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Psychogenic Origins of Multiple Chemical Sensitivities Syndrome: A Critical Review of the Research Literature

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ABSTRACT. The purpose of this review was to critically evaluate research on the psychogenic origins of multiple chemical sensitivities (MCS) syndrome. Using as keywords *environmental illness, multiple chemical sensitivities,* and *clinical ecology,* two databases—PsychLit and Medline—were searched by computer; reference lists of all articles located were also searched manually. Ten articles meeting three criteria were selected for review. Five sample selection problems, seven measurement problems, and three study design problems were common in all but one of the articles reviewed. Current studies investigating psychogenic hypotheses of MCS syndrome are methodologically problematic and their conclusions questionable. Studies of psychiatric profiles observed in MCS syndrome need to be designed to differentiate between competing psychogenic and biogenic hypotheses.

MULTIPLE CHEMICAL SENSITIVITIES (MCS) SYNDROME (known also as environmental illness [EI], ecologic illness, environmental hypersensitivity, total allergy syndrome) has been described as "the most puzzling clinical entity emerging in the 1980s."[1] MCS lacks a standard case definition, but, in one survey,[2] more than 50% of physician respondents agreed that case selection criteria for the condition should include the following characteristics: (1) affected individuals experience symptoms following exposures at very low levels to multiple, structurally unrelated chemical substances; (2) the responses are reproducible; (3) the symptoms resolve or improve when the incitants are removed; and (4) the condition is chronic. Other defining characteristics of MCS syndrome are symptoms representing multiple organ systems,[3] including systemic (e.g., chronic, overwhelming fatigue), neuropsychiatric (e.g., confusion, short-term memory deficits, sudden sleepiness), musculoskeletal (e.g., muscle spasm and pain), lower respiratory (e.g., difficulty breathing), upper respiratory (e.g., rhinitis, congestion, sore throat), and gastrointestinal (e.g., bloating, cramps, indigestion) systems.[4] Individuals reporting environmental hypersensitivities experience varying degrees of morbidity; some are unable to work or to carry on normal activities.[1,5,6]

Although the prevalence of MCS syndrome is unknown, some authors believe that the condition is relatively common.[1,5,6] Intolerance to low levels of environmental chemicals has been reported after varied occupational exposures,[7] exposure to "tight" or "sick" buildings,[8] organophosphate exposures,[9] and solvent exposures.[10] Moreover, a mild MCS-like condition is widely believed to be characteristic of patients with rhinitis, sinusitis, asthma, and other upper and lower respiratory conditions, as well as those with metabolic and toxic conditions such as hypothyroidism, hyperthyroid-

ism, diabetes mellitus, and drug use.[11-13] Our own as yet unpublished research and that of others[14] also indicate that some degree of chemical hypersensitivity is common in the general population.

The origins of MCS syndrome are unknown but highly controversial in the medical community. Physicians at one extreme consider the syndrome to be pathophysiologically induced. Physicians at the other extreme argue that the chemical sensitivity in MCS syndrome is imaginary, attributable to the patient's misinterpretation, or the physician's misdiagnosis, of a traditional psychiatric disorder (e.g., major depressive, phobic, generalized anxiety, or somatoform disorders). Yet, other physicians take an intermediate stance on the origins of MCS syndrome, one that implicates both personality and environment as etiologic factors. In a survey of MCS syndrome-related practices and attitudes, 9% of occupational physician respondents reported believing that the syndrome resulted from predominantly physical roots, whereas 82% reported believing that it resulted from a combination of psychogenic and biogenic factors.[15] Among physicians with a particular interest in MCS, at least 70% of the entire sample and of the three specialist groups who see the most patients—allergists, occupational physicians, and clinical ecologists—considered the physical environment important in causing the syndrome.[16] However, more than 70% of allergists, 50% of occupational physicians, and 20% of clinical ecologists reported believing that the patient's personality was also important in causing the condition. These data suggest that MCS syndrome is perceived by many physicians to be at least partially induced by psychogenic conditions.

The purpose of this research was to critically review research studies that are considered supportive of the psychogenic hypothesis of MCS syndrome.

