Psikiyatride Güncel Yaklaşımlar-Current Approaches in Psychiatry 2021; 13(3):573-587
doi: 10.18863/pgy.827416

Intolerance of Uncertainty as a Transdiagnostic Factor

Transdiagnostik Faktör Olarak Belirsizliğe Tahammülsüzlük

Fatih Yığman [1], Selim Fidan [2]

Abstract

With the rapidly changing world and the impact of life conditions, uncertainty has become one of the concepts that we encounter in all areas of life. Uncertainty, which makes its presence felt almost every moment of time in daily life, is a disturbing and anxious situation for most people in the face of events or situations. Intolerance to uncertainty is the cognitive, emotional and behavioral response generated by the biased information process, which leads to high threat level, misconception and difficult to deal with. Intolerance to uncertainty is a concept developed against the backdrop of widespread anxiety disorder, after which its relationship with many mental disorders is revealed. Researches; it shows that people with depression, post-traumatic stress disorder, generalized anxiety disorder, obsessive-compulsive disorder, and social anxiety disorder have higher intolerance to uncertainty levels than healthy controls. For many mental disorders, it is considered as a transdiagnostic factor, because it is a revealing and sustaining factor. Recently, the importance of transdiagnostic factors in mental disorders is emphasized.The literature on the intolerance of uncertainty is increasing. In this review, intolerance to uncertainty is examined with a general perspective in line with the current literature, and the findings will be discussed both conceptually, measurement methods and clinical results will be evaluated. As a transdiagnostic factor, intolerance to uncertainty should be considered in the clinical approach because of its cognitive, emotional and behavioral structure.

Keywords: Intolerance of uncertainty, anxiety disorders, obsesive compulsive disorder, review

Öz

Günümüzde hızla değişen dünya ve hayat şartlarının etkisi ile birlikte belirsizlik, hayatın her alanında karşımıza çıkan kavramlardan birisi haline gelmiştir. Günlük hayatta zamanın neredeyse her anında varlığını hissettiren belirsizlik, olaylar veya durumlar karşısında çoğu kişi için rahatsız edici ve kaygı verici bir durumdur. Belirsizliğe tahammülsüzlük, tehdit düzeyi yüksek, hatalı algılamaya yol açan ve başa çıkmanın güç olduğu, önyargılı bilgi işleminin oluşturduğu bilişsel, duygusal ve davranışsal tepkidir. Belirsizliğe tahammülsüzlük, yaygın anksiyete bozukluğu zemininde geliştirilen, sonrasında birçok ruhsal bozukluk ile ilişkisi ortaya konan bir kavramdır. Yapılan araştırmalar; depresyon, travma sonrası stres bozukluğu, yaygın anksiyete bozukluğu, obsesif kompulsif bozukluk ve sosyal anksiyete bozukluğu olan kişilerin sağlıklı kontrollerden daha yüksek belirsizliğe tahammülsüzlük düzeylerine sahip olduklarını göstermektedir. Birçok ruhsal bozukluk için, ortaya çıkarıcı, sürdürücü bir faktör olması sebebiyle de transdiagnostik bir faktör olarak ele alınmaktadır. Son zamanlarda ruhsal bozukluklarda transdiganostik faktörlerin önemine dikkat çekilmektedir. Belirsizliğe tahammülsüzlük ile ilgili yazın giderek artmaktadır. Bu gözden geçirmede belirsizliğe tahammülsüzlük genel bir bakış açısı ile güncel yazın doğrultusunda incelenmiş olup, bulgular hem kavramsal olarak ele alınacak, hem de ölçüm yöntemleri ve klinik sonuçları değerlendirilecektir. Transdiagnostik bir faktör olarak belirsizliğe tahammülsüzlük bilişsel, duygusal ve davranışsal bir yapı olmasından dolayı klinik yaklaşımda göz önünde bulundurulması gerekir.

Anahtar sözcükler: Belirsizliğe tahammülsüzlük, anksiyete bozuklukları, obsesif kompulsif bozukluk, derleme

[1]Ufuk University, Ankara, Turkey
[2]University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

✉ Fatih Yığman, Ufuk University Faculty of Medicine Department of Psychiatry, Ankara, Turkey
dr.yigman@gmail.com | 0000-0001-6052-7662

Received: 17.11.2020 | Accepted: 17.01.2021 | Published online: 03.06.2021

INTOLERANCE of uncertainty is a concept that has been on the agenda especially since the mid-90s, and it is expressed by people experiencing difficulties in situations of uncertainty.

The concept of intolerance of uncertainty was first used in 1949 (Frenkel-Brunswik 1949). According to a definition accepted since the mid-90s, it is "a cognitive, emotional and behavioral response created by biased information processing, which has a high level of threat, causes erroneous perception and is difficult to cope with" (Freeston et al. 1994). More recent reviews define IU as "a dispositional feature reflecting a set of negative beliefs about uncertainty and its effects" (Dugas et al. 2007).

In recent years, it has been considered as a factor that reveals, maintains, has an effect on comorbidity conditions and treatment for many diseases; therefore it has been evaluated as a transdiagnostic factor. Studies on this subject are limited in the domestic literature. With this review, we planned to review the conceptual information about the intolerance of uncertainty and its clinical equivalents in the literature.

