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Educational case report

Two of three patients with multiple chemical sensitivity had less symptoms and secondary hyperalgesia after transcranially applied pulsed electromagnetic fields

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HIGHLIGHTS

- Pulsed electromagnetic fields applied transcranially in 3 cases with multiple chemical sensitivity.
- Symptoms and functional impairments improved in 2 of 3 cases.
- Capsaicin-induced secondary hyperalgesia was reduced in 2 of 3 cases.
- Pulsed electromagnetic fields applied transcranially was a feasible treatment modality in all 3 cases with multiple chemical sensitivity.

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ABSTRACT

Background: Multiple chemical sensitivity (MCS) is a chronic, disabling condition characterized by recurrent multisystem symptoms triggered by common airborne chemicals. Evidence points towards abnormal sensory processing in the central nervous system (CNS) as a likely pathophysiological mechanism. No effective treatment has yet been reported, but clinical observations suggest that as pulsed electromagnetic fields (PEMF) is a treatment for some CNS disorders (depression and chronic pain), it may also be a treatment modality for MCS.
Methods: In an open case study, the effects of PEMF were assessed in three MCS patients. All cases received 30 min daily treatment 5 days a week for 8 consecutive weeks. Symptoms and functional impairments related to MCS, depressive symptoms, and capsaicin-induced secondary punctate hyperalgesia were assessed at baseline and weekly until an 18-week follow-up.
Results: Two of the three cases showed considerable improvement on all measures of symptoms and functional impairments related to MCS in response to PEMF therapy. One case showed no improvement and during the treatment period was unexpectedly diagnosed with depression.
Conclusion: Our findings indicate potential benefits of PEMF therapy in MCS.
Implication: The therapeutic effect of PEMF in MCS needs to be investigated by a randomized placebo-controlled trial.

1. Introduction

Multiple chemical sensitivity (MCS) is a chronic condition characterized by recurrent multisystem symptoms triggered by common airborne chemicals, such as fragranced products, new furnishing or smoke from woodburners, at levels below those expected to produce symptoms [1,2,3]. Symptoms from the central nervous system (CNS) such as headache, exhaustion and cognitive deficits are particularly frequent in MCS but symptoms from airways, muscles and joints are also commonly reported [4,5,6].

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Abbreviations: MCS, multiple chemical sensitivity; PEMF, pulsed electromagnetic fields; CNS, central nervous system; QEESI, quick environmental exposure and sensitivity inventory; LIS, life impact scale; OIS, other intolerances scale; CIS, chemical intolerance scale; SSS, symptom severity scale; SDS, Sheehan disability scale; SCL-92, symptom checklist 92.
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The pathophysiology of MCS is unexplained, but many theories have been suggested [7,8]; perhaps the most persistent is that of abnormal and amplified processing of sensory signals in the CNS, i.e., neural sensitization. Neural sensitization is defined as an increased central response to a normal sensory input [9,10]. Several recent scientific findings support this hypothesis. Firstly, brain imaging studies have shown reduced brain activation of odour processing regions during odour provocation in MCS patients compared with healthy controls [11,12]. This has been suggested to reflect a reduced cerebral inhibitory activity, thus resulting in neural sensitization [12]. Secondly, controlled experimental pain studies with capsaicin (the active component in chilli peppers) in MCS patients have demonstrated enlarged areas of capsaicin-induced secondary mechanical hyperalgesia [13,14]. Secondary mechanical hyperalgesia reflects an increased mechanical sensitivity in the skin surrounding the capsaicin injection site and is regarded as a CNS response. In accordance with these findings and observations, a single high-level exposure or chronic low-level chemical exposures as well as life stressors have been reported to precede MCS [15] and may trigger plastic CNS changes resulting in an altered response to chemosensory input [9].

