SOCIETY OF TOXICOLOGY

Poster #3?

ABSTRACT FORM

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AUDITORY AND VISUAL EVOKED POTENTIALS IN CHILDREN WITH UNDUE LEAD ABSORPTION. D.A. Otto, S.B. Baumann, G.S. Robinson, S.R. Schroeder, D.G. Kleinbaum, C.N. Barton and P. Mushak. U.S. Environmental Protection Agency, Research Triangle Park, NC. Sponsor: R.S. Dyer

Visual impairments have been demonstrated behaviorally and electrophsiologically in rats and monkeys neonatally exposed to lead (Pb). Little evidence exists on auditory and visual effects of Pb exposure in humans, although we observed increased latencies of brainstem auditory evoked potentials (BAEP) in children with histories of undue Pb absorption (Otto et al. Environ. Res., in press). BAEPs and pattern-reversal visual evoked potentials (PREP) were recorded in 80 children aged 3 to 7 with blood lead (PbB) levels ranging from 6 to 47 μ g/dl. Elevated hearing thresholds were observed in children with higher PbB levels. The latencies of BAEP waves I and III varied inversely with PbB contrary to prediction, a possible result of adjusting stimulation level for hearing threshold. P1 latency, the most clinically relevant PREP measure, did not vary significantly with blood lead (PbB) level. An exploratory analysis of P1N2 amplitude, however, varied inversely with PbB consistent with other data suggestive of Pb-related visual impairment. Since the PREP reflects cone-mediated photopic visual function, other measures of scotopic visual function may provide more sensitive indices of lead exposure effects in humans.

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TYPE OF STUDY	TYPE OF TOXICANT	TYPE OF TARGET
Analytical	Air Pollutants/Gases	Cardiovascular
Aquatic	Drug/Cosmetic	Cellular
Clinical	Food Additives	Central Nervous System
Developmental/Reproduction	Halogenated Hydrocarbon	Dermal
Environmental	Metal	Hematological
General Toxicology Evaluation	Natural Products	Hepatic or Gastrointestinal
Hypersensitivity	*Pesticides*	*Immune*
Inhalation	Solvents/Vapors	Molecular/Genetic
In Vitro	Other	Ocular
Mechanism		Peripheral Nervous System
Metabolism/Disposition		Pulmonary
Mutagenesis		Renal
Oncogenesis		Reproductive
Reactive Intermediates		
Regulatory		

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OBJECTIVE

To replicate and extend results of previous work (Otto et al, 1985) on the relationship of blood lead (PbB) levels and sensory evoked potentials in young children.

HYPOTHESES

(1) Auditory nerve conduction velocity as indexed by the latencies of waves III and V of the brainstem auditory evoked potential (BAEP) will increase directly with PbB levels.

(2) N1P1 amplitude of the pattern-reversal visual evoked potential (PREP) will vary inversely with PbB.

METHODS

Subjects. Eighty children (50 girls) aged three to seven from low-income Black families considered to be at risk for Pb poisoning and referred by county health departments were evaluated. Pb-based paint from deteriorated housing was the primary source of exposure.

BAEP. Children were screened for middle ear infection by otoscopic examination or tympanometry. Hearing thresholds were determined audiometrically using a 2KHz pure tone or electrophysiologically using descending BAEP intensities. Two averages of 2000 alternating polarity binaural clicks (11.1/sec) presented at 60 dBSL were recorded from children lying down in a darkened mobile laboratory. BAEPs were recorded between the vertex (Cz) and linked mastoids using a 0.1-3 KHz bandpass.

PREP. Visual acuity was checked using a children's eye chart. Children were seated 5 ft. from a Grass Visual Pattern Generator (VPG-1) for full-field presentation of a black and white checkerboard pattern reversing twice per sec. 24' squares at 90% contrast were used. Two averages of 200 reversals were recorded binocularly from an Oz-Cz derivation using a 1-300 Hz bandpass.

PbB Measurement. Venipuncture samples were drawn on test day. PbB levels were determined by the Ediger and Coleman (1972) modification of the Delves cup micro atomic absorption spectrometric procedure (Delves, 1970). Previous PbB levels of children were also obtained from county health departments when available.

RESULTS

Table I. Descriptive statistics for control, PbB and electrophysiological variables.

Table II. Summary of statistical analyses of BAEP/PREP measures

Fig. 1. Hearing thresholds increased linearly with maximal PbB

Fig. 2. Representative BAEPs from five boys with varying maximal PbB histories (click intensity 80±5 dBSPL)

Fig. 3. Linear (wave I) and curvilinear (waves III, V, IPLs I-V, I-III) relationships of BAEP measures and maximal PbB. Wave I latency decreased linearly as PbB increased, while latencies of waves III, V, I-V and I-III decreased below 25 mg/dl, but increased above this level.

