Multiple chemical sensitivities: review

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Purpose of review

There have been a number of recent studies examining behavioural and social factors in the potential cause of Multiple Chemical Sensitivities, or Idiopathic Environmental Intolerance. The current review will draw together recent research and suggest directions for future investigation.

Recent findings

Recent studies have implicated a number of different perspectives which may be helpful in understanding the cause of chemical sensitivities. A multifactorial model incorporating behavioural, physiological and sociological approaches may be useful. Cultural and historical factors, alongside individual expectations and beliefs, as well as maladaptive learning and conditioning processes, may be important in the specific cause of chemical sensitivities. Iatrogenesis, through the promise of unproven 'therapies', may perpetuate reported symptoms further. Although there are many recent experiments implicating potential behavioural or psychological causes for Multiple Chemical Sensitivities, there remains a paucity of treatment trials for this condition.

Summary

Good-quality treatment trials examining psychological/behavioural approaches in the management of Multiple Chemical Sensitivities are urgently needed.

Keywords

functional somatic syndromes, idiopathic environmental intolerance, IEI, MCS, multiple chemical sensitivity

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Abbreviation

MCS Multiple Chemical Sensitivities

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Introduction

Multiple Chemical Sensitivities (MCS) or Idiopathic Environmental Intolerance was first reported in the 1950s to define a syndrome of nonspecific symptoms affecting a wide range of organ systems after low-level exposure to chemicals commonly found in the environment [1]. The condition remains controversial, partly because the suggested causal mechanisms fall outside of traditional immunological or hypersensitivity mechanisms, and partly because of the involvement of a group of people defining themselves as 'clinical ecologists', who claim to have specialist skills in the treatment of the condition, and who have elicited further skepticism from various authoritative bodies [2–4].

Diagnosis and epidemiology

At the heart of controversies surrounding the definition and diagnostic status of MCS is the absence of any specific biological tests to confirm its presence. To date, biological studies have failed to implicate MCS-specific causes (e.g. [5]). For example, a recent study [6] suggested that people with MCS showed a nonsignificant trend towards lymphocyte depletion, but this is also known to occur in major depression, possibly as a result of hypercortisolaemia [7], and widespread immunological differences have also been shown in people with somatization disorders [8]. The controversy over diagnosing MCS is reflected by the number of different diagnostic criteria that have been proposed [9–13].

Table 1 [14–21] summarizes epidemiological studies for MCS conducted in general populations. Prevalence rates vary widely, depending on the criteria used. In one recent population-based survey [15], subjects reporting annoyance from odours also scored higher on the General Health Questionnaire, and lower on the self-reported health questionnaire, indicating associated impaired subjective and mental health well-being [15].

Table 1 does not specifically show prevalence rates of MCS as reported in specific groups of people, such as in military personnel. A recent systematic review [22••], however, confirmed that veterans deployed to the Gulf are approximately three-and-a-half times more likely to report MCS than those not deployed. MCS in combat veterans is associated with psychiatric morbidity [23,24] and low levels of preparedness for combat [24].

Differing prevalence figures for MCS may also be due to the nosological validity of MCS as a culture-bound entity,

Table 1 Epidemiological surveys examining MCS prevalence

Reference	Year/population	Criteria	Total sample	Prevalence	Risk factors
Hausteiner *et al.* [14]	2005/Germany	Self-reported chemical sensitivity or doctor-diagnosed MCS	2032	9% of sample reported sensitivity to odours; 0.5% reported physician-diagnosed MCS	
Carlsson *et al.* [15]	1999–2000/community survey, Scania, Sweden	During the past 14 days, have you experienced annoyance from: breathing air that smells of chemicals or other smells?	13 604	12.5% of sample reported some or much annoyance to chemicals; 16.2% reported some or much annoyance to other smells	Female sex
Caress and Steinemann [16,17]	1999–2000/community survey, Georgia, USA	Ever been diagnosed with MCS? Consider yourself sensitive to everyday chemicals?	1582	12.6% of sample reported sensitivity to chemicals; 3.1% reported previous medical diagnosis of MCS	Female sex
Levallois *et al.* [18]	1998/community survey, California, USA	Ever been diagnosed with MCS? Consider yourself sensitive to everyday chemicals?	2063	24.4% of sample reported sensitivity to chemicals	Female sex
Kreutzer *et al.* [19]	1995/community survey, California, USA	Ever been diagnosed with MCS? Consider yourself sensitive to everyday chemicals?	4046	15.9% of sample reported sensitivity to chemicals; 6.3% reported previous medical diagnosis of MCS	Female sex (for self-report MCS); Hispanic ethnicity (for doctor-diagnosed MCS)
Meggs *et al.* [20]	1993/rural population of North Carolina, USA	Reports of feeling ill after smelling odours	1027	33% reported feeling ill after smelling odours/chemicals	
Bell *et al.* [21]	1993/college psychology students, USA	Self-reported chemical sensitivity or doctor-diagnosed MCS	643	66% reported feeling ill after smelling one or more chemicals	Female sex