MCS can severely impact patients' lives, often in terms of social and/or occupational disability. Hence, an effective treatment for MCS is urgently needed. However, only few intervention studies on MCS have been published [16,17]. One case study reported a successful treatment outcome using a therapeutic approach combining psychological desensitization and pharmacological treatment with a selective serotonin reuptake inhibitor [18]. Another case study reported a transient but, nevertheless, substantial effect of electroconvulsive therapy (ECT) in cases with MCS [19]. However, ECT is a less attractive treatment as it depends on general anaesthesia and muscle relaxants and may be associated with adverse effects such as transient amnesia. Pulsed electromagnetic fields (PEMF) are a newer technology that utilizes magnetic stimulation to achieve electrical currents in the brain without the disadvantages of ECT. The principle of PEMF is based on alternating magnetic fields, which may activate the underlying neural tissue through activation of intracellular signalling [20]. PEMF has been used for several purposes [21,22,23,24,25,26,27] including neuronal activation [28], enhancing peripheral nerve regeneration [29,30,31,32], and treating depression [33,34] and chronic pain [35,36]. In a previous placebo-controlled study applying PEMF for treatment-resistant depression, the following adverse effects were reported in 1–3 of 25 patients in the active group: increased dream activity, suicidal ideation, tremor, paresthesia, dizziness, constipation, stranguria/voiding problems, increased sweating, helmet felt heavy, flu-like symptoms, lower back pain and stabbing pain in the head [34]. The aims of the present study were to investigate whether PEMF therapy was associated with positive effects on MCS in terms of symptom severity and functional impairments and whether this therapeutic procedure was feasible in MCS patients.

2. Materials and methods

The study was approved by the Danish Data Protection Agency and the Committees on Biomedical Research Ethics of the Capital Region of Denmark. All participants gave signed informed consent and agreed to having their history published.

Cases were recruited from the patient research register at The Danish Research Centre for Chemical Sensitivities. Thirty-seven patients who lived in or near the Copenhagen area were contacted by telephone and invited to participate. Cases were screened by a telephone interview and selected according to the extended consensus criteria for MCS [6] which were applied as follows: (1) symptom duration of at least 6 months, (2) symptoms in response to at least 2 of 11 categories of chemical exposures often associated with MCS, (3) at least one CNS symptom and one symptom from another organ system, (4) a severity score ≥ 5 (on a scale from 0 to 10) on one important area of functioning, i.e., work, social or family life, (5) symptoms occurring when exposed and improving or resolving when triggering exposures are removed and (6) symptoms triggered by exposure levels that do not evoke symptoms in other individuals exposed to the same levels.

All cases received transcranial PEMF therapy at the Danish Research Centre for Chemical Sensitivities for 30 min daily on all weekdays for 8 consecutive weeks totalling 39 treatments per patient. Treatment duration was set at 8 weeks as suggested in a previous PEMF study on treatment-resistant depression [34]. PEMF was delivered by the Re5 Independent System® (model I2010, Re5 Aps, Frederiksberg, Denmark) with a pulse generator providing pulses for the applicator. The pulses alternate between +50 and −50 V and have a frequency of 55 Hz. The pulse patterns are designed to mimic the electrical fields occurring outside nerves and muscles due to the propagation of action potentials. The Re5 head applicator is worn as a helmet and consists of seven electromagnetic coils of which two coils are located over the anterior and posterior temporal region bilaterally, one coil over the upper parietal region bilaterally and one coil over the centre of the lower occipital region. The coil generates an alternating magnetic field with a calculated maximum of 1.9 mT (19G) at a distance of 0.5 cm from the coil. The magnetic fields can induce electrical fields in tissue with a magnitude of 2.2 mV/cm at a distance of 0.5 cm from each individual coil, decreasing with distance to around 30 μV/cm 10 cm from the coil [34,20].

