

Long-Term Neurobehavioral Health Effects of Methyl Parathion Exposure in Children in Mississippi and Ohio

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Methyl parathion (MP), an organophosphate pesticide licensed only for agricultural uses, was sprayed illegally for pest control in Mississippi and Ohio residences. To evaluate the association between MP exposure and neurobehavioral development, we assessed children 6 years or younger at the time of the spraying and local comparison groups of unexposed children using the Pediatric Environmental Neurobehavioral Test Battery (PENTB). The PENTB is composed of informant-based procedures (parent interview and questionnaires) and performance-based procedures (neurobehavioral tests for children 4 years or older) that evaluate cognitive, motor, sensory, and affect domains essential to neurobehavioral assessment. Children were classified as exposed or unexposed on the basis of urinary *para*-nitrophenol levels and environmental wipe samples for MP. Exposed children had more difficulties with tasks involving short-term memory and attention. Additionally, parents of exposed children reported that their children had more behavioral and motor skill problems than did parents of unexposed children. However, these effects were not consistently seen at both sites. There were no differences between exposed and unexposed children in tests for general intelligence, the integration of visual and motor skills, and multistep processing. Our findings suggest that MP might be associated with subtle changes to short-term memory and attention and contribute to problems with motor skills and some behaviors, but the results of the study are not conclusive. **Key words:** children's health, methyl parathion, neurobehavioral development, neurologic functioning, organophosphate pesticide. *Environ Health Perspect* 112:46–51 (2004). doi:10.1289/ehp.6430 available via <http://dx.doi.org/> [Online 25 September 2003]

Methyl parathion (MP), also known as “cotton poison,” is an organophosphate insecticide that was first registered for use in the United States in 1954 [Agency for Toxic Substances and Disease Registry (ATSDR) 1999; U.S. Environmental Protection Agency (EPA) Office of Pesticide Programs 2000]. In 1978, MP was classified as a “Restricted Use Pesticide” because of its potential to harm humans and birds (U.S. EPA Office of Pesticide Programs 2000). In the United States, MP is licensed only to control insects on certain agricultural crops in open fields. It is most commonly used on cotton, but other major uses include field corn, peaches, wheat, barley, soybeans, and rice fields (Anonymous 1997a; ATSDR 1999). MP has been marketed under the names Nitrox, Dithon 63, Ketokil 52, Seis-Tres 6-3, Metaspray 5E, Paraspray 6-3, and Penncap-M (Anonymous 1997a, 1997b; ATSDR 1999; U.S. EPA Office of Pesticide Programs 2000).

MP is not licensed for indoor use, but it was used illegally as a pesticide for cockroaches possibly because *a*) it is effective against these pests, *b*) it is relatively inexpensive, and *c*) it persists for long periods of time when used indoors so that frequent respraying may not be necessary (Anonymous 1997c; U.S. EPA Office of Pesticide Programs 2000). Illegal indoor residential spraying of MP for pest control has been identified in nine states: Alabama, Arkansas, Illinois, Louisiana, Michigan, Mississippi, Ohio, Tennessee, and

Texas (Anonymous 1997b). All sprayed areas in these states have been designated as Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA 1986) or “Superfund” sites. These sites were placed on the National Priorities List (NPL) that identifies sites most in need of remediation. These sites are different from typical NPL sites, such as industrial facilities, which are generally defined by a structural boundary. In contrast, the MP sites consist of contaminated residences and businesses that are intermingled with other structures that were never sprayed with MP. In addition, these sites are spread over several counties in several states, which makes the planning of targeted remedial actions more challenging.

