Behavioral Effects of Water Toxicity:

An Unexpected Problem in Experimental Methodology

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Abstract

Are the effects of environmental toxins on brain chemistry and behavior relevant to experimental methods in evolutionary psychology? The question is raised by a study by Crabbe, Wahlsten and Dudek, who conducted six experiments with eight mouse strains at three laboratories (Portland, Oregon; Albany, New York, and Edmonton, Alberta). Results were influenced by unanticipated local factors. Reanalysis of this study suggests that local drinking water, used in all sites, may have contributed to a tendency for lower behavioral inhibition in Edmonton, where public water supplies are treated with hydrofluosilicic acid. Although this chemical and sodium silicofluoride are widely used in the U.S., neither of the silicofluorides is added to the water in Portland or Albany. Silicofluorides are acetylcholinesterase inhibitors whose use in water treatment has been associated with enhanced uptake of environmental lead as well as increased disinhibition of behaviors likely to be influenced by lead neurotoxicity. Granted prudence is needed when interpreting correlational findings, two methodological conclusions follow: first, important behavioral experiments may need replication using more than one genotype in different sites; second, even an apparently innocuous variable such as tap water may be a source of behavioral neurotoxicity (with unexpected effects on replicating experimental outcomes).

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Introduction: Can Toxins Undermine Behavioral Research?

Environmental toxins often interact with genetic variation to produce distinct outcomes in health and behavior. For example, complex relationships between gene expression and toxins – recently called "toxicogenomics" (Olden, Guthrie & Newton, 2001; Gershon, 2002) -- might account for otherwise puzzling inconsistencies in the health effects of a given exposure to methylmercury (Castoldi, Coccini, Ceccatelli, Manzo, 2001). In laboratory studies of behavior, analysis of similar interactions between environmental toxins and genes could call in question some traditional methods and findings.

To illustrate the importance of "toxicogenomics," it is useful to reconsider the findings in a research paper on "Genetics of Mouse Behavior: Interactions with Laboratory Environment" (Crabbe, Wahlsten, & Dudek, 1999). This study compared responses of eight mouse strains in six experimental tests at three laboratories. Unexpectedly, in four of these experiments there were significant differences in responses at one of the three locations. Although the authors had difficulty identifying the environmental factors involved, there is reason to suggest that chemicals in the drinking water may have been responsible. Given the possibility that such a factor could undermine the reliability of many research studies in health as well as behavior, this hypothesis deserves careful attention.

I. The Study of "Genetics of Mouse Behavior"

The authors of "Genetics of Mouse Behavior" carefully designed experiments to explore whether "subtle environmental differences among labs" could lead to "discrepancies in the outcomes reported by different labs testing the same genotypes for ostensibly the same behaviors." (Ibid., p. 1670). To reanalyze the interactions between

genotype and laboratory environment, the original methodological description of this study needs to be cited in detail:

> "We addressed this problem by testing six mouse behaviors simultaneously in three laboratories (Albany, New York; Edmonton, Alberta, Canada; and Portland Oregon) using exactly the same inbred strains and one null mutant strain. We went to extraordinary lengths to equate test apparatus, testing protocols, and all possible features of animal husbandry. One potentially important feature was varied systematically. Because many believe that mice tested after shipping from a supplier behave differently from those reared in-house, we compared mice either shipped or bred locally at the same age (77 days) starting at the same time (0830 to 0900 hours local time on 20 April 1998) in all three labs. Each mouse was given the same order of tests: [Day 1: locomotor activity in an open field; Day 2: an anxiety test, exploration of two enclosed and two open arms of an elevated plus maze; Day 3: walking and balancing on a rotating rod; Day 4: learning to swim to a visible platform; Day 5: locomotor activation after cocaine injection; Days 6 to 11: preference for drinking ethanol versus tap water].
>
> "Despite our efforts to equate laboratory environments, significant and, in some cases, large effects of site were found for nearly all variables. Furthermore, the pattern of strain differences varied substantially among the sites for several tests. Sex differences were only occasionally detected and, much to our surprise, there were almost no effects of shipping animals before testing. Large genetic effects on all behaviors were confirmed, which is not surprising because we chose strains known to differ markedly on these tasks." (Ibid., pp. 1670-1671).

In short, while expected behavioral differences were found between genetic mutant strains, the three sites were significantly different on six of eight measures -- and on four

measures, there were statistically significant interactions between site and genotype in observed behaviors.

To explain why the same procedures in Edmonton, Portland, and Albany yielded different results, with the site influencing some genetic mutants in six cases but not others, it is essential to identify the variables that were consciously controlled or known to vary:

> "Variables explicitly equated across laboratories included apparatus, exact testing protocols, age of shipped and laboratory-reared mice, method and time of marking before testing, food (Purina 5001; Purina 5000 for breeders), bedding (Bed-o-cob, 1/4 inch, Animal Specialties, Inc., Hubbard, OR), stainless steel cage tops, four to five mice per cage, light/dark cycle, cage changing frequency and specific days, male left in cage after births, culling only of obvious runts, postpartum pregnancy allowed, weaned at 21 days, specific days of body weight recording, and gloved handling without use of forceps. Unmatched variables included local tap water, requirement of filters over cage tops in Portland only, variation of physical arrangement of colonies and testing rooms across sites, different air handling and humidity, and different sources of batches of cocaine and alcohol." (Ibid., note 4, p. 1672).

The experimenters did not suspect any of these "unmatched variables" but noted that "specific experimenters performing the testing were unique to each laboratory and could have influenced behavior of the mice. The experimenter in Edmonton, for example, was highly allergic to mice and performed all tests while wearing a respirator -- a laboratory-specific (and uncontrolled) variable." (Ibid., p. 1672).

In letters to *Science*, several critics attributed site differences to “handling” the mice (noting the “fan motors” in respiratory helmets), while another cited “group housing” and “social rank” of mice as well as “idiosyncratic differences” in the “behavior of personnel,” and another commentator suggested “diet” as a possible explanation. [i]

Because functional mechanisms were not cited to explain the observed behavioral variability attributed to these factors, further analysis is appropriate.[ii] To this end, it will be useful to consider whether neurotoxic effects of chemicals in "local tap water" – most notably lead (or other heavy metals) and silicofluorides -- could have influenced the behaviors that differed between laboratories in ways sometimes also dependent on mouse strain.[1]

Four steps are needed to formulate and test this hypothesis. First, precisely which behaviors varied in each location? Second, among uncontrolled variables, why is tap water a source of neurotoxicity that could produce these effects – and if so, why is it reasonable to test the toxicity hypothesis with data on the use of silicofluorides in water treatment? Third, an empirical test of the hypothesis begins by determining whether silicofluoride usage in public water at these three sites varied in a way consistent with the experimental results. Finally, the empirical test concludes by comparing previously reported data on behavioral effects of silicofluoride treated water with the experimental results reported by Crabbe, Wahlsten, and Dudek. As will be shown, the toxins had similar functional consequences in both animal and human studies with interactive effects like those predicted by toxicogenomics.

II. Behavioral Differences by Site

For four of the six behavioral tests not entailing consumption of alcohol, the pattern of variation between laboratories could be described as greater physical activity and lowered inhibition in Edmonton than in Portland or Albany. Table 1 indicates for each

[1] After drafting this manuscript, publication of another anomaly in the Edmonton, Albert water supply has appeared: Naomi Lubick, "More nitrosamines in drinking water Two nitrosamines, considered to be potential carcinogens, have been detected in drinking water for the first time," *Science News* (Nov. 8, 2006), http://pubs.acs.org/subscribe/journals/esthag-w/2006/nov/science/nl_nitrosamines.html. For the original article: Yuan-Yuan Zhao, Jessica Boyd, Steve E. Hrudey, and Xing-Fang Li, "Characterization of New Nitrosamines in Drinking Water Using Liquid Chromatography Tandem Mass Spectrometry," *Environ. Sci. Technol.*; 2006**;** ASAP Web Release Date: 08-Nov-2006;DOI: 10.1021/es061332s

test the number of genetic strains that was most active, least active, intermediate, or the same as at other sites. For the 32 tests at each site (8 genetic strains in each of four experiments), mice in Edmonton were most active in 26 tests, while the number of genetic strains in Portland or Albany that were of lowest activity differed by test and by site.

The researchers present data for one more experiment -- the tendency of mice to prefer ethanol to tap water as measured by the grams of ethanol consumed. For this behavior, which concerns choice of liquid rather than locomotion, the researchers note that "laboratory environment was not critical. For example, ethanol drinking scores were closely comparable across all three labs, and genotypes alone accounted for 48 of the variance." (Crabbe, Wahlsted, & Dudek, 1999; p. 1671). As Table 2 shows, while there were differences between Portland and Albany among the 8 strains in this experiment, responses were usually intermediate in Edmonton, suggesting that the results in Table 1 are not due to a consistent error in record-keeping.[iii]

As Tables 1 and 2 indicate, the most consistent difference between laboratories was the tendency for most strains of mice to exhibit more active and less fearful locomotor behavior in Edmonton. That brain chemistry was a factor in these findings is, moreover, implied by the differential increase in locomotion after administration of cocaine.

These results are clearest when summarized as the proportion of the 32 locomotor tests in each category at each site (Table 3). Whereas mice in Edmonton were the most active in three-quarters of the 32 tests, those in Portland and Albany where either the least active or intermediate in more than three-quarters of the tests. Hence the principal research question concerns the factor or factors that increased locomotor behavior or reduced behavioral inhibition in Edmonton.

Table 1: Levels of Behavioral Activity in Four Tests in the Three Laboratory Sites*

(Number = number of the 8 strains at each of the experimental sites.)

	Edmonton	Portland	Albany
Test #1: "Open field horizonal activity," Day 1 (Fig. 1A)			
Most active	6	1	0
Intermediate	1	4	1
Least active	0	2	7
Same in all	1	1	0
Test #2: "Activity change after cocaine," Day 5 minus Day 1 (Fig 1B)			
Most active	4	1	1
Intermediate	1	2	4
Least active	1	3	1
Same in all	2	2	2
Test #3: "Total Arm Entries" in Maze, Day 2 (Fig. 2A)			
Most active	7	1	0
Intermediate	1	2	4
Least active	0	5	4
Same in all	0	0	0
Test #4: "Time in Open Arms" in Maze, Day 2 (Fig. 2B)			
Most active	7	0	0
Intermediate	0	1	5
Least active	0	7	2
Same in all	1	0	1

SOURCE: Crabbe, Wahlsten, & Dudek, 1999. The ANOVA results include statistically significant ($p < .10$) two-way interactions of genotype and site for at least one behavior in each of these experiments (Table 1).

Table 2: Preference for Ethanol over Tap Water*

Test #6: Comparison of Ethanol Consumed (g/Kg) by 8 Strains, Days 6 to 10

	Edmonton	Portland	Albany
Most consumed	1/8 (12.5%)	4/8 (50%)	3/8 (37.5%)
Intermediate	4/8 (50%)	2/8 (25%)	1/8 (12.5%)
Least consumed	2/8 (25%)	1/8 (3.1%)	4/8 (50%)
Same as 1 other site	1/8 (12.5%)	1/8 (12.5%)	0/8 (---%)

*Source: ibid., Fig. 3. ANOVA results show no statistical significance for site or for the interaction of genotype and site (Ibid., Table 1).