Uncertainty

Uncertainty is defined as "ambiguity, ignorance, vagueness, nebulousness" (TDK 2019). Research on uncertainty has shown that uncertainty is associated with an increased fear response. When the unconditional stimulus (eg electrical stimulation) was given predictably, the magnitude of the fear response decreased (Badia et al. 1966, Lanzetta and Driscoll 1966). Although the emotion emphasized at the first stage is fear; in fact, fear is related to the present and it is a relatively clear affect. Anxiety is forward-looking and relatively uncertain (Gu et al.2020). In more recent experimental studies, uncertainty and higher negative affect, startle response and physiological responses were also found (Vansteenwegen et al.2008, Grupe and Nitschke 2011). Uncertainty blocks us from preparing effectively for what will happen in the future and thus can cause worry and anxiety (Grupe and Nitschke 2013). Previous studies have suggested that fear of the unknown may be the most basic component of pathological anxiety and one of the main components of all anxiety disorders (Carleton et al.2007a, Carleton 2016). Although, in the first stage, studies are conducted on negative affect; as examples from life, the series ends in the most exciting place, the excitement, and uncertainty created at the very beginning of romantic relationships can also have a rewarding effect when the context is positive. In other words, uncertainty can increase positive and negative affect depending on its context. In a study conducted on Facebook profiles, it was reported that positive emotions increased more when people of the opposite gender did not state whether they like them or not (Bar-Anan et al.2009). It has been suggested that uncertainty can increase attention and curiosity, and in this way, it may have an effect on positive affect, similar to the Zeigarnik effect. The Zeigarnik effect is a psychological concept that expresses that people can remember unfinished situations better than completed situations, and can explain the "tomorrow" effect we see in daily life in TV series and movies (Denmark 2010).

Generally, uncertainty is associated with 3 main situations; Encountering an unpredictable new situation is a predictable but complex situation, and finally, different predictions present different information and there is a contradiction in this case (Stanley Budner 1962).

Intolerance of uncertainty (IU)

In every area of life, we actually live a life with many uncertainties. For example, there is no guarantee that we will not crash in traffic, or we do not know if the people reading this review will give ruthless criticism. However, for people with low IU, they feel confident enough when there are no clear threat stimuli (for example, if one of the tires of the car is not lowered). Further, people with high IU may feel a perception of threat ("what if I crash?") even without clear threat stimuli. In summary, while people with low IU are satisfied with being "confident enough", people with high IU cannot be "sure enough" and exaggerate the importance of this unsure.

In studies conducted with people with high intolerance to uncertainty, some differences were obtained compared to control groups. To summarize these studies; while individuals with high IU anticipate a threat, there is a greater increase in blood pressure (Greco and Roger 2003), more anxiety response (Buhr and Dugas 2009), and higher perception of threat/disaster in uncertain situations (Davey et al. 2007), they have more "what if" thoughts (Ottaviani et al. 2014), exhibit more positive beliefs about anxiety (Davey et al. 2007), have negative problem orientations (Zlomke and Jeter 2014), and use more cognitive avoidance. (Kertz et al. 2015). In general, it has been suggested that IU plays a central role in the development and maintenance of anxiety (Laugesen et al. 2003).

Development of intolerance of uncertainty and neuroanatomy

In studies on the development of the concept of IU, it was stated that overprotective and controlling parenting styles can reduce children's perceived control and self-efficacy, and negative cognition and strategies related to uncertainty can play a role in their development (Chorpita and Barlow 1998, Buhr and Dugas 2006). In another study, 174 young adults were included, and it was reported that there is a relationship between parents' anxious upbringing and rejecting attitudes and high levels of IU (Zlomke and Young 2009). Also, in this study, it was found that IU mediates the relationship between anxious parenting and anxiety. In a prospective study examining the relationship between IU and anxiety in adolescence, they reported that changes in IU mediate changes in anxiety (Dugas et al. 2012). When evaluated on personality traits, it was found that neuroticism was highly correlated with IU (r=.55) and extraversion was negatively correlated with IU (r=.18) (McEvoy and Mahoney 2012a). Studies focusing on neurological bases have focused on the role of the dorsal anterior cingulate cortex (dACC), rostral ACC (rACC), and amygdala in the presence of uncertainty. In a predictive period, dACC and amygdala get activated, and when conflict is detected, rACC suppresses the amygdala and associated physiological responses (Whalen et al. 2001, Shin and Liberzon 2010). In a functional MRI study with 30 adult women, uncertainty was found to be associated with activation of the posterior frontomedial cortex

(pFMC), dorsolateral prefrontal cortex (dlPFC), and anterior cingulate cortex (ACC). IU also positively correlated with amygdala activation and negatively correlated with pFMC activity. Based on these results, it has been interpreted that cognitive mechanisms may not be used sufficiently in the face of uncertainty in individuals with high IU (Schienle et al. 2010). One of the interesting results among the studies is that patients with ventromedial prefrontal cortex (vmPFC) damage were compared with the control group; as a result, bilateral insula activity and correlated heart rate variability were shown in the control group in the face of uncertainty. In the study, an abnormal neural activity pattern was shown in bilateral insulae in patients with vmPFC damage (Motzkin et al. 2014). In other studies, functional magnetic resonance imaging results including the insula, amygdala, anterior singulate cortex, orbitofrontal cortex, ventromedial prefrontal cortex, dorsolateral prefrontal cortex, and posterior frontomedial cortex were reported in relation to IU (Krain et al. 2006, Sarinop Simmons et al. 2008, Sarinopoulos et al. 2010, Thayer et al. 2012).

