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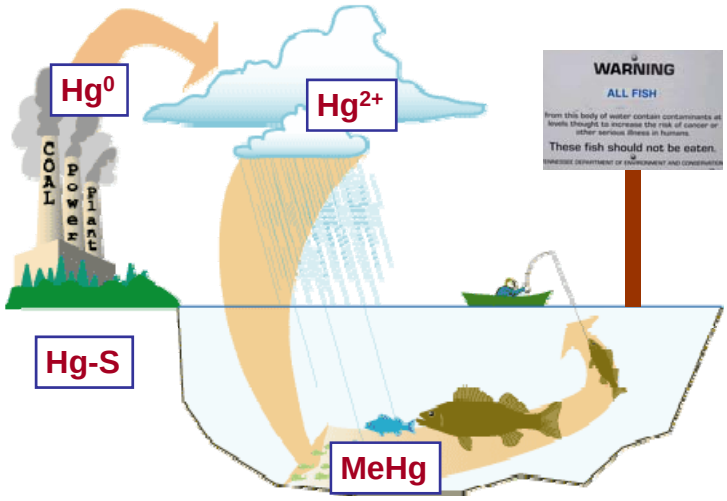
Assessing Methylmercury's Health Impact on Piscivorous Wildlife by Use of Neurochemical Biomarkers

NIL BASU

Department of Environmental Health Sciences
School of Public Health, University of Michigan
Ann Arbor, MI

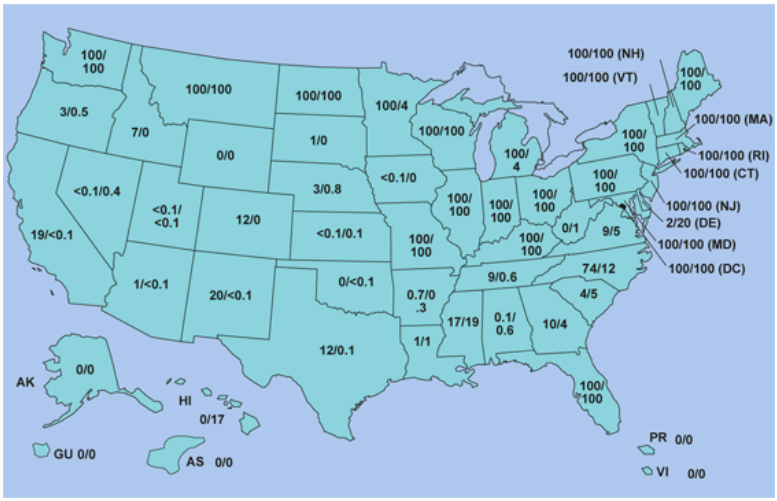
niladri@umich.edu
sitemaker.umich.edu/ecotoxicology.lab

A Simplified Mercury Cycle



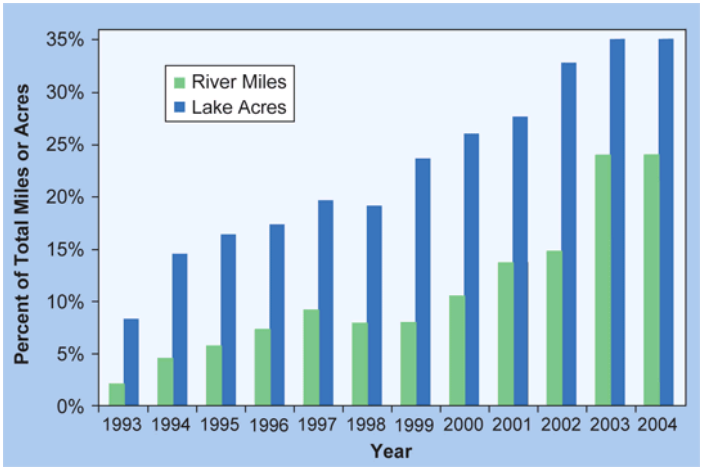
*** all steps are extremely complex!!!