Method

Selection and overview of articles reviewed. For this study, two databases—PsychLit (American Psychological Association) and Medline (National Library of Medicine)—were searched by computer; the keywords used were *environmental illness, multiple chemical sensitivities,* and *clinical ecology.* The reference lists of all articles located by the search were also reviewed for additional articles. All articles meeting the following criteria were selected for analysis: (1) original data were gathered on a human sample by the authors, (2) the psychogenic origins of MCS syndrome were addressed implicitly or explicitly, and (3) the findings were published during or after 1980. Our literature search yielded 11 articles. One article[17] was subsequently eliminated because all the data on MCS syndrome subjects were analyzed in a second article,[18] which was retained, leaving 10 articles for review.

Categories of articles reviewed. The 10 articles selected were categorized according to the following measurement strategies used for the findings presented: (1) case histories, relying typically upon multiple nonstandardized strategies, especially interviews and case records; (2) standardized psychiatric or psychologic measurements; (3) medical measurements; and (4) both psychiatric or psychologic and medical measurements. The articles, organized by category, are summarized in Table 1 in terms of objectives, design, and conclusions. Objectives ranged from very specific (e.g., to determine whether specific physiologic characteristics and depression are characteristic of MCS syndrome) to very general (e.g., to review medical records for support of the environmental illness concept). Six of the 10 studies used a descriptive case history design with no control group; 3 studies used a case-control design; and 1 study used a quasi-experimental design.

Procedure. Initial readings of the articles led to the list of problems described in Table 2. The problems were conceptualized as concerning (1) sample selection, (2) measurement, or (3) study design.

Five sample selection problems were identified, including small sample size, and nonrepresentative sample sources (those with obvious biases, such as psychiatric referrals or workman's compensation claimants). Using as a sample source only patients being seen by a clinical ecologist was also considered a biased sampling strategy for two reasons: (1) communications from clinical ecologists are widely believed to channel patients' concepts of their illness in specific directions,[18] and (2) patients consulting clinical ecologists are only a subset of patients alleging MCS syndrome.[4] Small sample size was defined arbitrarily as 20 or fewer participants. It seemed justifiable to classify a sample size of 20 or fewer index subjects as inadequate on the grounds that a controlled study with 20 index subjects and 20 controls would have only a 46% chance of detecting a true difference, assuming a medium effect size, between the means of the two groups, which would be significant at the .05 level of probability using a one-tailed test.[19] Likewise, estimates derived from a group of 20 subjects would be imprecise; for example, a prevalence estimate of 50%, based on a sample of 20 subjects, would have a 95% confidence interval of 39% to 61%.

Seven measurement problems were identified, including no control for investigator bias and insufficient information about the assessment instruments. Three study design problems were identified, including inadequate controls for a chronic illness explanation of symptoms and conclusions about cause and effect in the absence of both a testable hypothesis about cause and effect and a study design capable of elucidating cause and effect relationships.

This list of methodologic problems was used as a guide as both authors evaluated each article independently. The few differences between the authors' evaluations—attributable in all cases to the need to further differentiate between definitions of related categories—were resolved by discussion.

Results

Consensus tabulations of methodologic problems in the articles appear in Table 3. Only one study reviewed was judged to have fewer than 8 methodologic problems. The number of methodologic problems per article ranged from a low of 3 to a high of 13 (maximum possible: 15). The mean number of methodologic problems

Table 1.—Objectives, Design, and Conclusions of Studies Reviewed

Article/objective	Design	Conclusion
	Case Histories	
Brodsky[18] To present model cases and elements that recur in sample; to examine medical subculture that shaped "illness careers" of EI patients	Case histories, based on 2- to 3-h psychiatric examination	"This subsculture seems to appeal to patients with a history of chronic psychiatric symptoms, and, for this reason, psychiatrists must be aware of this problem population . . ." (p. 742).
Rosenberg et al.[25] To contrast the clinical presentation of the EI patient with an obsessive/paranoid style to the hysteric/somatizing EI patient	Single case history, based on interview, medical records, and a projective test	"The treatment approach for . . . environmental illness patients has to be markedly different if one sees these patients as obsessive or paranoid characters, rather than exhibiting a variation of hysteria . . . or somatization disorder" (p. 680).
Stewart and Raskin[22] To illustrate the case presentation and management of patients with "20th-century disease" suffering from a recognizable psychiatric disorder	Case histories, based on psychiatric interviews	"Psychiatric disorders were found in all 18 patients with 20th-century disease. . . . Twentieth century disease appears to be not a new illness but rather a fashionable name for a condition known to physicians for centuries" (p. 1006).
	Psychiatric/psychological measurements	
Black et al.[26] To explore the associations between EI and psychiatric disorder	Comparison of index subjects to first-degree relatives of psychiatrically normal subjects, using standardized psychiatric tests	"Patients with EI who consented to a diagnostic interview were significantly more likely than controls to meet lifetime criteria for a major mental disorder . . . suggest[ing] that psychiatric diagnoses must be considered as an explanation for patients with multiple ill-defined symptoms in the absense of clinical or laboratory findings" (p. 3170).
Simon et al.[27] To study psychological factors associated with EI in a population not selected for psychiatric illness	Comparison of index subjects to exposed sick subjects not meeting criteria for MCS syndrome, using structured diagnostic interviews and standardized self-report measures	"These findings suggest that psychological vulnerability strongly influences chemical sensitivity following chemical exposure" (p. 901).

