A Controlled Comparison of Multiple Chemical Sensitivities and Chronic Fatigue Syndrome

NANCY FIEDLER, PHD, HOWARD M. KIPEN, MD, MPH, JOHN DELUCA, PHD, KATHIE KELLY-MCNEIL, BA, AND BENJAMIN NATELSON, MD

The present study had two objectives: 1) to determine the characteristics that differentiated subjects with multiple chemical sensitivities (MCS), chemical sensitivities (CS), and chronic fatigue syndrome (CFS); and 2) to evaluate the psychiatric and neuropsychological complaints of these groups relative to normal controls. A cross-sectional comparison was made of the following groups matched for age, sex, and education: 1) patients whose sensitivities to multiple low level chemical exposures began with a defined exposure (MCS; $N = 23$); 2) patients with sensitivities to multiple chemicals without a clear date of onset (CS; $N = 13$); 3) patients meeting CDC criteria for Chronic Fatigue Syndrome (CFS; $N = 18$); and 4) normal controls ($N = 18$). Subjects with sensitivities to chemicals (MCS and CS) reported significantly more lifestyle changes due to chemical sensitivities and significantly more chemical substances that made them ill compared with chronic fatigue and normal controls. MCS, CS, and CFS patients had significantly higher rates of current psychiatric disorders than normal controls and reported significantly more physical symptoms with no medical explanation. Seventy-four percent of MCS and 61% of CFS did not qualify for any current Axis I psychiatric diagnosis. Chemically sensitive subjects without a defined date of onset (CS) had the highest rate of Axis I psychiatric disorders (69%). On the MMPI-2, 44% of MCS, 42% of CS, 53% of CFS, and none of the controls achieved clinically significant elevations on scales associated with somatoform disorders. With the exception of one complex test of visual memory, no significant differences were noted among the groups on tests of neuropsychological function. Standardized measures of psychiatric and neuropsychological function did not differentiate subjects with sensitivities to chemicals from those with chronic fatigue. Subjects with sensitivities to chemicals and no clear date of onset had the highest rate of psychiatric morbidity. Standardized neuropsychological tests did not substantiate the cognitive impairment reported symptomatically. Cognitive deficits may become apparent under controlled exposure conditions.

Key words: chemical sensitivities, chronic fatigue, psychiatric, neuropsychiatric.

INTRODUCTION

In the last decade, chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS) have received increasing attention in the medical literature. Because no consistent physical finding or laboratory abnormality has been discovered to account for the symptoms associated with these illnesses, they are regarded frequently as manifestations of psychiatric disorders such as depression, anxiety, and somatization disorder (1–3). The Centers for Disease Control and Prevention (CDCP) have developed a clinical case definition for the diagnosis of CFS (4, 5). Although no comparable case definition for MCS has been accepted, MCS has been characterized by symptoms reflective of multiple organ systems that arise in the presence of low level chemical exposures (6).

Case series suggest that MCS and CFS occur predominantly in relatively well educated adult females (7, 8). However, MCS and CFS appear to have different origins and different ongoing symptom triggers. The onset and ongoing triggers, at least for a prominent subset of MCS patients, has been associated with chemical exposure, while CFS often arises following a flu-like illness with exertion as an ongoing trigger. However, both share many prominent symptoms in common, including the complaint of impaired cognitive function unaccompanied by significant clinical signs. While the symptoms, lack of demonstrated organic explanation, and demographics of these groups suggest similarity, few direct comparisons have been made. The purpose of this project was to compare the psychiatric, neuropsychological, medical, and immunological function of

From the UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Department of Environmental and Community Medicine, Piscataway, New Jersey (N.F., H.M.K., K.K-M); Kessler Institute, West Orange, New Jersey (J.D.); and VA Medical Center, East Orange, New Jersey (B.N.).

Address reprint requests to: Dr. Nancy Fiedler, UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Department of Environmental and Community Medicine, 681 Frelinghuysen Road Piscataway, NJ 08855.

Received for publication August 15, 1994; revision received May 1, 1995.

0033-3174/96/5801-0038$03.00/0

CFS, MCS, and normal controls. The present communication describes the comparison of standardized psychiatric and neuropsychological measures between these groups while the medical and immunological results will be reported separately.

Several studies have investigated the psychiatric status of MCS or CFS patients. For example, two controlled studies of MCS patients, identified by their use of clinical ecologists or allergists specializing in treatment of MCS, concluded that a significantly greater number of MCS subjects (50%) than controls had premorbid or current psychiatric disorders such as anxiety and depression that might explain their current symptoms (2, 9). However, Fiedler et al. (8) reported in a case series that MCS subjects who met more specific criteria infrequently had a history of psychiatric disorder before onset of MCS.

Higher rates of anxiety and depression have also been observed among CFS patients (10, 11). However, as is the case for MCS, it remains unresolved whether these symptoms are primary, secondary, or co-morbid to CFS. Also, use of the CDC criteria, which include multiple physical complaints, by definition may select for patients with a high rate of psychiatric diagnoses because the latter are associated with multiple physical complaints (12).

Relatively fewer studies have been published in which the neuropsychological function of these patients was evaluated. Recently, Simon et al. (9) recruited MCS subjects from a community allergist and compared their immunological, psychiatric, and neuropsychological function with patients who had musculoskeletal injuries. They reported no significant differences among the groups on standardized neuropsychological measures of concentration and memory. Again, no information was provided to establish that the MCS symptoms had a definable onset, one of Cullen's (6) key criteria. Also, although MCS and the musculoskeletal subjects were of comparable age, sex, and education, no estimate of intellectual ability was included to establish that these groups were of comparable premorbid ability. The most significant limitation was that no normal, healthy control group was included in this study.

Individuals with CFS also present cognitive complaints of poor attention and memory. However, the results of the few studies examining cognitive dysfunction were mixed and suffer from methodological constraints similar to studies of MCS. Some studies found significant differences from normal controls in functions such as complex information processing (13) or memory consolidation and vulnerability to interference (14). Others concluded that cognitive abilities in CFS were intact (15). At least one study of CFS patients described a subset with MCS symptoms such as sensitivity to solvents and perfumes (16). As for MCS, case selection criteria may account partially for discrepant findings. The present study is a cross-sectional comparison of the standardized neuropsychological and psychiatric function of MCS patients who met and did not meet Cullen's (6) criteria compared with patients meeting the CDC definition for CFS and with normal controls.