2004: % of waterways under advisory

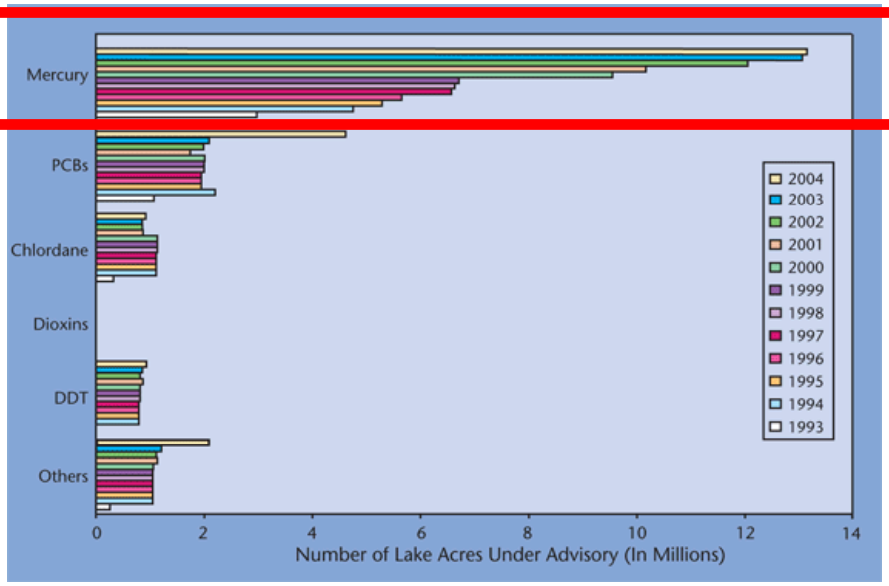


Percentage of Lake Acres/River Miles under Advisory in 2004
2004 National Listing of Fish Advisories (www.epa.gov/waterscience/fish)

1993-2004: over-time trends increasing

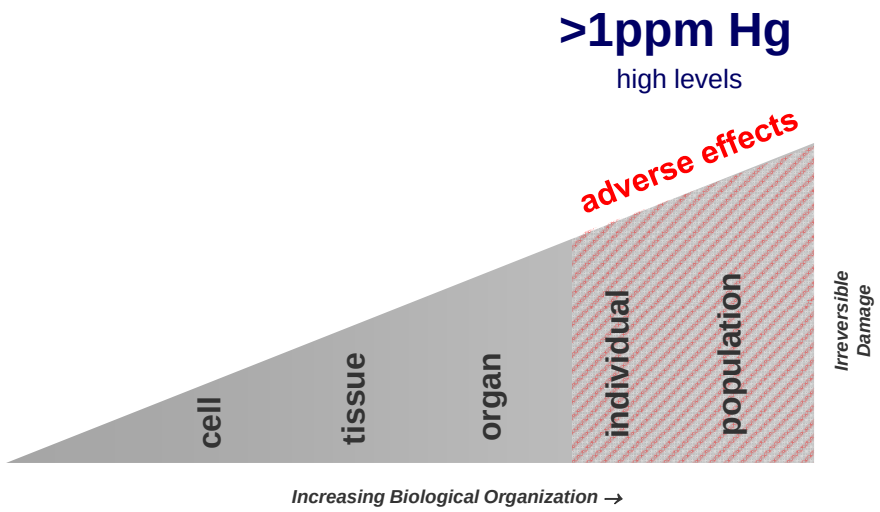


Percentage of River Miles and Lake Acres Under Advisory (1993-2004)
2004 National Listing of Fish Advisories (www.epa.gov/waterscience/fish)



Number of Lake Acres Under Advisory for Various Pollutants in 2004
2004 National Listing of Fish Advisories (www.epa.gov/waterscience/fish)