(Table 1 continued on page 319)

was 9.6; the median number of methodologic problems was 10.0.

Sample selection problems. All but 2 studies reviewed[20,21] had more than two sample selection problems. Sample sizes in the range of 1 to 20, judged to be problematic, affected 6 of the 10 studies. Nine of the 10 studies were judged to use nonrepresentative sample sources, such as psychiatric clinic patients, cases pursuing litigation or compensation, or patients of a clinical ecologist. A less common sampling problem (found in 4 of the 10 studies) was the inclusion of individuals with food sensitivity or candidiasis diagnoses without clarifying their status with regard to chemical hypersensitivity. Only Schottenfeld and Cullen,[20] Doty et al.,[21] and Terr[24] specifically described excluding from their index group individuals with medical conditions other than MCS syndrome that could account for their hypersensitivity symptoms. Seven of the 10 studies committed another sampling error, using vague selection criteria for defining index subjects. For example, 3 studies defined cases in terms of being "identified as EI by a clinical ecologist." Another 3 studies defined cases in terms of being "self-identified as having environmental hypersensitivities." The criteria used by physicians or patients, respectively, in these studies were not specified.

Measurement problems. Measurement problems were also common in the studies reviewed. Five of the studies[18,20,22–24] described findings based on a measurement protocol that varied without describing the criteria used for differential treatment. Six studies[18,23–27] based conclusions about psychopathology in MCS syndrome largely or exclusively on measurement instruments or strategies that could not distinguish persisting psychopathologic traits from either unexplained medical symptoms or distress caused by medical symptoms.

Two of the research instruments used in the Simon et al. study[27] were examined in detail for illustrative purposes. Item analyses were performed by computing the percentage of items that, in the authors' judgments, based on interview studies,[4] would be anticipated if

Table 1.—Objectives, Design, and Conclusions of Studies Reviewed *(Continued)*

Article/objective	Design	Conclusion
	Medical measurements	
Schottenfeld and Cullen[20] To apply diagnostic criteria for atypical posttraumatic stress disorder (PTSD) and other conditions to disabling conditions that are medically unexplained	Analysis of case records during specified time period	"Although not specifically tested by our study, the results of the study suggest that patients with chronic or repeated exposure . . . or with histories of exposure to solvents are perhaps more likely to develop atypical rather than typical PTSD" (p. 369).
Staudenmayer and Selner[30] To facilitate differential diagnosis between verifiable medical disease and psychosomatic illness	Comparison of index and control groups (one with and one without psychological symptoms) on psychophysiological measures during relaxation	"The . . . results [confirm and extend] previous work which hypothesized that universal reactors manifest psychosomatic illness rather than true environmental disease" (p. 270).
Terr[24] To assess whether (1) environmentally induced illness is a disease entity with an identifiable set of clinical features, and (2) a significant immunologic abnormality distinguishes the patients from normal persons	Analysis of medical records, medical histories, and findings from physical examinations and laboratory tests (if appropriate)	"The subgroup of 31 patients with multiple symptoms most likely of psychological origin corresponds to the type of patient described repeatedly in the clinical ecology literature. . . . Treatment . . . failed in every case to produce a remission; in fact, the number of symptoms reported by most of these patients significantly increased after such treatment, probably reflecting increasing fear of other possible environmental hazards" (p. 149).
Terr[23] To review medical records for support for the concept of environmental illness	Analysis of medical records; medical, environmental, and occupational histories; findings from physical examinations and diagnostic tests, as warranted	"Medical histories showed that medical illnesses were minimal but previous psychologic difficulties . . . were prominent" (p. 261). "Examining physicians who were not clinical ecologists invariably arrived at other diagnoses, usually psychiatric. This retrospective review lends no support to the clinical ecology concept of 'environmental illness'" (p. 257).
	Medical and psychiatric measurements	
Doty et al.[21] To determine whether persons with MCS display alterations in olfactory sensitivity, blood pressure, heart rate, respiratory rate, nasal airflow resistance, and/or psychologic depression	Comparison of MCS syndrome patients and controls on varied physiologic and psychologic measures	"It is apparent from these observations that individuals suffering from MCS are experiencing alterations in a variety of autonomic functions. . . . However, why or how such symptoms are triggered remains a mystery" (p. 1427). "[As regards depression data] it is difficult to disentangle cause from effect" (p. 1427).

