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## ARTICLES

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### Neuropsychological Performance of Patients Following Mold Exposure

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*This study investigated the effects of mold exposure (ME) on human cognition by analyzing neuropsychological data from patients who were exposed to mold in their homes or workplaces. Compared to normative data, ME patients were impaired (< 10th percentile) on a number of cognitive measures, with the most consistent deficits in visuospatial learning, visuospatial memory, verbal learning, and psychomotor speed. We also examined emotional functioning and found that a number of ME patients showed evidence of both Axis I and Axis II pathology. Interestingly, there was a significant correlation among patients' scores on the Beck Depression Inventory–Second Edition and the number of neuropsychological tests falling within the impaired range. Given the limited understanding of ME and its effect on the human central nervous system, we provide a working model that attempts to capture the complex interactions of impaired cognition, psychosocial stressors, poor physical health, and emotional functioning in patients following ME.*

*Keywords: mold exposure, mild traumatic brain injury, toxic exposure*

Adverse health effects due to mold exposure (ME) have been reported in humans for thousands of years (Sorenson, 1993; Ueno, 1980, 1983). Ergotism, a syndrome associated with ingestion of fungus-contaminated grains, involves symptoms such as convulsions and gangrene and has been hypothesized as the basis for unusual behavior that was interpreted as demonic possession in medieval times (Donaldson, Cavanagh, & Rankin, 1997). In the late 1800s, a Japanese scientist showed that moldy rice contained toxins that were responsible for symptoms such as vomiting, convulsions, paralysis, and respiratory arrest (Ueno, 1983).

More rigorous research on ME has taken place in the last 100 years and has shown that certain toxic fungal (mold) metabolites, known as mycotoxins, are associated with a number of health effects, including respiratory disease, cardiac disease, cancer, and even death (Coulombe, 1993; Reijula, 1999; Sorenson, 1993; Ueno, 1980, 1983). In recent years, airborne mycotoxins have been posited as the basis for adverse health effects in water-damaged buildings (so-called sick building syndrome), but documenting a causal link has proven difficult (Fung, Clark, & Williams, 1998; Hodgson et al., 1998).

Recently, it has been suggested that ME may also result in central nervous system (CNS) changes (K. E. Gordon, Johanning, & Haddad, 1999; W. A. Gordon, Masotti, & Waddell, 1993; Johanning & Landsbergis, 1999; Sudakin, 1998). A recent case study reported that a teenage boy presented with tremorgenic encephalopathy following exposure to moldy fodder on his family's

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farm (K. E. Gordon et al., 1993). The boy, in addition to other family members, experienced an acute illness of headache, fatigue, and flulike symptoms while cleaning out a grain silo. Though the other family members quickly recovered, the boy progressed, and at 48 hr following exposure, he had a severe tremor and displayed confusion. Upon examination, he was found to be disoriented and slow to respond, and his attention capacity was reduced. EEG tests revealed a dysrhythmia "consistent with a toxic encephalopathy" (p. 238). He recovered 7 days postonset without significant residua.

In a larger, retrospective study, Johannig and Landsbergis (1999) reviewed 151 cases that presented at an occupational and environmental health clinic for evaluation following ME. Fungal exposure was assessed via environmental survey of the affected home or workplace. Patients were given a symptom survey and were tested for evidence of fungal reactions and altered immune system function. In addition to respiratory symptoms, Johannig and Landsbergis found that almost 80% of patients reported CNS-related symptoms, with 52% endorsing three or more such complaints. These symptoms included headaches, difficulty concentrating, fatigue, dizziness, and nervousness. A follow-up survey revealed that a majority of patients (68%) had a reduction in symptoms once their exposure to mold ended or was reduced (e.g., due to moving, repairs, etc.). A caveat of the study, however, was the finding that the correlation between CNS changes and elevated immunoglobulin G (an indication of allergic reactivity) was not significant. Furthermore, approximately 50% of a nonaffected, demographically matched control group also experienced CNS symptoms.

