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Cumulative lead exposure in community-dwelling adults and fine motor function: comparing standard and novel tasks in the VA Normative Aging Study

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Abstract

Background and Aims—Lead exposure in children and occupationally-exposed adults has been associated with reduced visuomotor and fine motor function. However, associations in environmentally-exposed adults remain relatively unexplored. To address this, we examined the association between cumulative lead exposure—as measured by lead in bone—and performance on the Grooved Pegboard (GP) manual dexterity task, as well as on handwriting tasks using a novel assessment approach, among men in the VA Normative Aging Study (NAS).

Methods—GP testing was done with 362 NAS participants, and handwriting assessment with 328, who also had tibia and patella lead measurements made with K-X-Ray Fluorescence (KXRF). GP scores were time (sec) to complete the task with the dominant hand. The handwriting assessment approach assessed the production of signature and cursive lowercase l and m letter samples. Signature and lm task scores reflect consistency in repeated trials. We used linear regression to estimate associations and 95% confidence intervals (CI) with adjustment for age, smoking, education, income and computer experience. A backward elimination algorithm was used in the subset with both GP and handwriting assessment to identify variables predictive of each outcome.

Results—The mean (SD) participant age was 69.1 (7.2) years; mean patella and tibia concentrations were 25.0 (20.7) μg/g and 19.2 (14.6) μg/g, respectively. In multivariable-adjusted analyses, GP performance was associated with tibia (β per 15 μg/g bone = 4.66, 95% CI: 1.73,

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Conflict of Interest Statement

The development of the Neuroskill device was funded in part by a NIH Small Business Innovation Award to VeriFax Corporation. The Neuroskill technology was conceived and developed by R. Shrairman and A. Landau, who are the President and Vice President for Research & Development of VeriFax, respectively. The other authors have no conflicts of interest to report.

7.58, p=0.002) and patella (β per 20 μg/g = 3.93, 95% CI: 1.11, 6.76, p = 0.006). In multivariable adjusted models of handwriting production, only the lm-pattern task showed a significant association with tibia (β per 15 μg/g bone = 1.27, 95% CI: 0.24, 2.29, p = 0.015), such that lm pattern production was more stable with increasing lead exposure. GP and handwriting scores were differentially sensitive to education, smoking, computer experience, financial stability, income and alcohol consumption.

Conclusions—Long-term cumulative environmental lead exposure was associated with deficits in GP performance, but not handwriting production. Higher lead appeared to be associated with greater consistency on the lm task. Lead sensitivity differences could suggest that lead affects neural processing speed rather than motor function *per se*, or could result from distinct brain areas involved in the execution of different motor tasks.

Search terms

Grooved pegboard; lead; NAS; fine motor; visuomotor

1. Introduction

The elderly population in the U.S. is growing rapidly (Rice et al., 2004), and independence in this age group relies on maintaining functional levels of fine motor control that enable bathing, dressing, taking medication, phone usage and more (Christensen et al., 2009). Looking across the entire U.S. elderly population, small changes in fine motor function would shift the distribution such that some portion of the population would move out of independence and into requiring more care. Any factor--such as an environmental exposure--that limits fine motor function would result in changes in the amount of time an elderly individual is independent and subsequently affect medical care and caretaking costs on a large scale (Spillman et al., 2000).

As one of the most studied neurotoxicants, lead (Pb) has been shown to produce a diverse array of neurological deficits in occupationally-exposed adults and environmentally-exposed children and adults. In children, studies of lead-related visuomotor effects have helped identify developmentally vulnerable windows of exposure. Occupational exposure studies in adults have provided insight into visuomotor and fine motor deficits resulting from lead exposure occurring at relatively high lead exposure levels (Balbus-Kornfeld et al., 1995, Seeber et al., 2002, Shih et al., 2007). However, there has been limited exploration into the effects of lead on fine motor function in environmentally-exposed adults. Deficits in fine motor function can be detrimental occupationally and socially, where daily tasks in the home and at work require fine motor coordination and dexterity. Here, we asked a cohort of elderly men with non-occupational exposure to lead to complete a series of fine motor tasks that included a grooved pegboard task, and two tests (a handwriting task and a signature task) using a novel assessment device.

Lead exposure either prenatally or in childhood has been linked to a spectrum of neurological deficits, including intelligence quotients, memory and other cognitive abilities (Bellinger, 2008, Lanphear et al., 2005, Mazumdar et al., 2011, Needleman et al., 1990). Gross motor dysfunction in children, including gait, postural balance, arm control and locomotion has been linked to environmental lead exposure (Bhattacharya et al., 2007, Despres et al., 2005, Fraser et al., 2006, Wasserman et al., 2000). Fine motor function impairment resulting from childhood lead exposure specifically measured with the grooved pegboard task has been shown to be apparent in childhood (Chiodo et al., 2004), adolescence (Ris et al., 2004) and in adulthood (White et al., 1993).