dependent on historical and cultural conditions [25,26]. For example, Bornschein and colleagues [27] describe the results of a study conducted in the former German Democratic Republic, where, despite doctors being as familiar with the concept as West German counterparts, and despite presumed environmental exposures being (at best) similar to those in former West Germany, MCS is relatively rare, whereas, in former West Germany, it is diagnosed more frequently [27]. Similar observations have been made for other ill-defined and controversial syndromes [28,29].

Cause of Multiple Chemical Sensitivities

In a recent systematic review [30••] of provocation studies, we reviewed responses of MCS sufferers to controlled provocation challenges involving chemicals. We noted that many studies which have attempted to study this effect in people describing MCS did not blind chemical/odour provocations adequately [30••]. In those studies in which blinding was adequate, people reporting MCS were not better able to discern active compared with sham exposures over chance [30••]. In some of the studies reviewed, people reporting MCS showed severe responses to sham provocations when they believed these to be active chemicals; in the case of one study [31], responses were so severe that the trial had to be stopped.

In one reviewed study [32], painters reporting MCS reported more adverse effects when exposed to coffee fumes (the control exposure) over acetone and volatile organic chemicals (the active exposures); the authors of this study speculated that this was because coffee fumes were interpreted more negatively by painters, who were less accustomed to this odour than to acetone. In another study [33], information was given to study participants prior to chemical challenges regarding the nature of exposures [study participants were told that provocations were either healthy ('natural extracts with relaxing effects'), neutral (odorants 'approved for olfactory research') or toxic (odorants which were 'industrial solvents')]. Being informed that they were to be exposed to the 'harmful' odour had powerful effects in increasing associated somatic symptom reporting and discomfort reporting by participants, particularly by those participants scoring higher on 'odour reactivity' indices [33]. In another experiment, Lorber and colleagues [34••] demonstrated that healthy volunteers who inhaled an inert placebo and were informed that this was a 'suspected environmental toxin' were more likely to report somatic symptoms; this was more likely in women who had observed a female 'confederate' role-playing such symptoms after also inhaling the placebo [34••]. Investigators [35] have also been able to demonstrate the impact of exposure to adverse media warnings prior to controlled exposure with odours as well as CO_2-enriched

air in healthy volunteers. In this experiment, individuals reported more somatic symptoms after exposure to both noxious and pleasant odours, but this only occurred in participants who had also been given prior negative information about the environment and its relationship to MCS [35]. These studies suggest important effects from prior expectations, experiences and observing other people's behavior (modelling) in the pathogenesis of MCS.

In a series of experiments [35–37,38••,39], Omer van den Bergh and colleagues showed that when healthy volunteers were exposed to odours in conjunction with CO_2-enriched air, participants subsequently displayed somatic symptoms, after provocation with the odour only. This effect has been re-created in subjects using hyperventilation (thereby inducing hypocapnia [38••]), implicating an overlap with panic disorder. Learnt symptoms may persist for a week after exposure and, in some cases, generalize to odours not used in initial experiments [39]. This finding has been replicated [40] using healthy volunteers exposed to noxious odours whilst exercising.

A more recent study [41•] has suggested that high levels of preexisting trait neuroticism as well as dissatisfaction with work situations may also be associated with the reporting of chemical sensitivities.

Multiple Chemical Sensitivities, other functional somatic syndromes and other comorbidities

A large amount of evidence suggests that MCS shares a considerable degree of overlap with a number of other conditions, as they are frequently reported in people also reporting Sick Building Syndrome [42], Electrical Sensitivity [18], Chronic Fatigue Syndrome [43] and Gulf War Syndrome [22••,44,45]. All of these conditions share similarities in that conventional biomedicine does not account for their causes. A significant overlap also exists in the diagnostic criteria for these conditions, as well as the common occurrence of nonspecific somatic symptoms. High rates of comorbid somatoform, anxiety and depression have been confirmed in these populations, as well as in people reporting MCS [46–49]. In a study [49] investigating comorbidity, age and sex-matched controls (who were semiconductor industry workers) were compared with people reporting MCS; higher rates of psychiatric comorbidity were found in the MCS group compared with controls, but controls had higher concentrations of metal in their urine compared with the MCS group, suggesting that chemical exposure and psychological symptoms were not causally related. Other studies [50,51] have used psychometric testing, such as the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) scale, on MCS claimants. MCS claimants were not more likely to exaggerate psychological problems, but were more likely to deny them, tending to express distress through somatization, as is seen in other functional somatic syndromes. Psychological factors (e.g. beliefs around causation and toxicity) may influence MCS claimants' motives for litigation [50,51].