IU measurement tools

The first scale developed for IU measurements is the 27-item Intolerance of Uncertainty Scale (Freeston et al. 1994). The internal consistency of the scale was found to be.91 and the test-retest reliability was.78. The Turkish validity and reliability study was conducted with 441 university students and the scale was found to be valid and reliable (Cronbach α=.79) (Sari and Dağ 2009). However, it has been suggested that this scale includes items on generalized anxiety disorder (GAD) and worries, and may affect transdiagnostic practices (Gentes and Ruscio 2011). It has been suggested that some items in the IUS do not validate and measure the default results related to IU rather than directly IU. Therefore, IUS-12 was developed, which consists of two factors as prospective IU and inhibitory IU (Carleton et al. 2007a). IUS-12 has strong psychometric properties (Cronbach α=.91 in the non-clinical population,.92 in the clinical population) and is a viable transdiagnostic assessment tool (Khawaja and Yu 2010). The Turkish validity and reliability study of the scale was conducted with 593 university students (Cronbach α =.88), and the two-factor structure was supported (Sarıçam et al. 2014).

As a third measure, the 45-item IU Inventory (IUI) was developed (Carleton et al. 2010). IUI consists of two parts; it distinguishes six behavioral and cognitive expressions (i.e. avoidance, doubt, overestimation, worry, control, assurance; Part B) (Cronbach α=.96) associated with trait IU (Part A) (Cronbach α=93).

It is the Intolerance of Uncertainty Scale for Children (IUSC), which revised the IUI items for children and it was the first IU measure validated for children (Comer et al. 2009). It was evaluated in clinical and non-clinical samples; Cronbach was α.92 for children and.96 for parents. The scale consists of 27 items and includes the evaluation of the same concepts as child and parent forms.

In addition, the Situation-Specific IU scale (IU-SS) (Mahoney and McEvoy 2012a), which is an adapted version of IUS-12, was developed as a result of theoretical distinctions between trait and disorder-specific IU based on sub-dimensions. This scale includes the

items of the IUS-12 scale but evaluates general expressions by customizing them according to situations in which people experience uncertainty.

A 24-item Disorder-Specific Intolerance of Uncertainty Scale (DSIU) was designed to evaluate IU by focusing on separate symptom categories (Thibodeau et al.2015). The scale evaluates IU over 8 different tables: GAD, obsessive-compulsive disorder (OCD), social anxiety, health anxiety, panic disorder, specific phobia, post-traumatic stress disorder, and depressive disorder. In the study, the scale was found to be valid and reliable (α >.83 for all tables).

Conceptualization and sub-dimensions of IU

Along with the first measurements, intolerance of uncertainty was categorized in four dimensions. These are; a) desire for predictability ("I want to know what will happen in the future"), b) uncertainty paralysis ("I stand still in an uncertain situation"), c) distress in the face of uncertainty ("Uncertainty hurts me") and d) dysfunctional beliefs of uncertainty ("Everything in life should be clear"). In this sense, IU seems to be a general concept that includes cognitions, metacognitive beliefs, emotions, and behaviors. The desire for predictability and the uncertainty paralysis will be explained separately as concepts that form the basis of further research. While distress in the face of uncertainty is associated with the emotional component of the concept, dysfunctional uncertainty beliefs refer to both cognitive and metacognitive beliefs.

Desire for predictability (prospective IU) - uncertainty paralysis (inhibitory IU)

While conceptualizing, an important grouping that stands out as a result of the studies is the desire for predictability and the uncertainty paralysis. As a result of the studies, after the re-evaluation of the first IU scale, the IUI-12 scale was created; afterward, while the studies in the literature evaluated IU, one of the focal points was the desire for predictability and uncertainty paralysis. While the desire for predictability directly increases anxiety, uncertainty paralysis seems to be more related to avoidance behaviors (Berenbaum et al. 2008).

The desire for predictability is a person's search for clarity about what will happen in the future. Uncertainty paralysis, on the other hand, seems to be associated with inhibition when an uncertain situation occurs or avoiding the situation that reveals uncertainty. In this sense, the desire for predictability seems more like a cognitive component, whereas uncertainty paralysis seems to be a behavioral component (Carleton et al. 2007b, Einstein 2014). In other words, the desire for predictability expresses the desire to know what the future will bring; it motivates attempts to increase predictability by seeking new information and taking behavioral actions. Uncertainty paralysis, on the other hand, explains the situation of being stuck and being unable to respond effectively when faced with uncertainty, which results in freezing in cognition and action (Birrell et al. 2011).

Different components of IU may show different levels of association with various clinical pictures. For example, the desire for predictability (the cognitive component) is uniquely associated with GAD (ie anxiety) and OCD symptoms; and uncertainty paralysis (the behavioral component) is associated with panic/agoraphobia, social anxiety, and depression symptoms (McEvoy and Mahoney 2012b). In a study conducted with 110 patients, it was reported that procrastination behaviors were only associated with "uncertainty paralysis", but control behaviors were equally associated with both "uncertainty paralysis" and desire for predictability (Fourtounas and Thomas 2016). An overview of the literature suggests that uncertainty paralysis is more strongly associated with anxiety and depression symptoms; it can be said that the desire for predictability is related to control behaviors and anxiety, especially in OCD and GAD (Shihata et al. 2016).