Table 3: Overall Percentages of Differences in Behavioral Activity

(Number of Strains as Proportion of 32 tests in Table 1)

	Edmonton	Portland	Albany
Most active	24/32 (***75%***)	3/32 (*9.4%*)	1/32 (*3.1%*)
Intermediate	3/32	9/32	14/32
Intermediate	3/32 (*9.4%*)	9/32 (*28.1%*)	14/32 (***43.8%***)
Least active	1/32	17/32	14/32
Least active	1/32 (*3.1%*)	17/32 ***53.1%***)	14/32 (***43.8%***)
Same as 1 other site	4/32 (*12.5%*)	3/32 (*9.4%*)	3/32 (*9.4%)*

III. Hypothesis: Differences in Local Tap Water Can Influence Experimental Behavior

The principal variable suggested as explaining between-site variation was the manner in which individual experimenters handled mice. Were such factors as respirator use responsible for higher behavioral activity in Edmonton, why would preferences for ethanol over tap water be primarily due to the genetic strain with no consistent effect of laboratory site? No one has cited a behavioral mechanism linking the experimenter's touching behavior, odor, or noise to increased motor activity and disinhibition of mice or other species in otherwise fearful environments while not having effects on increased intake of ethanol. Without specifying a plausible functional mechanism, it is difficult to distinguish among the factors cited by the critics.

A possible step further could be consideration of "local tap water," an uncontrolled variable which has often been linked to uptake of heavy metals. This factor is important because heavy metals are known to modify neurotransmitter function in ways that could account for some of the behavioral differences noted in Tables 1-3 (Schauss, 1981; Marlow, Schneider, & Bliss, 1991; Brockel & Cory-Slechta, 1998). For example, numerous studies show that lead is associated with lowered dopamine function (especially in the basal ganglia) and, as a result, poor behavioral inhibition and higher motor activity levels (Needleman, 1992; Cory-Sletcha, 1995).

Behaviors that have been linked to lead neurotoxicity include hyperactivity or ADHD (Kahn, Kelly, & Walker, 1995; CorySletcha, 1998; Walker, 1998), attention deficit disorder (Tuthill, 1996; Needleman, 1999), impaired cognition (Bryce-Smith, 1983; Needleman & Tatsonis, 1990), and violent crime (Pihl & Ervin, 1990; Denno, 1994; Needleman, Riess, Tobin, Blesecker, & Greenhouse, 1996; Masters, Hone, & Doshi, 1997; Masters, Hone, Greloti, Gonzalez, & Jones, 1998). In addition to laboratory studies and geographical data, time series analysis of the sales of leaded gasoline have been associated with higher rates of violent crime and unwed pregnancy (both plausibly mediated by loss of inhibition) and lower IQ (Nevin, 2000; Masters, 2001).

Lead neurotoxicity has also been linked to increased response to given doses of ethanol (Cezard, Demarquilly, Boniface, Haguencoer, 1992) and increased consumption of cocaine, which compensates for reduced dopamine function (Kuhar, 1992; Slusher, Tiffany, Olkowski, 1997).

Another toxin linked with several of these effects, including increased rates of violent crime, is manganese, which downregulates serotonin as well as dopamine and other neurotransmitters (Donaldson, Labella, & Gesser, 1981; Donaldson & Barbeau, 1985; Donaldson, 1987; Subhash & Pamashree, 1990; Gottschalk, Rebello, Buchsbaum, Tucker, & Hodges, 1991). Since water systems sometimes contain potentially dangerous levels of lead or manganese, tap water seems a plausible uncontrolled variable to explore more fully as a source of between-laboratory differences in responses to the same experimental paradigm.

This hypothesis is reinforced by considering the whether public water supplies are treated with fluosilicic acid (H_2SiF_6) or sodium silicofluoride (Na_2SiF_6), a practice that has been associated with both increased uptake of lead (and perhaps other toxins) from the environment and greater behavioral disinhibition. Although these two chemicals – jointly called silicofluorides – are widely used in water treatment in the U.S. and Canada, they are toxins whose effects when injected in water were never tested for effects on health and behavior (Thurnau, 2001).[iv] When fluoridaton using silicofluoride instead of sodium fluoride was approved by the Public Health Service in 1950, this action was based on a theoretical assumption that the compounds would dissociate "virtually completely" (Zipkin & McClure, 1951). Earlier experiments in Europe were inconsistent with this belief and more recent German studies revealed the persistence of "residual" chemical species that have important biochemical effects (Rees & Hudleston, 1936; Ryss & Slutskaya,, 1940; Westendorf, 1975). Moreover, three recent epidemiological studies (population samples totalling over 400,000) indicate that, unlike sodium fluoride, silicofluorides enhance lead uptake from environmental sources such as lead paint in old housing or industrial pollution with lead (Masters & Coplan,1999; Coplan, Masters, &

Hone, 1999; Coplan, Masters, Hone, & Dykes, 2000; Masters, 2001). Combined with human behavioral data on effects of silicofluoride-treated water (Masters, 2001; Masters, Coplan, Hone, Grelotti, Gonzalez, & Jones, in press; Masters & Coplan, in press; Masters, in press), there is reason to examine the hypothesis that use of municipal tap water treated with these chemicals could modify mouse behavior.

To ascertain whether toxicity in local tap water helps explain enhanced locomotor activity and reduced inhibition across divergent genetic strains in these experiments, there are practical reasons to focus on silicofluorides. On the one hand, the only reliable measure of lead or other toxic uptake in the experimental mice would have been analysis of these chemicals in hair or blood at the time of the experiment. On the other, silicofluoride usage in the experimental sites is documented and empirical studies have associated silicofluoride treated water with acetylcholinesterase inhibition (Knappwost & Westendorf, 1974; Westendorf, 1975) as well as enhanced lead uptake (e.g., Figures 1a-b below) and behavioral differences like those in the Crabbe et al. experiments (e.g., Figures 2a-b below).[v] Hence silicofluorides provide a practical and theoretically interesting way to check the toxicity hypothesis.[vi]

IV. Silicofluoride Usage in Local Communities

The first test of this version of the "tap water" hypothesis is whether the public water of Edmonton (where behavioral disinhibition was more pronounced) is treated with silicofluorides whereas these chemicals are not use in either Portland or Albany. Two enquiries have confirmed that Edmondton's public tap water is treated with fluosilicic acid (H_2SiF_6).[vii] In contrast, the U.S. Center for Disease Control's "Fluoridation" Census for 1993 indicates that neither Portland, Oregon nor Albany, New York, fluoridates with these chemicals (CDC, 1993) -- and recent follow-up enquiries have confirmed this is still the case.[viii]

This difference is worth considering because controversies over "fluoridation" have routinely ignored the specific chemicals used for this purpose. Although

silicofluorides are today used in over 90% of fluoridated public water supplies, delivered to approximately 140 million Americans, sodium fluoride (familiar from toothpaste) was the chemical original tested for safety. Given the biochemical differences between sodium fluoride and the silicofluorides (Coplan & Masters, 2001), testing the hypothesis that silicofluoride-treated water was responsible for differing experimental results between Edmonton and either Portland or Albany could benefit public policy as well as research methods in evolutionary psychology.

V. Silicofluoride Treated Water, Lead Uptake, and Hyperactivity or Poor Impulse Control

The four behavioral responses often (but not always) higher in Edmonton than Portland and Albany were: "locomotor activity in an open field," measured by "horizontal distances (centimeters) traveled in 15 minutes on the first test on Day 1; "cocaine induced activation, expressed as the difference between horizontal activity (centimeters in 15 min) after cocaine (20mg/dkg) on Day 5 minus the score on Day 1"; "total number of entries into any arm (defined as all four limbs in the arm)" when mice are "videotaped for 5 min. on elevated plus mazes having two open and two enclosed arms"; and "time (seconds) spent in the two open arms during the 300-s test," with "smaller amounts of time" indicating "higher levels of anxiety" (or, in less emotional terms, lower levels of inhibition).

Because lead neurotoxicity can decrease inhibition and increase locomotor activity, it is important to note that the enhancement of lead uptake in humans exposed to silicofluorides shows a statistically significant interaction between race and exposure to water treated with these chemicals (Figures 1a-b). That is, not only is public tap water treated with this chemical a significant risk-factor for higher uptake of lead, but this effect shows a genotype-site interaction similar to those found by Crabbe et al. (1999: Table 1).

Analyses of the effects of silicofluorides on behavioral disinhibition among humans have focused on geographic differences in rates of hyperactivity, cocaine usage, and violent crime. The best data are FBI crime reports for all U.S. counties of populations above 500,000, which show that controlling for lead pollution in the environment, silicofluoride treated water is a risk factor for higher rates of violent crime (for 1985: Figure 2a; for 1991: Figure 2b). That this is effect is not due to a spurious correlation is shown by multiple regression analysis of this data: after controlling for socio-economic, demographic, and other environmental variables associated with violent crime, silicofluoride-treated water is a significant predictive factor for this type of behavioral disinhibition (Table 4). Comparable national data on arrests for drunken behavior also show that, controlling for other variables, silicofluoride usage is a significant risk factor for loss of inhibition (Table 4). Because such arrests reflect addiction and loss of inhibition rather than preference for ethanol (cf. Hyman & Malenka, 2001), these last results do not contradict the data on preference for ethanol in the Edmonton samples studied by Crabbe et al. (see note 3 above).

The hypothesis that water treated with silicofluorides may have behavioral effects is also confirmed by other data. In a National Institute of Justice study of cocaine use at time of criminal arrest (n = 30,000), silicofluorides were significantly associated with higher substance abuse (Masters & Coplan, 1999). And while reliable data on hyperactivity (ADHD) among children are difficult to obtain, a private survey in Massachusetts towns found that where silicofluorides are used, rates of learning disabilities are higher, especially where lead levels in 90^{th} % first draw water were above 20 ppb (Fig. 3).

Since these effects do not seem to occur where water is fluoridated with sodium fluoride or not fluoridated at all, they support the hypothesis of water treatment chemistry as a factor in higher locomotor activity and poor inhibition. Moreover, because the toxic effects of silicofluorides differ by race, the human data is consistent with the differences in mouse strain observed in the study by Crabbe, Wahlsten, and Dudek. While such correlational data does not “prove” that silicofluoride treated tap water was a key factor,

it indicates the need for further laboratory experimentation on “tap water” as a potential confounding factor in behavioral research.

