Fluoride & IQ Studies: The Context

Michael Connett, Esq

Fluoride Action Network

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Dr. Mullenix's Prediction

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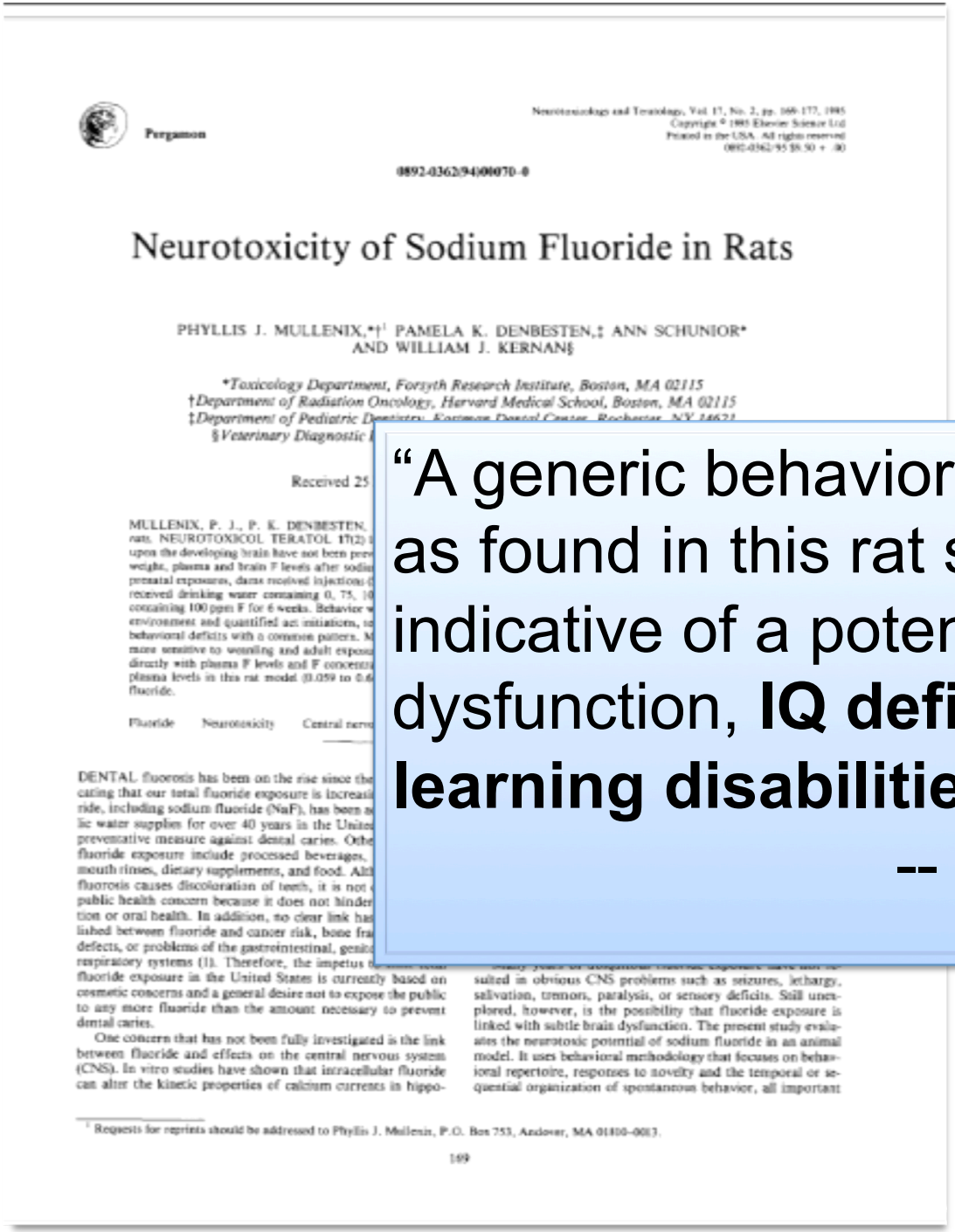

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Neurotoxicity of Sodium Fluoride in Rats

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Received 25

MULLENIX, P. J., P. K. DENBESTEN, rats. NEUROTOXICOL TERATOL 17(2) upon the developing brain have not been prev weight, plasma and brain F levels after sodiu prenatal exposures, dams received injections received drinking water containing 0, 75, containing 100 ppm F for 6 weeks. Behavior environment and quantified act initiations, behavioral deficits with a common pattern. M more sensitive to weanling and adult expos directly with plasma F levels and F concentr plasma levels in this rat model (0.059 to 0.6 fluoride.

