

Intolerance of Uncertainty

Shaping an Agenda for Research on Coping with Multiple Sclerosis

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*Multiple sclerosis (MS) is a chronic and progressive neurologic condition that, by its nature, carries uncertainty as a hallmark characteristic. Although all patients face uncertainty, there is variability in how individuals cope with its presence. In other populations, the concept of “intolerance of uncertainty” has been conceptualized to explain this variability such that individuals who have difficulty tolerating the possibility of future occurrences may engage in thoughts or behaviors by which they attempt to exert control over that possibility or lessen the uncertainty but may, as a result, experience worse outcomes, particularly in terms of psychological well-being. This topical review introduces MS-focused researchers, clinicians, and patients to intolerance of uncertainty, integrates the concept with what is already understood about coping with MS, and suggests future steps for conceptual, assessment, and treatment-focused research that may benefit from integrating intolerance of uncertainty as a central feature. *Int J MS Care.* 2015;17:153–158.*

Multiple sclerosis (MS) is a chronic and progressive neurologic condition that, by its nature, carries uncertainty as a hallmark characteristic. Individuals with MS experience an uneven and unpredictable progression of symptoms. Most individuals with MS (85%) have a relapsing-remitting disease course, characterized by periods of stability followed by an episode of worsened symptoms that may or may not fully remit.^{1,2} The timing of these relapses is typically unknown, and the extent to which they will result in residual symptoms is often equally unclear. For individuals with progressive forms of MS, the rate of decline is uneven, and the severity and location of symptoms remain a constant unknown. Undoubtedly, concerns about whether, when, and how symptoms will progress are central to the experience of MS regardless of disease

course. Successfully coping with these concerns is central to psychological well-being.

All patients with MS face uncertainty. However, there is significant variability in how individuals cope with that uncertainty. The reasons for this variability are not entirely clear. In contrast, there is extensive research from other populations on how individuals tolerate uncertainty and how that relates to important outcomes. Originally proposed by Freeston and colleagues,³ the concept of “intolerance of uncertainty” (IU) introduced the idea that individuals who have difficulty tolerating the possibility of a future occurrence (ie, uncertainty)—and, more specifically, have greater difficulty coexisting with the cognitive and emotional unpleasantness that accompanies uncertainty—may experience worse psychological outcomes.

The purpose of this review is to explore the possibility that the concept of IU may help improve our understanding of how individuals cope with the indeterminacy of MS. We first introduce MS specialists to the concept of IU and the impact of IU on well-being and functioning based on research found in other populations. Then, we integrate the concept of IU with what we already know about individuals with MS. We hope that this review encourages future research on IU and subsequent targeted interventions.

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What Is IU?

Intolerance of uncertainty was introduced under the premise that all people face uncertainty and that the presence of uncertainty is often unpleasant in nature, but individuals vary along a continuum in terms of the extent to which they are comfortable coexisting with that uncertainty.

Intolerance of uncertainty is defined as “a cognitive bias that affects how a person perceives, interprets, and responds to uncertain situations on a cognitive, emotional, and behavioral level.”^{4(p835)} The concept has been operationalized through the Intolerance of Uncertainty Scale,⁵ which yields a continuous score and, therefore, suggests that the extent to which an individual tolerates uncertainty resides along a continuum. People who are the most intolerant of uncertainty reside at the end of the continuum where individuals may find it more difficult to coexist with uncertainty and are, therefore, more likely to take efforts to try to control the situation or eliminate the uncertainty; as a result, they may be more likely to use coping strategies that have been associated with poorer outcomes. Therefore, IU may be viewed as a risk factor for poorer outcomes, but it is not itself diagnostic or pathologic.

In a seminal paper, Freeston and colleagues³ introduced IU in the context of worry, noting that a primary reason individuals worry is to attempt to exert control over situations in hopes of preventing negative future outcomes. Individuals who are high in IU have a negative bias toward uncertainty,⁵ are distracted from using effective problem-solving skills (also reported empirically by Dugas et al.⁶), require a greater amount of evidence to change their beliefs, and may overestimate the possibility of negative outcomes.³ The subsequent engagement in worry may reflect low confidence in problem-solving skills and a decreased sense of control.³

The extent to which an individual tolerates uncertainty is suggested to be modifiable such that emerging treatments are now focusing on this important aspect in efforts to improve coping in individuals with a variety of emotional disorders.⁷ As with any treatment, the value of intervening in IU is based on the empirical link between the target (IU) and important outcomes.

How Does IU Relate to Patient Well-being and Functioning?