Many cognitive deficits have been attributed to high occupational lead exposure in men, including mood, memory and executive function (Seeber, 2002). Studies have incorporated tests of fine motor function, specifically using a pegboard task (Baker et al., 1983, Bleecker et al., 1997, Hanninen et al., 1998, Maizlish et al., 1995, Ryan et al., 1987, Schwartz et al., 2001, Stewart et al., 1999). In each of these studies, pegboard tasks using the grooved pegboard, Purdue pegboard or Santa Ana pegboard showed significant associations with lead measured in blood (Baker, 1983, Bleecker, 1997, Hanninen, 1998, Maizlish, 1995, Ryan, 1987, Schwartz, 2001) and also in bone (Bleecker, 1997, Stewart, 1999). In one study on low-level occupational exposure, the grooved pegboard task was the only measure found to be associated with blood lead levels out of a battery that also looked at memory, visuospatial ability, learning and attention (Ryan, 1987). These associations, as well as similar ones found in Bleecker et al. (1997), were increased at older ages, indicating an enhanced age-related effect of lead on grooved pegboard performance.

Environmental-level exposure to lead—in particular cumulative exposure as measured by lead in bone—has been shown in older populations to affect cognitive function across a number of domains, including measures of attention, executive function, processing speed, memory, language and more (Bandeen-Roche et al., 2009, Glass et al., 2009, Peters et al., 2010, Rajan et al., 2008, Shih, 2007, van Wijngaarden et al., 2009, Weuve et al., 2009). To our knowledge, the effects of cumulative lead exposure on fine motor function in a community dwelling group has only been explored in two settings: the Department of Veterans Affairs Normative Aging Study (NAS) and the Baltimore Memory Study (BMS). In our work in the NAS, we have examined several aspects of the relation between cumulative lead exposure and cognitive function. In 2003, Wright et al. found that higher lead in blood and patella bone, as well as age, was associated with worse Mini-Mental Status Examination (MMSE) performance (Wright et al., 2003). Patella lead was also associated with greater decline in MMSE performance over time (Weisskopf, 2004). When performance on a whole battery of cognitive tests was considered, one interquartile range higher patella bone lead was associated with worse change in scores over time in spatial orientation, memory, attention, language abilities, and figure copying (Weisskopf et al., 2007). The figure copying task—a visuomotor function—had one of the clearest associations with lead exposure. Rajan et al. (2008) subsequently found that the association between lead exposure and performance on the figure copying test was modified by the delta-aminolevulinic acid dehydratase (ALAD) gene polymorphism.

In the BMS, a cohort of community dwelling men and women, ages 50–70 years in the Baltimore, MD area, Shih et al. (2006) examined the association between tibia lead and performance on several cognitive tests, including a composite “hand eye coordination” score made up of performance on the Purdue grooved pegboard and the Trailmaking A task. They found that after adjusting for age, sex, technician and presence of the APOE- ε4 gene mutation, higher tibia lead level was significantly associated with worse eye-hand coordination. Relationships weakened when race/ethnicity, and wealth were included in models. In a another study in the same population, tibia lead was significantly associated with progressive decline in the same hand-eye coordination score over time (Bandeen-Roche, 2009). However, stratified analysis showed the effect to be significant only in African-American and combined subject pools, but not for white subjects. Thus, the evidence for motor effects of lead exposure at environmental levels is limited, and the data that do exist involve only a couple of motor tests.

In order to further examine the association between cumulative lead exposure and motor function, we explored, in the NAS, the association between bone lead concentration and performance on both a traditional and a novel test of fine motor function: the grooved pegboard and a new handwriting analysis device, the Neuroskill (Verifax Corporation,

Boulder, CO). Tests of manual dexterity and fine motor functioning range from simple movements like finger tapping (where subjects press a button as many times as possible over ten seconds), to more complex tasks like the grooved pegboard that may involve visual integration, executive function and attention. Neuroskill assesses fine motor control through analysis of handwriting and signature dynamics (Shrairman et al., 2005). This device takes a novel approach to assessing the stability of the production of the elemental motor components that make up handwriting, and has been used only once in an environmental context: signature stability measured in welders occupationally exposed to manganese (Mn) showed a negative association with Mn exposure over a work shift (Laohaudomchok et al., 2011). An important unique aspect of the Neuroskill is that the motor assessment is independent of the speed of response, providing information about visuomotor cognitive function that is currently unmeasured in standard test batteries.

