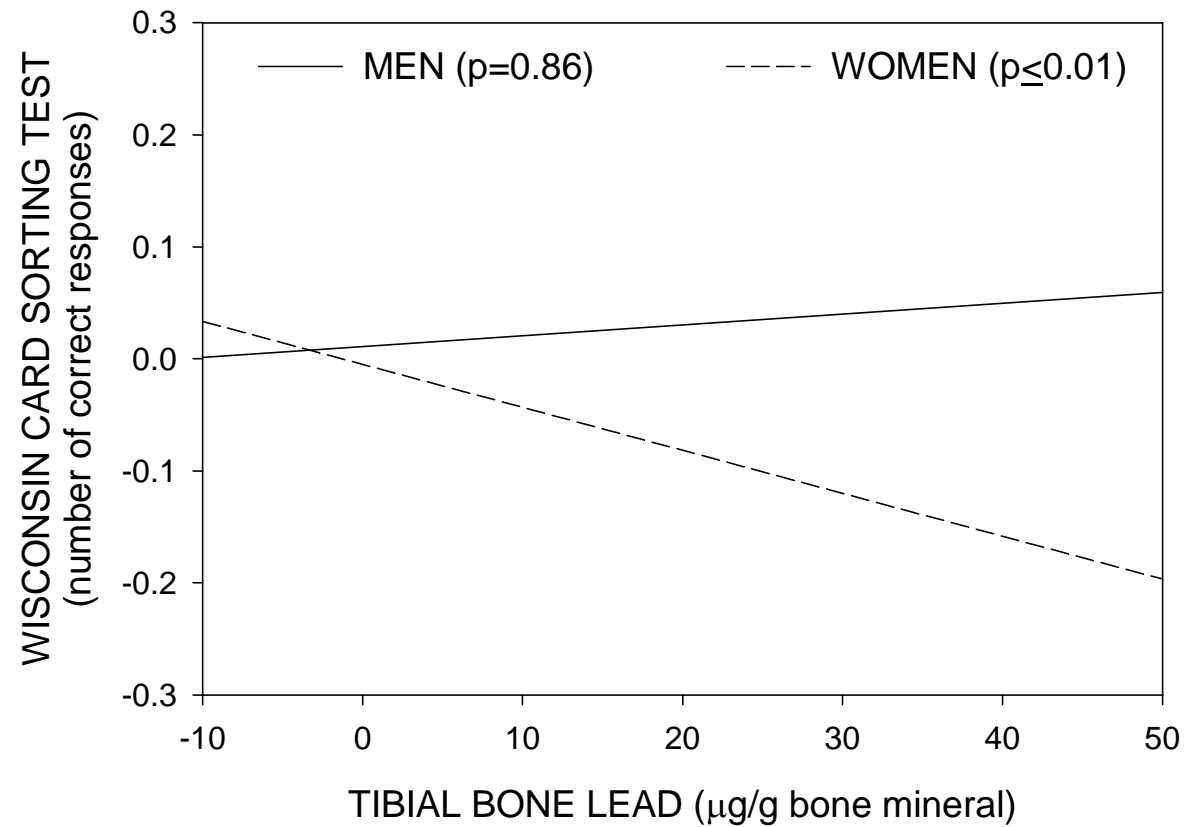
Executive Function describes mental processes that help connect past experience with present action. We use executive function when we perform such activities as planning, organizing, strategizing and paying attention to and remembering details.