Most IU research focuses on anxiety and worry. Broadly, research is separated into studies of individuals with anxiety disorders and individuals with medical conditions (often focused on health anxiety). However,

some of the newest studies identify IU as a common thread across a variety of psychological disorders.⁷

IU and Psychological Well-being

Recent publications suggest that IU may be a central construct underlying anxiety disorders and depression.^{7,8} In the case of psychiatric conditions, individuals may identify undesired outcomes that could occur (eg, “I will become so anxious I will faint when speaking in public”), may distort the possibility that the outcome will occur (eg, “This is definitely going to happen when I give this presentation”), or may distort how severe the outcome will be if it occurs (eg, “I will be too embarrassed to go on”). Intolerance of uncertainty is then implicated via the individual’s attempt to minimize the unsettling nature of this possible future occurrence through engagement in thoughts or behaviors that provide a sense of control, including by avoiding the scenario altogether to eliminate the potential outcome. In this case, the extent to which an individual experiences IU may be central to their display of the corresponding psychiatric disorder.

For example, Boswell and colleagues⁷ note that maladaptive cognitive and behavioral efforts to control uncertainty are central to generalized anxiety disorder (worry to increase the perception of control of future events), obsessive-compulsive disorder (obsessions and compulsions to reduce uncertainty and increase the perception of control), panic disorder (avoidance of stimuli of panic attacks to control the likelihood of future occurrences), social phobia (avoidance of specific social situations to eliminate the need to worry about an uncertain social interaction), and major depressive disorder (engagement in rumination about past events in an attempt to make meaning of events that are difficult to understand).

IU in Medical Settings

There is also a small body of research focused on IU in individuals with medical conditions. In medical conditions, the risk of the uncertain outcome may be less exaggerated than in psychiatric conditions, but the impact of IU describes a similar process with respect to how individuals manage the uncertainty that they experience or perceive. In the case of medical conditions, too, individuals scoring higher on measures of IU are more likely to engage in maladaptive coping strategies that negatively affect psychological outcomes.⁹⁻¹⁹ Therefore, for individuals with medical conditions, IU may help explain how they experience their condition, particularly in terms of psychological outcomes. Unlike psychiatric

conditions, it is not necessarily intended to describe a pathologic response.

We are aware of only one study examining IU in individuals with MS; IU emerged as a key variable associated with less patient acceptance of the medical condition.⁹ Research available in other health conditions presents interesting findings: increased stress and lower emotional well-being are associated with patients with cancer scoring high on measures of IU.¹⁰ Individuals with higher IU, across health conditions, are understood to have more worries about their health, higher health anxiety, and increased threat perception, and they may feel more out of control.¹¹⁻¹⁸ Not surprisingly, IU is also implicated in patients' efforts to find answers regarding their health conditions. In one study, IU moderated the relationship between checking the Internet regarding a health condition and health anxiety such that people with higher IU checked the Internet more frequently.¹⁹

Therefore, although the source of the uncertainty may be different for medical patients relative to individuals with psychiatric conditions, the resulting cognitive and behavioral response by individuals who are more intolerant of uncertainty is similar in that the response represents efforts to reduce the uncertainty and increase the perception of control so as to eliminate the distress of uncertainty. Although this has a negative effect on psychological outcomes for the patients studied, evidence does not suggest that they have worse health outcomes.²⁰

IU and MS

How Might IU Affect Individuals with MS?

Individuals with MS face disproportionately high levels of uncertainty owing to the characteristics of this medical condition. In fact, individuals with MS report that uncertainty is among the primary challenges they face in coping with their condition.²¹ In qualitative research, uncertainty emerges as a common thread when individuals describe concerns about the future. For example, employed patients wonder about their ability to maintain a career and their financial stability; patients with children wonder about their ability to satisfactorily participate in parenting; and, more broadly, patients worry about how disease progression will affect their identity²² and quality of life. The impact of uncertainty even extends to families such that families report that the presence of uncertainty disrupts family routines.²³

Despite the presence of these types of uncertainty-related concerns, there is significant variability in how well patients cope with the presence of uncertainty.

Specifically, although it might be suggested that all individuals with MS face resulting uncertainty, responses vary from persistence to significant struggle. Using IU as a framework, one might suggest that this variation is a sign of the extent to which an individual has identified strategies that help them effectively cope with—or perhaps more aptly put, coexist with—the uncertainty. Although IU has been minimally explored in MS, the existing literature on IU in health conditions and anxiety disorders provides information from which a theoretical framework can be constructed.

