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Adverse effects of childhood lead poisoning: The clinical neuropsychological perspective

T.I. Lidsky[a,*], J.S. Schneider[b]

[a]Department of Psychobiology, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY 10314, USA
[b]Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, College of Medicine, Philadelphia, PA 19107, USA

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Abstract

Elevated blood lead levels in children can result in brain injury and, as a consequence, have negative effects on cognitive functioning and behavior. Risk assessment studies have focused on psychological measures, especially IQ, and also school achievement and behavioral adjustment as endpoints. Such studies, like epidemiological work in other areas, by necessity examine effects in large groups rather than in individuals. Since the peer-reviewed literature primarily describes those adverse effects noted in epidemiological studies, little or no attention has been directed to what is observed in the individual. The present review describes the presentation of individual lead-poisoned children from the perspective of the clinical neuropsychologist. The sequelae of lead poisoning typically observed in evaluation of individuals provide information in addition to that gained from risk assessment studies and has implications for the mechanisms and treatment of this disease. In addition, attention to certain aspects of individual case presentation does provide information relevant to issues of public health.

Keywords: Lead poisoning; Adverse effects; Clinical neuropsychology; Risk assessment; Neuropsychological testing; IQ; Children

1. Introduction

Identification of a toxic agent's adverse effects is a prerequisite not only to diagnosis, treatment, and prevention, but also to risk assessment. In the case of childhood lead poisoning, given the exposure levels seen the majority of current cases, the long-term negative effects that are most typically experienced by patients fall under the rubric of impaired neurocognitive development. For this reason, after diagnosis and treatment of immediate medical problems by physicians, lead-poisoned children typically come to the attention of psychologists and educational specialists. However, as Bellinger (2003) has explained in a recent review, the features that are of concern to a clinician for diagnosis and treatment differ somewhat from those that are used by the epidemiologist to establish population risk. Because much of the attention to childhood lead poisoning has been in the context of public health regulation, considerable efforts have been made in the peer-reviewed literature to describe those adverse effects that are within the purview of epidemiological studies. In contrast, the clinical presentation of lead poisoning in individual children, a picture that cannot be unequivocally adduced from examination of epidemiological studies, has received little attention and has not been otherwise presented. Accordingly, knowledge of the signs and symptoms of lead poisoning in the individual child is gained by psychologists and educational specialists primarily through direct experience in performing evaluations.

Similarly to other toxins, the behavioral manifestations of lead poisoning are dose-dependent. Lead at blood lead levels $\geqslant 70\,\mu g/dl$ is life-threatening and can cause encephalopathy in children. Such poisoning has

*Corresponding author. Fax: +1 718 698 3803.
E-mail address: tlidsky@monmouth.com (T.I. Lidsky).

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symptoms that may initially include lethargy, abdominal cramps, anorexia, and irritability and can progress to vomiting, clumsiness, ataxia, alternating periods of hyperirritability and stupor, and then finally coma and seizures. The sequelae include neurological signs and mental retardation (Adams and Victor, 1993). However, due to the prohibition of the use of leaded paint in 1978 and the elimination of leaded gasoline in 1985, average blood lead levels in the United States have decreased and children with blood lead levels $\geqslant 70\,\mu g/dl$ are relatively rare (Brody et al., 1994). Since children with potentially lethal blood lead levels are now infrequently encountered, the poisoned patient who comes to the attention of clinicians presents with entirely different symptoms. Patients with lower levels of exposure may complain of stomach pains and loss of appetite and could have anemia. These symptoms "…are not present in all poisoned children, or even the majority, and in any case, do not unequivocally point to lead as the culprit" (Lidsky and Schneider, 2003). Low lead levels may still be neurotoxic and numerous investigations have documented that these patients' symptoms are in the realm of neurobehavioral functioning.

The present paper discusses the clinical picture observed by psychologists and educational specialists when a lead-poisoned child is evaluated. Consideration of the behavioral signs and symptoms of lead poisoning typically encountered in such cases has implications for the mechanisms and treatment of this disease. In addition, although it has been persuasively argued that nosology based on clinical observations would be an awkward and inefficient basis for population studies aimed at determining risk (Bellinger, 2003), it is our opinion that attention to various aspects of individual case presentation also provides information relevant to issues of public health.

2. The lead-poisoned child in epidemiological studies

The majority of risk assessment studies have used the averaged performance of a large group of children on a traditional IQ test as the behavioral endpoint. IQ has been used for this purpose because it has "… good psychometric properties, is sufficiently well standardized to be comparable across studies, and exhibits attractive simplicity for the regulator in a public health context" (Winneke and Krämer, 1997). Numerous such investigations have been done and, despite differences in a variety of important factors (e.g., nationality, SES), there has been general consistency in the finding of an inverse relationship between indices of lead exposure and IQ (e.g., Needleman and Gatsonis, 1990; Schwartz, 1994). Taken together with recent analyses (Bellinger and Needleman, 2003; Canfield et al., 2003; Schwartz, 1994), there is a loss of about 7–8 points in Full Scale IQ as blood lead level increases to $10\,\mu g/dl$ and at least an additional 1–3-point decrement as the blood lead level reaches $20\,\mu g/dl$. The magnitude of this loss is substantial, amounting to about two-thirds of a standard deviation.