WECHSLER MEMORY SCALE



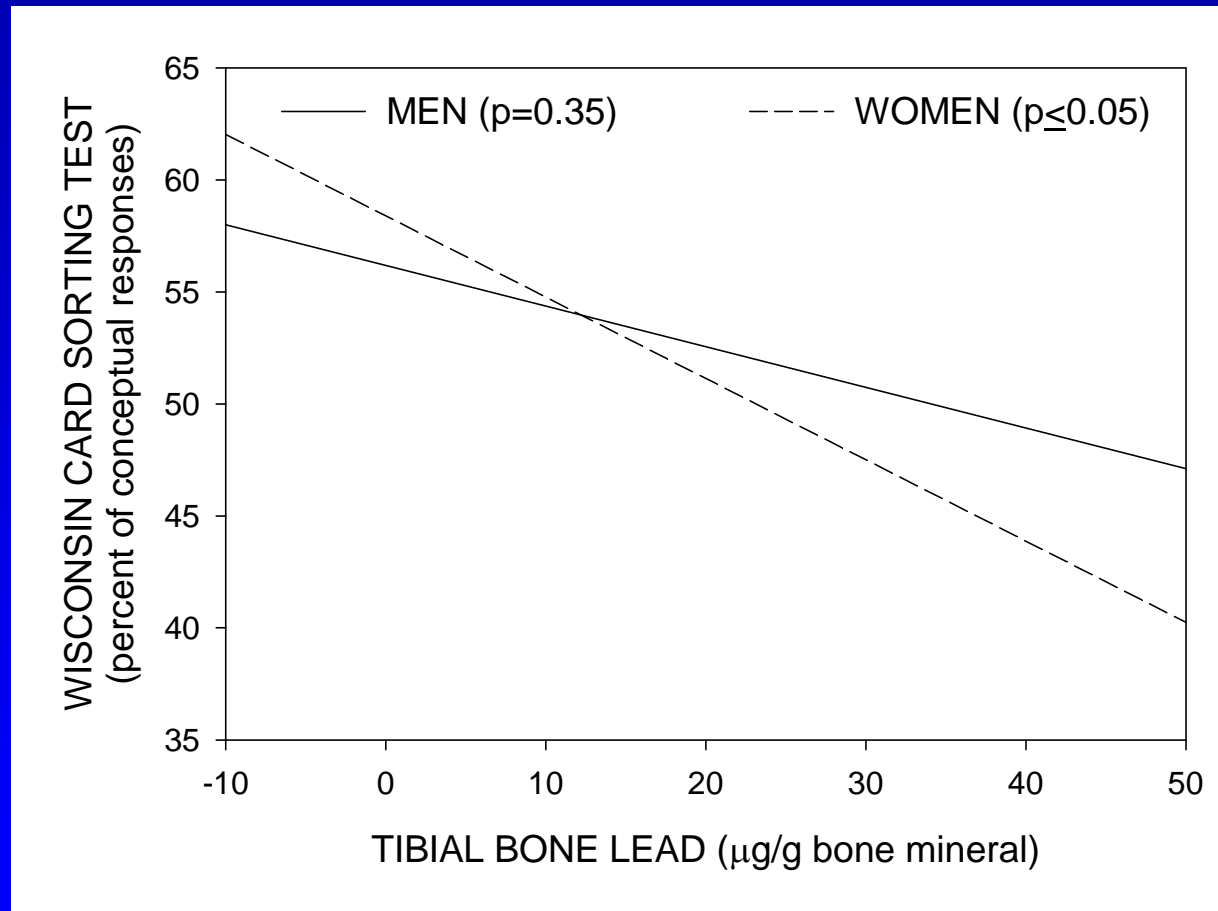
Adjusted for age, education, smoking in the past year, occupational exposure to solvents, state anxiety

WISCONSIN CARD SORTING TEST (number of correct responses)