Although MP degrades rapidly outdoors, it degrades more slowly indoors under most conditions (ATSDR 1999). However, MP dissipates more rapidly from the indoor air than from contaminated indoor surfaces such as drywall, wood, or heating ducts. Under some situations, MP may be released back into the air, such as when heaters are turned on or when carpets are chemically cleaned (Esteban et al. 1996). Acute exposure to high levels of MP affects the nervous system by inhibiting activity of the enzyme acetylcholinesterase (AChE) (ATSDR 1999; Eskenazi et al. 1999; U.S. EPA Office of Pesticide Programs 2000). At normal levels, AChE breaks down acetylcholine, which helps transmit signals in the nervous system. When AChE is inhibited, an

excess of acetylcholine accumulates and impairs the proper functioning of the nervous system (Eskenazi et al. 1999; U.S. EPA Office of Pesticide Programs 2000). Signs and symptoms of acute high-dose exposure include loss of consciousness, headache, dizziness, confusion, difficulty breathing, loss of coordination, muscle twitching, tremor, nausea, vomiting, abdominal cramps, diarrhea, blurred vision, and excessive perspiration and salivation (Anonymous 1997a, 1997b; ATSDR 1999; Eskenazi et al. 1999; U.S. EPA Office of Pesticide Programs 2000). Symptoms usually appear within hours of exposure and generally disappear after days or weeks as new cholinesterase is synthesized.

In 1984, seven children in Mississippi became ill (two ultimately died) after acute indoor exposure to MP in a concentration nearly three times that used for outdoor agricultural spraying. The signs and symptoms included two children in respiratory arrest and five children with various degrees of lethargy, increased salivation, increased respiratory secretions, abdominal pain, and pinpoint pupils [Centers for Disease Control and Prevention (CDC) 1984].

Health effects resulting from long-term exposure to MP are unknown. MP can enter the body through inhalation, ingestion, and dermal absorption, but dermal absorption is the most common means of exposure (Anonymous 1997a, 1997b; ATSDR 1999). Once it is absorbed, MP is metabolized by the liver. *para*-Nitrophenol (PNP), a metabolite of MP, has been measured in urine as a biologic marker for exposure to MP. Urinary levels of PNP can reflect the direct intake of environmental MP, the assimilated MP that biodegrades into PNP, or both sources. Urine testing for PNP is reliable only for about 24 hr after exposure because MP breaks down quickly and exits the body (ATSDR 1999; Morgan et al. 1977).

The length of time between spraying and sample collection is not known in this study. The spraying in Mississippi occurred during a

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2-year period ending in 1996 (Anonymous 1997a); in Ohio, the spraying occurred from January 1991 through November 1994 (Esteban et al. 1996). A study conducted in Lorain County, Ohio, showed that PNP was still present in the urine of some people whose homes were sprayed more than a year before the sample was collected (Esteban et al. 1996). The fact that PNP was detected in the urine after this length of time may indicate continual exposure via MP-contaminated households or personal items (Esteban et al. 1996).

Animal studies have shown that exposure to organophosphate pesticides affects neurologic functioning in developing rats by altering behavior and producing slight changes in learning ability (ATSDR 1999; Eskenazi et al. 1999). A study of 90 pesticide applicators suggested that organophosphate exposure was associated with a loss of peripheral nerve function (Stokes et al. 1995). Another cohort of pesticide applicators acutely exposed to organophosphates several years before testing were more likely to have mood changes and difficulties with memory and motor reflexes than was an unexposed comparison population (Savage et al. 1988). Agricultural workers in Nicaragua who were tested 2 years after exposure to organophosphate pesticides performed worse on tests that measured verbal and visual attention, visual memory, visuomotor speed, sequencing and problem solving, and motor steadiness and dexterity than did an unexposed comparison population (Rosenstock et al. 1991). A 1994 study examined the chronic effects of acute organophosphate poisoning using California surveillance data and found that exposed men performed significantly worse on tests that measured sustained visual attention and mood scales (Steenland et al. 1994). A study of sheep farmers with long-term exposure to organophosphates found subtle peripheral neuropathy (Beach et al. 1996). Fifty-two male workers occupationally exposed to organophosphate pesticides for at least 3 years were compared with 50 unexposed male controls; the pesticide applicators performed worse on tests that measured visuomotor speed, verbal abstraction, attention, and memory (Farahat et al. 2003). These studies suggest evidence of neurologic deficits in workers who were occupationally exposed to organophosphate pesticides.