What we know

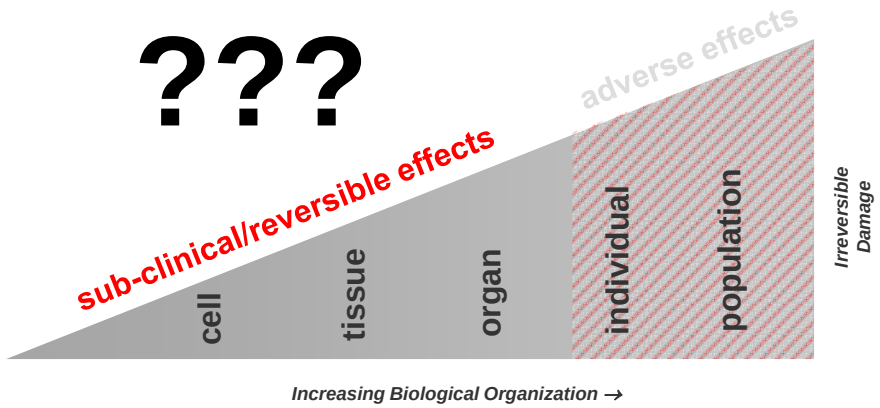


What we do NOT know

< 1ppm Hg
relevant levels

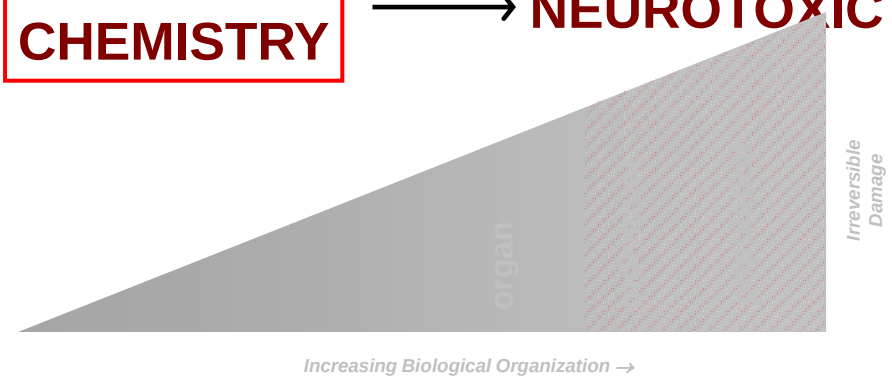
???

>1ppm Hg
high levels



MERCURY

BRAIN CHEMISTRY → **NEUROTOXIC**



Research Hypothesis

Neurochemical research can further our knowledge of the mechanisms and impacts of aquatic pollutants towards the health of humans, wildlife, and ecosystems.

Mercury → BRAIN CHEMISTRY → Neurotoxic

↓

objective/quantitative method to assess early/subtle effects

model pathway – **Cholinergic System**

- **well-studied neurochemical pathway**
- **sensitive to Hg (*in vitro* and *in vivo*)**

Cholinergic disorders		Mercury poisoning
☑	salivation	☑
☑	ataxia	☑
☑	loss of vision	☑
Alzheimer's	relevant diseases	Minamata

Wess et al., 2005; Kobayashi, 1981

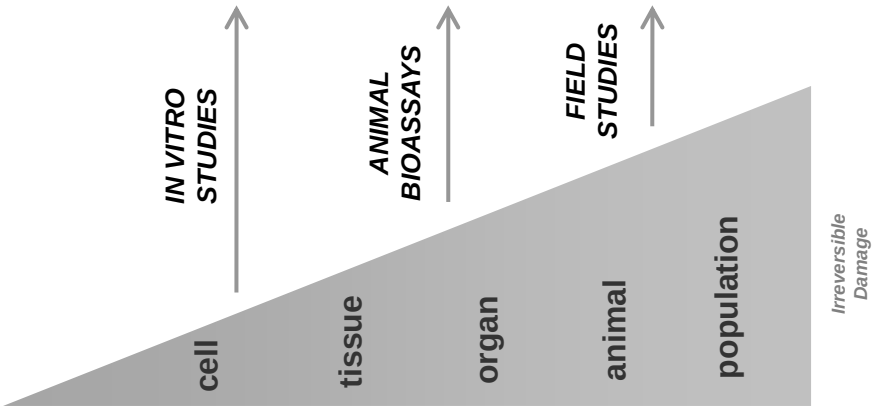
model organism – **Mink**

- high-trophic, fish-eating mammal common across North America & Europe
- Hg-related effects (lesions, behavior) similar to other wildlife and humans
- declines in wild mink populations associated with Hg pollution
- studied in nature and the laboratory