Conclusion

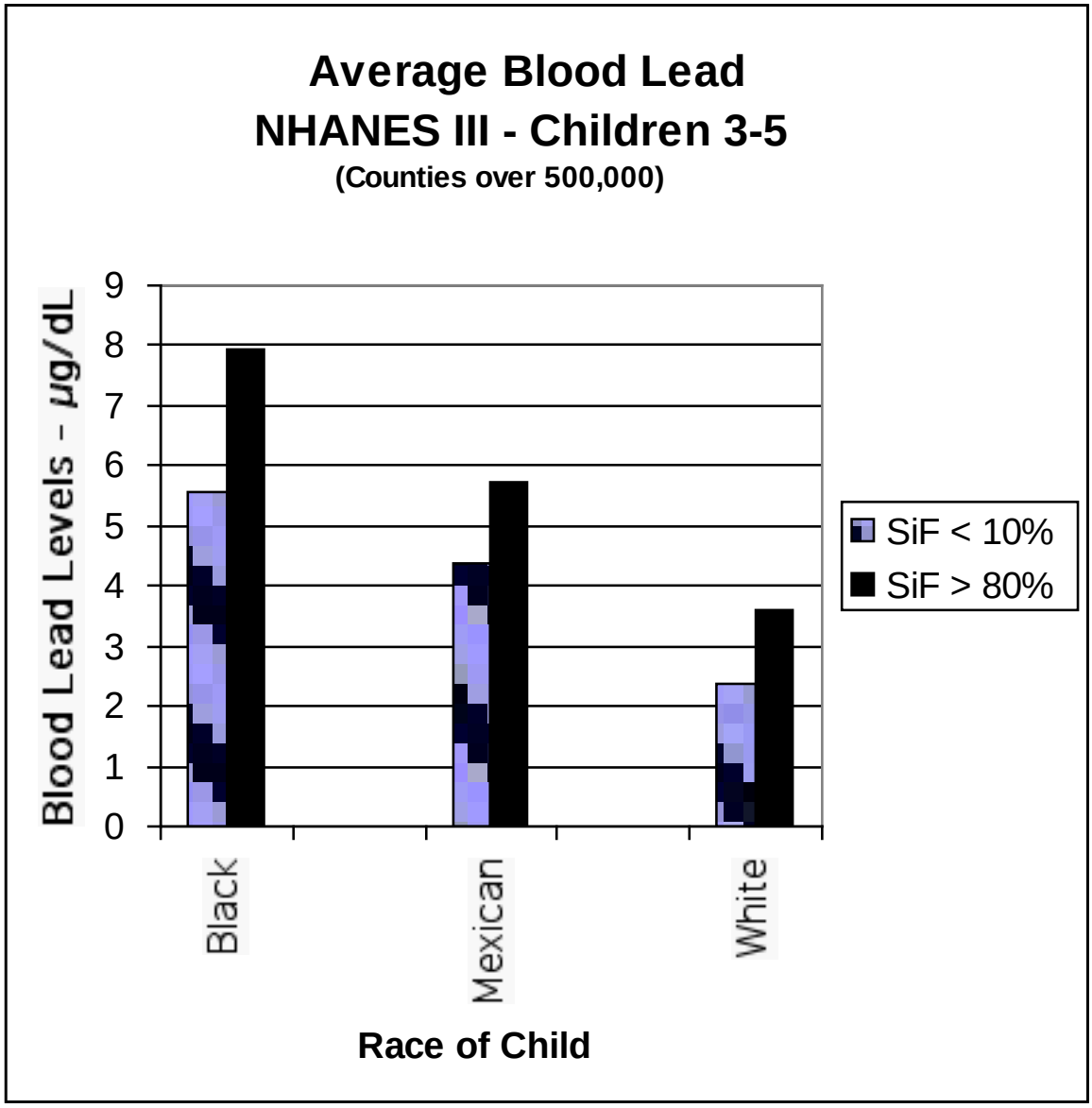
By focusing simultaneously on genetic and environmental factors in behavior, the study by Crabbe, Wahlsten, and Dudek was an important contribution. As two commentators on this paper noted, in such studies evidence of “interlab variability generates controversies that stimulate further investigation, resulting in methodological improvement over time.” (Picciotto & Self, 1999). Consideration of an environmental factor like local tap water is especially important because toxins often found in public water supplies have known behavioral effects. Indeed, the irony in this case is that prior studies in human toxicology may help explain experimental observations of mouse behavior and contribute to improved laboratory techniques in evolutionary psychology.

The hypothesis that silicofluorides produced experimental differences in mouse behavior also has implications for public policy. Because silicofluorides have never been tested for safety, ecological studies that show an association between silicofluorides and lead uptake, substance abuse, and violent crime have attracted attention. Combined with the data reported by Crabbe et al (1999), the epidemiological data show the urgent need for experimental studies to test the association between silicofluoride treated water and such human effects as learning disabilities, increased locomotor behaviors (e.g., ADHD in children), and behavioral disinhibition (e.g., higher rates of violence).

The need for animal studies of this hypothesis is reinforced by an additional parallel between the experimental data described in Tables 1-3 and ecological findings concerning humans exposed to silicofluorides. The mice studied by Crabbe et al. often differed by genetic strain in their responses to identical test situations. The proposed hypothesis is consistent with human data showing that where silicofluorides are used in public water supplies, the enhancement of lead uptake differs by race, being most serious for Blacks, least serious for Whites, and intermediate for Hispanics (Figures 1a-b). In both the experiment with mice and human epidemiological data in the U.S., the

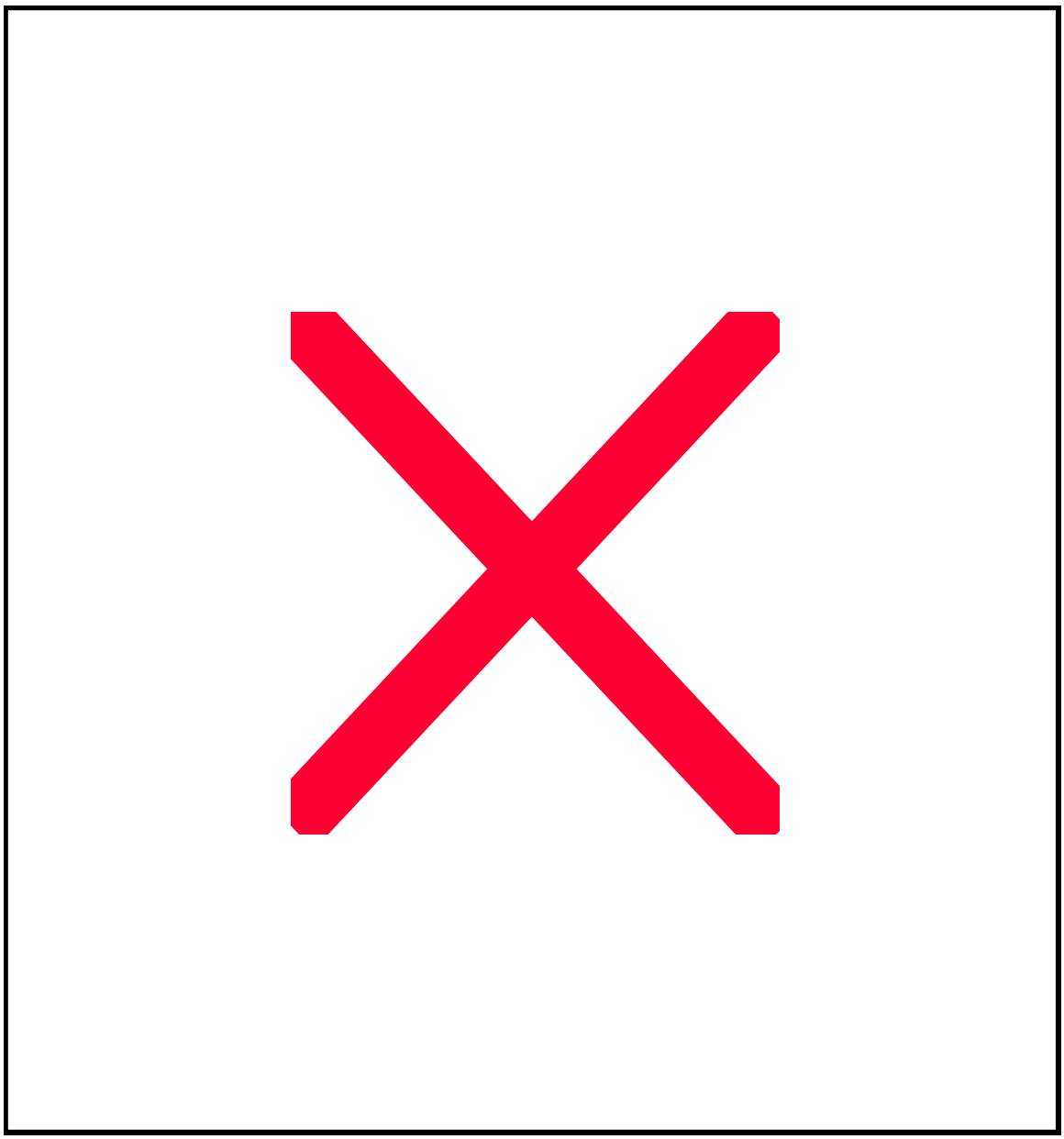
interaction term of the ANOVA (analysis of variance) is statistically significant. Hence, in addition to indicating an important variable needing controls in laboratory behavioral experimentation, this analysis points to a long overdue need to reconsider a public policy that may be harmful to 140 million Americans with especially serious effects among minorities. As this example suggests, evolutionary psychology has the potential to make great contributions to public health and safety.

FIGURE 1a



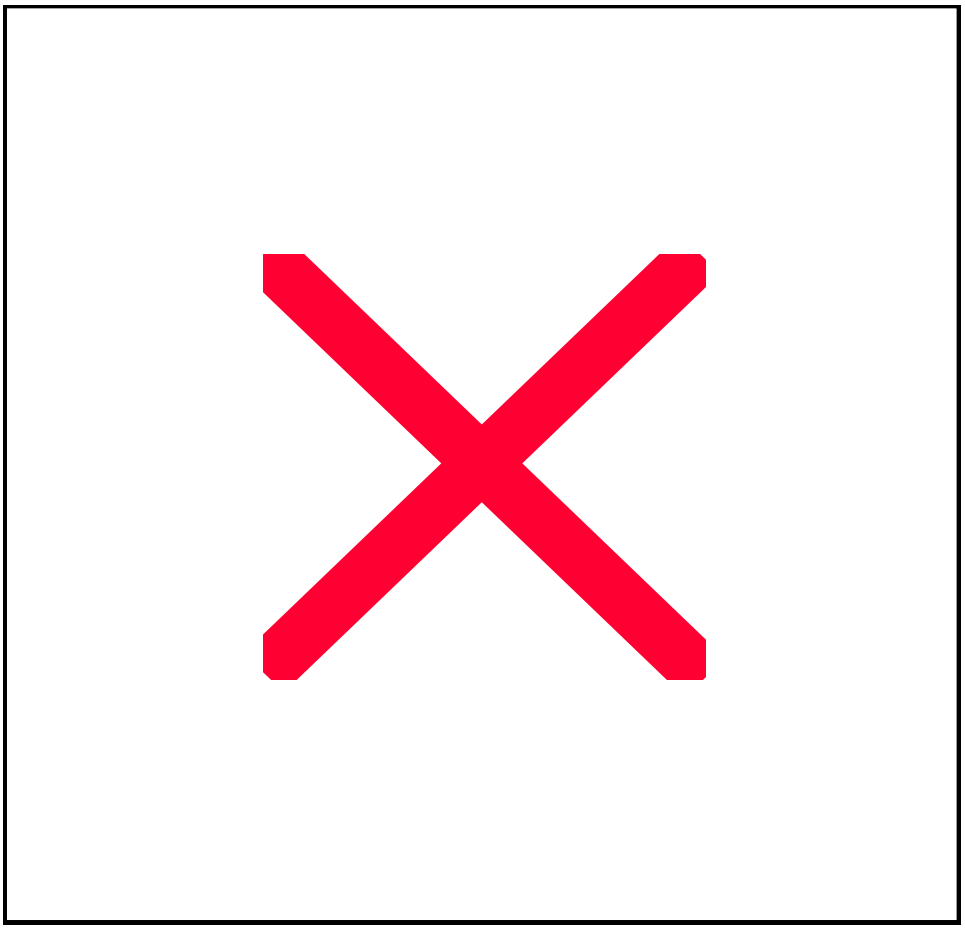
For NHANES III Children 3-5, mean blood lead is significantly associated with fluoridation status (DF 3, F 17.14, $p < .0001$) and race (DF 2, F 19.35, $p < .0001$) as well as for poverty income ratio (DF 1, F 66.55, $p < .0001$). Interaction effect between race and fluoridation status: DF 6, F ;3.333, $p < .0029$. (Source: Masters, 2001).