The overlap between MCS and other functional somatic syndromes like Chronic Fatigue Syndrome has led Wessely and colleagues [52] to suggest that conditions like MCS are artefacts of medical sub-specialization and that each organ 'system', with its associated cluster of symptoms, is a symptomatic manifestation of similar underlying processes. They suggest that one functional somatic syndrome, accounting for each of these idiosyncratic conditions, may better encapsulate the phenomenon of MCS and other related conditions, although they do not advocate transferring of all of these syndromes to psychiatry, nor dismissing these syndromes as simply 'imaginary' [52]. Some [53,54] disagree with this view, however, arguing that such approaches alienate patients further, who may then feel that they are being dismissed as having 'psychosomatic' complaints. Those who disagree with a general functional somatic syndrome approach also argue that 'lumping' together all functional somatic syndromes may prevent research into specific causes and may impede the development of treatments for individual conditions [53,54].

In addition, two recent studies reported high prevalence rates of delusional disorders comorbid with MCS [55], and high prevalence rates of MCS in people also diagnosed with bipolar affective disorder [56]. The available evidence therefore continues to suggest that psychiatric comorbidity is a frequent occurrence in people with MCS and so should be routinely screened for and, where appropriate, any comorbidity should be treated using usual approaches, although, arguably, MCS is itself a functional somatic syndrome and potential treatment approaches might incorporate this paradigm.

Treatments

A review of the literature shows a paucity of trials examining effective treatment modalities (psychological or otherwise) for MCS, and it is clear that such studies are urgently needed. In addition, those studies which have attempted to examine potential treatments in MCS are frequently of a poor quality. In North America, the issue of 'treatment' is also acutely political [26,57]; for example, people reporting MCS may be refused Worker's Compensation on the grounds that it is psychological [57,58], and there is a widespread feeling amongst those reporting MCS that the medical establishment has misunderstood their needs [57,58].

Clinical ecology

A survey [59] of people reporting MCS in the United States reported that more than 100 types of treatment

were commonly used by people reporting MCS. These included treatments as diverse as nutritional supplements, filters, saunas, special diets, as well as more intrusive procedures, such as amalgam-filling removal, colonic irrigation, gall bladder/liver flushes and the use of over-the-counter/prescription medications such as antibiotics, antifungal medications and acyclovir. The evidence base for most of these therapies is limited; in addition, some therapies have iatrogenic effects [60,61]. Survey responders admitted spending, on average, $51 000 on treatments, of which $7000 was spent in the previous year, averaging 15% of their annual household income, and had spent an average of $57 000 in attempting to make their homes safer [59]. Participants rated chemical avoidance, creating a chemical-free living space and prayer as the three most useful interventions [59].

Psychological treatments

Despite much evidence to suggest that MCS is a functional somatic syndrome with a psychological or behavioural basis, there have been no good-quality large-scale trials examining the efficacy of psychological interventions in the management of MCS and such trials are urgently needed.

Many authors suggest a nonjudgmental approach which establishes rapport at the outset and with a view to reducing longer-term disability as helpful [27]. Some evidence [62–65] suggests that the responses of people with MCS to odour triggers are akin to responses also seen in people who suffer from panic disorder, so approaches which 'extinguish' such responses may be helpful. For example, Van den Bergh and colleagues [66] demonstrated successful 'extinction' of maladaptive responses to odours which had been learnt in the same experiments by healthy volunteers. A number of case reports in the literature confirm that such approaches (occasionally incorporating the use of psychotropic medication such as an antidepressant [67,68]) may be useful in people who report MCS [67–72], although large-scale randomized–controlled studies are still lacking.