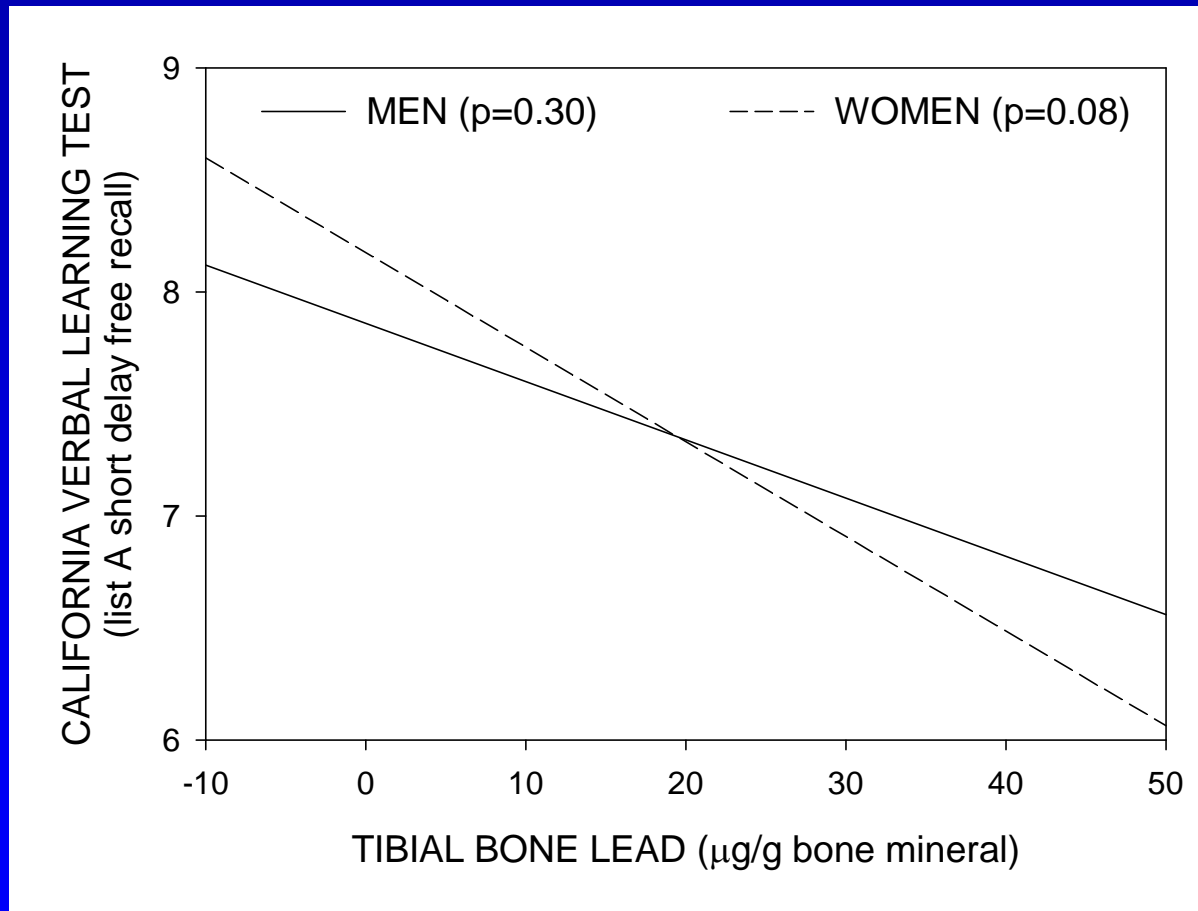
Adjusted for education, smoking in the past year

WISCONSIN CARD SORTING TEST (understanding the sorting principle)



Adjusted for age, education, state anxiety, other NSAIDs

CALIFORNIA VERBAL LEARNING TEST



Adjusted for age, education

WHY ARE PCBs NOT ASSOCIATED WITH NEUROCOGNITIVE DEFICITS?

- HEALTHY WORKER EFFECT
 - PCB Exposure was so high that some workers may have chosen not to participate
- PCBs MAY BE LESS NEUROTOXIC IN ADULTS THAN IN INFANTS AND CHILDREN
- OCCUPATIONAL EXPOSURE WAS ALMOST EXCLUSIVELY TO PCBs
- CONTAMINATED FISH CONTAIN MANY NEUROTOXICANTS (MERCURY, PESTICIDES) THAT INTERACT TO AFFECT BRAIN FUNCTION

TAKE HOME MESSAGES

1. PCBs are persistent – serum levels today are two times higher in the worker population than in the general population
2. Occupational PCB exposure may be associated with increased Parkinson's disease mortality in women
3. Bone lead levels in the worker population are similar to those in the general population, but are correlated with IH ratings for job categories with high lead exposure
4. Bone lead levels are associated with deficits in performance on motor, memory and executive function, with a greater number of findings for women

THANKS!