2. Materials and Methods

2.1 Study Population

To assess visuomotor deficits in environmental lead exposed elderly men, we tested participants in the NAS, a cohort of community-dwelling elderly, majority Caucasian men originally recruited from the greater Boston, Massachusetts area in the 1960s who report for medical examinations every three to five years (Bell et al., 1966, Hu et al., 1996, Shih, 2007, Weisskopf, 2007). Because the NAS is a cohort of men drawn from the general population, the participants' lead exposure levels generally reflect those of people exposed to lead in the general environment, although a small number of participants may actually have exposures from their jobs. Nonetheless, because of the community-dwelling origins of the NAS, we use the term environmentally-exposed to distinguish this population from a specifically occupationally-exposed cohort.

After 1991, subjects were invited to have their bone lead concentration measured using K-shell x-ray fluorescence (KXRF). Among active NAS participants at the time of initial KXRF testing, 876 (68%) agreed to have their bone lead measured. Grooved pegboard testing was conducted at NAS participants' regular NAS study visits between May of 2005 and December of 2009, and testing with the Neuroskill device was done at study visits between July of 2004 and November, 2007. This study was approved by the Institutional Review Boards of the VA Boston Healthcare System, Brigham and Women's Hospital, and the Harvard School of Public Health. All participants provided written informed consent to participate.

Grooved pegboard task performance was assessed in 484 NAS participants as part of a separate study on cognitive function. There were 452 NAS participants tested with the Neuroskill device, although data from 6 of these men were excluded because of equipment malfunction. Of those men with Neuroskill data 174 provided both signature and lm-pattern samples at two separate times during the same NAS visit in order to examine test-retest reliability of the Neuroskill device. Among these men, for all analyses of Neuroskill results other than the test-retest reliability, the first Neuroskill performance results were used. Among the 484 NAS participants who were administered the grooved pegboard test, 385 were also tested with the Neuroskill device.

Of the 484 men with grooved pegboard data, 362 (74.8%) also had bone lead data. Of the 446 men with valid Neuroskill data, 328 (73.5%) also had bone lead data. One man's patella lead measurement was excluded because it was extremely low (−88μg/g of bone, or 4.4 standard deviations from the mean) and thus was considered invalid. Some negative values are expected given uncertainties around measurements when true bonelead levels are close

to 0, but −88μg/g is around 10 times greater than typical uncertainties and so suggests an invalid reading.

2.2 Bone lead KXRF Measurements

Bone lead concentration was measured at the patella and the midtibial shaft using an ABIOMED KXRF instrument (ABIOMED, Danvers, MA) as previously described (Aro et al., 1994, Chettle et al., 2003, Hu et al., 1998). Tibia and patella sites were cleaned with a 50% solution of isopropyl alcohol, prior to a 30-minute measurement. The tibial midshaft was defined as the midpoint between the medial malleolus and the tibial plateau. The KXRF beam collimator was positioned 30° in the lateral direction of the patella, and perpendicular to the flat bony surface of the tibia. When X-rays are directed toward bone near the skin's surface (such as in the patellar knee bone or the tibia bone along the shin), lead atoms that were in the bone matrix are ejected in direct proportion to the concentration of lead in the bone, measured in μg of lead per g of bone. Tibia and patella bone lead concentrations reflect cumulative lead exposure over different time windows: patella lead reflects exposure over the last decade, while tibia lead half-life is on the order of decades (Wilker et al., 2011).

2.3 Grooved Pegboard test

The grooved pegboard apparatus (Lafayette Instrument Co., Lafayette, IN) is a symmetrical board with 25 slotted holes in a 5 by 5 matrix and a well in which metal pegs with slotted edges are placed at the start of the protocol (Lezak, 1995). With the pegboard centered in front of the subject at the edge of a table and the board positioned so that the peg well was further away from the participant than the holes, subjects were asked to insert the metal pegs into each of the 25 holes in sequence as quickly as possible with their dominant hand without practice trials. We recorded the time in seconds from the insertion of the first pin to the insertion of the last one.

2.4 Neuroskill Handwriting and Signature Test

For the Neuroskill portion of the test, subjects were asked to provide five samples of their signature in succession—written in their natural manner—and five samples of a series of cursive "lm"s (lm-pattern) using the instrumented pen. The Neuroskill measure of handwriting uniformity is an indication of the correlation between all pairs of handwriting samples (either the 5 signature samples, or the 5 cursive "lm" sequences) provided by the participants at each test session and provides a measure of reproducibility across the samples (Shrairman, 2005).