Fluoride Neurotoxicity Central nerv

DENTAL fluorosis has been on the rise since the caring that our total fluoride exposure is increasi ride, including sodium fluoride (NaF), has been lic water supplies for over 40 years in the Unite preventative measure against dental caries. Othe fluoride exposure include processed beverages, mouth rinses, dietary supplements, and food. Alt fluorosis causes discoloration of teeth, it is not public health concern because it does not hinder tion or oral health. In addition, no clear link ha lished between fluoride and cancer risk, bone fra defects, or problems of the gastrointestinal, geni respiratory systems (1). Therefore, the impetus fluoride exposure in the United States is currently based on cosmetic concerns and a general desire not to expose the public to any more fluoride than the amount necessary to prevent dental caries.

One concern that has not been fully investigated is the link between fluoride and effects on the central nervous system (CNS). In vitro studies have shown that intracellular fluoride can alter the kinetic properties of calcium currents in hippo- sulted in obvious CNS problems such as seizures, lethargy, salivation, tremors, paralysis, or sensory deficits. Still unexplored, however, is the possibility that fluoride exposure is linked with subtle brain dysfunction. The present study evaluates the neurotoxic potential of sodium fluoride in an animal model. It uses behavioral methodology that focuses on behavioral repertoire, responses to novelty and the temporal or sequential organization of spontaneous behavior, all important

[1] Requests for reprints should be addressed to Phyllis J. Mullenix, P.O. Box 753, Andover, MA 01810-0013.

"A generic behavioral pattern disruption as found in this rat study can be indicative of a potential for motor dysfunction, **IQ deficits** and/or **learning disabilities** in humans."

-- Mullenix (1995)

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What Mullenix Did Not Know…

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…the F/IQ Studies had Already Begun

1989-1995:
12 Studies

Ren (1989)
Hu (1989)
Qin (1990)
Sun (1991)
Chen (1991)
Guo (1991)
Lin (1991)
An (1992)
Yang (1994)
Li (1994)
Xu (1994)
Duan (1995)

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And the IQ studies kept on coming

Review

Developmental Fluoride Neurotoxicity: A Systematic Review and Meta-Analysis

Anna L. Choi,[1] Guifan Sun,[2] Ying Zhang,[3] and Philippe Grandjean[1,4]

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BACKGROUND: Although fluoride may cause neurotoxicity in animal models and acute fluoride poisoning causes neurotoxicity in adults, very little is known of its effects on children's neurodevelopment.

OBJECTIVE: We performed a systematic review and meta-analysis of published studies to investigate the effects of increased fluoride exposure and delayed neurobehavioral development.

METHODS: We searched the MEDLINE, EMBASE, Water Resources Abstracts, and TOXNET databases through 2011 for eligible studies. We also searched the China National Knowledge Infrastructure (CNKI) database, because many studies on fluoride neurotoxicity have been published in Chinese journals only. In total, we identified 27 eligible epidemiological studies with high and reference exposures, end points of IQ scores, or related cognitive function measures with means and variances for the two exposure groups. Using random-effects models, we estimated the standardized mean difference between exposed and reference groups across all studies. We conducted sensitivity analyses restricted to studies using the same outcome assessment and having drinking-water fluoride as the only exposure. We performed the Cochran test for heterogeneity between studies, Begg's funnel plot, and Egger test to assess publication bias, and conducted meta-regressions to explore sources of variation in mean differences among the studies.

Registry 2003). Fluoride exposure to the developing brain, which is much more susceptible to injury caused by toxicants than is the mature brain, may possibly lead to permanent damage (Grandjean and Landrigan 2006). In response to the recommendation of the NRC (2006), the U.S. Department of Health and Human Services (DHHS) and the U.S. EPA recently announced that DHHS is proposing to change the recommended level of fluoride in drinking water to 0.7 mg/L from the currently recommended range of 0.7–1.2 mg/L, and the U.S. EPA is reviewing the maximum amount of fluoride allowed in drinking water, which currently is set at 4.0 mg/L (U.S. EPA 2011).