Other aspects of lead's effects on child development have also been studied in the context of risk assessment. Children who have had elevated lead levels as infants have decreased proficiency in basic academic skills (e.g., reading, arithmetic) and decreased achievement at school (e.g., Fergusson et al., 1997; Lanphear et al., 2000; Needleman et al., 1990; Wang et al., 2002). In addition, in adolescence such children are also at increased risk for antisocial behavior and delinquency (e.g., Dietrich et al., 2001; Needleman et al., 1996, 2002).

The picture that emerges from risk assessment research therefore is of a child with a diminished overall level of intellectual functioning, decreased academic attainment, and problematic behavior. Such a symptom triad is certainly not uncommon in the general population and, in and of itself, can be related to any of a multitude of etiologies. Are there symptoms that are more specific to the lead-poisoned child?

In evaluating an individual lead-poisoned child, one must be mindful that this metal's effects on neurocognitive development are mediated by its neurotoxic effects on the developing brain (Bressler et al., 1999; Lidsky and Schneider, 2003; Silbergeld, 1992). Thus, techniques must be selected that are designed to detect the manifestations of brain dysfunction. Although intuitively it might seem that an IQ test battery would be an ideal measure, this assumption would be ill founded. While brain injury can certainly affect IQ, these test batteries were not designed to assess brain dysfunction and are remarkably insensitive to its effects (Lezak, 1995). Brain injury, from a variety of causes (e.g., trauma, ischemia/hypoxia, toxic agents), frequently affects functioning in a limited number of neurobehavioral systems. For example, it is not unusual when evaluations of brain-injured patients reveal deficits affecting only circumscribed aspects of language (e.g., object naming) or specific memory functions (e.g., working memory only), leaving other aspects of memory (procedural, semantic, episodic) as well as other cognitive functions intact. Intelligence tests, because the aggregate IQ is based on summed performance of multiple subtests that tap a vast array of cognitive functions, obscure the telltale focal impairments that are the stigmata of brain injury. Indeed, although the averaged IQ of a large group of patients often will show some decrement as a result of brain damage, the size of the decrease underestimates the functional significance of the impairments with respect to the patients' ability to perform activities of daily living. In addition, the IQ of some individuals within that group will show no change or will actually increase (Dlugos

et al., 1999). The other endpoints used in risk assessment, school performance and antisocial behavior, are actually more sensitive to the effects of brain injury than is IQ but less informative concerning mechanisms.

3. The lead-poisoned child in neuropsychological studies

"Neuropsychology is an applied science concerned with the behavioral expression of brain dysfunction." (Lezak, 1995). Neuropsychological tests, more narrowly focused on behavioral functions controlled by specific neural systems, have been designed to detect the functional effects of brain injury. Due, in part, to the insensitivity of IQ tests to the effects of brain injury, the use of neuropsychological tests has been receiving increasing attention over the past two decades for the description of the effects of lead exposure in children. These studies, like those employing IQ as an endpoint, differed from each other with respect to important factors such as choice of tests, age at testing, and blood lead levels. Averaged performance of cohorts of lead-exposed children, or adults who had been lead-exposed as children, were compared to control groups on tests of fine motor skills, language, memory and learning, attention, and executive functioning. In most of this work different investigators focused on different behaviors so that no one investigation assessed a complete spectrum of neuropsychological functions.

Considered as a group, these studies reported deficient average performance on tests that assess fine motor skills, language, aspects of memory and learning, attention, and executive functioning (e.g., Bellinger et al., 1994; Campbell et al., 2000; Canfield et al., 2004; Dietrich et al., 1992; Faust and Brown, 1987; Ris et al., 2004; Stiles and Bellinger, 1993; Stokes et al., 1998; Walkowiak et al., 1998; Wasserman et al., 2000; White et al., 1993; Winneke and Krämer, 1997). One investigation, that of Faust and Brown, did assess a wide spectrum of neuropsychological domains in children (average age ~7 years 9 months) that the authors characterized as having "moderately elevated blood lead levels" (<30 μg/dl for the previous year and never exceeding 60 μg/dl at any time). In comparison to controls and also to average performance, the lead-poisoned group was deficient in 3 of 4 aspects of fine motor functioning, 4 of 4 aspects of visuoperceptual abilities, 4 of 4 aspects of aspects of memory, 7 of 8 aspects of language, 2 of 3 aspects of attention, and 4 of 4 aspects of executive functioning.