Neuroskill assesses the central mechanism of motor control through analysis of complex signals of handwriting dynamics. The Neuroskill system evaluates handwriting as "quanta" of preprocessed neural information encoding fine motor movements that are about 100ms in duration (Morasso et al., 1982, Schomaker et al., 1995). These quantal segments are stationary, to which Neuroskill applies correlation function analysis in order to establish the criterion of "consistency" in motor control. The measure of consistency characterizes the ability of the patient to stably reproduce the preprogrammed micro-movements (strokes) from sample to sample. Thus, the Neuroskill does not assess how handwriting looks, but rather how consistently a given sample is performed.

The Neuroskill device is an ordinary-size instrumented pen with accompanying software and a computer interface electronic module. The pen's motor-sensing electronics consist of accelerometers that measure motions along the X and Y-axes of the writing surface, and a pressure transducer that measures dynamics along the pen body, or Z-axis. These analog signals are sampled 200 to 400 times per second and converted into a digital bit stream representing up to 2000 data points. Parameters used with the Neuroskill software for data

analysis were: interval from 10 to 1010; sigma multiplier = 1; shadow lead = 60; shadow lag = 60; window size = 200; step 6 =; shadow step = 1; acceptable correlation = 75%; and acceptable correlation for expanded search = 67%. We computed the maximum of the cross correlation function for the dynamic signals that represent sequences of the elementary motor movements. The stability score can range from 0 to 100 percent. As an example, for two identical signals the value of the criterion of stability would be equal to 100 (or 100% correlation).

2.5 Data analysis

Linear regression was used to evaluate the relationship between lead biomarkers and continuous measures of test performance. Linear models were run using PROC GENMOD in SAS software version 9.2 (SAS Institute, Inc., Cary, NC). Tibia and patella lead were modeled separately. Based on a priori hypotheses from other studies of cognitive function and motor function, initial models were adjusted for age, education, smoking (pack years), financial stability, computer experience (Yes/No) and income. Education was categorized into ≤12 years, >12 but ≤16, and >16. Financial stability was assessed using a questionnaire, in which subjects were asked to select the statement that best describes their current financial status: “I can’t make ends meet with the income I now have”, “I just about manage to get by with the income I now have”, “I have enough to get along, and even a little extra” and “I can buy pretty much anything I want with the income I now have”. There were less than 5 subjects in the lowest financial stability category so the first two were combined. Income categories included ≤$34,999, $35K–$49,999, $50K–$74,999 and ≥$75K. Additional analyses in a subset of the study population also included alcohol (drinks/week), handedness, English as a first language (Yes/No), and retirement status. Alcohol can diminish performance on motor tasks (Lex et al., 1988, Vorstius et al., 2008), and handedness is differentially represented in motor cortices and may affect task performance (Hammond, 2002). The other two variables we considered further indicators of socioeconomic status, which may be related to fine motor coordination (Piek et al., 2008). Retirement status was broken down into the following categories: “Retired, not employed”, “Retired, work part-time”, “Retired, work full-time”, “Work part-time”, “Work full-time”, and “Unemployed”.

All models were evaluated for outliers, and heteroscedasticity. Missing categorical data were assigned “missing” category indicators and included in models. Subjects missing smoking packyear data (n=13) were assigned the mean, and a missing smoking data indicator variable was included in the model. Because the sets of participants completing the grooved pegboard and Neuroskill tasks differed, the model results cannot be directly compared. Therefore, we explored predictors of performance on these tasks in the subset of NAS participants that did both tasks and had bone lead measurements (n= 282) in order to better understand how predictors of performance on the novel Neuroskill device compare to predictors of grooved pegboard performance. For this we used a Wald test-based backward elimination algorithm, with a threshold for inclusion of p=0.1 to identify covariates that were associated with task performance.

3. Results

Motor test performance by different subject characteristics are shown in Table 1. The average age of this population was 69.1 years (standard deviation or SD = 7.2). Mean patella lead was 25.0 μg/g bone (SD = 20.7), and mean tibia lead was 19.2 (SD = 14.6), comparable to levels seen in other studies (Bandeen-Roche, 2009). The average time to complete the Grooved Pegboard task was 101.7 seconds (SD = 27.5). The average Neuroskill signature score was 66.0% (SD = 9.7%), and the average lm-pattern score was 54.5% (SD = 9.6). An average of 2.1 (SD = 3.2 years elapsed between the KXRF measurements and the grooved

pegboard testing. An average of 2.0 (SD = 3.3) years elapsed between the KXRF measurements and the Neuroskill testing. The NAS participants with bone lead measurements who took part in the fine motor function tests were younger, had lower bone lead concentrations, were less likely to be smokers, and had slightly more years of education that those who were not tested. After adjusting for all of these factors, there was no difference in bone lead level among those who participated in the fine motor tasks versus those who did not (data not shown).

