



Virginia Commonwealth University
VCU Scholars Compass

Theses and Dissertations

Graduate School

2005

Blood Lead and Decision Speed in Working Age Adults

S. W. Harkins

Virginia Commonwealth University

Follow this and additional works at: <http://scholarscompass.vcu.edu/etd>

 Part of the [Epidemiology Commons](#)

© The Author

Downloaded from

<http://scholarscompass.vcu.edu/etd/772>

This Thesis is brought to you for free and open access by the Graduate School at VCU Scholars Compass. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of VCU Scholars Compass. For more information, please contact libcompass@vcu.edu.

Blood Lead and Decision Speed in Working Age Adults

by

S. W. Harkins, PhD, FGSA

Leonard Vance, PhD, J.D.
Advisor

Department of Epidemiology and Community Health
Master of Public Health Program
MPH Research Project: PMCH 691

August 2005

HARKINS, S. W.

Research Project Agreement Form
Department of Epidemiology and Community Health

Student name: S. W. Harkins E-mail address:
Street address:
Home phone: Work phone: Fax:
Number of semester hours (3-6): 3 Semester: Spring Year: 2005

Please complete the following outline. **Do not exceed 2 pages (A-H).**

A. PROJECT TITLE: LEAD TOXICITY IN WORKING AGE ADULTS:
NEUROBEHAVIORAL CORRELATES IN THE THIRD NATIONAL HEALTH
AND NUTRITION SURVEY

B. PURPOSE (state hypothesis/research question): Hypotheses: Blood lead levels are not related to simple signaled reaction time, digit symbol substitution test accuracy or digit symbol substitution test time to completion.

C. SPECIFIC OBJECTIVES (list major aims of the study): Test hypotheses in B

D. DESCRIPTION OF METHODS

D.1. Identify source(s) of data (eg, existing data set, data collection plans, etc): THE THIRD NATIONAL HEALTH AND NUTRITION SURVEY-Analyses require use of the Adult, Exam and Lab files.

D.2. State the type of study design (eg, cross-sectional, cohort, case-control, intervention, etc): Cross-sectional design.

D.3. Describe the study population and sample size: Individuals age 20 to 59 from NHANES-III who have neurobehavioral test results and blood lead levels. N ~ 5,092, with over representation of non-Hispanic blacks and Hispanics.

D.4. List variables to be included (If a qualitative study, describe types of information to be collected) Outcomes of interest are simple reaction times (msec), accuracy of performance of the digit substitution task and time to complete this task in relation to the following independent variables (blood lead level controlling variously for age, sex, race/ethnicity, education, and selected health behaviors -- smoking, and Ethol by self-report and cotinine and blood Ethol levels).

D.5. Describe methods to be used for data analysis (If a qualitative study, describe general approach to compiling the information collected)
SAS callable SUDAAN (v. 8) and SUDAAN stand alone Beta V9.00 linear regression.

E. ANTICIPATED RESULTS: Possible demonstration that lead is a risk factor for impaired neurobehavioral test performance in adults

F. SIGNIFICANCE OF PROJECT TO PUBLIC HEALTH: Evidence that current accepted NIOSH AND OSHA blood lead levels for adults are perhaps too high.

HARKINS, S. W.

G. IRB Status:

1) Do you plan to collect data through direct intervention or interaction with human subjects? **No**

2) Will you have access to any existing identifiable private information? **_ no**
If you answered "no" to both of the questions above, IRB review is not required.
If you answered "yes" to either one of these questions, your proposed study must be reviewed by the VCU Institutional Review Board (IRB). Please contact Dr. Turf or Dr. Buzzard for assistance with this procedure.

Please indicate your IRB status:

- to be submitted (targeted date _____)
- submitted (date of submission _____; VCU IRB # _____)
- IRB exempt review approved (date _____)
- IRB expedited review approved (date _____)
- IRB approval not required

H. PROPOSED SCHEDULE: Start Date: In progress End Date: 5/05

I. INDICATE WHICH OF THE FOLLOWING AREAS OF PUBLIC HEALTH KNOWLEDGE WILL BE DEMONSTRATED:

1. Biostatistics – collection, storage, retrieval, analysis and interpretation of health data; design and analysis of health-related surveys and experiments; and concepts and practice of statistical data analysis. **yes**
2. Epidemiology – distributions and determinants of disease, disabilities and death in human populations; the characteristics and dynamics of human populations; and the natural history of disease and the biologic basis of health. **yes** (if yes, briefly describe): **Simple descriptive summary of blood lead burden in working age Americans (age 20 to 59), by age, gender, race-ethnicity and impact, if any, of lead on neurobehavioral deficits.**
3. Environmental Health Sciences – environmental factors including biological, physical and chemical factors which affect the health of a community. **yes** (if yes, briefly describe): **Lead burden in adults.** Time permitting this in relation of occupation.
4. Health Services Administration – planning, organization, administration, management, evaluation and policy analysis of health programs. **no** (if yes, briefly describe):
5. Social/Behavioral Sciences – concepts and methods of social and behavioral sciences relevant to the identification and the solution of public health problems. **yes** (if yes, briefly describe): **Secondary findings possible involving evaluation of neurobehavioral indices in survey research in diverse populations of adult Americans and health behaviors of smoking and Ethol. use hx.**