MCS syndrome were a bonafide pathophysiologically based illness. Specifically, items in three categories were identified: (1) physical symptoms reported frequently in MCS syndrome; (2) likely correlates of any untreated, poorly understood, chronic medical condition; and (3) commonly reported social/psychological sequelae peculiar to MCS syndrome, such as avoidance of commonly reported incitants. Out of 14 items on the Whitely Index of Hypochondriasis, 12 items (86%) related to one of these three categories; of 90 items on the Hopkins Symptom Checklist, 54 items (60%) related to one of the three categories. In other words, the identical test findings used by Simon and his colleagues to support a psychogenic hypothesis could have been used to support a biogenic hypothesis. The tests are unable to distinguish between the two hypotheses. Given that somatic symptoms usually inflate scores on tests of psychopathology, psychometric instruments that avoid questions about somatic symptoms—such as the Geriatric Depression Scale[28] and the Neuroticism Extroversion Openness Personality Inventory–Revised[29]—are better choices for studying psychopathology in a condition presenting with medical symptoms.

Another methodologic problem, basing inferences about psychogenic etiology largely or completely on de-

Table 2.—Definition of Methodological Problem Categories

Sample selection problems

1. Likely selection bias due to small sample size. Size of sample is small for meaningful generalizations to the population of interest. Conclusions were based on an *n* of 1, in one case; in five additional cases, *n* was less than 20.
2. Likely selection bias due to sample source. Nonrepresentative sample sources, such as psychiatric referrals, workmen's compensation claimants, and patients of clinical ecologists, make generalizations to the population of interest inappropriate.
3. Sample includes individuals whose status with regards to MCS syndrome is unspecified. For example, patients whose major complaint was food sensitivities or chronic candidiasis are included in the index sample.
4. Patients with allergy, asthma, or other conditions associated with nonspecific hypersensitivity to environmental chemicals are not explicitly excluded from the index sample.
5. Selection criteria for the index sample are vague or unspecified and, therefore, selection bias cannot be evaluated. For example, the authors of three articles used Environmental Illness diagnoses (based on undisclosed criteria) by clinical ecologists as the basis for inclusion in the index sample.

Measurement problems

1. Variable protocol. Measurements collected differ from subject to subject, and no criteria are specified to justify the differential treatment.
2. Inappropriate instruments. One or more study measures cannot distinguish unexplained medical symptoms and distress secondary to medical symptoms from persisting psychopathologic traits, but investigators assume the data are indicative of psychopathologic traits.
3. Mostly self-report data. Study conclusions rely on patients' subjective perceptions (e.g., interview data or psychological tests) in contrast to behavioral observations or physiologic assays.
4. Largely qualitative data are collected. For example, the investigator's personal observations.
5. Controls for investigator bias are absent. Investigators are not blind to the subjects' group membership.
6. Insufficient information. Measurement instruments are not named or described; therefore evaluation is impossible.
7. Selective information. Although both biogenic and psychogenic explanations of the data are plausible, investigators endorse psychogenic explanations without discussing biogenic explanations. Psychiatric symptoms that could represent consequences, rather than causes of MCS syndrome are considered indicative of psychogenic causation.

