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Multiple Chemical Sensitivity Syndrome (MCS) – suggestions for an extension of the US MCS-case definition

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Abstract

Purpose: To validate and extend the US case definition for the Multiple Chemical Sensitivity Syndrome (MCS) from 1999 by a systematic literature-review.

Data source: MEDLINE-research from 1997 to August 2003, research in the Cochrane-Library in August 2003, earlier reviews since 1997.

Study selection: Headings and abstracts were screened by one reviewer. All references dealing with multiple chemical sensitivities (MCS) which covered topics of interest such as symptom-profiles, differential diagnostic procedures, etc. were included in the analysis.

Data extraction and synthesis: Topic-specific data extraction and synthesis was done by one reviewer. Data interpretation was discussed by all other authors.

Results: Out of 1429 references 36 publications proved to be suitable for the review . The results can be summarized as follows: exposure-related symptoms associated with self-reported multiple chemical sensitivities can be divided into non-specific complaints of the central nervous system – CNS (main characteristics) and functional disturbances in other organ systems (optional complaints). There is a significant overlap of MCS, CFS and fibromyalgie. At present no standards for a diagnostic procedure based on the criteria outlined above are existing

Conclusions: MCS should only be diagnosed in patients who are mainly suffering from exposure-related non-specific complaints of the Central nervous system. The suggested diagnostic procedure follows the guidelines for CFS which are extended by diagnostic clarification of functional disturbances in other organ systems.

Keywords: Multiple chemical sensitivity; Multiple chemical sensitivities; Multiple chemical sensitivity syndrome – MCS; Idiopathic environmental illness – IEI

Introduction

In recent years greater attention has been devoted to the phenomenon of self-reported multiple chemical sensitivities in Germany (Eis et al., 1997). First described

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by Randolph in 1954 and later by Rea et al. in 1978, it was not before 1987 until an attempt was made by Cullen (1987) as well as Levin and Byers (1987) to define a so-called "Multiple Chemical Sensitivity Syndrome" (MCS). At present, at least 9 case definitions for MCS are existing (Kreutzer, 2000). The most profound and well-known case definition was developed in the United States in 1999 (MCS consensus conference, 1999). As in the case definition of Nethercott et al. (1993), the US-proposal showed a high discriminant validity as determined by the Toronto's Health Survey self-administered questionnaire (McKeown-Eyssen et al., 2001). The combined criteria of the consensus-conference definition take into account self-reported, exposure-related circumstances that patients experience as multiple chemical sensitivities. These experiences of exposition to anticipated noxious stimuli cannot easily be objectivied by chamber challenges (Lenzoff and Binkley, 2000). This may be one of the reasons why a closer differentiation of the symptom-profile in MCS has not been offered yet. The resultant heterogeneity and vagueness of symptoms, which are considered of diagnostic relevance for MCS gives ground for casting justifiable doubt on the assumption that MCS is at all a nosological entity with a specific underlying etiology and pathogenesis. The lack of agreement concerning an empirically validated symptom profile which is characteristic of MCS also prevents a definition of comprehensive diagnostic procedures which is a set back for clinical practice as well as for scientific investigation (Executive Committee of the AAAI, 1986; American College of Physicians, 1989; Council on Scientific Affairs - AMA, 1992; Gots, 1993; Terr, 1993; AAAAI Board of Directors, 1999; Altenkirch, 2000; Labarge and McCaffrey, 2000; Staudenmayer, 2001; Bolt and Kiesswetter, 2002; Schafer, 2002; Winder, 2002).

In the present paper we have tried to validate the US MCS-case definition on the basis of a systematic literature-review and to derive standards for a differential diagnostic procedure.