One could easily get the impression from the group studies employing neuropsychological testing that, like the dampening effect on IQ, childhood lead exposure causes a generalized decrease in functioning across neurocognitive domains. If diffuse neurocognitive dulling was the characteristic outcome of pediatric lead poisoning, this information could have utility for diagnosis. Brain injuries from the majority of etiologies do not produce a diffuse dampening of neurocognitive functioning in individuals—rather, symptoms are typically focal impairments of specific neuropsychological processes observed in association with relatively normal functioning in other neuropsychological domains (Lezak, 1995). Thus, if as a result of lead poisoning a child presented with impairments affecting a broad array of neurocognitive functions, this would be a rather unique set of symptoms of brain injury. Unfortunately, the impression that childhood lead poisoning causes this particular generalized pattern of behavioral symptoms is an artifact due to the use of test score averaging in group studies.

4. The lead-poisoned child in clinical neuropsychology

4.1. Rationale

The methodology and rationale underlying a clinical neuropsychological assessment of an individual and the conclusions drawn therefrom substantially differ from those of epidemiological studies of groups. Both types of assessment depend upon results from administration of neuropsychological tests. However, rather than using parametric statistics to compare averaged results from groups that differ with respect to exposure to a neurotoxic event, clinical neuropsychological assessment depends on an examination of individuals test results to determine if observed performance differs from expected results (see below).

Neuropsychological testing in a clinical setting is designed to measure the cognitive/behavioral manifestations of normal and abnormal brain function in an individual to determine if a diagnosis of brain injury is appropriate. The neuropsychological functions targeted by these tests are behaviors, identified in clinical and research studies and increasingly confirmed with functional scanning, that are associated with functioning in identifiable discrete or distributed neural systems. These functions are broadly categorized as sensory/perceptual, motor, language, attention, memory and executive. Each of these categories are subdivided; for example, major processes subsumed under the rubric of memory include short-term and long-term storage, free recall, recognition, working, and procedural and episodic memory with different systems for remembering auditory, verbal, and visual information as well as information conveyed by other sensory modalities.

Tests commonly used in clinical practice aim to quantify the relevant behavior in a way that allows objective scoring. For example, the critical score derived from administration of the Purdue Pegboard, a test of visuomotor functioning, is the number of pegs inserted

into holes within a fixed time period; the particulars of the patient's grasp and positioning movements, while often noted, are irrelevant to the total score. Once a patient's score for a given test is calculated, it is compared to a normative group to determine the relative level of performance, often expressed in standard scores and ultimately as a percentile.

Decisions as to whether or not there is abnormality are based on the pattern of test results rather than on any individual score taken in isolation. The underlying rationale is that with the majority of brain injuries, some neural systems are unaffected, while the functioning of others are diminished. The neuropsychological functions mediated by the damaged areas will be negatively impacted, while the behaviors controlled by the intact systems will be less affected. Accordingly, neuropsychological test performance that depends on behaviors controlled by damaged areas will decline, while tests less reliant on such behaviors will be normal.

"Reliable neuropsychological assessment based on impairment patterns requires a fairly broad review of functions. A minor or well-circumscribed cognitive deficit may show up on only one or a very few depressed test scores, or may not become evident at all if the test battery samples a narrow range of behaviors" (Lezak, 1995). A neuropsychological evaluation typically includes tests for major sensory/perceptual, motor, language, attention, memory, and executive processes—striking a balance between the need to be comprehensive and the necessity to avoid tiring the patient with overlong testing.

To determine whether a depressed test score represents the normal fluctuation of cognitive strengths and weaknesses in an intact individual rather than a score indicative of impairment due to brain injury, use is made of a standard of comparison specific to that particular individual. Determination of this standard (or baseline) rests on the well-founded assumption that under normal conditions (e.g., absent brain damage or psychiatric illness), there is "…one performance level that best represents each person's cognitive abilities and skills generally." Thus, "…the performance level of most normally developed healthy persons on most tests of cognitive functioning probably provides a reasonable estimate of their performance level on other kinds of cognitive tasks" (Lezak, 1995). Accordingly, test performance that is significantly below expectation for an individual's overall level of cognitive functioning is considered to be abnormal. For cognitive functions (e.g., memory) that are normally distributed in the population, tests results that are at least one standard deviation below an individual's baseline (Hebben and Milberg, 2002) or greater than one standard deviation (Lezak et al., 2004) are classified as clinically significant.