Study design problems

1. Unjustifiable conclusions. Cause-and-effect hypotheses are neither specified nor tested, given the study design; yet cause-and-effect relationships are inferred. For example, researchers who investigated associations between psychopathology and MCS syndrome, retrospectively, and calculated lifetime prevalences of psychiatric diagnoses concluded that psychiatric conditions preceded and caused MCS syndrome.
2. Controls for the "environmental induction" explanation of psychiatric symptoms are not described. Psychiatric symptoms (e.g., depression, fatigue) that could be induced by exposures to environmental incitants are considered evidence of psychogenic causation.
3. Controls for "adjustment responses to chronic, stigmatizing, isolating illness" are not described.

scriptive self-report data from patients, was found in 5 of the 10 studies reviewed.[18,22,25-27] Four studies reviewed[18,20,22,25] used qualitative data—in this case, the observers' unblinded impressions—to infer psychogenic etiology in MCS syndrome. None of the studies described procedures to control or minimize investigator bias beyond the unblinded use of standardized tests and interviews.

Omissions of important methodologic information were also common in the reviewed articles. Six authors[18,20,22-25] referred to medical or psychological data that had been collected, but did not describe some, or all, of the measurement instruments used and did not quantify some, or all, of the data collected. Two studies omitted information pertaining to alternative biogenic hypotheses. For example, in the Staudenmayer-Selner study,[30] neurophysiologic signs (e.g., high levels of EEG beta activity) were interpreted as indicative of psychosomatic disorders, but are, in fact, nonspecific as to etiology and are often found in populations after known overexposures to environmental toxicants.[31-33] In the Rosenberg et al. study[25] of a single case hospitalized for asthmatic symptoms, medical data were not even discussed. Furthermore, authors concluding psychogenic etiology from associations between MCS syndrome and psychiatric traits/disorders (see Brodsky[18] and Black et al.,[26] for example) failed to mention that the psychiatric profiles of medical populations are often indistinguishable from those of psychiatric populations (see, for example, Enders,[34] Cripe,[35] and Ahles et al.[36]).

Study design problems. Study design problems were judged to be prominent in 9 of the 10 articles reviewed, the exception being Doty et al.[21] None of the authors advanced testable cause and effect hypotheses or used a study design that could distinguish correlation from causation, yet 8 authors considered their data supportive of psychogenic explanations. For example, although Black et al.[26] and Simon et al.[27] reported that their goals were to explore *associations* between MCS syndrome and psychiatric disorder, the conclusions of both groups suggested that study data supported the thesis that MCS syndrome was attributable to "psychological vulnerability" or psychopathology. Plausible illness-related explanations for the psychiatric profile—for example, responses to environmental chemical triggers or adjustment to a chronic, distressing, and isolating illness—were not explored adequately by any author and were described by only two research teams.[21,30]

Additional problems. Two additional problems were common in 9 of the 10 articles reviewed, the exception being Doty et al.[21] Nine studies required rigorous evidence about medical contributions, but not about psychological contributions to MCS syndrome. Most frequently, this was reflected in mistaking the failure to support specific medical hypotheses in their own or in someone else's research (usually, reported as case notes or case histories) for positive support of psychiatric causation. Furthermore, 5 authors[23,24,26,27,30] failed to comment on the implications for the psychogenic hypothesis advanced of finding that a substantial percentage of their MCS syndrome sample failed to meet the study criteria for psychopathology.

Discussion

This review suggests that existing research studies, considered widely supportive of a psychogenic origin for

Table 3.—Methodological Problems in Articles Reviewed

Methodological problems	Brodsky[18]	Rosenberg et al.[25]	Stewart and Raskin[22]	Black et al.[26]	Simon et al.[27]	Schottenfeld and Cullen[20]	Staudenmayer and Selner[30]	Terr[24]	Terr[23]	Doty et al.[21]
Sample selection problems										
Small sample size	X	X	X		X	X				X
Questionable sample source	X	X	X	X	X		X	X	X	X
MCS syndrome status of index subjects unspecified			X	X				X	X	
Asthmatic, allergic, etc., subjects not excluded from MCS syndrome sample	X	X	X	X	X		X		X	
Unspecified selection criteria for MCS syndrome subjects	X	X	X	X			X	X	X	
Measurement problems										
Variable protocol	X	n/a*	X			X		X	X	
Measures confound symptoms and sequelae of illness with psychopathological traits	X	X	n/a	X	X			X	X	
Self-report data largely	X	X	X	X	X					
Qualitative data largely	X	X	X			X				
Investigator bias uncontrolled	X	X	X	X	X	X	X	X	X	X
Insufficient information	X	X	X			X		X	X	
Selective information	n/a	X	n/a	n/a	n/a		X			
Study design problems										
Unjustifiable conclusions	X	X	X	X	X	X	X	X	n/a	
Inadequate controls for environment-induction explanation	X	X	X	X	X	X	X	X	X	n/a
Inadequate controls for adjustment to illness explanation	X	X	X	X	n/a	X	X	X	X	n/a

*n/a—pertinent information is lacking or the issue in question is not applicable to the particular study.