To our knowledge, only one published study has conducted a detailed investigation of the neuropsychological effects of ME. W. A. Gordon et al. (1999) studied 20 patients who were exposed to *Stachybotrys*, a toxic mold associated with adverse health effects (Fung et al., 1998). Patients were administered a standard battery of neuropsychological measures, and the following impairment criteria were used: Verbal IQ (VIQ) > Performance IQ (PIQ; by 10 points); visual memory > verbal memory (by 10 points); general memory > attention/concentration (by 10 points); verbal learning scores one standard score below the mean; and impaired problem solving on the Booklet Category test. Although overall means on IQ and memory tests were in the normal range, all patients met at least one of the aforementioned criteria, and 45% of the patients met three of the criteria. W. A. Gordon et al. (1999) con-

cluded that long-term ME was associated with cognitive impairment, especially in the areas of visuospatial integration, verbal learning, attention, and set-shifting. However, firm conclusions awaited further studies. Interestingly, the authors noted that the pattern of impairment observed in these ME patients was similar to that observed following mild traumatic brain injury (MTBI).

This study further explores the relationship between ME and cognitive changes. We analyzed neuropsychological data collected from a group of ME patients involved in litigation. An important question not addressed by previous studies is the extent to which emotional and psychosocial factors may play a role in the presentation of ME patients. Therefore, in this study, both cognitive and emotional functioning were assessed using standardized neuropsychological and psychological measures. As suggested by W. A. Gordon et al. (1999), we compared ME patients to individuals diagnosed with MTBI to directly compare the groups' neuropsychological test performance. To control for the effects of litigation, patients in the MTBI group were chosen who were also involved in litigation. The two main goals of this study were to (a) explore the interaction of cognitive and emotional changes in the presentation of patients with ME; and (b) determine the specificity of test performance in ME patients compared to another group of patients experiencing mild cognitive symptomatology.

## Method

### Participants

We analyzed neuropsychological data from 10 patients who presented in a structured clinical interview with physical and cognitive changes following ME. Of these 10 patients, 7 were exposed to mold in their homes, and 3 were exposed at their workplaces. All patients had been involved in litigation regarding their exposure. The type of mold varied across cases, including, but not limited to, *Stachybotrys atra*, *Penicillium*, and *Aspergillus*. The average duration of ME was 2.3 years (range = 0.5–3.0 years), estimated from the time that patients first reported being aware of the mold. The average duration since onset of exposure to time of testing was 3.17 years (range = 0.9–3.8 years).

Common physical complaints in ME patients included fatigue, respiratory problems, recurring bloody noses, nausea, frequent sore throats, head-

aches, congestion, lung infections, chronic cough, bronchitis, and skin rashes. These physical symptoms were also generally documented in patients' medical records. Common cognitive complaints included difficulty concentrating, memory loss, decreased attention span, difficulty following conversations, and slowed mental processing. Many patients complained of emotional difficulties as well, including depressed mood, anxiety, and increased emotionality (e.g., increased anger, crying more often). At the time of the evaluation, the majority (9 out of 10) of ME patients were no longer living or working in the ME environment.

The ME patients were compared to 10 gender-, age-, and education-matched patients who were diagnosed with MTBI using the American Congress of Rehabilitation Medicine criteria (Mild Traumatic Brain Injury Committee, 1993). They were also involved in litigation. In this group, 3 of the patients' injuries were due to a motor vehicle accident, 3 were due to blows to the head, 3 were due to falls, and 1 was due to a pedestrian accident. At the time of testing, MTBI patients were an average of 1.7 years postinjury (range = 0.2–2.7 years). In all MTBI patients, the time of loss of consciousness did not exceed 30 min, and the duration of posttraumatic amnesia did not exceed 24 hr. Cognitive and emotional complaints in the MTBI group overlapped to a significant degree with symptoms described by the ME patients (previously discussed). Physical complaints, however, were more distinct from ME patients and commonly included symptoms such as headaches, chronic pain, and fatigue.