Trait IU versus disorder-specific IU

Although the studies mostly focus on the uncertainty paralysis and the desire for predictability, another prominent grouping in conceptualization is the individual handling of the uncertainty experienced by individuals structurally or specific to the disorder. Different studies have suggested that the experience of uncertainty may differ according to the situation and the disorder (Tolin et al. 2003, Carleton et al. 2010), and while examining IU, trait and disorder-specific components were evaluated. For example, the uncertainty about how to evaluate the person experienced with social anxiety disorder is different from the uncertainty related to whether the person will have an attack in panic disorder or to check whether the person has locked the door in OCD. For this reason; a trait IU that refers to the general personality traits of individuals and the concept of IU specific to a disorder (condition), caused by the mental state (or condition) they are in, have been proposed.

In previous studies, it was found that clinical participants reported higher disorder-specific IU than trait IU (Mahoney and McEvoy 2012a, Jensen and Heimberg 2015). In another study, 507 participants were evaluated with disease-specific cognitive factors (OCD, GAD, social anxiety disorder, and panic disorder). It has been shown that the relationship between trait IU and symptoms is mediated by disorder-specific IU and disease-specific cognitive factors (Shihata et al. 2017). In a study conducted on this subject showed that while trait IU was more closely related to generalized anxiety disorder and obsessive-compulsive disorder symptoms, disorder-specific IU was found to be a stronger predictor of social anxiety and panic disorder symptoms (Thibodeau et al. 2015). In addition, trait and disorder-specific IU predicted depression and specific phobia symptoms similarly. Also, trait IU was strongly associated with each of the disorder-specific IU subscales, and weaknesses specific to disorders (i.e., negative metacognitions, fear of negative evaluation, inflated responsibility and agoraphobic cognitions) and symptoms of the disorder (i.e., generalized anxiety disorder, social anxiety, and obsessive compulsive disorder). These results contribute to studies showing that IU is associated with a wide range of disease symptomatology, supporting the conceptualization of IU as transdiagnostic (Mahoney and McEvoy 2012a, Hong and Cheung 2015)

IU in behavior

The effects of uncertainty on behavior have also been intriguing for many studies (Pleskac et al. 2015, Carleton et al. 2016). In general, it has been shown that uncertainty activates fight-or-flight response (Thayer et al. 2012) and behavioral inhibition (Gray and McNaughton 2003) and that IU affects psychopathology and decision-making processes. In addition, uncertainty was triggered experimentally in studies and the responses with high IU were examined. The results showed that people with higher IU prefer rewards that can be obtained immediately, even if they are less likely or less valuable (Luhmann et al. 2011). It has been found that they are less confident about high-risk decisions and are less likely to change their decisions, despite receiving new information (Jensen et al. 2014). In non-clinical samples, they were found to be more likely to seek additional information to increase precision (Rosen et al. 2010, Jacoby et al. 2014, Jacoby et al. 2016). In clinical (Jacoby et al. 2014) and non-clinical samples (Jacoby et al. 2014, Jacoby et al. 2016), they were found to be more likely to increase precision by acting slower or making decisions, but it was shown that moving slower was not associated with more errors. (Thibodeau et al. 2013).

In the light of all these experimental results, it can be said that uncertainty can negatively affect behaviors and decision-making in people with high IU, even at relatively low threat levels. However, these relationships appear to be complex, and significant additional research is needed to understand how clinically meaningful IU will affect pathology-related behaviors (Carleton et al. 2016).

IU from a cognitive behavioral perspective

From a cognitive behavioral point of view, people must first have basic beliefs about uncertainty ("uncertainty is sad, uncertainty should be avoided"). After people have basic beliefs about uncertainty, they use biased information processing within the framework of these basic beliefs. They misinterpret uncertainty related information ("the reason for my heart palpitations may be caused by something bad") and have increased attention to issues in the focus of uncertainty ("they pay attention to news about heart attacks around them"). In case of uncertainty or suspicion, people make threatening secondary comments (my heart palpitations may indicate a serious heart disease). Emotional anxiety and distress arise. In the behavioral part, there are two ways in front of people. The first is to provide certainty to remove uncertainty (eg, to have continuous examinations), and the second is to avoid situations that create uncertainty (eg to quit the exercise). While these behaviors provide instant relief, they nourish the process by acting as negative reinforcement on basic beliefs in the long term (Jacoby 2020).

To summarize, according to the cognitive behavioral model, IU does not only cause exaggerated anxiety about daily life events. At the same time, security behaviors prepare the ground for delaying, controlling, and avoiding behaviors to reduce uncertainty. These behaviors play a negative reinforcing role in the process and the problem becomes more rooted (Robichaud 2013).