The Pearson correlation between time to complete the grooved pegboard and the stability score of the signature samples was −0.25 (negative because the handwriting and grooved pegboard scales are in opposite directions). The grooved pegboard correlation with the lm-pattern samples was −0.18. The Pearson correlation between stability scores for the lm-pattern and signature tasks was 0.61. The Neuroskill device demonstrated good test-retest correlation for both signature samples (0.70) and lm-pattern cursive script (0.78) over a mean interval of 103 minutes. The signature and lm scores decreased slightly over this interval, which was most likely a result of fatigue associated with the tests.

For both tibia and patella, higher bone lead concentration was associated with longer pegboard completion times in age-adjusted models (Table 2). These associations were changed little with further adjustments for additional potential confounders. Age-adjusted models of signature and lm-pattern consistency did not show a relationship with either bone lead measurement (Table 2). With further adjustment there was little change to the relation with signature score, but for the lm-pattern higher bone lead appeared associated with more stable scores (Table 2).

We then used backward elimination to determine which covariates were predictive of performance on the different fine motor tasks. We used normalized task scores to be able to directly compare results. Table 3 shows the results of the final models for the normalized grooved pegboard, signature and lm-pattern scores when tibia lead was included in the model. Longer times to complete the grooved pegboard were predicted by higher tibia lead, older age, higher education and not having computer experience. Greater stability in the Neuroskill signature task was predicted by less smoking, computer experience, less financial stability, higher income, and greater alcohol consumption. For the lm-pattern task, greater stability was predicted by higher tibia lead, higher education, and higher income. The association with education was not monotonic. The results when patella bone lead were included in the model were similar, except that the Neuroskill signature stability score was not predicted by smoking or computer experience (Table 4). English as a first language, handedness and retirement status were not associated with performance on any of the three fine motor tasks.

The same backward elimination criteria were applied to all men that took both types of tests, regardless of whether or not bone lead had been measured (bone lead was not included in the model; data not shown). We found that the variables associated with GP remained the same. Variables associated with signature stability scores were the same as those found in Table 2. Finally, variables associated with lm pattern scores remained the same except that alcohol remained in the model.

4. Discussion

The results of our study describe the association between cumulative lead exposure—as measured by lead in bone—and fine motor function using two different types of motor assessments: the established grooved pegboard task and the novel Neuroskill handwriting analyses. We found an association between higher cumulative lead exposure and slower completion times on the grooved pegboard task. Cumulative lead exposure was not

associated with stability of signature production as assessed with the Neuroskill, but was associated with increased stability in the production of the cursive lm sequence.

The grooved pegboard completion times among the NAS men was slower, with larger standard deviations, than norms established for this age group (Lafayette Instrument Company, 2002). This could be because of other factors such as altered sensation in the fingers from carpal tunnel syndrome or peripheral neuropathy, or medications. However, as such factors shouldn't increase lead exposure, they would not account for the association we find between lead exposure and GP performance. To the extent that such factors are caused by lead exposure, they could be mediators of the association we found.

The association between cumulative lead exposure and fine motor function among groups not occupationally exposed to lead has not been extensively studied. The few studies that have explored this have found reduced performance on motor tasks with increasing lead exposure (Bandeen-Roche, 2009, Shih, 2006). The motor performance assessments used in these studies were combinations of different motor tasks including grooved pegboard and the Trailmaking A task. Our grooved pegboard results concur with these prior findings, but our Neuroskill results do not. Our results, however, do suggest differences in predictors of performance on the grooved pegboard and performance on the Neuroskill, which could suggest that the two assessments measure somewhat different aspects of brain function.

Performance on the grooved pegboard was predicted by tibia lead, patella lead, age, education, and computer experience. The Neuroskill assessment of signature production was predicted by smoking, financial stability, income and alcohol consumption, and assessment of the cursive lm sequence was predicted by tibia lead, patella lead, education, and income. Specific brain regions subserve specific motor task components, and differences in associations with lead using distinct motor tasks may reflect differential actions of lead across brain areas.

The production of well-learned, frequently-used samples of handwriting, for example signatures, is considered to be accomplished by the sequential activation of elemental open-loop (not under feedback control) motor commands, or strokes (Morasso, 1982, Thomassen et al., 1985) The production of sequential cursive lm series is a less familiar task than one's signature and thus likely has more of a closed-loop component (involving visuomotor feedback control) than production of a signature. The Neuroskill device analyzes the assembly of these elemental strokes and the manner in which the intervals between them occur in an entire handwriting example, and so is sensitive to delays in initialization and distortions in production and sequencing of the elementary strokes. Switching from stroke to stroke to create continuous smooth writing is thought to rely heavily on the parietal and frontal cortices, as well as the cerebellum and thalamus (De Smet et al., 2011, Hodges, 1991, Marien et al., 2007), regions implicated in lead toxicity (Sanders et al., 2009, Verstraeten et al., 2008). To the extent that grooved pegboard performance—or performance of the other motor tests used in prior studies of non-occupational lead exposure—depends on other brain regions, this could explain the different findings.