The ME and MTBI groups did not differ in terms of gender (8 women and 2 men in each group); age (40.7 and 42.4 years, respectively),  $F(1, 19) = .17$ ,  $p = .69$ ; or education (15.1 and 14.4 years, respectively),  $F(1, 19) = .53$ ,  $p = .48$ . Moreover, the ME and MTBI groups did not differ on an assessment of pre-morbid intelligence (the vocabulary subtest on the Wechsler Adult Intelligence Scale–Third Edition [WAIS–III; Wechsler, 1997]  $M = 70$ th vs. 69th percentile, respectively),  $F(1, 19) = .04$ ,  $p = .85$ .

Institutional Review Board approval was obtained for the study at the first author's primary setting, the Veterans Affairs Northern California Health Care System.

### Procedure

All patients were evaluated with the San Diego Neuropsychological Test Battery (Baser & Ruff, 1987), which has been used previously in the diagno-

sis of toxic encephalopathy (Troster & Ruff, 1990; Troster, Ruff, & Watson, 1991). The tests included in this battery are listed in Table 1 and were administered according to standard procedures. The normative data used for comparison were those published in each of the individual tests as referenced in Table 1. To screen for poor motivation and malingering, the Rey 15-Item Test and the Rey Dot Counting Test were administered (Spreeen & Strauss, 1998). On the former, all participants recalled between 12 and 15 items (within normal limits), and the two groups did not differ on this measure,  $F(1, 19) = .11$ ,  $p = .74$  (ME  $M = 14.1$  and MTBI  $M = 14.3$ ). In addition, all participants performed in the normal range on the Dot Counting Test. These data suggested adequate motivation, allowing the observed deficits to be interpreted with reasonable certainty.

## Results

### ME Versus Normative Data

Neuropsychological data from patients with ME were compared to normative data. Performance below the 10th percentile was considered an indication of impairment. Between 1 and 5 ME patients performed below the 10th percentile on all but one cognitive measure, as shown in Table 1. A number of measures revealed impaired performance in 4 or more ME patients, including psychomotor speed (Ruff 2 & 7 Selective Attention Test), verbal learning (Selective Reminding Test), spatial span with a 20-sec delay, spatial learning (Ruff-Light Trail Learning Test), and visuospatial memory (Rey Complex Figure Test, 3-min delay). The latter three tests all have in common a reliance on visuospatial memory. However, considerable variability existed within the group. For example, on the Rey Complex Figure Test (3-min delay), 4 patients scored at the 1st to 2nd percentile, whereas 4 patients scored between the 69th and 88th percentiles. Mean percentiles across all tests are shown in Figure 1.

In contrast to the more specific cognitive measures, performance on the WAIS–III revealed very little impairment. Only 1 patient with ME was impaired (< 10th percentile) on a number of the WAIS–III subtests, scoring in the impaired range on 10 out of 13 of the subtests given. One other ME patient scored at the 9th percentile on Block Design. Otherwise, all ME patients scored in the low to high average range on all subtests (10th to 99th percentile). As a group, ME patients' mean Full Scale IQ

Table 1. Neuropsychological Deficits in Mold Exposure Versus Mild Traumatic Brain Injury Patients