IU as a transdiagnostic factor

In general, it is reported that there are factors that not only contribute to the emergence of a particular disorder but are also partially responsible for comorbidity among disorders. Factors that go beyond the specific nature of such disorders are referred to as transdiagnostic factors (Harvey et al. 2004, Ehring and Watkins 2008). Although transdiagnostic factors are generally a risk factor and a maintenance factor for disorders, they are common in many clinical pictures and a relationship between their changes and changes in symptoms is determined. Although the mechanism of IU may be different in diverse clinical pictures, it seems to be effective in revealing and maintaining the symptomatology. For example in post-traumatic stress disorder, there is an uncertainty that he will never know the outcome, such as whether the same results would have occurred if he had done a different behavior. Or in OCD, it may appear as uncertainty whether he has cleaned his hands sufficiently. Another example for eating disorder; if the amount he ate is excessive, and whether this amount will affect his physical appearance. IU was originally developed on anxiety, which is a distinctive symptom of GAD (Freeston et al. 1994, Dugas et al. 1998). IU is thought to differentiate people with GAD from other heterogeneous anxiety disorders (Dugas et al. 2004, Buhr and Dugas 2006). The relationship between anxiety/worry and IU in children and adolescents has also been emphasized in studies (Osman ağaoğlu et al. 2018). However, many studies did not support the specificity results of IU regarding GAD (Norton and Mehta 2007, Gentes and Ruscio 2011, McEvoy and Mahoney 2011, Hong and Cheung 2015).

Subsequently, studies focused on OCD. The Obsessive Compulsive Cognitive Working Group (OCCWG) defined intolerance of uncertainty as "believing that everything should be certain and free from uncertainty, thinking that you cannot cope in case of uncertainty, and having problems with functionality in case of uncertainty" and defined it as one of the six obsessive cognitions (OCCWG 1997).

The relationship between IU and OCD has been emphasized in many studies (Tolin et al. 2003, Holaway et al. 2006, Jacoby et al. 2013). Studies have also shown a strong relationship between IU and perfectionism in the population with OCD (Calleo et al. 2010). Interestingly, the increased responsibility in one study did not appear to have a direct effect on OCD symptoms after controlling trait IU and disorder-specific IU. Therefore, if people can tolerate uncertainty, it seems that they can tolerate their responsibility to prevent the consequences they fear. In addition, studies have emphasized the relationship between IU and OCD-related disorders such as hoarding disorder and body dysmorphic disorder. They reported that IU was predictive regarding hoarding disorder (Oglesby et al. 2013, Wheaton et al. 2016). Clinically, higher IU levels were found in patients with hoarding disorder compared to healthy individuals and the anxiety group (Wheaton et al. 2016). In addition, a significant relationship was found with the urge to acquire more items than the symptoms of hoarding and disposal of items with IU, and it was reported that high pre-treatment IU scores indicate the possibility of non-response to treatment (Castriotta et al.

2019). In studies conducted on body dysmorphic disorder, it has been reported that IU and body dysmorphic disorder symptoms are predictive of anxiety and depression symptoms in clinical samples (Summers et al. 2016). In a study conducted on personality traits, IU mediated the relationship between obsessive-compulsive personality disorder and low quality of life (Wheaton and Ward 2020).

The effect of IU in relation to anxiety disorders has been emphasized in many studies. For example, in social anxiety disorder, the relationship between IU and social anxiety has been shown (Boelen and Reijntjes 2009). In a study conducted with 472 undergraduate students, it was found that "uncertainty paralysis" played a greater role in performance type social anxiety than "desire for predictability"; on the other hand, "uncertainty paralysis" has been reported to play a role in interaction type social anxiety (Whiting et al. 2014). It is thought that the probability of occurrence of an adverse situation related to panic disorder may be related to IU. In a study, it has been shown that "uncertainty paralysis" has a more critical role than anxiety sensitivity, especially on avoidance behaviors (Carleton et al. 2013). Regarding health anxiety, it has been shown that "desire for predictability" is associated with symptoms in both undergraduate students and other participants (Fetzner et al. 2014). In the same study, IU scores in health anxiety were compared with other anxiety disorders and IU scores in OCD, and low differences were found. Again, in a study conducted with 128 adolescents, the relationship between IU and health anxiety was emphasized (Wright et al. 2016).

In addition, post-traumatic stress symptoms and disorder (PTSD) among other mental disorders have come to the fore in recent years. In a study conducted with 122 people with a history of trauma, it was stated that "uncertainty paralysis" was associated with all PTSD symptoms except for re-experiencing symptoms (Fetzner et al. 2013). In another study, evaluations were made on 265 participants and after 6 months of follow-up, it was shown that "uncertainty paralysis" was associated with PTSD and depression symptom levels, but prolonged grief was not associated with symptom levels (Boelen et al. 2016). In an experimentally designed prospective study, 77 undergraduate students' data were analyzed; the relationship between pre-traumatic high IU scores and PTSD symptoms has been shown (Oglesby et al. 2016).

The relationship between depression and IU has also been another focus of studies. For example, it has been shown that depression, ruminative thinking, and IU are strongly associated (de Jong-Meyer et al. 2009). In another study, it was reported that IU and anxiety and depression symptoms were associated in the clinical sample group (Dar et al. 2017).

Another mental illness group that has been noted in studies is eating disorders. In a study of 134 people with eating disorders, IU was found to be associated with eating, weight, overestimation of physical appearance, and emotional symptoms (Renjan et al. 2016). In a meta-analysis, it was shown that women with eating disorders had higher IU scores compared to healthy controls (Brown et al. 2017). According to meta-analysis results, IU has been reported to be vulnerability and a sustaining factor for eating disorders.