METHOD

Subjects

Twenty-three MCS, 13 CS, 18 CFS, and 18 normal controls participated in the study. MCS subjects who met the following five criteria derived from Cullen (6) were recruited from patients referred to our Environmental and Occupational Health Clinical Center: 1) symptoms acquired in relation to an initial identifiable environmental exposure(s); 2) symptoms currently involve more than one organ system (e.g., respiratory and nervous system); 3) symptoms recur and abate in response to exposure to chemical/substances; 4) symptoms are elicited by exposures to very low levels of chemicals of diverse structural classes (e.g., solvents, pesticides); 5) other medical conditions do not account for the symptoms. MCS subjects currently involved in a legal case related to their exposures were not included.

During a 3-year period, 53 patients were self- or physician-referred for evaluation of chemical sensitivities. Thirty of those patients were not included as MCS subjects because they did not meet one or more of the eligibility criteria. With regard to the defining criteria for MCS, 13 could not report a clear onset for the development of chemical sensitivities and six did not report sensitivities to multiple substances. Two patients had other pre-existing explanatory medical conditions (i.e., hypothyroidism, viral illness/chronic fatigue), and one had a previous psychiatric hospitalization with electroconvulsive shock therapy for severe depression. Three patients were in litigation, two were unwilling to participate, one moved out of the region, and two were not included because they were employed as a psychologist/psychiatrist. Thus, 23 subjects met the full criteria for MCS. Thirteen subjects who met criteria for MCS, with the exception of a clear onset, completed the research and were analyzed as a separate group (i.e., CS).

Twenty-three CFS patients were referred to the study by one of the co-authors, who is the Director of the CFS Center at the New Jersey Medical School. Three of these subjects were not eligible to participate because they no longer reported a sufficient number of CFS symptoms to meet CDC criteria. The CDC criteria were as follows: debilitating fatigue lasting at least 6 months that reduces activity 50% below premorbid levels; and 8 minor symptoms (i.e, mild fever, sore throat, muscle weakness, painful lymph nodes, myalgia, severe fatigue after mild exercise, headaches, and neuropsychological complaints). Two subjects declined participation because of pregnancy and difficulty traveling, respectively. None of the CFS subjects were considered to have MCS based on the criteria listed above. Thus, a total of 18 subjects who met the Centers for Disease Control criteria for CFS participated in the study (5).

Eighteen normal healthy controls were recruited from a general

internal medicine clinic population and from newspaper advertisements. Based on physical examination, no subject from any group had serious concomitant medical disorders including neurologic disease or brain injury, stroke or cardiovascular disease, serious pulmonary disease, liver or kidney disease, serious gastrointestinal disorders (e.g., colitis), significant toxic exposure, or major psychiatric conditions (i.e., psychoses, bipolar disorder, or substance abuse). As with serious physical disorders, inclusion of subjects with serious psychiatric disorders could confound performance on neuropsychological tests (17, 18). Across all subject groups, only one subject (MCS) was not studied solely because of a premorbid history of a psychiatric condition (i.e., hospitalization for depression with ECT).

All subjects were told that this was a study to understand individual responses to chemicals encountered routinely at work and home. The study was approved by the Institutional Review Board of UMDNJ-Robert Wood Johnson Medical School. Upon completion of the study, each subject was paid $50.

Evaluation Measures

Subjects completed a questionnaire in which they were instructed to check off those substances from a list of 122 that caused them to have symptoms when exposed (19). Subjects were asked the following lifestyle questions as a measure of chemical sensitivities: 1) Do you now need to follow any special diet because of chemical or food sensitivity?; 2) Do you now take special precautions in your home or home furnishings (furniture, drapes, carpets) because of chemical sensitivities?; 3) Do you now need to wear particular clothes because of chemical sensitivities?; and 4) Do you have trouble shopping in stores or eating in restaurants because of chemical sensitivities? To examine the lifetime and current (at time of the study) Axis I psychiatric diagnoses of subjects, the Structured Clinical Interview for the Diagnostic and Statistical Manual, 3rd edition, Revised (20) was administered. The Minnesota Multiphasic Personality Inventory-2 (21) was also administered. The response set of over- or under-reporting psychopathology was evaluated for each subject by using the configuration of scores on L, F, and K, the traditional validity scales (22). These response sets, the traditional clinical scales, and the content scales were scored for each subject.

In addition, the somatization section of the Diagnostic Interview Survey-III-A (23) was administered by a nurse to ascertain the rate of medically explained and unexplained symptoms. The date of onset for each symptom was determined. Symptoms were initially classified according to DIS-III-A guidelines as medically explained if the subject gave a physician's medical diagnosis. A symptom was regarded as medically unexplained or a somatization symptom if no medical diagnosis was given by the subject. To reduce misattribution, and thus falsely negative findings of somatization symptoms, a physician co-investigator who was blind to group status reviewed the written record of medical explanations given by the subjects to ascertain medical plausibility. If the recorded medical explanation was not a specific recognized diagnosis, the symptom was shifted into the medically unexplained category. Examples that were shifted to the medically unexplained category included "weak chest," "MCS" or "CFS," "low blood sugar," "low blood pressure," "irritable bowel syndrome," "fibromyalgia," and "dietary problems." Symptoms were classified as indeterminate if the explanatory diagnosis was a recognized organic cause of symptoms in some cases but seemed to be invoked nonspecifically and without careful diagnostic evaluation, e.g., lumbar strain, disc degeneration, migraines, food allergies, esophageal spasm, or TMJ syndrome. No symptoms were moved by the physician review process from the unexplained to the explained category biasing this added review process toward meeting somatization criteria.

Those tests in the neuropsychological battery that have been described previously (8) are listed with their original references. The computerized tests listed below are from a battery of neuropsychological tests developed for epidemiological studies of the effects of neurotoxicants (24). The dependent measures used in the analyses are in parentheses after each test listed below.

Tests of concentration included computerized Simple Reaction Time, dominant and nondominant hand (mean response latency in milliseconds) and computerized Continuous Performance Test (median reaction time in milliseconds) (25), Digit Span (scaled score) (26), and the Stroop Color Word Task (number of correct responses minus incorrect responses) (27). Tests of visuomotor skills included Digit Symbol (scaled score) (26), computerized Hand-Eye Coordination (mean absolute error of two best trials) (25), and Grooved Pegboard, dominant and nondominant hand (for each hand, time in seconds required to fill pegboard) (28). Tests of memory included the California Verbal Learning Test (raw scores) (29), the Continuous Visual Memory Test (raw scores) (30), and Visual Reproduction I and II (raw score) (31).