Measure	Function(s) Assessed	Number Impaired out of 10	
		ME	MTBI
Finger Tapping Test (Ruff & Parker, 1993)	Motor speed	2	1
Grooved Pegboard (Ruff & Parker, 1993)	Psychomotor speed and dexterity	3	3
Ruff 2 & 7 Selective Attention Test (Ruff & Allen, 1996)	Psychomotor speed and accuracy, attention	4	4
Block-Tapping Test Block-Tapping (Baser & Ruff, 1987)	Spatial immediate memory	2	1
Test (20-sec delay; Baser & Ruff, 1987)	Spatial short-term memory	4	3
Selective Reminding Test (Buschke & Fuld, 1974)	Verbal learning	4	1
Ruff-Light Trail Learning Test (Ruff & Allen, 1999)	Visuospatial learning	5	4
WMS-III Logical Memory I (Wechsler, 1997b)	Verbal Memory	1	1
WMS-III Logical Memory II (Wechsler, 1997b)	Verbal long-term memory	2	1
Rey Complex Figure, 3 min delay	Verbal Memory	4	2
Rey Complex Figure, 30 min delay (Mitruskina, Boone, & D'Elia, 1999)	Spatial long-term memory	3	2
Controlled Oral Word Association Test (Ruff, Light, Parker, & Levin, 1996)	Verbal fluency	2	1
Ruff Figural Fluency (Ruff, 1996)	Nonverbal fluency	2	3
Trailmaking Test (Heaton, Grant, & Matthews, 1991)	Cognitive flexibility	2	2
WCST (Heaton, Chelune, Talley, Kay, & Curtis, 1993)	Cognitive shifting and problem solving	1	1
Stroop Color-Word Naming (Spreen & Strausa, 1998)	Selective attention	0	4
WAIS-III (Wechsler, 1997a)	VIQ and PIQ	1	1

Note: ME = mold exposure; MTBI = mild traumatic brain injury; WMS-III = Wechsler Memory Scale-Third Edition; WCST = Wisconsin Card Sorting Test; WAIS-III = Wechsler Adult Intelligence Scale-Third Edition; VIQ = Verbal IQ; PIQ = Performance IQ.

(FSIQ) was at the 62nd percentile, mean VIQ was at the 65th percentile, and mean PIQ was at the 53rd percentile.

In sum, ME patients exhibited a number of weaknesses on testing, most consistently on tests of visuospatial memory, but there was no single, consistent pattern of neuropsychological test performance across patients. Also, the group was heterogeneous in that some patients scored in the impaired range on a number of measures whereas other patients exhibited very few deficits.

### ME Versus MTBI

To assess whether the observed effects of ME were specific to this disorder, we compared the ME group to a group of patients with MTBI. Across the battery of tests, only one cognitive measure (the Stroop Color Word Test) distinguished between the groups when mean percentiles were compared (two-tailed *t* tests, alpha set at  $p = .05$ ). That is, the ME and MTBI groups had statistically comparable performance across neuropsychological measures when con-

sidering mean performance. Visual inspection of Figure 1 shows that the ME and MTBI patients had a number of similar strengths and weaknesses. Again, however, there was a broad range of performance within both groups: Some individuals in each group were quite impaired whereas others performed in the average to high average range (see Table 1).

The largest numeric differences between the ME and MTBI patients were observed on the Stroop Color Word Test and the Rey Complex Figure Test. Four MTBI but no ME patients were impaired on the Stroop test, a measure of attention and executive functioning. Mean performance on this test differed significantly between the groups,  $F(1, 19) = 5.38, p < .05$ . In contrast, 4 ME patients but only 2 MTBI patients were impaired on the Rey Complex Figure task (3-min delay), a test of visuospatial memory. However, the difference in mean performance on this test did not reach statistical significance.

WAIS-III scores also did not distinguish the ME from MTBI patients. *T* tests comparing the groups on FSIQ, VIQ, PIQ, processing speed, working memory, perceptual organization, and verbal comprehension re-