2.1. Outcomes

The following outcomes were used to measure the effects of PEMF therapy:

(1) Quick Environmental Exposure and Sensitivity Inventory (QEESI) which was developed as a screening questionnaire for MCS. In this study, four of five scales were employed using an evaluated Danish translation [37] i.e. Chemical Intolerance Scale (CIS), Other Intolerances Scale (OIS), Life Impact Scale (LIS) and Symptom Severity Scale (SSS). The LIS measures the impact of MCS on everyday life, such as the ability to perform domestic chores, take part in social activities, attend to work etc. The SSS and CIS measure the severity of general symptoms and of exposure-related symptoms, respectively. Each scale contains 10 items and produces a score ranging from 0 to 100 [38].
(2) Sheehan Disability Scale (SDS) which is widely used in psychiatry and in relation to many other chronic illnesses. It uses visuo-spatial, numeric and descriptive anchors to measure impaired functioning in three domains: work, social life and family life. The scale generates a disability score for each domain ranging from 0 to 10 [39].
(3) Symptom Checklist 92 (SCL-92) subscale for depressive symptoms which is a screening questionnaire and cannot be used for diagnostic purposes. The subscale comprises 13 items on which each item is rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much). The total score is the mean of all items. The SCL-92 has been validated in a general Danish population and normative data have been established [40].
(4) The mean area of capsaicin-induced secondary punctate hyperalgesia. The capsaicin procedure applied to MCS patients has been described elsewhere [14]. In brief, 0.1 ml capsaicin (3.3 μM, 1 μg/ml or 0.01% solution) was injected intradermally in the volar side of the right forearm. After 15 and 35 min, a mechanical probe was applied to the skin starting from a point well outside the capsaicin injection site and then sequentially

Table 1
Outcome measures for all cases at baseline, post-treatment, and 13-week and 18-week follow-up.

Measure	Case	Baseline	Post-treatment	13-week follow-up	18-week follow-up
QEESI					
CIS	1	89	87	87	87
	2	67	46	54	59
	3	91	60	59	†
OIS	1	71	69	72	70
	2	79	46	54	45
	3	56	32	28	†
LIS	1	92	88	87	87
	2	78	46	51	60
	3	86	56	52	†
SSS	1	100	100	100	100
	2	60	30	39	58
	3	43	18	21	†
SDS					
Work	1	10	10	10	10
	2	7	4	4	6
	3	10	7	7	†
Social life	1	9	8	8	8
	2	7	4	5	5
	3	8	6	7	†
Family life	1	9	8	8	8
	2	8	5	5	5
	3	7	2	3	†
Depressive symptoms (SCL-92)	1	2.2	2.4	2.0	2.2
	2	1.7	0.6	0.6	1.2
	3	0.8	0.5	0.8	†
Secondary hyperalgesia (cm^2)	1	73	78	†	†
	2	19	7	†	†
	3	52	44	†	†

QEESI, Quick Environmental Exposure And Sensitivity Inventory; CIS, Chemical Intolerance Scale; OIS, Other Intolerances Scale; LIS, Life Impact Scale; SSS, Symptom Severity Scale; SDS, Sheehan Disability Scale; SCL-92, Symptom Check List 92.
† Data are not available.

reapplied to the skin moving along a vector towards the injection site. The participants were instructed to report when the pricking sensation changed in intensity or character. When this occurred, the point was marked. This procedure was repeated along eight vectors and the eight marks were connected to form an area of secondary punctate hyperalgesia. The double assessment of the area of secondary punctate hyperalgesia was used to derive a mean area of capsaicin-induced secondary punctate hyperalgesia.

Outcomes were measured at baseline and weekly until 18-week follow-up except for the area of capsaicin-induced secondary punctate hyperalgesia, which was assessed only at baseline and post-treatment.

3. Results

Table 1 and Figs. 1–3 show the baseline, post-treatment and follow-up scores on the QEESI and SCL-92 for all three cases.

3.1. Case 1

A 36-year-old woman with a 5-year history of MCS starting after the growth of mould in her home as a result of water damage. She felt obliged to leave her home and is currently living in a holiday cottage, not having found a suitable new residence. Her MCS symptoms impair her both socially and occupationally. They prevent her from using public transportation, enjoying social activities and doing sport. She stopped working as a hairdresser and sold her saloons. Currently, she is unemployed, and is looking for a job