Method

Data sources and search strategy

Search was done in PubMed (from 1/1997 to 8/2003) and the Cochrane Library (date of search: 8th August 2003). It was performed by using medical subject headings ("multiple chemical sensitivity") and free-text citation ("multiple chemical sensitivity", "multiple chemical sensitivities", "multiple chemical sensitivity syndrome", "MCS", "idiopathic environmental intolerance", "IEI"). Search in The Cochrane Library covered additional free-text citations ("chemical sensitivity", "chemical sensitivities", "chemical intolerance"). One MCS-report from 1999 (which covered a search in EMBASE, MEDLINE, PASC, Science Citation Index, Toxline, and Biosis Previews in 1997), three other MCS-reviews from 2000, 1999 and 1998 (which covered a MEDLINE and hand search in 1997), their references, a standard reference of the CFS-case definition as proposed by Fukuda et al. (1994) and additional hand search were also included (Lacour et al., 1998; MCS consensus conference, 1999; Bartenstein et al., 1999; Health Council of the Netherlands Gezondheidsraad, 1999; Labarge and McCaffrey, 2000; Maschewsky and Oppl, 2000; Miller and Prihoda, 2000).

Data selection

Headings and abstracts of all search results were screened by one reviewer.

References which covered the following topics:

1. Symptom-profiles and clinical picture (including also the overlap with other functional syndromes like Chronic Fatigue Syndrome (CFS) and primary fibromyalgia (FM), course of the disease, quality of life functional impairment and
2. Diagnostic procedures were included in the analysis.

Epidemiological studies were only taken into account if symptom-profiles of MCS were reported. There were no restrictions concerning quality standards and publication type. The search was generally limited to English and German language-publications (marked with square brackets in the references).

Data extraction

Studies and reviews were evaluated on the basis of the original literature by one reviewer. Involved organ-systems, symptom-profiles, symptom-severity, and circumstances of symptom-development (exposure-related, recurrent, chronic, not specified) were surveyed in tabular form. An estimation of the frequencies of the leading symptoms was made by adding the frequencies of single investigations that give detailed information. Furthermore, special attention was paid to information dealing with self-reported odor-hypersensitivity (or hyposmia), course of disease, quality of life, functional impairment and differential diagnostic procedures. These are summarized in free style.

Data interpretation

Data interpretation was undertaken by one reviewer and discussed with all authors. In reviewing the literature three questions were evaluated:

1. Which of the exposure-related symptoms should be considered as mandatory for the diagnosis of MCS?

2. Which of the exposure-related symptoms should be considered as optional?
3. Which general characteristics such as the duration of symptoms, the functional impairment etc. should be taken into account in diagnosing MCS?

The differential diagnostic procedures were discussed under the following aspects:

1. Which diagnostic procedures are necessary and appropriate in order to detect and clarify the mandatory and optional symptoms of MCS?
2. How can MCS be differentiated from other related functional syndromes such as CFS and FM?

Results

In total 1429 references were screened.
As the search-strategy was sensitive but not specific for MCS and selection-criteria were complex, the reasons for excluding literature cannot be presented in detail here. The excluded literature covered topics like age and sex distribution, epidemiology, etiology, pathogenesis, psychiatric disturbances, and therapy. Some references did not deal with MCS as a potentially environment-associated syndrome. Duplicates, PubMed-citations without abstracts, and citations which were not available were also excluded. Of the remaining references seven studies were not included because no symptom-profiles were presented or the case-definition was insufficient (e.g., not restricted to *multiple* chemical sensitivities, Fiedler et al., 1996; Donnay and Ziem, 1999; Janson et al., 2000; Ciccone and Natelson, 2003). The same applied to other studies, which investigated MCS or Chemical Sensitivity in Gulf War Veterans (Black et al., 2000a). Studies which reported symptom-profiles without detailed information of the symptom frequency or which did not survey the complete spectrum of complaints (e.g. restriction to CFS-symptoms) were only excluded from the analysis of global symptoms frequencies (Buchwald and Garrity, 1994; Lax and Henneberger, 1995; Miller and Mitzel, 1995; Ziem and McTamney, 1997; Black et al., 2000a; McKeown-Eyssen et al., 2000; Miller and Prihoda, 2000).

Thus, 36 publications proved to be suitable for the review: 31 articles, which contributed to the US MCS-case definition, 10 publications with of symptom profiles (Table 1), 3 publications that estimated global symptom frequencies (Fig. 1) and 13 papers dealing with standards for differential diagnostic procedures.