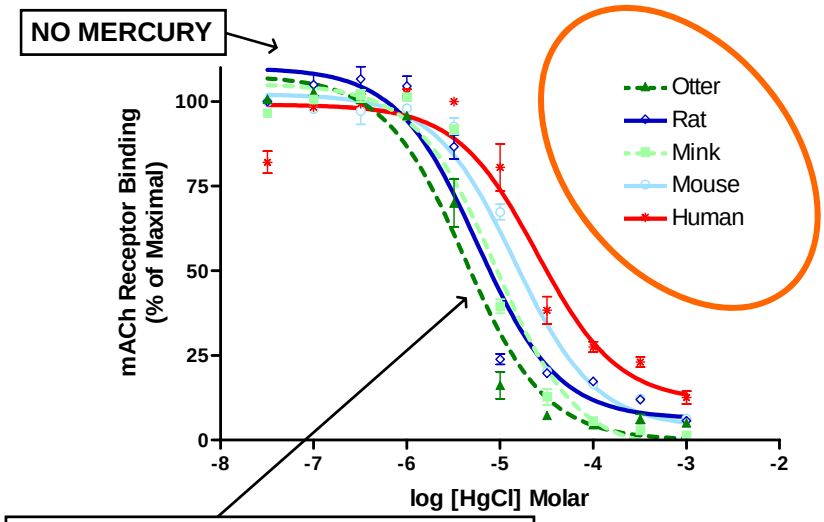
Basu et al., 2007; Aulerich et al., 1999

Integrative Approach

Does mercury affect the cholinergic receptor in mink?

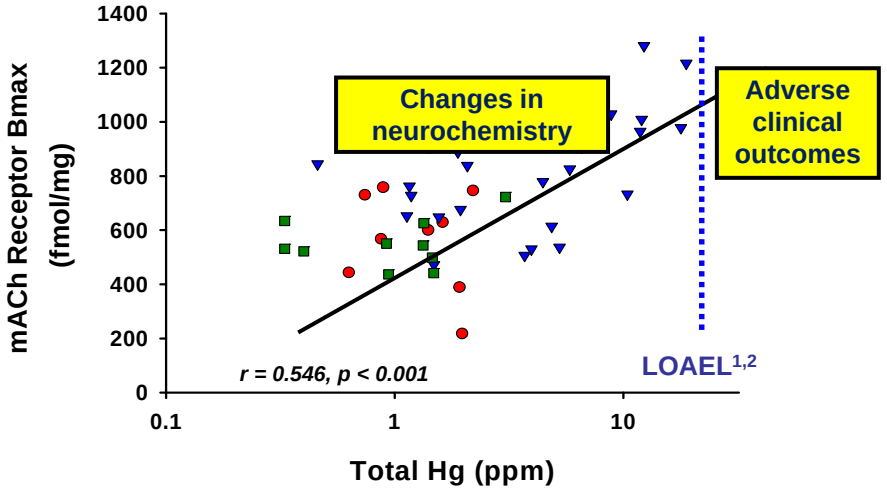


In vitro study – does Hg inhibit mAChR?



Toxicol Appl Pharmacol 205: 71-76

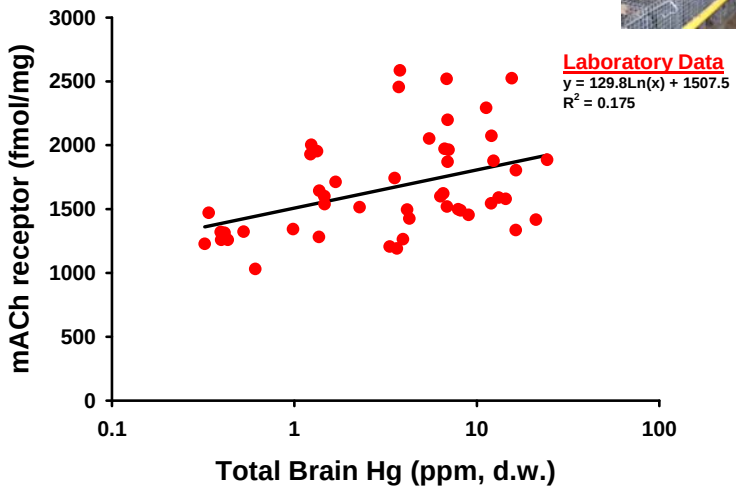
Field study –Hg α mAChR?



