Why Do People Misdiagnose Themselves with Food Hypersensitivity? An Exploration of the Role of Biopsychosocial Factors

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Abstract

Up to 35% of people self-diagnose food allergy or intolerance (food hypersensitivity [FH]), or diagnose it in their child, and self-manage the condition rather than seek a clinical diagnosis. This is much higher than the latest FH prevalence rate, estimated to affect 2–5% of the general population. The actual prevalence rate may be underestimated due to the lack of diagnostic services; however, this can only account for a small proportion of the discrepancy because only a small percentage of self-reported FH can be clinically confirmed. Many people are therefore misdiagnosing their or their child's symptoms as FH and needlessly removing foods from their or their child's diet. There are a number of possible reasons for this misdiagnosis, which can be considered from a biopsychosocial perspective. Psychological factors include a confusion over the diagnosis, coincidental pairing of food and symptom, psychological or psychosomatic reactions, and taste aversions. There are also biological mechanisms that have not been fully considered in food allergy research that may be relevant, such as conditioning of the immune system or stress responses. A social context pertains to a greater awareness of FH due to media coverage and changes in food labelling laws. Any of these theories are plausible, but the research to date has a number of methodological issues. Most studies report on small self-selected samples recruited from clinics and there is a lack of general population data. Studies also tend to be cross-sectional, which does not allow cause and effect to be established. Future research needs to include longitudinal designs that incorporate qualitative elements to enable a detailed exploration of reasons why people self and misdiagnose FH.

INTRODUCTION

Food hypersensitivity (FH), which includes food allergy and intolerance, is an adverse reaction to food causing unpleasant and sometimes life-threatening symptoms.[1] Recent estimates put the prevalence rate of food allergy at around 2% of adults and 5% of children in the general population,[2] and there is evidence that the prevalence is increasing.[3] There is currently no cure for FH and management requires constant vigilance to avoid the food in question. Having this condition or caring for someone with FH

has therefore been associated with stress, worry, anxiety, and depression, and can impact quality of life.[4-6] Allergy service provision in primary and secondary care is limited across Europe,[7] with the number of certified allergists as low as 1 per 25 million of the population in some areas.[8] There is also a paucity of knowledge about FH in primary care[9-10] and physicians experience difficulties in arriving at correct diagnoses,[11] meaning that FH could go unrecognised and undiagnosed for some years.[12] However, FH is well known in the public domain, with widespread media coverage on the topic in recent years and more awareness due to changes in food labelling laws for unpackaged food.[13]

It may therefore be unsurprising that many people self-diagnose FH or diagnose it in their child and self-manage, rather than attaining a clinical diagnosis. Recent meta-analyses have reported that up to 35% of people self-report food allergy or intolerance or report it in their child.[3,14] Nwaru et al.[3] found a pooled lifetime prevalence of self-reported FH of 17.3% but only 2.7% prevalence as confirmed by skin prick tests and 0.9% confirmed by food challenges. This discrepancy is not just confined to FH, but it is also seen in other allergic conditions. Two large randomised controlled trials found that self-reported allergic triggers were not confirmed by skin prick testing in 41% of a paediatric population[15] and 78% of an adult population[16] with asthma or rhinitis.

It is unclear why there is such a large discrepancy between perceived self-reported FH and that which can be confirmed clinically. The actual FH prevalence rates may be underestimated because of a lack of diagnostic services,[3] but this may only account for a small proportion of this discrepancy. Many people may therefore be misdiagnosing their symptoms as FH and needlessly removing foods from their or their child's diet. There are a number of possible reasons for this misdiagnosis, which can be considered from a biopsychosocial perspective. Psychological factors contributing to misdiagnosis include confusion over definitions, coincidental pairing of food and symptom, taste aversions, and psychosomatic reactions. Biological factors encompass mechanisms that have been given less consideration in FH research, such as conditioning of the immune system or stress responses. This is set within

a social context, where there is greater public awareness (but not necessarily knowledge and understanding) of FH due to media coverage of fatal reactions and changes in labelling laws. This paper takes a biopsychosocial approach to explore possible reasons for the discrepancy between self-diagnosed and clinically diagnosed FH and provides new directions for research.

COINCIDENCE AND CONFUSION

For many years, the academic literature used different terms to refer to food allergy or intolerance, and there was a lack of consensus over the definitions of food allergy, intolerance, hypersensitivity, and aversion. To address this, a position statement was published that gave definitions for food allergy (both IgE and non-IgE mediated) and food intolerance (which does not involve the immune system).[17] However, these definitions were not clearly transmitted to the public and often people do not understand the difference between the two, with knowledge about FH being poor even in those with a clinical diagnosis.[18,19] As a result, people may label themselves as allergic to a food when they have a food intolerance or even have another condition entirely. A high prevalence of irritable bowel disease has been found in people with self-reported FH,[20] and, although up to 70% of those with irritable bowel disease have been found to have immune activation, this was not typical of an IgE-mediated reaction.[20] Therefore, these cases would not be diagnosed by standard skin prick testing for IgE. Coeliac disease and rarer diseases, such as hydatid disease,[21] also have symptoms in common with FH and may be misdiagnosed as such. A proportion of the discrepancy between self-reported and clinically confirmed FH may, therefore, be due to a lack of knowledge resulting in a misdiagnosis of food-induced symptoms.

