NEUROPSYCHOLOGY AND PSYCHOLOGY OF MCS

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Neurological symptoms are frequently reported by patients with multiple chemical sensitivities (MCS). Methods to compare the psychiatric, personality, and neuropsychological function of patients with MCS, chronic fatigue syndrome (CFS), and normal controls are described. Increased rates of Axis I psychiatric diagnoses are observed in the literature for MCS and CFS subjects relative to controls. Findings on the MMPI-2 and the Toronto Alexithymia Scale reveal profiles consistent with the tendency to report somatic rather than emotional symptoms in response to stress. However, many of the reported somatic symptoms also coincide with those found in neurologic disorders. The overall neuropsychological profile for MCS subjects does not reflect cognitive impairment. Relative to normal controls, the only difference in neuropsychological performance observed is reduced recognition of nontarget designs on a visual memory task. More fruitful areas for future psychological research will include measurement of the interaction between behavioral response styles and attentional processes in cognition, as well as observations under controlled challenge conditions.

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2. Abbreviations: CFS, Chronic Fatigue Syndrome; CVMT, Continuous Visual Memory Test; DIS, Diagnostic Interview Survey; MCS, Multiple Chemical Sensitivity; MMPI, Minnesota Multiphasic Personality Inventory; SCID, Structured Clinical Interview for the Diagnostic and Statistical Manual.

3. Key Words: Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, Neuropsychology, Psychiatric.

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INTRODUCTION

Neurotoxicants such as pesticides and solvents are ubiquitous in the environment and cause acute, as well as chronic, emotional and cognitive symptoms (e.g., Anger and Johnson, 1992). Patients exposed to neurotoxicants often complain of poor memory, difficulty in concentration, and changes in mood (Hartman, 1988). Standardized neuropsychological tests can quantify these symptoms. For example, these tests have documented cognitive impairments of memory and concentration due to chronic solvent exposure (NIOSH, 1987).

Exposure standards have been established to protect the health of workers using neurotoxicants. However, the concentration and duration of exposure that may result in permanent cognitive and emotional symptoms is not clearly defined and probably interacts with host factors. Recently, we have seen a group of patients with multiple nervous system and other symptoms which they attribute to environmental chemical exposures well below accepted exposure standards. A subgroup of such individuals are clinically defined to have multiple chemical sensitivities (MCS).

MCS patients frequently complain of cognitive and emotional symptoms, yet few data are available to quantify these complaints (e.g., concentration and memory). The purpose of this component of our research is to evaluate objectively the psychiatric and neuropsychological function of MCS patients and to compare them to patients with similar health complaints not attributed to chemicals (i.e., chronic fatigue syndrome (CFS)) and to normal controls.

Based on a description of their symptom profile, MCS patients resemble patients with psychiatric diagnoses such as post–traumatic stress (Schottenfeld and Cullen, 1986) or somatoform disorders (e.g., Brodsky, 1983; Stewart and Raskin, 1985). These similarities have lead some investigators to hypothesize that MCS can be explained by preexisting psychiatric disorders (e.g., Brodsky, 1983). Due to these observations, several recent studies investigated the premorbid psychiatric status of MCS patients. For example, as compared to musculoskeletal injury patients (Simon et al., 1993) and community controls (Black et al., 1990), a significantly greater proportion of MCS subjects had premorbid psychiatric disorders. However, a significant proportion of MCS subjects also did not qualify for a preexisting psychiatric diagnosis (53% in Simon et al., 1993; 35% in Black et al., 1990). Fiedler et al. (1992a) reported in a case series that MCS subjects, chosen according to the more specific criteria proposed by Cullen (1987), infrequently had a history of psychiatric disorder prior to the onset of MCS. The discrepancy in these investigations may be due, in part, to differences in the criteria used to select MCS patients.

Depending on the criteria employed, a broad range of patients may be considered chemically sensitive. For example, from the most inclusive perspective, clinical ecologists propose chemical sensitivity as an early manifestation of diseases involving any system (e.g. cardiovascular, renal) (Rea, 1992). Based on this conceptualization, patients diagnosed with traditional diseases are also said to suffer from chemical sensitivity. While not as broad,

previous investigators (e.g., Black et al., 1990; Simon et al., 1993) included patients under the care of clinical ecologists who were diagnosed with systemic candidiasis and chemical hypersensitivity. In part, the goal of these studies was to characterize the psychiatric, neuropsychologic, and immunologic status of the "typical" chemical sensitivity patient from a clinical ecology practice. In contrast, the goal of studies from our laboratory (Fiedler et al., 1992a; Fiedler et al., unpublished[1]) is to characterize patients who meet criteria proposed to define MCS as a primary problem generally in the absence of other known medical and psychiatric diagnoses. This allows a clear separation of findings related to chemical sensitivity from findings associated with known medical or psychiatric diagnoses.