TABLE OF CONTENTS

ABSTRACT	v
INTRODUCTION AND OBJECTIVE	1
METHODS	5
RESULTS	8
DISCUSSION AND CONCLUSION	11
REFERENCES	14
TABLES	19

ACKNOWLEDGEMENTS

My sincere thanks and appreciation to Dr. Saba Masho, M.D., Dr.P.H , whose joy for numbers makes epidemiological research come alive, to Dr. R. LEONARD VANCE, PH.D., JD, PE, CIH, CSP whose encyclopedic knowledge of the field of environmental health led to this effort and to Dr. Jack O. Lanier, Dr.PH., FACHE for allowing me to attempt to come to grips with research in this paper in relation to environmental and social injustice. While I failed in developing issues of injustice here perhaps the seeds are sown. There is much very important work still to be done and the search for causal relations is sorely needed, as is the political will to address critical problems contributing to environmental poison.

I thank Dr. Adera for all of his considerations. As we both know the ultimate directive, *Nosce te ipsum*, is always a process of successive approximations.

Blood Lead and Decision Speed in Working Age Adults:

S. W. Harkins

ABSTRACT

Lead is a central nervous system poison. Healthy People 2010 established a target blood lead level (BLL) for children of 0 $\mu\text{g}/\text{dL}$ by 2010, but is silent with regard to any changes in BLLs standards for working age adults. In this paper, the relation of BLL to performance on two neurobehavioral tests was assessed in working age adults (N = 4909; Age 20 to 59 years; 51.4% Female) employing data from the Third National Health and Nutrition Survey (NHANES III). Multiple linear regression analyses indicated a significant effect of BLL on time taken to complete an attention demanding cognitive task (Symbol Digit Substitution Task, SDST) but not accuracy of performance of the SDST or simple reaction time, after controlling for confounding variables of age, sex, race-ethnicity, and education. Persons with $\text{BLL} \geq 5 \mu\text{g}/\text{dL}$ took longer (multivariate adjusted mean = 23.6 Sec, SE = 0.30) compared to individuals with $\text{BLLs} < 5 \mu\text{g}/\text{dL}$ (mean = 22.5 Sec, SE = 0.14). The results suggest that lead burden in working age persons impairs central nervous processes involving executive mental functions (decision speed and attention). The findings, if confirmed by case control and or cohort studies would indicate a need to reconsider currently accepted lead levels in working age adults.

INTRODUCTION AND OBJECTIVE

Pliny The Elder (Gaius Plinius Secundus, A.D. 23-79) a close friend of Vespasian (Titus Flavius Vespasianus, Roman Emperor A.D. 69-79) died while observing the eruption of Vesuvius, but not before the publication of his major work, *Historia Naturalis*, (Dedicated to Titus, A.D.77). *Historia Naturalis* consists of some 37 volumes and is a major resource in the study of early Western Civilization.

Pliny wrote about the importance of protecting natural resources, appropriate selection and use of medicines, accuracy of diagnoses and quality of the physicians of his time. In Rome, during this period lead acetate was used to sweeten wine and for its antibacterial properties. Pliny's interest in wine and its preparation is reflected in his instructions for increasing the sugar content of "common wine" by boiling it in lead jars:

... new wine should be boiled [boiled-down like maple syrup] when there is no moon, which means at the conjunction of that planet, and not on any other day, and moreover **leaden and not copper jars should be used**, [emphasis added] and some walnuts should be thrown into the liquor, for those are said to absorb the smoke (XIV.136).

Today, some argue the decline and fall of the Roman Empire was due to the systematic poisoning of the population by lead.

Lead is a multi-system poison that can be breathed, ingested, and, in certain forms, absorbed through skin. Lead has a dose response effect on the developing nervous system, impairing cognitive, affective, and social development.^{1, 2} Beginning in 1978, the Centers for Disease Control and Prevention (CDC) lowered blood lead level (BLL) values for children from 60 µg /dL to a current value for intervention of 10 µg /dL.³ Deficits in mental abilities, however, have been observed in children with BLL below 10

$\mu\text{g}/\text{dL}$.⁴⁻⁷ Healthy Americans 2010 recognized the toxicity of lead at any level for the developing nervous system and established a target value of 0 $\mu\text{g}/\text{dL}$ for children by 2010.⁷ Considerably less attention has been devoted to possible effects of lead on mental abilities in working age and older adults.