There are several accepted ways to approximate a person's overall level of cognitive functioning to establish a baseline. Although with each method the baseline is an estimate, a rather wide range is set wherein test results are considered to be normal; only results below that range are classified as abnormal. The "best performance method" is often used, in which the baseline is taken to be the highest score or set of scores. The rationale underlying this approach includes the assumptions that the higher scores represent functioning in relatively undamaged systems and that "few persons consistently function at their maximum potential (Lezak et al., 2004).[1]" so that best test results are unlikely to be an overestimate of cognitive functioning. Another commonly used method is to use performance on an intelligence test battery, because of the relative insensitivity of IQ to brain injury, to establish the baseline. In the case of lead-poisoned children, however, this approach is complicated by the fact that lead clearly lowers IQ. For this reason, in neuropsychological evaluations of children with lead poisoning, as with other types of brain injuries that are sustained early in development, determinations of impairment are based on comparisons between test results and estimates of what the child's level of intellectual functioning *would have been* in the absence of injury. However, when determining a lead-poisoned child's reference baseline, the well-established effect of this toxin on overall IQ becomes part of the equation. As already discussed, blood lead levels of 10 μg/dl lead to a loss of about 7 Full Scale IQ points. Further increases in blood lead level produces the loss of an additional 1–3 Full Scale IQ points with a linear dose/response relationship for additional increases in lead level (Bellinger and Rappaport, 2002).

When a baseline is estimated using either the best performance method or IQ, the variability inherent in test performance with the former and with blood-lead/IQ relationships with the latter is counterbalanced by the fact that the baseline determines a wide range in which test results are considered to be normal. Further, the method of estimating baseline based on IQ is conservative since, due to the short half-life of lead in the blood and sporadic blood lead testing in the population, a child's exposure is likely to be underestimated. As a result the baseline is also likely to be underestimated and therefore one is less likely to classify deficient performance on a neuropsychological test as an impairment. In practice, with lead-poisoned children, use of IQ generally sets a lower baseline than the best performance method (cf. Fig. 1).

Based on the results of a neuropsychological evaluation, one can only conclude that functioning of neuropsychological processes is normal or impaired. When impairment is detected, consideration of addi-

[1]Lezak et al., 2004 provide a far more extensive discussion of the best performance method.

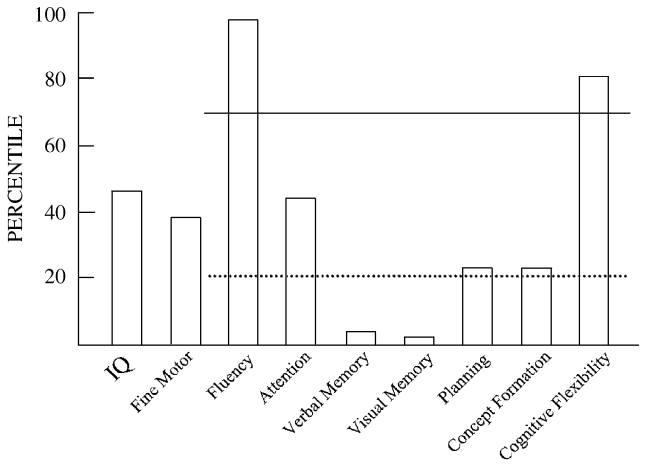

Fig. 1. Individual test result profile in which neuropsychological functioning was assessed with the following tests: fine motor—Purdue Pegboard; verbal fluency—Controlled Oral Word Association Test; attention—Brief Test of Attention; verbal memory—Story Memory from the Test of Memory and Learning; visual memory—Rey Oestereith Complex Figure Test; planning—Mazes subtest from the WISC-III; concept formation—Similarities subtest from the WISC-III, cognitive flexibility—Wisconsin Card Sorting Test. Shown are test results of a 10-year-old girl who was found to have elevated lead levels at about 24 months of age and whose blood lead levels peaked at 14 μg/dl during a 2-year period of poisoning. Her Full Scale IQ was 99 (47th percentile). It is estimated that, if not lead poisoned, her IQ would have been about 8 points higher and would have corresponded to overall functioning corresponding to the 68th percentile (solid horizontal line); the lower limit of the normal range of functioning (dotted horizontal line) is $1\frac{1}{3}$ standard deviations below. It should be noted that the test results indicating impairment (verbal and visual memory) would have been so classified even if no adjustments were made in the baseline based on her prior lead poisoning.

tional factors (e.g., medical records, lab reports) as well as other pertinent information allows the additional conclusion of whether or not there is brain injury or some other cause for the test deficiencies. If the conclusion reached is that brain damage is the cause of the test results, one cannot (except in very rare cases) determine the cause of that damage based simply on the specific pattern of behavioral performance. When a particular cause of brain damage results in a specific and unique set of symptoms that can be used for etiological diagnosis, that clinical presentation is termed a signature injury. Unfortunately, most etiologies of brain damage lack a signature injury and typically produce different patterns of impairments in different individuals; conclusions about cause rely on differential diagnosis. Thus, all pertinent information is considered (e.g., medical history, lab reports, physician's reports) and possible causes of the injury are identified, evaluated, and ruled in or out.