Patients with chronic fatigue also frequently complain of poor attention, impaired concentration and memory, as well as symptoms indicative of psychiatric illness (e.g., depression) (Katon and Russo, 1992). As with MCS patients, little evidence is available to suggest a consistent underlying organic basis for their symptoms. Nevertheless, data from some standardized neuropsychological tests are available to substantiate cognitive symptoms (e.g., DeLuca et al., 1993). It has also been suggested that chronic fatigue and MCS are modern variations of somatoform disorders (Stewart and Raskin, 1985). However, chronic fatigue patients do not attribute their symptoms to chemical exposures. Rather, the onset of their symptoms typically follows a flu-like illness and exacerbations of symptoms are attributed to exertion. Due to the symptomatic similarities of CFS and MCS, another goal of our studies has been to use standardized psychiatric and neuropsychological instruments to compare MCS and CFS patient groups.

Although the neuropsychological and psychiatric symptoms reported by MCS patients are often similar to those reported by patients with ongoing solvent exposures, the exposure history of these two groups appears to be different. In contrast to MCS, neuropsychological impairment among solvent-exposed patients typically occurs after considerably greater exposure duration (e.g., 7 to 10 years) and involves clearly higher concentrations of solvent exposure. The neuropsychological tests used in our laboratory overlap those used to evaluate the long-term effects of solvent exposure. Therefore, the pattern of performance in MCS and CFS patients can be compared to those seen among workers with chronic occupational solvent exposure.

RATIONALE FOR SUBJECT SELECTION CRITERIA

Based on the clinical similarities between MCS and CFS, a direct objective comparison of these groups could help resolve discrepant hypotheses about the conditions. For example, some investigators have suggested that the symptomatology of CFS is the somatic form of depression (Holmes et al., 1988). On the other hand, the symptoms of MCS have been

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[1]FIEDLER, N., KIPEN, H., DELUCA, J., KELLY-MCNEIL, K., and NATELSON, B. "A controlled comparison of Multiple Chemical Sensitivity and Chronic Fatigue."

compared to anxiety-based disorders such as phobias (Bolla-Wilson et al., 1988). In addition, healthy normal controls provide a nonclinical comparison standard.

MCS subjects entering our studies meet the following criteria suggested by Cullen (1987): 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. Subjects with a history of psychiatric hospitalizations or the following premorbid psychiatric conditions are excluded: psychoses, manic depression, alcoholism or drug abuse. Also, subjects currently involved in a legal case related to their exposure are not included.

Chronic fatigue subjects (CFS) evaluated for our studies meet the revised Centers for Disease Control criteria for CFS (Schluederberg et al., 1992). Severe fatigue that reduces activity 50% below premorbid levels for a minimum of six months is the "major" criterion. This fatigue cannot be explained by other medical or psychiatric illness. Minor criteria include at least 8 of 14 rheumatological, infectious, and neuropsychiatric symptoms (e.g., myalgia, sore throat, poor concentration).

Normal controls are recruited from a general internal medicine clinic population or from newspaper advertisements. Subjects with any of the following disorders are excluded: neurologic disease or brain injury, toxic exposure, stroke or cardiovascular disease, liver or kidney disease, serious gastrointestinal disorders (e.g., colitis), and major psychiatric conditions described previously.

RATIONALE AND SELECTION OF NEUROPSYCHOLOGIC AND PSYCHIATRIC MEASURES

A battery of neuropsychological tests that include traditional neuropsychological tests and performance based tests are used to assess cognitive function. Traditional neuropsychological tests have been used to evaluate dysfunction due to brain injury (Lezak, 1983). Since MCS and CFS patients report cognitive symptoms of permanent dysfunction, traditional tests reflecting neuropsychological impairment are being used as a part of the neuropsychological battery. On the other hand, performance based tests such as reaction time have been used as subtle indicators of changes in performance due to such environmental factors as stress or drugs (Wittenborn, 1987). In addition to general cognitive dysfunction, MCS patients report relatively subtle performance changes under exposure conditions. While MCS patients are accommodated as much as possible during testing, our testing rooms are not free of exposures reported to cause symptoms. Therefore, if subtle exposure and symptoms occur, the performance tests would be most sensitive in evaluating these effects.