Another interesting disease group is Autism Spectrum Disorders (ASD). Studies have shown that IU mediates anxiety symptoms in children with ASD (Boulter et al. 2014). In a study in which 172 adults with ASD were compared with healthy controls, people with ASD had higher IU scores (Hwang et al. 2020). In this study, it was also reported that IU mediated symptoms related to anxiety and insistence of sameness. In addition, it has been suggested that changes in predictive abilities in autism may be associated with greater intolerance of uncertainty (Paula-Pérez and Artigas-Pallarés 2020).

Again, in studies, it has been shown that the prolonged mourning process is related to IU (Boelen 2010). In addition, it was determined that the desire for predictability predicts the symptoms of prolonged grief disorder 6 months after the loss (Boelen et al. 2016). Also, in a study conducted with 215 adults, it was shown that IU was associated with separation anxiety (Boelen et al. 2014). Finally, in a study conducted with 95 adults, it was reported that IU was associated with problematic behaviors such as aggression, alcohol/marijuana use, problematic impulsivity, and problematic risky behaviors in the last 1 month. According to the results of the study, it has been suggested that difficulty tolerating uncertainty will increase the likelihood of individuals engaging in risky behaviors to alleviate negative emotions (Sadeh and Bredemeier 2019).

IU has also been found to be associated with increased comorbidity in studies. Studies have found higher IU scores in patients with GAD and comorbidities of depression (Dupuy and Ladouceur 2008, Yook et al. 2010). Again, in a clinical sample of 218 people, the relationship between comorbidity and IU was shown regardless of the diagnosis (Mahoney and McEvoy 2012).

In a recent meta-analysis, it was reported that the strength of the relationship between IU and symptoms in the study sample ranged from 0.40 (eating disorders) to 0.57 (GAD) (McEvoy et al. 2019). In this meta-analysis, the strength of the relationship of OCD comes after depression, social anxiety, and panic disorder. It refers to the role of IU in many different clinical pictures (Einstein 2014, Shihata et al. 2016, McEvoy et al. 2019).

Different treatment protocols targeting various anxiety disorders and depression are associated with reductions in IU (Dugas et al. 2007, van der Heiden et al. 2012, Boswell et al. 2013, McEvoy and Erceg-Hurn 2016). This information is consistent with the fact that IU is a transdiagnostic risk and the maintenance factor and mechanism of change. In addition, an effective cognitive behavioral therapy (CBT) targeting related factors were established to evaluate IU and symptom severity, and it was found that approximately 20-30% of the participants did not achieve complete remission after treatment. IU remains high in these individuals (Hebert and Dugas 2019). This situation draws attention to the relationship of IU with improvement in symptoms.

Conclusion

When the studies in the literature are examined, it is seen that uncertainty is at the center of especially anxiety-related pathologies and that IU has an important relationship with many clinical pictures. These findings have clinical significance. IU stands out as a potential

transdiagnostic treatment target. Further studies on IU in different groups and including IU in treatment protocols (exposure treatments or cognitive strategies) would potentially be beneficial.

References

Badia P, McBane B, Suter S (1966) Preference behavior in an immediate versus variably delayed shock situation with and without a warning signal. J Exp Psychol Gen, 72:847-852.

Bar-Anan Y, Wilson TD, Gilbert DT (2009) The feeling of uncertainty intensifies affective reactions. Emotion, 9:123-127.

Berenbaum H, Bredemeier K, Thompson RJ (2008) Intolerance of uncertainty: Exploring its dimensionality and associations with need for cognitive closure, psychopathology, and personality. J Anxiety Disord, 22:117-125.

Birrell J, Meares K, Wilkinson A, Freeston M (2011) Toward a definition of intolerance of uncertainty: A review of factor analytical studies of the Intolerance of Uncertainty Scale. Clin Psychol Rev, 31:1198-1208.

Boelen P (2010) Intolerance of uncertainty and emotional distress following the death of a loved one. Anxiety Stress Coping, 23:471-478.

Boelen PA, Reijntjes A (2009) Intolerance of uncertainty and social anxiety. J Anxiety Disord, 23:130-135.

Boelen PA, Reijntjes A, Carleton RN (2014) Intolerance of uncertainty and adult separation anxiety. Cogn Behav Ther, 43:133-144.

Boelen PA, Reijntjes A, Smid GE (2016) Concurrent and prospective associations of intolerance of uncertainty with symptoms of prolonged grief, posttraumatic stress, and depression after bereavement. J Anxiety Disord, 41:65-72.

Boswell JF, Thompson-Hollands J, Farchione TJ, Barlow DH (2013) Intolerance of uncertainty: A common factor in the treatment of emotional disorders. J Clin Psychol, 69:630-645.

Boulter C, Freeston M, South M, Rodgers J (2014) Intolerance of uncertainty as a framework for understanding anxiety in children and adolescents with autism spectrum disorders. J Autism Dev Disord, 44:1391-1402.

Brown M, Robinson L, Campione GC, Wuensch K, Hildebrandt T, Micali N (2017) Intolerance of uncertainty in eating disorders: A systematic review and meta-analysis. Eur Eat Disord Rev, 25:329-343.