Current National Institute of Occupational Safety and Health⁸ (NIOSH) and Occupational Safety and Health Administration⁹ (OSHA) guidelines for BLLs in occupationally-lead-exposed workers are considerable higher than that set for children ($\geq 25 \mu\text{g}/\text{dL}$ ⁸ and $\geq 40 \mu\text{g}/\text{dL}$ ⁹, respectively). While some studies found no relation between adult lead burden and neurobehavioral variables,¹⁰ most report that lead burden adversely influences mental development and impairs cognitive function,¹¹⁻¹⁴ particularly on effortful, attention-demanding, speeded-tasks involving executive functions. Old age may not be a barrier to adverse effects of lead on mental abilities. BLLs as low as 5 $\mu\text{g}/\text{dL}$ may adversely influence memory, language, visuospatial and sensory motor function in older women¹⁵ and men.¹⁶

Between NHANES II (1976 – 1980) and Part One of NHANES III (1988 to 1991) the prevalence of persons one year of age and older with a BLL of 10 $\mu\text{g}/\text{dL}$ or greater declined from 77.8% to 4.4%. The population estimated mean BLLs decreased from 12.8 $\mu\text{g}/\text{dL}$ in NHANES II to 2.9 $\mu\text{g}/\text{dL}$ in Phase I of NHANES III. The decline continued in the brief interval between the two phases of NHANES III, where individuals with BLLs of 10 $\mu\text{g}/\text{dL}$ or greater decreased from 4.4% in Phase I to 2.2% in Phase II (1991 – 1994).^{17,18} Nevertheless, heavy metal burden, often acquired early in life, likely has long-term effects on mental abilities later in life. Both occupational and general

environmental lead exposure appears to have a progressive effect on cognitive decline as a function of cumulative dose, particularly in the domains of executive mental abilities.

Figure 1 illustrates the success of both voluntary and regulatory activities designed to reduce lead load in the general population of the United States. Shown in this figure are age, sample weight adjusted mean values of BLLs from NHANES II AND NHANES III.

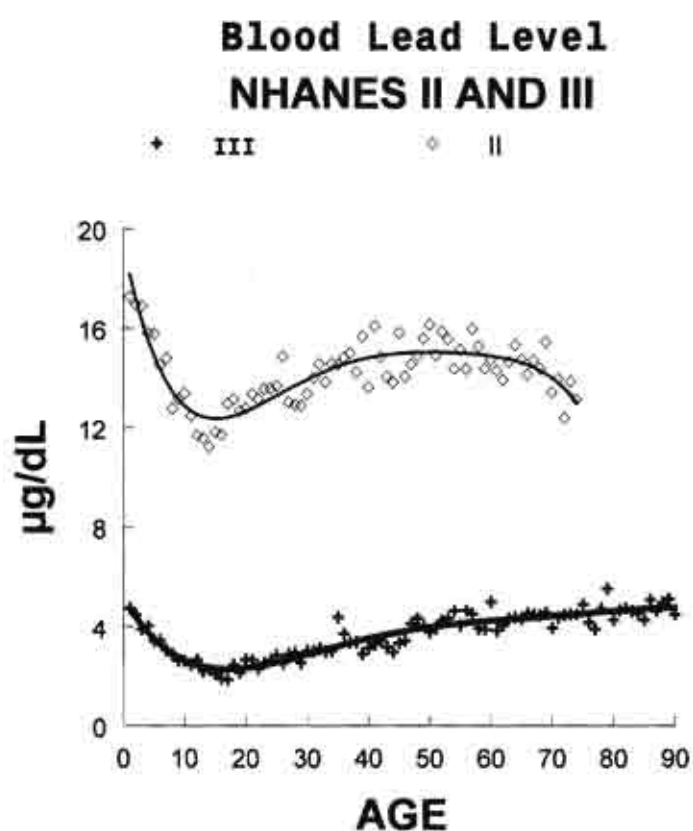


Figure 1: Blood lead levels from participants in NHANES II (Top curve) and III (Bottom curve). Note that BLLs decrease with age to approximately 15 to 17 years of age in both surveys and then increase. (Harkins, S. W. Analyses and graphic of 2005)

NHANES III included neurobehavioral testing on a subsample of persons age 20 to 59. This component of NHANES III involved tasks specifically designed to assess for impaired higher-order central nervous system functioning in populations at risk of exposure to neurotoxins and chemicals associated with impaired CNS function.¹⁹⁻²¹ One report found no relations of BLL with simple reaction times, accuracy of performance on a symbol-digit substitution task and serial digit learning.²² This report did not, however, comment with regard to time taken to complete the symbol-digit substitution task. Time taken to complete this type of test of mental abilities reflects mental decision time and executive function that can be independent of task performance. This is most clearly seen in differences in task performance where speed may be traded for accuracy (speed-accuracy trade off) and vice versa. Several studies^{10-16,21} suggest a relation between BLL and mental processes mediating timed performance on tasks such as the symbol-digit task employed in NHANES III. The objective of the present study was to replicate earlier findings of no effect of BLL on simple reaction times or symbol-digit substitution accuracy²² and extend the analyses to include decision speed on the symbol-digit substitution task, a task involving sustained, effortful attention and executive function.