To summarize the available literature,

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The Current Tally

- **48** = # of human studies on fluoride & IQ
- **41** = # of studies have found reduced IQ
- **17** = # of studies with reduced IQ at "safe" levels (<4 ppm)

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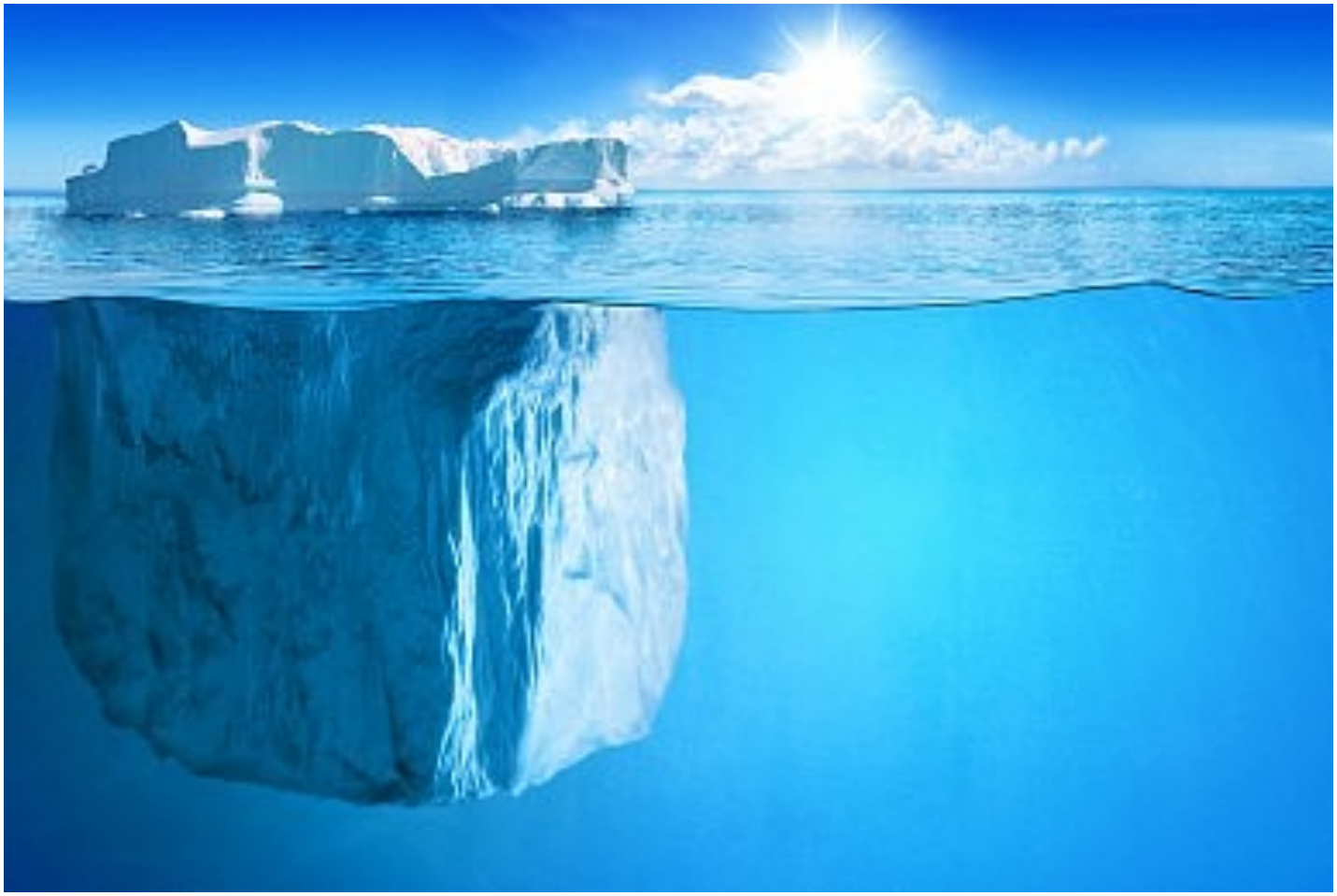
IQ Studies = Tip of the Iceberg



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Animal Studies

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Over 100 Animal Studies have found Fluoride Damages the Brain

- Damage to hippocampus
- Increase in oxidative stress
- Neuronal degeneration
- Damage to nicotinic receptors
- Deceased brain glucose utilization
- Inhibitions of cholinesterase

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30 Animal Studies Have Found Fluoride Impairs Learning/Memory

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Learning/Memory Studies

- **30 of 32 studies** have found an effect
- Different types of tests:
  - Y maze
  - T maze
  - Morris water maze
  - Novel object recognition test
  - Open field test
- **Low Doses:** 5 ppm (Lu 2014)

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Learning/Memory:
Published Research from 2014

"We found that **NaF treatment impaired learning and memory** in these rats."

