

From: Bill Osmunson [redacted]

Sent: Friday, October 28, 2016 4:39 PM

To: Thayer, Kristina (NIH/NIEHS) [E] <thayer@niehs.nih.gov>

Subject: RE: Rocha Amador's F/IQ study (Prenatal Exposure) - Latest results

Dear Kristina,

Please note the attached research by Zhang (2015) et al and graphic.

Would it be possible to include COMT SNP testing with the animal studies NTP is currently doing?

Note the rather low fluoride concentrations (1.4 mg/l vs 0.6 mg/l) and fluoride urine and serum were measured, increasing confidence in individual total exposure.

Zhang (2015) reports that some people with certain genetic variations (SNPs or single nucleotide polymorphisms) had a greater reduction in IQ than people without those variations. It is my understanding that SNPs are not the same as genetic diseases. Some SNPs can be common, with 10, 20 or more percent of the population having a particular SNP. Zhang (2015) reported that people with two "fluoride susceptibility" SNPs (in this case "Val" and Met" variants) had lower IQ than those with a single SNP.

For all the subjects, there was a very strong negative relationship: the higher the serum or urine F level, the lower the IQ. Subjects with the highest serum or urine F had IQs that averaged about 12 points less than those with the lowest F levels. See Zhang (2015) Figure 1

For people with no copy of the "val" "susceptibility SNP" the decrease in IQ averaged only about 1.45 points per 1.0 mg/L increase in urine F, a small and difficult to detect decrease in IQ. But for people with two "val"s the average decrease in IQ was 9.67 points per 1.0 mg/L increase in urine F. These people were therefore 650% more sensitive than the people with two "met"s. People with one each "val" and "met" had an intermediate decrease in IQ of 4.67 points per 1.0 mg/L increase in urine F. All of this is shown in Table 3 of the paper.

Urine fluoride concentrations were higher than US children with similar water fluoride concentrations. Either they drank more water or had another source of fluoride.

If the dose-response relationship found in this study is extrapolated to 0.0 mg/L, for someone with the val/val genotype, they loose about 10 IQ points per 1.0 mg/L increase in urine F. Therefore, such a person drinking 0.1 mg/L water might be predicted to loose 1 IQ point compared to if they were drinking water with 0.0 mg/L F. Current HHS recommendation of (0.7 mg/L F) compared to drinking low F water with 0.1 mg/L is about 6 points lost.

Presumably the parents of these children had similar exposures.

In addition, the synergistic effects of other neurotoxicants should be considered.

Regards,

Bill

References cited (this citation was added by the National Toxicology Program):

Zhang S, Zhang X, Liu H, Qu W, Guan Z, Zeng Q, Jiang C, Gao H, Zhan C, Lei R, TXia T, Wang Z, Yang L, Chen Y, Wu X, Cui Y, Yu L, Wang A. 2015. Modifying Effect of COMT Gene Polymorphism and a Predictive Role for Proteomics Analysis in Children's Intelligence in Endemic Fluorosis Area in Tianjin, China. *Toxicological sciences : an official journal of the Society of Toxicology* 144(2):238-245.