FIGURE 1b



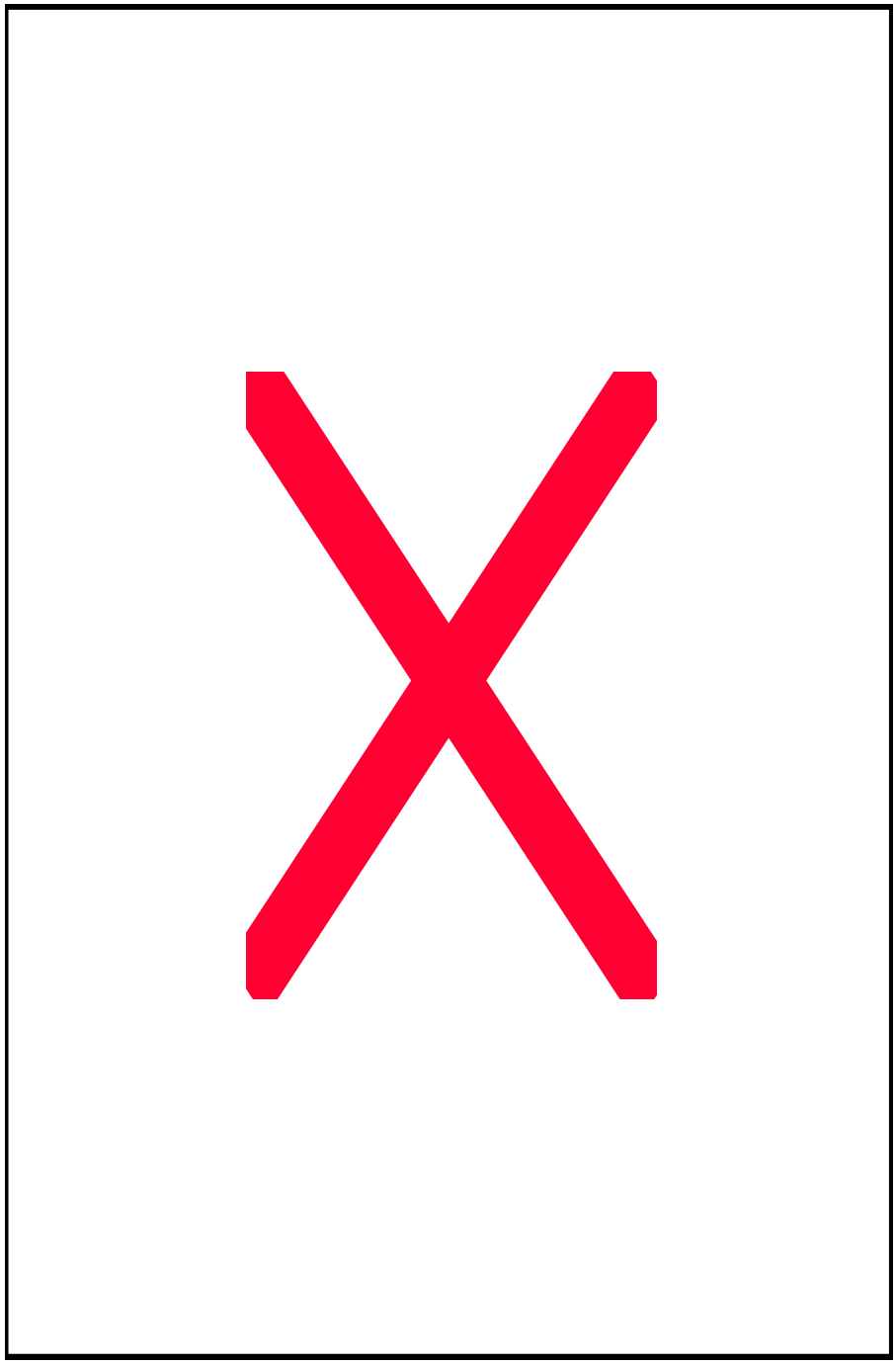
Significance, for ages 5-17: fluoridation status (DF 3, F 57.67, $p < .0001$), race (DF2, 28.68, $p < .0001$), Poverty-Income Ratio (DF 1, 252.88, $p < .0001$). Interaction between race and fluoridation status DF 6, F 11.17, $p < .0001$ (Source:Masters, 2001).

FIGURE 2a.



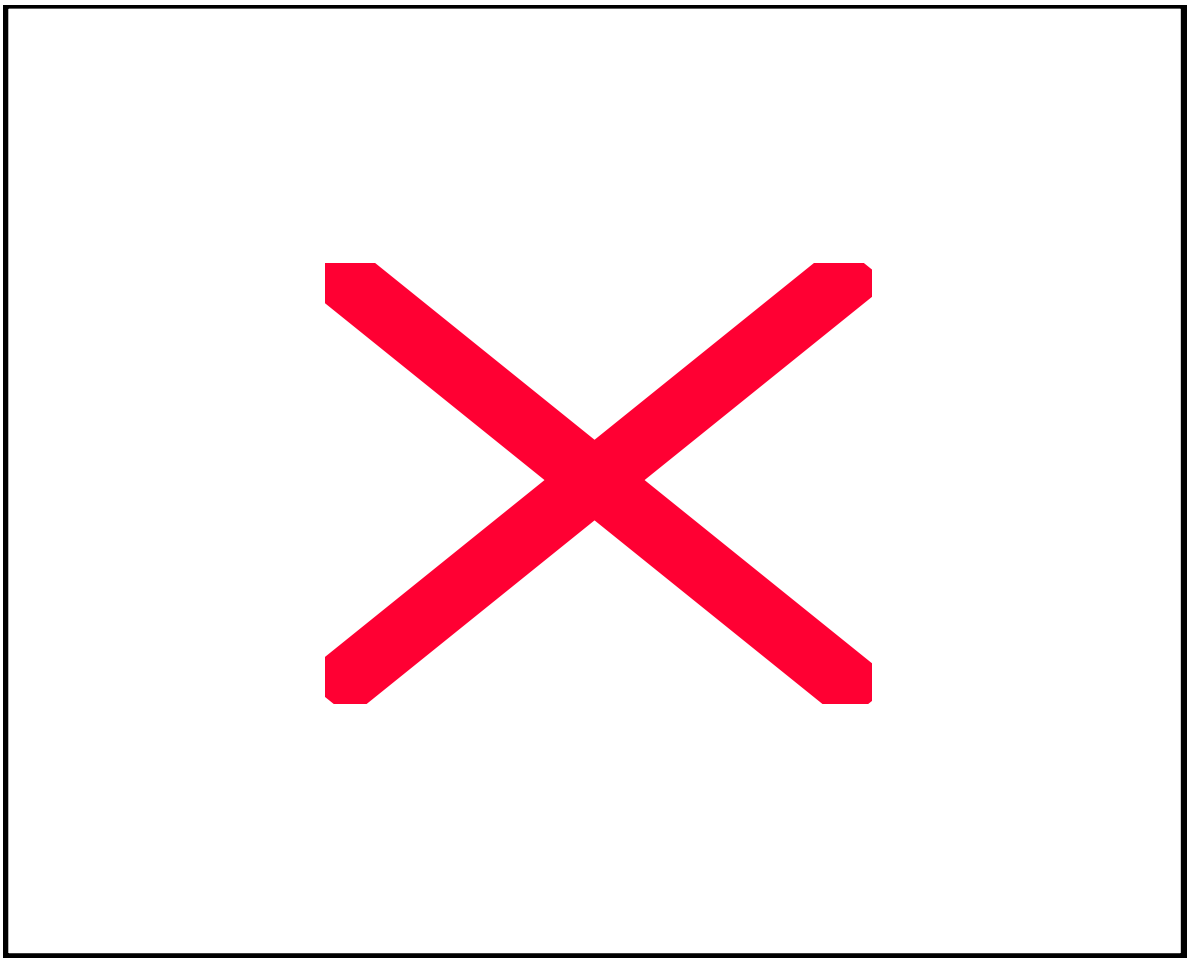
(Source: Masters et al, in press; Masters & Coplan, in press). Lead Pollution is measured by EPA Toxic Release Inventory

FIGURE 2b



Source: see Figure 2a.

Figure 3



Lead Levels in Public Water Supply: 90th % first draw sample of water had lead level above or below 20 ppb. SiF: Community water supply does or does not use either fluosilicic acid or sodium silicofluoride (SiFs) as fluoridation agents (CDC Fluoridation Census).
% Learning Disabilities: Results of author's informal survey. Sample is too small for statistical reliability, but note same pattern found elsewhere: SiF enhances negative effects of lead pollution in environment.

	Lead in Water	
	< 20ppm	>20ppb
No SiF	n=7	n=1
SiF	n=2	n=5

Average % Learning Disabled Students by SiF use: No SiF = 10.2% (n=8)
SiF = 15.8% (n = 7):