Environ Toxicol Chem 24: 1444-1450

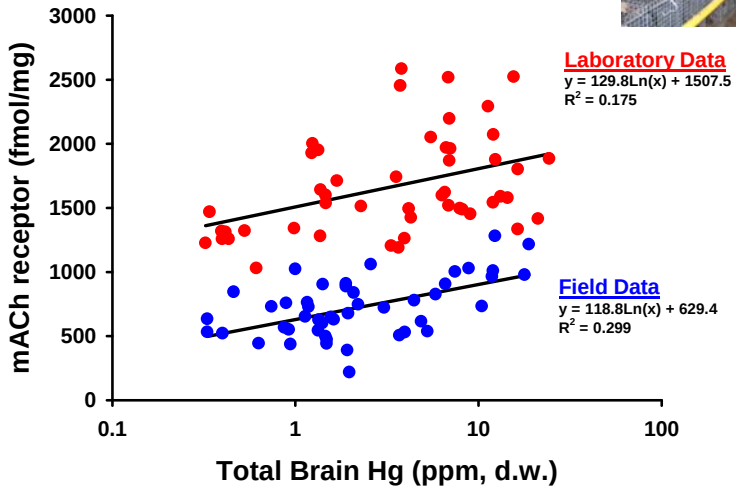
[1] Wren et al. 1987
[2] Wobesor et al. 1976

Lab study – corroboration?



Toxicological Sciences 91: 202-209

Lab study – corroboration?



SIMILAR SLOPE-RESPONSE RELATIONSHIPS

Toxicological Sciences 91: 202-209

Mid-Talk Summary

Mercury disrupts the cholinergic receptor in mink

- ecologically relevant levels disrupt brain neurochemistry
- changes are potentially of physiological and ecological significance
- continuum of effects is established

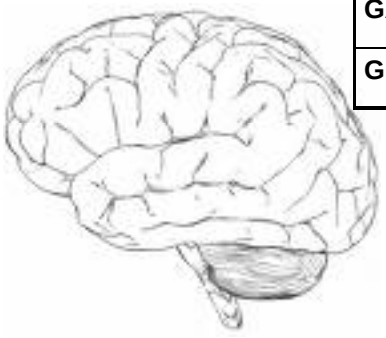
WHAT ABOUT OTHER SIGNALING PATHWAYS?

WHAT ABOUT OTHER FISH-EATING WILDLIFE?

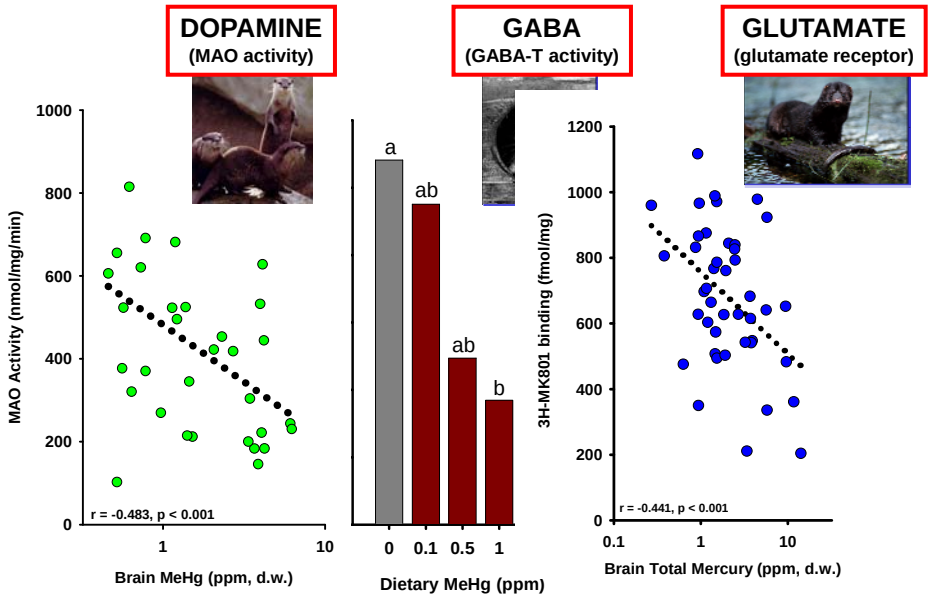
Comparative Approach

Multiple neurochemical pathways affected by mercury in rodents

Cholinergic	Cognitive/sensory
Dopamine	Motor deficits
GABA	Inhibitory function
Glutamate	Excitatory function