4.2. Clinical findings

The clinical presentation of the lead-poisoned child, and how this differs from the impression that is gained from epidemiological studies, is illustrated by a series of cases from the authors' practice. For illustrative purposes, comparisons were made between the average effects of lead (peak blood lead levels: 7–15 μg/dl) on neuropsychological test performance of a group of 21 children, poisoned as infants, and the specific effects in the individual members of the group. Considered as a group, mean IQ was below the population average of 100 and performance in tests of memory, attention, and executive functioning was also below average (Fig. 2), thereby giving the impression that lead poisoning caused a generalized diminution of intellectual and neuropsychological functioning. In contrast, consideration of each case individually, as in a clinical evaluation, indicated that lead's effects in the individual child were quite different. Shown in Fig. 1 is the pattern of test results in a single individual, a 10-year-old girl who was found to have elevated lead levels at about 24 months of age and whose blood lead levels peaked at 14 μg/dl during a 2-year period of poisoning. It was estimated that, if she had not been poisoned, her Full Scale IQ, measured as 99 (47th percentile), would have been about 8 points higher and would have corresponded to overall functioning corresponding to the 68th percentile. Her neuropsychological test performance in many areas, including fine motor, attention, planning, and concept formation, was in the normal range and in two areas, verbal fluency and cognitive flexibility, was well above average. However, performance in two areas, verbal memory and visual memory, was markedly depressed and well outside the range of neurocognitive strengths and weaknesses seen in normal individuals. This child, with memory of a short story at the fifth percentile and free recall of a geometric figure at the third percentile,

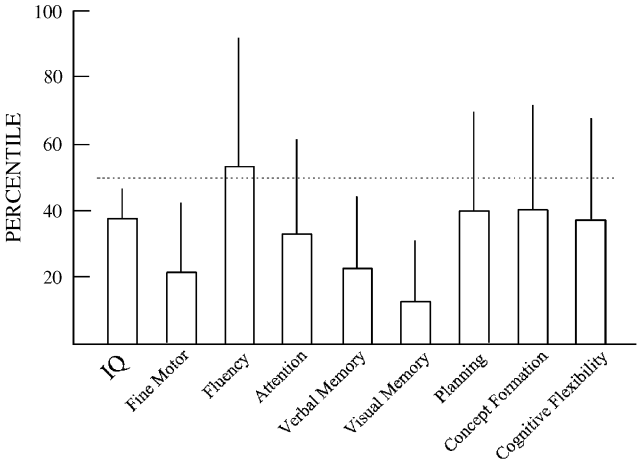

Fig. 2. Average performance of a group of lead-exposed children ($N = 21$) on psychological and neuropsychological testing (same tests as in Fig. 1). Averaged IQ (95), based on performance of the Wechsler Intelligence Scale for Children (WISC-III), was in the average range. The dotted line indicates the 50th percentile, bars indicate mean performance, and lines indicate standard deviations.

has impaired verbal and visual memory. It should be noted that these test results would have been classified as impaired even if no adjustments were made in the baseline based on her prior lead poisoning.

The general pattern of test results shown by the child in Fig. 2 was observed in each of the lead-poisoned children in this group. Each child showed areas of complete normality with test results in specific cognitive domains in the average or above-average range. However, coupled with this adequate performance were test results in other cognitive domains that reflected severe impairment. This pattern of test results in the individual is characteristic of brain injury rather than of a nonspecific dampening of intellectual functioning.

However, despite the similarity with respect to a pattern of results typical of brain injury, detailed comparisons of children's deficits indicates that lead, like most other causes of brain injury, does not produce exactly the same set of impairments in each patient. Fig. 3 shows areas of impairment and normality in neuropsychological domains (e.g., verbal memory and visual memory) for each of the 21 children discussed earlier. Clearly, the pattern of results differs for each child and no one single set of results unequivocally indicates lead poisoning rather than some other etiology. Although visuospatial memory deficits were very common, they were not seen in all children and are also commonly observed with brain damage with nonlead etiologies.

Pb	Motor	Fluency	Attention	Verbal memory	Visual Memory	Planning	Concept Form	Cog, Flex
5					■			
6		■		■	■	■		
7	■			■	■			
7					■			
9	■				■			■
10	■				■	■	■	■
10	■			■	■			■
12	■		■		■			
12			■	■	■			■
12	■				■			
13		■			■			■
13	■				■			
14	■	■		■				■
14			■		■		■	
14	■	■			■	■		
14				■	■			
14	■				■	■		■
14	■		■		■			
15			■		■			
15	■		■					
15		■			■			

Fig. 3. Summary of neuropsychological test results for each child of group whose averaged data are presented in Fig. 1. Peak lead levels are listed at left. Unfilled cells indicate performance in the normal range; cells with black squares indicate impaired performance. Each child showed areas of normality coupled with performance in other cognitive domains that reflected impairment. The specific areas of impairment varied from child to child.