Fig. 4. Representative PREPs from five children with varying maximal PbB histories. Only P1N2 amplitude varied significantly (decreased) with PbB level. P1 latency increased (nonsignificantly) with increasing PbB.

Fig. 5. Relationship of P1N2 amplitude and maximal PbB.

CONCLUSIONS

(1) Curvilinear relationships of BAEP waves III, V and interpeak latencies I-III and I-V suggest possible biphasic effect of Pb on nerve conduction in auditory pathway. Only the ascending portions of curves above 25 mg/dl are consistent with predictions.

(2) Observations of elevated hearing thresholds and decreased wave I latencies in children with elevated PbB are ~~incompatible~~. ~~Electrophysiological data suggest that Pb may alter higher level auditory perceptual processes involved in psychophysical judgment without really changing hearing threshold.~~ compatible with a sensorineural recruiting hearing loss.

(3) Visual evoked potential findings did not confirm hypothesis 2, although P1N2 amplitude varied in predicted direction. Inconsistencies of present and earlier (Otto et al, 1985) findings may be due to the photopic nature of PREPs. Animal studies suggest that Pb selectively alters scotopic (rod) function. Further study of Pb effects on scotopic vision in man is needed to resolve this question.

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TABLE I. SAMPLE MEANS FOR DEMOGRAPHIC

AND ELECTROPHYSIOLOGICAL VARIABLES

VARIABLE	N	MEAN	SD	MIN	MAX
AGE (Months)	75	58.4	11.7	33	94
SES	75	70.8	6.2	55	84
CHILD IQ	75	86.1	11.7	60	119
MATERNAL IQ	75	63.4	11.3	40	94
HOME	75	59.8	15.1	20	87
CURRENT PbB (μg/dl)	75	20.6	9.7	6.2	47.4
MAXIMUM PbB	75	26.7	14.1	6.2	56.0
BRAINSTEM AUDITORY EVOKED POTENTIAL					
LATENCY I (MSEC)	64	1.72	0.14	1.47	2.14
LATENCY III	65	3.85	0.19	3.51	4.50
LATENCY V	65	5.72	0.24	5.26	6.46
IPL I-III	64	2.13	0.15	1.89	2.55
IPL III-V	65	1.86	0.13	1.57	2.17
IPL I-V	64	3.99	0.22	3.63	4.45
PATTERN-REVERSAL VISUAL EVOKED POTENTIAL					
N1 LATENCY (MSEC)	70	68.6	3.6	60.5	81.0
P1 LATENCY	70	100.3	5.9	90.0	129.5
N2 LATENCY	70	145.2	15.2	123.5	197.5
N1P1 AMPLITUDE (μV)	70	15.5	7.2	2.95	40.6
P1N2 AMPLITUDE	70	10.9	5.5	2.17	26.7

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TABLE II. EXPLORATORY ANALYSIS OF LINEAR, QUADRATIC AND CUBIC TRENDS IN THE RELATIONSHIP OF MAXIMUM PbB LEVELS AND ELECTROPHYSIOLOGICAL MEASURES: p-VALUES

Dependent Variable	Polynomial*	Linear	Quadratic	Cubic
BRAINSTEM AUDITORY EVOKED POTENTIAL				
LATENCY I	.035	.008	.28	.60
LATENCY III	.020	.44	.003	.98
LATENCY V	.06	.98	.007	.98
IPL I-III	.016	.12	.005	.60
IPL I-V	.037	.08	.020	.76
IPL III-V	.63	.26	.51	.92
PATTERN-REVERSAL VISUAL EVOKED POTENTIAL				
N1 LATENCY	.048	.12	.06	.16
P1 LATENCY	.14	.08	.38	.19
N2 LATENCY	.77	.58	.55	.50
N1P1 AMPLITUDE	.35	.17	.26	.72
P1N2 AMPLITUDE	.013	.001	.64	.68

