Medically Unexplained Symptoms Explained

For years, the term “Medically Unexplained Symptoms” has been used to describe patients with persistent physical symptoms but no detectable disease. In clinical care these have often been referred to as 'heartsink' patients [1] – a term reflecting the frustration of both patient and doctor in finding effective treatments for the symptoms. But are these symptoms really unexplained?

Physical symptoms, like all perceptual experiences, come from complex neural activity in the brain. Although these symptoms often are triggered by bodily signals, such as tissue damage, the same symptoms can arise without any such input [2]. For example, the brain generates pain whenever it anticipates or believes there is a reason for us to feel pain [3]. This process explains why we can experience severe pain without injury [4] and, conversely, experience severe injury without any pain [5]. Studies of hypnotic suggestions to induce pain have shown that the hypnotic pain triggers neural activation in pain-related areas, as if the pain was caused by tissue damage [6]. Furthermore, associative learning enables physical symptoms to be triggered by sounds [7] or smells [2], and even viewing distressing pictures can trigger physical symptoms. Compared with healthy control individuals, the effect of distressing pictures on symptoms is considerably more pronounced among patients with persistent physical symptoms [8], the neural correlates of this effect involve somatosensory and nociceptive brain patterns, regions intimately connected to pain processing [8].

The accumulation of these scientific findings and others have substantially improved our capacity to explain previously unexplained physical symptoms. There is an urgent need for translating this knowledge into more effective interventions. If done successfully, these approaches could surpass the efficacy of previous interventions. In some, they could even result in recovery [9], as seen in patients with chronic low back pain in 2022 [10].

In The Lancet, Christopher Burton and collegaues [11] present a prime example of such an intervention. By recruiting general practitioners (GPs) with an extended role to dedicated symptoms clinics, the approach offered a targeted intervention for patients with persistent physical symptoms. The intervention, aptly named ecognition, explanation, action, and learning (REAL), included four unique components. First was recognition, in which the GP with an extended role validated the patient’s experience and symptoms as legitimate. Second, the explanation, in which a credible explanation of symptom perception was offered, including plausible mechanisms of symptom causes [12]. The third component, action, provided techniques and strategies that corresponded to the explanation. Finally, during learning, the patient implemented the acquired techniques and evaluated the effects on their symptoms.

Of the 354 participants recruited to this pragmatic, multicentre, parallel-group, individually randomized controlled trial, 291 (82%) identified as women and 63 (18%) identified as men; 25 (7%) identified as a minoritised ethnic group. 136 (38%) participants reported no academic qualifications after age 16 years, whereas See Editorial page 2565 See Articles page 2619 Halfpoint Images via Getty ImagesComment www.thelancet.com Vol 403 June 15, 2024 2569 119 (34%) had at least one university degree. According to the HLS-EU6 survey, at baseline, only 122 (35%) of 354 participants met the cutoff for “sufficient” health literacy, 167 (47%) had scores in the range suggesting “problematic” health literacy, and 50 (14%) had “inadequate” health literacy. The primary outcome was self-reported Patient Health Questionnaire-15 score 52 weeks after randomisation, which were 14·1 (SD 3·7) in the group receiving usual care and 12·2 (4·5) in the group receiving the intervention. The significant adjusted between-group difference (–1·82, 95% CI –2·67 to –0·97) was in favour of the intervention group (p<0·0001).

The trial has several strengths, among them a large sample size and robust design. Remote online delivery further showed equivalent effectiveness to in-person encounters, which implies versatility in methods of delivery. Despite little ethnic diversity, recruitment included areas of socioeconomic disadvantage and a high rate of individuals with low health literacy. There were high adherence rates to the intervention, which supports both generalisability and real-world relevance. Another crucial finding was the absence of any observed adverse events deemed to be related to the trial intervention. Concerns might occur about the possibility that the intervention could lead to delayed medical attention if symptoms are mistakenly attributed to no particular cause, rather than to an underlying medical condition. Nonetheless, Burton and colleagues [11] showed no evidence of any delay in appropriate medical care or any other unfavorable outcomes.

A weakness of the trial is the absence of an attention control group, which raises the possibility of nocebo effects in the usual-care group. Although this is critique is common in clinical trials, the shown long-term effects somewhat mitigate this concern. A more important concern, however, is the potential for scalability and broad implementation of the symptoms clinics. How interested GPs might be in adopting this method is unclear, and patient acceptability within the target group was not thoroughly explored —except for a moderate acceptance rate among those invited to participate. Furthermore, the trial does not address whether symptom improvements led to better real-life functioning, such as decreased work disability. Cost-effectiveness considerations were also absent, although forthcoming publications are anticipated to address this gap.

The delivery of care to patients by GPs with an extended role in separate clinics offers both advantages and challenges. As all GPs commonly see these patients, integrating the intervention principles into regular primary-care practices might be feasible via the existing GP-patient relationship. However, a distinct advantage of providing care in separate clinics is the potential to offer more comprehensive and effective care for these patients, as convincingly illustrated by Burton and colleagues.

In summary, scientific developments since 2015 challenge the accuracy of the term medically unexplained symptoms, suggesting that these symptoms are both explainable and treatable [2, 9, 12]. The trial by Burton and colleagues [11] corroborates this notion by offering an effective treatment for patients with persistent physical symptoms in which the symptoms are validated, explained, and managed. This paradigm shift offers renewed hope for a previously misunderstood and mistreated patient group, providing and opportunity for improved treatment outcomes and the possibility of recovery.

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