Children may be more likely to be exposed to MP because crawling and play activities put them close to the ground, where they have increased chances of exposure to contaminated surfaces such as baseboards (ATSDR 1999; Bearer 1995; Eskenazi et al. 1999; Guzelian et al. 1992; Landrigan and Carlson 1995). Additionally, children may be more susceptible to health effects from MP exposure because of their developing organ systems (ATSDR 1999; Eskenazi et al. 1999; Kolb and Fantie 1997).

No studies have examined the neurobehavioral effects of MP exposure in children.

Because children have unique characteristics that often place them at greater risk of adverse health effects when exposed to hazardous chemicals, this study examined the neurobehavioral development in children subacutely exposed to MP in doses lower than those seen in occupationally exposed workers.

Materials and Methods

Study population. Potential participants were identified using data files provided to the ATSDR by the Mississippi and Ohio state health departments. These states were selected because environmental data collection and urine testing were available. Children residing in Mississippi and Ohio who were 6 years or younger when their homes were sprayed with MP were eligible for inclusion in the study. In one Ohio county, the spraying occurred in a multifamily, subsidized housing facility that was last sprayed in 1994. In Mississippi, the spraying was more widespread and included 29 counties with residences sprayed as recently as late 1996.

Results of environmental wipe samples for MP taken from residences (household MP) and urine testing for creatinine-adjusted PNP, a metabolite of MP, were provided by the state health departments. The samples were collected for residents in areas known to be illegally sprayed with MP. Household MP samples were analyzed by laboratories approved by the U.S. EPA employing the same analytical methods, and PNP samples were analyzed by the CDC. Testing was done in Ohio in 1994 and in Mississippi from late 1996 through mid-1997. Exposure status was defined on the basis of the test results. Both household MP and urinary PNP levels were used to define exposure status.

In Mississippi, exposure was defined as at least one household MP sample $\geq 150 \mu\text{g}/100 \text{ cm}^2$ or urinary PNP $\geq 100 \text{ ppb}$ for at least one person in the household. For Ohio, exposure was defined as household MP $\geq 132.9 \mu\text{g}/100 \text{ cm}^2$ or urinary PNP $\geq 100 \text{ ppb}$ for at least one person in the household. To include enough exposed children in Ohio, it was necessary to set a lower cutoff value for household MP.

Comparison groups of unexposed children residing in the same communities as the exposed children were also identified. Local comparison groups were chosen to minimize confounding from sociocultural factors (e.g., regional variations in education, IQ, race, and cultural factors).

In Mississippi, unexposed children were selected through state records from houses that tested $< 25 \mu\text{g}/100 \text{ cm}^2$ for household MP; no urine testing was done for children at these levels of MP. In Ohio, unexposed children were selected in two ways. State records

were reviewed from houses that tested $< 35 \mu\text{g}/100 \text{ cm}^2$ for household MP and where no one in the household had a urinary PNP level $> 25 \text{ ppb}$. The cutoff value for household MP in Ohio was increased to include enough unexposed children. Because an insufficient number of unexposed children were identified through existing records, a special census was done in the sprayed complex after it was remediated and in a nearby housing complex that was not sprayed, to identify additional unexposed children.

Children whose household MP levels were between the lower and upper cutoff values for a particular site and who did not have at least one person in the household with a urinary PNP level $\geq 100 \text{ ppb}$ were not invited to participate in the study. For example, a child in Mississippi with a household MP level of $90 \mu\text{g}/100 \text{ cm}^2$ and where no one in the household had a urinary PNP level $\geq 100 \text{ ppb}$ would not be invited to participate in the study because their household MP level was not $< 25 \mu\text{g}/100 \text{ cm}^2$ or $\geq 150 \mu\text{g}/100 \text{ cm}^2$ and the urinary PNP requirement was not met.

