

December 20, 2006



**VIA HAND DELIVERY**

TSCA Confidential Business Information Center (7407M)  
EPA East - Room 6428 Attn: Section 8(e)  
1201 Constitution Ave NW  
Washington DC 20004-3302

Attention: TSCA 8(e) Coordinator

RE: Supplemental Information on Submission Number 8EHQ-05-16202

Dear TSCA 8(e) Coordinator:

The American Chemistry Council's Diisocyanates Panel (Panel), on behalf of its members,<sup>1</sup> is submitting the attached published case reports "Examination of three cases with acute and chronic symptoms caused by exposure to MDI" and "Neuropsychological toxicology of methylene diphenyl diisocyanate: a report of five cases," to the EPA pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA).

While being submitted in accordance with TSCA 8(e), the Panel has made no determination as to whether this information presents a substantial risk of injury to health or the environment is actually presented by this information.

If you have any questions, please contact me, the Diisocyanates Panel Manager, at 703-741-5607 or [sarah\\_mclallen@americanchemistry.com](mailto:sarah_mclallen@americanchemistry.com).

Best regards,

Sarah Loftus McLallen  
Manager, Diisocyanates Panel



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Cc: DII Panel



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<sup>1</sup> The members of the Panel are BASF Corporation, Bayer MaterialScience, The Dow Chemical Company, and Huntsman Polyurethanes.



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## Examination of three cases with acute and chronic symptoms caused by exposure to MDI (Case report)

The 77<sup>th</sup> Annual Meeting of Japan Society for Occupational Health; Oral presentation: April 2004

Yohich NAKAMURA, H..OGURA, et al.

**Case :** 43 years old man(#1), 46 years old man(#2), 48 years old man(#3)

### **Symptom :**

Irritation of mucosa; sore throat , cough, dyspnea, chest pain

Disorder of autonomic nerve; numbness on extremities, diarrhea, nausea

### **History of previous disease :**

No allergic disease, #2: mild diabetes mellitus

**Occupation :** Tunneling worker for 5 years(#1), 20years(#2) and 7 years(#3):

**Case of disease:** In July, 2002, while he was working in the tunnel, he felt coughing and difficulty breathing et al. So, they went to the doctor after several days.

### **Data:**

From the history taking of the patient and measurement of MDI at workplace, it was suspected that symptoms caused by MDI. We detected MDA in their serum, the concentrations of MDA were 0.045mg/l(#1), 0.329mg/l(#2) and 0.671mg/l(#3). The serum DMA disappeared after 1-3 months. There were no findings about hypersensitivity pneumonitis in every chest CT, but mild hypoxemia was detected at the admission. MDI-RAST test was positive in #1 and #2 case, bronchial hypersensitivity test was positive in #2 and #3 case. The autonomic nerve function test indicted unstable response of the pupil size by electrical pupil size meter in ever cases.

### **Clinical course:**

Symptoms related irritation of mucosa disappeared in few days. Symptoms related disorder of autonomic nerve persist for long time and hypersensitivity to other chemicals occurred.

### **Conclusion.:**

We detected three MDI toxicosis. The cause of persistent symptoms related disorder of autonomic nerve is unknown, more research for neurotoxicity is need.

## Case report

# Neuropsychological toxicology of methylene diphenyl diisocyanate: a report of five cases

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The neuropsychological functioning of five men suffering alleged physical, cognitive and behavioural changes following exposure to methylene diphenyl diisocyanate (MDI), an industrial chemical, was investigated in the present study. At the time of assessment, four of the five patients remained symptomatic despite having no contact with MDI for periods ranging from 5 to 9 months. All patients reported experiencing subjective symptoms consisting of respiratory distress, headaches, depression, irritability, forgetfulness, decreased calculating ability, word-finding problems and reduced concentration. While the pattern of neuropsychological deficits varied among the patients, common findings for the group included intact psychomotor, psychosensory, visuographic and language functions accompanied by decreased concentration, mental efficiency, rate of information processing, learning ability and abstract reasoning. All five patients also revealed significant emotional distress on an objective personality measure. In general, the neuropsychological test data support the presence of behavioural and cognitive correlates of CNS injury following exposure to MDI.