Parallels Between IU and Difficulty Coping with Uncertainty in MS

Studies of IU identify three important themes that parallel coping with MS: 1) there is an awareness of the presence and challenge of uncertainty, 2) there may be negative consequences to specific responses to uncertainty, and 3) common psychological consequences of high IU are also common psychological sequelae experienced by individuals with MS.

First, individuals with MS are aware of the presence and challenge of uncertainty.²⁴ For example, when asked to define the prognostic risk of developing specific MS-related symptoms, participants acknowledge the factual presence of uncertainty (often noting an approximately 50% chance of developing a specific problem) but also seem to subjectively modify their expectancies based on intra-individual differences in the relevance or reality of that uncertain outcome.²⁴ For example, individuals may be more likely to believe in the likelihood of an uncertain outcome (eg, needing a wheelchair for ambulation) based on the extent to which they believe that their situation relates to individuals who have that outcome and the extent to which they can envision being in that situation. Individuals with MS are aware of the importance of learning to cope with uncertainty for healthy adaptation.²⁵

Second, how some individuals respond to uncertainty in MS undoubtedly contributes to their suffering. However, unlike other populations in which IU has been studied, there are often competing ways in which the same responses may be adaptive. For example, there is evidence that avoidance may at times be adaptive and at other times maladaptive. Empirical evidence suggests that individuals living with MS often avoid thoughts about disease progression.^{26,27} When one chooses not to focus on the potential progression of their MS despite the threat of future outcomes—"I am not going to worry about this future possibility, as it is not here at present"—it may be adaptive. However, when individuals choose not to engage in specific activities out

of concern that some day they may not be able to do the activity, the avoidance may be more maladaptive. For example, we have observed several patients, with relatively few symptoms and a stable course, choose not to engage in desired vocational training out of fear that by the time they finish, substantial symptoms will have developed, impeding their ability to pursue that career path. Such inaction is unfortunate and potentially maladaptive in light of recent research examining those with MS who are “precariously adjusted.” These examined individuals expressed worry about the future, stating that they would be unable to tolerate the progression of particular symptoms. However, even in those who experience such circumstances, there were no instances in which a participant was unable to cope with the circumstance.²⁶ Other responses beyond avoidance may also be concerning, such as responding to uncertainty with hopelessness. For example, patients may feel as if they are in a futile battle with MS. In this case, the individual might believe that no opportunities are worth pursuing. Such responses (eg, avoidance, hopelessness) are consistent with the increased worry, threat perception, health-related anxiety, and depression displayed in individuals who are more intolerant of uncertainty in other medical populations.⁹⁻¹⁸

Third, in IU study populations, higher IU is associated with increased symptoms of depression and anxiety, two prevalent conditions in individuals with MS. Depression and anxiety are important to consider because they have detrimental effects on patient outcomes and may even be related to confirmed exacerbations and pseudoexacerbations.²⁸⁻³³ Given what has been observed in other populations, it may be reasonable to consider whether the presence and impact of depression and anxiety in MS are mediated by how an individual copes with uncertainty. Indeed, previous studies established that individuals with MS who indicate the presence of uncertainty are more depressed and less hopeful³⁴⁻³⁶; it is unclear whether the central issue here is the presence of uncertainty, how the individual copes with that uncertainty, or both. Clinically, we observe that most mental health referrals citing depression, anxiety, and adjustment to MS ultimately result in a focus on how the patient is coping with the uncertainty surrounding his or her MS. Therefore, we wonder whether how one copes with uncertainty is a central, cross-cutting feature related to psychology and MS, in similar fashion to how depression and anxiety have been repeatedly linked to IU in other medical and nonmedical populations.^{7,9-18}

Taken together, given the prominent role of uncertainty in MS, the myriad of ways that individuals cope with uncertainty, and the parallel features of IU and the experience of coping with MS, there is reason to consider the importance and relevance of IU to life with MS. However, to date, there is a paucity of research supporting this theoretical relationship.

Future Directions for IU in Individuals with MS

Establishing the Presence and Effect of IU in MS

In the absence of research on IU in MS, an obvious first step is cross-sectional research that improves our understanding of IU in MS. Methodologically, this is a relatively easy step. It simply requires the use of measures such as the Intolerance of Uncertainty Scale⁵ as part of any MS-related research. Incorporating this measure into primary or secondary analyses would help provide evidence for the presence or absence of IU in this population and would help define how IU is manifested in this population. Such research could also explore the extent to which IU is associated with biopsychosocial outcomes. If relevant observations come to light, additional research assessing empirical relationships between IU and important MS-related variables would establish its impact.