Symptom-profile and clinical picture

Although not generally consistent, non-specific complaints of the central nervous system (CNS), especially headaches, fatigue and cognitive deficits, were the symptoms most frequently described in patients suffering from multiple chemical sensitivities in studies (Table 1) and reviews (Ross, 1992; Thomas, 1996; Levy, 1997; Lacour et al., 1998; Bolla, 2000; Labarge and McCaffrey, 2000; Hall, 2002). Furthermore, non-specific CNS-symptoms are the leading complaints showing exposure-related circumstances, highest severity-rates and highest symptoms total agreement, as shown in a reproducibility study (Miller and Mitzel, 1995; McKeown-Eyssen et al., 2000; Miller and Prihoda, 2000). An overview on the prevalence of symptoms in MCS is shown in Fig. 1 (Black et al., 1990; Lohmann et al., 1996; Maschewsky and Oppl, 2000). Other common symptoms of MCS which are not ranked in Fig. 1 and which are also clinically relevant are self-reported odor hypersensitivity, allergic diathesis, and self-reported food or alcohol intolerance (Bell et al., 1995, 1996; Levy, 1997; Ross, 1997; Lacour et al., 1998; Ross et al., 1999a; Dalton et al., 2000; Maschewsky and Oppl, 2000).

There is a significant overlap of symptoms between MCS, CFS and primary fibromyalgia (Buchwald and Garrity, 1994; Slotkoff et al., 1997; Donnay and Ziem, 1999; Janson et al., 2000; Aaron and Buchwald, 2001, 2003; Ciccone and Natelson, 2003). The overlap of symptoms (especially with CFS) may amount to as much as 90%. Therefore many authors consider MCS as a chronic condition in which symptoms show only a slight or no tendency to spontaneous resolution (Council on Scientific Affairs - AMA, 1992; Levin and Byers, 1987; Fiedler et al., 1996; MCS consensus conference, 1999; Black et al., 2000b). As in CFS, MCS-patients experience a significant loss in lifestyle and functional impairment (Davidoff and Keyl, 1996; Black et al., 1999, 2000b; Janson et al., 2000). Although this is not specific for MCS it should also be taken into account as a criterion for diagnosis.

Based on these reports we suggest to extend the diagnostic criteria of the US-consensus conference by defining CNS-related symptoms as obligatory for the diagnosis of MCS. In addition functional symptoms in at least one further organ system should occur and the syndrome should last more than six months and be associated with significant life-style or functional impairment. Table 2 gives an overview how these criteria compare with the 1999-US-MCS-case definition.

Diagnostic procedure

The diagnostic procedure to establish a MCS-diagnosis had not been the focus of the MCS consensus-conference in 1999. To our knowledge it had neither been an explicit issue of any other recent investigation. A first attempt to establish standards of

Table 1. Overview of the original literature of symptom-profiles in patients with self-reported multiple chemical sensitivities/MCS

Literature	Study-type	Cases	Main symptoms	Main controls	Main symptoms
Black et al. (1990)	Clinical cross-sectional study	Diagnosis of EI by clinical ecologist ($n = 26$)	Respiratory (58%), neurologic (including headaches) (38%), fatigue/weakness (35%)	Normal subjects ($n = 33$)	n.d.
Black et al. (2000b)	Clinical follow-up study	MCS-diagnosis by clinical ecologist ($n = 18$)	Headaches (61%), gastrointestinal (44%), dermatologic (44%), pain (44%)	None	
Buchwald and Garrity (1994)	Clinical cross-sectional study	MCS-diagnosis by allergist/clinical ecologist ($n = 30$)	Fatigue (90%), muscle weakness (67%), headaches (63%), myalgias (63%)	CFS-diagnosis ($n = 30$)	Fatigue (100%), muscle weakness (67%), headaches (83%), myalgias (77%)
Lax and Henneberger (1995)	Clinical cross-sectional and follow-up study	MCS-diagnosis according to modified Cullen-criteria ($n = 35$)	Symptoms of nervous system (majority)	Non-MCS ($n = 557$)	n.d.
Lohmann et al. (1996)	Retrospective clinical evaluation	MCS-diagnosis by clinical ecologist ($n = 136$)	Headaches (83.8%), vertigo (83.1%), sensation of coldness of extremities (75%)	Diagnosis of neurotoxic disorders by neurologist	Headaches (76.6%), vertigo (57.1%), coldness of extremities (64.1%)
McKeown-Eyssen et al. (2000)	Cross-sectional and follow-up study by questionnaire	sr-MCS ($n = 134$)	Exposure-dependent CNS-symptoms (majority)	Follow-up of sr-MCS ($n = 134$)	Agreement (76.1%)
Miller and Mitzel (1995)	Cross-sectional study by questionnaire	sr-MCS attributed to pesticide exposures ($n = 37$)	Cognitive symptoms (highest severity)	sr-MCS attributed to remodeling of buildings ($n = 75$)	Cognitive symptoms (highest severity)
Miller and Prihoda (2000)	Cross-sectional study by questionnaire	sr-MCS with reported exposures ($n = 96$)	Cognitive symptoms (highest severity)	Female conference-members and others	Cognitive symptoms (less severity, $p = 0.0001$)
Maschewsky and Oppl (2000)	Cross-sectional study by questionnaire	sr-MCS ($n = 613$)	Fatigue (82%), cognitive deficits (77%), headaches (76%)	None	
Ziem and McTamney (1997)	Cross-sectional study by questionnaire	sr-MCS ($n = 91$)	Fatigue, confusion, memory problems (60–70% daily or several days/week)	None	