Buhr K, Dugas MJ (2006) Investigating the construct validity of intolerance of uncertainty and its unique relationship with worry. J Anxiety Disord, 20:222-236.

Buhr K, Dugas MJ (2009) The role of fear of anxiety and intolerance of uncertainty in worry: An experimental manipulation. Behav Res Ther, 47:215-223.

Calleo JS, Hart J, Björgvinsson T, Stanley MA (2010) Obsessions and worry beliefs in an inpatient OCD population. J Anxiety Disord, 24:903-908.

Carleton RN (2016) Into the unknown: A review and synthesis of contemporary models involving uncertainty. J Anxiety Disord, 39:30-43.

Carleton RN, Duranceau S, Shulman EP, Zerff M, Gonzales J, Mishra S (2016) Self-reported intolerance of uncertainty and behavioural decisions. J Behav Ther Exp Psychiatry, 51:58-65.

Carleton RN, Fetzner MG, Hackl JL, McEvoy P (2013) Intolerance of uncertainty as a contributor to fear and avoidance symptoms of panic attacks. Cogn Behav Ther, 42:328-341.

Carleton RN, Gosselin P, Asmundson GJ (2010) Psychol Assess, 22: 396-406.

Carleton RN, Norton MPJ, Asmundson GJ (2007a) Fearing the unknown: A short version of the Intolerance of Uncertainty Scale. J Anxiety Disord, 21:105-117.

Carleton RN, Sharpe D, Asmundson GJ(2007b) Anxiety sensitivity and intolerance of uncertainty: Requisites of the fundamental fears? Behav Res Ther 45:2307-2316.

Castriotta N, Dozier ME, Taylor CT, Mayes T, Ayers CR (2019) Intolerance of uncertainty in hoarding disorder. J Obsessive Compuls Relat Disord, 21:97-101.

Chorpita BF, Barlow DH (1998) The development of anxiety: the role of control in the early environment. Psychol Bull, 124:3-21.

Comer JS, Roy AK, Furr JM, Gotimer K, Beidas RS, Dugas MJ et al. (2009) The intolerance of uncertainty scale for children: a psychometric evaluation. Psychol Assess, 21:402-411.

Dar KA, Iqbal N, Mushtaq A (2017) Intolerance of uncertainty, depression, and anxiety: Examining the indirect and moderating effects of worry. Asian J Psychiatr, 29:129-133.

Davey GC, Eldridge F, Drost J, MacDonald BA (2007) What ends a worry bout? An analysis of changes in mood and stop rule use across the catastrophising interview task. Behav Res Ther, 45:1231-1243.

De Jong-Meyer, Beck RB, Riede K (2009) Relationships between rumination, worry, intolerance of uncertainty and metacognitive beliefs. Pers Individ Dif, 46:547-551.

Denmark FL (2010) Zeigarnik effect. The Corsini Encyclopedia of Psychology 4th edition(Eds IB Weiner, WE Craighead):1873-1874. Hoboken, NJ, Wiley.

Dugas MJ, Gagnon F, Ladouceur R, Freeston MH (1998) Generalized anxiety disorder: A preliminary test of a conceptual model. Behav Res Ther, 36:215-226.

Dugas MJ, Laugesen N, Bukowski WM (2012) Intolerance of uncertainty, fear of anxiety, and adolescent worry. J Abnorm Child Psychol, 40:863-870.

Dugas MJ, Savard P, Gaudet A, Turcotte J, Laugesen N, Robichaud M et al. (2007) Can the components of a cognitive model predict the severity of generalized anxiety disorder? Behav Ther, 38:169-178.

Dugas MJ, Schwartz A, Francis K (2004) Brief report: Intolerance of uncertainty, worry, and depression. Cognit Ther Res, 28:835-842.

Dupuy JB, Ladouceur R (2008) Cognitive processes of generalized anxiety disorder in comorbid generalized anxiety disorder and major depressive disorder. J Anxiety Disord, 22:505-514.

Ehring T, Watkins ER (2008) Repetitive negative thinking as a transdiagnostic process. Int J Cogn Ther, 1:192-205.

Einstein DA (2014) Extension of the transdiagnostic model to focus on intolerance of uncertainty: a review of the literature and implications for treatment. Clin Psychol, 21:280-300.

Fetzner MG, Asmundson GJ, Carey C, Thibodeau MA, Brandt C, Zvolensky MJ et al. (2014) How do elements of a reduced capacity to withstand uncertainty relate to the severity of health anxiety? Cogn Behav Ther, 43:262-274.

Fetzner MG, Horswill SC, Boelen PA, Carleton RN (2013) Intolerance of uncertainty and PTSD symptoms: Exploring the construct relationship in a community sample with a heterogeneous trauma history. Cognit Ther Res, 37:725-734.

Fourtounas A, Thomas SJ (2016) Cognitive factors predicting checking, procrastination and other maladaptive behaviours: prospective versus inhibitory intolerance of uncertainty. J Obsessive Compuls Relat Disord, 9:30-35.

Freeston MH, Rhéaume J, Letarte H, Dugas MJ, Ladouceur R (1994) Why do people worry? Pers Individ Dif, 17:791-802.

Frenkel-Brunswik E (1949) Intolerance of ambiguity as an emotional and perceptual personality variable. J Pers, 18:108-143.

