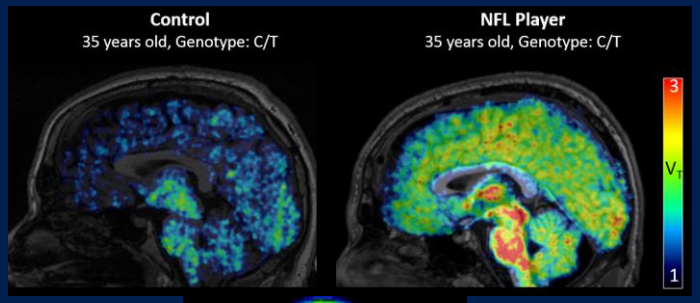

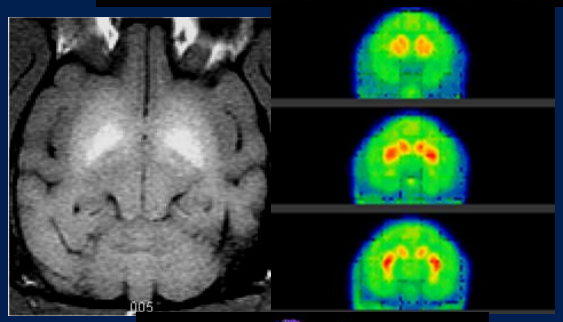

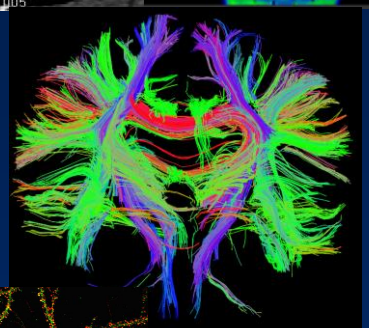

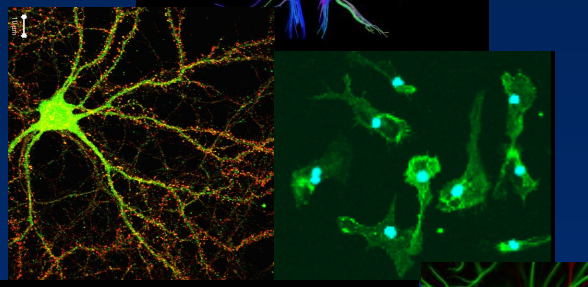

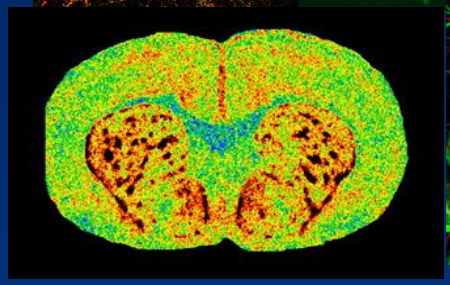

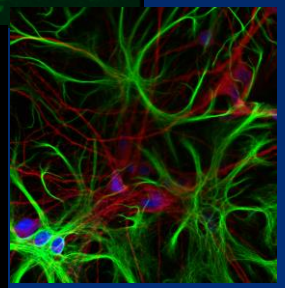

The Environment and Brain Health:
Identifying environmental risk factors of neurological disease

Tomás R. Guilarte, PhD
Dean, Robert Stempel College of Public Health & Social Work
Professor, Dept. of Environmental Health Sciences
Professor, Cognitive Neuroscience & Imaging
Director: Brain, Behavior & the Environment
Member: Biomolecular Sciences Institute
Florida International University
Miami, FL

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Brain Health & the Environment
It's all inter-connected

What if I tell you that there are over **800 million** children around the world (including the US), or **40%** of the world's children, that have a condition that slowly takes away their intelligence and a bright future [UNICEF 2020 Report]

This condition results in:
-learning deficits and a need for special education
-poor school performance & increased school dropout
-delinquent behavior & incarceration
-risk of psychiatric disease such as depression & schizophrenia
-increased risk of drug use & abuse
-increased risk of Alzheimer's disease later in life

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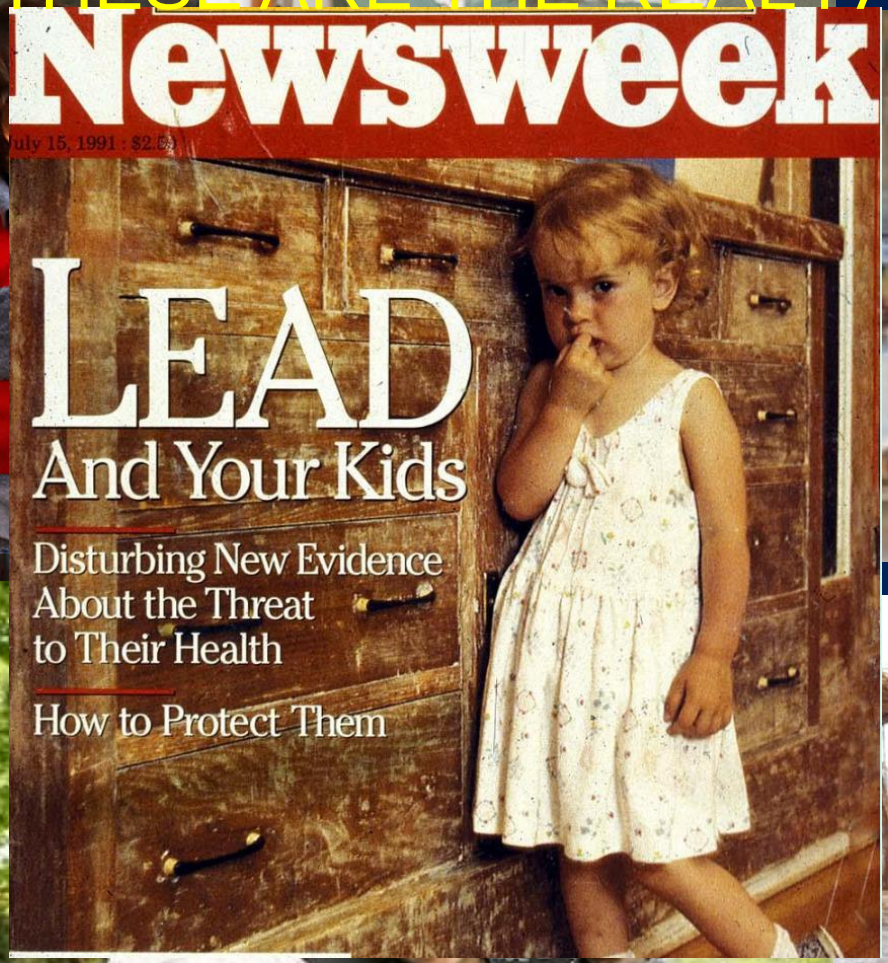
These are the same children that will be responsible for our world in the decades to come……

THESE ARE THE REAL FACES



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The Toxic Truth: Children's Exposure to Lead Pollution Undermines a Generation of Future Potential

UNICEF REPORT 2020

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theguardian

US world opinion sports soccer tech arts lifestyle fashion business travel environment science browse all sections

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Michigan

'We were paying to poison our kids': lead in Michigan city's water hits children

Flint declared a public health emergency this week after a dangerous spike in its water's lead levels. But parents say they've been 'screaming' about the issue for months in an area where water prices are among the country's highest

Ryan Felton in Flint, Michigan

Sunday 4 October 2015 07.00 EDT

- April 2014 – To save costs, Flint, MI switched the source of it's drinking water supply from Detroit city water to the Flint River

- The Flint Water Study found that 10% of the homes tested had 25 ppb of lead, far exceeding the EPA's action level of 15 ppb.

- The highest test came back at 13,200 ppb; at 5,000 ppb, water is considered hazardous waste.

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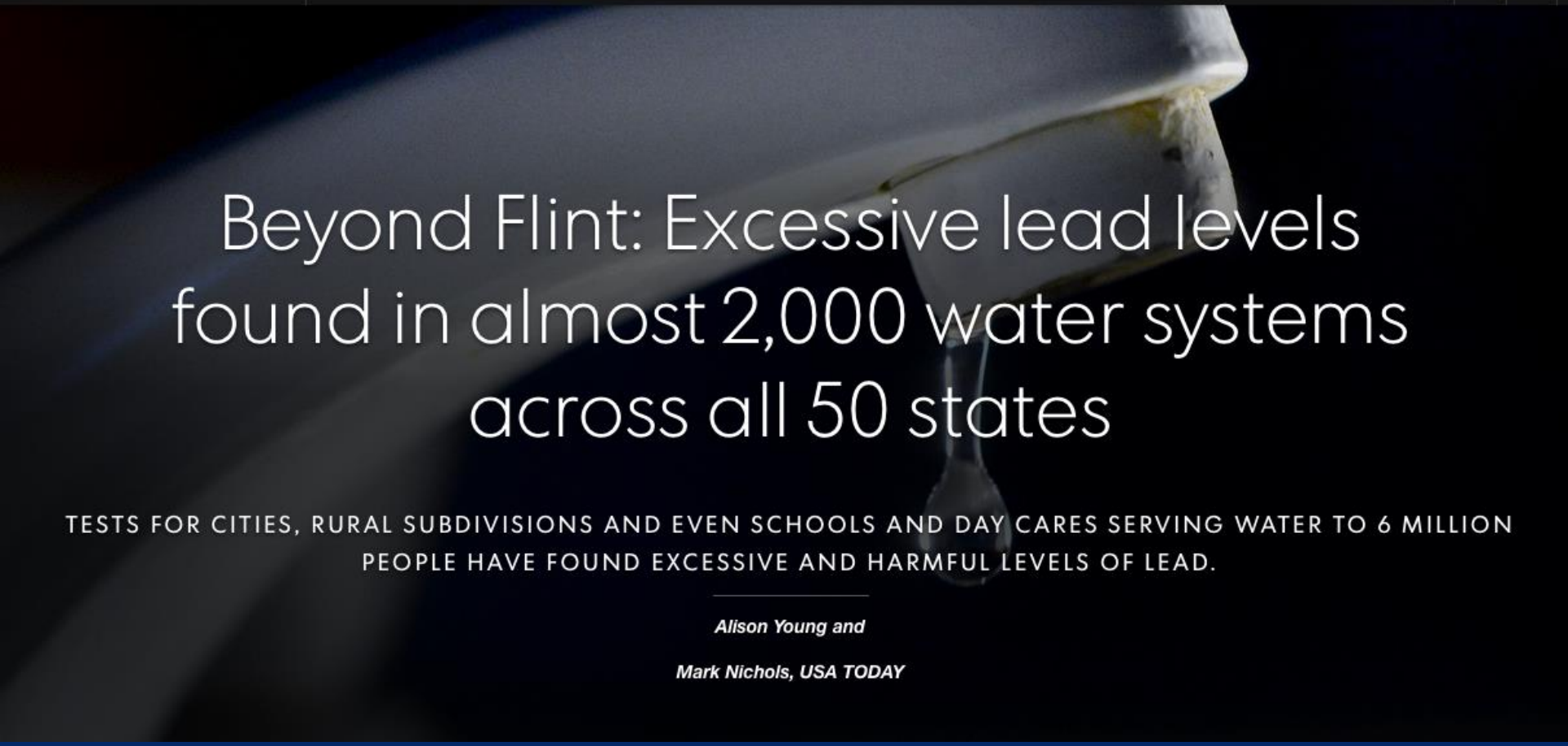


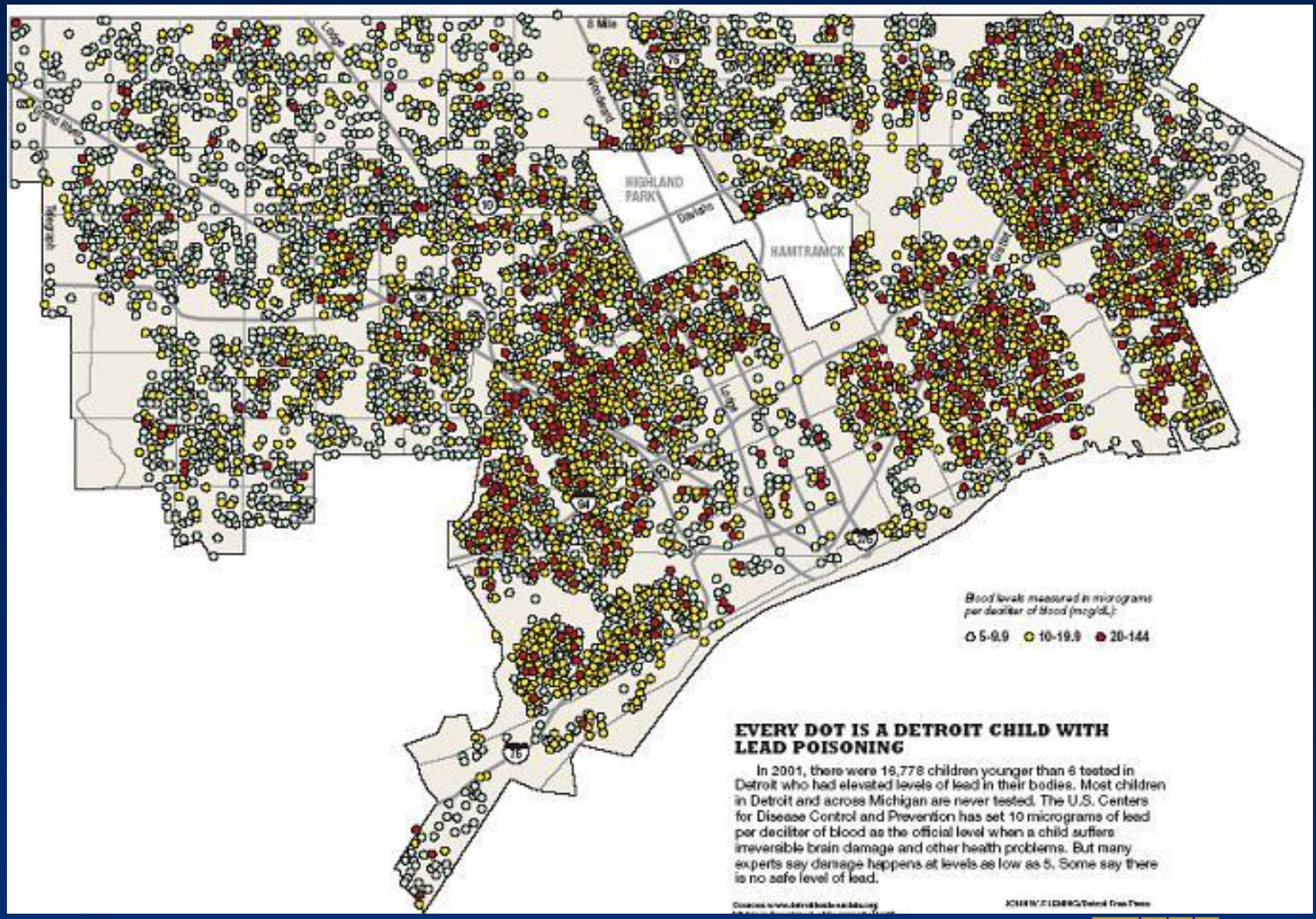
Beyond Flint: Excessive lead levels found in almost 2,000 water systems across all 50 states

TESTS FOR CITIES, RURAL SUBDIVISIONS AND EVEN SCHOOLS AND DAY CARES SERVING WATER TO 6 MILLION PEOPLE HAVE FOUND EXCESSIVE AND HARMFUL LEVELS OF LEAD.