EI, environmental illness; MCS, multiple chemical sensitivity syndrome; CFS, chronic fatigue syndrome; sr-MCS, self-reported multiple chemical sensitivities; CNS, central nervous system.

the diagnostic procedure in MCS was made in 1998: the recommendations which were then given mainly defined procedures in agreement with the CFS-standards as described by Fukuda et al. (1994). In addition to an evaluation of the leading symptom they focused on the diagnostic clarification of additional functional symptoms and on the psychiatric evaluation according to DSM-IV (Fukuda et al., 1994; Lacour et al., 1998; Simon, 1998). It is noteworthy that only the need for a psychiatric evaluation is based on empirical evidence, because a high prevalence rate of psychiatric morbidity and psychiatric symptoms such as panic-response in association with provocation challenges, personality disorders, family psychiatric disorders, negative paternal relationship and a poor "home environment", physical and sexual abuse, and other early life stress in MCS-patients was reported in a great number of studies providing substantial evidence for the necessity of a psychiatric assessment in MCS (Black, 2000). In contrast the recommendations of other diagnostic procedures are based rather on clinical experience than on a systematic analysis of the literature (Lacour et al., 1998; Sparks, 2000). Given this lack of empirical evidence, the following steps of the diagnostic procedure of MCS are based on clinical considerations:

Clarification of the CNS-symptoms (mandatory diagnostic criterion)

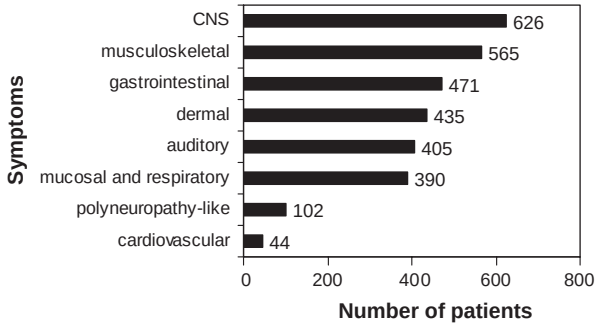

Fig. 1. Self-reported complaints of 777 MCS-patients.

The relevant diagnostic procedures pertinent to neurological symptoms are described in detail in the CFS-standards (Fukuda et al., 1994). Some of the differential diagnoses, which have to be ruled out, are listed in Table 3.

Clarification of additional functional symptoms (optional diagnostic criterion)

Procedures that are recommended for diagnostic clarification of additional functional symptoms are listed in Table 4 (an overview on diagnoses which might be comorbid is given in Table 5). Due to the heterogeneity of symptoms in MCS, Table 4 hardly can be considered as complete. As stated above the recommendations given are based only on clinical experience. They are not drawn from empirical investigation or from the review of the literature.