MCS syndrome, have serious methodologic flaws regarding sample selection, measurement, and study design. Given the magnitude of the methodologic shortcomings, both comprehensive discussions of study limitations and cautious conclusions are warranted. But 8 of the 10 studies reviewed suggested—for the most part, explicitly—that psychogenic hypotheses derived support from the data obtained.

Competing hypotheses about psychiatric features. Few investigators would deny that psychiatric symptoms (such as depression, anxiety, memory impairment, and overwhelming fatigue) are usually, but not always,[37] observed in individuals with MCS syndrome. What is controversial is the nature, timing, and origin of these features, which can be explained plausibly by at least six competing hypotheses (see Table 4).

Hypotheses 1 and 2 assume that psychiatric characteristics preceded both exposure and MCS syndrome onset. Hypothesis 1 posits that psychopathology preceded and contributed to the onset of MCS syndrome, conceptualized as an emotional disorder. Hypothesis 2 stipulates that psychiatric characteristics are a correlate of risk factors for MCS syndrome. For example, malaise and fatigue could be correlates of a predisposing biological characteristic, such as atopy or upper airway disorders, which are reported as predating MCS syndrome by some affected individuals.

Four equally plausible hypotheses place the emergence of psychiatric characteristics after either exposure or illness onset. Hypothesis 3 suggests that malaise, fatigue, and other psychiatric characteristics represent early preclinical manifestations of MCS syndrome, conceived as a medical condition that often develops gradually over time after repeated exposures. Hypothesis 4 posits that psychiatric symptoms constitute the subjective component of certain neurological/physiological responses to incitants, appearing first after the onset of MCS syndrome. Hypothesis 5 assumes that psychiatric characteristics represent transient, or lasting, psychosocial consequences of an illness-inducing chemical expo-

Table 4.—Alternative Hypotheses for Psychiatric Profile Seen in MCS Syndrome

Origins of psychiatric symptoms	Chronicity/timing of psychiatric symptoms	Role of psychiatric symptoms
1. Psychopathology contributes to onset of MCS syndrome, an emotional disorder.	Longstanding; precede exposure and MCS syndrome onset	Contribute to MCS syndrome
2. Psychopathology derives from a characteristic (such as hypersusceptibility to irritants or atopy), which directly contributes to MCS syndrome, a medical disorder.	Longstanding; precede exposure and MCS syndrome onset	Correlate of factor predisposing MCS syndrome
3. Unexplained medical symptoms and malaise, comprising preclinical manifestations of MCS syndrome, are misinterpreted as a pre-existing emotional disorder.	Longstanding; follow exposure, precede MCS syndrome onset	Correlate of MCS syndrome onset
4. Psychiatric features derive from episodic medical responses to incitants.	Longstanding, episodic; follow both exposure and MCS syndrome onset	Consequence of MCS syndrome
5. Psychiatric features are a result of an illness-inducing exposure(s) and/or a chronic, debilitating, stigmatizing, medical condition.	Transient or longlasting; follow exposure or follow exposure and MCS syndrome onset	Consequence of exposure or MCS syndrome
6. Stress associated with a chemical exposure precipitates an emotional disorder, MCS syndrome.	Longstanding; follow exposure, contemporaneous with MCS syndrome onset	Consequence of stress attending chemical exposure

sure and/or a chronic, confusing, debilitating, isolating, and stigmatizing medical disorder. Hypothesis 6 stipulates that MCS syndrome is an emotional disorder (e.g., a maladaptive conditioned response or an atypical variant of post-traumatic stress disorder) that is precipitated often by the stress associated with certain types of environmental exposures; a psychiatric history is not required.