Procedure

Before entrance into the study, all potential MCS subjects were given an exhaustive history and physical examination at the Environmental and Occupational Health Clinical Center. CFS subjects were evaluated at the CFS Center. Medical records and a standardized history were reviewed to rule out the conditions listed previously. In addition to routine laboratory evaluations for all subjects, further testing such as spirometry or chest roentgenogram was done as needed to evaluate possible medical conditions that reasonably might explain the symptomatology. Patients were evaluated in a meeting of the investigators, and those who met the entrance criteria were invited to participate. All subjects were evaluated according to the five criteria for MCS to ensure correct group classification. Before participation, all subjects gave informed consent.

All neuropsychological tests and the SCID-III-R were administered during the same day. At the time of testing, no subject was on any medication that would affect neuropsychological performance. The MMPI-2 was administered when subjects returned to have delayed hypersensitivity skin tests read for the immunological study. The somatization section of the DIS-III-A was administered subsequently in a telephone interview. The SCID-III-R was administered by a clinical psychologist or by a clinical social worker, and the neuropsychological test battery was administered by a trained research technician. The interviewers administering the SCID-III-R and the DIS-III-A could not be blinded to group membership because of the nature of the interview. The research technician administering the neuropsychological tests was not told the group membership of the subjects before testing. Because of the nature of the patients tested, she often was able to distinguish normal controls from the patient groups. However, she could not distinguish MCS from CFS subjects.

Statistical Analyses

Because of the exploratory nature of the present study and the paucity of information about the patient groups under study,

separate univariate analyses of variance were conducted to explore potential group differences on each measure. This procedure was recommended by Huberty and Morris (32) as a legitimate approach for exploratory studies. When the univariate analyses of variance were significant, Student Neuman-Keuls post hoc tests were conducted. Significant results were interpreted with caution given the number of intercorrelated comparisons made. Fisher's Exact Test was used to compare categorical prevalence rates data such as diagnostic categories from the SCID-III-R.

To understand the variables that may explain any differences between MCS and normal controls on tests of neuropsychological performance, multiple regression analyses were conducted to predict neuropsychological scores: group membership, age, WRAT-R, education, MMPI-2 content scales of depression, anxiety, and health concerns. Age, education, and WRAT-R, as indicators of premorbid ability, were chosen because these variables are known to influence performance on neuropsychological tests (33). In addition, anxiety, depression, and health concerns are psychological variables that may influence neuropsychological performance (17, 33).

RESULTS

Subject Characteristics

In each of the subsequent analyses, the following subject groups were compared: 1) multiple chemical sensitivities with a defined onset of illness (MCS); 2) sensitivities to multiple chemicals with no date of onset (CS); 3) chronic fatigue syndrome (CFS); and 4) normal controls. Since age, sex, education, and premorbid ability (estimated with Wide Range Achievement Test (WRAT)-Reading) (34) affect performance on neuropsychological tests, univariate analyses compared subject groups on these variables first (see Table 1). No significant differences between the groups were noted for age and WRAT-Reading. Although the overall ANOVA revealed a significant difference in years of education, the SNK post-hoc test showed no significant differences among the individual groups. As can be seen from the means in Table 1, educational differences were relatively minor. There were no significant gender differences among the groups. Finally, MCS and CFS subjects were not significantly different in age of illness onset. Thus, the groups were comparable on relevant demographic variables.

Lifestyle Questions and Substance Questionnaire

Univariate analyses followed by SNK post hoc tests revealed that MCS and CS were comparable with each other but reported a significantly greater number of lifestyle changes due to chemical sensitivities than CFS or normal controls. However, CFS subjects also reported significantly more lifestyle changes than did controls. CS reported significantly more substances that made them ill than did MCS, whereas MCS and CS subjects reported significantly more substances than CFS and normal controls (Table 2). No differences were observed between CFS and normals.

Psychiatric Evaluation

Axis I psychiatric diagnoses, excluding somatoform disorders, were evaluated with the SCID-III-R. Seventeen percent (4/23) of MCS, 38% (5/13) of CS, and 22% (4/18) of CFS qualified for a current (at time of study) diagnosis of either dysthymia or a major depressive episode, whereas none of the normals qualified for this diagnosis (Table 3). The CS ($p < .007$) and CFS ($p < .05$) groups each had a significantly higher rate of dysthymia/major depression than normal controls, whereas the difference in rates of dysthymia/major depression between MCS and

TABLE 1. Demographics of Subject Groups

	Multiple chemical sensitivities ($N = 23$)[a]	Chemical sensitivities (no onset) ($N = 13$)[a]	Chronic fatigue syndrome ($N = 18$)[a]	Normals ($N = 18$)[a]	F	P
Sex ratio	M(4) F(19)	M(0) F(13)	M(3) F(15)	M(4) F(14)	*	.35
Age (yr)	43 (2.0)	46 (1.8)	40 (1.6)	45 (2.3)	1.53	.22
	28–58	35–58	29–53	28–63		
Education	15 (.5)	14 (.6)	16 (.5)	16 (.6)	3.05	.03
	11–20	12–18	14–20	12–20		
WRAT-Reading	103 (2.7)	103 (3.0)	111 (2.2)	106 (3.4)	1.82	.15
	82–122	84–123	87–125	82–126		
Age of onset (yr)	39 (2.5)		36 (1.6)		3.02	.39
	8–57		26–50			

[a] Expressed as mean (SE) and range.

* Fisher's Exact Test.

M, male; F, female.

TABLE 2. Questionnaire Results to Describe Chemical Sensitivities

	N	Mean	SE	Range	F	p
Chemical sensitivity and lifestyle changes[a]						
Multiple chemical sensitivities	22	3.1	.2	2–4	22.2	0001
Chemical sensitivities	10	3.3	.3	1–4		
Chronic fatigue syndrome	17	1.9	.3	0–4		
Normals	16	.6	.2	0–3		
Substance questionnaire[b]						
Multiple chemical sensitivities	23	38.2	4.7	9–85	22.0	.0001
Chemical sensitivities	13	76.2	8.1	13–111		
Chronic fatigue syndrome	16	22.3	6.3	0–79		
Normals	18	12.3	3.3	0–50		

[a] Four yes-no questions reflect changes in lifestyle due to chemical sensitivities (e.g., diet, clothing, shopping, home furnishings). Scores range from 0 (no changes) to a maximum of 4 changes.
[b] Number of substances reported to produce symptoms.

normals approached significance ($p < .08$). However, MCS, CS, and CFS did not differ from each other in the rate of depression ($p < .39$). Twenty-three percent (3/13) of the CS and 17% (3/18) of the CFS subjects had an anxiety disorder. These rates of anxiety disorders each approached significance when compared with normal controls ($p < .06$ for CS; $p < .11$ for CFS). Based on the DIS somatization interview, 18% (4/22) of MCS, 12% (2/17) of CFS, and 10% (1/10) of CS subjects reported 13 or more unexplained symptoms. One MCS subject had no unexplained symptoms before age 30. Therefore, at the time of the study, 14% (3/22) of MCS, 12% (2/17) of CFS, and 10% (1/10) of CS subjects met the full criteria for somatization disorder. These rates of somatization were not significantly different from normal controls ($p < .16$ for MCS; $p < .23$ for CFS; $p < .36$ for CS). In summary, the only current psychiatric diagnostic group that statistically differentiated each patient group from normals was the depressive disorders. For all current psychiatric diagnoses, MCS ($p < .02$), CS ($p < .0001$), and CFS ($p < .003$) each had a significantly higher rate of current psychiatric disorders than normals.