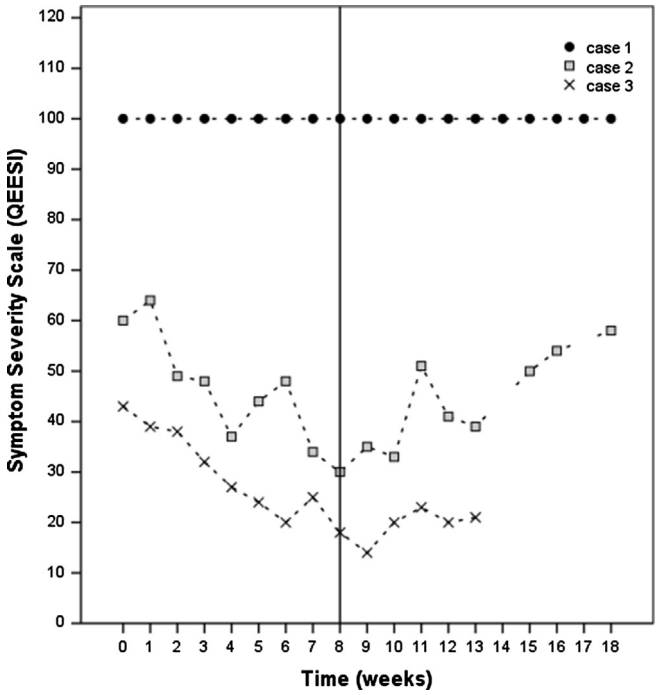

Fig. 1. The scores on the Symptom Severity Scale of the Quick Environmental Exposure and Sensitivity Inventory (QEESI) at baseline (week 0), during treatment (week 1–7), post-treatment (week 8) and during follow-up (week 9–18). Data were unavailable for case 2 at week 14 and 17. Case 3 was lost to follow-up after 13 weeks.

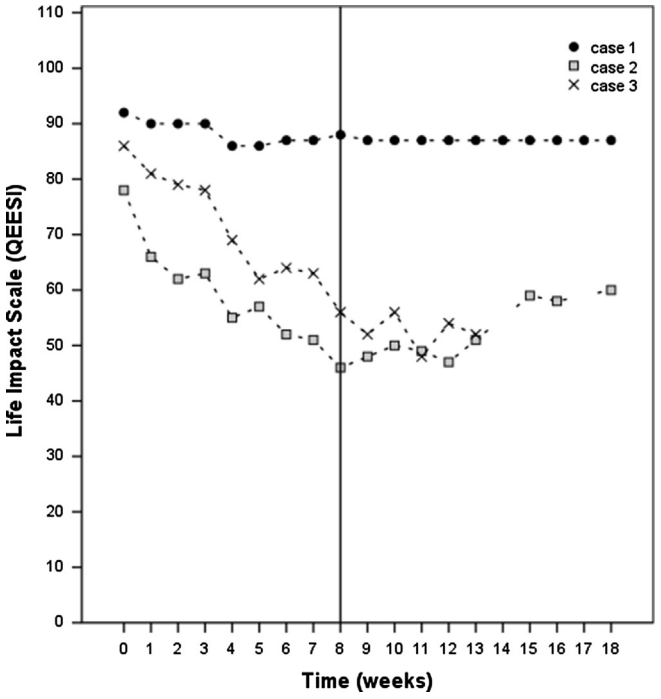

Fig. 2. The scores on the Life Impact Scale of the Quick Environmental Exposure and Sensitivity Inventory (QEESI) at baseline (week 0), during treatment (week 1–7), post-treatment (week 8) and during follow-up (week 9–18). Data were unavailable for case 2 at week 14 and 17. Case 3 was lost to follow-up after 13 weeks.