METHODS

Subjects: Analyses here were based on the Central Nervous System (CNS) Examination Subsample of the Third National Health and Nutrition Examination Survey (NHANES III).²³ The National Health and Nutrition Examination Survey (NHANES) is a periodic survey conducted by the National Center for Health Statistics (NCHS). NHANES III, conducted from 1988 through 1994 in two parts, was the seventh in a series. NHANES III was designed to provide national estimates of the health and nutritional status of the United States' civilian, noninstitutionalized population aged two months and older. Selected populations (younger and older persons, non-Hispanic blacks, and Hispanics) were over sampled to improve prevalence estimates in these persons.

A sub-sample of non-pregnant, English and Spanish speaking examinees between the ages of 20 and 59 years were randomly selected for the Central Nervous System Function Evaluation.^{23,24} The sample used in the present study (N = 4925; Mean age 37.1 years; SE = 0.23; Range 20 – 59; 50.8% female) consisted of persons with complete information on the variables of interest.

Blood Lead Level: Using blood collected by venipuncture during the physical examination component of NHANES III, blood lead concentration was assessed employing graphite furnace atomic absorption spectrophotometry.^{25, 26}

Central Nervous System (CNS) Function: Three computerized neurobehavioral tests were used to evaluate cognitive functioning in the CNS-subsample of NHANES III¹⁹⁻²⁰.

²⁴ These neurobehavioral tests are part of a computerized test battery (the Neurobehavioral Evaluation System; NES) originally designed to measure

neurobehavioral performance in populations at risk of environmental or occupational exposure to neurotoxins and poisons.²⁴ The tests employed in NHANES III were: (1) a simple reaction time test (SRTT), a measure of motor response speed to a visual stimulus; (2) a symbol-digit substitution test (SDST), a test of coding ability involving effortful attention; and (3) a serial-digit learning test (SDLT), a short-term memory test. The current study was restricted to the two speeded tests, the SRTT and the SDST.

The SRTT measures simple reaction time (RT). It requires minimal information processing load or mental operation. Simple RT tasks are highly sensitive to chronological age and generally are performed faster by men than women.

The SDST, based on the Wechsler Adult Intelligence Scale, Digit Substitution Task,²⁷ is a timed task involving matching a series of single digit numbers and non-sense shapes. It requires effortful attention for accurate performance. It assesses “mental efficiency” and executive functions. Time taken to complete this task and to a lesser degree accuracy are non-specific indicators of possible CNS impairment at multiple levels of information processing and complex-decision making, including motor function, visual-motor coordination, perceptual organization and selective attention.²⁸ Performance on this task correlates in the .30 to .50 range with both verbal and performance IQ scores.²⁸ Both accuracy and time to complete this type of task are age sensitive.²⁹

Demographic variables: Demographic variables of age, sex, race-ethnic background and education were employed as possible confounding variables in regression analyses testing relations among the neurobehavioral measures and BLLs. Race was based on

NHANES – III categories: white-Non-Hispanic; Black-Non-Hispanic; Hispanic; and Other. Education was coded as completing versus not-completing high school.

Statistical Analyses: Demographic variables were calculated as means and variance estimates for continuous variables and percentages for categorical variables by race and gender. Interactions between lead and race and lead and gender were examined. Age- and multivariate-adjusted linear regression models were used to test relations of BLL with the neurobehavioral performance variables, stratified by race and gender. Following Vupputuri, et al., (2003)³⁰ we modeled effects of higher lead levels (BLL => 5ug/dL) on performance of the SDST.

All analyses were weighted for the complex sampling methodology of NHANES III using SAS³¹ callable SUDAAN.³² The total NHANES III CNS examination component final weight (WTPFCNS6) was employed in all analyses in these analyses.³²

RESULTS

Mean age of the sample was 37.1 years (SE = 0.24; Range 20 to 59 years).

Demographic information is summarized in Table 1. Also shown in Table 1 are findings concerning BLL and neurobehavioral performance for the sample and for each of the demographic subgroups. As shown in Table 1 mean BLL for the study sample was 3.26 $\mu\text{g/dL}$ (SE = 0.23; N = 4925), a value substantially below current OSHA or NIOSH guidelines for working age adults in occupations involving lead exposure risk. As shown in Table 1, BLLs were higher in males (4.19 $\mu\text{g/dL}$; SE = 0.12) than females (2.37 $\mu\text{g/dL}$; SE = 0.10), were lowest in the white non-Hispanic sample and were higher in individuals with less than a high-school education compared to those with a high-school or more education (See Table 1).

Table 1 also shows simple reactions times (SRTT), accuracy on the symbol digit substitution task (SDST) and time taken to complete the SDST for the sample and for each demographic group. Simple reaction times (in milliseconds) were remarkably stable across the different groups and accuracy on the digit substitution task approached the ceiling value of 8 (Population M = 7.71; SE 0.01) with little variation among the groups. In contrast, there was greater variability between the groups in time taken to complete the symbol digit substitution task.