SOURCE: Jiang C, et al. (2014). Low Glucose Utilization and Neurodegenerative Changes Caused by Sodium Fluoride Exposure in Rat's Developmental Brain. Neuromolecular Medicine 16(1):94-105.

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Learning/Memory:
Published Research from 2014

"These data indicate that fluoride and arsenic, either alone or combined, can **decrease learning and memory ability** in rats."

SOURCE: Jiang S, et al. (2014). Fluoride and Arsenic Exposure Impairs Learning and Memory and Decreases mGluR5 Expression in the Hippocampus and Cortex in Rats. PLoS One. 2014 Apr 23;9(4):e96041.

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Learning/Memory:
Published Research from 2014

"Collectively, our data indicate that **developmental exposure to NaF induces cognitive deficits** and anxiety-depression-like behaviors in mice."

SOURCE: Liu F, et al. (2014). Fluoride exposure during development affects both cognition and emotion in mice. Physiology & Behavior 124:1-7.

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Learning/Memory:
Published Research from 2014

"Taken together, these results indicated that long-term fluoride administration can enhance the excitement of male mice [and] **impair recognition memory**…."

SOURCE: Han H, et al. (2014). Effects of chronic fluoride exposure on object recognition memory and mRNA expression of SNARE complex in hippocampus of male mice. Biological Trace Element Research [Epub ahead of print]

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Human (non-IQ) Studies

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Human (non-IQ) Studies

- Fetal Brain Studies
  - *Yu (1996); Dong (1989); Du (1992); Han (1989)*
- Neonatal Behavioral Neurological Assessment (NBNA)
  - *Li (2004)*
- Rey-Osterrieth Complex Figure Test (ROCF)
  - *Rocha Amador (2009)*
- Neurobehavioral Core Test Battery (NCTB)
  - *Yazdi (2011) and Guo (2001)*

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Fetal Brain Studies

Fetal Brain Studies
Du (1992)