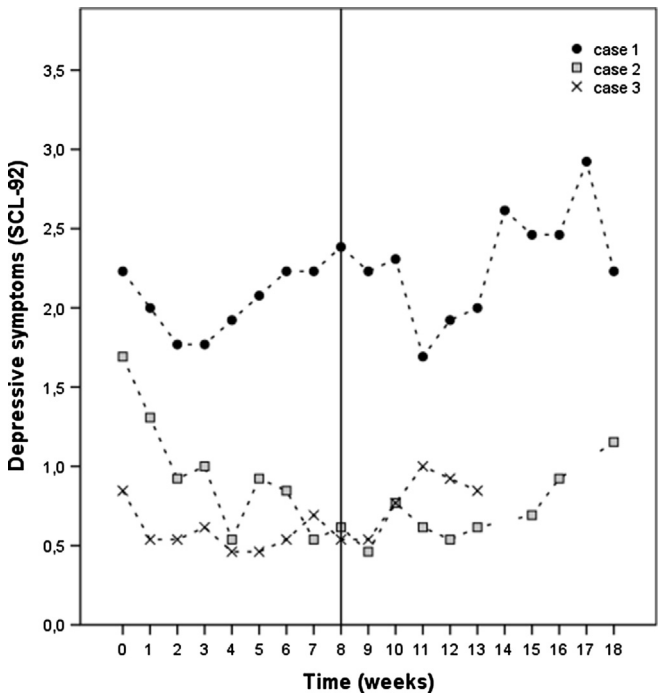

Fig. 3. The scores on depressive symptoms of the Symptom Check List (SCL-92) at baseline (week 0), during treatment (week 1–7), post-treatment (week 8) and during follow-up (week 9–18). Data were unavailable for case 2 at week 14 and 17. Case 3 was lost to follow-up after 13 weeks.

where she can work from home. Before and during the study period she daily took methylphenidate for attention deficit hyperactivity disorder and cetirizine (antihistamine) for itch.

Case 1 received 36 of the 39 treatments. The baseline scores on QEESI were 89 (CIS), 92 (LIS) and 100 (SSS) and at post-treatment the scores were 87, 88 and 100, respectively (Table 1, Figs. 1 and 2). At 18-week follow-up the QEESI scores were 87, 87 and 100, respectively. The scores on depressive symptoms (SCL-92) were 2.2 at baseline, 2.4 at post-treatment and 2.2 at 18 week follow-up (Table 1, Fig. 3).The mean area of capsaicin-induced secondary punctuate hyperalgesia was assessed to be 73 cm^2 at baseline and 78 cm^2 at post-treatment. Four days before the end of treatment, Case 1 received a diagnosis of depression and antidepressive treatment with citalopram was initiated by a psychiatrist.

3.2. Case 2

A 31-year-old man whose MCS problems began gradually 4 years ago without an attributed inciting event. During the past 2 years his MCS has intensified, preventing him from enjoying social activities, having guests at home, travelling and doing sport. To keep his job, he arranged to have a private office, constructed a plexiglass box to cover his computer screen and accommodated his work routines to his intolerance, e.g. minimizing the time spent in the copy room and holding his breath when in there. Medication used before the study was ibuprofen for muscle aches about every third day and during the study ibuprofen was taken daily for headache in the initial 3 weeks.

Case 2 received 38 of the 39 treatments. The QEESI baseline scores were 67 (CIS), 78 (LIS) and 60 (SSS) and at post-treatment the scores were 46, 46 and 30, respectively (Figs. 1 and 2). At 18-week follow-up, the QEESI scores were 59, 60 and 58, respectively.

The depressive symptoms scores (SCL-92) were 1.7 at baseline, 0.6 at post-treatment and 1.2 at 18-week follow-up (Fig. 3). The mean area of capsaicin-induced secondary punctuate hyperalgesia was assessed to be 19 cm^2 at baseline and 7 cm^2 at post-treatment.

3.3. Case 3

A 37-year-old man who developed MCS 4 years ago after the growth of mould in his home as a result of water damage. He then moved to a new flat, which he was able to tolerate. However, since then, his MCS symptoms have limited his social life to the extent that he avoids using public transportation, refrains from inviting guests, and is unable to enjoy social activities and indoor sports. His MCS has also had consequences occupationally. Prior to his current period of sick leave, it was often necessary for him to work from home and he often had to call in sick. He was eventually dismissed because of prolonged sick leave. He is planning to return to the labour market and is looking for a job where he can work from home. He has doctor-diagnosed depression, which is well treated with mirtazapine. To cope with his airway symptoms due to MCS, he daily took montelukast (leucotriene receptor antagonist), a nasal spray with fluticason furoate (glucocorticoid), and an inhaler with a combination of budesonide (glucocorticoid) and formeterol (β_2 agonist) before the study.