Regression analyses employing these data are summarized in Table 2. BLLs were not related to simple RT or accuracy on the digit substitution task, confirming earlier findings.²² Mean RT on the SRTT were significantly related to all demographic variables (See Table 2). Being younger, male, better educated, or non-Hispanic white

was associated with faster simple RTs (Means values provided in Table 1). While accuracy on the SDST approached the maximum of eight correct responses in each subgroup based on the demographic variables (Table 1) it was also significantly related to the demographic variables. Being younger, male, better educated and non-Hispanic white but not BLL were all related to more accurate performance of the SDST (Tables 1 & 2).

Lead load was related to time taken to complete the digit substitution task. On average it took nearly 23 seconds (Mean 22.75; SE = 0.21; Table 1) to complete the SDST. Being younger, female, having a high school or greater education, and being non-Hispanic white were associated with shorter total time to complete the SDST. After controlling for these demographic variables, BLLs were directly related to time taken to complete the SDST (beta = 0.16; SE = 0.05; $p = 0.003$; Model $R^2 = 0.354$; Table 2).

Following Vupputuri, et al.,³⁰ the sample was divided into groups based on BLL below 5 $\mu\text{g}/\text{dL}$ or a value of 5 $\mu\text{g}/\text{dL}$ or greater. Individuals with low BLLs ($< 5 \mu\text{g}/\text{dL}$; $M = 2.29 \mu\text{g}/\text{dL}$; $SE = 0.05$; $N = 3893$) took less time to complete the SDST compared to those with high lead levels ($\geq 5 \mu\text{g}/\text{dL}$; $7.96 \mu\text{g}/\text{dL}$; $SE = 0.16$; $N = 1032$). The unweighted, unadjusted mean time taken to complete the SDST was approximately 4.4 seconds longer in the high lead (Mean = 28.73 Sec; $SD = 11.71$) compared to the low lead group (Mean 24.32; $SD = 9.32$). After controlling for the demographic variables, individuals in the high-lead group were more than 1 second slower in time taken to complete the SDST compared to those in the low-lead group (beta = 1.05; $SE = 0.35$; $p = 0.004$; $R^2 = 0.34$). Individuals in the Low-BLL group had a weighted, adjusted mean of

22.56 seconds (SE = 0.14) while those in the High-BLL group took 23.67 (SE = 0.30) seconds to complete this test.

DISCUSSION AND CONCLUSION:

The findings indicate that time to complete a cognitively demanding mental task, but not accuracy of performance or simple reaction time is related to BLL in working age adults. We confirmed earlier findings showing simple reaction time as well as accuracy on the digit substitution task are not related to BLLs in working age adults (age 20 to 59 years) participating in NHANES III.²² and contrast this with the measure of complex mental decision processing time (the digit substitution task). Lead load in adults of working age, appears to adversely affect speed of CNS processes involving attention, effort and complex decision making.

Performance on the neurobehavioral tests was influenced by the demographic variables. Simple RT and time to complete the SDST increased with age while accuracy of performance on the SDST decreased. Simple RTs were faster in men than women. SDST accuracy was significantly higher in men than women but decision time was faster in women. The finding that women were slower on the simple RT task but faster on the more complex digit substitution task (the SDST), suggests a gender difference in performance strategy on the SDST. Women may trade speed for accuracy (speed-accuracy-trade-off) on this attention-demanding test of mental abilities.

High school or more education was associated with better performance on all tasks. Compared to non-Hispanic whites, non-Hispanic blacks and Hispanics had significantly slower simple RTs, more errors on the SDST, and longer completion times on the SDST. The "Other" race-ethnicity category did not differ from non-Hispanic whites on simple RTs and errors on the SDST but were slower on the SDST.

There has been a substantial reduction in lead burden in the general population of the United States over the past several decades. This is a reflection of both regulatory and voluntary efforts to reduce sources of lead in the environment. The target level of no measurable blood lead in children in Healthy People 2010 is a response to the fact that lead is detrimental at any level in children.⁷ In adults, the levels considered by both OSHA and NIOSH are well above the current trigger point of interest in children (10 µg/dL) and these standards are likely to remain for the near future. The findings here suggested that BLL in the currently acceptable range have adverse effects on speed of mental operations associated with complex information processing and decisions in adults.

The magnitude of this slowing on the SDST (LS adjusted means) was on the order of one in approximately 22 seconds or about a 7% slowing in overall decision time in the High Lead Group (individuals with BLLs => 5µg/dL). The findings represent inference to the general population of some 125,971,217 persons age 20 to 59 years and a loss of productivity of 7% in decision speed may have rather far reaching economic consequences.