Alison Young and

Mark Nichols, USA TODAY

In cities like Detroit, your zip code dictates lead exposure level



3.5 ug/dL is the current CDC level of action

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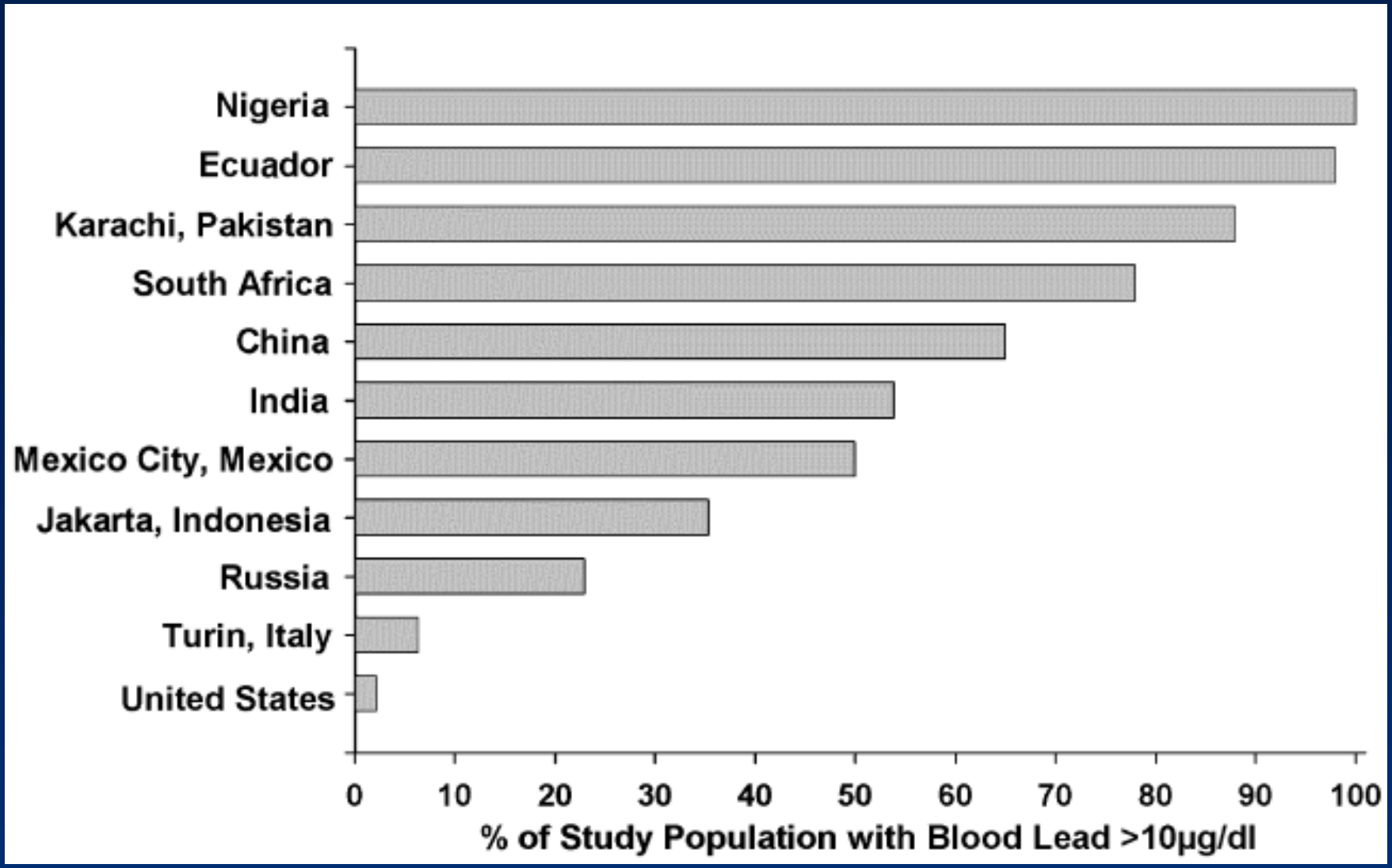
CHILDHOOD LEAD INTOXICATION IS A GLOBAL PUBLIC HEALTH PROBLEM



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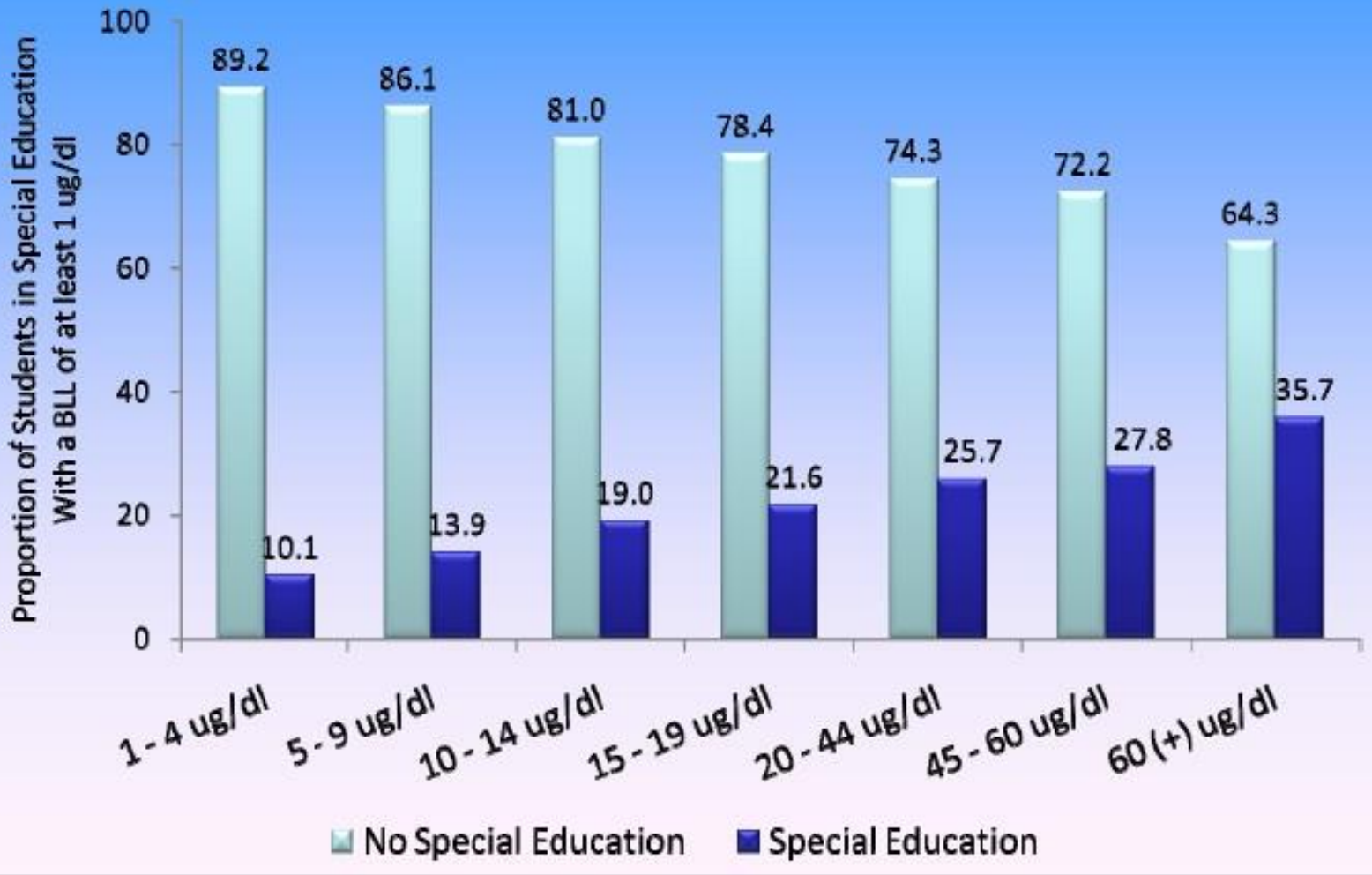
Special Education Status by Blood Lead Level



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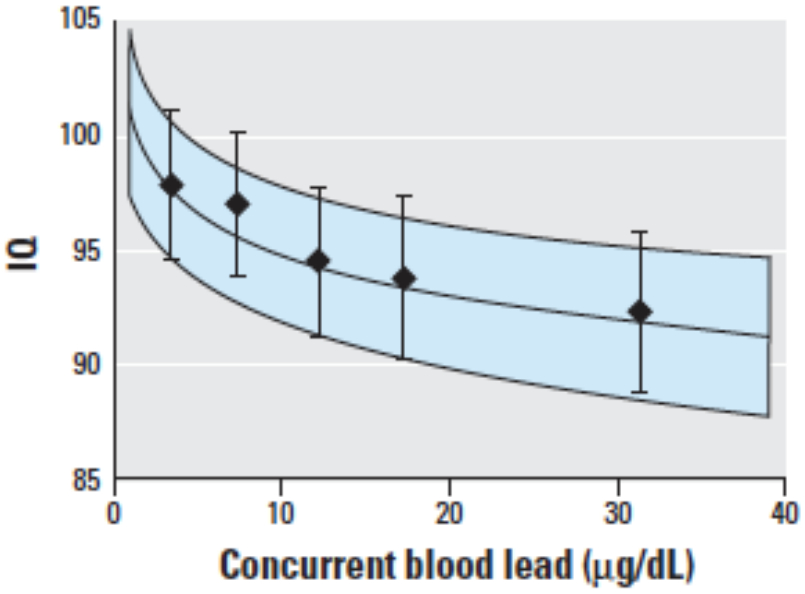
Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis

Bruce P. Lanphear,[1,2] Richard Hornung,[1,2,3] Jane Khoury,[1,2] Kimberly Yolton,[1] Peter Baghurst,[4] David C. Bellinger,[5] Richard L. Canfield,[6] Kim N. Dietrich,[1,2] Robert Bornschein,[2] Tom Greene,[7] Stephen J. Rothenberg,[8,9] Herbert L. Needleman,[10] Lourdes Schnaas,[11] Gail Wasserman,[12] Joseph Graziano,[13] and Russell Roberts[14]

[1]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA; [2]Department of Environmental Health, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA; [3]Institute for Health Policy and Health Services Research, Department of Environmental Health, University of Cincinnati, Cincinnati, Ohio, USA; [4]Women and Children's Hospital, North Adelaide, South Australia; [5]Department of Neurology, Children's Hospital Boston and Harvard Medical School, Boston, Massachusetts, USA; [6]Division of Nutritional Sciences, Cornell University, Ithaca, New York, USA; [7]Department of Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio, USA; [8]Center for Research in Population Health, National Institute of Public Health, Cuernavaca, Morelos, Mexico; [9]Drew University, Los Angeles, California, USA; [10]University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA; [11]National Institute of Perinatology, Mexico City, Mexico; [12]Department of Child Psychiatry, Columbia University, New York, New York, USA; [13]Department of Environmental Health Sciences, Columbia University, New York, New York, USA; [14]School of Applied Psychology, Griffith University, Queensland, Australia



Mean IQ effect as a function of blood lead adjusted for HOME score, maternal education, maternal IQ, and birth weight.

Env Hlth Persp 113: 894, 2005

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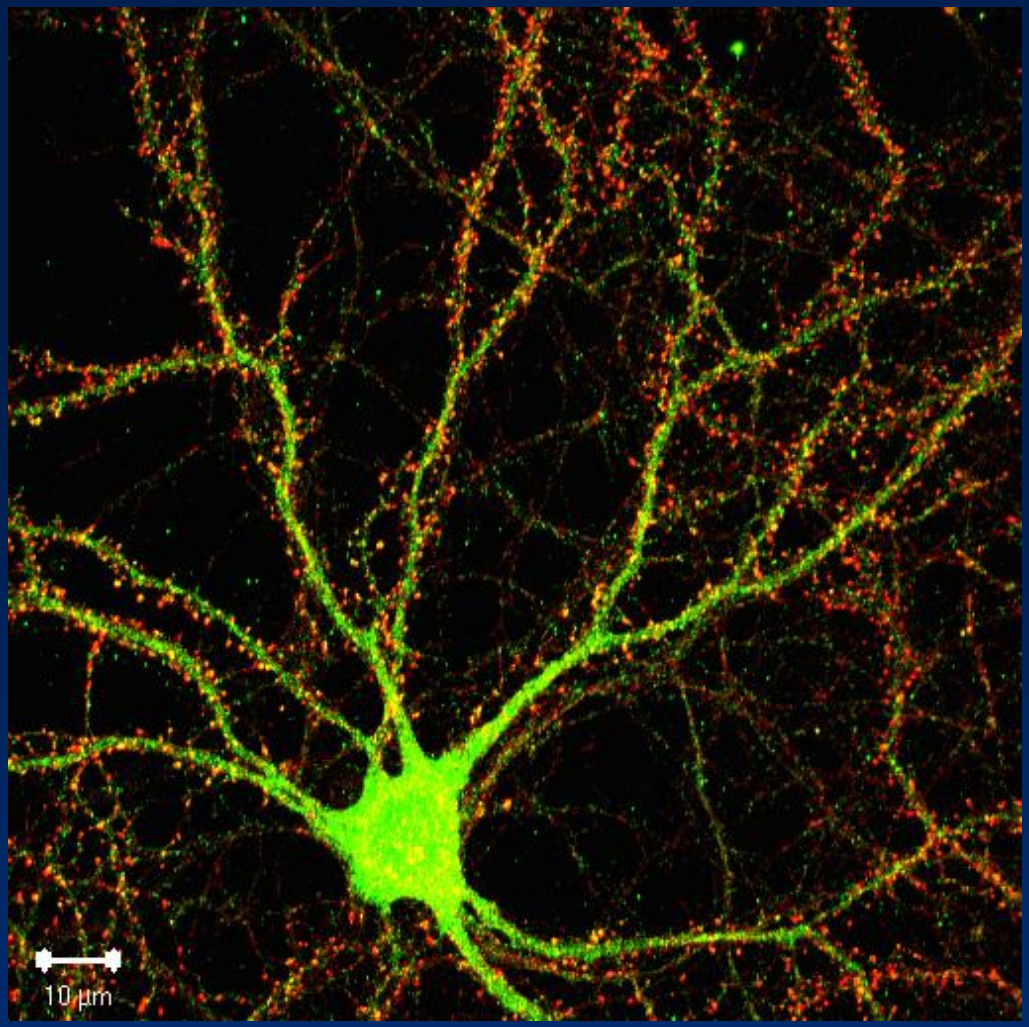
HOW DOES LEAD AFFECT THE BRAIN?