*Polynomial-test of the set of three trends

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Fig. 1

RELATIONSHIP OF HEARING THRESHOLD VS. PbB

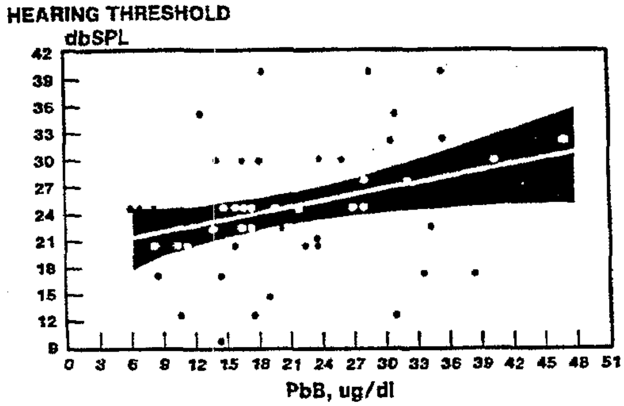
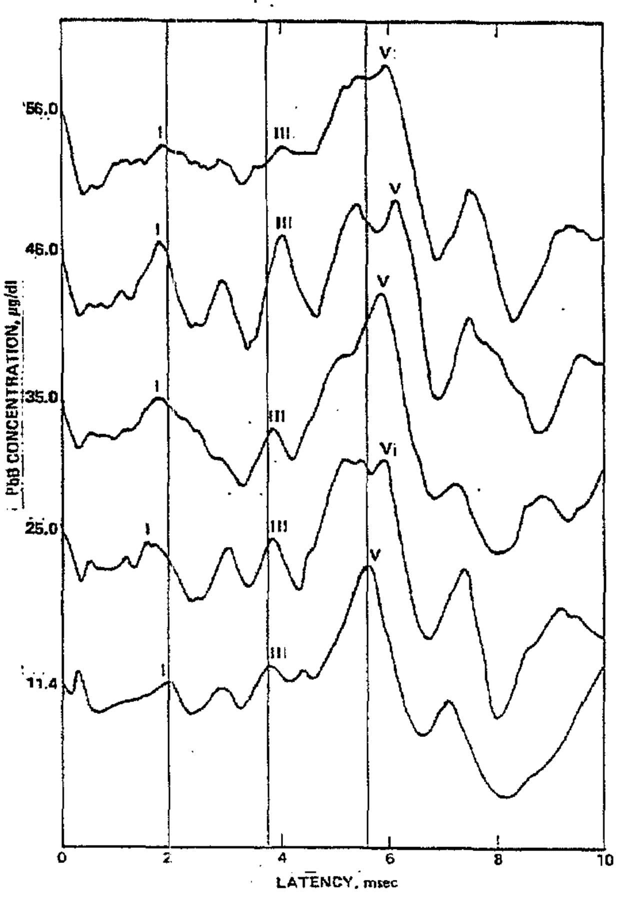


Fig. 2

BRAINSTEM AUDITORY EVOKED POTENTIALS IN BOYS WITH VARYING Pb EXPOSURE HISTORIES



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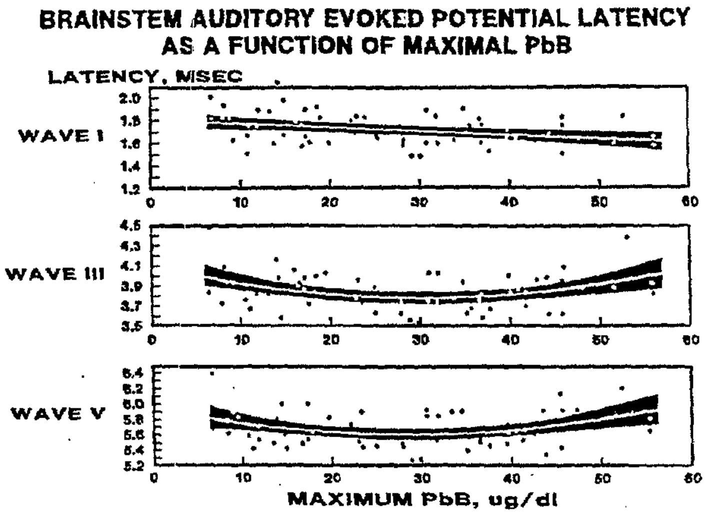