Tests of concentration include computerized Simple Reaction Time (dominant and nondominant hand) and Continuous Performance Test (Baker et al., 1985), Digit Span (Wechsler, 1981), and the Stroop Color Word Test (Trenerry et al., 1989). Tests of visuomotor skills are Digit Symbol (Wechsler, 1981), computerized Hand-Eye Coordination (Baker et al., 1985), and Grooved Pegboard, dominant and nondominant hand (Trites, 1981). Tests of memory are the California Verbal Learning Test (Delis et al., 1987), the Continuous Visual Memory Test (Trahan and Larrabee, 1988), and Visual Reproduction I and II (Wechsler, 1987). The Metamemory Questionnaire (Mateer et al., 1987) is administered to assess subjects' perception of memory function.

To examine the current psychiatric status of subjects, the Structured Clinical Interview for the Diagnostic and Statistical Manual, 3rd Edition Revised (Spitzer et al., 1990) and the Minnesota Multiphasic Personality Inventory-2 are administered (Hathaway and McKinley, 1989). In addition, the somatization section of the Diagnostic Interview Survey, III-A (Robins and Helzer, 1985) is administered by a nurse to ascertain the rate of medically explained and unexplained symptoms. These instruments assessed traditional psychiatric diagnostic categories. Results from these measures provide an objective comparison of the rates of psychiatric disorders between MCS and CFS. In addition to the traditional clinical scales, the MMPI-2 provides content scales based on single symptom dimensions such as depression and health concerns. The latter allows separation of somatic (health concerns) from emotional symptoms (anxiety). The Toronto Alexithymia Scale is administered to assess the tendency to express feelings in somatic rather than verbal or symbolic terms (Taylor et al., 1988). Performance on this scale has been associated with psychosomatic illness and somatization (Taylor et al., 1988).

PSYCHIATRIC AND PERSONALITY STATUS OF MCS PATIENTS

Our studies as well as those from other investigators (e.g., Simon et al., 1993), evaluating Axis I psychiatric diagnoses with structured psychiatric interviews, suggest that MCS subjects have significantly higher rates of psychiatric diagnoses than age-, gender-, and education-matched controls.

The diagnoses occurring most frequently among MCS subjects are depression and anxiety disorders. For example, our preliminary results with MCS patients suggests a rate of current depression at 17% (Fiedler et al., 1992a). These rates are lower than the rates of current depression (29%) and anxiety (34%) reported in the most recent study by Simon et al. (1993). MCS and CFS subjects have a significantly higher overall rate of current psychiatric diagnoses than various control groups (e.g., normal controls, musculoskeletal injury), a significant proportion of subjects from our studies as well as other laboratories (e.g., Simon et al., 1993) have no current psychiatric diagnosis. The data do not support that anxiety based disorders are more prevalent among MCS patients. Also, a significant proportion of subjects from our studies (e.g., 83%) (Fiedler et al., 1992a) as well as other investigators (e.g., Simon et al., 1993) have no current psychiatric diagnosis.

For several reasons, traditional Axis I psychiatric diagnoses may not provide the most useful information regarding the psychological attributes that contribute to this disorder. First, thus far, the data has not shown MCS to be fully explained by premorbid or current psychiatric disorders. Even though considerable overlap exists between the symptoms of somatoform disorders and MCS, a majority of these patients do not meet the criteria for somatization disorder as currently outlined in DSM-III-R. Second, the cause and effect relationship between MCS and psychiatric disorders cannot be addressed among individuals who are already ill with MCS at the time of testing. That is, it can be effectively argued that psychiatric disorders such as depression or anxiety may have been a consequence of MCS.

Instead of focusing on the dichotomous diagnostic categories within psychiatry, use of measures that assess personality traits associated with physical symptom reporting may be of greater heuristic value. For example, our studies with the MMPI-2 reveal that the group profile for MCS subjects is consistent with somatoform disorders (Fiedler et al., 1992a). That is, the peak scale elevations are on scales of hypochondriasis and hysteria. When the items from these scales are analyzed based on their content, the primary symptoms expressed by MCS subjects load on a scale of Health Concerns. This scale includes somatic items that are psychologically based as well as somatic items endorsed by neurologically impaired populations such as closed head injury and multiple sclerosis (Meyerink et al., 1988; Alfano et al., 1990).

Other studies have shown that MCS subjects also scored significantly higher than controls on scales associated with somatization such as the Barsky Amplification Scale (Simon et al., 1990), and the Illness Behavior Questionnaire (Black et al., 1993). The Toronto Alexithymia Scale, a measure reflective of difficulty with verbal and symbolic expression of emotion, was selected in our laboratory to assess the personality construct hypothesized to be associated with post–traumatic syndromes and psychosomatic disease (Taylor et al., 1988). That is, MCS subjects are hypothesized to express symptoms of distress in somatic rather than emotional terms.