Primary neuron in culture - Hippocampus

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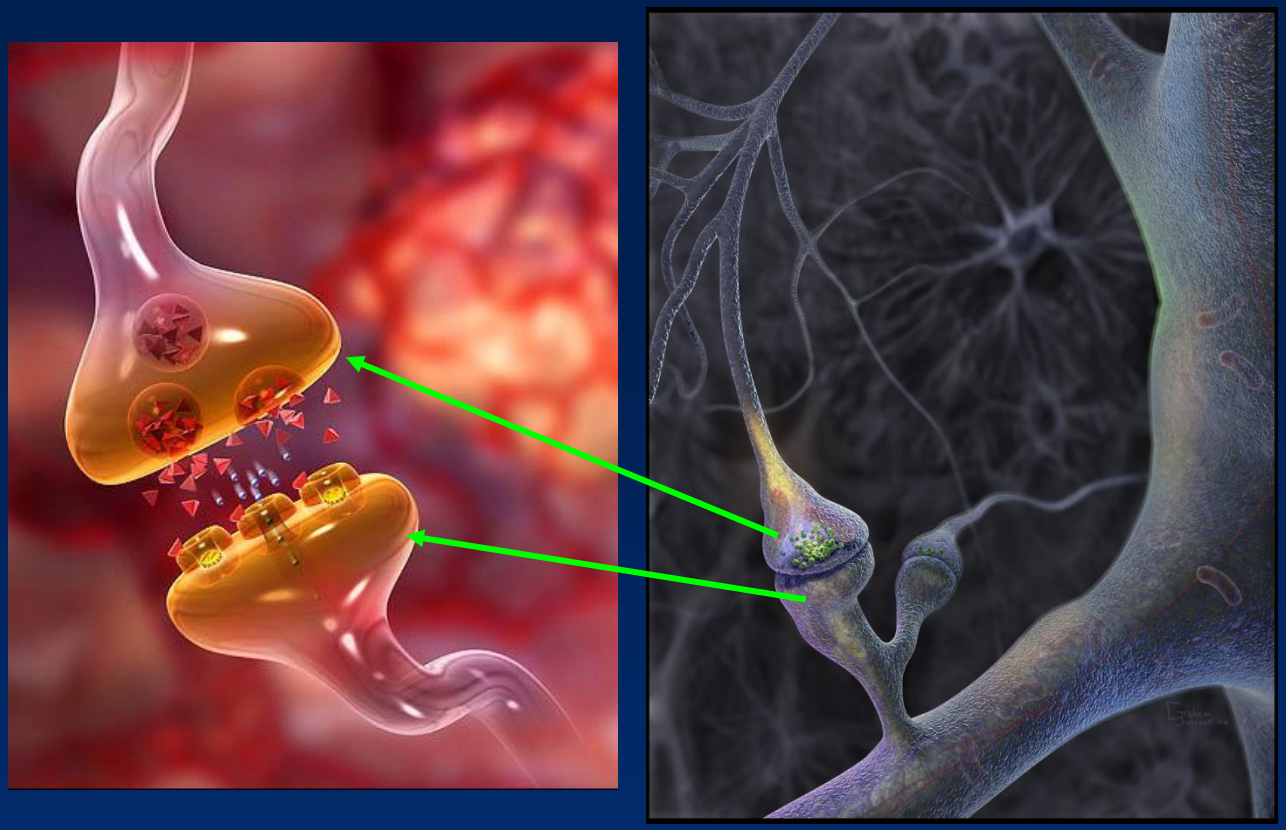
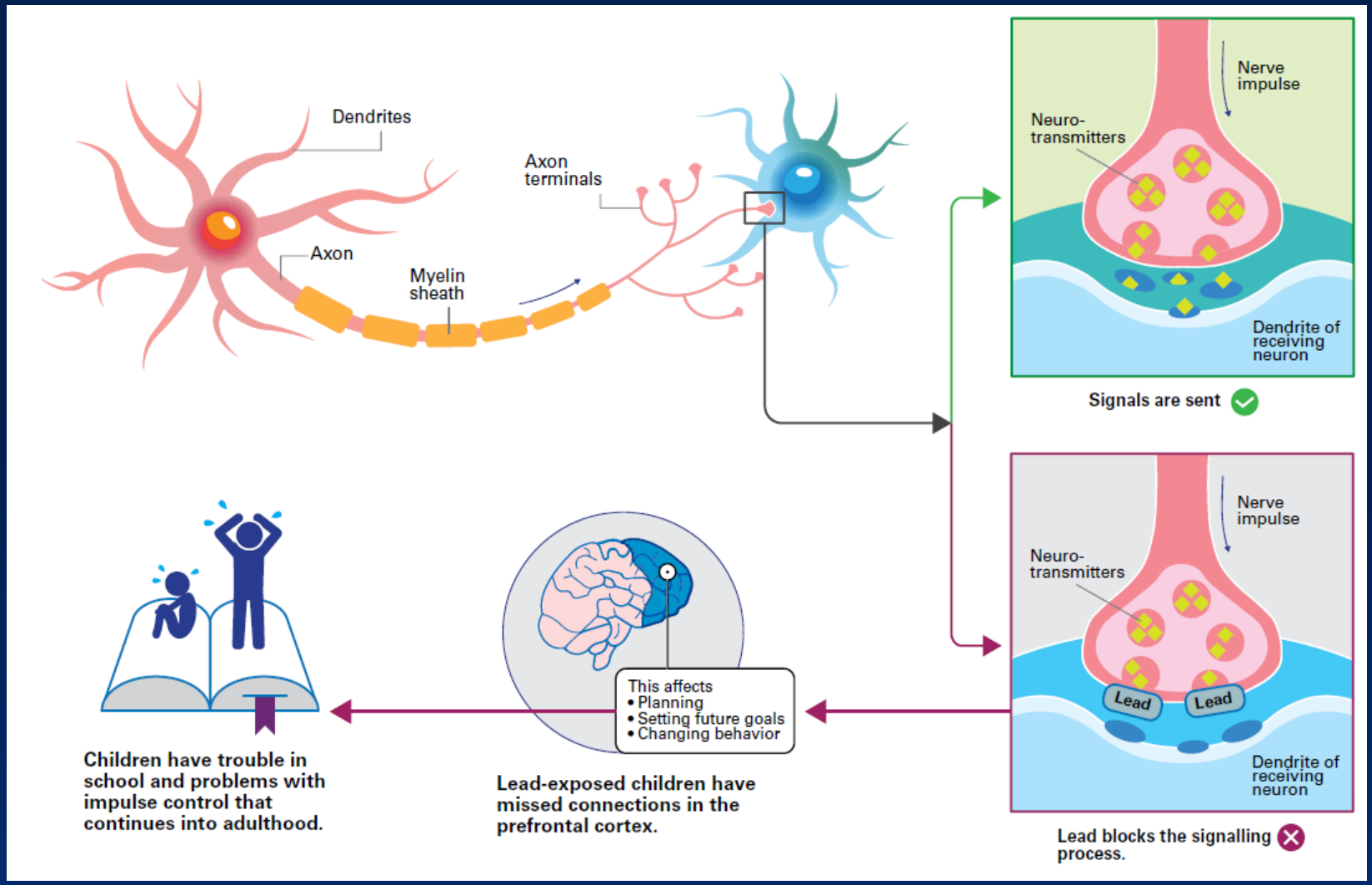
SYNAPSES ARE POINTS OF INFORMATION TRANSFER FROM NEURON TO NEURON



Research has discovered:



Lead interferes with the ability of NEURONS to grow, connect, and communicate.

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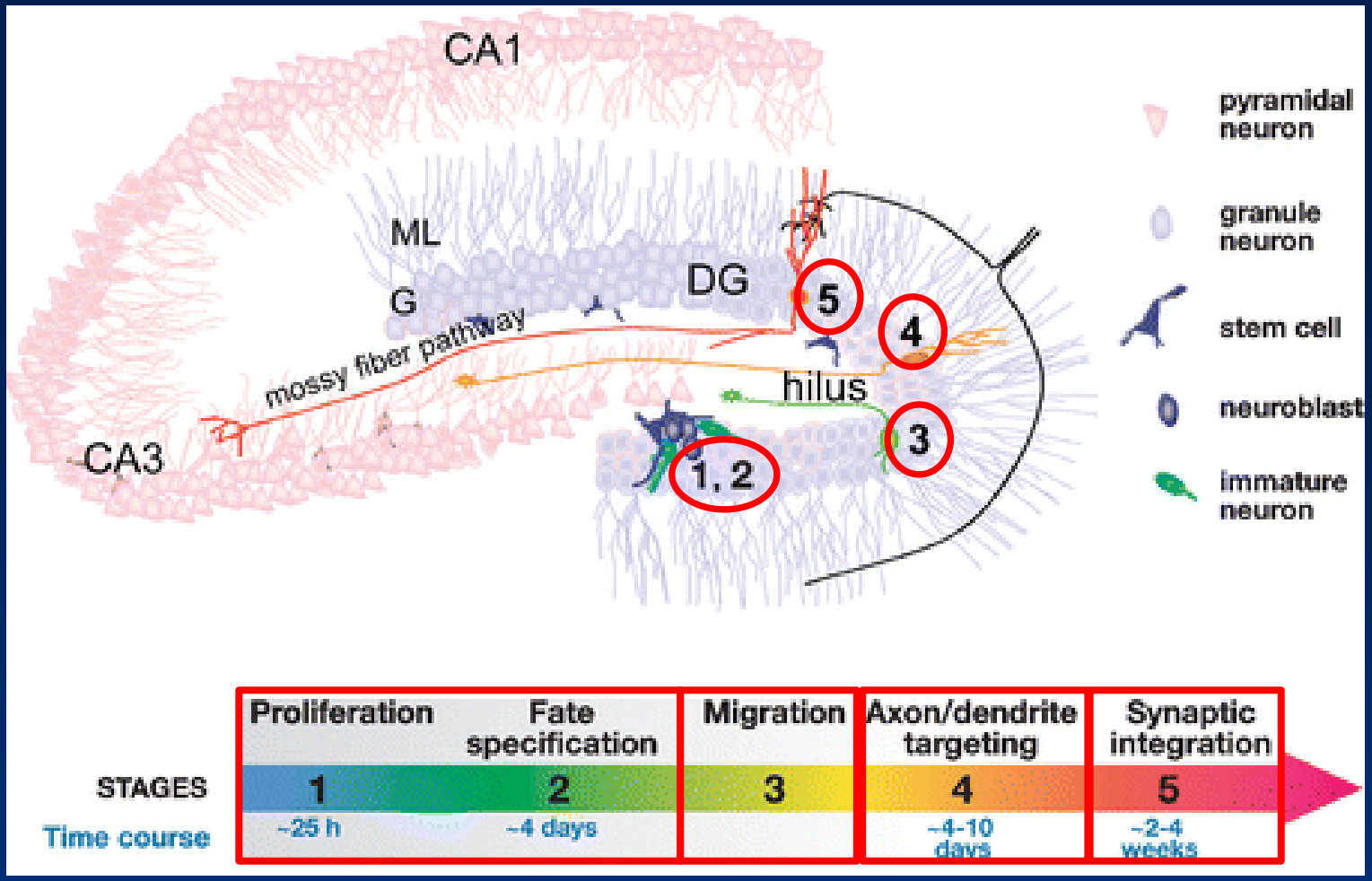
What are the consequences of lead exposure at the cellular level?

ADULT NEUROGENESIS



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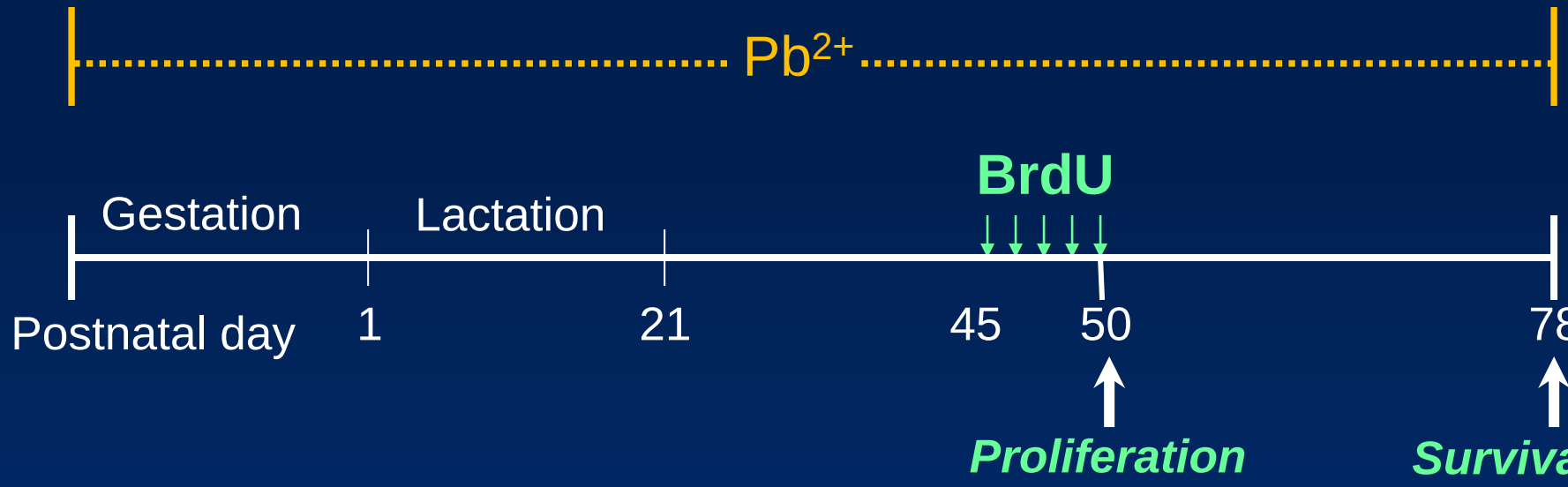
LEAD EXPOSURE & ADULT NEUROGENESIS: EXPERIMENTAL DESIGN