The findings here have, perhaps, greater relevance to public health of an aging population, than might be apparent at first. The SDST is sensitive to a number of mental abilities including motor persistence, ability to maintain attention, visual – motor coordination, and organization.²⁸ Accuracy and speed on such tasks are affected by CNS non-specific dysfunction which is common in the elderly. Slowing in task performance with aging is widely reported and accuracy is related to presence of a diagnosis of dementia of the Alzheimer type³³ Longitudinal findings suggest SDST

performance is more sensitive to subsequent development of Alzheimer's disease in later life than many other known risk factors (age, gender, and education).³⁴

While adult lead levels have limited use in understanding childhood lead toxicity effects³⁵ the converse is far from true. Approximately 90% of lead acquired early in life is sequestered in bone, where it not only competes with calcium related physiological processes but is constantly interchanged with body tissues with remodeling across the adult life-span. Recent findings indicate that age related cataract risk is increased by accumulated lead exposure in older men,³⁶ likely reflecting altered lens redox status and decreased transparency. In individuals with a childhood history of lead exposure, later age related osteopenia (both sexes) and osteoporosis (women) likely increases risk of low level, chronic toxicity in the later years of life. Lead accumulated early in life is incorporated into bone during development (See Figure 1), may well increase risk for a number of age related oxidative-stress disorders including hypertension and cognitive impairment in addition to such slow metabolic processes as cataract development.³⁶⁻³⁸

Weiss³⁹ notes that vulnerability to toxic processes, well recognized as great in infants, rises again in late life and "in many ways recapitulates the imperfect defenses deployed by the immature organism." Aging is not a mechanism for age-related disorders, but is frequently so invoked. Life long environmental factors may account for many, avoidable, age-related chronic health problems. This is well recognized in the obvious cases of health-related-behaviors but is not so well considered for subtler, long-term environmental risk hazards. It has been suggested that one form of Alzheimer's, for example, is mediated by an interaction of genetic (apoE4) and environmental factors (hyperlipidaemic lifestyles) acting via the Ca^{2+} - energy - redox triangle.⁴⁰ This system is

implicated in the relation between lifetime lead burden and age related cataracts in men.

³⁶ Such expression in a long term, low energy demand system should raise concern of lead and its release with bone remodeling in later life on more metabolically active body systems.

The data presented in this paper reflect cross-sectional findings and no inferences concerning causality can be made. Further, lead poisoning, even at low levels, can damage different body systems in different individuals. Such multi-system damage and difference between individual sensitivity may easily account for the findings here without causing any direct CNS damage. In the absence of knowledge of specific actions of lead on the CNS and in the absence of appropriate panel or case-control studies, the present data must be suspect as indicating low-level lead effects on CNS activity in working age adults.

REFERENCES

- ¹ Baghurst PA, McMichael AJ, Wigg NR, et al. (1992). Environmental exposure to lead and children's intelligence at the age of seven years. *N Engl J Med.* 327:1279-1284.
- ² Rice DC. (1993) Lead-induced changes in learning: Evidence for behavioral Mechanisms from experimental animal studies. *Neurotoxicology*, 14:167-178
- ³ Children's Blood Lead Levels in the United States. National Center for Environmental Health CDC 1, February 2005. <http://www.cdc.gov/nceh/lead/research/kidsBL.L.htm>
- ⁴ Canfield, R., Henderson, M.A., Cory-Slechta, D,et al. (2003). Intellectual impairment in children with blood lead concentrations below 10 ug per Deciliter. *The New England Journal of Medicine*; 348:1517-26.
- ⁵ Brown, M.J., Meehan, P.J. (2004). Health effects of blood lead levels lower than 10ug/dL in children. *Am J. Public Health* 94:8-9.
- ⁶ Work Group of the Advisory Committee on Childhood Lead Poisoning Prevention. (2004). A review of evidence of health effects of blood lead levels <10ug/dL in children, Draft Final for ACCLPP Review, February 23, 2004. <http://www.cdc.gov/nceh/lead/ACCLPP/meetingMinutes/lessThan10MtgMAR04.pdf>
- ⁷ Healthy Americans 2010, Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services (<http://www.healthypeople.gov/>).
- ⁸ **Morbidity and Mortality Weekly Report, July 9, 2004. NIOSH Adult Blood Lead Epidemiology and Surveillance -- United States, 2002**
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5326a2.htm>
- ⁹ U.S. Department of Labor. Medical Surveillance Guidelines – 1926.62 App C
http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10644
- ¹⁰ Ryan CM, Morrow L, Parkinson D, Bromet E., (1987). Low-level lead exposure and neuropsychological functioning in blue-collar males. *Int J Neurosci.*36:29-39.
- ¹¹ Schwartz, BS, Lee, BK, Lee GS, Stewart, WF, Lee SS., Hwang, KY, Ahn KD, Kim YB, Bolla KI, Simon D., Parsons PJ, Todd, AC. (2001) Associations of blood lead, dimercaptosuccinic acid-chelatable lead, and tibia lead with neurobehavioral test scores in south Korean lead workers., *American Journal of Epidemiology* 153: 453-464.
- ¹² Schwartz BS, Bolla KI, Stewart W, Ford DP, Agnew J, Frumkin H. (1993). Decrements in neurobehavioral performance associated with mixed exposure to organic and inorganic lead. *Am J Epidemiol.* 137:1006-21.