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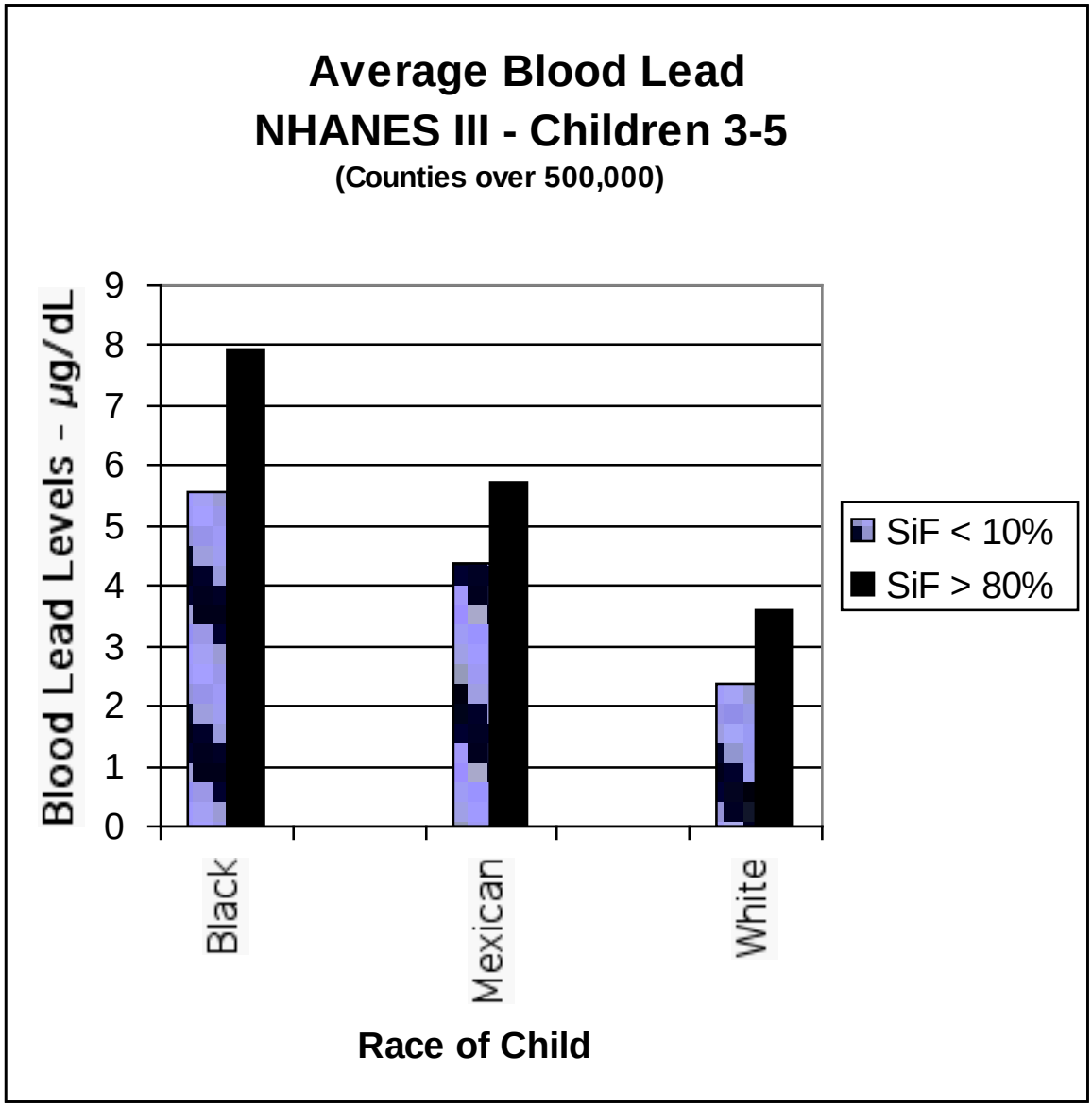
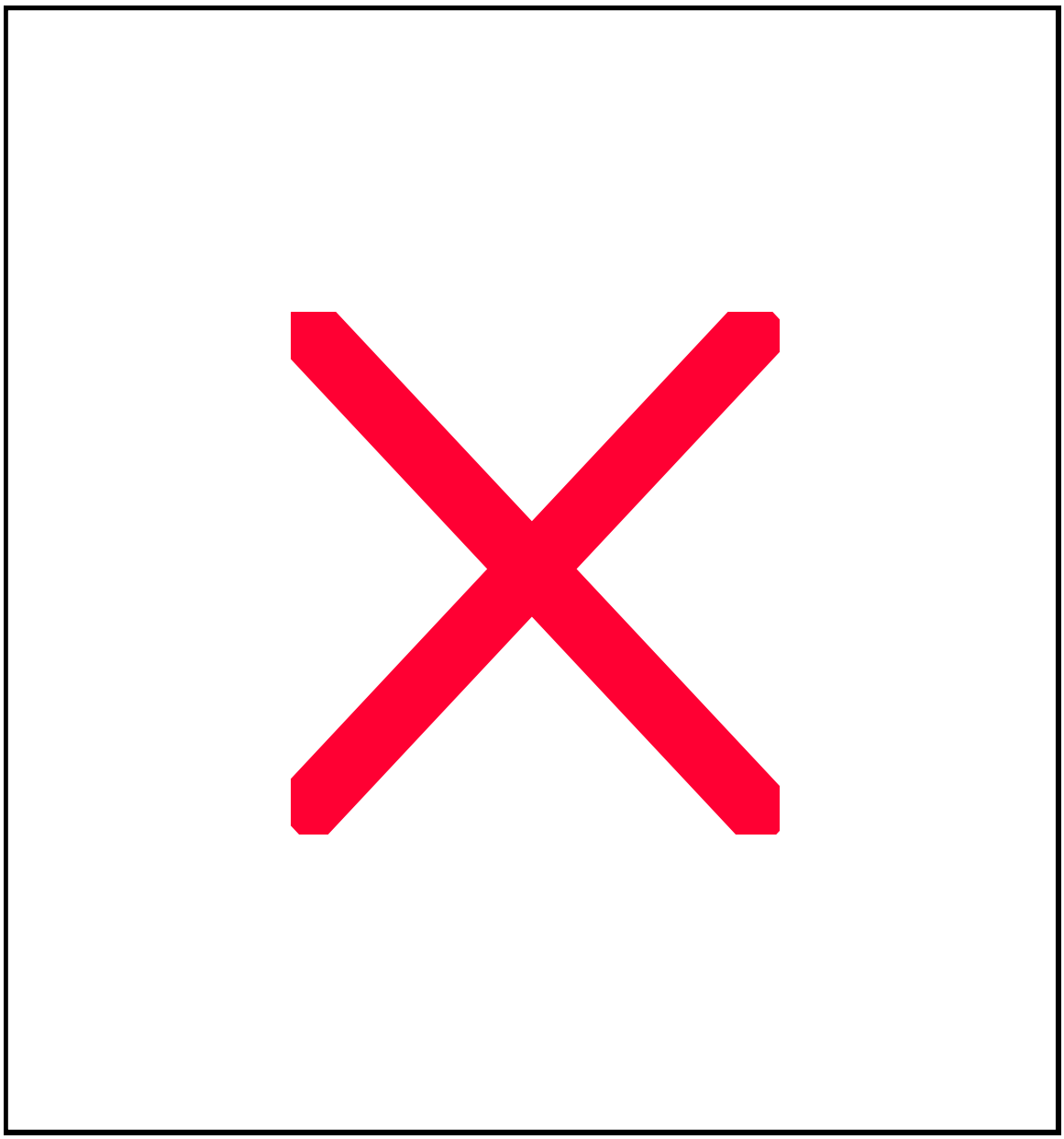
FIGURE 1a



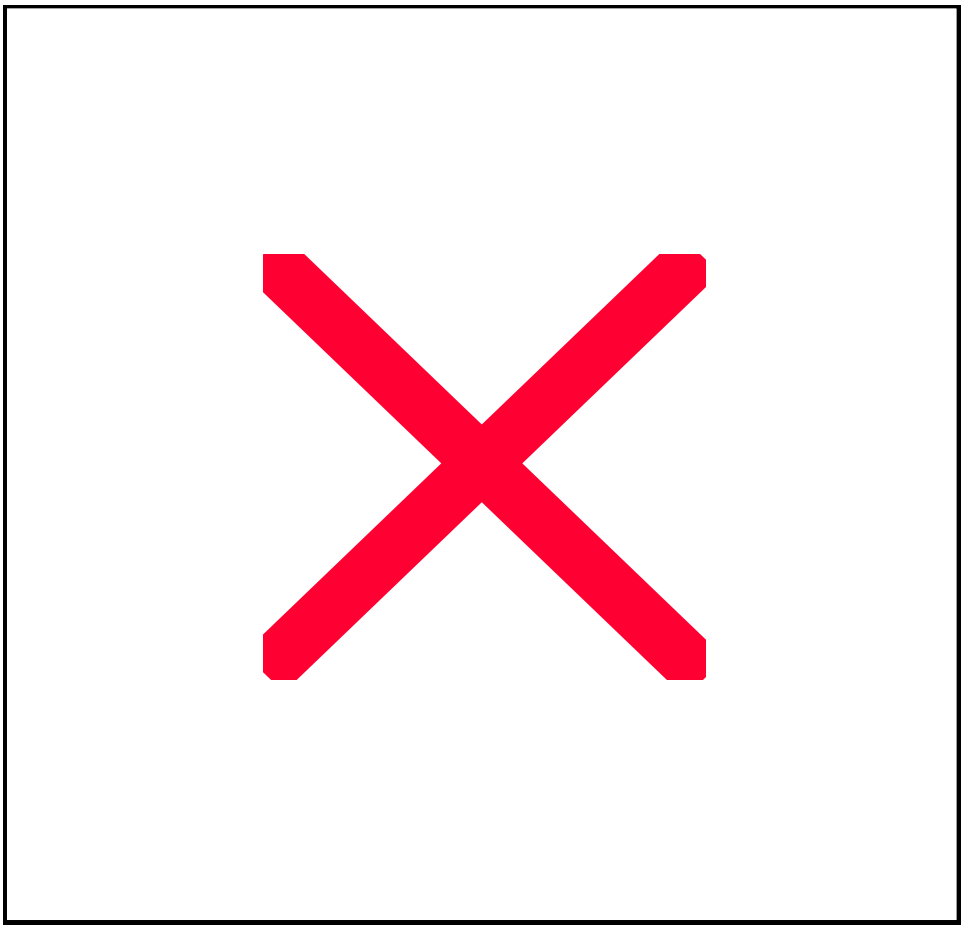
For NHANES III Children 3-5, mean blood lead is significantly associated with fluoridation status (DF 3, F 17.14, $p < .0001$) and race (DF 2, F 19.35, $p < .0001$) as well as for poverty income ratio (DF 1, F 66.55, $p < .0001$). Interaction effect between race and fluoridation status: DF 6, F ;3.333, $p < .0029$. (Source: Masters, 2001).

FIGURE 1b



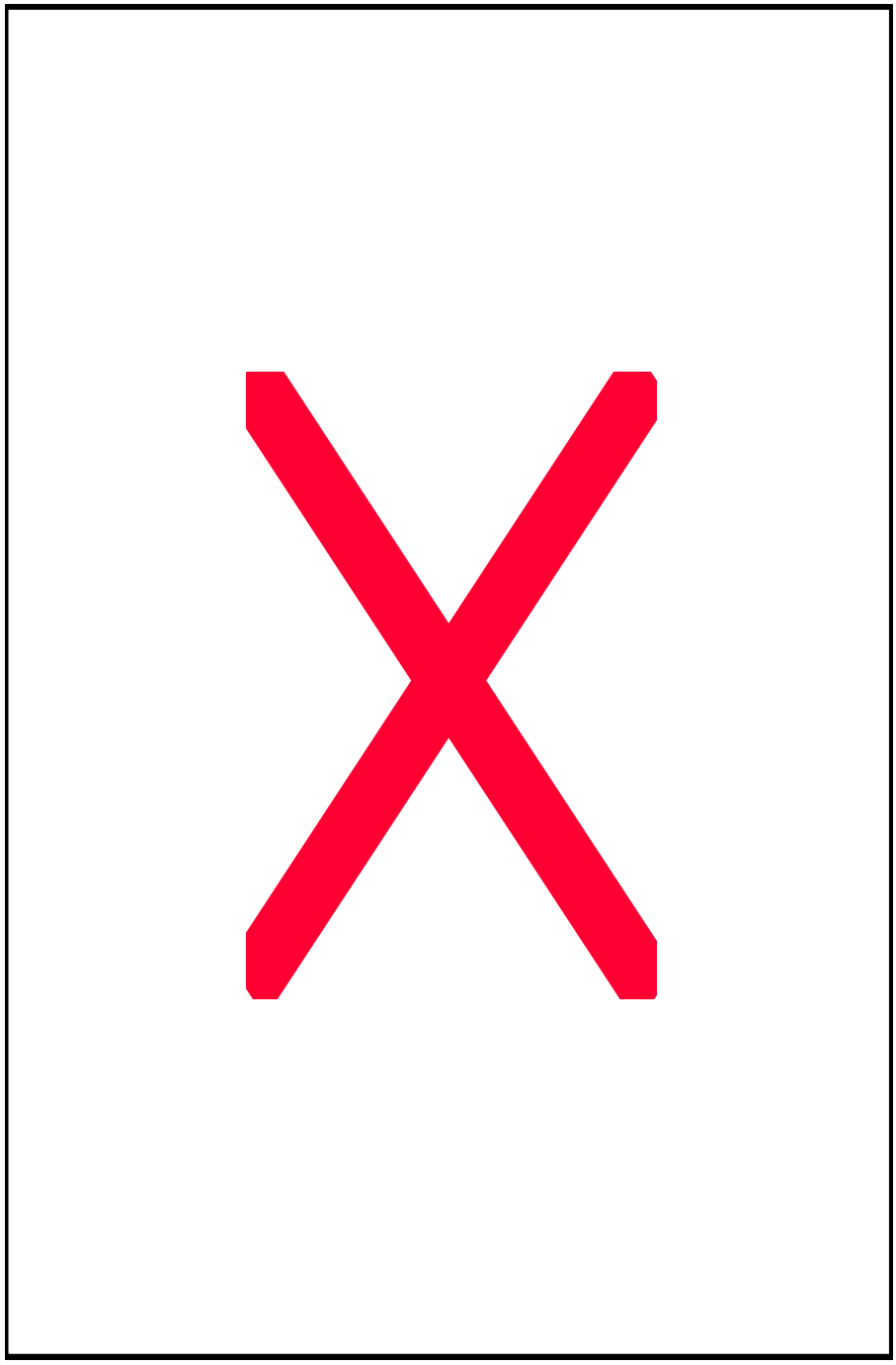
Significance, for ages 5-17: fluoridation status (DF 3, F 57.67, $p < .0001$), race (DF2, 28.68, $p < .0001$), Poverty-Income Ratio (DF 1, 252.88, $p < .0001$). Interaction between race and fluoridation status DF 6, F 11.17, $p < .0001$ (Source:Masters, 2001).