## COGNITIVE EFFECTS OF MOLD EXPOSURE

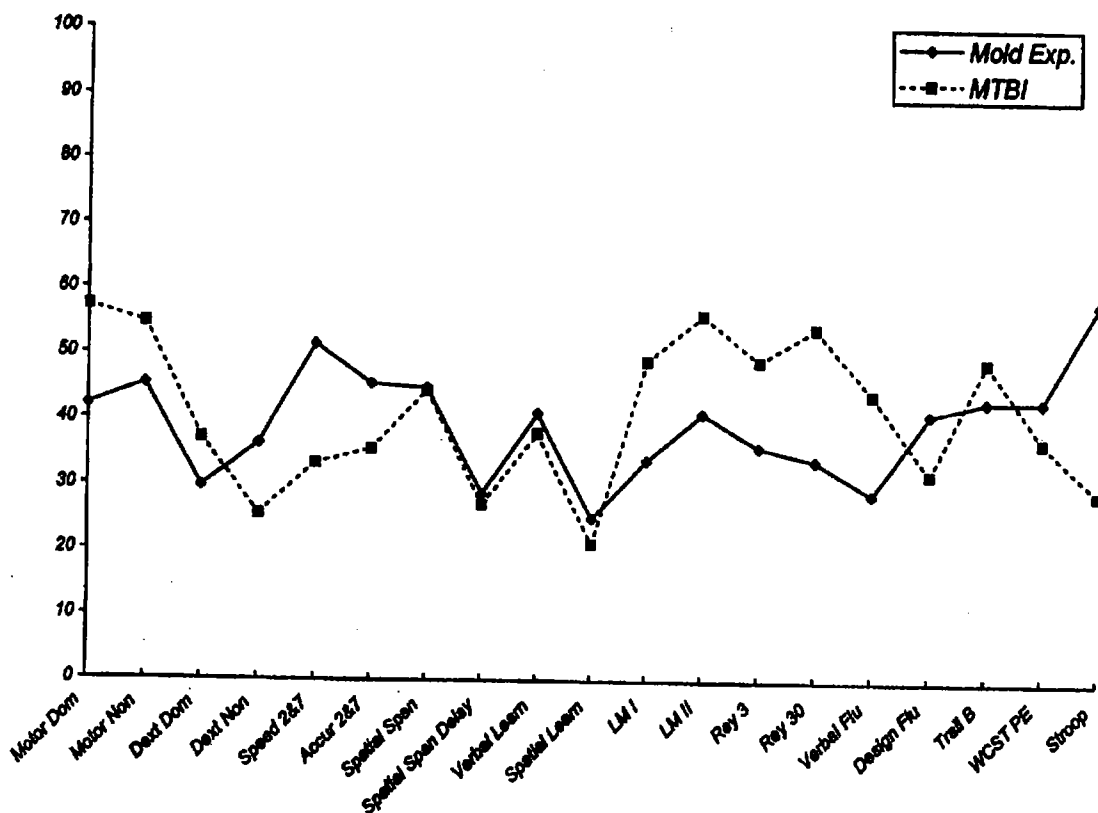


Figure 1. Performance of mold exposure (ME) and mild traumatic brain-injured (MTBI) patients on various measures in the neuropsychological battery. Motor Dom = Finger Tapping with dominant hand; Motor Non = Finger Tapping with nondominant hand; Dext Dom = Grooved Pegboard with dominant hand; Dext Non = Grooved Pegboard with nondominant hand; Speed 2&7 = speed on the Ruff 2&7 test; Accur 2&7 = accuracy on the Ruff 2&7 test; LM I = Logical Memory I; LM II = Logical Memory II; Rey 3 = Rey Complex Figure Test (3-min delay); Rey 30 = Rey Complex Figure Test (30-min delay); Verbal Flu = verbal fluency; Design Flu = design fluency; Trail B = part B of Trailmaking Test; WCST PE = perseverative errors on the Wisconsin Card Sorting Task.

vealed no significant group differences when comparing mean performance between ME and MTBI patients (all  $p > .05$ ; see Figure 2). Visual inspection of Figure 2, however, suggests a relative weakness in perceptual-organization skills in ME patients.