Not only does the overall pattern of impairments differ from child to child, but even the particulars of deficits within neuropsychological domains show patient-specific patterns. Fig. 4 illustrates the performance of three children on a test of visuospatial memory, the Rey Oestereith Complex Figure Test (ROCFT). In the ROCFT, the child is shown a complex geometric figure (Fig. 4, Model) and instructed to copy it. After the drawing is completed, both the model and the copy are filed away and the child is engaged in a verbal task for about 3 min. Following this, the child is instructed to draw the figure from memory (immediate free recall—Recall 1); after 30 min the child is again instructed to draw the figure from memory (delayed free recall—Recall 2). Finally, in the recognition phase of the ROCFT the child is shown a series of drawings, of which some are components of the geometric figure that served as the model for the original copy and others that were not part of the model. The child is instructed to identify the drawings that were part of the model. The immediate and delayed free-recall drawings are scored according to objective criteria (Meyers and Myers, 1995) and the outcomes compared to a reference baseline of children of similar age. In the recognition trial, the number of copy components correctly identified is tallied, the number of components incorrectly identified subtracted, and the total also compared to a reference baseline of children of similar age. Fig. 4 illustrates three general patterns that were observed in lead-poisoned children. In the first (Fig. 4A), relatively similar normal levels of performance were observed in immediate and delayed free recall as well as in recognition, as is typical of unimpaired visuospatial memory. In the second (Fig. 4B), very low levels of performance were seen in all three components of the task, as is observed in memory problems due to impaired storage of information. In the third (Fig. 4C), recognition was performed at a much higher level than were immediate and delayed free recall, a pattern observed when information is stored but is abnormally difficult to retrieve.

Unlike the clinical neuropsychological findings in which individual children differ with respect to cognitive deficits, there has been discussion in the epidemiological literature about whether, when large groups of lead-poisoned children are considered, there is a signature injury. Several studies have documented neuropsychological deficiencies in fine motor, visuospatial, and executive functioning as well as in attention in large groups of children (e.g., Canfield et al., 2004; Ris et al., 2004), while other reports have firmly established that antisocial behavior and delinquency frequently are a long-term consequence of early poisoning (e.g., Dietrich et al., 2001; Needleman et al., 1996, 2002). The