More commonly, a misdiagnosis could be due to coincidence or confusion. People eat food regularly throughout the day and there are many reasons why symptoms are exhibited. Food poisoning may be experienced or a short-term virus that causes gastrointestinal symptoms. There are also a range of agents that can cause allergic reactions similar to food allergy, such as aeroallergens (e.g., pollen), reactions to animal dander, washing powders and latex, or

low molecular mass chemicals (e.g., salicylates, benzoates, and sulphites).[22] It is often difficult for a trained practitioner to properly diagnose food allergy or intolerance based on recalled history alone.[11] Kelsay[23] stated that patients and families could more accurately diagnose food allergy by flipping a coin rather than relying on symptoms. Histories can be unreliable,[24] and often people cannot recall much detail about past experiences regarding reactions to food.[25]

Thus, it can be extremely easy to make a mistake and think an innocent food has caused symptoms and that it will cause symptoms again if eaten.[26] In a large study, where 300 people were interviewed about their reasons for self-diagnosing FH, Knibb et al.[25] found that a vague recollection of instances where food was followed by symptoms correlated negatively with pathophysiological plausibility of actual FH, based on an assessment of their recalled clinical history. Many of the histories did not match typical clinical presentations of food allergy and could be explained by other factors, such as food poisoning, taste aversion, or a concomitant illness. In addition, approximately a fifth of those interviewed had decided that they had FH after experiencing symptoms just once after eating the food; they avoided the food after this incident and so never tested their assumption that the food was responsible for their symptoms.

This illustrates an important issue: people do not behave like scientists when testing a hypothesis that food causes a symptom. In a study exploring scientific decision-making, Croker and Knibb[27] provided adults without food allergy in the USA and the UK with a hypothetical situation where a person avoided peanuts because they thought they had an allergy to it. When asked what the person should do to find out if they were, in fact, allergic to peanuts, people were more likely to advise the person to continue avoiding peanuts rather than try eating peanuts to see if symptoms occurred. Thus, coincidental pairing of food and symptom on one occasion, coupled with an absence of symptoms on food avoidance and a reluctance to try the food again to see if symptoms reoccur, could explain a large proportion of misdiagnosed FH.

Judgement about the cause of symptoms may also be affected by a confirmation bias,[28] where the person reaches the view that they have FH and ignores additional information that conflicts with this view (e.g., they have eaten the food before and never experienced symptoms or they experience similar symptoms again even though they are now avoiding the food). As these people do not seek a clinical diagnosis for their perceived FH, these misattributions could lead to long-term food avoidance and reductions in health-related quality of life seen in those with clinically confirmed FH.[4-6] More qualitative research exploring reasons why people decide they have a FH is needed to determine the extent to which confusion and coincidence may be a causative factor.

TASTE AVERSIONS

A coincidental pairing of food and symptom leading to an erroneous assumption that the food caused the symptom may result in the development of an aversion to that food, which may perpetuate the belief that the food causes symptoms. Aversion to the taste of food occurs when the taste of food is paired with an unpleasant physiological reaction, most commonly nausea and vomiting.[29] Thereafter, the implicated food is often avoided and the sight or smell of that food can induce nausea without having to actually ingest it. However, aversions are not just related to nausea and vomiting; they have been reported in people with self-diagnosed FH.[30]

Knibb et al.[30] found that just over a third (35%) of the people interviewed with self-reported FH who avoided the food completely stated an acquired dislike for the food after they decided that consuming it caused symptoms. Aversion to the taste of the food occurred most often after nausea or vomiting; however, aversion also occurred equally as often to other symptoms, including behavioural and emotional states, such as hyperactivity, irritability, anxiety, and depression. Aversion to the flavour of alcoholic and non-alcoholic beverages (possibly due to the strong taste of these compared to other foods implicated in self-reported FH) occurred most often.

Interestingly, Knibb et al.[30] found that taste aversion was reported significantly more often in people who had less plausible recalled histories for FH. Those who reported fear of the symptoms as opposed to an aversion to the

taste were more likely to give more plausible accounts. This pattern of results was evident for foods inducing nausea and vomiting, as well as behavioural symptoms. The authors suggest that nausea and vomiting in particular (due to these symptoms' ability to provoke thoughts of the oral region) may bring sensory aversions to mind without any foundation for a real contingency between eating the food and suffering the illness.[30] Little empirical research has been conducted on taste aversions in those with self-reported FH and is needed to further explore its potential role in being a cause of misdiagnosed FH.