Identifying Risk Factors and Outcomes for IU in MS

If cross-sectional relationships are supported, a subsequent step would be to establish longitudinal cause-and-effect relationships between IU and the biopsychosocial experience of MS. This research would attempt to ascertain at least two elements. First, longitudinal research could assist with understanding which patients are most at risk for being intolerant of uncertainty and which individuals are least at risk—and why. Such information is particularly useful in clinical assessment so that providers can then be aware of risk factors for IU that would warrant closer monitoring. Second, longitudinal research could identify targets for intervention by identifying cause-and-effect relationships between IU and biopsychosocial outcomes using information obtained from individuals who are struggling with uncertainty and from those who are successfully navigating the challenge.

Developing Treatments That Target IU

Ultimately, an improved understanding of IU as an underlying construct in MS may present the opportunity for improved treatment. Research in other populations has focused on two advances to treatment as a result of improved understanding about IU. First, there is the opportunity to directly modify the way an individual copes with uncertainty. Second, there is the opportu-

nity to improve treatment outcomes by better accounting for the underlying impact of a treatment on IU.

Although no research on the intersection of IU with treatment is available specifically for individuals with MS, research from other populations may serve as a model for developing an MS-specific intervention that targets improved tolerance with the presence of MS-related uncertainty.

Treatments Empirically or Theoretically Linked to Modifying IU

In non-MS populations, a modest amount of research has been conducted on the extent to which interventions positively affect IU. This includes one treatment developed specifically to target IU called IU therapy,^{37,38} which focuses on increasing an individual's ability to tolerate uncertainty and accept its presence in daily life.

Other treatments have also received empirical support for their effect on IU or may be more successful when they improve on an individual's methods of coping with uncertainty despite the fact that these interventions were not developed specifically to affect IU. These treatments include cognitive-behavioral group therapy for social phobia,³⁹ acceptance-based behavioral therapy for generalized anxiety disorder,⁴⁰ behavioral activation for worry,⁴¹ the Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders,^{7,42} a self-help version of cognitive-behavioral therapy for worry delivered via bibliotherapy,⁴³ and spirituality-focused interventions.⁴⁴

There is theoretical support for a variety of additional treatments to positively affect how individuals cope with uncertainty. These are commonly used interventions in

psychology, including by psychologists who work with individuals with MS. Examples include cognitive-behavioral therapy and acceptance and commitment therapy.

Cognitive-behavioral therapy focuses on identifying thoughts and actions that may produce negative outcomes and teaches new strategies that might produce better outcomes; in the face of uncertainty, this includes exploring the extent to which an individual's cognitive and behavioral response to uncertainty is resulting in the best possible outcomes for the individual. Cognitive-behavioral therapy is a commonly used and effective intervention in MS psychology for a broad variety of aspects of coping.⁴⁵⁻⁴⁸

Acceptance and commitment therapy is a newer intervention that focuses on mindfulness, acceptance, and commitment to values-based living as a means to living a life that focuses on what is important and meaningful to an individual as opposed to living a life that is based on avoiding or being stuck on an individual's challenges.^{49,50} Acceptance and commitment therapy presents a particularly interesting avenue for addressing tolerance of uncertainty because a core of the intervention would be acceptance of the presence of uncertainty, followed by a conscious decision to put one's efforts on meaningful participation, as opposed to trying to combat the uncertainty. Preliminary research on the effectiveness of acceptance and commitment therapy as a treatment in MS indicates that it improves an individual's ability to accept undesirable thoughts and feelings.⁵¹ This is important because greater acceptance has been shown to relate to better adjustment to life with MS.⁵²

Conclusion

Individuals with MS are faced with the constant presence of uncertainty. The available research on uncertainty in MS suggests that the ability to cope with uncertainty relates to well-being. Indeed, this makes sense for individuals with MS: uncertainty is going to be a part of the MS experience, so individuals who can tolerate uncertainty would logically be less likely to suffer. Yet despite this logical connection, there is a paucity of research on the topic. It is important to understand how uncertainty and, more specifically, IU relate to well-being in individuals with MS. If the expected effect is present, then increased efforts to develop IU-specific interventions are warranted. □

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Practice Points

- MS is a chronic and progressive neurologic condition that, by its nature, carries uncertainty as a hallmark characteristic. Although all patients face uncertainty, there is substantial variability in how individuals cope with its presence.
- The concept of "intolerance of uncertainty" (ie, difficulty tolerating the possibility of future occurrences) may serve as a useful basis for understanding this variability and the subsequent effect on patient outcomes.
- This review considers how the concept of intolerance of uncertainty can be integrated into conceptual, assessment, and treatment-focused research.

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