## Introduction

The emergence of neuropsychological toxicology as a subspecialty of neuropsychology [1] has led to a proliferation of studies documenting cognitive and behavioural correlates of acute and subacute exposure to toxic chemicals in the workplace. A wide array of chemicals acting on the nervous system (for example, solvents, metals, pesticides and carbon monoxide) have been studied using epidemiological, experimental and case study formats [2-4].

The central nervous system (CNS) functions most adversely impacted by neurotoxins typically include attention, concentration, rate of information processing, memory, rate of new learning, psychomotor speed, fine motor dexterity, visuoconstructive ability and reaction time [2, 4, 5]. Vague subjective physical complaints and affective disturbance may also accompany neurotoxic exposure arising from either primary neurotoxin-induced effects [5, 7, 8], functional reaction to illness [9, 10] or mixed organic-functional psychological disturbance [11]. Various neurological symptoms have additionally been reported as sequelae following exposure to neurotoxic chemicals, including vestibular changes [12, 13], impaired colour discrimination [14, 15], olfactory hypersensitivity [16], optic neuropathy, peripheral neuropathy [5] and Parkinsonism [17].

Industrial workers are at great risk of potential toxic exposure, but few data are available on the CNS effects of many industrially employed chemicals. Methylene diphenyl diisocyanate (MDI), an organic isocyanide, is one such chemical used in a

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variety of industrial applications and is the key ingredient in spray foam packaging. Although infrequent, hazardous airborne exposures can occur with MDI if it is heated [18]. The current permissible exposure limit for MDI is 0.005 parts per million (ppm). While it is known that workers exposed to MDI are at risk for adverse respiratory effects, including occupational asthma, allergic disease and immunologic injury [19], no studies pertaining to the neuropsychological effects of MDI exposure have been reported in the literature. However, a related isocyanate, toluene diisocyanate (TDI), has been shown to cause headache, fatigue, concentration problems, irritability, depression, sleep disturbance, memory and sexual dysfunction [20].

Neuropsychological reactions to airborne neurotoxins do not constitute a single syndrome, but rather a number of syndromes, each of which is associated with a particular type of chemical. Case studies have the advantage of yielding detailed documentation of neuropsychological dysfunction which may constitute a particular pattern of neuropsychological disturbance for a specific substance or set of substances [21]. The purpose of the present case report is to evaluate the pattern of neuropsychological functions in five men suffering from physical, cognitive and emotional changes following acute and chronic MDI exposure.

## Method

### *Subjects*

Five right-handed male patients referred by their workers' compensation attorney for a comprehensive neuropsychological evaluation served as subjects for the study. Each subject had been exposed to MDI and hydrocarbon solvent vapours within the workplace. While hydrocarbon solvent vapours are known to cause acute and chronic CNS intoxication, none of the subjects became symptomatic until MDI was introduced into their work environment. The duration and severity of exposure to MDI also varied considerably among the subjects owing to differences in work-related activities and responsibilities. Instances of exposure for each subject occurred over a 2-year span, and adequate ventilation or other safety precautions were not used during that time period (for example, heating MDI-based glue beyond the temperature recommended by the manufacturer). The time since MDI exposure assessment varied as well. In all but one case, several months had elapsed since MDI exposure when the subjects were first seen for the neuropsychological evaluation. Subject 5 reported that he continued to be intermittently exposed to MDI in his workplace. All other subjects were not gainfully employed at the time of assessment. Formal analysis of MDI exposure levels was unfortunately not completed during any periods in which the subjects were being exposed.

The demographic characteristics for each subject can be found in Table 1. Except in the case of Subject 3, the premorbid medical, neurological, ethanol/drug use and psychological history for each subject was unremarkable and non-contributory. Subject 3 reported a positive history of having had a minor closed head injury from an automobile accident approximately 6 years earlier. He did not, however, report any residual sequelae from the head injury. Subject 5 was also suspected of having a learning disability associated with early life academic difficulties. While he did not recall participating in special education services, none of his academic records was made available. None of the subjects had completed neuroradiographic (that is, CT, MRI), electrophysiological (that is, EEG, BEAM, BEAR, VER, SEP) or functional