We identified 365 children in Mississippi (147 exposed and 218 unexposed) and 287 children in Ohio (104 exposed and 183 unexposed). We attempted to enroll two unexposed children for every exposed child to ensure an adequate number of unexposed children for analysis in subsequent study years. All children who participated in year 1 (summer 1999) were invited to be retested in year 2 (summer 2000) to see whether any differences in neurobehavioral testing between exposed and unexposed children persisted or disappeared.

Data collection. Parents/guardians of eligible children invited to take part in the study were contacted initially by letter, which was followed up with a telephone call. All parents/guardians gave written informed consent for their child to be in the study. Children 7 years and older provided assent for their participation in the study. All testing protocols were approved by the CDC's institutional review board.

A computer-assisted personal interview was administered by trained interviewers to the parent/guardian to obtain information on potential confounders. The interview collected information on demographic and personal characteristics such as parents' and child's medical history, mother's pregnancy history with regard to the index child, parental occupational histories, workplace chemical use, and child's residential history.

The Pediatric Environmental Neurobehavioral Test Battery (PENTB) was used to assess the neurobehavioral functioning of the children (Amler and Gibertini 1996). The PENTB consists of performance-based and informant-based tests, as described below.

Performance-based tests. The Developmental Test of Visual-Motor Integration (VMI) measures the integration of visual and motor skills. The Kaufman Brief Intelligence test (K-BIT) measures general intelligence, verbal ability, and nonverbal reasoning. The Purdue Pegboard tests visual-motor coordination, manual dexterity, and motor speed. The Story Memory and Story Memory-Delay from Wide Range Assessment of Memory and Learning tests verbal memory; immediate and delayed recall of both specific and general items are assessed. The Trail-Making test, Part A and Part B, assesses multistep processing involving more than one cognitive function area (visual perception, motor speed, sequential skills, and symbol recognition) and is administered to children 9 years and older. The Verbal Cancellation test measures sustained selective attention.

Informant-based tests. The Parenting Stress Index (PSI) estimates the occurrence of common signs and symptoms of child and family dysfunction; this test yields a child domain score composed of six subscales (adaptability, acceptability, demandingness, mood, distractibility/hyperactivity, and reinforces parent), a parent domain score composed of seven subscales (depression, attachment, restrictions of role, sense of competence, social isolation, relationship with spouse, and parent health) and a total stress score, and was completed by parents/guardians of children 1–3 years of age. The Personality Inventory for Children (PIC) assesses the child's behavior, affect, and cognitive status. This test yields four factor scores (undisciplined/poor self-control, social incompetence, internalization/somatic symptoms, cognitive development) and is completed by the parent or guardian of children 4 years or older. The Vineland Adaptive Behavior Scales (VABS) measure communication; daily living skills such as eating and dressing, household tasks, and time and money skills; socialization; and motor skills.

Detailed information about the PENTB, including specific PENTB tests and scoring, is presented elsewhere (Zeitl et al. 2002). For the individual PENTB tests, both raw scores and age-scaled scores (where appropriate) were computed using the appropriate scoring manuals. Children were also assigned to one of four overall PENTB outcome groups (expected, equivocal, below expected, or undetermined) on the basis of the number of completed tests and their scores on the individual tests. Children classified as expected scored in the average range or better on most tests, with only one or two test scores below average; children classified as equivocal scored average or better for some tests but below average on three or four tests or well below average on one or two tests, and showed no pattern or consistency; children classified as

below expected scored below average on five or more tests, well below average on three tests, or in the lower extreme on two tests; and children classified as undetermined completed too few tests.

Data analysis. We redefined the initial exposure status to identify a more highly exposed group of children. High exposure was defined as household MP $\geq 1,000$ $\mu\text{g}/100$ cm^2 or a urinary PNP level ≥ 300 ppb. Exposed children not meeting this requirement were assigned to the moderate exposure group. The unexposed group remained unchanged. Analyses were computed for both the initial exposure status and the redefined exposure status.

We analyzed continuous test scores using linear regression. A higher mean difference score between exposed and unexposed children indicates better performance for the following tests: K-BIT, Story Memory and Story Memory Delay, VMI, Purdue Pegboard, Verbal Cancellation, and VABS. A lower mean difference score indicates better performance for the Story Memory Difference, Trail Making, PSI, and PIC.