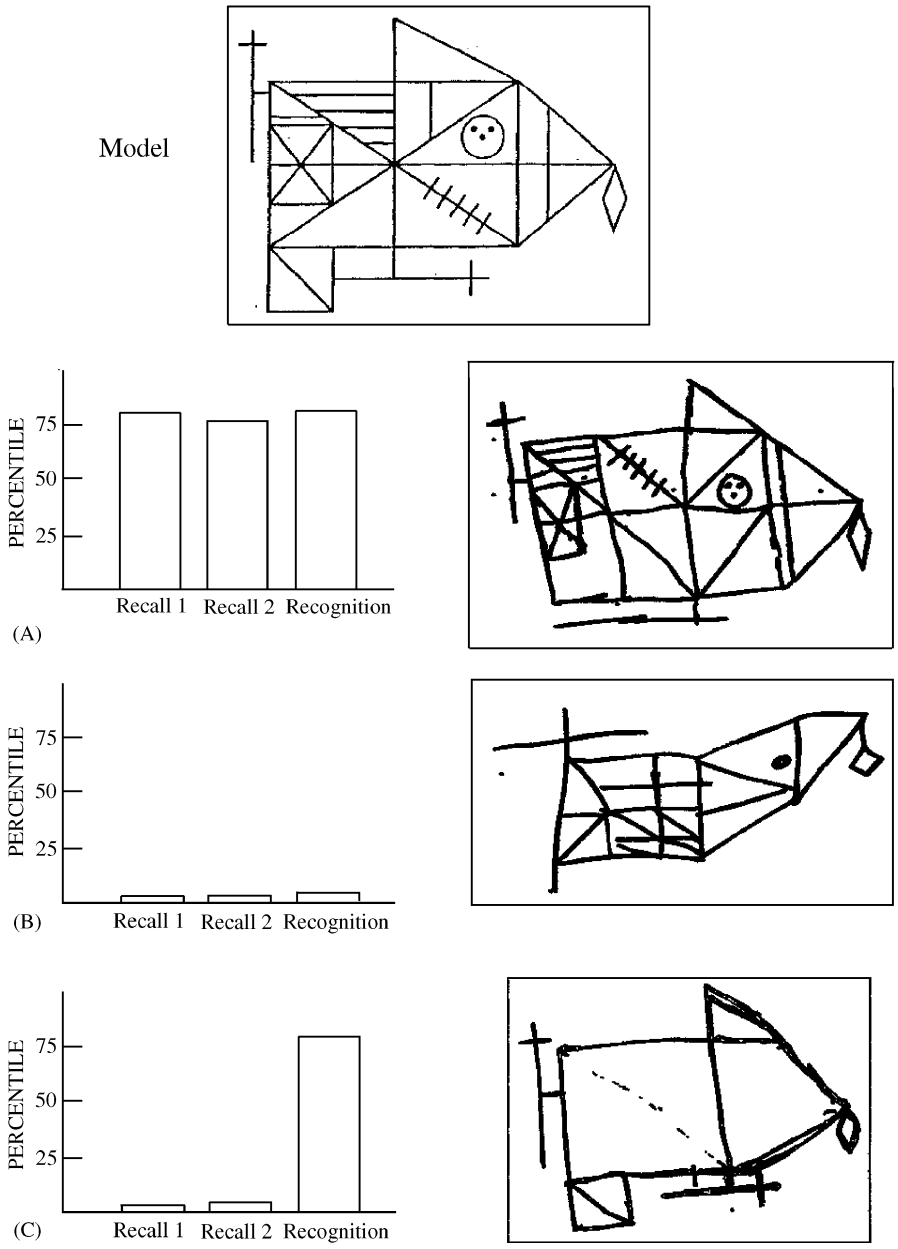

Fig. 4. Visual memory performance of three lead-poisoned children. The model at the top is the complex geometric figure that the child copies at the beginning of the Rey Oestereith Complex Figure Test (ROCFT). Three minutes after the copy is completed and removed from view the child is then instructed to draw it from memory (Recall 1), and after 30 min the child is again instructed to draw the figure from memory (Recall 2). Finally, the child is shown a series of drawings of which some are components of the geometric figure that served as a model for the original copy and others that were not part of the model. The child is instructed to identify the components of the copy model (Recognition). Shown at right is each child's Recall 2 results and at left performance in each phase of the test. The performance of Child A was normal with free recall trials and recognition performed at similar unimpaired levels. Child B's free recall of the figure shows spatial distortions and absence of details. In addition, this child also was unable to simply recognize components of the figure. This pattern of results is indicative of impaired information storage. The child in C shows a marked absence of detail from the recall trial but, in contrast, was able to accurately identify components of the model during the recognition trial. This pattern of results indicates a child who stores information but has difficulty retrieving it. Each child was about 10 years old at testing, had been poisoned before the age of 24 months, and had a peak lead level below 30 μg/dl (Child A: 26 μg/dl; Child B: 22 μg/dl; Child C: 28 μg/dl).

discussion over whether or not these findings constitute a signature injury is more a matter of semantics than a dispute over the significance of findings. If one defined signature injury as a set of consequences that generally follow a particular injury then one could suggest that the epidemiological findings do indeed indicate a signature injury. However, if the definition used is that which is commonly applied in clinical neuropsychology, wherein

the behavioral sequelae are so specific as to indicate etiology, one's conclusions would be different, viz., "Given the absence of specificity in the findings associated with an EBLL, a child's specific deficits are of little use in making a diagnosis of past or present EBLL" (Bellinger and Rappaport, 2002).

There are probably multiple reasons that, in individual evaluations, each lead-poisoned child presents with a patient-specific set of impairments. Lead targets developing brain cells (reviewed in Lidsky and Schneider, 2003; Silbergeld, 1992) and different neural systems mature at different times during development (Giedd, 2004; Huttenlocher, 1990). Children are exposed to lead at different times during development and therefore different neuronal systems, with associated behavioral functions, can be affected by poisoning. In addition, a variety of genetic factors, which differ from child to child, may affect the brain's vulnerability to the neurotoxic effects of lead (Onalaja and Claudio, 2000; Stewart et al., 2002).

As discussed, due to variability in exposures as well as biological factors, it is unlikely that different lead-poisoned children will have similar brain damage. However, even if each member of a group of lead-poisoned children has similar brain damage, it is likely that the behavioral manifestations will still differ from child to child. "Even when focal lesions of different types involve similar brain regions, they often produce substantially different manifestations that would impede deriving etiologically specific conclusions from the test data" (Alexander et al., 1996). Accordingly it is not surprising that lead poisoning's lack of a neurobehavioral signature is a property shared, not only by the overwhelming majority of neurotoxic agents (Hartman, 1995), but by virtually all causes of acquired brain injury (e.g., penetrating brain wounds, anoxia).

That patient-specific behavioral impairments are ubiquitous with different forms of brain injury may also be due, in large part, to the diversity of personality characteristics typical in a set of individuals, coupled with specific characteristics of neuropsychological tests that lend themselves to solutions using alternative cognitive strategies. For example, many tests of visual memory, such as the task illustrated in Fig. 3, involve the patient viewing a picture and then, after a delay, reproducing or identifying the picture. Correct performance of tasks of this type is open to at least two alternative strategies; the subject can either depend on visual memory or, less obviously, on verbal memory. The latter is accomplished by translating the figure into words and remembering that information. Although realistic scenes of everyday occurrences are most easy to verbalize, even memorization of abstract geometric figures can be approached in this way. For example, in the ROCFT (Fig. 3), one young child offered the following information concerning her impression of the figure: "It's a house on its side." Various components were described as a door and windows. For a child of her age, what was verbalized and drawn in her free recall trials was sufficient for unimpaired performance. The degree to which brain-damaged patients can rely on alternative strategies to compensate for deficiencies depends on personal characteristics as well as the nature of the brain injury. For example, an individual with impairments of both visual memory and also cognitive flexibility (or verbal memory) would be less likely to be able to switch to a verbal approach.