Table 1. Neuropsychological test results by subject

Test	Subjects				
	1	2	3	4	5
<i>Demographics</i>					
Age	52	43	29	40	29
Education	13	16	11	12	12
Months, post-exposure	8	5	9	6	Cont.
<i>Intellectual (WAIS-R)</i>					
VIQ	122	105	100	96	86
PIQ	117	105	104	94	93
FSIQ	122	106	101	95	87
Information	15	10	9	9	7
Digit Span	9	12	9	7	8
Vocabulary	15	10	12	9	8
Arithmetic	10	9	9	8	4
Comprehension	15	10	10	11	7
Similarities	14	15	13	12	13
Picture Completion	11	11	12	12	8
Picture Arrangement	12	10	11	8	8
Block Design	11	13	11	10	13
Object Assembly	12	10	13	10	10
Digit Symbol	8	11	6	6	6
<i>Motor speed and co-ordination (DH/NDH)</i>					
Grip strength (kg)	34/34	38/36	29/27	45/44	42/43
Finger oscillation	62/57	55/53	51/49	50/49	54/37
Grooved Pegboard (sec)	77/94	66/71	67/68	47/53	59/56
<i>Tactile sensory-perceptual (RH/LH)</i>					
Suppressions	0/0	0/0	0/0	0/0	0/0
Finger gnosis errors	0/0	0/0	0/0	0/0	0/0
Graphesthesia errors	1/1	0/0	0/0	9/10	0/7
Form recognition errors	0/0	0/0	0/0	0/0	0/0
<i>Auditory sensory-perceptual</i>					
Suppressions (RE/LE)	0/0	0/0	0/0	0/0	0/0
Speech sounds per. err.	2	5	17	5	8
Seashore tonal mem. err.	4	3	15	14	7
<i>Visual sensory-perceptual</i>					
Suppressions (RF/LF)	0/0	0/0	0/0	0/0	0/0
HVOT errors	1	6	3	4	3
Embedded figure errors	0	3	2	1	2
<i>Attention-concentration</i>					
WMS-R attent/conc. index	97	110	106	81	78
PASAT time/correct resp.					
Trial one	5.14	4.36	2.94	8.47	20.50
Trial two	4.62	3.53	3.16	5.45	d/c
Trial three	4.17	5.33	3.43	5.64	d/c
Trial four	24.00	6.00	3.60	4.50	d/c
<i>Cognitive efficiency-flexibility</i>					
Reaction time (msec)					
Simple	259	293	257	290	287
Complex	538	510	563	496	500
Trail Making Test (sec)					
Part A	52	21	26	35	28
Part B	71	68	71	104	97

Stroop Color Word ( <i>t</i> score)					
Words	37	41	44	31	20
Colors	31	49	49	38	<20
Color Words	26	36	47	39	20
<i>Language</i>					
COWA (raw)	33	31	41	33	34
Boston Naming (raw)	60	NA	NA	57	53
Benton Sentence Rep (raw)	10	10	13	13	13
<i>Visuographic</i>					
Rey CFD	36	36	36	35	36
<i>Memory-learning</i>					
WMS-R					
General index	120	76	96	90	92
Verbal index	110	77	103	95	84
Visual index	132	80	86	84	116
Delay index	125	92	97	79	97
CVLT (raw)					
Total list A	50	35	43	39	41
Trial 1	6	6	6	6	6
Trial 5	14	9	11	9	10
Learning slope	2.1	0.9	1.1	0.8	0.7
% Recall consistency	92	85	86	87	77
Semantic clustering	3.0	1.2	0.7	1.3	1.4
Serial clustering	1	9	5.9	4.1	3.9
List B	3	4	6	4	5
Short delay free rec.	11	6	7	4	8
Short delay cued rec.	11	8	12	6	12
Long delay free rec.	13	8	9	7	12
Long delay cued rec.	12	9	10	7	11
Perseverations	3	4	1	3	0
Intrusions	2	4	0	17	1
Correct recognition	15	16	15	11	15
Discriminability (%)	91	91	93	80	95
False positives	3	4	2	4	1
Response bias	0.5	0.6	0.3	-0.11	0
<i>Abstraction</i>					
Category test (errors)	23	103	73	60	71
Shipley abstr. ( <i>t</i> -score)	66	56	56	36	48
<i>Emotionality</i>					
MMPI ( <i>t</i> -score)					
L	53	66	53	53	40
F	60	50	64	66	56
K	44	57	61	44	44
Sum O/S difference	40	-59	36	16	138
TR (raw)	2	1	0	0	1
Carelessness (raw)	3	2	1	1	2
Hs	67	62	103	62	65
D	75	75	84	87	77
Hy	65	75	91	62	60
Pd	48	62	62	48	74
Mf	63	61	49	53	73
Pa	44	47	62	65	67
Pt	50	71	75	48	93
Sc	57	71	90	63	94
Ma	53	63	60	53	68
Si	64	46	46	73	75

metabolic/perfusion studies (that is, PET, SPECT) at the time of the assessment that could have otherwise assisted in confirming structural or metabolic CNS anomalies associated with MDI exposure.