- FOR YOUR ATTENTION
- TO THE STUDY PARTICIPANTS
 - Especially Ed Bloch and the IBEW
- TO THE STUDY INVESTIGATORS
- THE FUNDING AGENCIES

THE EPI STUDY STAFF



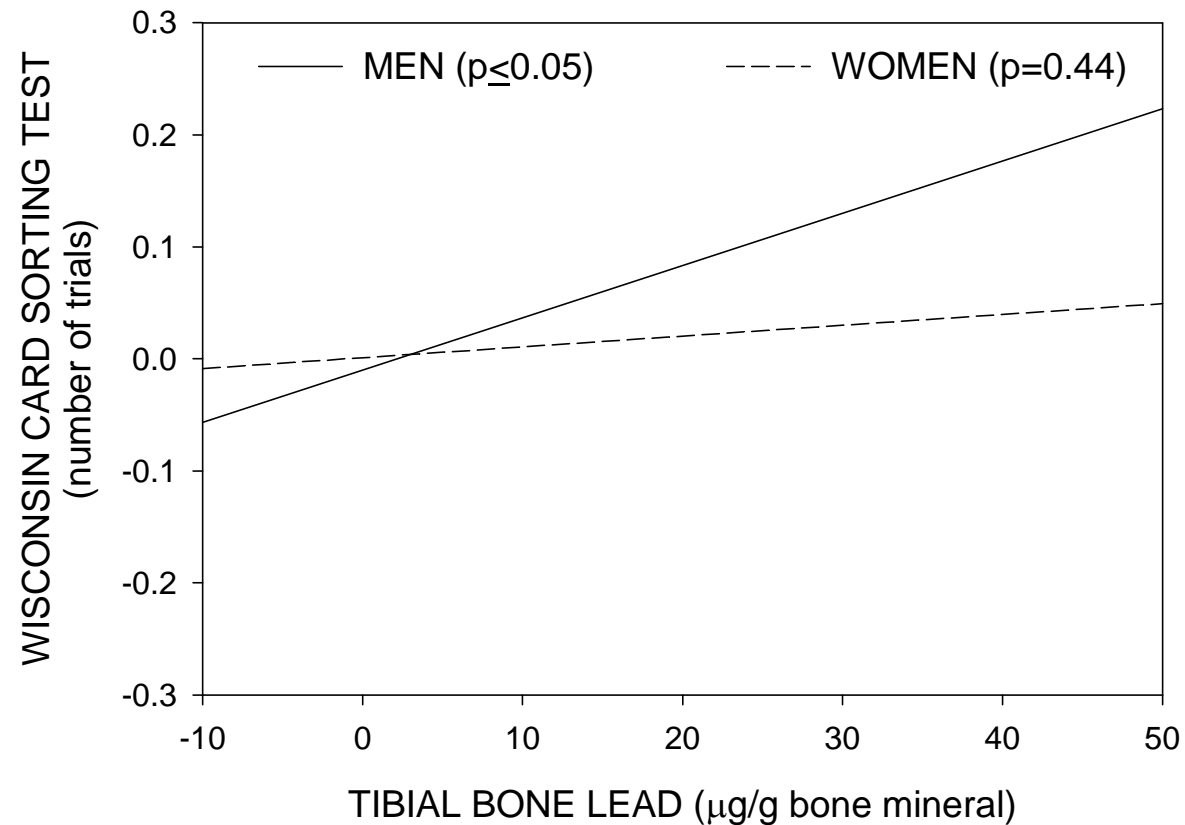
SUPPORT

**United States Army Medical
Research and Materiel Command**

NIH/NIEHS

USEPA

WISCONSIN CARD SORTING TEST (number of errors)



Adjusted for age, other NSAIDs, psychotherapeutic agents

Results Suggest that Only Women are at Risk For Parkinson's disease Following Occupational Exposure to PCBs

Only Women Show Inverse Relationship
Between PCB Body Burden and Dopamine
Terminal Densities (Our study)

Highly Exposed Women Show Greater Mortality
From PD than do Men (Steenland *et al.*)