The lifetime rate of psychiatric diagnoses included current and previous diagnoses. For individual diagnostic categories, the only significant difference observed between groups was that CS ($p < .01$) and CFS ($p < .0007$) had significantly higher rates of dysthymia/major depression than normal controls. For total lifetime psychiatric diagnoses summing across all categories MCS ($p < .02$), CS ($p < .003$), and CFS ($p < .000$) each had significantly higher rates of psychiatric diagnoses than normals.

The rate of medically explained and unexplained somatic symptoms from the DIS were also analyzed in four separate univariate analyses of variance comparing MCS, CS, CFS, and normal controls. MCS had significantly more medically explained symptoms than CFS and normal controls, but not more than CS (Table 4). CS did not differ significantly from CFS or normals in the number of medically explained symptoms. CFS, MCS, and CS did not differ among themselves but had significantly more medically unexplained symptoms than normal controls. CS tended to have more indeterminate symptoms than MCS subjects, but not more than CFS or normals. CFS, normals, and MCS did not differ in the number of indeterminate symptoms.

MMPI-2: Response Set

Two MCS subjects' and one normal control subject's MMPI-2 profiles were classified as invalid because L and K were both ≥70. For these subjects, response sets were so defensive that responses on the Clinical/Content Scales were likely to be significantly reduced because of under-reporting of symptomatology (22). One additional MCS profile was invalid because of an extreme elevation on F ($F \approx 82$). For this case, the response set was so exaggerated that the Clinical/Content Scales could be invalid because of over-reporting of pathology. No subjects from the CS or CFS groups were eliminated because of profile invalidity.

Clinical and Content Scales

Significant differences between the groups were observed in the Lie and F Validity scales and all clinical scales except MF and Hypomania. The specific between group differences are noted in Table 5. Although many significant differences were observed, the scales with clinically significant elevations (ie, ≥65) for the groups were relatively fewer in number. To summarize, Hypochondriasis, Hysteria, Schizophrenia, and Social Introversion were significantly elevated for MCS, CS, and CFS, whereas Depression, Psychasthenia, and Psychopathic Deviate were elevated for CS and CFS. Similarly, for the Content scales the only scale elevated at a clinically significant level for MCS, CS, and CFS was Health Concerns (Table 6). Thus, the group profile for MCS, CS, and CFS subjects was consistent with patients who have significant distress primarily related to somatic symptoms.

TABLE 3. Current and Lifetime Psychiatric Diagnoses[a]

	Multiple chemical sensitivities[b]	Chemical sensitivities (no onset)[b]	Chronic fatigue syndrome[b,c]	Normals[b]	p
Current					
Depression	17 (4/23)	38 (5/13)	22 (4/18)	0	.02
Anxiety disorders	0	23 (3/13)	17 (3/18)	0	.01
Somatization disorder	14 (3/22)	10 (1/10)	12 (2/17)	0	.37
Total current psychiatric	26 (6/23)	62 (8/13)	39 (7/18)	0 (0/18)	.002
Lifetime[d]					
Depression	30 (7/23)	54 (7/13)	67 (12/18)	11 (2/18)	.003
Anxiety	9 (2/23)	31 (4/13)	28 (5/18)	6 (1/18)	.11
Prescription drug abuse	0	0	11 (2/18)	0	.15
Bulimia	0	8 (1/13)	0	0	.18
Somatization disorder	14 (3/22)	10 (1/10)	12 (2/17)	0	.37
Total lifetime psychiatric	43 (10/23)	69 (9/13)	72 (13/18)	11 (2/18)	.004

[a] Diagnoses are based on Structured Clinical Interview and Diagnostic Interview Survey (Somatization only) for DSM-III-R. One MCS, one CS, and two CFS subjects had more than one diagnosis.
[b] Expressed as percentage (*N*).
[c] Four subjects qualified for a psychiatric diagnosis since the onset of illness but were in remission at the time of the study.
[d] Two MCS, four CS, eight CFS, and one normal subject had more than one diagnosis.

TABLE 4. DIS-III-R Somatization[a]

	Multiple chemical sensitivities ($N = 22$)[b]	Chemical sensitivities (no onset) ($N = 10$)[b]	Chronic fatigue syndrome ($N = 17$)[b]	Normals ($N = 18$)[b]	F	p
Symptoms with medical explanation	3.7 (.5) 0–9	2.9 (.7) 0–8	1.4 (.4) 0–6	1.2 (.3) 0–6	7.2	.0003
Symptoms with no medical explanation	8.4 (1.1) 0–21	6.5 (1.1) 4–15	10.8 (1.0) 6–19	1.3 (.4) 0–4	14.7	.0001
Indeterminate symptoms	.8 (.3) 0–4	2.2 (.6) 0–6	1.6 (.3) 0–3	1.4 (.4) 0–7	2.5	.07

[a] Number of somatic symptoms associated with somatization disorder.
[b] Expressed as mean (SE) and range.

Codetypes

For the MCS, CS, and CFS groups, the codetypes with Hypochondriasis and Hysteria (1–3/3–1) as peak elevations were most frequent, ie, 44% (8/18) for MCS, 42% (5/12) for CS, and 53% (9/17) for CFS. The next most frequent profile for MCS (2/18 = 11%) and CFS (3/17 = 18%) was the Depression and Hypochondriasis (2–1) profile. Overall, 66% (12/18) of MCS (1 Ss = 2–6; 1 Ss = 3–2), 100% of CS (3 Ss = 1–7 or 1–8; 2 Ss = 2–6 or 2–7; 1 Ss = 3–6), and 94% (16/17) of CFS subjects (1 Ss = 3–2; 2 Ss = 3–7; 1 Ss = 4–7) met criteria for a 2-point code-type, whereas 94% (16/17) (1 Ss = 5–9) of normals did not.

Neuropsychological Tests

With the exception of a complex test of visual memory, i.e., CVMT, no significant differences were observed among the groups on any test of neuropsychologic function (see Table 7).