A second possibility relates to the fact that of all the motor tests used in prior studies of lead exposure—and the grooved pegboard used in our study—the Neuroskill assessment is the only one that does not have a time component, i.e., in most motor tasks the outcome measured is time to complete the task. This raises the possibility that the associations seen between lead exposure and motor function in other studies (and with the grooved pegboard in our study) relate not to effects on motor function *per se*, but rather to effects of lead more generally on neuronal signal propagation speed, which would be a more brain-wide effect that could affect motor performance speed among other things.

In our data, higher tibia lead concentration, and to a lesser extent patella lead concentration, appeared to be associated with increased stability scores in the lm-pattern task. Initial tests of the Neuroskill device found that handwriting stability scores were worse with higher stress (NASA, 1997), and we also previously found that among welders exposed to low-levels of manganese, higher workday manganese exposure was associated with reduced lm task stability, but not with longer term cumulative Mn exposure measures (Laohaudomchok, 2011). It is possible that exposures do not have a universal effect on handwriting production and stability—exposures such as metals and environmental pollutants may differentially affect brain areas to produce varied effects on fine motor function. For example, the thalamus and basal ganglia are well-known targets of manganese (Bagga et al., 2012, Guilarte, 2010, Stanwood et al., 2009), which could explain the association with worse lm-pattern stability. We also cannot rule out the possibility that this was a chance finding or that this association was the result of confounding by some other variable that we did not account for.

The Neuroskill handwriting stability scores showed little, if any, variation with age. In contrast, finger tapping and the grooved pegboard test show rather strong changes with increasing age (Homann et al., 2003, Mitrushina et al., 1999, Nutt et al., 2000). The reduced dependence of the Neuroskill tasks on age could simplify the tracking of motor dysfunction over time. New additions to the current battery of fine motor and visuomotor tasks offer the opportunity to better tease out subtle differences in brain function and susceptibilities to relatively low-level environmental exposures.

This study was limited in that the NAS study is a very racially homogenous group of elderly men. Both previous Baltimore studies saw changes in associations when race/ethnicity was incorporated into their model, something we were unable to explore here because of the homogenous subject pool. Further work is necessary to determine whether grooved pegboard alone and handwriting task performance is differently sensitive based on race/ethnicity and gender. Previous studies have shown overall higher stability scores for both the lm-pattern and signature tasks when compared to the NAS participants described here (Laohaudomchok, 2011, NASA, 1997). However, the populations in these studies were younger, included men and women, and used participants from different geographical regions who may have had less lifetime exposures to lead and other neurotoxicants. Thus, identifying the reason for the differences is difficult. Further studies using the Neuroskill in other populations may be able to better discern whether regional exposures or other variables produce changes in Neuroskill test performance across a wider distribution of population characteristics.

In conclusion, our results suggest that while lead exposure is associated with motor function, it may be associated only with specific aspects of motor tasks. The exploration of associations with distinct types of motor tasks could allow for a better understanding of specific functions affected by any exposure, such as differentially affected brain regions or neural processing changes. The possibility that associations with many typical motor tasks are the result of effects of lead exposure on neural processing speed rather than motor function *per se* should be further explored.

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Highlights

- We explored fine motor function in elderly men exposed to environmental lead
- We used the grooved pegboard test, as well as a non-timed novel handwriting test
- Higher bone lead was associated with longer completion time on the grooved pegboard
- Higher bone lead was associated with increased performance stability on the novel tests
- Lead effects on fine motor test performance may be related to processing speed

Table 1

Mean (sd) Neuroskill stability scores or signature and lm-pattern handwriting samples, and mean (sd) time to complete the grooved pegboard (GP), by subject characteristics.