FIGURE 2a.



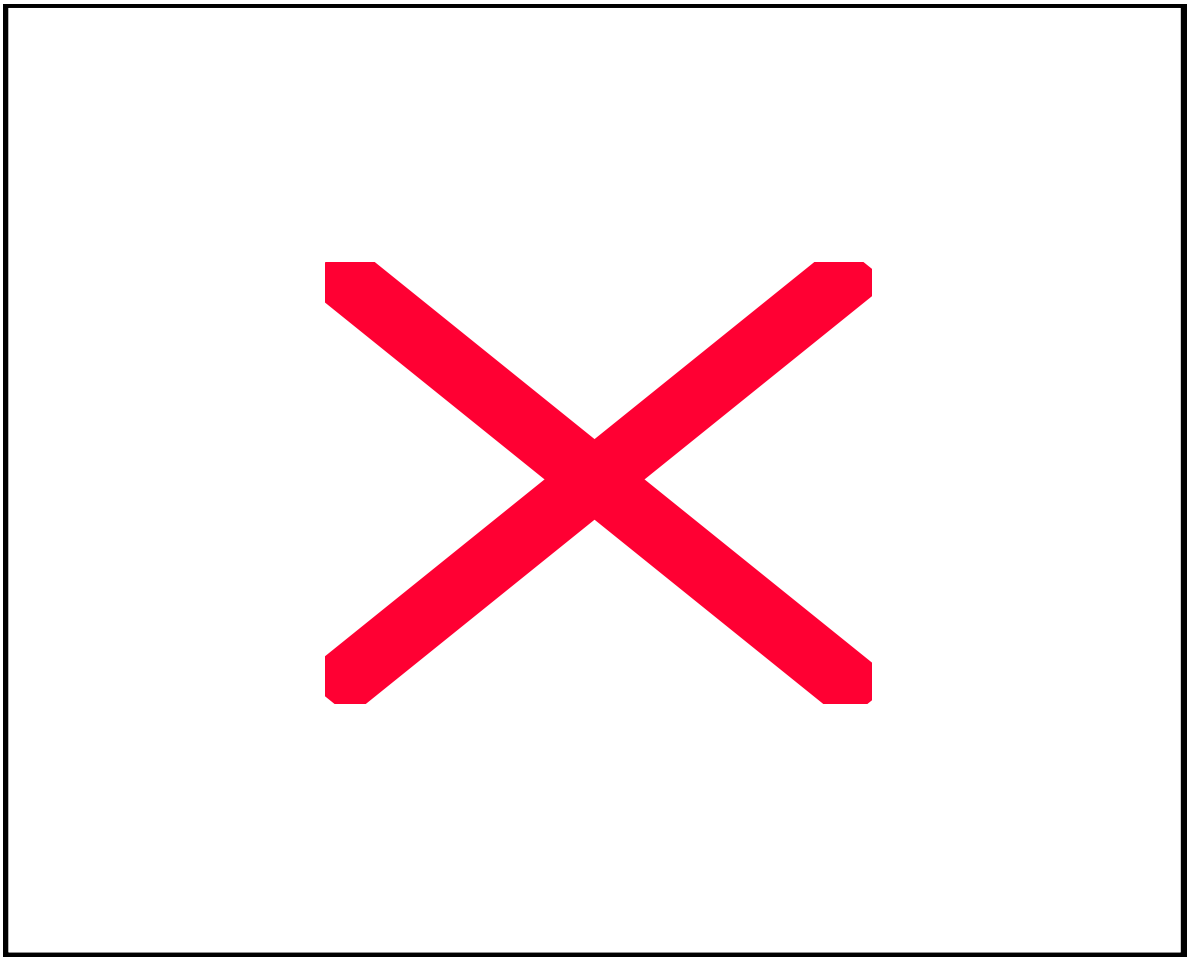
(Source: Masters et al, in press; Masters & Coplan, in press). Lead Pollution is measured by EPA Toxic Release Inventory

FIGURE 2b



Source: see Figure 2a.

Figure 3



Lead Levels in Public Water Supply: 90th % first draw sample of water had lead level above or below 20 ppb. SiF: Community water supply does or does not use either fluosilicic acid or sodium silicofluoride (SiFs) as fluoridation agents (CDC Fluoridation Census).
% Learning Disabilities: Results of author's informal survey. Sample is too small for statistical reliability, but note same pattern found elsewhere: SiF enhances negative effects of lead pollution in environment.

	Lead in Water	
	< 20ppm	>20ppb
No SiF	n=7	n=1
SiF	n=2	n=5

Average % Learning Disabled Students by SiF use: No SiF = 10.2% (n=8)
SiF = 15.8% (n = 7):

Table 1: Levels of Behavioral Activity in Four Tests in the Three Laboratory Sites*

(Number = number of the 8 strains at each of the experimental sites.)

	Edmonton	Portland	Albany
Test #1: "Open field horizonal activity," Day 1 (Fig. 1A)			
Most active	6	1	0
Intermediate	1	4	1
Least active	0	2	7
Same in all	1	1	0
Test #2: "Activity change after cocaine," Day 5 minus Day 1 (Fig 1B)			
Most active	4	1	1
Intermediate	1	2	4
Least active	1	3	1
Same in all	2	2	2
Test #3: "Total Arm Entries" in Maze, Day 2 (Fig. 2A)			
Most active	7	1	0
Intermediate	1	2	4
Least active	0	5	4
Same in all	0	0	0
Test #4: "Time in Open Arms" in Maze, Day 2 (Fig. 2B)			
Most active	7	0	0
Intermediate	0	1	5
Least active	0	7	2
Same in all	1	0	1

SOURCE: Crabbe, Wahlsten, & Dudek, 1999. The ANOVA results include statistically significant ($p < .10$) two-way interactions of genotype and site for at least one behavior in each of these experiments (Table 1).

Table 2: Preference for Ethanol over Tap Water*

Test #6: Comparison of Ethanol Consumed (g/Kg) by 8 Strains, Days 6 to 10

	Edmonton	Portland	Albany
Most consumed	1/8 (12.5%)	4/8 (50%)	3/8 (37.5%)
Intermediate	4/8 (50%)	2/8 (25%)	1/8 (12.5%)
Least consumed	2/8 (25%)	1/8 (3.1%)	4/8 (50%)
Same as 1 other site	1/8 (12.5%)	1/8 (12.5%)	0/8 (---%)

*Source: ibid., Fig. 3. ANOVA results show no statistical significance for site or for the interaction of genotype and site (Ibid., Table 1).

Table 3: Overall Percentages of Differences in Behavioral Activity

(Number of Strains as Proportion of 32 tests in Table 1)

	Edmonton	Portland	Albany
Most active	24/32 (***75%***)	3/32 (*9.4%*)	1/32 (*3.1%*)
Intermediate	3/32	9/32	14/32
Intermediate	3/32 (*9.4%*)	9/32 (*28.1%*)	14/32 (***43.8%***)
Least active	1/32	17/32	14/32
Least active	1/32 (*3.1%*)	17/32 ***53.1%***)	14/32 (***43.8%***)
Same as 1 other site	4/32 (*12.5%*)	3/32 (*9.4%*)	3/32 (*9.4%)*

Notes

[i] See, respectively, the letters to *Science* by Larissa A. Phorecky; by Gerard B. Dawson, Jonathan Flint, and Lawrence S.Wilkinson; by René Hen; and by Michael G. Tordoff, Alexander A. Bachmanov, Mark I. Friedman, and Gary K. Beauchamp; and by Marina R. Picciotto and David W. Self, in "Testing the Genetics of Behavior," *Science,* 285 (1999) 2067. Another letter in this group, by Marina R. Picciotto and David W. Self, refers to "differences in investigators" or "unforeseen environmental factors." That Crabbe, Wahlsten, and Dudek were aware of a wide variety of potential confounding variations in experimental procedure is evident in the web site giving "details of procedures and test protocols" (http://www.albany.edu/psy/obssr).

[ii] In their reply to the letters cited in note 1, Crabbe, Wahlsten and Dudek do not exclude the possibility that any of these factors might interact with genotype in producing different behaviors. Indeed, they explicitly endorse the view of Picciotto and Self, who said: "We should not conclude from this study that behavioral analysis is beyond rigorous scientific investigation or that genetic engineering will not help elucidate the molecular basis of complex behaviors. We should instead use these results to highlight that scientific progress is a changing mosaic of overlapping studies that correct, build, and expand on earlier findings." (ibid.) It might be added that, in assessing the effect of the experimentor wearing a respirator in Edmonton, all sites had an exhaust fan which could conceivably have masked this effect or substituted a comparable one.

[iii] Although the authors do not explain this difference, they note that for the contrast between two strains which had earlier differed four times on this test in Portland, there was no difference at any site in the experiment reported in 1999 (Crabbe, Waldren, & Dudek, note 9). The authors suggest that perhaps genes from the embryonic stem cell substrains might "have subsequently been fixed differentially in the $5\text{-}HT_{1B}$+/+ and -/- strains maintained at Columbia University" (ibid.) Though an "undetected variable (for example a change in animal care personnel)" at Portland is also mentioned (ibid), it is conceivable that prenatal or neonatal effects of some environmental factor at the breeding laboratory influenced serotonergic functions linked to alcohol consumption. Although mouse strains were originally reared in three different locations (Bar Harbor, ME; Germantown, NY; and New York City – ibid., note 3), the absence of reported differences between mice shipped to experimental sites and their offspring reared on site would seem to exclude this possibility. Such questions are relevant althoujgh the absence of a preference for alcohol in Edmonton might seem to contradict the hypothesis presented below, this is not the case. As for violent crime, an obvious example of disinhibition,analysis of U.S. national data show that the percent of county population exposed to silicofluorides is strongly predictive of arrest frequency for drunken behavior after controlling for manyh other variables (Table 4). This finding does not contradict the experiment measuring preference for alcohol, which is not predictive of addiction or its behavioral manifestations such as arrests for drunken behavior (see Hyman and Malenka, 2001).

[iv] Robert Thurnau (National Risk Management Research Laboratory, US EPA) to Roger D. Masters, November 16, 2000 (letter available at: http://www.dartmouth.edu/~rmasters/ahabs.htm). The essential passage reads: "To answer your first queston on whether we have in our possession empirical scientific data on the effects of fluosilicic acid of sodium silicofluoride on health and behavior, our answer is no. Health effects research is primarily conductded by our National Health and Environmental Effects Research Laboratory (NHEERL). We have contacted our colleagues at NHEERL and they report that with the exception of some acute toxicity data,

they were unable to find any information on the effects of silicofluorides on health and behavior."