Discussion

Extension of the 1999 US MCS-case definition

The literature review revealed that in MCS exposure-related unspecific symptoms of the CNS are a predominant feature (see Table 1 and Fig. 1). Therefore the existence of CNS-symptoms should be regarded as an obligatory diagnostic criterion for the diagnosis of MCS. In addition, only those conditions should yield a diagnosis of MCS in which a significant loss in life-style and in functional impairment leading to a chronic state of the disease has occurred (Council on Scientific Affairs - AMA, 1992; Levin and Byers, 1987; Davidoff and Keyl, 1996; Fiedler and Kipen, 1997; Black et al., 1999; MCS consensus conference, 1999; Black et al., 2000b; Janson et al., 2000). While the case definition of the US MCS-conference has provided a still useful and valid basis of diagnostic criteria for MCS the results of the present review suggest to specify these criteria as follows (Table 2): the predominant complaint in MCS involves a symptom of the CNS in association with

Table 2. Proposals for a further extension of the US MCS-case definition from 1999

US MCS-case definition MCS is:	Proposals
(1) A chronic condition	Of at least 6 months, that causes significant life-style or functional impairments
(2) With symptoms that recur reproducibly	In the CNS in association with self-reported odor hypersensitivity
(3) In multiple organ systems	Obligatory in the CNS and at least one symptom of another organ system (see Fig. 1)
(4) In response to low levels of exposure	
(5) To multiple unrelated chemicals and which	
(6) Improve or are resolved when incitants are removed	

CNS, central nervous system.

Table 3. Examples of diseases or disorders that may overlap with MCS-defining symptoms

1. *Lifetime or at present point in time*:
Psychosomatic medicine/psychiatry:
Any type of schizophrenia, schizophreniform disorder, schizoaffective disorder, paranoia or other mental illness in the psychotic realm of illness
Major depression with psychotic, catatonic or melancholic components or any bipolar disorder
Anorexia nervosa or bulimia
Delirium, dementia or amnestic disorder
2. *Two years before onset of illness or at any time thereafter*
Drug-abuse or drug-dependence
3. *Manifest, inadequately treated or incompletely cured Neurology*
Cerebrovascular diseases
Degenerative diseases of the CNS or dementia
Inflammatory diseases of the CNS
Pneumology
Sleep-apnea syndrome
Narcolepsy
Chronic disease of the bronchial system analogous to NYHA class II or above an attack frequency of >1x/day
Chronic lung disease analogous to NYHA class II
Cardiology
Chronic disease of the coronary vessels
Coronary insufficiency from NYHA stage – II
Arterial hypertonia for which medication does not provide a satisfactory treatment
Insulin-dependent diabetes mellitus
Obesity (body mass-index ≥ 30)
Gastroenterology
Chronic hepatopathy
Chronic inflammatory bowel disease
Nephrology
Chronic kidney disease: creatinine >1.5 mg/dl
Endocrinology and metabolic disturbances
Hypothyroidism and hyperthyroidism
Adrenal insufficiency
Pituitary insufficiency
Cushing's syndrome
Porphyrias
Hematology/Oncology
Anemia
Oncological disease
Rheumatology/Immunology
Collagen vascular diseases
Primary systemic vasculitides
Other immunopathies
Infectious diseases
Chronic hepatitis C (or B) virus infection
HIV-infection
Lues
Chronic Borrelia infection
Toxoplasmosis
TBC
Other chronic infections
4. *Present point in time*
Other conditions
Intake of sedating medication and psychopharmacologic drugs (benzodiazepine, barbiturates, anti-depressants with sedating components, neuroleptic drugs)

Table 4. Standardized diagnostics on the facultative, chemical exposure related symptoms of MCS to exclude relevant organic disease

Standardized diagnostic procedure encompasses the general case history, physical examination, and laboratory tests as proposed by Fukuda et al. (1994). Certain complaints need special investigations