PSYCHOSOMATIC OR PSYCHOLOGICAL REACTIONS

One reason for misdiagnosis of FH that has received a lot of attention in the literature is a psychosomatic or psychological reaction. It may be that some people are more prone to misinterpret bodily sensations as an adverse reaction to food. Anxiety can increase vigilance for bodily symptoms and people with high trait anxiety tend to report more symptoms and be more concerned about those symptoms.[31] This bias may mean that patients are reluctant to see a connection between symptoms, anxiety, and stress, and this may partly be due to the stigma associated with psychological factors as a cause of symptoms.[32]

In the UK in 1984, the Royal College of Physicians (RCP) defined food intolerance as an unpleasant reaction to food caused by emotions associated with the food rather than being caused by the food itself.[33] Research published around this time suggested that people reporting FH that could not be clinically confirmed were likely to be suffering from psychosomatic reactions (subjective symptoms with a psychological rather than medical or biological explanation). Their evidence was that these people were more likely to score higher for hypochondria, hysteria, somatisation, and symptom distress than patients with clinically confirmed FH.[34-36] It was also reported that people with self-diagnosed FH complained of more subjective somatic symptoms or symptoms related to the central nervous system (CNS), such as headaches; hyperactivity; learning problems; behavioural problems; insomnia; and emotional symptoms, such as anxiety, fatigue, and general aches

and pains. Objective symptoms, such as skin symptoms or angioedema were reported less often.[37] At the time, there was no proof of a consistent relationship between the CNS and food allergy;[38] however, more recent research on conditioning of the immune system is providing evidence that the CNS may indeed play a role. It has now been demonstrated that substances do not need to cross the blood–brain barrier to affect emotions and behaviour but can affect the CNS through neural pathways.[39]

More recently, Nekam et al.[40] have looked at food allergy symptoms as a possible consequence of a subconscious response to stress and anxiety in a small sample of 14 female patients where double-blind placebo-controlled food challenges could not establish food allergy beyond any doubt. Compared to a control group of patients with anxiety and social phobia with no physical disease, the patients reporting food allergy had significantly lower stress scores, elevated state anxiety (but not trait anxiety) scores, and moderately serious depression. The Szondi test (a projective test of subconsciously perceived stress and anxiety) showed that patients had a high level of anxiety related to a feeling of guilt, losing attachments, and feeling inhibited. The authors concluded that these patients do not consciously perceive their own stress and may convert their anxiety into somatic symptoms, which the patients attribute to food allergy.[40] Polloni et al.[41] have also reported higher levels of alexithymia (difficulty in recognising and expressing emotions) in children and young adults with confirmed food allergy compared to healthy controls.

The research focussing on a psychosomatic or psychiatric explanation for misdiagnosis has often been limited to small self-selecting samples of people attending an allergy clinic. These people may be very different to a general population sample self-diagnosing FH. Larger scale studies have been conducted and found that those with self-reported FH often have more self-reported depression, anxiety, somatisation, and subjective health complaints than those with no self-reported FH.[42,43] In a large, general population survey, Knibb et al.[44] found significantly higher levels of neuroticism and psychological distress in people with self-reported FH compared to healthy people. However, there was no greater prevalence of psychiatric disorders than that

seen in a reference sample of NHS and university staff and no differences in neuroticism compared to normative data. In a similar study, Peveler et al.[45] could find no evidence for greater psychological symptoms in a self-reported FH group compared to a control group. A recent study has also shown that parents who have diagnosed FH in their child do not have higher levels of stress, depression, or anxiety than those with a clinical diagnosis.[46]

Many of these larger studies do not verify the self-reported diagnosis through clinical testing and rely on self-report of psychological distress. One study to overcome these limitations involved the conduction of diagnostic interviews with 76 patients with self-reported FH and found that 57% of patients met the DSM-IV criteria for at least one psychiatric disorder, but only 8% of FH cases could be confirmed by double-blind placebo-controlled food challenges.[47] The authors noted the possibility of somatisation being involved in the presentation of FH, suggesting that the symptoms may be a result of stress, which can affect gastrointestinal function and increase gut motility, or depression, which has been associated with constipation. Conversely, they also suggested that suffering from prolonged symptoms could cause psychological distress.[47]

The limitation of all of these cross-sectional studies is the inability to determine the causal pathways between somatic symptoms, psychological distress, and self-diagnosed FH. Chida et al.[48] have reported evidence of a bi-directional relationship between stress, anxiety, depression, and allergy. The meta-analysis showed a small, but statistically significant, positive association between psychological distress and future atopic disorders, as well as between atopic disorders and future psychological distress.[48] Therefore, it is important for future research to separate the role of psychological factors in the cause of supposed FH from the consequences of such a condition. Longitudinal research is needed to determine this.