Analysis of the Continuous Visual Memory Test (CVMT) subscores revealed a significantly higher rate of CVMT False Alarms than normals and CS, but

TABLE 5. MMPI-2 Clinical Scales *T* Scores[a]

	Multiple chemical sensitivities (N = 18)[b,c]	Chemical sensitivities (no onset) (N = 12)[b,c]	Chronic fatigue syndrome (N = 17)[b,c]	Normals (N = 17)[c]	F (df = 3,63)	p
Lie (L)	60.9 (2.3) 47–78	57.3 (3.0) 38–76	48.3 (1.6) 38–62	52.9 (2.3) 38–66	6.21	.001[d]
Validity (F)	51.4 (2.3) 36–68	54.5 (2.3) 44–68	55.1 (2.3) 41–72	45.0 (1.4) 37–55	4.85	.004[e]
K	57.1 (2.1) 37–72	52.8 (2.7) 37–74	54.9 (2.0) 41–70	56.8 (2.1) 39–70	0 74	NS
Hypochondriasis (Hs)	70.3 (3.1) 43–99	77.2 (3.6) 46–92	78.2 (2.7) 54–95	49.3 (1.8) 30–63	23.70	.0001[e]
Depression (D)	62.8 (3.1) 42–92	72.8 (4.1) 53–99	71.1 (3.0) 49–103	45.4 (1.2) 34–53	18.93	.0001[f]
Hysteria (Hy)	73.4 (2.9) 47–96	77.3 (2.8) 63–92	80.3 (2.5) 65–104	49.5 (2.3) 34–68	28.91	.0001[e]
Psychopathic deviate (Pd)	49.9 (2.0) 36–73	55.4 (2.0) 47–73	58.6 (2.5) 45–81	45.8 (1.8) 30–59	7.41	.0003[g]
Masculinity-femininity (Mf)	49.6 (2.4) 30–69	48.1 (3.2) 38–77	45.2 (2.5) 30–72	54.8 (2.7) 38–77	2.40	.08
Paranoia (Pa)	57.6 (2.2) 37–74	57 6 (3.9) 37–81	52.9 (2.7) 32–70	46.5 (1.5) 34–59	3.82	.01[h]
Psychasthenia (Pt)	58.0 (2.2) 40–75	64.7 (3.2) 53–86	66.5 (2.9) 40–86	44.1 (1.4) 31–55	17.82	.0001[i]
Schizophrenia (Sc)	57.8 (2.5) 39–75	64.8 (2.3) 48–78	64.2 (2.9) 39–85	45.6 (1.6) 32–60	13.54	.0001[e]
Hypomania (Ma)	48.4 (2.5) 33–74	49.7 (3.6) 31–71	50.4 (2.4) 31–65	50.6 (2.2) 39–71	.16	NS
Social introversion (Si)	49.4 (2.4) 38–70	55.8 (3.2) 42–77	49.6 (1.9) 37–70	41 3 (1.6) 30–59	6.50	.0007[e]

[a] Minnesota Multiphasic Personality Inventory-2 *T* scores.
[b] Two MCS, one CS, and one CFS subject did not complete the MMPI-2.
[c] Expressed as mean (SE) and range.
[d] L Scale: MCS significantly higher than CFS and normals; CS significantly higher than CFS.
[e] F, Hs, Hy, Sc, Si Scale: CFS, CS, and MCS significantly higher than normals.
[f] D Scale: CS and CFS significantly higher than MCS and normals; MCS significantly higher than normals.
[g] Pd Scale: CFS significantly higher than MCS and normals; CS significantly higher than normals.
[h] Pa Scale: CS and MCS significantly higher than normals.
[i] Pt Scale: CFS significantly higher than MCS and normals, CS and MCS significantly higher than normals.
NS, not significant.

not CFS (Table 8). CFS also did not differ significantly from normals or CS in their CVMT False Alarm rate. The simplest multiple regression model with the maximum adjusted R-square was selected after the variables representing group were included. Achievement test (WRAT-R) score, age, health concerns, and membership in the CS group were the variables that accounted for a significant amount of the variance in CVMT total score (Table 9).

The concordance of symptom complaints and objective performance deficits on neuropsychologic tests were compared. Eighty-seven percent (20/23) of MCS, 92% (12/13) of CS, 94% (16/17) of CFS, and 28% (5/18) of normals reported symptoms of poor concentration and/or memory problems during the past year (review of systems). To develop an objective indicator of overall impairment, an average z-score for each subject was computed across all neuropsychological variables. The mean and standard deviation for the normal controls was the standard mean. Thirty percent (7/23) of MCS subjects, 8% (1/13) of CS, and 17% (3/18) of CFS achieved an average z-score that was one-half to one standard deviation below the normal control performance mean. Thus, many more subjects complained of neuropsychological symptoms than could be detected with objective testing.

DISCUSSION

The present study had two primary objectives: 1) to determine the characteristics that differentiated chemical sensitivities from chronic fatigue syn-

TABLE 6. MMPI-2 Content Scales *T* Scores

	Multiple chemical sensitivities (N = 18)[a]	Chemical sensitivities (no onset) (N = 12)[a]	Chronic fatigue syndrome (N = 16)[a]	Normals (N = 17)[a]	F (df = 3,62)	p
Anxiety	51.6 (2.3) 37–71	57.9 (3.2) 40–71	59.7 (3.5) 40–89	44.0 (1.5) 34–56	7.36	.0003[b]
Fears	46.4 (1.9) 35–65	47.3 (2.8) 35–65	49.5 (2.9) 35–75	43.2 (1.7) 31–53	1.34	NS
Obsessiveness	44.2 (1.6) 32–59	49.7 (2.9) 37–71	50 7 (2.1) 41–67	40.8 (1.5) 32–56	5.73	.002[f]
Depression	49.1 (2.4) 34–70	54.0 (3.1) 34–73	52.9 (2.4) 34–68	41.5 (1.4) 34–50	5.81	.002[b]
Health concerns	65.6 (2.9) 51–90	70.9 (3.0) 55–90	71.4 (3.2) 49–96	46.6 (1.5) 36–57	18.79	.0001[b]
Bizarre mentation	46.6 (1.8) 39–58	49.2 (3.0) 39–67	49.0 (2.0) 39–61	44.9 (1.4) 39–52	1.04	NS
Anger	45.2 (1.9) 31–60	51.8 (3.2) 39–68	49.1 (1.9) 36–60	43.9 (1.4) 31–56	3.86	.04[d]
Cynicism	42.8 (1.5) 31–53	46.7 (2.3) 35–64	46.9 (1.5) 35–56	46.1 (1.9) 32–67	1.22	NS
Antisocial practices	41.4 (1.1) 36–49	46.5 (2.3) 36–59	45.9 (1.5) 36–56	46.5 (1.6) 39–66	2.65	.06
Type A	44.0 (2.4) 30–64	48.8 (2.9) 30–64	50.9 (2.3) 41–77	46.7 (2.1) 33–64	1.64	NS
Low self-esteem	46.1 (2.2) 35–70	52.8 (2.9) 35–70	48.7 (1.2) 40–60	42.3 (1.4) 35–54	4.76	.005[e]
Social discomfort	50.6 (2.9) 35–84	54.7 (3.4) 41–80	48.1 (2.1) 35–68	43.5 (1.9) 32–60	3.05	.04[d]
Family problems	48.3 (2.6) 32–75	51.0 (3.4) 39–75	48.3 (2.5) 36–70	43.4 (1.8) 33–60	1.48	NS
Work interference	49.2 (1.6) 37–61	58.5 (3.1) 45–76	56.3 (2.5) 43–76	42.5 (1.2) 31–50	12.02	.0001[c]
Negative treatment indicators	46.2 (1.9) 32–61	47.8 (2.2) 39–59	49.4 (1.6) 39–61	40.4 (1.2) 35–53	5.33	.003[b]