Hypotheses 1 and 6 assume that MCS syndrome is an emotional disorder, precipitated by stress or exposure, in a patient with or without predisposing psychopathology. Hypotheses 2 through 5 assume MCS is a medical condition; the psychiatric characteristics are conceptualized as correlates or sequelae of that medical condition. These hypotheses are not necessarily mutually exclusive. For example, MCS syndrome could be a grouping of unrelated conditions with varied origins or a medical condition that presents with neuropsychiatric characteristics due to incitant-induced CNS symptoms and psychosocial consequences of developing a chronic, confusing, debilitating, isolating, and stigmatizing medical disorder.

Popularity of psychogenic explanations and emotional disorder concepts. Studies conducted to date on psychiatric features of MCS syndrome cannot differentiate between the six hypotheses described in the preceding section, yet variations on Hypotheses 1 and 6 are very popular in the medical community. In the absence of supportive evidence, why is it widely assumed that MCS syndrome is an emotional disorder of psychogenic origin? We believe that there are four interrelated reasons why a scantily researched condition of unknown etiology appears to the medical community to be a psychogenic emotional disorder.

1. Information about how common depression, anxiety, and distress are well-documented chronic medical conditions is not widely appreciated. Chronic medical conditions are commonly attended by psychiatric sequelae such as depression, anxiety, fatigue, and distress.[38-43] The link is so strong that psychological and psychiatric test and interview data alone may not differentiate between psychiatric patients and medical patients with well-documented biogenic disorders.[34-36] This link between medical conditions and psychiatric sequelae deserves to be better known.

2. The mere presence of distress, neuropsychiatric symptoms (depression, anxiety, tension, etc.), or psychiatric diagnoses is often misinterpreted as demonstrating that presenting symptoms derive from an emotional disorder of psychogenic origin. According to consensus within the American Psychiatric Association,[43] psychiatric diagnoses are descriptive entities that subsume signs and symptoms without explaining them. In other words, psychiatric symptoms and diagnoses are "nonspecific" in terms of etiology; these phenomena may have diverse causes.[41,44,45] Consider as an illustration what is commonly called "depression": a constellation of negative affects (such as hopelessness, fatigue), negative cognitions (such as pessimism), passivity, and anhedonia. Depression may arise because of a psychological loss, trauma, conflict, or another type of psychosocial stress. In addition, depression may arise in the absence of psychosocial stress because of a structural brain lesion (e.g., stroke, brain tumor); metabolic or endocrine dysfunction (e.g., hypothyroidism, hypoadrenocorticalism, B12 deficiency); medication (e.g., steroids, sedatives, estrogens, analgesics, antihypertensives); or toxic exposure (e.g., lead, organic solvents). Physicians need to understand that neither tests nor clinicians can distinguish origin when presented with a symptom complex alone.

3. The limitations of the psychometric data derived from psychiatric/psychologic tests are not well known. There appear to be misconceptions within the medical

community about the meaning of psychometric data. Psychometric data are not comparable to findings from a medical laboratory. Although some psychological and psychiatric tests and interviews may be scored reliably and are considered "objective" for that reason, scores on these self-report instruments depend ultimately on patient candor and accuracy. Furthermore, interpreting psychometric scores is based on comparing the test taker to a normative sample, composed, typically, of medically healthy people living in the community. Although endorsement of medical items—"Do you often have headaches?" "Are you fatigued a lot?"—may be unusual in a well community sample and, hence, may be construed as evidence of emotional problems in that group, endorsement of medical items is neither unusual nor indicative of emotional problems in people whose medical complaints are chronic and central. At most, psychometric data provide information about symptoms, traits, emotions, beliefs, attitudes, memories, judgments, and the like. They were not intended to, and cannot reveal, the origins of those characteristics and conditions (see #2 above).

4. Some physicians assume that medical conditions with psychogenic origins are differentiated from those with biogenic origins by such phenomena as the appearance of "secondary gain," improvement due to suggestion, presentation with multiple system symptoms, and selective focusing on illness. However, these phenomena appear common in illnesses with known biogenic origins. Secondary gain is defined as using symptoms of illness consciously or unconsciously for extraneous benefits (e.g., avoiding noxious activities; gaining support that would otherwise be denied). There is no evidence that trying to benefit from an illness is unique to psychologically unhealthy individuals. Instead, it is widely believed that psychologically healthy people make the best of circumstances and emphasize the positives in negative situations.[46–49] Moreover, because the sick role (e.g., staying home from work, staying in bed) is a legitimate and, in some cases, beneficial role for many symptomatic conditions—regardless of symptom origin—it is usually difficult to know whether acts construed as secondary gain are really motivated by any benefits beyond trying to feel better. In addition, assessments of secondary gain are prone to bias and uncertainty because the construct cannot be measured objectively and because specialists' judgments tend to be based on informal cross-sectional observations and inferences—without information about patients' health and mental health histories and habitual coping strategies.