[v] Other considerations reinforce using silicofluoride to test the hypothesis that toxins in tap water can modify behavior in a laboratory experiment. While exposure to heavy metals such as lead could also explain the observed behavioral differences in the data of Crabbe et al., the actual levels of lead, manganese, or other heavy metals in the tap water used in the experiment cannot be reliably assessed ex post facto. While base-line levels of lead or manganese are often recorded for an entire public water system, variations from one building to another can easily confound these data. In addition, lead from paint in old housing or the pipes and pipe joints may vary sharply from one building to another in the same community. Finally, if lead or other toxins were present in other aspects of laboratory environments as well as in tap water, silicofluoride-treated water could probably have been a factor increasing toxin uptake in the test animals.

[7] As will be shown below (Tables 1a-b), the importance of toxicogenomics in behavioral research is underscored by its relevance to racial differences in human health and behavior. While not the principal reason for encouraging this approach, it provides an substantial benefit (especially insofar as some racial stereotypes may be influenced by the behavioral effects of neurotoxins). For example, Table 4 shows that controlling for 15 other variables including percent of population receiving water treated with silicofluorides, the percent of Blacks in a county's population is no longer a significant predictor of violent crime – and is *negatively* associated with the rate of arrest for drunken behavior.

[8]Myron J. Coplan, telephone call to Edmonton water quality laboratory (780-412-7638) on June 27, 1999. Jeffrey Kemnitz, telephone call to Epcor Water Services, Edmonton (703-412-7601) on August 8, 2001.

[viii] Jeffrey Kemnitz, telephone calls to Portland Water Bureau, Portland, Oregon (503 823 7770) on August 8, 2001; and to Albany Department of Water and Water Supply, Albany, N. Y. (518 343 5300) on August 8, 2001. In both cases, respondents confirmed that these cities do not use any fluoridation chemicals in their water supplies.

TO: ASSEMBLEE NATIONALE, PROVINCE OF QUEBEC

FROM: Prof. Roger Masters, Dartmouth College, Hanover, NH 03755

I've been informed of your desire for professional expertise with regard to the effects of "water fluoridation" as a public policy to be expanded in the Province of Quebec. My own research has concerned the differing side-effects of the COMPOUNDS used for the purpose of water fluoridation. At the outset, however, it is essential to establish several basic points of importance.

FIRST: The element FLUORINE (with an "N") is not generally stable unless in a compound -- and when in a compound, this element is called "FLUORIDE" (with a "D"). This matters because water fluoridation -- for the purpose of increasing the contact of fluoride on dental surfaces as a means of reducing tooth decay -- is necessarily a process using one of several different chemical compounds which carry a fluorine atom. They are:

sodium fluoride (NaF)
fluorosilicic acid (H2SiF6)
sodium silicofluoride (Na2SiF6)

SECOND: There is a major difference in the safety of these three chemical compounds. Sodium fluoride, familiar in toothpaste, has been extensively tested for safety and to my knowledge doesn't pose any health problems except for the bizarre case of a child who swallows several entire tubes of toothpaste. As normally used in toothpaste or in water treatment, on contact with water, the sodium fluoride splits into sodium + fluoride. If the fluoride bonds to the tooth surface (as is especially likely for sodium fluoride in toothpaste), caries frequency is reduced.

THIRD: The two silicofluorides are very different compounds than sodium fluoride. While the use of silicofluorides in water treatment was approved in 1950 by the U.S. Public Health Service, this action was taken without any testing whatsoever and based entirely on the "assumption" that the silicofluorides would "dissociate" into their component elements (Hydrogen + silicon + fluoride) or (sodium + silicon + fluoride). This assumption had never been adequately tested until it was observed in the following important article:

W. A. Finney, et al., "Reexamination of Hexafluorosilicate Hydrolysis by 19F NMR and pH Measurement,"
ENVIRON. SCI. TECHNOL. 40 (2006) 2572-2577.

Contrary to Westendorf's claim, the Finney et al. study does NOT show that silicofluorides leave behind a "residual species" that has biological activity that includes the inhibition of the enzyme acetylcholinesterase. What the Finney et al show is when added to water, the silicofluoride molecule does dissociate, with the following effects:

- the acidity of the water is increased (as shown by lower pH), which has the effect of inhibiting acetylcholinesterase function

• the silicon atoms dissociated from either H2SiF6 or Na2SiF6 cluster in what Finney et al describe as "oligomerization of silicic acid to discrete oligosilicates and colloidal silica"

What this means in plain English is that unlike sodium fluoride (which leaves behind merely atoms of sodium separated from atoms of fluorine), the silicon atoms from silicofluoride dissociation form structures or sheets of silicate.
As the history of "silicon breast implants" might remind us, this formation of silicates can produce dangerous biological changes, especially if the "oligosilicates and colloidal silica" are deposed in the brain, since they can easily block neurotransmitter receptors that play important roles in regulating behavior.

This is NOT merely a theoretical hypothesis: quite the contrary. Over a decade of peer-reviewed studies has shown that where American public water supplies use either of the silicofluorides for water fluoridation (which is the case for over 90% of artificially fluoridated water IN THE U.S.;sodium fluoride is only used to fluoridate relatively small community water systems -- as is the case in Hanover, NH where I live). Unlike sodium fluoride, public water treated with silicofluorides is significantly associated with the following:

• higher children's blood lead levels (due to greater absorption of lead from environmental exposures to sources like old housing or industrial pollution)
• lower grades in 9 different subjects and grades on the MCAS standardized educational tests use in Massachusetts schools.
• higher rates of arrest for driving under the influence of cocaine in New York state.
• higher rates of violent crime in multivariate analyses (using up to 12 independent variables) of official crime statistics for all
3141 counties in the U.S. (a study confirmed by separate analyses of violent crime data for 1985 and 1991).

Since none of these effects are observed where sodium fluoride is in use -- and the study by Finney et al. confirms a significant difference in the side-effects of sodium fluoride and silicofluorides (in their study, significant lowering of pH), it is not scientifically justifiable to consider water "fluoridation" without reference to the compounds used for this purpose. Sodium fluoride is, to my knowledge, quite safe when used as directed. In contrast, there is no research to my knowledge that contradicts the existence of harmful side-effects where silicofluorides are added to water; rather, a recent manuscript has just been sent me concerning unexpectly high levels of arsenic in much of the silicofluoride now use in the U.S., which consequent harmful effects on consumers).

The side-effect of acetylcholinesterase inhibition (which had been found by Westendorf in Germany in 1974, and is confirmed by Finney et al) entails the inactivation of the enzyme breaking down the neurotransmitter acetylcholine, which is a principal neurotransmitter activating motor behavior throughout the human body. (Put simply, for body activity, acethylcholine is an "ON" switch, and acetylcholinesterase is an "OFF" switch.

Putting silicofluorides in the water is therefore having the effect of turning the OFF switch OFF -- that is, increasing bodily activity. In short,
while a complete experimental study has never been done, it would seem plausible to hypothesize that among the factors responsible for the striking increase in rates of ADHD in the U.S., silicofluoride water treatment deserves careful study. This is particularly important because the other effects of

silicofluoride treated water cited above (all of which have been documented in scientific publications) can all be subsumed in the general functional category of poor behavioral inhibition or greater impulsivity (which is reinforced by the higher blood lead levels).

I have enclosed three files as a summary of over a decade of research coauthored by Myron J. Coplan (former Vice President of Albany Chemical, Inc.) and the undersigned.

Crabbe28b : is a reanalysis of animal studies in three cities, which revealed greater implusiveness in the behavior of laboratory animals (as measured by the frequency of choosing dark arm of a "Y" maze in a city using silicofluoride in water, whereas in the two other cities studied -- which didn't add silicofluoride to tap water -- laboratory animals always preferred the lighted arm of the "Y" maze.)

Adverse Effects Silicic Acid2: is a summary of the side-effects of water treated with either fluorosilicic acid or sodium silicofluoride.

SiFPubs7-28-11: is a bibliography of a decade of research on behavioral side effects of either H2Sif6 or Na2SiF6, of which the other attachments are merely examples.

None of these studies (or others of which I'm aware) show comparable negative side-effects where sodium fluoride is used in water fluoridation. As this indicates, the issue should NOT be "water fluoridation"; rather, the scientific question concerns the safety of substituting silicofluorides (which on one occasion were classified in Australia as "dangerous poisons" and are still considered "Hazardous" compounds) for sodium fluoride.

If requested I will gladly present the foregoing information as a legal deposition sworn under oath. For my credentials, feel free to consult WHO'S WHO IN AMERICA or other such documents.

Sincerely yours,

Roger D. Masters
Research Professor and Nelson A. Rockefeller Professor Emeritus, Department of Government, Dartmouth College, Hanover, NH 0375t

From ???@??? Sun Mar 22 03:54:29 2009
Date: 22 Mar 2009 03:54:29 -0400
From: Roger D. Masters
Subject: Fwd: More re siliic acid
To: MikeCoplan@aol.com
Bcc: Roger D. Masters

Adverse Effects of Silicic Acid 298K

Mike:

I've had this enclosure, which you sent me on Mar. 18, in my files since it was first written -- and I frequently have had the following thought.

It seems it would be possible to shape this into an important bibliographic notice to submit for publication (whether to Joan Cranmer for publication in NEUROTOXICOLOGY and/or presentation to the next Neurotoxicology conference, or to another scientific publication). What do you think?

My point is that the manuscript should have the form of a bibliographic essay on a seriously neglected toxin (without primary reference to our work though a footnote listing our major publications would be appropriate).

I don't think much editorial tinkering is involved. I'd obviously prefer that you do this if you agree. However, if you would like me to play with it for your consideration, I'll give it a try.

For example, a possible introductory paragraph could read:

"This bibliographic note presents evidence that "silicic acid" is a largely ignored toxic compound which should be the subject of extensive research due to its potential for biochemical effects harmful to human health and behavior. Before presenting a bibliographic survey of what is known about this compound, a brief rationale is needed:

"ONE: What is Silicic Acid and Why Should It Be Studied Further? (bold title)

(text on first page)

"TWO: Iler's Description of Silicic Acid Toxicity" (bold title)

p. 764 of THE CHEMISTRY OF SILICA

"THREE: Annotated Bibliography of Silicic Acid Biochemistry" --

  remainder of your file,with any changes you think appropriate.

"FOUR: Conclusion"
   Any final remark (a single paragraph will do) on your view of what needs
doing (starting of course with action on the NTP nomination). AND in so doing,
should that nomination be copied into the file?

You should of course be the sole author of this Research Note.

(I presume the half line "polymers registers with that of the repeat units of
polypeptides" should be moved up to follow immediately the words "bonding sites
of" (and before the structural sketch of oligomers of Si(OH)4.

--- Forwarded Message from MikeCoplan@aol.com ---

>From: MikeCoplan@aol.com
>Date: Wed, 18 Mar 2009 16:42:54 EDT
>Subject: Fwd: More re siliic acid
>To: Roger.d.Masters@Dartmouth.edu

I. Publications

Masters, R,, Hone, B, and Doshi, A. (1998). "Environmental Pollution, Neurotoxicity, and Criminal Violence," in J. Rose, ed., *Environmental Toxicology: Current Developments* (London: Gordon and Breach, 1998), pp. 13-48.

Survey of evidence linking lead and manganese neurotoxicity to aggressive behavior and crime, presenting multivariate analysis correlating Toxic Release Inventory for lead and manganese with crime data for 1991 from all 3141 US counties Emphasizes effects of heavy metals on neurotransmitter function and behavior.

Masters, Roger D., with Baldwin Way, Brian T. Hone, David J. Grelotti, David Gonzalez, and David Jones (1998) "Neurotoxicity and Violence," *Vermont Law Review*, 22:358-382.