#### *Procedure*

A comprehensive neuropsychological evaluation was completed for each subject by the primary author (T.J.R.). All tests were administered according to standardized instructions provided by each publisher. Subjects completed the test battery in a single session. The order of test administration was the same for all subjects. The tests selected for inclusion in the battery of tests were chosen so as to adequately assess a broad array of neuropsychological functions involving intellectual, motor speed and coordination, sensory-perceptual (tactile, auditory and visual modalities), attention-concentration, cognitive efficiency-flexibility, language, visuographic, memory and learning, abstract reasoning and emotionality. The administered tests included the Wechsler Adult Intelligence Scale—Revised (WAIS—R) [22], portions of the Halstead Reitan Neuropsychological Test Battery [23], Grooved Pegboard Test [24], Tonal Memory Test [25], Hooper Visual Organization Test (HVOT) [26], Embedded Figures Test [27], Paced Auditory Serial Addition Test (PASAT) [28], Simple and Complex Reaction Time [29], Stroop Colour Word Test [30], Controlled Oral Word Association Test (COWA) [31], Boston Naming Test [32], Sentence Repetition Test [31], Rey Complex Figure Drawing (RCFD) [33], Wechsler Memory Scale—Revised (WMS—R) [22], California Verbal Learning Test (CVLT) [35], Shipley Institute of Living Scale [36] and Minnesota Multiphasic Personality Inventory (MMPI) [37].

#### **Results**

At initial contact, all subjects reported a similar pattern of subjective symptoms consisting of flu-like symptoms, headaches, respiratory distress, depression, irritability, forgetfulness, disorientation, decreased calculating ability, word-finding problems, reduced concentration, numbness of the hands and feet, altered sense of smell, chronic fatigue, decreased libido, decreased exercise tolerance and skin rash. Subject 4 was the only patient diagnosed as having a mild sensory peripheral polyneuropathy. Otherwise neurological examinations on each of the subjects did not reveal a pattern of cerebellar, motor or sensory disturbances. All of the subjects, however, were diagnosed with isocyanate-induced occupational asthma and allergic rhinitis, which physically supports the fact that they did suffer from MDI exposure. Owing to the small sample size and heterogeneous nature of the sample, no group data are presented. A total of 12 functional categories were evaluated for a total of 84 reportable scores on each subject. The individual test results for each subject are presented in Table 1.

*Intellectual.* WAIS—R Full Scale IQ (FSIQ) scores fell within or above the average range of ability, with the exception of Subject 5, who earned a Low Average FSIQ. Subject 5 was, however, the only patient suspected of having premorbid learning difficulties, which could account for his lower-than-average measured intellect. The level of general intelligence for the group appeared to be consistent with premorbid educational and occupational histories. Also, no consistent pattern of Verbal-Performance IQ discrepancy emerged across the subjects in support of a lateralized cortical dysfunction. While the age-corrected subtest profiles revealed considerable variability between subjects, in most instances weaknesses were found on subtests (Digit Span and Arithmetic) comprising the Freedom from Distractability (FD)

factor [38]. Four of five subjects also revealed an additional relative weakness on the Digit Symbol subtest, a measure which inconsistently loads the FD factor among adults. Taken together, however, these findings imply subtle difficulties with concentration and encoding of information used in cognitive processing among the subjects.

*Motor speed and co-ordination.* On tests of motor speed and co-ordination, mild variability was noted with respect to left-right discrepancies among the subjects, the most notable being Subject 5's poor rate of finger oscillation in the left hand. There was, however, no consistent pattern of lateralized deficits in motor functions observed and the results typically fell within the normal range.