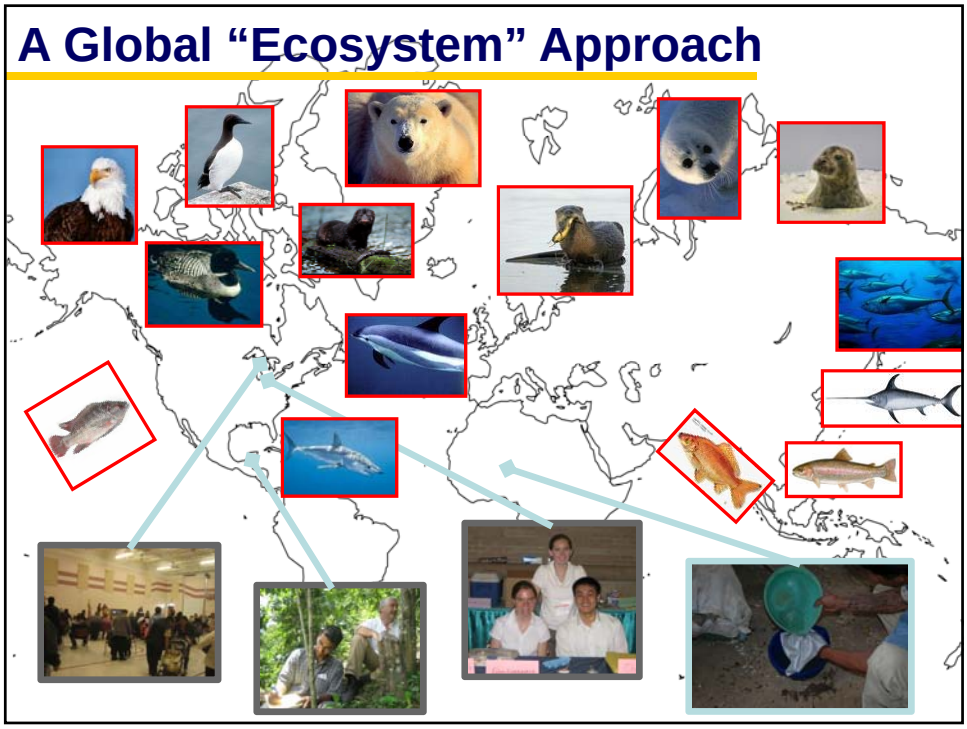
Changes in other pathways observed



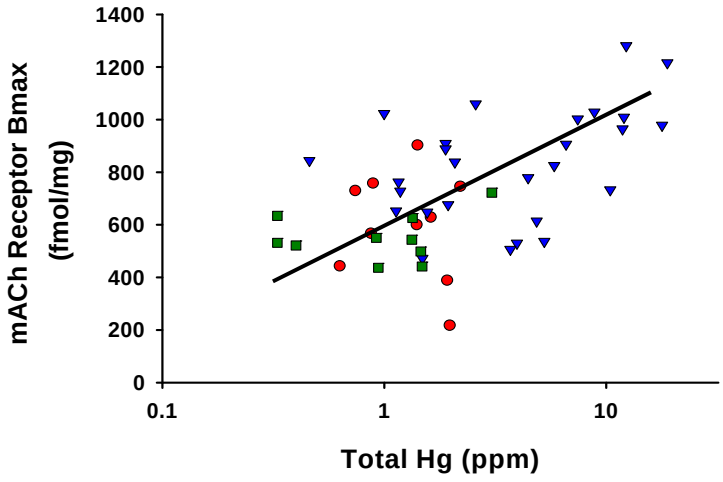
"In ecoepidemiology, the occurrence of an association in more than one species and species population is very strong evidence for causation."