Legal implications of the evidence linking neurotoxicity and crime (including data from Toxic Release Inventory and crime for partial sample of US counties)

Masters, R. and Coplan, M. (1999a) "Water Treatment with Silicofluorides and Lead Toxicity," *International Journal of Environmental Studies*, 56: 435-49

First published analysis of data linking silicofluoride treatment of public water supplies with higher uptake of lead, focused on survey of children's blood lead in Massachusetts (by town).

Masters, R. and Coplan, M. (1999b) "A Dynamic, Multifactorial Model of Alcohol, Drug Abuse, and Crime: Linking Neuroscience and Behavior to Toxicology," *Social Science Information*, 38:591-624.

Articulation of the linkages between neurotoxicity, brain chemistry, environmental pollution, and behavior (with focus on substance abuse and crime), using data from National Institute of Justice study of drug use in over 30,000 criminal offenders at time of arrest). Data show that where silicofluorides are in use, criminals are more likely to consume alcohol, more likely to have used cocaine at time of arrest – and that communities have significantly higher crime rates.

Coplan, M.J. and Masters, R.D. (1999). "Is Silicofluoride Safe? Comments Re EPA Response to Rep. Calvert's Inquiry" Submission to Representative Kenneth Calvert, Subcommittee on Energy and Science, Committee on Scienc e, U. S. House of Representative (August 12, 1999).

Analysis and rejoinder to letter dated 12 June 1999 from J. Charles Fox, Assistant Administrator, EPA, to Hon.Kenneth Calvert, U. S. House of Representative, commenting on errors and omissions in a "Question and Answer" statement and "Fluorosilicate Fact Sheet" enclosed by Mr. Fox. This document contains a preliminary review of scientific data on the differences between sodium fluoride (NaF) and the silicofluorides (H_2SiF_6 and Na_2SiF_6), with an emphasis on the complex production process and chemical interactions of the latter compounds.

Masters, R. and Coplan, M. (1999b) "A Dynamic, Multifactorial Model of Alcohol, Drug Abuse, and Crime: Linking Neuroscience and Behavior to Toxicology," *Social Science Information*, 38:591-624.

Articulation of the linkages between neurotoxicity, brain chemistry, environmental pollution, and behavior (with focus on substance abuse and crime), using data from National Institute of Justice study of drug use in over 30,000 criminal offenders at time of arrest). Data show that where silicofluorides are in use, criminals are more likely to consume alcohol, more likely to have used cocaine at time of arrest – and that communities have significantly higher crime rates.

Masters, R.D. and Coplan, M.J. (1999c). "The Triune Brain, the Environment, and Human Behavior: Hommage to Paul MacLean," to appear in Russell Gardner, ed. *Festschrift in Honor of Paul MacLean* . First presented at Back Bay Hilton Hotel, Boston, Mass. – July 16, 1999

Wilson, Jim (1999). "The Chemistry of Violence," *Popular Mechanics*, (April), pp. 42-43.

Journalist's report on Masters' earlier research on toxins and violence, and its extension in collaborative work with Coplan.

Coplan, M.J. and Masters, R.D. (1999). "Is Silicofluoride Safe? Comments Re EPA Response to Rep. Calvert's Inquiry" Submission to Representative Kenneth Calvert, Subcommittee on Energy and Science, Committee on Science, U. S. House of Representatives (August 12, 1999).

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preliminary review of scientific data on the differences between sodium fluoride (NaF) and the silicofluorides (H_2SiF_6 and Na_2SiF_6), with an emphasis on the complex production process and chemical interactions of the latter compounds.

Masters, R.D., Coplan, M. J., Hone, B.T., and Dykes, J.E. (2000)."Association of Silicofluoride Treated Water with Elevated Blood Lead," *Neurotoxicology* 21: 101-1100.

Follow-up epidemiological study of the association between silicofluoride treated community water and enhanced child blood lead parameters. This statistical study of 151,225 venous blood lead (VBL) tests taken from children ages 0-6 inclusive, living in 105 communities with populations from 15,000 to 75,000 in New York state, shows for every age and racial group a significant association between silicofluoride treated community water and elevated blood lead.

Roger D. Masters (2001), "Biology and Politics: Linking Nature and Nurture" in Nelson W. Polsby, ed., *Annual Review of Political Science*, vol. 4, pp. 45-369.

A survey of the scope of the emerging subfield called "biopolitics," reflecting the activities of the membership of the Association for Politics and the Life Sciences. Four areas are discussed in some detail: 1). genetics and health; 2), toxins and behavior (including hyperactivity, depression, and violent crime), 3) the specific case of silicofluorides in water treatment and their effect in enhancing lead uptake; and 4) biopolitics and political theory.

Note: one-time e-print available at following URL:
http://polisci.annualreviews.org/cgi/content/full/4/1/345?ijkey=0K1GnNcUKf2Gg&keytype=ref&siteid=arjournals

Myron J. Coplan and Roger Masters. 2001. "Guest Editorial: Silicofluorides and fluoridation," *Fluoride Quarterly Journal of the International Society for Fluoride Research,* 34: 161-220.

Masters, R.D. (2002). "MacLean's Evolutionary Neuroethology: Environmental Pollution, Brain Chemistry, and Violent Crime," Gerald A. Corey Jr. & Russell Gardner Jr., eds. *The Evolutionary Neuroethology of Paul MacLean* (Westport: Praeger), pp. 275-296 (Ch. 15).

Survey of research on neurotoxicity, brain chemistry and behavior, including evidence of the role of lead and other heavy metal pollution and crime (as demonstrated by individual data, neurochemistry, and both geographic and longitudinal data) as well as survey of data linking silicofluorides to enhanced lead uptake. First publication of findings on the extremely high correlation ($r = .90$) between gallons of leaded gasoline sold and the crime rates sixteen years later, confirming special vulnerability of pregnant mothers and newborns to lead toxicity.

First presented at conference in 1999 (see under conference presentations).

Roger D. Masters, 2003. "Neurotoxicology and Violence," in Richard W. Bloom and Nancy K. Dess, eds., *Evolutionary Psychology and Violence: A Primer for Policymakers and Public Policy Advocates* (Praeger/Greenwood), Ch. 2, pp. 23-56.

Analysis of evidence of neurotransmitter dysfunction due to toxins associated with increased rates of violent crime, with extensive discussion of silicofluoride neurotoxicity as an important instance.

Masters, R. D. and Coplan, M. J., with Hone, B.T., Grelotti, D. J., Gonzalez, D. and Jones, D. (in press). "Brain Biochemistry and the Violence Epidemic: Toward a 'Win-Win' Strategy for Reducing Crime," in Stuart Nagel, ed., *Super-Optimizing Examples Across Public Policy Problems* (NOVA Science Publishers) (in press).

Review of the evidence linking neurotoxicity and crime, using data from both county-level study (correlating EPA Toxic Release Inventory with FBI crime reports) and Massachusetts data on silicofluorides and lead uptake.

Masters, Roger D. "Science, Bureaucracy, and Public Policy: Can Scientific Inquiry Prevail Over Entrenched Institutional Self-Interest?" *New England Journal of Political Science*, in press (2005).

Coplan, Myron J., Patch Steven C., Masters, Roger D., and Bachman, Marcia S. (2007), "Confirmation of and explanations for elevated blood lead and other disorders in children exposed to water disinfection and fluoridation chemicals,"*Neurotoxicology* 28:1032-1042.

Confirmation of significant association between silicofluoride use in local water water supplies and significant increase in absorption of lead from environmental sources, based on children's blood lead data from National Health and Nutrition Evaluation Survey III, counties of over 150,000 population.

Research Activities

Silicofluorides, Neurotoxicity and Behavior (with Myron J. Coplan, P.E., Intellequity Consulting, Natick, MA). See list of "recent publications" on this area below.

Principal empirical work in this area has focused on epidemiological analysis of samples of children's blood lead or other geograhical data on health and behavior, exploring the effects of the injection of fluosilicic acid of sodium silicofluoride (chemicals never properly tested for health and behavioral effects). Because of the highly controversial nature of this research, it has entailed extensive contacts with staff at the House and Senate as well as EPA, NIH, and CDC personnel.

Superfund sites and toxic uptake among the Oujé Bougaumau Cree (with Christopher Covel, geological engineer, Lyndeborough, NH).

A new area based on Covel's field work among the Oujé Bougaumau Cree of Quebec, based on soil samples, water samples, and fish samples (as evidence of environmental pollution from mine tailings) and head hair samples (as measures of toxic uptake among Cree). Data now under analysis.

Web-site:

Research on Silicofluorides, Neurotoxicity, and Behavior

Myron J. Coplan, Roger D. Masters, and assistants

Overall site for Roger Masters' research:
http://www.dartmouth.edu/~rmasters/

Recent Presentations to Scientific Conferences:

Masters, R.D. and Coplan, M.J. "Silicofluoride Usage and Lead Uptake," Presentation to XXIInd Conference of the International Society for Fluoride Research, Bellingham, Washington, August 24-27, 1998.

> Report on findings of elevated blood lead associated with communities using silicofluoride, based on sample of over 250,000 children in Massachusetts (see Masters and Coplan, 1999a)

Masters, R.D. and Coplan, M.J. "The Triune Brain, the Environment, and Human Behavior," Presentation to *Festschrift in Honor of Paul MacLean* . Back Bay Hilton Hotel, Boston, Mass. – July 16, 1999 (see Masters and Coplan, 1999c).

Masters, R. D. . "Poisoning the Well: Neurotoxic Metals, Water Treatment and Human Behavior," Plenary address to Annual Conference of the Association for Politics and the Life Sciences," Four Seasons Hotel, Atlanta, GA (September 2, 1999).

> Review of evidence linking heavy metal pollution with substance abuse and crime, including presentation of data linking ban on sales of leaded gasoline with decline in crime 16 years later. Summary of geographical data analyses contradicting the "null hypothesis" that there is no difference in the effects of sodium fluoride and the silicofluorides.

Coplan, M. J., Masters, R. D., and Hone, B. (1999a) "Silicofluoride Usage, Tooth Decay and Children's Blood Lead," Poster presentation to Conference on "Environmental Influences on Children: Brain, Development and Behavior, New York Academy of Medicine, Mt. Sinai Hospital, New York, May 24-25, 1999.

> Preliminary report on data from analysis of national sample of over 4,000 children in NHANES III, showing that while water fluoridation is associated with a significant increase in children's blood lead (with especially strong effects among minority children), data on tooth decay from the same survey show limited benefits that are no longer evident among those aged 15-17.

Coplan, M.J., Masters, R.D., and Hone, B. (1999b) "Association of Silicofluoride Treated Water with Elevated Blood Lead," Poster presentation to 17th International Nerotoxicology Conference, Little Rock, AR, October 17

> Preliminary report on data from analysis of sample of blood lead testing of over 150,000 children in New York State communities of 15,000 to 75,000 population.

Once again, average blood lead levels were significantly higher ($p < .0001$) in communities using silicofluorides in water treatment than in those with unfluoridated water. The effect was found independently in every age group for three ethnic subsamples

Masters, R.D. and Coplan, M. J. (2001). "Silicofluorides and Enhanced Lead Uptake," Behavaioral Toxicology Society, ,annual meetings, Research Triangle Park, NC., May 6
Suvey of findings in research in this area.

Masters, R.D. (2002), "Toxins and Behavior: Implications of 'Toxicogenomics' for Public Policy," Paper presented to XXth International Neurotoxicology Conference, Little Rock, ARK-Nov. 19.