5. Implications of clinical neuropsychology for risk assessment

Observations from clinical neuropsychological evaluations provide information in addition to the description of the lead-poisoned child that emerges from epidemiological studies. Rather than simply dulling a child's intellect, a perception that is at least implicit in the findings of IQ-based group studies, clinical evaluations indicate that lead poisoning leads to a cognitive profile that is typical of brain injury. In this context, lead is similar to numerous other causes of brain damage that may not dramatically diminish IQ but result in neuropsychological impairments that significantly decrease academic potential and impair abilities to perform activities of daily living. Also similarly to other etiologies, lead-poisoning-induced brain damage produces different patterns of deficits in different children.

The information from clinical neuropsychology has direct implications for the treatment of lead-poisoned children. In contrast to the approaches that are typically taken with children who have learning disabilities or who are intellectually slow, the same modalities used with brain-injured children (cognitive rehabilitation, pharmacotherapy, and behavioral engineering (Lezak, 1987; Mateer et al., 1996) should also be used with children who have been lead poisoned. Cognitive rehabilitation involves retraining damaged functions or teaching the patient to use remaining cognitive abilities to compensate for impaired functions. Behavioral engineering entails changing the patient's environment to minimize the deleterious effects of specific cognitive impairments and to maximize the use of residual capabilities. For example, a child with lead-induced problems of attention should be taught in surroundings structured to eliminate sources of extraneous stimulation or distraction that would be benign to a cognitively intact student. Instruction for a child with attention problems can be structured to keep presentation of information brief and concise, provide repetition, and allow frequent breaks. Pharmacotherapy has been used principally in individuals with attention problems; a

variety of stimulant drugs have been used with success in some patients who have problems of concentration.

Bellinger notes that although a primary focus of epidemiological studies, "small shifts in the mean of a risk factor," differs from the variables that concern clinicians, data from risk assessment studies nonetheless have direct implications for individual evaluations. "…[S]mall shifts in the mean of a risk factor toward a less optimal function implies a corresponding increase in the prevalence of clinically defined cases that would be observed empirically…" (Bellinger, 2003). As discussed here, however, the converse is also true; clinical neuropsychological evaluations inform the epidemiologist by providing additional information concerning the *nature* of the risk posed by childhood lead poisoning. Clinical evaluations indicate that the victim of lead poisoning is brain damaged rather than simply a less intelligent child. Therefore those considering treatments for such children and the associated costs, should realize that standard special educational services that target children with lower intelligence or with typical learning disabilities are unlikely to be effective. Further, the fact that lead-poisoned children show idiosyncratic patterns of deficits means that the details of a rehabilitation program must be tailored to the individual child; one cannot design a generic treatment regimen for all lead-poisoned children.

The practical significance of epidemiological studies of lead poisoning can be most easily appreciated in examination of the tails of the distribution of IQs in the exposed population. Needleman et al. (1982) reported that with a 4-point downward shift in mean Full Scale IQ, there were about three times more children with IQs in the borderline range or lower (IQ $\leqslant 80$; $\leqslant$9th percentile) in the high-lead as compared to the low-lead group and a comparable but opposite shift in the proportions of children with high IQs (IQ $\geqslant 125$; $\geqslant$95th percentile). Clinical neuropsychological evaluations provide additional information about the sequelae of lead poisoning, effects that are apparent throughout the distribution, including for those children with average IQs. For example, the child whose neuropsychological test results are shown in Fig. 1 has a Full Scale IQ that is very nearly at the population mean. Yet despite an IQ that is solidly in the average range, she is experiencing considerable difficulty at school. Neuropsychological test results indicate an important reason: her ability to remember either verbal or visual information is impaired.

In conclusion, risk assessment studies and clinical neuropsychological evaluations provide different perspectives of the lead-poisoned child. Bellinger (2003) has indicated that the causes of "…small shifts in the population means on health indicators…" are clinically significant because they indicate "…that some members of the population who were formerly considered to be healthy have crossed the not-so-bright line separating the normal and abnormal and now warrant the label of patient." Clinical observations are a crucial adjunct to the epidemiological work because, unlike risk assessment studies that obscure individual differences, individual neuropsychological evaluations allow one to identify the specific impairments experienced by the patient. That information is crucial to public health administrators who are charged with the responsibility of ameliorating the effects of lead poisoning giving them a more realistic appreciation of the types of programs that will be needed to treat lead-poisoned children and what will be the likely cost.

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