Glen Fox. 1991. J Toxicol Environ Health 33: 359-373

A Global "Ecosystem" Approach

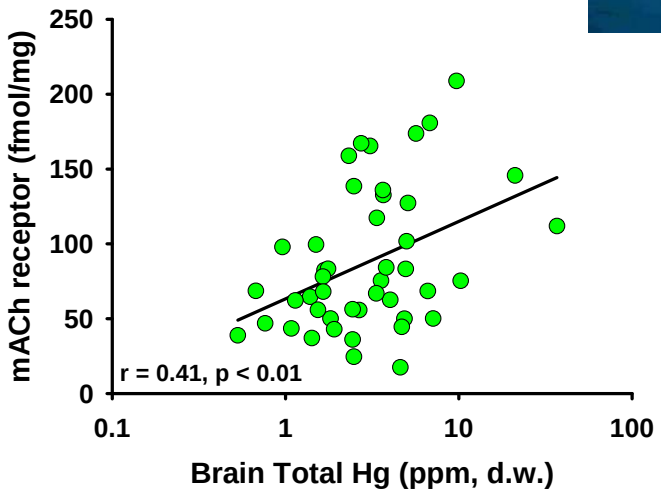


Hg & mAChR: MINK



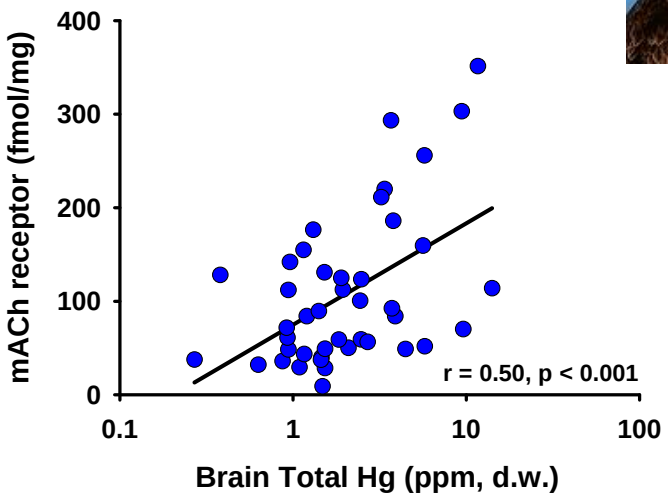
Environ Toxicol Chem 24: 1444-1450

Hg & mAChR: COMMON LOON



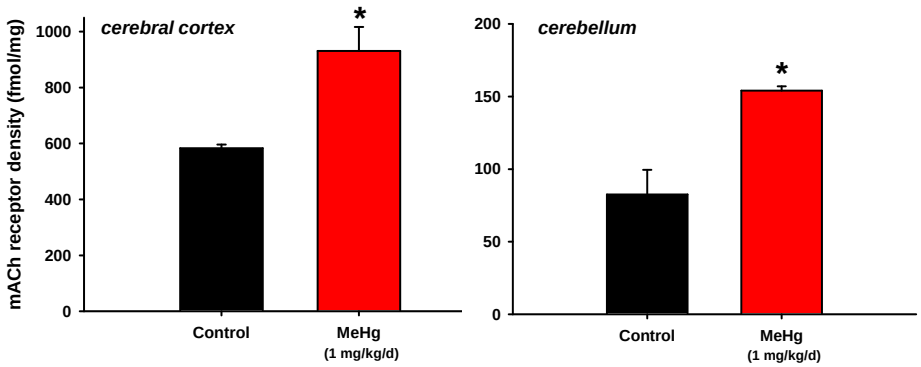
Ecotoxicology 17: 93-101

Hg & mAChR: BALD EAGLE



Ecotoxicology 17: 93-101

Hg & mAChR: LAB RAT



Coccini et al., 2006. Neurotoxicology. 27: 468-477

Quick Summary

Mercury disrupts cholinergic receptor in mink

↓

Mercury disrupts the brain chemistry in mink

↓

Mercury disrupts the brain chemistry in several fish-eating wildlife, lab animals (and humans?)

↓

“SO WHAT”???

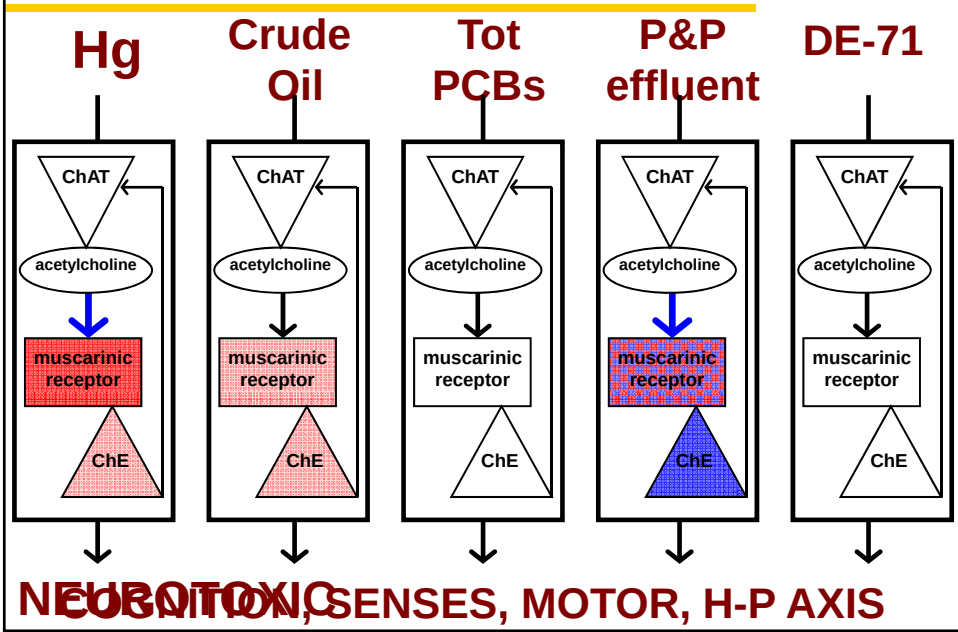
Implications to **Policy and Assessment #1**