We computed unadjusted and adjusted results and calculated 90% confidence intervals (CIs) for the parameter estimates. In the unadjusted models, we adjusted all raw (non-standardized) test scores for age to make the scores comparable. For each PENTB test, potential confounders were entered individually in the regression model with the exposure status. Variables that contributed to a change in the parameter estimate of the exposure status of 10% or more were included in the final adjusted model. Income ($< \$20,000/\text{year}$ compared with $\geq \$20,000/\text{year}$) and race (white, black, other) were included in the final adjusted model regardless of their effect on the parameter estimate of the exposure variable. Other variables adjusted for in the final model were ethnicity (Hispanic or Latino compared with non-Hispanic or non-Latino); mother's use of chemicals at work; mother had one or more of the following conditions: diabetes or epilepsy/seizures before pregnancy, hospitalized or confined to bed during pregnancy, fever, X rays, or vaginal bleeding during pregnancy; and parent reported that a doctor told them their child had lead or mercury poisoning. A site term was included in the models. Adjusted results are presented only if the adjusted and unadjusted results differed by $> 10\%$.

Test scores were also dichotomized to compare those children who scored in the worst 10% for a test with those children who scored in the other 90%. Dichotomized test scores were analyzed using logistic regression. Raw (nonstandardized) test scores were adjusted for age. Unadjusted odds ratios (ORs) and 90% CIs were computed.

Secondary analyses were conducted for each site separately and are presented when there are major differences between the two sites, such as effects seen in one site but not the other or large differences in the magnitude of the effects. For the Ohio participants, models could not be adjusted for "child had lead or mercury poisoning" because none of the parents reported that a doctor told them their child had lead or mercury poisoning. A full report of the site-specific analyses has been published elsewhere (ATSDR 2003).

We interpreted the results on the basis of the strength of association including the magnitude of the measures of effect and the precision of the estimates, exposure-response trends, and consistency of the findings across the different ways the data were analyzed (i.e., linear and logistic regression produced the same results). Here we present the overall PENTB outcome group and test-specific results for year 1. The overall PENTB outcome group results for year 2 were compared with overall PENTB outcome group results for year 1 to see whether any differences in neurobehavioral testing between exposed and unexposed children persisted or disappeared. A full report of the year 2 analyses is published elsewhere (ATSDR 2003).

Results

Table 1 presents the number of initially identified, scheduled, and tested participants in year 1. A comparison of available demographic characteristics for participating and nonparticipating children who were scheduled for testing in year 1 is presented in Table 2. Participating and nonparticipating children were similar with respect to age at scheduled testing and sex. In year 2, 226 (81%) of the children who participated in the first year of the study were retested (107 exposed and 119 unexposed).

Overall PENTB outcome group. The overall PENTB outcome group (expected, equivocal, below expected, or undetermined) for children who participated in year 1 is presented in Table 3. A similar number of exposed and unexposed children were classified as below expected. More exposed children than unexposed children were classified as expected, and fewer exposed children than unexposed children were classified as undetermined.

Each child's overall PENTB outcome group for year 1 was compared with their overall PENTB outcome group for year 2. A child was considered to have an improved overall outcome group from year 1 to year 2 if the child went from below expected to equivocal, from below expected to expected, or from equivocal to expected. For children who completed performance-based tests in both years of the study and who were not classified as undetermined in either year, 33% of the exposed children who were classified as below expected

in year 1 did not improve their classification from year 1 to year 2, compared with 60% of the unexposed children. Additionally, 61% of the exposed children who were classified as equivocal in year 1 did not improve their classification from year 1 to year 2, compared with 75% of the unexposed children. These results indicated that MP exposure was not associated with persistent deficits in year 2 among children who performed lower than expected in year 1. Overall PENTB outcome group results for years 1 and 2 were not compared for children whose parent/guardian completed informant-based tests in both years of the study because of small numbers.