*Tactile sensory-perceptual.* Except in a few instances, the subjects typically manifested intact tactile sensory-perceptual functions. Consistent with his diagnosed peripheral polyneuropathy, Subject 4 revealed bilateral graphaesthesia errors but otherwise intact cortical tactile functions. The left-sided graphaesthesia errors seen in Subject 5 also correlated with his poor finger oscillation rate in that extremity. Tactile suppressions, finger agnosia or astereognosis errors were otherwise not observed in the subjects.

*Auditory sensory-perceptual.* The subjects did not reveal auditory suppression errors with bilateral stimulation. With the exception of Subjects 3 and 4, the group appeared to have intact speech sound and tonal discrimination abilities. Subject 3 performed poorly on both the speech sound and tonal discrimination, while Subject 4 only revealed difficulty with the latter task. In view of the fact that auditory perceptual tasks such as these are easily disrupted by attention problems [33], it is possible that their difficulty can be explained on the basis of poor concentration as opposed to centrally mediated auditory processing deficits. Furthermore, each of these subjects reported a premorbid history of auditory acuity weakness of peripheral origin. This problem was particularly evident in Subject 3.

*Visual sensory-perceptual.* Visual sensory-perceptual functions appeared to be intact for each subject. No cortical suppressions were observed in either visual hemifield for subjects and each appeared to have adequate perceptual organization skills and figure-ground perception.

*Attention-concentration.* While the major of subjects revealed an intact simple attention span, significant weaknesses were observed in concentration for the group as a whole. Except in the case of Subject 3, subjects' performances across the four trials of the PASAT were above the established cut-off for impairment of 3.45 seconds per correct response [28]. The PASAT results almost uniformly revealed marked slowing in rate of information processing for the subjects despite the presence of at least average measured intelligence.

*Cognitive efficiency-flexibility.* Simple and four-choice reaction times appeared to be adequate in the group as a whole. Some variability was evident between the subjects with the simple mental and double mental tracking tasks but the results largely fell within normal limits for the group. Although no specific pattern of impaired mental flexibility was evident on the Stroop, reduced rate of mental processing contributed to a generalized slowing on this task in the majority of the subjects.

*Language.* Despite the subjects' commonly reported complaint of word retrieval problems, no language deficits were observed in the group. The subjects revealed intact verbal fluency, naming ability and sentence repetition.

*Visuographic.* As a group, the subjects performed well on the measure of visuographic reproduction. Their reproductions were free of significant perceptual distortions, misalignments, omissions or other visuoconstructive deficits.

*Memory-learning.* The majority of subjects demonstrated at least average ability to store and immediately recall new material. Only Subject 2 earned a General Memory Index below average. No consistent pattern of a modality-specific memory (verbal vs. visual) deficit at immediate recall emerged for the subjects. However, three of the subjects revealed significant discrepancies (greater than 15) between their ability to immediately recall verbal vs. non-verbal material, and one demonstrated a similarly large (11) discrepancy. The majority of subjects also revealed at least average long-term retention of learning material. Only Subject 4 revealed a relatively rapid rate of forgetting with a Delayed Recall Index falling within the Borderline ability range.

Despite their average capacity to store and recall material over time (WMS-R) following a single exposure, the majority of subjects revealed marked deficiencies in learning ability on a list-learning task (CVLT). Repetitive exposure with a list of 16 words demonstrated generally poor learning ability with a low incremental learning slope and frequent reliance on an ineffective learning strategy, serial clustering. Recall consistency across learning trials otherwise appeared to be adequate. The generally poor performance for immediate recall with List B implicated a tendency towards proactive interference, while the large discrepancy (three or more words) between Short-Delay Free Recall and Trial 5 of List A implied forgetting in the form of retroactive interference. The subjects also revealed improved performances at Short Delay Cued Recall, suggesting that problems with retrieval were contributing to the poor free recall. An underlying weakness in retrieval processes was further supported by the groups normal recall at Recognition testing and adequate Discriminability.

*Abstraction.* Simple verbal abstract reasoning, as measured by the Shipley test, was performed adequately by the majority of the subjects. More complex non-verbal abstract reasoning requiring hypothesis formulation, hypothesis testing, self-monitoring and use of feedback, and rule generalization was, however, performed poorly by the majority of the subjects. Four of the five patients scored 51 or more errors on the Category test, a value established as the cut-off for impairment [23].