Characteristic	Grooved Pegboard		Neuroskill		
	N	time, seconds	N	Signature score, %	lm-pattern score, %
Age group					
<60	41	90.34 (25.5)	35	68.39 (9.0)	54.26 (7.1)
60–64	66	94.1 (23.6)	58	67.49 (9.0)	55.42 (8.5)
65–69	88	97.10 (22.4)	76	64.0 (8.0)	52.61 (7.5)
70–74	103	104.40 (30.6)	94	67.78 (10.3)	55.90 (12.2)
75–79	49	113.55 (25.6)	51[a]	62.78 (9.3)	53.75 (7.3)
>80	16	132.38 (22.3)	21	54.68 (13.9)	54.95 (13.9)
Education					
High school graduate or less	113	102.29 (28.8)	108 [a]	64.47 (10.0)	52.94 (9.5)
Some college or college graduate	175	98.66 (24.5)	158	66.99 (8.9)	55.56 (9.7)
Graduate school	71	106.27 (29.0)	66	66.72 (10.8)	54.70 (9.4)
Missing	4	132.5 (59.2)	3	56.97 (13.9)	51.30 (11.0)
Financial stability					
“Can’t make ends meet”	7	106.86 (28.5)	7	75.07 (9.8)	62.32 (7.0)
“Just manage to get by”	58	104.26 (28.1)	49	66.69 (8.9)	53.19 (7.6)
“Have enough to get along, and extra”	163	102.04 (27.9)	145 [a]	64.93 (10.2)	54.34 (10.7)
“Can buy anything I want”	119	99.9 (25.6)	115	66.72 (8.8)	54.62 (8.8)
Missing	16	98.88 (35.8)	19	65.28 (12.2)	55.70 (10.5)
Computer experience					
Yes	211	95.96 (23.0)	185	67.17 (8.7)	54.69 (8.4)
No	148	109.12 (30.1)	147 [a]	64.81 (10.7)	54.47 (11.1)
Missing	4	125.75 (65.5)	3	56.60 (13.3)	45.69 (1.8)
Income					
Less than 34,999	92	107.93 (29.7)	80 [a]	65.11 (10.4)	53.65 (11.3)

Characteristic	Grooved Pegboard		Neuroskill		
	N	time, seconds	N	Signature score, %	lm-pattern score, %
$35K– $49,999	78	104.51 (27.8)	75	64.84 (9.3)	52.92 (8.4)
$50K– $74,999	87	97.66 (23.4)	76	67.08 (9.7)	55.93 (9.8)
More than $75K	72	98.11 (27.6)	68	68.32 (9.0)	56.13 (8.8)
Missing	34	95.85 (27.7)	36	64.07 (10.2)	53.70 (8.6)

[a] lm pattern test has one fewer subject

Table 2

Effect estimates (and 95% CI) per 20 μg/g patella [a] and per 15 μg/g tibia [a] bone lead concentration for fine motor task performance.

Variable	Grooved Pegboard		Neuroskill			
	Dominant hand completion time, s		Signature score, %		lm pattern score, %	
	Age-adjusted	Multi-variable [b] -adjusted	Age-adjusted	Multi-variable [b] -adjusted	Age-adjusted	Multi-variable [b] -adjusted
Patella	4.34 (1.66, 7.03) p= 0.002 n=354	3.93 (1.11, 6.76) p = 0.006 n=354	−0.59 (−1.67, 0.49) p= 0.28 n = 320	0.16 (−0.94, 1.26) p = 0.78 n = 320	0.35 (−0.63, 1.32) p = 0.49 n = 319	0.90 (−0.09, 1.90) p = 0.08 n = 319
Tibia	4.82 (2.05, 7.59) p =0.0006 n=362	4.66 (1.73, 7.58) p =0.002 n=362	−0.34 (−1.46, 0.79) p = 0.56 n = 328	0.44 (−0.72, 1.59) p = 0.46 n = 328	0.62 (−0.39, 1.64) p = 0.228 n = 327	1.27 (0.24, 2.29) p = 0.02 n= 327

[a] The interquartile range among the parent population (Weisskopf, 2007)

[b] Adjusted for age, smoking, education, computer experience and income.

Table 3

Backward elimination regression analysis of predictors of normalized fine motor task performance among subjects with tibia bone lead measurements.