### Emotional Factors

In addition to cognitive functioning, we were also interested in assessing current emotional state, as well as long-term personality features. To assess long-term personality style and emotional functioning, the ME and MTBI patients completed the Millon Clinical Multiaxial Inventory—Third Edition (MCMI-III). A number of patients in both groups scored in the clinically significant range (base rate  $> 85$ ) on both MCMI Axis I and II categories. Specifically, 3 ME and 2 MTBI pa-

tients scored in the clinically significant range on at least one MCMI Axis I category, and 4 ME and 3 MTBI patients scored in the significant range on at least one MCMI Axis II category. In the ME group, MCMI Axis I categories included anxiety, somatoform disorder, and major depression, and MCMI Axis II categories included histrionic and compulsive personality disorders.

In terms of mean base rates, the ME and MTBI patients had almost identical patterns of data across the MCMI Axis II diagnostic categories, as shown in Figure 3 (two-tailed  $t$  tests, all  $p > .05$ ). There was also a great deal of concordance across MCMI Axis I diagnostic categories, except for a numerically higher base rate on dysthymia and lower base rates on drug dependence and delusional disorder in the ME patients (see Figure 4). Only delusional disorder differed significantly between the groups,  $F(1, 18) = 10.61, p < .01$ .

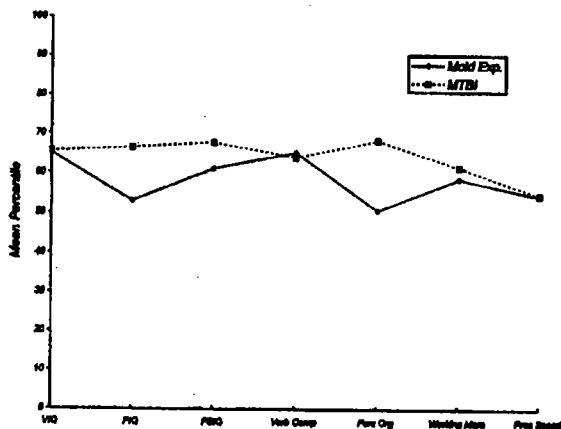


Figure 2. Performance of mold exposure (ME) and mild traumatic brain-injured (MTBI) patients on the Wechsler Adult Intelligence Scale-Third Edition. VIQ = Verbal IQ; PIQ = Performance IQ; FSIQ = Full Scale IQ; Verb Comp = Verbal Comprehension Index; Perc Org = Perceptual Organization Index; Working Mem = Working Memory Index; Proc Speed = Processing Speed Index.

A subset of patients in each group (7 ME and 6 MTBI) also completed the Beck Depression Inventory-Second Edition (BDI-II). In the ME group, 3 patients rated as severe, 2 as moderate, 1 as mild, and 1 as minimally depressed. In the MTBI group, 4 patients rated as moderate and 2 as minimally depressed. Given the literature suggesting that depressed mood can contribute to poor cognitive performance, we predicted that ME patients who had concomitant depression would have more neuropsychological test scores in the impaired range. We tested this idea in this study by comparing patients' BDI scores with overall test performance. Strikingly, correlational analysis (Pearson product moment correlation, one-tailed) revealed a significant relationship between patients' BDI scores and the number of cognitive measures in the impaired range,  $R = .47$ ,  $p < .05$ . That is, the greater the severity of the depression, the more likely a patient was to have a number of cognitive impairments on testing.