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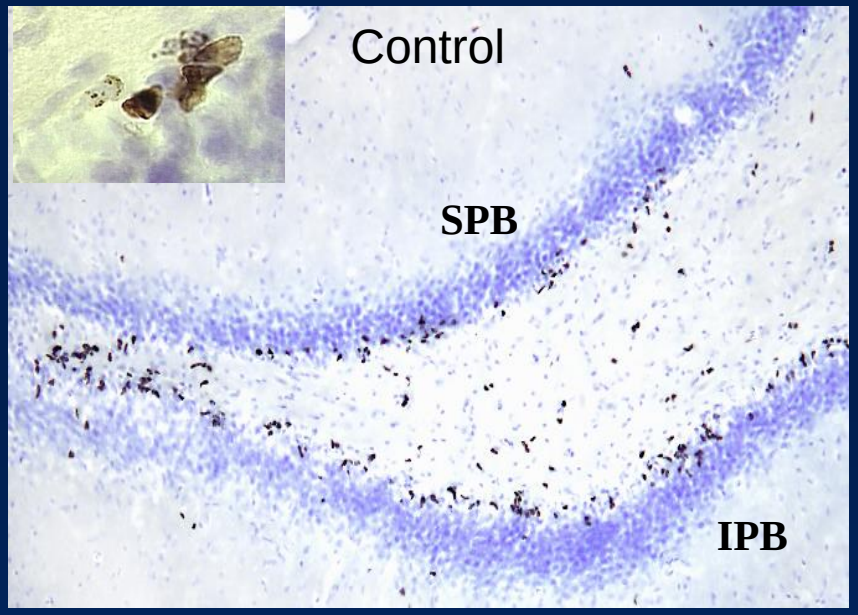
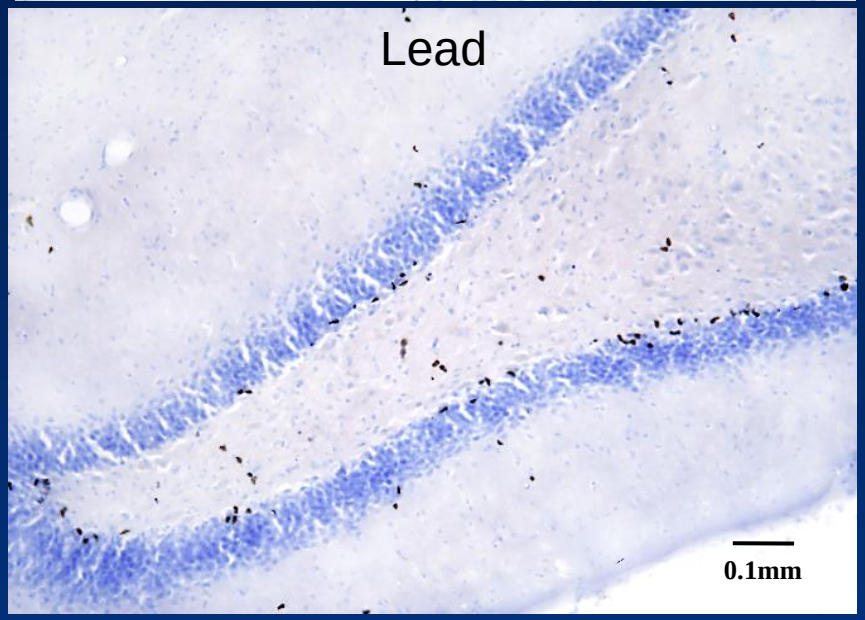
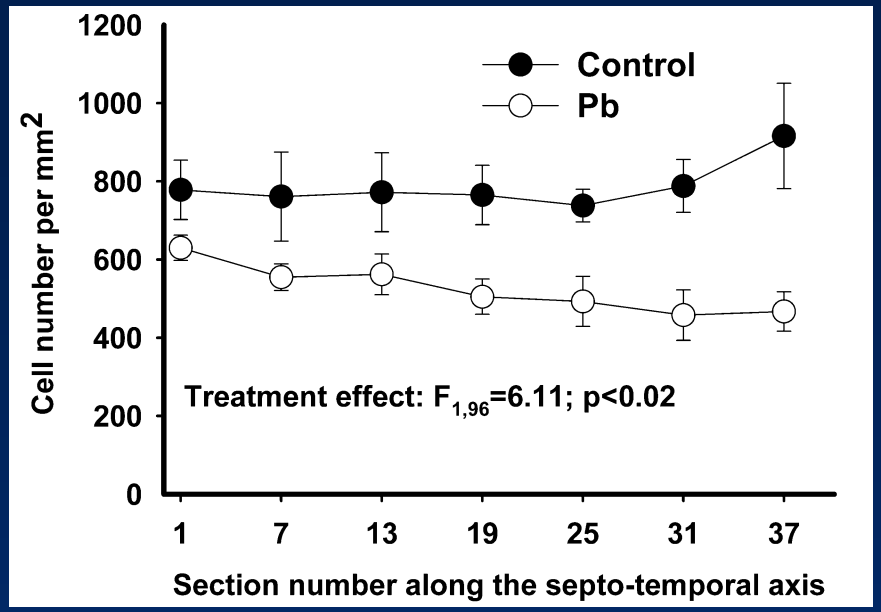
PROLIFERATION OF NEWLY BORN CELLS IN THE SUBGRANULAR ZONE - DENTATE GYRUS







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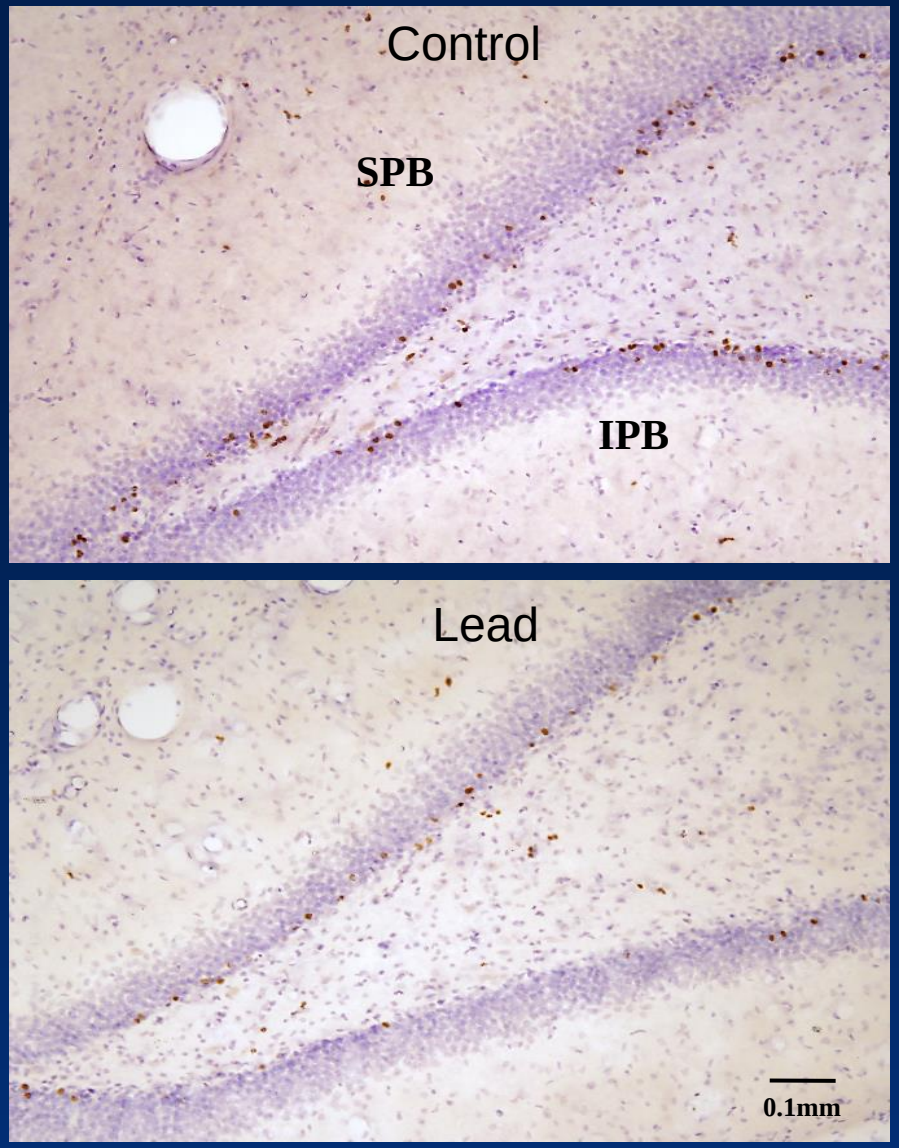
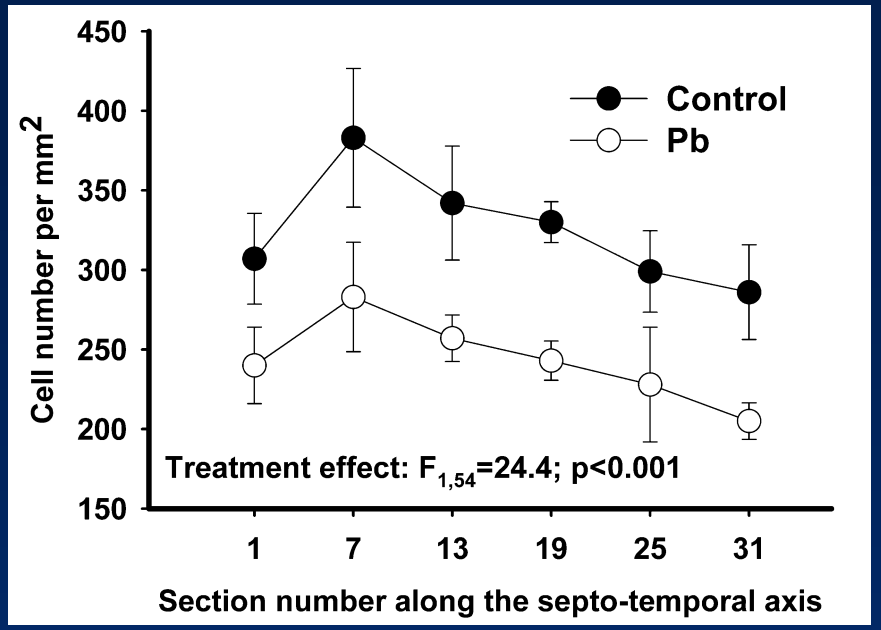
SURVIVAL OF NEWLY BORN CELLS IN THE DENTATE GYRUS





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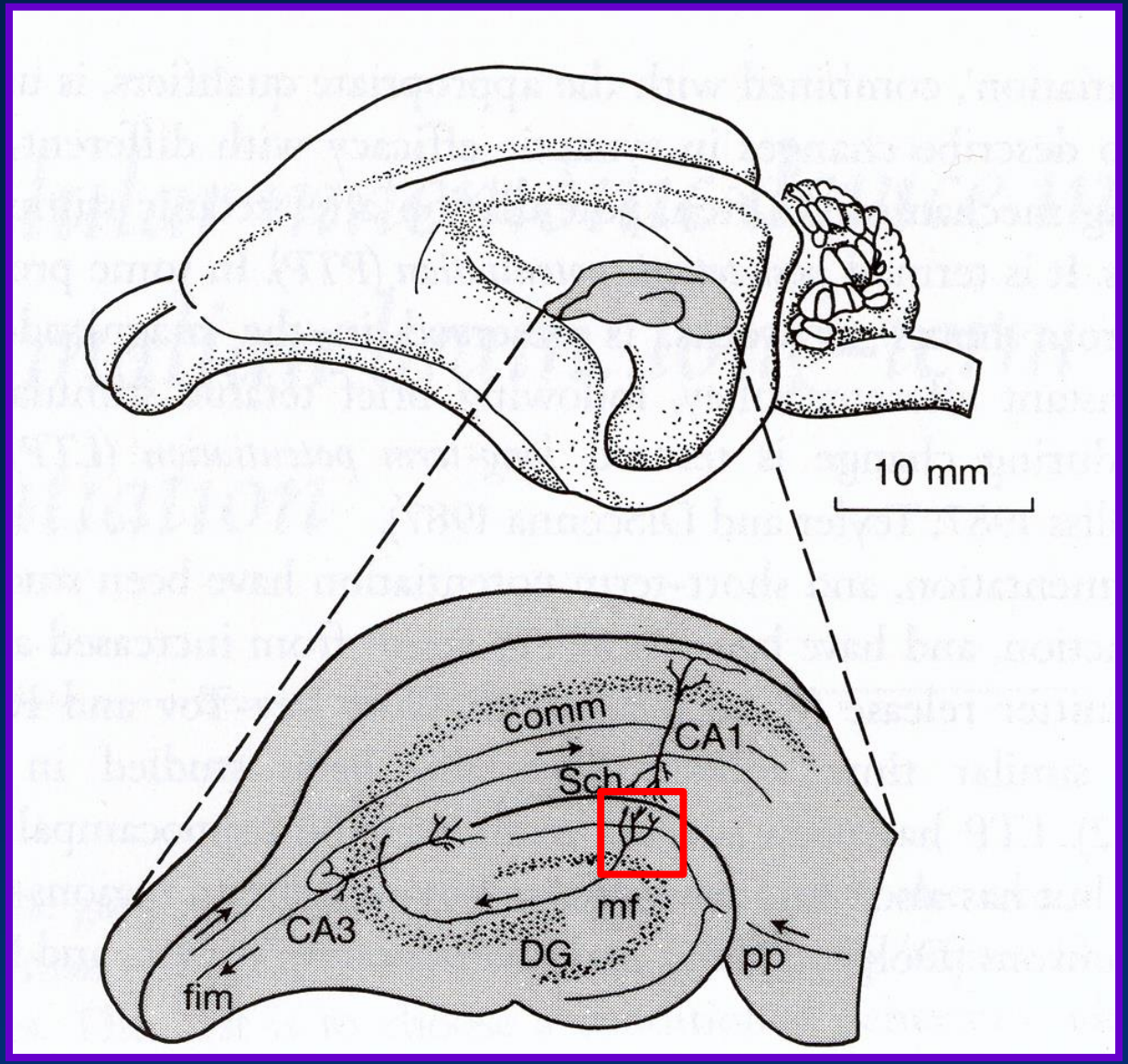
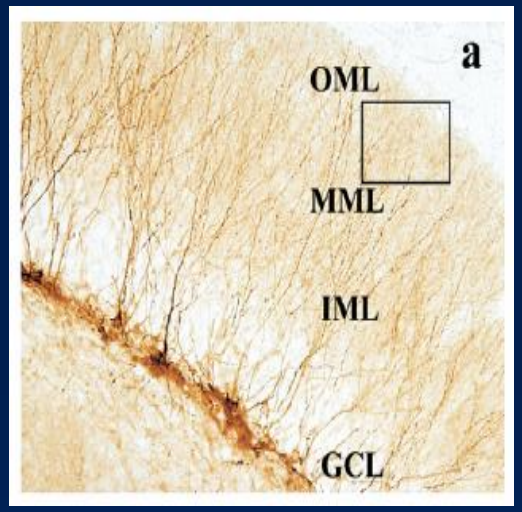
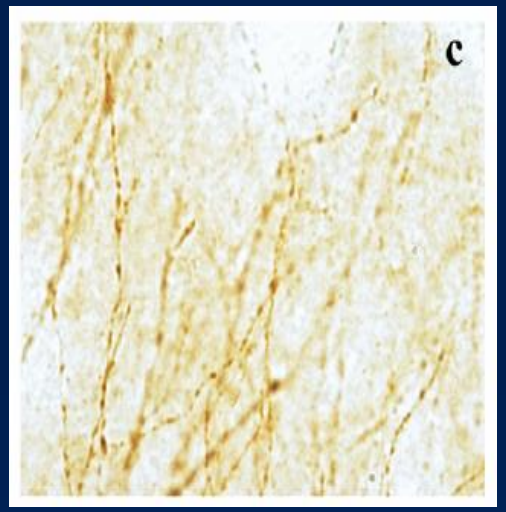
HIPPOCAMPUS CONNECTIVITY

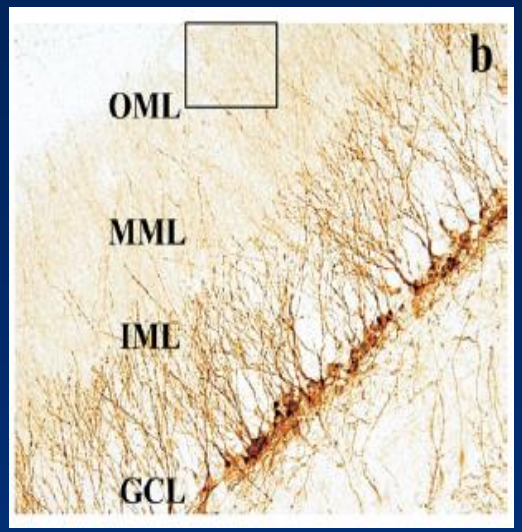


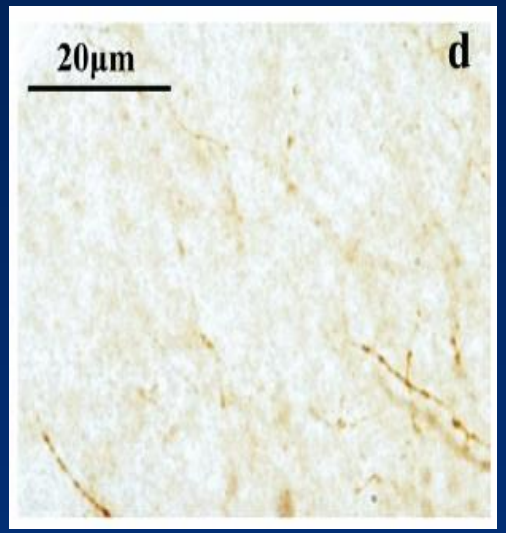
DENSITY & MORPHOLOGY OF APICAL DENDRITES IN NEWLY BORN NEURONS (DOUBLECORTIN LABELING)