Performance-based tests. No effects were seen for the K-BIT, VMI, or Trail-Making tests (ATSDR 2003). These tests measure general intelligence, the integration of visual and motor skills, and multistep processing. Table 4 presents the results of performance-based tests where exposed children performed worse than unexposed children in year 1.

For the Verbal Cancellation test, an effect was seen for the mean difference only in Ohio (highly exposed ordered form adjusted $\beta = -6.02$, 90% CI, -11.27 to -0.78 ; highly exposed nonordered form adjusted $\beta = -8.09$, 90% CI, -13.41 to -2.78), and there was a trend with exposure. When test scores were dichotomized, an effect was seen only in Mississippi (ordered form OR = 2.27, 90% CI, 0.80–6.45; nonordered form OR = 10.29, 90% CI, 2.23–47.41).

For the Story Memory tests, the only effect was seen for dichotomized Story Memory Difference scores (OR = 1.27, 90% CI, 0.61–2.67), and the effect was strongest in Ohio (OR = 1.71, 90% CI, 0.50–3.37). This subtest measures the ability to recall details of a story after a period of delay.

For the Purdue Pegboard test, the findings were not consistent across subtests or across sites. In Ohio, the only effect was seen for the nonpreferred hand (adjusted $\beta = -1.82$, 90% CI, -10.08 to 6.44; OR = 1.20, 90% CI, 0.42–3.49). In Mississippi, the only effect was seen for the dichotomized preferred hand score (OR = 1.39, 90% CI, 0.66–2.94).

Informant-based tests. Table 5 presents the results of informant-based tests where exposed children performed worse than unexposed children in year 1. The PSI was administered only in Mississippi because no children among those tested in the study in Ohio were younger than 4 years at the time of testing. Effects were seen for mean difference scores on all domains (Table 5). Effects were also seen when child domain and total stress scores were dichotomized (child domain OR = 1.90, 90% CI, 0.24–15.24; total stress OR = 4.22, 90% CI, 0.62–28.71). However, an OR could not be computed for the Parent domain because there were no unexposed

children who scored in the worst 10% for this subtest.

For the VABS, an effect was seen for the motor skills domain (highly exposed $\beta = -9.05$, 90% CI, -15.50 to 2.60; OR = 3.10, 90% CI, 0.90–10.63), and there was a trend with exposure for the mean difference scores. In Mississippi, an effect was seen for the mean difference and dichotomized test scores for all other subtests (Table 5). For the mean difference, a trend with exposure was seen for all subtests except the communications domain; for dichotomized test scores, a trend with exposure was seen for the daily living skills and social skills domains.

For the PIC, an effect was seen for the mean difference score for PIC factor 1, undisciplined/poor self control ($\beta = 2.73$, 90% CI, -1.16 to 6.62), and the effect was strongest among the highly exposed children in Mississippi (Table 5). In Mississippi, an effect was seen among highly exposed children for the dichotomized test scores for PIC factor 4, cognitive development (OR = 1.79, 90% CI, 0.52–6.25). In Ohio, an effect was seen for PIC factor 1 when scores were dichotomized and for PIC factor 3, internalization/somatic symptoms (Table 5). A trend with exposure

was present for the mean difference scores for PIC factor 3.

Discussion

Exposure to MP was not associated with poorer performance on most neurobehavioral tests, and effects were not consistently seen in both sites. Effects were seen for tasks that involve short-term memory and attention, and parents of exposed children reported that their children had more behavioral and motor skills problems than did parents of unexposed children. The reported behavioral problems included children misbehaving, acting on impulse, having problems with anger, being sad or shy, and having problems relating to other children. A comparison of overall PENTB outcome group scores indicated that MP exposure was not associated with persistent deficits in year 2 among children who performed lower than expected in year 1. This suggests that if there are neurobehavioral effects from subacute exposure to low levels of MP, they may be transient in children who were 6 years or younger when they were exposed. A previous study found major impairment of memory and concentration in workers who had exposures to various

Table 1. Number of eligible and tested participants in year 1.