- ¹³ Stollery, B.T. (1996). Reaction time changes in workers exposed to lead. *Neurotoxicol Teratol*, 18:477-83.
- ¹⁴ Fiedler, N., Weisel, C. Lynch, R., Kelly-McNeil, K. Wedeen R., Jones, K., Udasin, II, Ohman-Strickland, P., Gochfeld, M. (2003). Cognitive effects of chronic exposure to lead and solvents. *American Journal of Industrial Medicine*. 44:413-423.
- ¹⁵ Muldoon SB, Cauley JA, Kuller LH, Morrow L, Needleman HL, Scott J, Hooper FJ, 1996. Effects of blood lead levels on cognitive function of older women. *Neuroepidemiol* 15: 62-72.
- ¹⁶ Payton, M. Riggs, KM, Weiss, ST., Hu, H (1998). Relations of bone and blood lead to cognitive function: The VA Normative Aging Study.
- ¹⁷ MMWR (1997). Update: Blood lead levels – United States, 1991 – 1994.
- ¹⁸ Pirkle, J.L, Brody, DJ., Gunter, EW., et al., (1994). The decline of blood lead levels in the United States: The National Health and Nutrition Examination Surveys (NHANES). *JAMA* 1994; 272:289-91.
- ¹⁹ Krieg, E.J., Chrislip, D.W., Letz, R.E., Otto, D.A., Crespo, C.J. Brightwell, W.S., & Ehrenberg, R.L. (2001). Neurobehavioral test performance in the third National Health and Nutrition Examination Survey. *Neurotoxicology and Teratology*, 23:569-589
- ²⁰ Baker, El., Letz, RE, Fidler, AT., Shalat, S., Plantamura, D., Lyndon, M. (1985). A computer-based neurobehavioral evaluation system of occupational and environmental Epidemiology: Mythology and validation studies. *Neurohehav Teratol.*, 7:369-77.
- ²¹ Fiedler, N. (1996). Neuropsychological approaches for the detection and evaluation of toxic symptoms. *Environ Health Perspect.*, 104:239-245
- ²² Krieg, E.F., Chrislip, D.W., Crespo CJ., Brightwell WS., Ehrenberg, RL., Otto, DA., (2005). The Relationship between blood lead levels and neurobehavioral test performance in NHANES III and related occupational studies. *Public Health Reports* 120:240-251.
- ²³ U.S. Department of Health and Human Services (DHHS). National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988-94, Reference manuals and reports: http://www.cdc.gov/nchs/products/elec_prods/subject/han3rom.htm
- ²⁴ Anger, KW. (2003). Neurobehavioral tests and systems to assess neurotoxic exposures in the workplace and community. *Occupational and Environmental Medicine*. 60:531-538
- ²⁵ Gunter EW, Lewis BL, Koncikowski SM. Laboratory Methods Used for the Third National Health and Nutrition Examination Survey (NHANES III), 1984–1994. Hyattsville, Md: Centers for Disease Control and Prevention; 1996. [Context Link]

- ²⁶ Miller DT, Paschal DC, Gunter EW, Stroud PE, D'Angelo J. Determination of lead in blood using electrothermal atomization atomic absorption spectrometry with a L'vov platform and matrix modifier. *Analyst*. 1987; 112: 1701–1704. [Bibliographic Links](#) [[Context Link](#)]
- ²⁷ Wechsler D: *The Measurement and Appraisal of Adult Intelligence* (4th ed.). Baltimore: Williams and Wilkins, 1958
- ²⁸ Lezak M: (1995). *Neuropsychological Assessment*, (3rd ed.). New York: Oxford University Press.
- ²⁹ Tun, P. A., Wingfield, A., Lindfield, K. C. (1994). Motor-baseline for the Digit-Symbol Substitution test. *Clinical gerontologist*, 18, 47-51.
- ³⁰ Vupputuri, S., He, J., Muntner, P., Bazzano, L.A., Whelton, P.K., Batuman, V. (2003). Blood Lead Level Is Associated With Elevated Blood Pressure in Blacks. *Hypertension*, 41: 463-468.
- ³¹ Statistical Analysis System V.8.2. <http://support.sas.com/documentation/onlinedoc/>
- ³² ANALYTIC AND REPORTING GUIDELINES: The Third National Health and Nutrition Examination Survey, NHANES III (1988-94), October, 1996 National Center for Health Statistics Centers for Disease Control and Prevention Hyattsville, Maryland <http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf>
- ³³ Storandt, M., and Hill, R. D. (1989). Very mild senile dementia of the Alzheimer type: II. Psychometric test performance. *Archives of Neurology*, 46, 383-386.
- ³⁴ Papp, M. A., & reischies, F.M. (2005), Attention and executive control predict Alzheimer disease in late life., *American J. Geriatric Psychiatry*, 13:134-141.
- ³⁵ Bellinger, DC. (2004). Lead. *Pediatrics*, 113:1016-1022.
- ³⁶ Schaumberg, D.a., Mendes, F., Bataram, M., Dana, M.R., Sparrow, D., Hu, H., (2004). Accumulated lead exposure and reisk of age-related cataract in men. *JAMA*, 292:2750-2754.
- ³⁷ Kondrashov1, V. Rothenberg, SJ, Chettle, D.,Zerwekh, J. (2005). Evaluation of potentially significant increase of lead in the blood during long-term bed rest and space flight. *Physiol. Meas.* 26 (2005) 1–12 .
http://ej.iop.org.proxy.library.vcu.edu/links/q21/RWcVp0d+665hzR68J5Y8lw/pm5_1_001.pdf
- ³⁸ Brito, Jose A. A.; McNeill, Fiona E.; Stronach, Ian; Webber, Colin E.; Wells, Sue; Richard, Norbert; Chettle, David R. (2001). Longitudinal changes in bone lead concentration: implications for modelling of human bone lead metabolism. *Journal of*