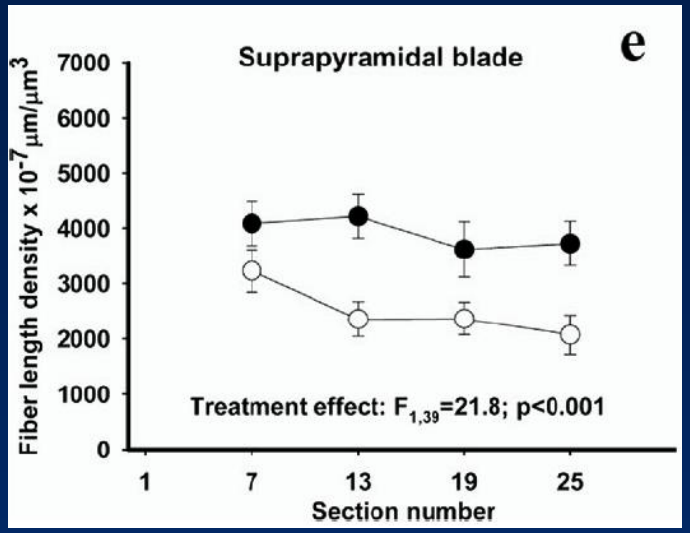


CONTROL





LEAD EXPOSED



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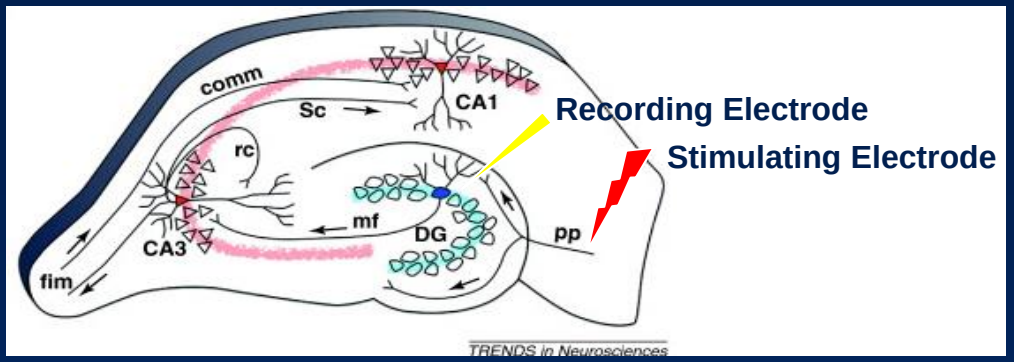
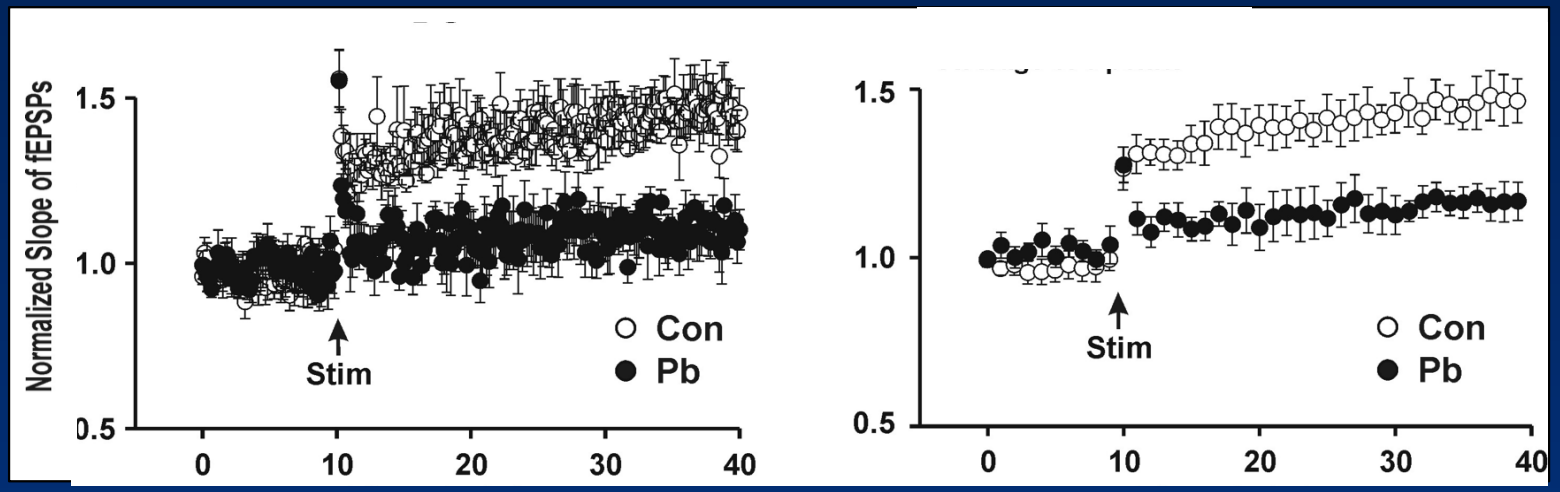
EFFECT OF LEAD EXPOSURE ON DENTATE GYRUS LTP IN THE RAT HIPPOCAMPUS

LTP= Long-Term Potentiation is a long-lasting increase in synaptic efficacy believed to be involved in information storage in the brain





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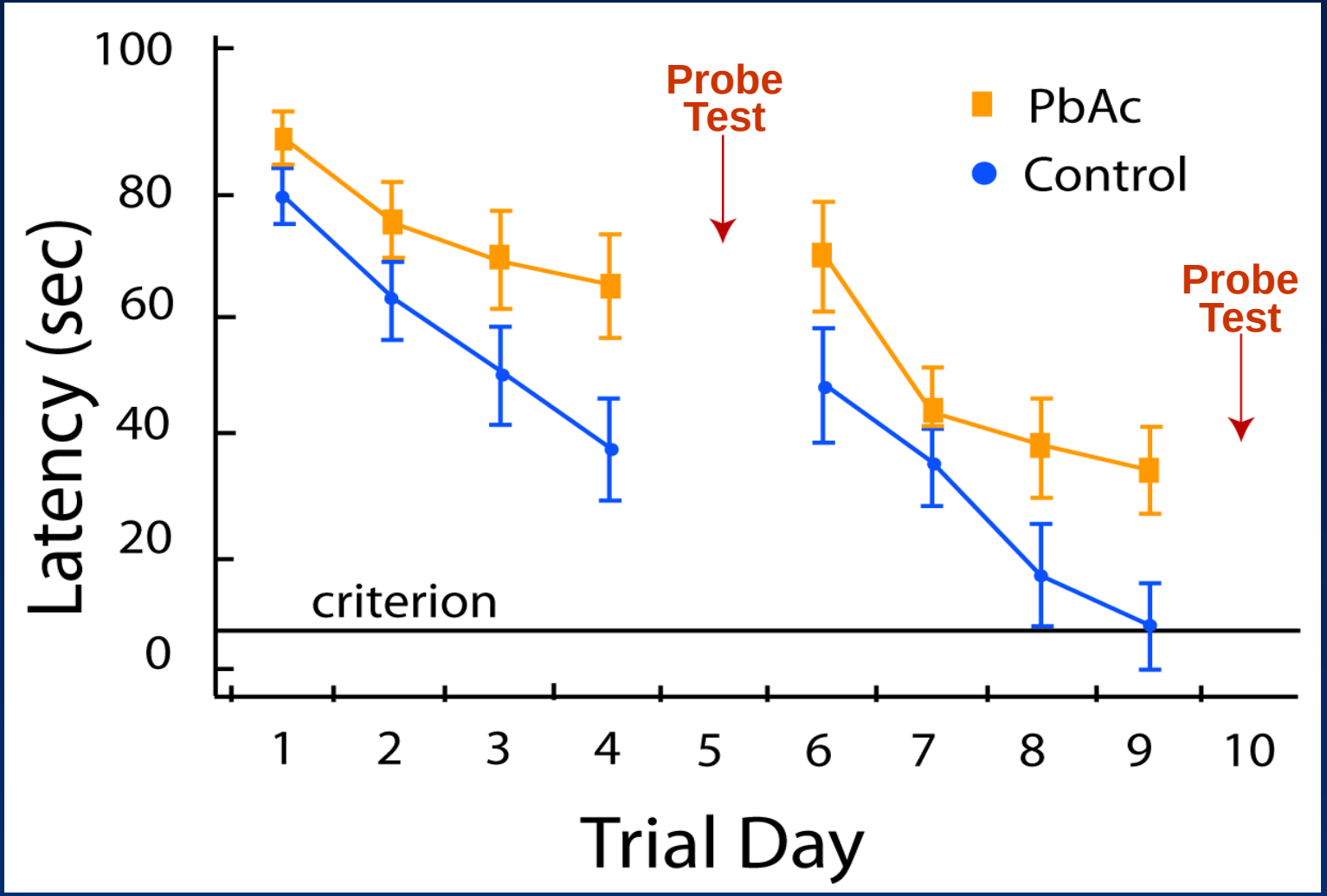
ACQUISITION OF LEARNING BEHAVIOR
SPATIAL LEARNING – MORRIS WATER MAZE



[Nihei, et al., Neuroscience *99:233, 2000]*

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SUMMARY

- Early life lead exposure alters adult neurogenesis and the morphology of newly born neuron in the hippocampus of adolescent animals.

- These effects alter neuronal circuitry in the hippocampus with detrimental effects on synaptic plasticity and cognitive function.

TAKE-HOME MESSAGE

Lead attacks the most fundamental aspect of the human brain,

the synapse

It undermines the ability of children to develop the mind.

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THANK YOU!!

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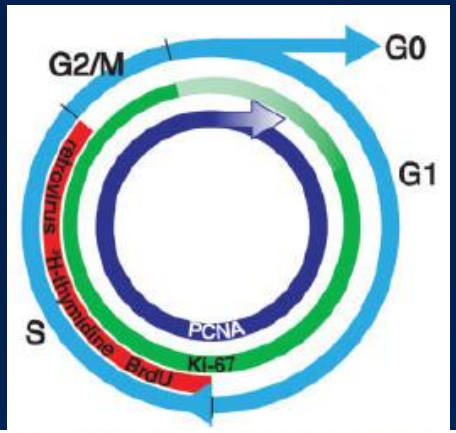
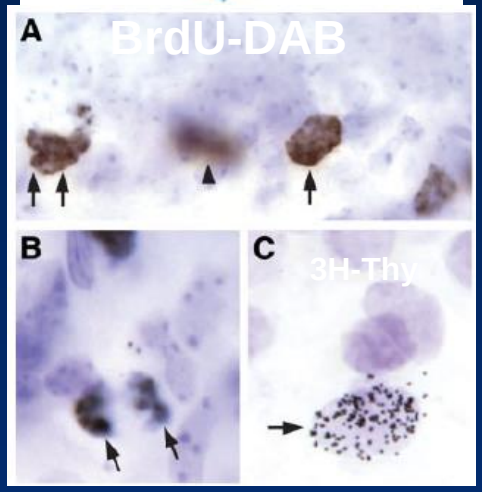
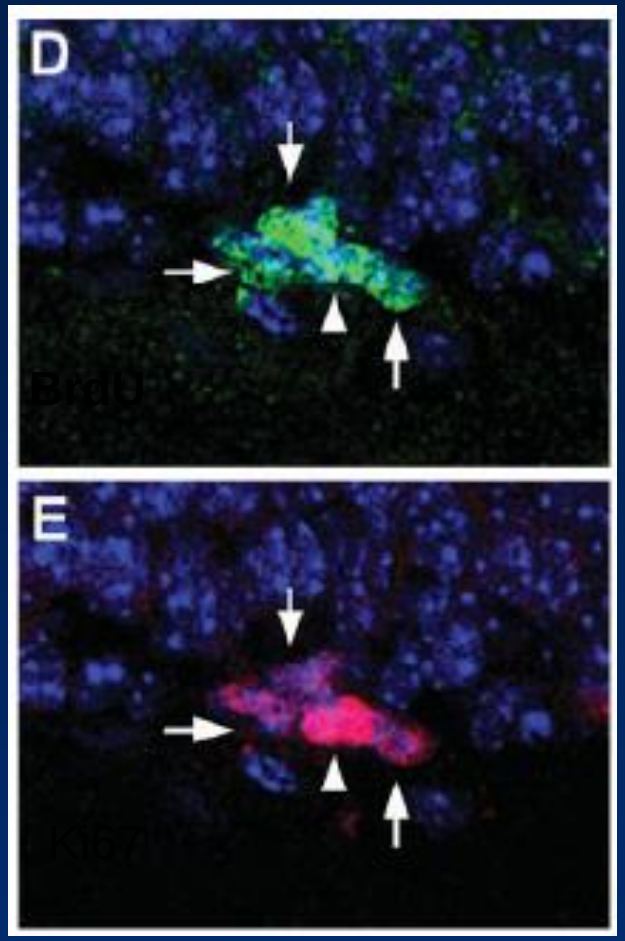
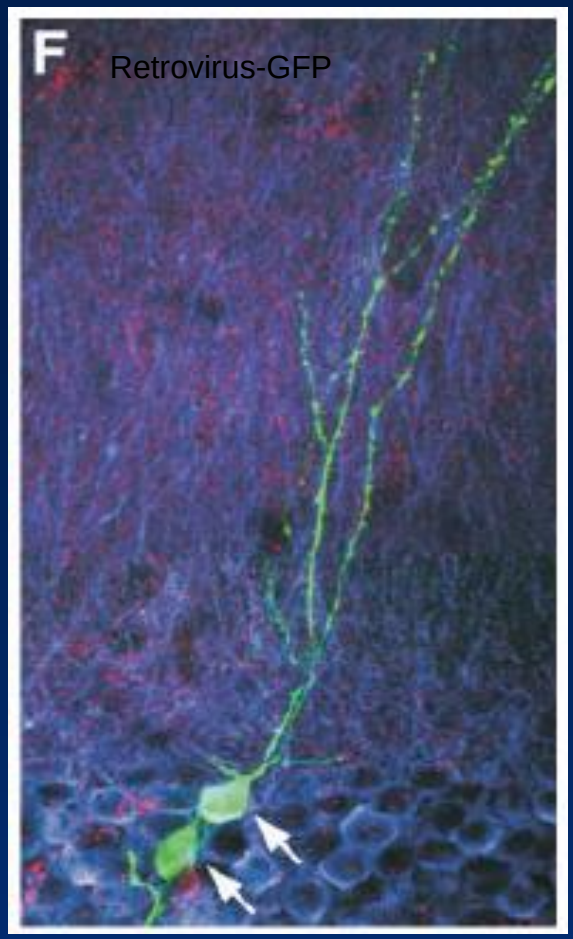
LABELING OF PROGENITOR CELLS IN THE SGZ









Source: Christie and Cameron. (2006). *Hippocampus*.