Case 3 received all 39 treatments. At baseline, the QEESI scores were 91 (CIS), 86 (LIS) and 43 (SSS) and at post-treatment the scores were 60, 56 and 18, respectively (Figs. 1 and 2). Case 3 was lost to follow-up at 18 weeks but at 13-week follow-up, the QEESI scores were 59, 52 and 21, respectively. The scores on depressive symptoms (SCL-92) were 0.8 at baseline, 0.5 at post-treatment and 0.8 at 13-week follow-up (Fig. 3). The mean area of capsaicin-induced secondary punctuate hyperalgesia was assessed to be 52 cm^2 at baseline and 44 cm^2 at post-treatment. During treatment, Case 3 had stopped taking some of his ordinary medications, the nasal spray with glucocorticoid after 4 weeks of treatment and montelukast after 6 weeks of treatment due to symptom alleviation.

3.4. Adverse effects

During treatment, tiredness, mild headache, and a dazed state were reported by two cases as possible adverse effects of Re5 therapy. One case reported no adverse effects.

4. Discussion

This report describes three cases of MCS with considerable functional impairments who received PEMF therapy for 8 weeks. In a Danish MCS patient sample the median scores of the CIS, LIS and SSS of QEESI were found to be 82, 65, and 47, respectively [37]. At baseline, all three cases were above the patient sample median on the LIS which was intentional and due to case selection on the basis of severity. This also explains why the baseline scores on the other scales of QEESI were above the patient sample median as symptom severity and functional impairment are closely linked. The mean score of depressive symptoms using SCL-92 in the Danish MCS patient sample was 0.88 [37], so at baseline the degree of depressive symptoms was unexpectedly above average in two of the cases. Two out of three cases showed 35–60% improvement on all QEESI scales. The improvement in functional impairments was also reflected in reduced scores on the SDS at post-treatment. One case also experienced a 40% decrease on depressive symptoms, which is in accordance with a positive effect of PEMF on refractory depression in a previous study [34]. PEMF has been shown to activate intracellular signalling, and to promote angiogenesis and vasodilatation [20,24,35]. Although speculative, the observed effect of PEMF therapy on MCS may stem from an activation of the inhibitory brain circuits in odour processing regions, which

previous studies have suggested to be hypoactive [11,12]. However, there are several limitations of this case study. A placebo effect, as well as the attention given to the participants during treatment, or the natural fluctuations of the condition cannot be ruled out as explanations for the positive effect observed in two of the cases. Further studies are needed to determine this. Interestingly, an improvement in MCS-related measures was associated with a reduced mean area of capsaicin-induced secondary punctate hyperalgesia at post-treatment, which is in keeping with the hypothesis of neural sensitization.

One of the two cases who benefited from PEMF therapy, showed partial regression of MCS at 18-week follow-up. In line with this, regression after the end of treatment has also been observed with ECT for MCS and chronic pain disorders, where maintenance treatment was attempted with success [19,41]. Similarly, maintenance treatment with PEMF therapy may also be necessary to prevent relapse of illness.

Total remission of MCS was not achieved with PEMF therapy within the present time frame. However, since the observed effect did not reach a plateau at post-treatment, an additional treatment effect may be obtained by prolonging the duration of treatment in weeks and/or intensifying the treatment by increasing the number of doses per day. When considering a new treatment, the effect of treatment should always be weighed against its adverse effects. With this aspect in mind, PEMF therapy was well tolerated by the three cases and only few and mild adverse effects were reported which is in accordance with previous studies [33,34,36]. Although one of the cases was diagnosed with depression during the intervention, we find it unlikely that the depression was related to PEMF. The depression coincided with several stressful events in the participant's life which were reflected in a high depressive score even at baseline and these events were more likely to be the cause.

5. Conclusion

This case report indicates a beneficial effect of PEMF therapy for MCS.

6. Implication

The therapeutic effect of transcranially applied PEMF in MCS needs to be investigated by a randomized placebo-controlled trial.

Conflicts of interest

The authors have no conflicts of interest.

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