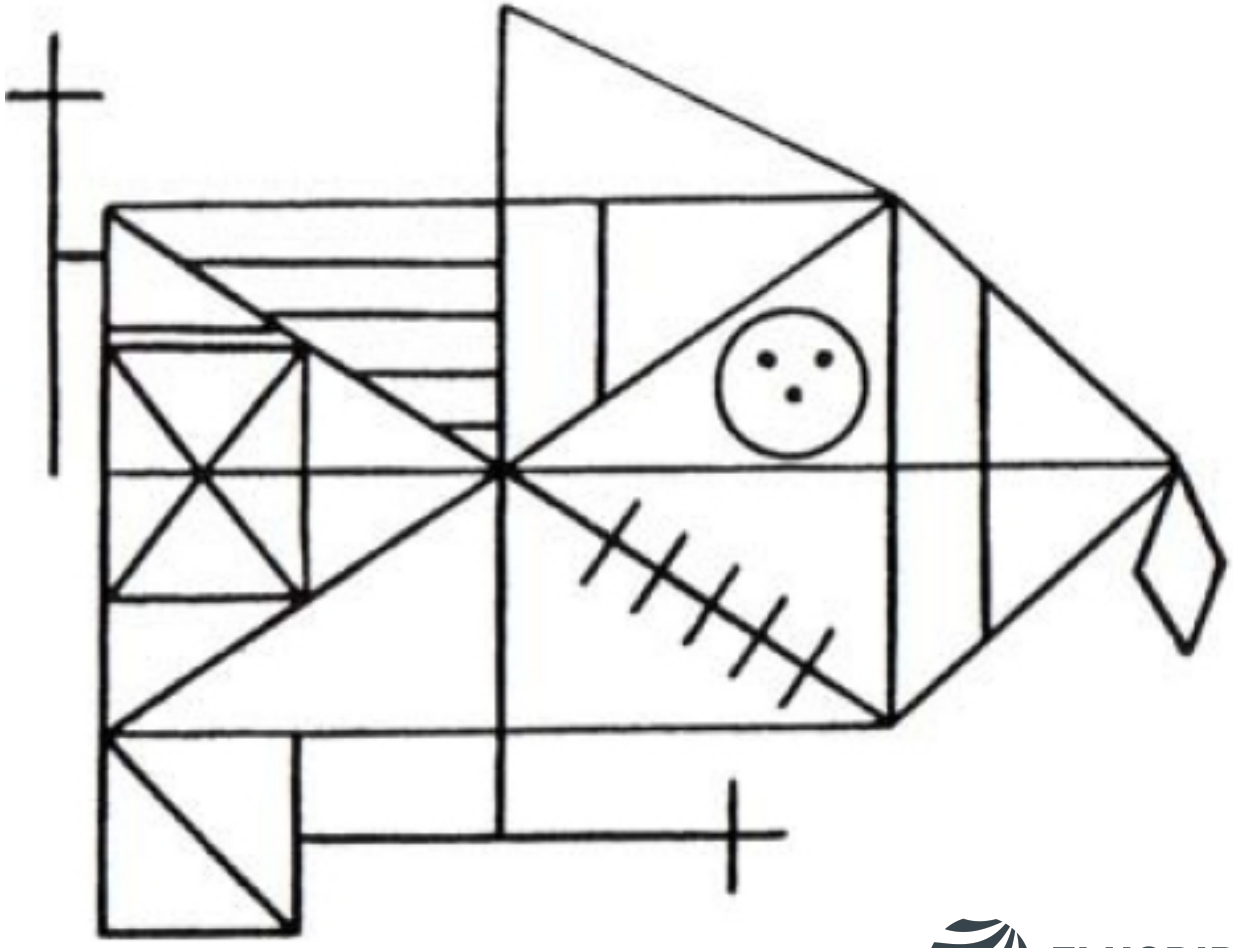
"In summary, the passage of fluorine through the placenta of mothers with chronic fluorosis and its accumulation within the brain of the fetus impacts the developing central nervous system and stunts neuron development."

SOURCE: Du L. (1992). The effect of fluorine on the developing human brain. Chinese Journal of Pathology 21(4):218-20.

Neonatal Behavioral Neurological Assessment

- "The present observations indicate that fluoride, as a toxic material to nerve development **can have an adverse impact on the neurobehavioral development of neonates** and can cause abnormal changes of neurobehavioral capability during the neonate period."
- SOURCE: Li J, et al. (2004). Effects of high fluoride level on neonatal neurobehavioral development. Chinese Journal of Endemiology 23(5):463-65.

Rey-Osterrieth Complex Figure Test



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Rey Osterrieth Complex Figure Test
Rocha Amador (2009)

- High quality study
  - Controlled for key variables (e.g., education, nutritional status, exposure to other contaminants)
  - Individual-based fluoride exposures (urine F levels)
- Findings:
  - "Approximately **9 out of 10 children** were unable to copy the ROCF as expected for their age."
  - "For Immediate Recall, almost **6 out of 10 children** were unable to draw the figure as expected for their age."

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Neurobehavioral Core Test Battery (NCTB)

- **Background:**
  - Developed in 1980s by the World Health Organization and National Institute for Occupational Safety and Health
  - The key test for identifying neurotoxins in the workplace
  - Tests ability to learn, reaction time, memory, and coordination

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Aluminum workers in Iran *(Yazdi 2011)*

- **Conclusion:**
  - "In summary, **this study found that neurobehavioral testing can detect impairments in psychomotor performance from occupational F exposure."**

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Aluminum workers in China *(Guo 2001)*

- **Conclusion:**
  - "By relating these test results to fluoride exposure, our study **demonstrated various effects of occupational fluoride exposure on the central nervous system,** thereby providing early earning indicators that can be used to protect the health of workers who have occupational contact with fluoride."

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Summary

- Fluoride & IQ studies are tip of iceberg for studies on fluoride's neurotoxicity
- Animal Studies:
  - Over 100 studies show F damages brain
  - 30 studies show F impairs learning/memory
- Human Studies:
  - F can damage fetal brain
  - F affects behavior of neonates
  - F affects performance on Rey-Osterrieth Complex Figure Test
  - F damages central nervous system of workers

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