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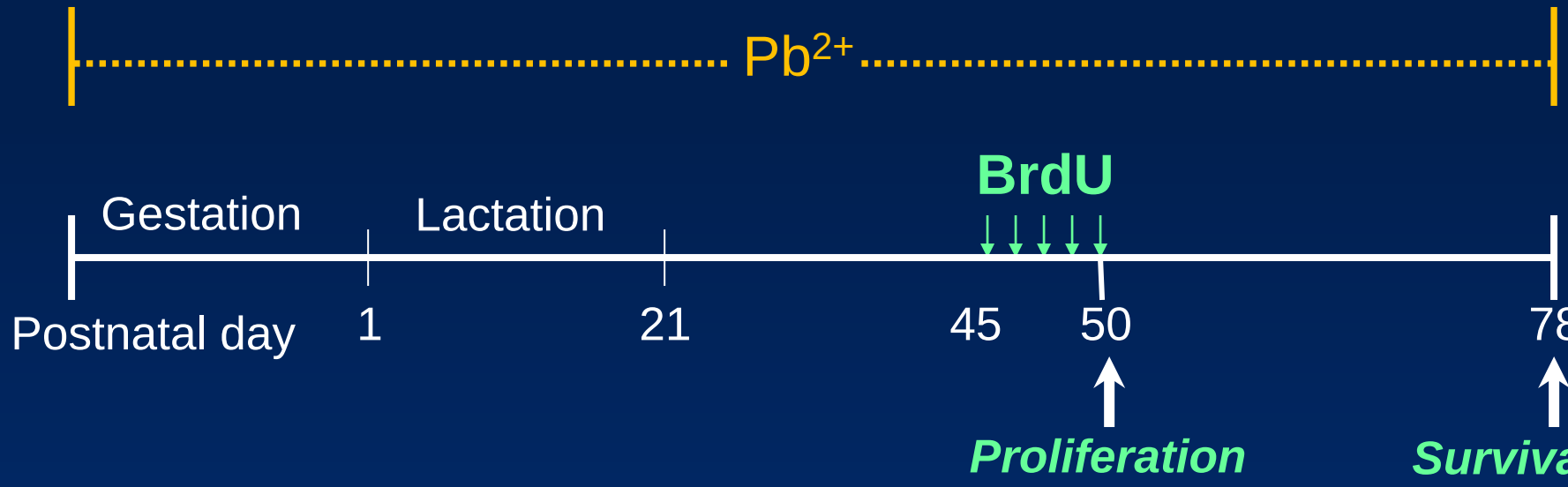
LEAD EXPOSURE & ADULT NEUROGENESIS: EXPERIMENTAL DESIGN



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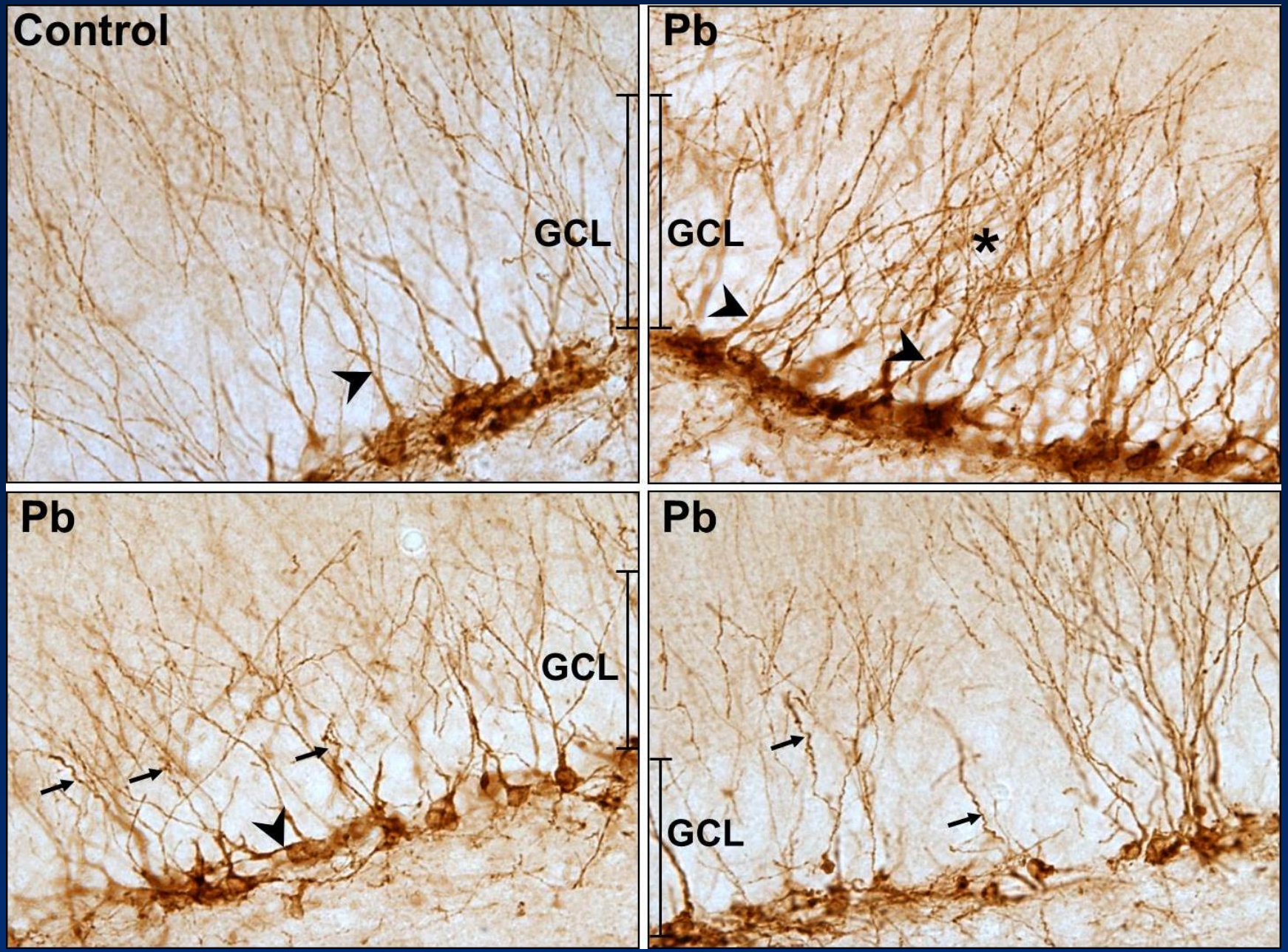

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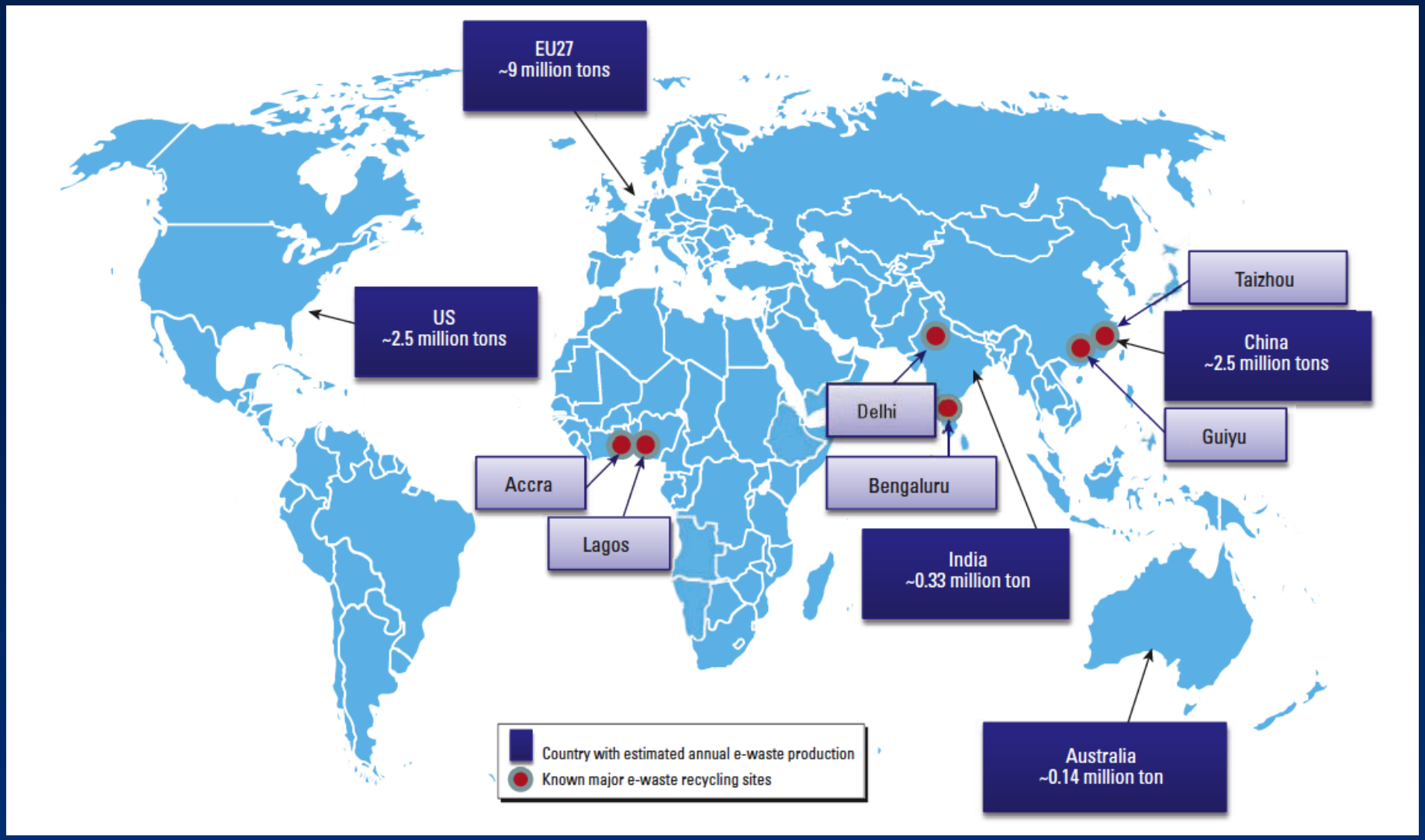
E-WASTE: A NEW GLOBAL SOURCE OF LEAD AND OTHER TOXIC METALS EXPOSURE IN CHILDREN



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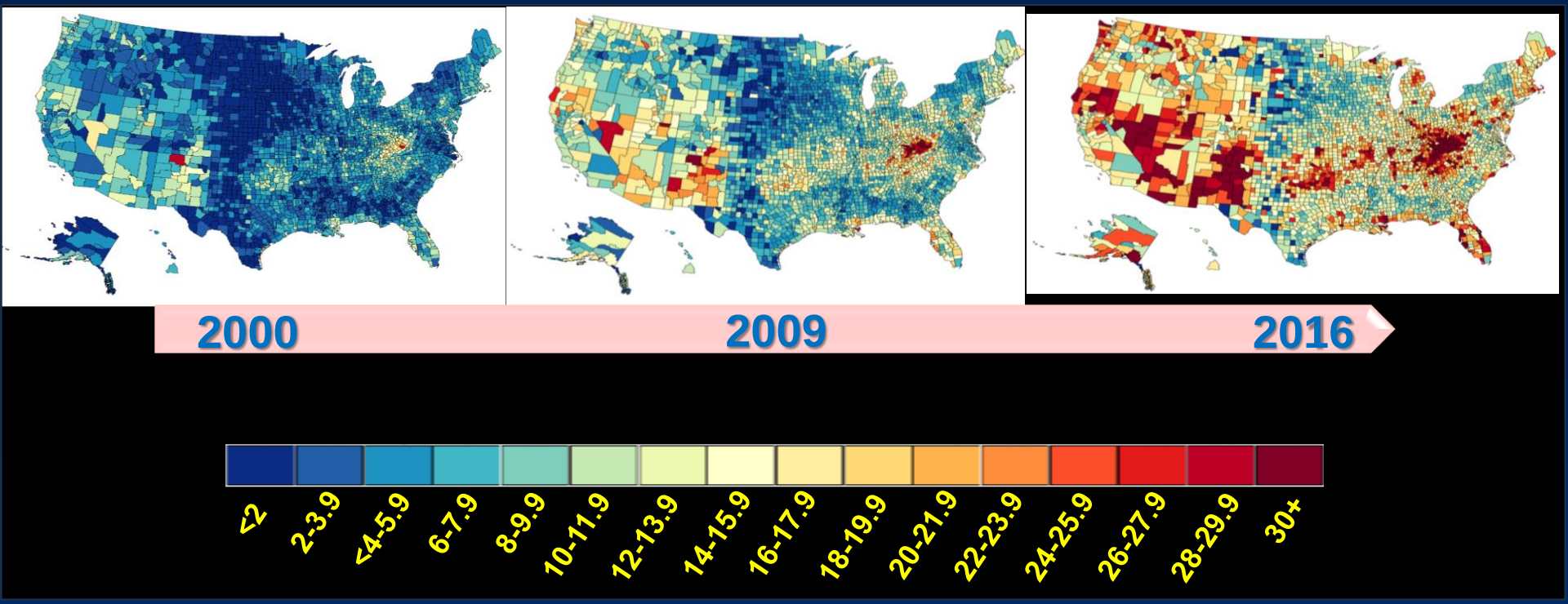
Heat-map of drug-poisoning mortality estimated age-adjusted death rate per 100,000 in the United States in the years 2000, 2009 and 2016.