Conditions that are helped by suggestion or support, at least in the short term, are sometimes presumed to be largely psychogenic. But suggestion and support can be very helpful to people with biogenic conditions. Approximately 35 of every 100 people receiving placebos report experiencing relief,[50] which can be profound in some cases.[51] Beyond the psychological benefits that many bonafide medical patients say they receive from support groups and other types of counseling, credible research has documented authentic medical benefits—in one case, increased survival in breast cancer patients given group therapy.[52]

The reporting of multiple organ symptoms in the absence of obvious pathophysiologic signs or positive findings on standard laboratory tests is not evidence of psychogenic causation. Disorders based on endocrine, metabolic, nervous, and immune systems often result in multiple organ system complaints that are difficult to diagnose (e.g., multiple sclerosis, systemic mastocytosis, Lyme disease). Likewise, health complaints attributable to chemical exposures (e.g., lead poisoning, mercury poisoning, solvent encephalopathy, etc.) are frequently missed because they span multiple organ systems and require specialized tests that are not performed routinely. The presence of multisystem complaints, coupled with the absence of positive findings on routine medical tests, does not constitute evidence for psychogenic causation in the case of a condition that has not been studied rigorously.

Persons seeking help for a condition perceived as medical often focus on symptoms and ill health. "Obsessive" reporting of "substantiating" evidence is what might be expected from patients trying to convince skeptical potential caregivers of the reality of their distress. Psychopathology explanations for preoccupation with illness in MCS syndrome[25] assume that patients are not medically ill, an assumption that has not yet been tested adequately.

Origins of psychiatric features in MCS syndrome. If understanding is to be advanced about the origins of the psychiatric features observed in MCS syndrome, or in any other condition of unknown etiology, studies must be designed to differentiate between competing hypotheses about those psychiatric features. Studies addressing the following questions could help distinguish between competing hypotheses:

1. What is the nature of the psychiatric manifestations observed? Are psychiatric manifestations best explained as transient neurologic or physiologic responses to specific incitants, distress, or adjustment difficulties? These are all plausible sequelae of chronic illnesses and, as such, are consistent with a biogenic hypothesis. Or, are the psychiatric manifestations better characterized as persistant, pervasive psychopathologic traits, as is consistent with an emotional disorder hypothesis?
2. When did the psychiatric manifestations first appear? Finding evidence of psychopathology predating an initial "sensitizing" exposure and early manifestations of illness is consistent with psychogenic causation but does not rule out biogenic causation (e.g., Hypothesis 2, Table 4).
3. Are "sensitizing" exposures invariably stressful? How have affected individuals coped with stress prior to the present illness? Stressful sensitizing exposures and histories of maladaptive coping with stress (especially by somatization and other psychiatric disorders) are both consistent with a psychogenic hypothesis and emotional disorder concept of MCS syndrome.
4. Are psychiatric traits characteristic of the entire MCS syndrome population throughout the entire course of the condition? It is important for investiga-

tors of emotional disorder hypotheses of MCS syndrome to establish that psychiatric traits are not associated transiently with MCS syndrome, for example, only at its earliest stage, only at its most symptomatic stage, or only during responses to incitants. It is also important to show that psychiatric traits are characteristic of affected people who do not seek medical help as well as those who do and of affected males as well as affected females.

5. Can psychosocial interventions cure MCS syndrome? The finding that psychosocial treatments cure and do not simply help MCS syndrome patients is consistent with psychogenic causation. The finding that psychosocial treatments merely help MCS syndrome patients cope more competently is as consistent with a biogenic hypothesis as with a psychogenic hypothesis, as described previously.
6. Have biogenic explanations proven to be inadequate in explaining the symptoms of MCS syndrome? It is important to test plausible biogenic explanations fairly and rigorously; to date, no such studies have been reported.

No one disputes the idea that a great deal of suffering accompanies MCS syndrome—whatever its origin. Science and ethics require that future studies of the psychiatric profile of affected individuals be designed to differentiate between competing hypotheses about the origins of the condition. Ultimately, prevention and treatment depend on such studies.

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