*Emotionality.* Except in the case of Subject 5, all subjects appeared to respond consistently and accurately to the objective personality inventory. Subject 5 revealed a tendency to endorse obvious indicators of psychopathology when contrasted against more subtle indicators [39], which no doubt contributed to his profile elevation. Every subject revealed at least one clinical scale from the MMPI above 70T, and the majority had two or more such scales elevated. While there was no common codetype observed for the group, clinically significant elevations were evident for all five subjects on Depression, three on Psychasthenia and three on Schizophrenia. The combination of these scales implies the presence of significant emotional distress among these subjects in the form of depression, anxiety and altered mentation, a finding which has become increasingly evident among neurotoxic-exposed patients [11].

### Discussion

Although the present results do not clearly identify a single pattern of neuropsychological deficits associated with MDI exposure, the data do suggest the presence of compromised cognitive functions characteristic of CNS involvement. All of the patients reported a high incidence of vague subjective complaints of the type typically seen in neurotoxic exposure, such as headaches, mood alterations, forgetfulness and decreased concentration [5, 7, 8, 11]. Similarly, the common group neuropsychological findings of intact psychomotor, psychosensory, visuographic and language

skills accompanied by decreased concentration, mental efficiency, rate of information processing, learning ability and abstract reasoning are largely consistent with neuropsychological deficits typically reported in neurotoxic studies [2, 5, 6, 40].

Additionally, the high incidence of emotional distress revealed by the subjects on the objective personality measure appears consistent with previous studies that have found affective and mood disturbances following toxic exposure [11]. Whether the emotional distress identified in these subjects arises from reactive issues, an organic affective disturbance, or some combination of the two is unclear. It is interesting to note, however, that decrements in regional cerebral blood flow have been identified in structures known to mediate emotions (for example, prefrontal and frontotemporal structures) among patients exposed to organic solvents [41]. It is unfortunate that specific neurodiagnostic information pertaining to the structural and functional integrity of these regions was not available for the present subjects. There is also a possibility that the associated cognitive deficits noted above are in part the direct result of emotional distress in these patients. Within a clinical setting, however, there appears to be no certain established way to rule this out, except to treat the affective distress and follow the patient over time to see if there is a correlated improvement in cognition.

The mechanism by which MDI acts on the nervous system to produce neuropsychological deficits is not known at the present time. Moreover, since it is possible that toxins affect the central nervous system through a number of mechanisms, it would be entirely speculative to comment on MDI's mode of action [42]. The possibilities, however, include interfering with energy production required to maintain normal neural structure and function through inactivation of enzymes or coenzymes essential for oxidative energy mechanisms, interfering with nutrition of the neural cells through involvement of the nutrient vessels, giving rise to allergic or immunologic responses that ultimately lead to structural or functional neural impairment, and altering neural function through effects on the neurochemistry, including neurotransmitters, acid-base balance and ionic concentrations. Equally speculative would be to posit a primary focus of central nervous system involvement. While it might be suggested the neuropsychological test results reflect a frontal diencephalic pattern of weakness, such a pattern is similarly evident in other non-specific disorders, such as closed head injury and chronic alcohol abuse [6] and may be of little value in localization.

Limitations imposed by the small sample make generalizing the present results to other clinical cases difficult. There is quite obviously a need for replication of the present findings. Since all of the subjects were involved in personal injury litigation, it can also be argued that the results reflect more the needs of the patients to be functionally impaired as opposed to their true neuropsychological status. However, there appears to be little support for simple malingering or exaggeration by the subjects given the data. In addition to weaknesses on testing, each of the subjects revealed areas of relative strengths. Moreover, each patient was re-evaluated approximately 1 year following their initial assessment and while some areas of continued weaknesses were identified, there were also clear indicators of functional improvement found in the group as a whole. In fact, one subject was found to be symptom-free at the 1 year follow-up. This pattern of improvement among the subjects arose in the presence of unsettled personal litigation. The results of this follow-up study will be published in the near future.

One additional confound with the study represents selection bias. Unfortunately, there were additional workers who suffered MDI exposure but did not come forward

with complaints. Several of the test subjects commented on these workers and speculated they were reluctant to come forward for fear of losing their jobs. It is also plausible that the test subjects were actually more affected by the exposure and therefore more likely to report symptoms. There were also a number of co-workers from foreign cultures who had obvious language and cultural differences that interfered with subjective reporting as well as objective neuropsychological testing.

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