Complaints	Case history: ascertain	Physical examination: carry out	Laboratory tests: complete by
Multiple arthralgias, soft-tissue rheumatic disorders or other rheumatic complaints	Assessment according to American College of Rheumatology (ACR) criteria, check-list for specific symptoms of systemic rheumatic diseases	Rheumatologic, neurologic and angiologic examination status	If necessary: rheumatologic, neurologic and angiologic examination by a specialist
Stool irregularities or other abdominal complaints	Food intolerance	Palpation and auscultation of the abdomen, rectal examination	3 x test for occult blood, α-amylase, lipase, IgE
Erythema, urticarial changes, (facial) swelling or other skin eruptions	Contact allergies[a], common allergens[b], environmental allergens[c], irritants[d]	Inspection of the oral cavity, the skin[e], the nails and check for dermographism	IgE if necessary: C1-esterase inhibitor concentration and function, dermatologic or allergologic examination by a specialist
Auditory complaints	Hypacusia, otitis media, tinnitus, Mennière's syndrome	Inspection of the ear, the external auditory, the tympanic membrane, Weber's- and Rinne's-hearing test, examination of the vestibular system	If necessary: ENT-examination
Mucosal irritation or other respiratory complaints	Common allergens[b], environmental allergens[c], irritants[d]	Inspection of the oro-pharyngeal mucosa, auscultation of the lung	IgE
Dysesthesia, muscle weakness or other complaints of the extremities	Anxiety-related situations and hyperventilation	Sensitivity testing, percussion of the retinaculum of the wrist, test for muscle strength, reflex status, pathological reflexes	If necessary: neurological and electrophysiological examination by a specialist
Cardiac arrhythmia, palpations or other cardiac complaints	Anxiety-related situations	Pulse check, auscultation of the heart	If necessary: ECG, 24-h ECG, exercise ECG, echocardiography
Pain and other disturbances of the urogenital tract	Infections, cycle-associated complaints, kidney stones, appendicitis	Suprapubic and hypogastric tenderness, rebound tenderness, guarding, renal beds sensitivity, rectal examination	If necessary: microbiologic examination of the urine, sonography of the kidneys and lower abdomen, plain abdominal radiography, urological and gynecological examination by a specialist

[a]E.g. nickel, pyrethroids.
[b]House dust mites, pollen.
[c]Molds, isozyanates, formaldehyde, 3-carenes, methyl benzoate, dimethyl maloate, foodstuffs.
[d]Solvents, aldehydes, ketones, pyrethroids.
[e]Face, hairline, scalp, wrists, popliteal cavities, extensor side of the extremities, rima ani.

self-reported odor hypersensitivity. The symptoms are lasting for at least 6 months and are associated with significant functional impairment and change in life-style. In addition at least one further functional symptom in another organ system has occurred. As none of the available studies (see Table 1) differentiates between exposure-related and non-exposure-related complaints in detail (the latter may have resulted from

Table 5. Examples of diseases that do not rule out a diagnosis of MCS
If one of these diseases or functional disturbances is detected, the symptoms should not be attributed to self-reported MCS

CNS-symptoms as a result of:	Disorders of the cervical spine
	Sinusitis
	Orthostatic collaps
Locomotor system:	Arthrotic conditions
Gastrointestinal tract:	Chronic gastritis
	Intolerance to foodstuffs without additives
	Lactose intolerance
	Gluten sensitive enteropathy
	Mild pancreas insufficiency without evidence of florid pancreatitis or alcohol abuse
	Status following surgery of the gastrointestinal tract for non-malignant disease which may lead to mild stool irregularities but without evidence of dumping syndrome
Skin:	Mild dermatologic diseases without requiring therapy which has systemic effect and where there is no underlying systemic disease
Auditory system:	Tinnitus
	Hypacusis
	Otitis media
Mucosa/respiratory tract:	Allergic conjunctivitis
	Allergic rhinitis
	Mild bronchial asthma (asthmatic symptoms maximally 1 x /day)
	Sicca symptoms without evidence of rheumatologic systemic disease or untreated hyperthyroidism
Symptoms of the peripherous nervous system:	Hyperventilation syndrome
	Carpal tunnel syndrome without evidence of other severe underlying cause such as insulin-dependent diabetes mellitus or rheumatological systemic disease
	Mild idiopathic polyneuropathy
Cardiovascular system:	Mitral valve prolapse
	Paroxysmal supraventricular tachycardia
	Ventricular arrhythmia up to Lown IV b without evidence of other underlying cardiac diseases
Urogenital tract and systemic complaints:	Premenstrual syndrome
	Menopausal complaints
	Known kidney stones

CNS, central nervous system.

other disorders), a complete and precise description of all potentially obligatory, exposure-related CNS-symptoms is not possible at present. According to our clinical experience we regard headache (or pressure in the head and light-headedness, but not fatigue) as the most common, exposure-related complaint, but this needs to be verified in further studies. Furthermore, in the literature a wide range of other symptoms is described (see Fig. 1; MCS consensus conference, 1999). Therefore, we suggest that exposure-related symptoms, which are associated with self-reported MCS, should be divided into a hierarchy of criteria: symptoms of the CNS, which we consider as main characteristics or mandatory criteria and non-CNS symptoms, which we consider as optional criteria.