[a] Expressed as mean (SE) and range.
[b] Anxiety, depression, health concerns, negative treatment indicators: CFS, CS, and MCS significantly higher than normals.
[c] Work interference: CS and CFS significantly higher than MCS and normals; MCS significantly higher than normals.
[d] Social discomfort, anger: CS significantly higher than normals.
[e] Low self-esteem: CS significantly higher than MCS and normals.
[f] Obsessiveness: CFS and CS significantly higher than normals.

drome (CFS); and 2) to evaluate the psychiatric and neuropsychological complaints of these groups relative to normal controls. In contrast to previous studies of chemical sensitivities (2, 9), this study applied restrictive case criteria for selection of subjects and contrasted those who had sensitivities to multiple chemicals beginning with a defined exposure (MCS) with those who had similar sensitivities without a clear date of onset (CS). Standardized measures of psychiatric and neuropsychological function did not distinguish chemically sensitive subjects (MCS and CS) from chronic fatigue subjects (CFS). However, factors that described the concomitants of illness differentiated these patient groups. For example, all chemical sensitivities subjects reported significantly more lifestyle changes and a significantly greater number of substances that made them ill than CFS subjects. As expected, MCS and CS subjects more clearly reported and attributed their symptoms to chemicals than did CFS subjects. Of note, however, was that CFS subjects also reported significantly more lifestyle changes due to chemical sensitivities than normal controls and reported twice as many substances on average that caused symptoms. Such lifestyle changes may have been due to CFS subjects' general level of illness rather than actual sensitivity to chemicals. However, the distribution of scores on the substance questionnaire suggested that 30% of CFS subjects reported no substance causing illness, whereas 39% (7) endorsed over 20 substances. In future studies, investigators may consider stratifying CFS patients by chemical sensitivities to elucidate the differences between CFS and chemical sensitivities.

TABLE 7. Neuropsychological Tests[a]

	Multiple chemical sensitivities (N = 23)[b]	Chemical sensitivities (no onset) (N = 13)[b]	Chronic fatigue syndrome (N = 18)[b]	Normals (N = 18)[b]	p
Attention/concentration					
Simple reaction time-mean response latency (msec)					
Right hand	294.2 (16.7)	316.5 (22.1)	322.2 (17.7)	297.8 (8.8)	.54
	261.5–326.9	273.2–359.8	287.5–356.9	280.6–315.0	
Left hand	277.4 (16.4)	294.9 (15.8)	285.5 (14.5)	266.7 (6.5)	.60
	245.3–309.5	263.9–325.9	257.1–313.9	254.0–279.4	
Continuous Performance-Median	388.4 (10.4)	394.7 (16.1)	404.4 (18.1)	386.8 (12.0)	.80
Reaction time (msec)	368.0–408.8	363.1–426.3	368.9–439.9	363.3–410.3	
Stroop Color-Word Task raw score	99.6 (3.2)	97.5 (5 9)	96.4 (4.1)	103.8 (2.1)	.53
	93.3–105.9	85.9–109.1	88.4–104.4	99.7–107.9	
Digit Span Total scaled score	9.7 (7)	10.1 (.6)	9.7 (.7)	10.7 (.8)	.72
	8.3–11.1	8.9–11 3	8.3–11.1	9.1–12.3	
Digit Span-Forward raw score	8 7 (.6)	8.7 (.7)	8.1 (6)	8.8 (.5)	.84
	7.5–9.9	7.3–10.1	6.9–9.3	7.8–9.8	
Digit Span-Backward raw score	6.8 (.6)	7.0 (.4)	7.3 (.6)	7.9 (.7)	54
	5.6–8.0	6.2–7.8	6.1–8.5	6.5–9.3	
Visuomotor coordination					
Digit Symbol-Scaled score	10.2 (.8)	10.7 (.8)	9.3 (.5)	10.4 (.6)	.57
	8.6–11.8	9.1–12.3	8.3–10.3	9.2–11.6	
Hand-eye Coordination mean absolute error	6.2 (.4)	7.0 (4)	6.7 (.5)	6.2 (.7)	.68
	5.4–7.0	6.2–7.8	5.7–7.7	4.8–7 6	
Grooved Pegboard-total seconds					
Dominant hand	65.2 (2.2)	67.6 (2.6)	67.9 (2.0)	66.4 (2.5)	.82
	60.9–69.5	62.5–72.7	64.0–71.8	61.5–71.3	
Nondominant hand	70.9 (2.4)	73.5 (2.5)	72.3 (2.5)	69.4 (2.0)	.69
	66.2–75.6	68.6–78 4	67.4–77.2	65.5–73.3	
Verbal memory					
California Verbal Learning Test	38.0 (2.4)	34 2 (2.7)	42.7 (3.3)	42.3 (2.1)	.13
List A total trials 1–5; standard score	33.3–42.7	28.9–39 5	36.2–49.2	38.2–46.4	
Visual memory					
Continuous Visual Memory Test total score	72.3 (1.8)	77.8 (1.5)	76.4 (1.7)	79.4 (1.0)	.009[c]
	68.8–75.8	74.9–80.7	73.1–79.7	77.4–81.4	
Visual Repro I raw score	32.3 (1.8)	34.8 (1.1)	34.6 (1.4)	36.4 (1.0)	.21
	28.8–35.8	32.6–37.0	31.9–37.3	34.4–38.4	
Visual Repro. II raw score	26 8 (2.4)	26.9 (2.1)	30.8 (1.7)	32.3 (1.8)	.14
	22 1–31.5	22.8–31.0	27.5–34.1	28.8–35.8	

[a] Higher scores indicate better performance for all variables except Simple Reaction Time, Continuous Performance, and Hand-eye Coordination where lower scores indicate better performance.
[b] Expressed as mean (SE) and 95% lower and upper confidence interval.
[c] Normals and CS significantly better than MCS but not CFS.