Environmental Monitoring 3: 343-351 <http://chemport.cas.org/cgi-in/sdcgi?APP=ftslink&action=reflink&origin=iopp&version=1.0&coi=1%3ACAS%3A528%3ADC%252BD3MXIsVCitbs%253D&pissn=0967-3334&md5=867ca8ab4ddcad114a6372c2b016ad6a>

39 Weiss, B. (200). Vulnerability to pesticide neurotoxicity is a lifetime issue. *Neurotoxicology*, 21:67073.

40 Heininger, K., (2000). A unifying hypothesis of Alzheimer's disease. III. Risk factors. *Human Psychopharmacology-Clinical and Experimental*, 15:1-70.

TABLE ONE: Sample summary showing demographic variables in relation to blood lead levels and neurobehavioral variables.

VARIABLE	Sample size	N Weighted population	Percent (SE)	BLOOD LEAD LEVEL		SIMPLE REACTION TIME TASK		SYMBOL DIGIT SUBSTITUTION TASK (SDST)			
				$\mu\text{g/dL}$ (SE)		(Milliseconds)		Accuracy		Time on task (Seconds)	
				Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
TOTAL	4925	123,108,237	100 (0.0)	3.26	0.23	233.2	1.36	7.71	0.01	22.75	0.21
SEX											
MALE	2252	60,609,400	49.2 (0.94)	4.19	0.13	233.5	1.34	7.72	0.01	22.15	0.2
FEMALE	2673	62,498,838	50.8 (0.94)	2.37	0.1	231.9	3.24	7.64	0.03	25.66	0.4
HIGH SCHOOL											
NO	1595	24,739,626	20.1 (1.23)	4.09	0.15	247.3	3.11	7.59	0.02	28.55	0.38
YES	3330	98,368,611	79.9 (1.23)	3.06	0.1	229.7	1.24	7.74	0.01	21.29	0.16
RACE											
White Non-Hispanic	1779	94,420,140	76.7 (1.34)	3.17	0.12	229.8	1.52	7.74	0.02	21.7	0.22
Black Non-Hispanic	1507	13,388,491	10.9 (0.76)	3.73	0.13	247.1	2.51	7.57	0.02	25.73	0.31
Hispanic	1457	6,834,132	5.5 (0.56)	3.57	0.11	246.7	1.81	7.56	0.02	27.56	0.47
Other	182	8,465,475	6.9 (0.76)	3.42	0.28	238.9	4.79	7.64	0.06	25.75	0.76

TABLE 2 Multiple regression of relations of Blood Lead Level (BLL) to task performance adjusted for demographic variables.

VARIABLE	Mean or %*	SRTT (Msec.)			DIGIT TASK (SDST) Accuracy			DIGIT TASK (SDST) Time on task (Sec.)		
		β	SE	P	β	SE	P	β	SE	P
AGE (yrs)	37.1	0.35	0.1	0.000	-0.01	0	0.000	0.24	0.01	0.000
SEX										
MALE	49.2	REF			REF			REF		
FEMALE	50.8	14.06	2.5	0.000	-0.14	0.04	0.001	-0.93	0.25	0.000
HIGH SCHOOL										
NO	20.1	REF			REF					
YES	79.9	-15.68	3.00	0.000	0.21	0.06	0.004	-5.99	0.38	0.000
RACE										
White Non-Hispanic	76.7	REF			REF			REF		
Black Non-Hispanic	10.9	16.25	2.6	0.000	-0.21	0.04	0.000	4.02	0.22	0.000
Hispanic	5.5	12.73	2.7	0.001	-0.30	0.06	0.000	4.45	0.45	0.000
Other	6.9	6.42	4.4	0.150	-0.1	0.12	0.386	3.22	0.67	0.000
LEAD LEVEL										
(ug/dL)	3.26	-0.3	0.4	0.409	-0.01	0.01	0.905	0.16	0.05	0.003
R²		0.066			0.03			0.354		