Advantage of the extended US MCS-case definition

By weighing symptom-frequencies and by focusing on the main characteristics of unspecific CNS-symptoms two of the four problems that according to the US consensus conference from 1999 are biasing the MCS-diagnosis can be alleviated: (1) the confusing heterogeneity of symptoms is eliminated and (2) this makes it easier to develop standards for differential diagnostic procedures.

Remaining problems

Unfortunately there are still some problems left: (1) the MCS-diagnosis is largely based on the patients' self-report and (2) the overlap of symptoms between MCS, CFS and FM provides a substantial diagnostic challenge (Buchwald and Garrity, 1994; Donnay and Ziem, 1999; Janson et al., 2000; Aaron and Buchwald, 2001, 2003; Schafer, 2002; Ciccone and Natelson, 2003). Thus, according to our opinion, syndromes which strongly overlap with MCS should exclude an MCS diagnosis. This applies in particular to CFS and to FM, if these conditions precede the symptoms of MCS. If CFS or

FM develop in the course of MCS they should be treated as co-morbidity and do not exclude a diagnosis of MCS.

Differential diagnostic procedure

The diagnostic procedure first should exclude diseases that might account for non-specific symptoms of the CNS, as described in the CFS-clarification standards by Fukuda et al. in (1994). In some cases a neurological examination should be carried out by a specialist, and EEG, or imaging procedure of the CNS (MRI or CT) for the exclusion of an epilepsy, a space-occupying lesion, degenerative, inflammatory or cerebro-vascular disease should be made. In contrast quantitative EEG, brain electrical activity mapping (BEAM), evoked potentials, functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT), which measure regional blood flow or brain metabolic function, seem insufficiently validated to solve the diagnostic problems addressed and should rather be reserved for scientific investigation (Simon et al., 1994; Bartenstein et al., 1999; Ross et al., 1999b; Sparks, 2000; Waxmann, 2000).

The second diagnostic step is to clarify the facultative (non CNS-associated) exposure-related (functional) symptoms of other organ systems. At present recommendations as shown in Table 4 are based only on clinical considerations and experience. In this context it should be kept in mind that some diseases and functional disturbances do not rule out a MCS-diagnosis (see Table 5).

Sometimes an allergologic and medical ear, nose and throat (ENT) examination is desirable in MCS-patients. However, as stated above, proven allergic diathesis (including food intolerance or alcohol intolerance) is not an exclusion criterion for MCS. On the contrary, it is a common co-morbidity in patients with MCS.

Finally there is evidence which supports a thorough psychiatric assessment in MCS. This may be performed either by a semi-structured psychiatric interview (e.g. SKID-interview according to DSM IV) or by clinical psychosomatic/psychiatric evaluation. Any type of psychotic disorder, anorexia nervosa, bulimia, delirium, dementia, amnestic disorder, drug or alcohol abuse or dependence, etc. must be excluded. Regarding the psychological assessment it should be kept in mind that until the etiology and pathogenesis of MCS has been clarified an organic cause of the MCS associated symptoms and symptom complexes cannot be entirely ruled out. Overhasty psychosomatic, i.e. psychiatric diagnoses of somatoform disorder, dissociative disorder, or anxiety disorder should not be made in MCS patients. As in cases of depression, these disorders should be regarded as overlapping MCS, or treated as co-morbidity. Confirmation of such a diagnosis should be carefully investigated in each case individually.

Future research

Further studies investigating the symptom-profiles of MCS-patients are highly desirable. These should be based on an international accepted MCS-case definition, should enclose an appropriate control-group, and should take into consideration exposure related complaints and symptoms' severity.

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