Based on the SCID-III-R psychiatric interview, there were more similarities than differences between chemical sensitivities and CFS. MCS, CS, and CFS had significantly elevated rates of diagnosable psychiatric disorders, and the disorder most frequently diagnosed was depression. Despite this significant elevation, 74% of MCS and 61% of CFS did not meet criteria for any current psychiatric disorder. However, chemical sensitivities patients who did not meet all case criteria (CS) had the highest rate of current and lifetime psychiatric disorders (i.e., 69%). Because these patients reported developing chemical sensitivities gradually, they may have had chemical sensitivities longer and developed more psychiatric illness in response to the stress of chemical sensitivities. On the other hand, those

TABLE 8. Continuous Visual Memory Test Subscores[a]

	Multiple chemical sensitivities (N = 23)[b]	Chemical sensitivities (no onset) (N = 13)[b]	Chronic fatigue syndrome (N = 18)[b]	Normals (N = 18)[b]	p
Hits	36.7 (1.0)	37.6 (1.0)	37.4 (.9)	38.3 (.6)	60
False alarms	18.4 (1.5)	13.8 (2.0)	15.0 (1.5)	12.9 (.9)	.04
Delayed recognition	3.9 (.3)	4.7 (.5)	4.9 (.4)	4.5 (.3)	.21
Total score	72.3 (1.8)	77.8 (1.5)	76.4 (1.7)	79.4 (1.0)	.009[c]

[a] Hits, recognition of target design; false alarms, identify nontarget as a target; delayed recognition, recognition memory for target designs; total score, combination of hits and false alarms.
[b] Expressed as mean (SE).
[c] Normals and CS significantly higher than MCS but not CFS.

TABLE 9. Multiple Regression Analysis: Dependent Variable: Continuous Visual Memory Test Total Score

Independent variables	Partial R-SQ[a]	p
Wide Range Achievement Test Standard Score	.23	.0001
Age	.13	.0010
Health concerns	.10	.0013
Chemically sensitive group	.05	.0170
Depression	.03	.0734
Normals group	.01	.2045
Chronic fatigue group	.00	.8604

[a] Overall adjusted R-sq = .4435.

patients who did not have a clear onset may represent a subgroup of chemical sensitivities in which psychiatric comorbidity plays a more significant role. This observation may clarify why Simon et al. (9) and Black et al. (2) reported higher rates of psychiatric disorder because neither investigator applied the current case criteria.

Axis II personality disorders were not evaluated in this study. Therefore, a higher rate of psychiatric disorders may have been observed if all possible disorders had been evaluated. For example, eight MCS, four CS, and nine CFS subjects who achieved clinically significant scale elevations on the MMPI-2 (i.e., 2-point code types) had no current Axis I diagnosis. These subjects may have had disorders from Axis II or subclinical psychiatric disturbance.

Along with depression, the most prominent symptoms presented by CFS, MCS, and CS subjects were symptoms associated with somatization disorder. In the present study, a conservative approach was taken to classify symptoms as medically unexplained. That is, the attribution of symptoms to chemical sensitivities or CFS was not regarded as a medical explanation. Using these criteria to score the DIS-III-R somatization interview, MCS, CFS, and CS had significantly more unexplained somatic symptoms than controls. However, only a minority of subjects qualified for the diagnosis of somatization disorder. As noted in the Black et al. (2) study, many subjects had several somatic symptoms, but their age of onset or the number of symptoms did not qualify them for a DSM-III-R diagnosis of somatization disorder.

Consistent with the DIS-III-R, the MMPI-2 scale scores reaching a clinically interpretable level (i.e., ≥65) for both groups were those associated with somatization disorder, i.e., hypochondriasis and hysteria. Forty-four percent of MCS, 42% of CS, and 53% of CFS qualified for the 2-point code type (1–3/3–1) associated with psychological distress expressed as somatic symptoms (22). Also, MCS and CS subjects were more defensive in their response to the MMPI-2 (L scale elevation). This response style was consistent with the tendency to emphasize physical rather than psychological interpretation of symptoms. Such defensiveness may be associated also with a higher level of physiological reactivity, which may produce, in turn, more symptoms. For example, Jamner et al. (35) reported a significant interaction between hostility and defensiveness to predict heart rate responses among paramedics. Alternatively, neurologically impaired populations also display MMPI-2 profiles suggestive of somatization disorder despite the physical origin of their symptoms. For example, patients with multiple sclerosis (36), closed head injuries (37–38), and a mixed neurologic population (37) present MMPI-2 profiles consistent with those seen in this study. The present data cannot distinguish a functional from an organic basis for the somatic symptoms reported by these patient groups.

Although MCS, CS, and CFS patients reported numerous neuropsychological symptoms, neuropsychological test results did not account for the level of impairment implied by the symptom reports. The only test showing significant differences between MCS and normal controls was a complex test of visual memory (CVMT). Subjects whose sensitivities began with a defined exposure (MCS) were unable to

discriminate target from nontarget designs (False Alarm rate). However, this result was not observed for chemical sensitivities subjects without a date of onset (CS), suggesting that poor performance on this measure was not a unique feature of sensitivity to chemicals. Somatic symptoms (Health Concerns) were significant predictors of CVMT performance. These findings suggest that subjects with numerous unexplained somatic symptoms have difficulty distinguishing relevant from irrelevant signals. Whether the relation between somatic symptoms and neuropsychological results reflects a primary neurological dysfunction (39), a behavioral response style, or a finding due to chance requires replication.

In summary, psychiatric and neuropsychological evaluation demonstrated more similarities than differences between patients with chronic fatigue and sensitivities to chemicals. In fact, a subset of CFS subjects reported a level of sensitivities to chemicals that was comparable with MCS subjects. If, as is reported clinically, patients with sensitivities to chemicals experience cognitive deficits only under exposure conditions, then controlled exposure studies will be needed to document these deficits. As Cullen suggested, selecting subjects with a clear date of onset for their sensitivities reduced the level of psychiatric co-morbidity. Therefore, psychiatric status and onset of illness associated with an exposure should be considered in future controlled exposure studies designed to test the phenomenon of multiple chemical sensitivities.