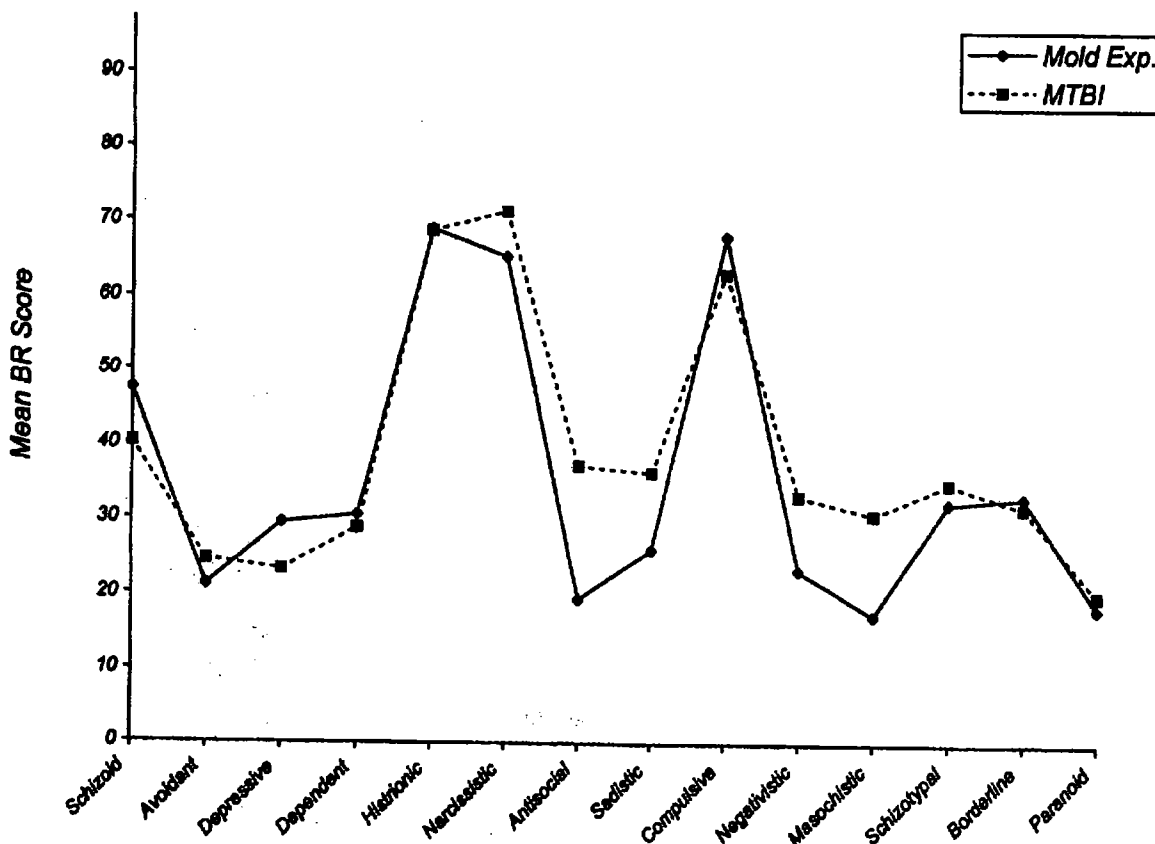


Figure 3. Mean base rates of mold exposure (ME) and mild traumatic brain-injured (MTBI) patients on the Axis II diagnostic categories of the Millon Clinical Multiaxial Inventory-Third Edition.