In summary, traditional, Axis I psychiatric diagnoses have not adequately described the majority of MCS subjects. However, several studies support that MCS subjects report a mixture of somatic symptoms that reflect both neurological and psychosomatic processes.

NEUROPSYCHOLOGICAL STATUS OF MCS PATIENTS

To date, few studies have systematically evaluated the neuropsychological symptoms reported by MCS patients and no studies have evaluated cognitive performance under controlled exposure conditions. Simon et al. (1993) administered traditional measures of neuropsychological performance including tests of memory, concentration, and visuo-motor speed. A few significant differences were noted between MCS and musculoskeletal injury controls on immediate verbal recall. However, the authors concluded that when the effects of

psychological distress (e.g., anxiety and depression) were controlled, differences in cognitive function were no longer apparent.

In our laboratory, applying the standardized neuropsychological tests described previously, we also detected few overall differences in performance between MCS subjects and normal controls. Relative to normative standards, we observed no differences on tests of concentration, which included Simple Reaction Time, Continuous Performance, Stroop Color-Word Task, and Digit Span (Fiedler et al., 1992a,b). We also detected no differences relative to normative standards on tests of visuomotor coordination such as Digit Symbol, Hand-eye Coordination, and Grooved Pegboard (Fiedler et al., 1992a,b). Preliminary comparisons with age, gender, and education matched CFS, and normal controls revealed no significant differences in performance on these measures.

We observed more mixed results on tests of verbal and visual memory. Preliminary data using the California Verbal Learning test revealed no significant overall differences in performance between MCS and normal controls. However, MCS subjects performed significantly more poorly on the initial trial of the word lists (Fiedler et al., 1992a). That is, the ability of MCS subjects to encode the list after one presentation was significantly lower for both lists presented within this task. After repetition of the word list (five learning trials), however, the overall recall as well as the slope of the learning curve for the MCS subjects was comparable to normal controls. This preliminary result is similar to the findings cited above by Simon et al. (1993). That is, initial verbal learning trials were reduced relative to controls. However, after a delay of 30 minutes, no differences in retention of the material were noted.

Preliminary data comparing MCS to normal controls on a complex signal detection task of visual memory, i.e., Continuous Visual Memory, reveals that MCS subjects commit significantly more False Alarms. That is, in signal detection terms, they have difficulty distinguishing target from nontarget designs or noise from the signal.

Thus far, performance on neuropsychological testing has not revealed evidence of cognitive impairment among MCS subjects. Even among the more sensitive tests of performance such as Reaction Time and Continuous Performance, the preliminary data from our laboratory do not show significant reductions in performance relative to normal controls. However, caution is indicated since only two laboratories to date have reported neuropsychological evaluation of MCS patients and none of these evaluations have been conducted under controlled exposure conditions.

SUMMARY

The most consistent finding in our studies as well as those of other investigators (e.g., Simon et al., 1993) is that MCS subjects report numerous somatic symptoms associated with Axis I psychiatric disorders such as depression, and with neurologic disorders such as multiple sclerosis (Alfano et al., 1990; Gass, 1991). The challenge from a psychological perspective is

to develop objective methods that will help us understand the conditions under which these symptoms are produced, their neurobiological basis, and their impact on cognitive performance.

Thus far, our research with MCS subjects has been conducted in relatively uncontrolled exposure conditions. Subjects travel to our clinical facility, and while we make every effort to minimize exposures, our facility is not free of substances to which MCS subjects report reactions (e.g., cleaning products). Despite these uncontrolled exposure conditions, with one exception, the overall neuropsychological test results do not reveal cognitive deficits. Thus, the neuropsychological performance pattern of MCS subjects has not reflected reductions in performance that resemble other groups reporting cognitive deficits due to neurotoxicant exposures (e.g., solvents) (Ryan et al., 1988) nor have they reflected permanent brain injury.

On tests associated with personality attributes of somatic concerns, MCS subjects have shown a consistent pattern of increased focus on bodily sensations. This behavioral style may reflect difficulty with filtering out irrelevant or subclinical stimuli. For example, James et al. (1987) reported that based on evoked response potential, somatization disorder patients had difficulty separating relevant from irrelevant stimuli. Our preliminary data from the CVMT, a behavioral task in which MCS subjects had to separate relevant from irrelevant stimuli, provides some impetus for further exploration of this behavioral response style.

In summary, our studies suggest that future research should focus on attentional processes and on personality factors that may contribute to symptomatology. Dichotomous psychiatric diagnoses and traditional neuropsychological test batteries are not likely to enhance our understanding of the psychological or neurobiological mechanisms of MCS.

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