Source: National Center for Health Statistics, National Vital Statistics System, mortality data
Rossen et al., 2017

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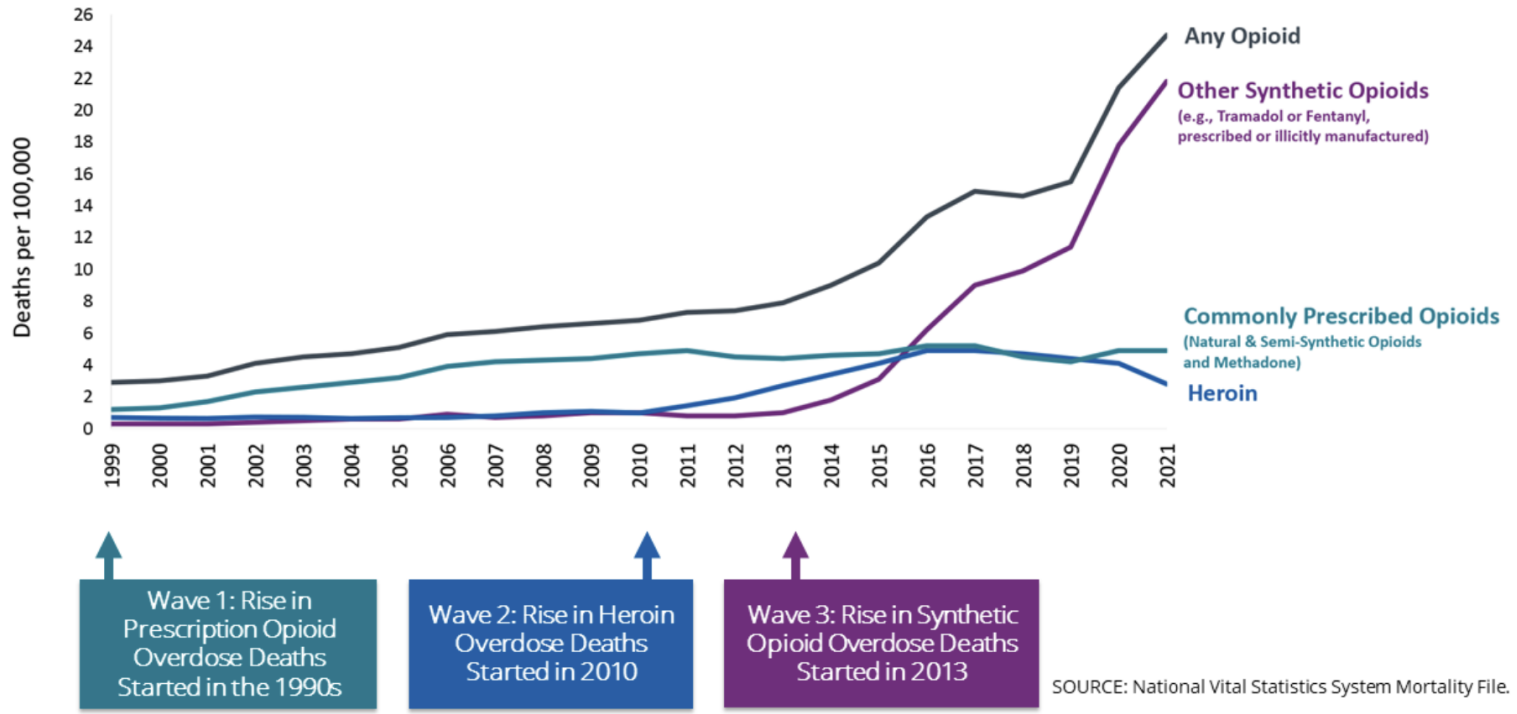
Three Waves of Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

From 1999-2021, nearly 645,000 people died from an overdose involving any opioid, including prescription and illicit opioids[1].

Fentanyl is a synthetic opioid that is up to 50 times stronger than heroin and 100 times stronger than morphine. It is approved by the FDA as an analgesic.

Fentanyl produces its pharmacological effects by activating mu-opioid receptors in the brain.

Source: Center for Disease Control & Prevention

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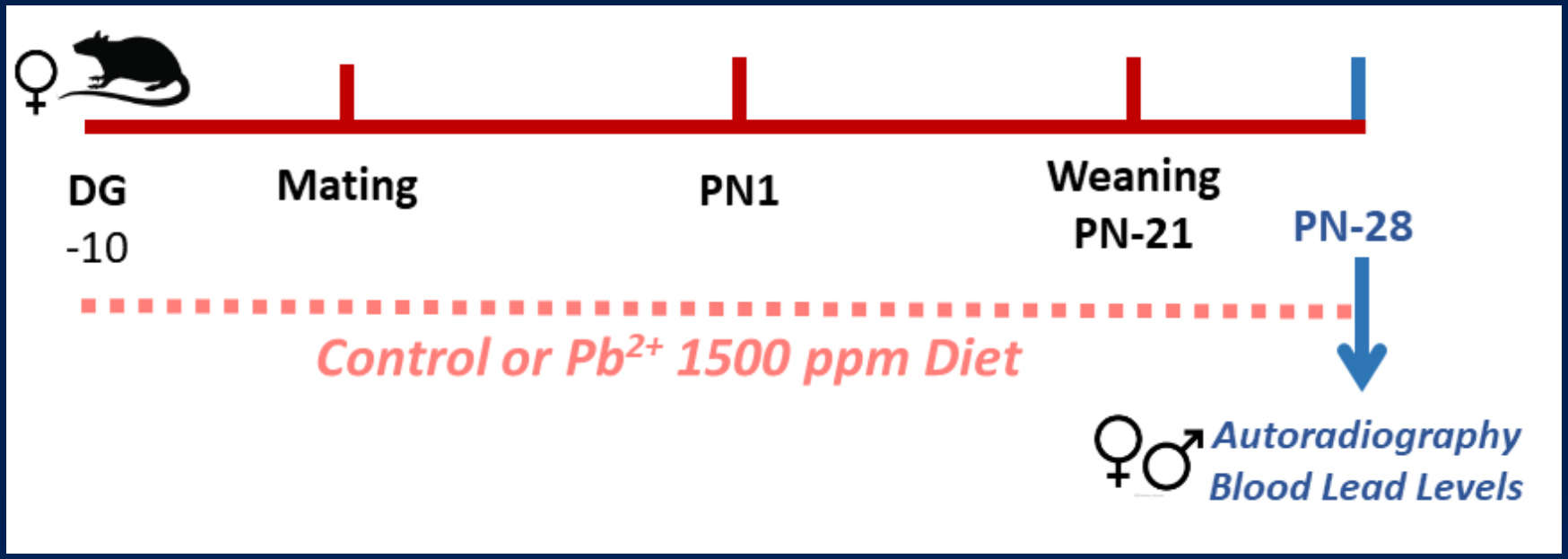

	Males PN-28	Females PN-28
	Blood Lead Levels (µg/dL)	
P value	≤0.0001	≤0.0001
Control	≤1.9 µg/dL *n=46*	≤1.9 µg/dL *n=40*
Pb^{2+}	19.93 ± 0.49 µg/dL *n=61*	24.49 ± 1.11 µg/dL *n=40*

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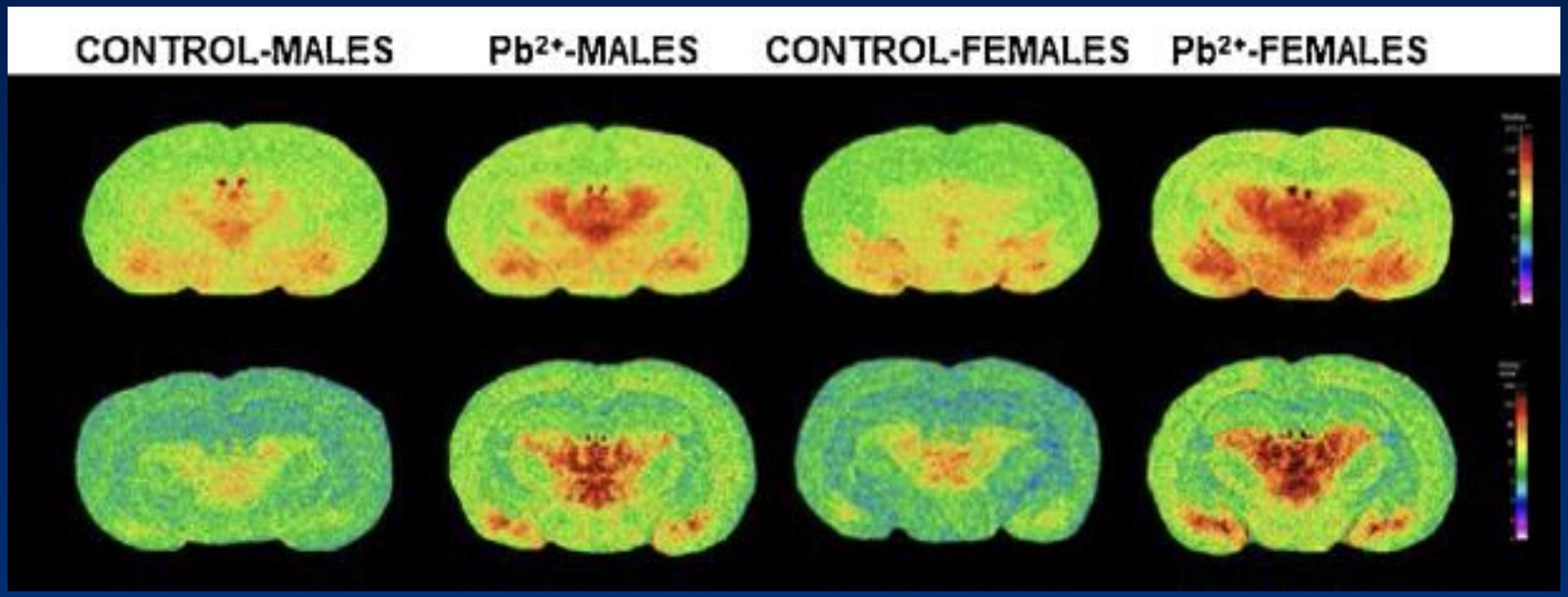
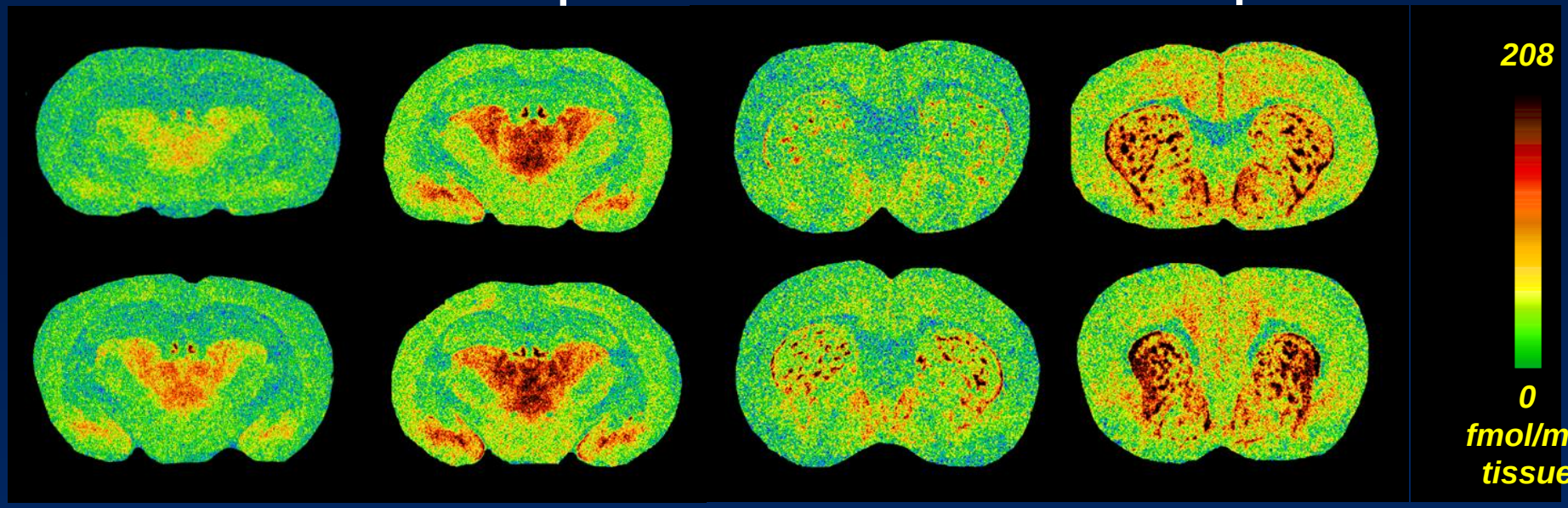
Chronic developmental lead exposure increases μ-opiate receptor levels in the adolescent rat brain

Damaris Albores-Garcia [a,b], Jennifer L. McGlothan [a,b], Zoran Bursac [c], Tomás R. Guilarte [a,b,*]



Spatial distribution of μ-Opioid Receptors in the rat brain using [^{3}H]-DAMGO autoradiography

CONTROL | Pb^{2+} exposed | CONTROL | Pb^{2+} exposed



-3.30 mm Bregma
(hypothalamus, thalamus, basolateral amygdala, stria medullaris of the thalamus)

1.30 mm Bregma
(striatum and nucleus accumbens)

Top Row= Males
Lower Row= Females

Males: Control n=8, Pb^{2+}-exposed n=7; Females: Control n=8, Pb^{2+}-exposed n=6.

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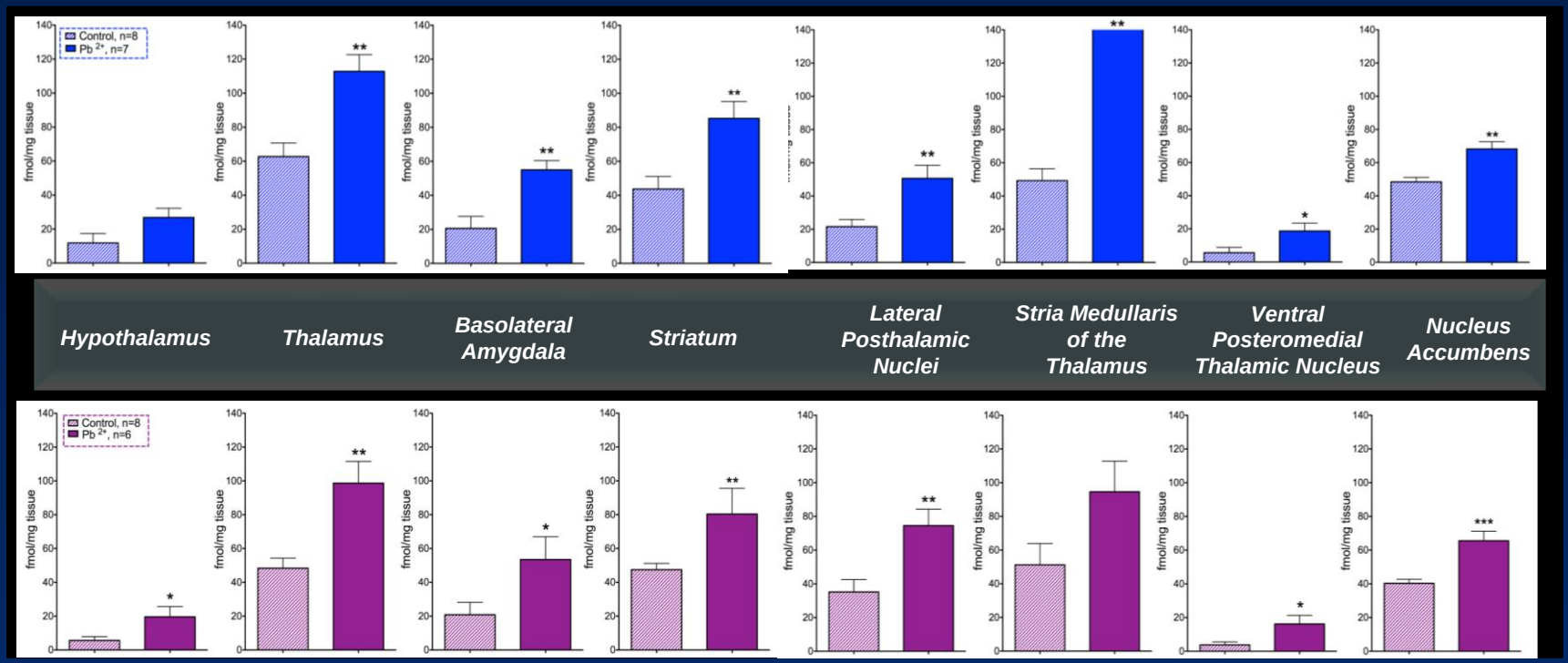
[^{3}H]-DAMGO specific binding to μ-opioid receptors in different brain regions of adolescent male and female rats exposed to Pb^{2+}