COGNITIVE EFFECTS OF MOLD EXPOSURE

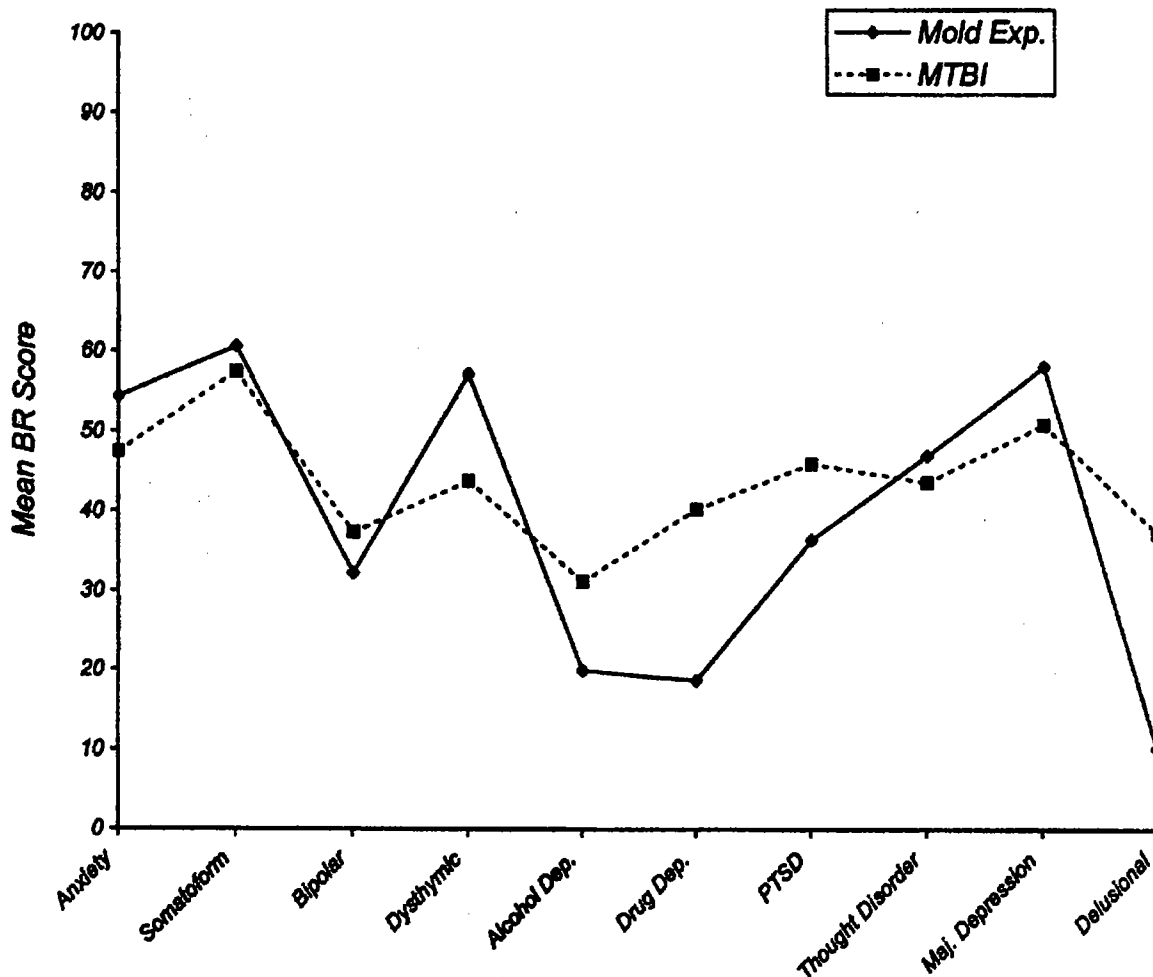


Figure 4. Mean base rates of mold exposure (ME) and mild traumatic brain-injured (MTBI) patients on the Axis I diagnostic categories of the Millon Clinical Multiaxial Inventory—Third Edition. Alcohol Dep. = alcohol dependence; Drug Dep. = drug dependence; PTSD = posttraumatic stress disorder; Maj. Depression = major depression.

Discussion

This study presents preliminary findings documenting a number of cognitive impairments in patients following ME. Areas that were most consistently affected in ME patients included psychomotor speed, verbal learning, visuospatial learning, and visuospatial memory. These findings are in part consistent with those of W. A. Gordon et al. (1999) who reported impaired visuospatial integration in patients following ME. As in that study, we also found that a subset of patients were impaired on verbal learning. This study's results are also similar to a recent study of solvent-exposed individuals that found reduced performance in the same cognitive domains (Morrow,

Stein, Bagovich, Condray, & Scott, 2001). It should be noted, however, that a great deal of variability existed in this study, such that on any given measure, some ME patients were very impaired whereas others were in the average to high average range. Thus, we did not find evidence of a single, consistent pattern of neuropsychological performance in patients exposed to mold.

To control for a number of factors, such as involvement in litigation and psychosocial stress, we compared patients with ME to a neurologic comparison group of MTBI patients who were also involved in litigation. We did not find any evidence of attempts to exaggerate deficits in either the ME or MTBI group. All patients appeared to exert full effort, and, in fact, many