continuum of effects established →

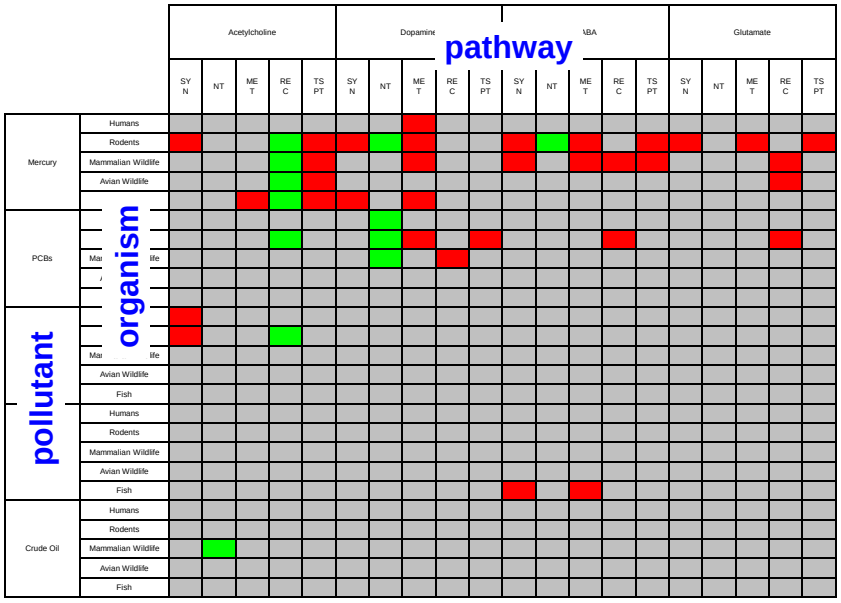
Fish MeHg	Brain Hg	Fur Hg	Outcome
5	20	150	Death
2	8	60	Tissue lesions, reproductive impairment, behavioural changes, death
1	4	30	
0.5	2	15	Biochemical (*sub-clinical?*)
0.1	0.5	3	Biochemical (*adaptive?*)

- **neurochemical disruption at relevant levels**
- **changes of physiological/ecological concern**

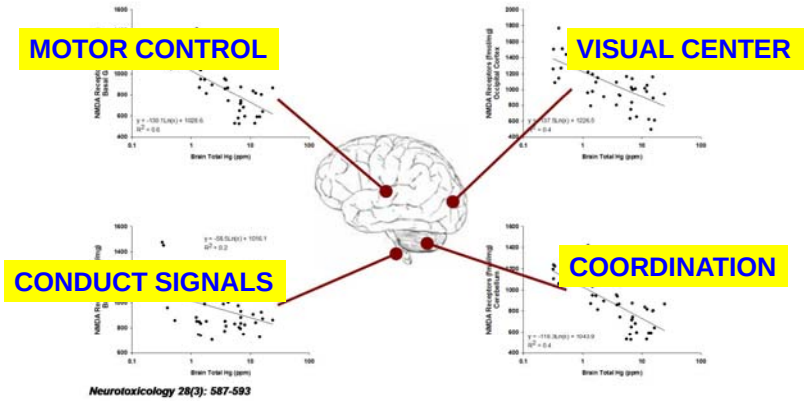
Implications to **Policy and Assessment #2**



A Neurochemical Fingerprint?



Implications to **Policy and Assessment #3**



- **brain regions have specific functions**
- **semi-quantitative, objective measure?**

Thanks!
Questions?

NIL BASU, PhD

Assistant Professor
Department of Environmental Health Sciences
School of Public Health, University of Michigan
Ann Arbor, MI

niladri@umich.edu
sitemaker.umich.edu/ecotoxicology.lab