This project was supported by a grant from the Hazardous Substance Management Research Center, A National Science Foundation Industry/University Cooperative Center, and a New Jersey Commission on Science and Technology Advanced Technology Center. NIEHS Center Grant ES05022, and NIEHS Superfund Grant ES05955. Dr. Kipen was supported in part by NIEHS Academic Award ES-00218. We acknowledge the contributions in the early phase of this project of Carol Natarelli, RN, MPH.

REFERENCES

1. Greenberg DB: Neurasthenia in the 1980's: Chronic mononucleosis, chronic fatigue syndrome, and anxiety and depressive disorders. Psychosomatics 31:129–137, 1990
2. Black EW, Rathe A, Goldstein RB: Environmental illness: A controlled study of 26 subjects with "20th century disease." JAMA 264:3166–3170, 1990
3. Stewart DE, Raskin J: Psychiatric assessment of patients with "20th century disease" ("Total Allergy Syndrome"). Can Med Assoc J 133:1001–1006, 1985
4. Holmes GP, Kaplan JE, Gantz NM, et al: Chronic fatigue syndrome: A working case definition. Ann Intern Med 108: 387–389, 1988
5. Schluederberg A, Straus S, Peterson P, et al: Chronic fatigue syndrome research: definition and medical outcome assessment. Ann Intern Med 117:325–331, 1992
6. Cullen MR, ed: Workers with Multiple Chemical Sensitivities. Philadelphia, Hanley & Belfus, Inc., 1987
7. Shafron SD: The chronic fatigue syndrome. Am J Med 90: 730–739, 1991
8. Fiedler N, Maccia C, Kipen H: Evaluation of chemically sensitive patients. J Occup Med 34:529–538, 1992
9. Simon GE, Daniell W, Stockbridge H, et al: Immunologic, psychological, and neuropsychological factors in multiple chemical sensitivity: A controlled study. Ann Intern Med 19:97–103, 1993
10. Katon WJ, Buchwald DS, Simon GE, et al: Psychiatric illness in patients with chronic fatigue and rheumatoid arthritis. J Gen Intern Med 6:277–285, 1991
11. Wood GC, Bentall RP, Gopfert M, et al: A comparative psychiatric assessment of patients with chronic fatigue syndrome and muscle disease. Psychol Med 21:619–628, 1991
12. Katon W, Russo J: Chronic fatigue syndrome criteria. A critique of the requirement for multiple physical complaints. Arch Intern Med 152:1604–1609, 1992
13. DeLuca J, Johnson S, Natelson B: Information processing efficiency in chronic fatigue syndrome and multiple sclerosis. Arch Neurol 50:301–304, 1993
14. Sandman C, Barron J, Nackoul K: Memory deficits associated with chronic fatigue immune dysfunction syndrome. Biol Psychiatry 33:618–623, 1993
15. Grafman J, Schwartz V, Dale JK, et al: Analysis of neuropsychological functioning in patients with CFS. J Neurol Neurosurg Psychiatry 56:684–689, 1993
16. Straus SE, Dale JK, Wright R, et al: Allergy and the chronic fatigue syndrome. J Allergy Clin Immunol 81:791–795, 1988
17. Massman PJ, Delis DC, Butters N, et al: The subcortical dysfunction hypothesis of memory deficits in depression: Neuropsychological validation in a subgroup of patients. J Clin Exp Neuropsychol 14:687–706, 1992
18. Grant I: Alcohol and the brain: Neuropsychological correlates. J Consult Clin Psychol 3:310–324, 1987
19. Kipen H, Hallman W, Kelly-McNeil K, et al: Measuring chemical sensitivity prevalence. Am J Public Health 1995:85: 574–577
20. Spitzer RL, Williams JBW, Gibbon M, et al: User's Guide for the Structured Clinical Interview for DSM-III-R. Washington, DC, American Psychiatric Press, Inc., 1990
21. Hathaway SR, McKinley JC: MMPI-2. University of Minnesota Press, Minneapolis, MN, 1989
22. Greene RL. The MMPI-2/MMPI: An Interpretive Manual. Needham Heights, MA, Allyn and Bacon. 1991
23. Robins LN, Helzer JE. Diagnostic Interview Schedule (DIS) Version III- A. St. Louis, Mo, Washington University School of Medicine, 1985
24. Letz R, Baker E: Neurobehavioral Evaluation System (NES). Neurobehavioral Systems, Inc., Winchester, MA, 1985
25. Baker E, Letz R, Fidler A: A computer-administered neurobehavioral evaluation system for occupational and environmental epidemiology. J Occup Med 27:206–212, 1985
26. Wechsler D: Wechsler Adult Intelligence Scale-Revised. New York, NY, The Psychological Corporation, 1981

27. Trenerry MR, Crosson B, DeBoe J, et al: Stroop Neuropsychological Screening Test Manual. Odessa FL, Psychological Assessment Resources, Inc., 1989
28. Trites RL: Neuropsychological Test Manual. Montreal, Canada, Technolab, 1981
29. Delis DC, Kramer JH, Kaplan E, et al: California Verbal Learning Test Manual. San Antonio, TX, The Psychological Corporation, 1987
30. Trahan DE, Larrabee GJ: Continuous Visual Memory Test. Odessa, FL, Psychological Assessment Resources, Inc., 1988
31. Wechsler D: Wechsler Memory Scale - Revised Manual. San Antonio, The Psychological Corporation, 1987
32. Huberty C, Morris J: Multivariate analysis versus multiple univariate analyses. Psychol Bull 105:302–308, 1989
33. Lezak MD: Neuropsychological Assessment. New York, NY, Oxford University Press, 1983
34. Jastak S, Wilkinson GS: Wide Range Achievement Test Administration Manual. Wilmington, DE, Jastak Associates, Inc., 1984
35. Jamner LD, Shapiro D, Jui KK, et al: Hostility and differences between clinic, self-determined, and ambulatory blood pressure. Psychosom Med 55:203–211, 1993
36. Meyerink LH, Reitan RM, Selz M: The validity of the MMPI with multiple sclerosis patients. J Clin Psychol 44:764–769, 1988
37. Alfano D, Finlayson M, Stearns G, et al: The MMPI and neurologic dysfunction: Profile configuration and analysis. Clin Neuropsychologist 4:69–79, 1990
38. Gass CS: MMPI-2 interpretation and closed head injury: A correction factor. J Consult Clin Psychol 3:27–31, 1991
39. Bell IR, Miller CS, Schwartz GE: An olfactory-limbic model of multiple chemical sensitivity syndrome: Possible relationships to kindling and affective spectrum disorders. Biol Psychiatry 32:218–242, 1992