	Exposed [No. (%)]	Unexposed [No. (%)]	Total [No. (%)]
Potential participants	251	401	652
Ineligible	77	141	218
Eligible	174 (100)	26 (100)	434 (100)
Refused	6 (3.4)	41 (15.8)	47 (10.8)
Scheduled for testing	168 (96.6)	219 (86.2)	387 (90.8)
Completed or partially completed testing	132 (75.9)	147 (56.5)	279 (64.3)

Table 2. Comparison of available demographic characteristics of participating and nonparticipating children who were scheduled for testing in year 1.

	Participant	Nonparticipant	χ^2
Exposure status [<i>n</i> (%)]			
Exposed	132 (47.3)	36 (33.3)	6.2, <i>p</i> = 0.01
Unexposed	147 (52.7)	72 (66.7)	
Mean age in years at testing (range) ^a	6.1 (2.5–11.5)	6.0 (1.9–12.5)	
Sex ^b [<i>n</i> (%)]			0.9, <i>p</i> = 0.35
Male	149 (53.4)	48 (48.0)	
Female	130 (46.6)	52 (52.0)	
Site [<i>n</i> (%)]			4.1, <i>p</i> = 0.04
Mississippi	179 (64.2)	81 (75.0)	
Ohio	100 (35.8)	27 (25.0)	
Total	279	108	

^aAge information missing for seven nonparticipating children in Mississippi. ^bSex information missing for eight nonparticipating children in Mississippi.

Table 3. Overall PENTB outcome group for children who participated in year 1.

Overall PENTB outcome group ^a	Exposed [No. (%)]	Unexposed [No. (%)]	Total [No. (%)]
Expected	72 (54.5)	60 (40.8)	132 (47.3)
Equivocal	41 (31.1)	54 (36.7)	95 (34.1)
Below expected	14 (10.6)	15 (10.2)	29 (10.4)
Undetermined	5 (3.8)	18 (12.2)	23 (8.2)
Total ^b	132 (100)	147 (99.9)	279 (100)

^aExpected, scored in the average range or better on most tests; equivocal, scored in the average range for some tests and below average on some tests; below expected, scored below average on most tests; undetermined, did not complete enough tests to score. ^bPercentages may not total 100% due to rounding.

organophosphates for several years, but the impairments disappeared 12 months after exposure ceased (ATSDR 1999). In this study, the time between the last spraying of the pesticide and the testing was at least 2.5 years in Mississippi and at least 4.5 years in Ohio. Incoordination is a common neurologic effect of severe MP poisoning, and slowed motor processes have been associated with acute mild exposure to MP (ATSDR 1999).

Inconsistencies in the results between Mississippi and Ohio may be due to the

differences in length of time between the spraying and testing in the two sites (the last spraying in Mississippi was in late 1996 and the last spraying in Ohio was in 1994; children in both sites were initially tested in 1999). Additionally, children in Ohio were older than children in Mississippi at the time of testing, and the older children may have outgrown any neurobehavioral effects that were caused by MP. Also, the exposure assessment of MP in household samples and in urine for each child represents only a snapshot in

time and may not reflect the total exposure received by the child. There were also inconsistencies in results within subtests of some tests. Additionally, there was a lack of trend with exposure for most tests.

Limitations of this study include the fact that the length of time between the last MP spraying, sample collection, and neurobehavioral testing was not known and was different in the two study sites. The frequency and duration of spraying were also unknown. Results for a particular test could be lacking because the neurobehavioral effects are transient and were no longer measurable when the children were tested. It might also be possible that the PENTB was not the appropriate test battery to examine neurobehavioral effects from exposure to MP. For example, even with a large sample size, the standard errors for several tests were quite large, making it difficult to find subtle effects.

Strengths of this study include the use of environmental wipe samples and urine testing to quantify the children's individual exposure to MP. The participation rate in year 1 was 64% (76% for exposed children and 57% for unexposed children). A test battery (PENTB) that was developed by a group of experts to examine the neurobehavioral effects of environmental exposures specifically in children was used. Extensive training of PENTB examiners who were blinded to the exposure status of the child and a thorough review of the collected data also contributed to the strengths of this study.