THE IMMUNE SYSTEM, STRESS, AND CONDITIONING

Allergic reactions to food involve the immune system; thus, studies investigating the conditioning of immune responses and evidence from the field of psychoneuroimmunology, exploring how the immune system responds to psychological stress, may provide further explanations for misattributed FH.

Early animal research has shown how conditioning can elicit an allergic reaction. In a study by Williams et al.,[49] rats were conditioned with audiovisual stimuli (a loud noise and flashing lights). The rats were sensitised to egg albumen and were then trained on three successive occasions to associate the injection of antigen with the audiovisual cue. Subsequently, the rats demonstrated significant rises in serum rat mast cell protease when exposed to the audiovisual cue alone. This rise was comparable to animals challenged with the antigen without a cue. It has been suggested that this mast cell activation may be partly triggered by the CNS via the peripheral nerves in the respiratory and GI tracts.[50] Histamine release (which is the cause of unpleasant allergy symptoms) as a response to stress has also been demonstrated in guinea pigs in a conditioning paradigm.[51]

As a result, food could act as a conditioned stimulus in humans if paired with something that stimulates an immune response, such that a conditioned response develops when a person is exposed to the food on subsequent occasions. Psychological stress affects the immune system and has been shown to reduce the rate of wound healing and affect responses to infectious diseases and vaccines.[52] In relation to allergic conditions, chronic stress can dysregulate the hypothalamic pituitary adrenal system, resulting in blunted cortisol release and increased eosinophil counts leading to reduced lung function in patients with asthma.[53,54] Active and passive stressors have also been shown to increase sympathetic nervous system activity, cortisol and inflammatory responses, and induce mild bronchoconstriction.[55] Similar immune responses to stress have been seen in patients with atopic dermatitis.[56]

In addition, when experiencing acute stress, activation of the sympathetic nervous and hypothalamic pituitary adrenal systems and an increase in adrenaline and cortisol induces symptoms, such as increased heart rate, blood pressure, and respiration rate, which can cause redness of the skin and irritation of the gastrointestinal tract.[31] If food has been paired

with symptoms in the past that caused distress, subsequent presentation of the food could induce anxiety or stress-related symptoms, which could be misinterpreted as being caused by the food.

These hypotheses offer possible psychopathophysiological pathways that may go some way to explain why certain people have real allergy-like symptoms for which they blame food but do not react to double blind placebo-controlled food challenge where they do not have the food as a cue. The lack of food cues may result in an absence of a stress-related or conditioned response; thus, leading to null or equivocal food challenge results. These hypotheses require full examination in human participants with self-reported FH to explore their potential as reasons for the discrepancy between self-reported and double-blind placebo-controlled food challenge confirmed FH.

THE SOCIAL CONTEXT OF FOOD HYPERSENSITIVITY

The factors explored in this paper are likely to be reinforced or influenced by a social context, which may increase the likelihood that someone attributes the symptoms that they have experienced to the food consumed. FH is now more in the public consciousness; people with FH have reported greater awareness of FH when eating out and increased confidence in communicating with catering staff about FH.[13] This is partly due to the change in European labelling laws meaning that catering establishments must publish information about the main allergens in the food they serve (European Union [EU] Food Information for Consumer Regulation No 1169/2011),[57] making FH more salient when people eat out or buy non-prepacked food. It is also partly due to widespread media coverage of fatal food allergy

related reactions, some of which have led to successful prosecutions for manslaughter where food has been served containing allergens despite the customer declaring an allergy. It has also become much easier for people to obtain health and illness related information from the internet, where there is a plethora of FH related websites, online discussion boards, and support groups. The availability of information related to FH could increase the chances of people attributing symptoms to food due to availability bias,[28] which increases the perception of an event's risk (therefore leading a person to believe they have developed a FH) for which an example can be easily recalled. The social context of increased awareness of FH requires further investigation as a reason for misdiagnosis to explore these hypotheses.

CONCLUSIONS

It is clear that one factor alone cannot explain the large discrepancy between self-diagnosed and clinically diagnosed FH. A biopsychosocial approach to health and illness recognises the interaction of factors in the cause of illness and a bidirectional relationship across them.[31,58] Thus, it is likely that more than one factor is responsible for misdiagnosed FH in any single case and that often symptoms are not merely due to a psychosomatic reaction, but have a plausible biological basis, whether those symptoms are caused by FH or not. How these factors interrelate and the direction of cause and effect requires further exploration to provide greater insight into why people misdiagnose not just FH, but other allergic conditions too. A mixed design longitudinal approach using quantitative and qualitative methods investigating biological, psychological, and social factors would be beneficial in furthering our knowledge in this important area.

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