Lacour and colleagues [73] reported findings of a non-randomized study of an 'interdisciplinary' approach which used a combination of self-help programmes, acupuncture and psychosomatic/group interventions on eight individuals reporting MCS. They advocated taking into consideration patients' physical explanations of illness, in order to improve engagement with psychological therapies, and reported statistically significant improvements in overall disability scores at the end of eight months' intervention [73]. Previously, Haller [74] described an in-patient approach using psychotherapy in three individuals reporting MCS, with apparent improvements in disability. Staudenmayer [75] advocates psychotherapy-based approaches, but suggests that the challenge in management is in overcoming patient beliefs of a toxic cause to their problems, although other studies [76] examining related syndromes such as Chronic Fatigue suggest that changing a person's causal attribution of symptoms is not necessary to improve quality of life. In an open-label study [77], investigators reported that revisiting medical work-up and excluding organic causes to presentations resulted in a reduction in preconsultation 'diagnoses' in study participants, but also resulted in a reduction in MCS symptoms at follow-up, with some of the study participants seeking psychotherapy in the intervening period. This suggests that there may be some therapeutic benefits in simple psychoeducational approaches coupled with medical investigations designed to reassure patients and exclude other potential organic causes.

If the cause of MCS lies in Pavlovian/learned responses to environmental triggers or cues, moves to ban odours in public spaces [57,78] may be somewhat premature. To a certain extent, such moves confound the issue further by promoting collusion with those reporting MCS at a societal level, inadvertently reinforcing avoidant behaviours. We remain doubtful that such moves would have an effect on reduction in overall prevalence of MCS.

Prognosis

A recent study [79••] examining the longitudinal course of MCS showed that MCS was still present in 92% of study subjects at 1-year follow-up. At baseline, these subjects scored higher on trait negativity as well as higher on somatic symptom attribution compared with non-MCS controls [79••]. People reporting MCS in this study had higher rates of service use and were more functionally impaired than non-MCS controls over the course of the year [79••]. Identifying negative body sensations as pathological and having prominent cognitions of environmental threat were both associated with ongoing MCS caseness at follow-up [79••]. A study [80] which examined the temporal stability of MCS over a 9-year period also confirmed the stability of the diagnosis over time.

Conclusion

MCS should perhaps be conceptualized using a multifactorial model, incorporating physiological, social and psychological factors, as recently proposed by Mayou and colleagues [81]. Physiological processes (e.g. exposure to odours under distressing circumstances) may interact with beliefs, engendered by media reporting, for example, which might reinforce the interpretation of somatic sensations as 'pathological'. A 'syndrome' of somatic symptoms at times associated with panic may develop. Eventually, a protracted course of avoidance may lead to chronic disability, in part perpetuated by the iatrogenesis of unproven therapies which the sufferer may have sought from numerous 'experts' [81]. Highly

comorbid anxiety/depressive illnesses may perpetuate the situation further, amplifying the distressing experience of somatic symptoms, such that a picture of chronicity is finally reinforced [81]. It is not surprising that sufferers seek the support of self-help groups, given the shared experience of developing disability, and a reaffirmation of the experience through an illness label, against the skepticism of the wider medical community [57,58].

Lessons learnt from managing other syndromes (e.g. Chronic Fatigue Syndrome) could be of some use. Physicians may have a dilemma over whether or not to 'give' patients a label or diagnosis [82•], although an alternative focus might be to engender a positive therapeutic alliance in which the patient is encouraged to take an active part in their recovery [82•]. Having established a therapeutic alliance, approaches based on cognitive–behavioural therapy, psychoeducation, group support or psychotherapy might be helpful, although, within the field of MCS, research investigating specific therapies is still needed.

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 294).

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Prospective study of 152 people fulfiling criteria for MCS, of which 140 were followed up 1 year later; 91.8% of participants reporting MCS at baseline met case criteria for MCS 1 year later, confirming that MCS is extremely temporally stable. High proportions of the MCS group were functionally impaired (75.5% reported difficulties shopping in stores or eating in restaurants and 79.6% reported taking special precautions at home) and 22.4% had lost a job or had stopped working at follow-up. Trait-negative affectivity and somatic symptom attribution continued to predict symptom severity in the MCS group at 1 year. Prominent cognitions of environmental threat, as well as the tendency to focus on bodily sensations and interpret these as pathological, were also found to be strongly associated with MCS caseness at 1-year follow-up.

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Narrative review of the literature on Chronic Fatigue Syndrome which, as in the case of MCS, highlights the conflict between medical models of CFS and user-led notions of CFS, in the absence of an established organic cause for the condition. The authors propose that the issue in the management of these patients should not be one of labelling but one of engendering a positive therapeutic encounter in which patients are encouraged to take an active role in their recovery without attributing blame, and are given accurate nonpartial advice around the condition. The authors also suggest that whilst it might be beneficial to the therapeutic alliance to acknowledge the patient's distress, this should be done sensitively without reinforcing sick role beliefs or 'maladaptive illness beliefs'.