Table 4. Individual performance-based PENTB tests where exposed children performed worse than unexposed children in year 1.

PENTB Test	OR (90% CI)	Mean difference (90% CI)
Story Memory Difference		
Overall	1.27 (0.61–2.67)	
Ohio	1.71 (0.50–3.37)	
Verbal Cancellation		
Ordered form		
Mississippi	2.27 (0.80–6.45)	
Ohio		–6.02 ^{a,b} (–11.27 to –0.78)
Nonordered form		
Mississippi	10.29 (2.23–47.41)	
Ohio		–8.09 ^{a,b} (–13.41 to –2.78)
Purdue Pegboard		
Preferred hand		
Mississippi	1.39 (0.66–2.94)	
Nonpreferred hand		
Ohio	1.20 (0.42–3.49)	–1.82 ^a (–10.08 to 6.44)

^aAdjusted for income, race, ethnicity; mother's use of chemicals at work; mother had one or more of the following conditions: diabetes or epilepsy/seizures before pregnancy, hospitalized or confined to bed during pregnancy, fever, X rays, or vaginal bleeding during pregnancy; and parent reported that a doctor told them their child had lead or mercury poisoning. ^bHighly exposed children = household MP $\geq 1,000 \mu\text{g}/100 \text{ cm}^2$ or urinary PNP level $\geq 300 \text{ ppb}$.

Table 5. Individual informant-based PENTB tests where exposed children performed worse than unexposed children in year 1.

PENTB Test	OR (90% CI)	Mean difference (90% CI)
VABS		
Communication skills		
Mississippi	1.16 (0.46–2.89)	–3.41 (–6.95 to 0.13)
Daily living skills		
Mississippi	2.75 ^a (0.95–7.93)	–7.29 ^a (–12.66 to –1.92)
Social skills		
Mississippi	1.37 ^a (0.48–3.91)	–6.15 ^{a,b} (–11.34 to –0.96)
Motor skills		
Overall	3.10 (0.90–10.63)	–9.05 ^a (–15.50 to 2.60)
Adaptive behavior composite		
Mississippi	1.58 (0.63–3.99)	–7.57 ^a (–12.68 to –2.46)
PIC		
Factor 1		
Overall	2.73 (–1.16 to 6.62)	
Mississippi		5.29 ^a (–2.14 to 12.72)
Ohio	1.25 (0.47–3.34)	
Factor 3		
Ohio	1.42 (0.39–5.24)	13.04 ^a (–3.06 to 23.03)
Factor 4		
Mississippi	1.79 ^a (0.52–6.25)	
PSI		
Child domain		
Mississippi	1.90 (0.24–15.24)	20.07 (6.36–33.79)
Parent domain		
Mississippi		10.62 (–3.08 to 24.32)
Total stress		
Mississippi	4.22 (0.62–28.71)	13.07 (–0.23 to 26.68)

^aHighly exposed children = household MP $\geq 1,000 \mu\text{g}/100 \text{ cm}^2$ or urinary PNP level $\geq 300 \text{ ppb}$. ^bAdjusted for income, race, ethnicity; mother's use of chemicals at work; mother had one or more of the following conditions: diabetes or epilepsy/seizures prior to pregnancy, hospitalized or confined to bed during pregnancy, fever, X-rays, or vaginal bleeding during pregnancy; and parent reported that a doctor told them their child had lead or mercury poisoning.

Conclusion

Our findings suggest that MP might cause subtle changes to short-term memory and attention and might contribute to problems with motor skills and some behaviors. However, the results of the study are not conclusive because these effects were not seen consistently in both sites. Although some domains essential to neurobehavioral development appear to have been affected by exposure to MP, the results are largely inconsistent. The usefulness of the PENTB should be evaluated to determine whether further refinement of the battery is needed. Suggested modifications to the PENTB include adding or deleting tests, as necessary or appropriate, for the environmental exposure and outcome being examined.

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