Variable		Grooved pegboard	Neuroskill	
			Signature score	lm pattern score
	N	Estimate (95% CI) p-value	Estimate (95% CI) p-value	Estimate (95% CI) p-value
Tibia	282	0.009 (0.0002, 0.018) p = 0.05	Eliminated	0.01 (0.003, 0.017) p = 0.008
Age	282	0.034 (0.017, 0.051) p < 0.0001	Eliminated	Eliminated
Smoking	282	Eliminated	−0.004 (−0.009,0.0007) p = 0.10	Eliminated
Education			Eliminated	
HS or less	88	Reference group		Reference group
Some or completed college	136	0.104 (−0.158, 0.366) p = 0.44		0.356 (0.132, 0.579) p = 0.002
Graduate school	55	0.512 (0.179, 0.846) p = 0.003		0.191 (−0.093, 0.475) p = 0.19
missing	3	1.404 (−0.018, 2.827) p = 0.05		−0.017 (−0.921, 0.888) p = 0.97
Computer experience				Eliminated
No	111	Reference group	Reference group	
Yes	168	−0.364 (−0.603, − 0.126) p = 0.003	0.24 (0.029, 0.451) p = 0.03	
Missing	3	0.142 (−1.277, 1.561) p = 0.88	−0.857 (−1.825, 0.111) p = 0.08	
Financial stability		Eliminated		Eliminated
“Can’t make ends meet” or “Just manage to get by”	53		Reference group	
“Have enough to get along, and extra”	122		−0.386 (−0.665, 0.107) p = 0.007	
“Can buy anything I want”	94		−0.313 (−0.614, − 0.013) p = 0.04	
Missing	13		−0.198 (−0.885, 0.49) p = 0.57	
Income		Eliminated		
Less than $34,999	70		Reference group	Reference group
$35K– $49,999	63		0.052 (−0.241, 0.345) p = 0.73	0.089 (−0.179, 0.357) p = 0.51
$50K– $74,999	66		0.258 (−0.043, 0.5588) p = 0.09	0.394 (0.12, 0.668) p = 0.0005
More than $75K	57		0.473 (0.1552, 0.791) p= 0.004	0.482 (0.196, 0.767) p = 0.001
Missing	26		−0.134 (−0.645, 0.377) p = 0.61	0.119 (−0.235, 0.472) p = 0.51
Alcohol (drinks per week)		Eliminated		Eliminated
0	72		Reference group	
More than zero, <= 10	103		0.161 (−0.095, 0.416)	

Variable		Grooved pegboard	Neuroskill	
			Signature score	lm pattern score
	N	Estimate (95% CI) p-value	Estimate (95% CI) p-value	Estimate (95% CI) p-value
			p = 0.22	
More than 10, <= 20	54		0.287 (−0.01, 0.585) p = 0.06	
More than 20	53		0.465 (0.161, 0.768) p = 0.003	

Table 4

Backward elimination regression analysis of predictors of normalized fine motor task performance among subjects with patella bone lead measurements.

Variable		Grooved pegboard	Neuroskill	
			Signature score	lm pattern score
	N	Estimate (95% CI) p-value	Estimate (95% CI) p-value	Estimate (95% CI) p-value
Patella	281	0.006 (−0.007, 0.012) p = 0.08	Eliminated	0.006 (0.0002, 0.011) p = 0.423
Age	281	0.035 (0.019, 0.051) p <0.0001	Eliminated	Eliminated
Education			Eliminated	
HS or less	88	Reference group		Reference group
Some or completed college	135	0.1426 (−0.119, 0.404) p = 0.2858		0.349 (0.115, 0.583) p = 0.004
Graduate school	55	0.557 (0.234, 0.881) p = 0.0007		0.185 (−0.102, 0.472) p = 0.207
Missing	3	1.55 (0.15, 2.95) p = 0.03		0.018 (−0.908, 0.944) p = 0.969
Computer experience			Eliminated	Eliminated
No	111	Reference group		
Yes	167	−0.32 (−0.56, −0.081) p = 0.009		
Missing	3	0.113 (−1.284, 1.509) p = 0.8744		
Financial stability		Eliminated		Eliminated
“Can’t make ends meet” or “Just manage to get by”	52		Reference group	
“Have enough to get along, and extra”	122		−0.423 (−0.705, − 0.141) p =0.0033	
“Can buy anything I want”	94		−0.3 (−0.604, 0.005) p = 0.0535	
Missing	13		−0.225 (−0.923, 0.4734) p = 0.5279	
Income		Eliminated		
Less than $34,999	69		Reference group	Reference group
$35K– $49,999	63		0.081 (−0.214, 0.377) p = 0.5891	0.044 (−0.237, 0.325) p = 0.759
$50K– $74,999	66		0.296 (−0.0034, 0.595) p = 0.0526	0.312 (0.026, 0.597) p = 0.032
More than $75K	57		0.552 (0.242, 0.863) p = 0.0005	0.398 (0.102, 0.693) p = 0.009
Missing	26		−0.073 (−0.584, 0.438) p= 0.7784	0.061 (−0.303, 0.426) p = 0.741
Alcohol (drinks per week)		Eliminated		Eliminated
0	72		Reference group	
More than zero, <= 10	102		0.174 (−0.088, 0.435) p = 0.1924	
More than 10, <= 20	54		0.294 (−0.01, 0.597)	

Variable		Grooved pegboard	Neuroskill	
			Signature score	lm pattern score
	N	Estimate (95% CI) p-value	Estimate (95% CI) p-value	Estimate (95% CI) p-value
			p = 0.058	
More than 20	53		0.453 (0.146, 0.761) p = 0.004	