MALE



FEMALE

*p<0.05 ,**p<0.01 and ,***p<0.001 compared to Control

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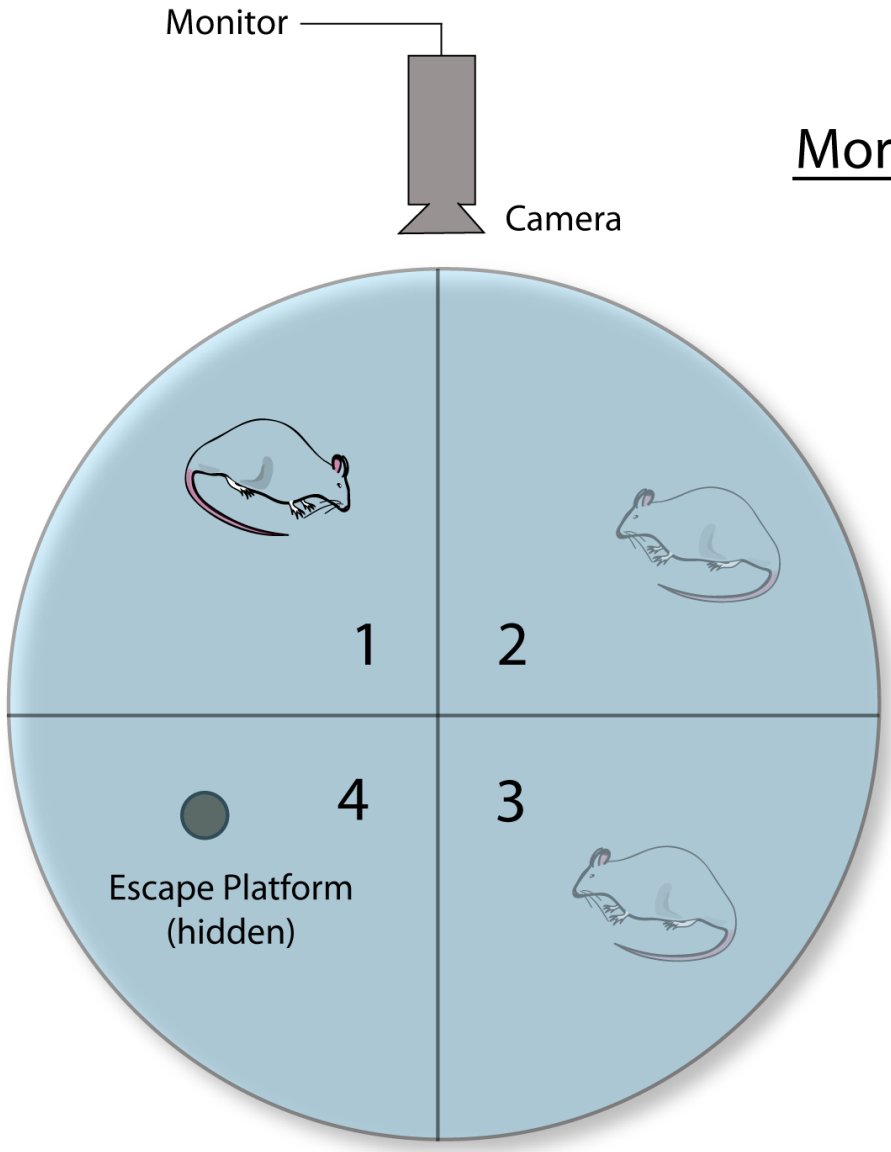
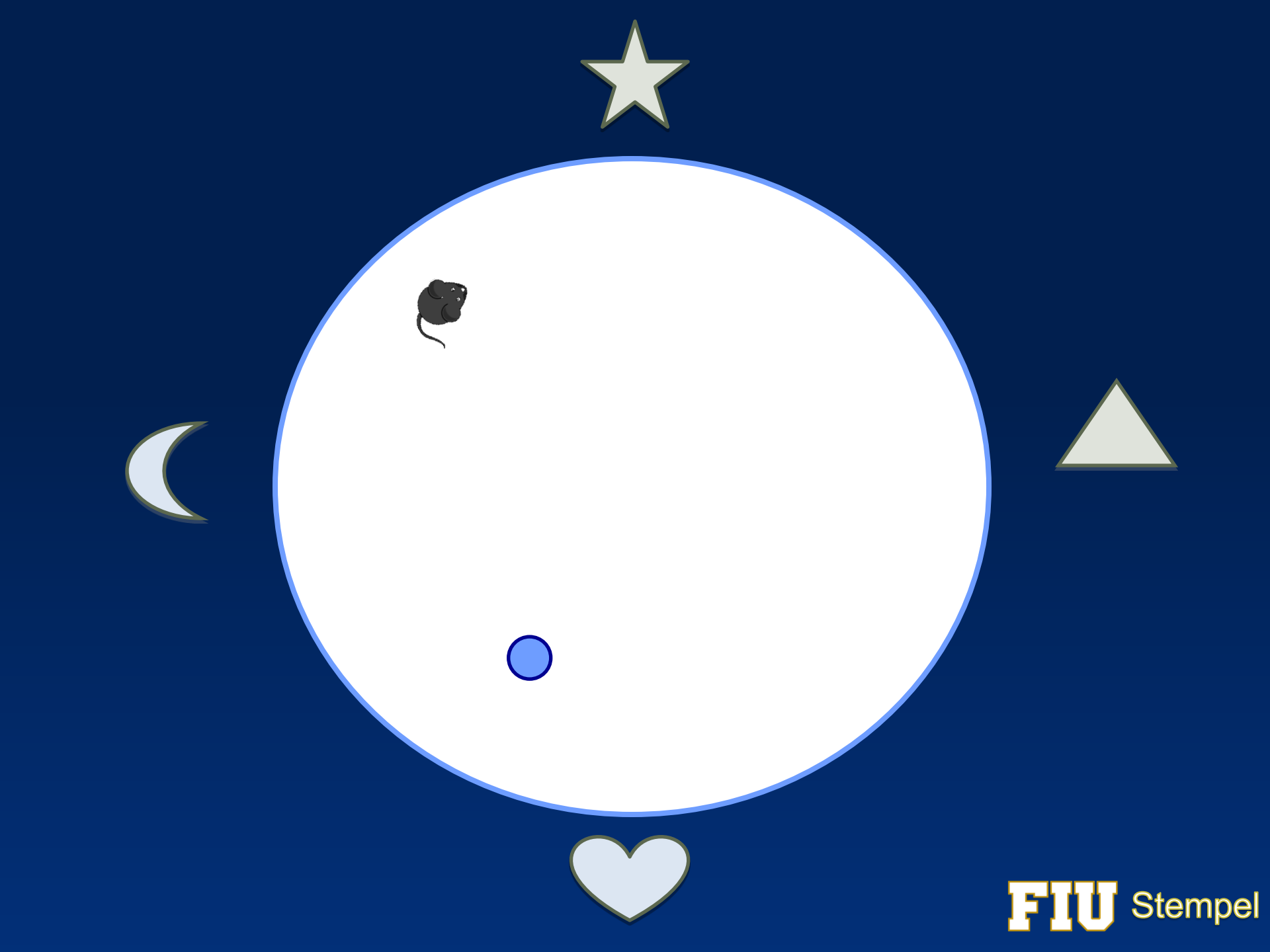
SPATIAL LEARNING TASK



Morris Water Maze

- Pool is filled with opaque water
- Rat placed in pool at 1,2 or 3 (random)
- Allowed to swim for 90 sec
- If goal is found in 90 sec, rat rests on platform for 20 sec
- If goal is not found, rat guided to platform and allowed to rest on platform for 20 sec
- ESCAPE LATENCY=Time to platform discovery



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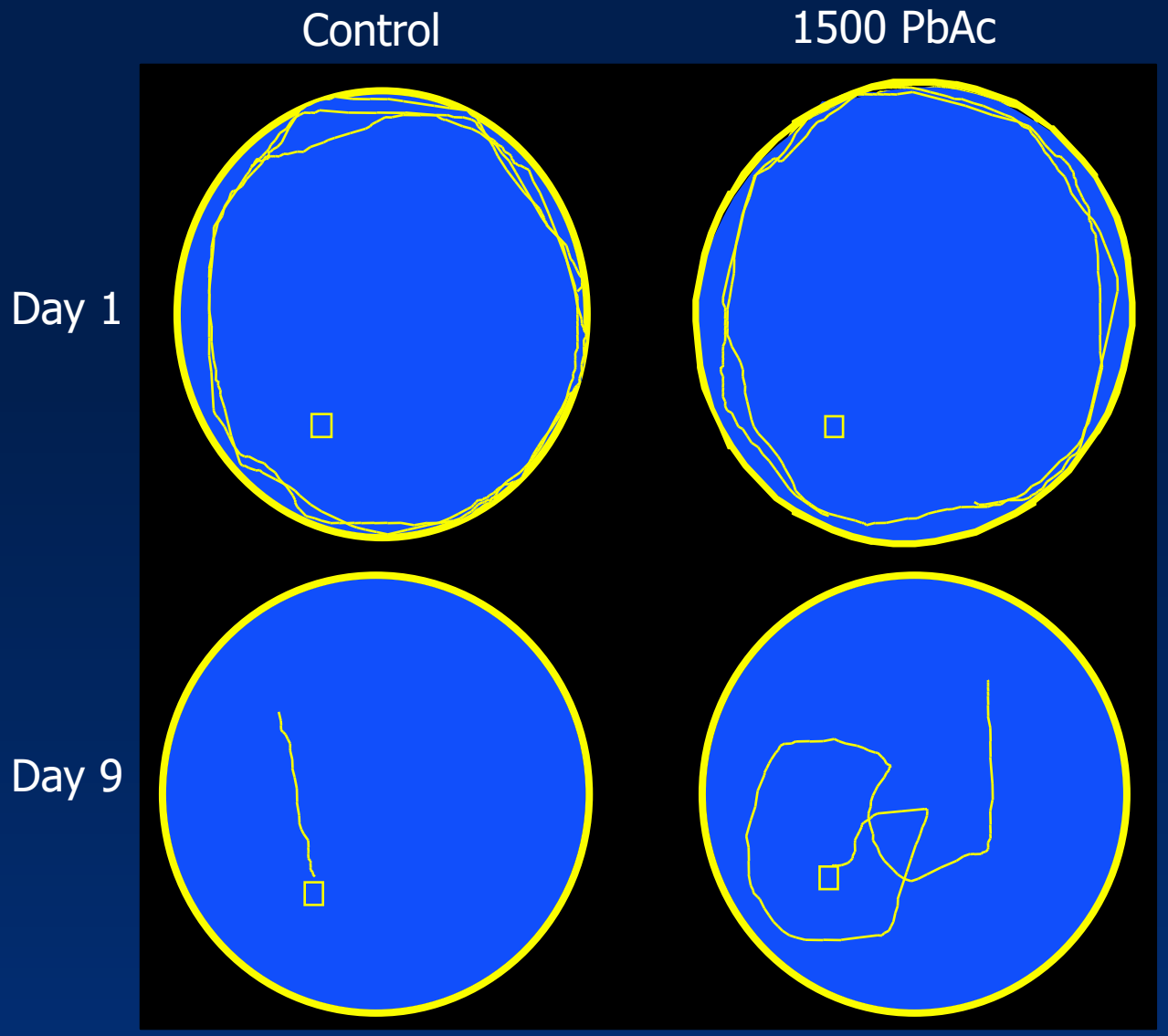
TRACKING OF SWIMMING PATH



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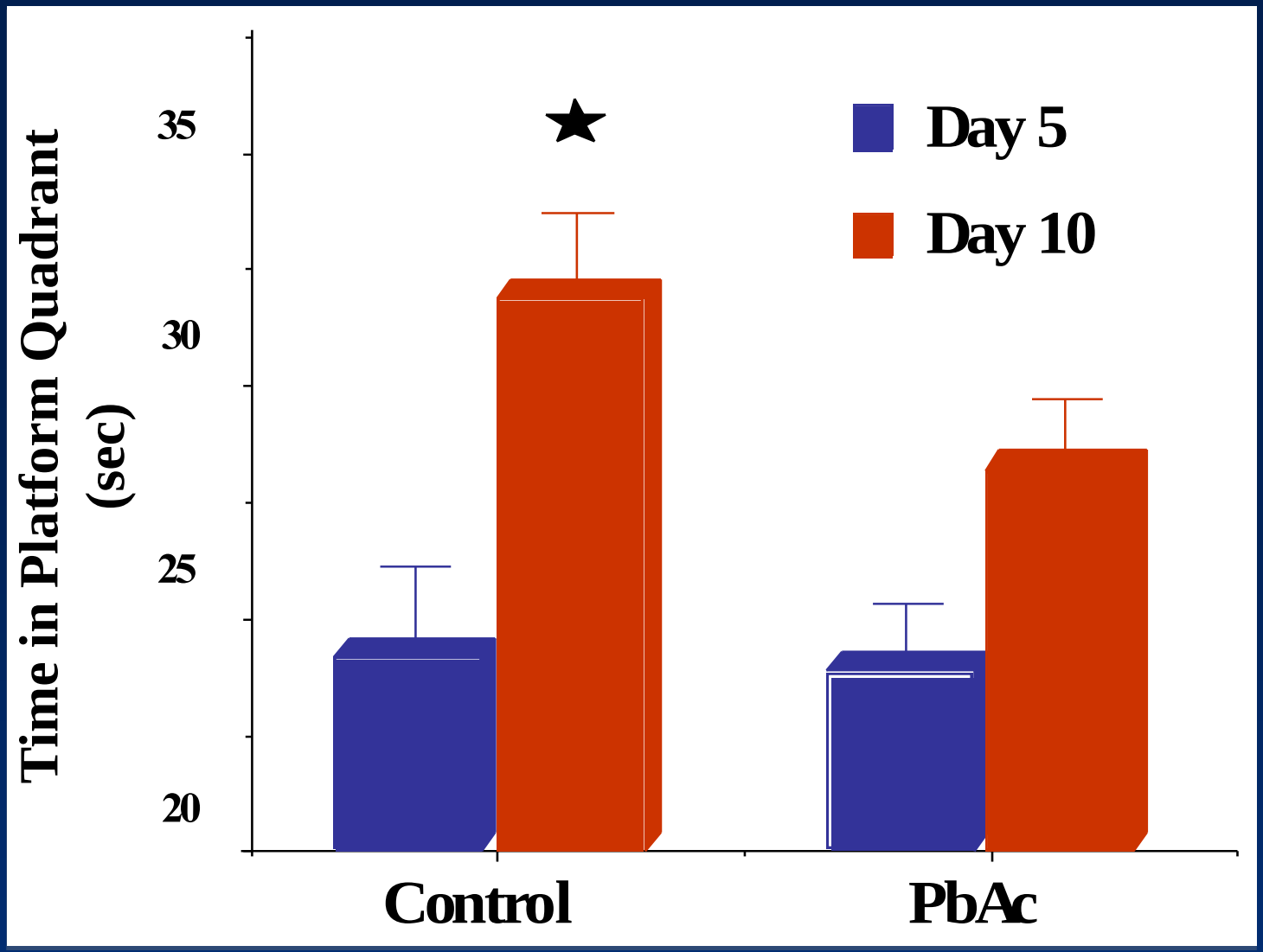
PROBE TEST-NO PLATFORM



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