Fig 3a

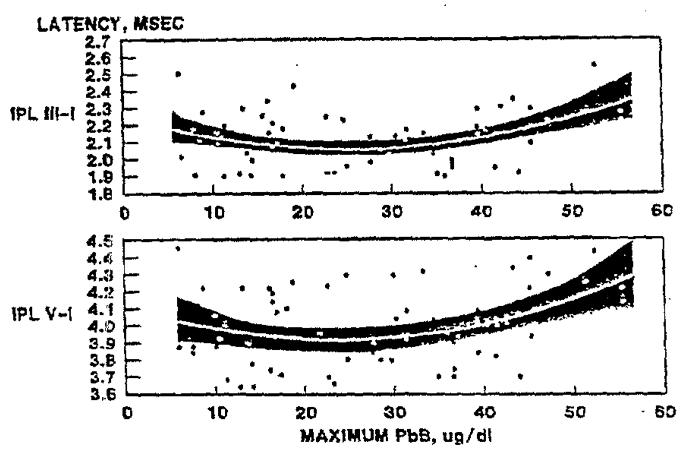

Fig 3b

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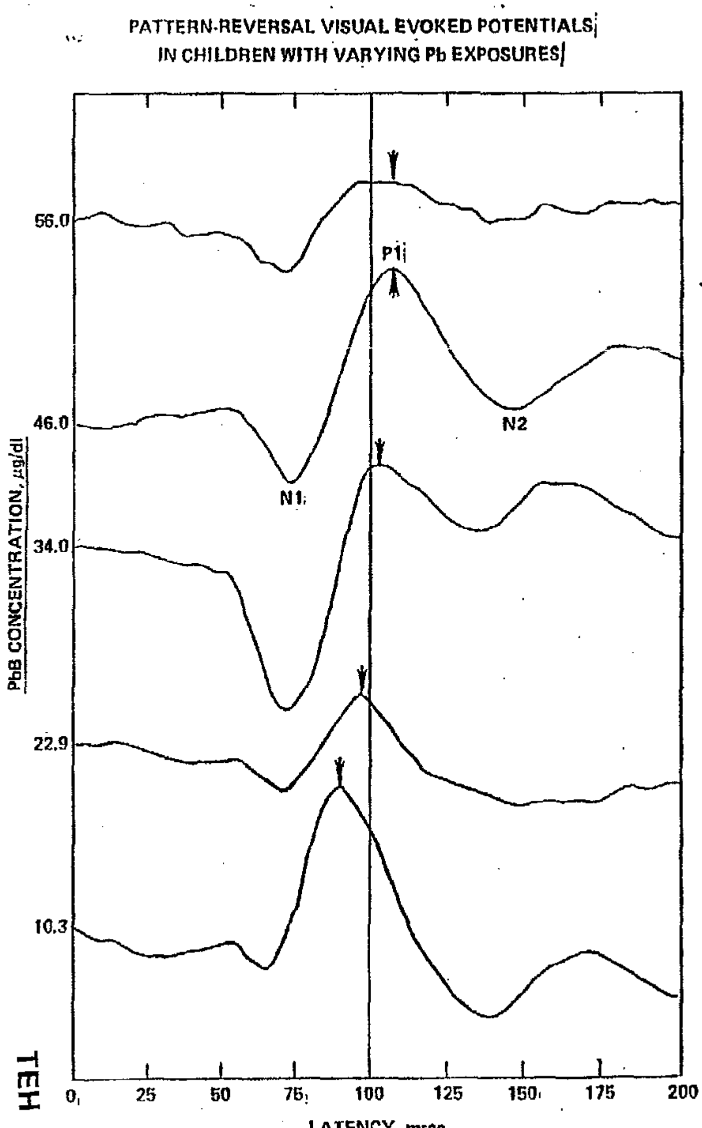
PATTERN-REVERSAL VISUAL EVOKED POTENTIALS
IN CHILDREN WITH VARYING Pb EXPOSURES
PbB CONCENTRATION, µg/dl
56.0
46.0
34.0
22.9
10.3
P1
N1
N2
0
25
50
75
100
125
150
175
200
LATENCY, msec

Fig. 4

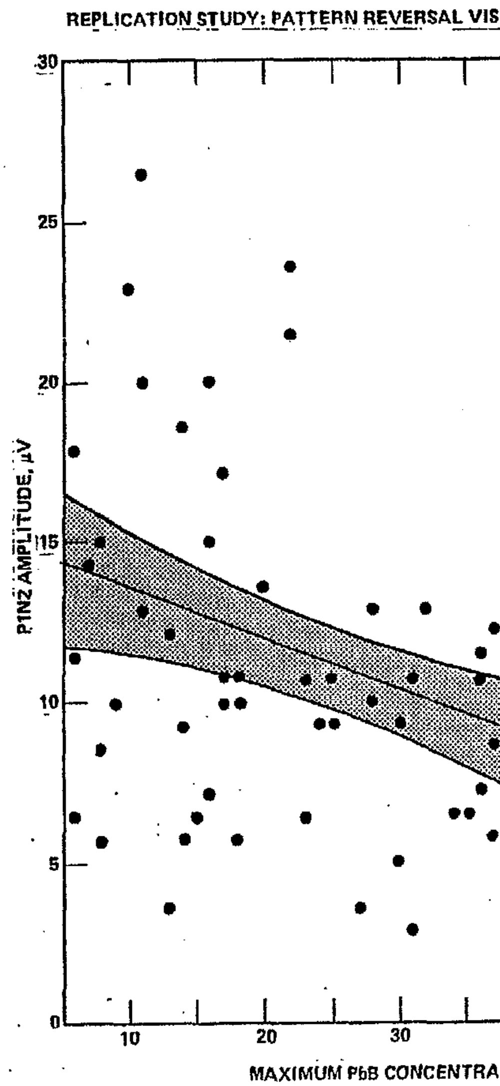
REPLICATION STUDY: PATTERN REVERSAL VIS
P1N2 AMPLITUDE, µV
30
25
20
15
10
5
0
10
20
30
MAXIMUM PbB CONCENTRA

Fig 5