Gentes EL, Ruscio AM (2011) A meta-analysis of the relation of intolerance of uncertainty to symptoms of generalized anxiety disorder, major depressive disorder, and obsessive-compulsive disorder. Clin Psychol Rev, 31:923-933.

Gray J, McNaughton N (2003) The Neuropsychology of Anxiety: An Enquiry into the Functions of the Septo-Hippocampal System. New York, Oxford University Press.

Greco V, Roger D (2003) Uncertainty, stress, and health. Pers Individ Dif, 34:1057-1068.

Grupe DW, Nitschke JB (2011) Uncertainty is associated with biased expectancies and heightened responses to aversion. Emotion, 11:413-424.

Grupe DW, Nitschke JB (2013) Uncertainty and anticipation in anxiety: an integrated neurobiological and psychological perspective. Nat Rev Neurosci, 14:488-501.

Gu Y, Gu S, Lei Y, Li H (2020) From uncertainty to anxiety: how uncertainty fuels anxiety in a process mediated by intolerance of uncertainty. Neural Plast, 2020:8866386.

Harvey A, Watkins E, Mansell W, Shafran R (2004). A Transdiagnostic Approach to Research and Treatment. New York, Oxford University Press.

Hebert EA, Dugas MJ (2019) Behavioral experiments for intolerance of uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. Cogn Behav Pract, 26:421-436.

Holaway RM, Heimberg RG, Coles ME (2006) A comparison of intolerance of uncertainty in analogue obsessive-compulsive disorder and generalized anxiety disorder. J Anxiety Disord, 20:158-174.

Hong RY, Cheung MWL (2015) The structure of cognitive vulnerabilities to depression and anxiety: Evidence for a common core etiologic process based on a meta-analytic review. Clin Psychol Sci, 3:892-912.

Hwang YI, Arnold S, Srasuebkul P, Trollor J (2020) Understanding anxiety in adults on the autism spectrum: An investigation of its relationship with intolerance of uncertainty, sensory sensitivities and repetitive behaviours. Autism, 24:411-422.

Jacoby RJ (2020) Intolerance of Uncertainty. Washington, DC, American Psychological Association.

Jacoby RJ, Abramowitz JS, Buck BE, Fabricant LE (2014) How is the Beads Task related to intolerance of uncertainty in anxiety disorders? J Anxiety Disord, 28:495-503.

Jacoby RJ, Abramowitz JS, Reuman L, Blakey SM (2016) Enhancing the ecological validity of the Beads Task as a behavioral measure of intolerance of uncertainty. J Anxiety Disord, 41:43-49.

Jacoby RJ, Fabricant LE, Leonard RC, Riemann BC, Abramowitz JS (2013) Just to be certain: Confirming the factor structure of the Intolerance of Uncertainty Scale in patients with obsessive-compulsive disorder. J Anxiety Disord, 27:535-542.

Jensen D, Heimberg RG (2015) Domain-specific intolerance of uncertainty in socially anxious and contamination-focused obsessive-compulsive individuals. Cogn Behav Ther, 44:54-62.

Jensen D, Kind AJ, Morrison AS, Heimberg RG (2014) Intolerance of uncertainty and immediate decision-making in high-risk situations. J Exp Psychopathol, 5:178-190.

Kertz SJ, Stevens KT, McHugh RK, Björgvinsson T (2015) Distress intolerance and worry: The mediating role of cognitive variables. Anxiety Stress Coping, 28:408-424.

Khawaja NG, Yu LNH (2010) A comparison of the 27-item and 12-item intolerance of uncertainty scales. Clin Psychol, 14:97-106.

Krain AL, Hefton S, Pine DS, Ernst M, Xavier Castellanos F, Klein RG et al. (2006) An fMRI examination of developmental differences in the neural correlates of uncertainty and decision-making. J Child Psychol Psychiatry, 47:1023-1030.

Lanzetta JT, Driscoll JM (1966) Preference for information about an uncertain but unavoidable outcome. J Pers Soc Psychol, 3:96-102.

Laugesen N, Dugas M, Bukowski WM (2003) Understanding adolescent worry: The application of a cognitive model. J Abnorm Child Psychol, 31:55-64.

Luhmann CC, Ishida K, Hajcak G (2011) Intolerance of uncertainty and decisions about delayed, probabilistic rewards. Behav Ther, 42:378-386.

Mahoney AE, McEvoy PM (2012a) Trait versus situation-specific intolerance of uncertainty in a clinical sample with anxiety and depressive disorders. Cogn Behav Ther, 41:26-39.

Mahoney AE, McEvoy PM (2012b) A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders. Cogn Behav Ther, 41:212-222.

McEvoy PM, Erceg-Hurn DM (2016) The search for universal transdiagnostic and trans-therapy change processes: Evidence for intolerance of uncertainty. J Anxiety Disord, 41:96-107.

McEvoy PM, Hyett MP, Shihata S, Price JE, Strachan L (2019) The impact of methodological and measurement factors on transdiagnostic associations with intolerance of uncertainty: A meta-analysis. Clin Psychol Rev, 73:101778.

McEvoy PM, Mahoney AE (2011) Achieving certainty about the structure of intolerance of uncertainty in a treatment-seeking sample with anxiety and depression. J Anxiety Disord, 25:112-122.

McEvoy PM, Mahoney AE (2012) To be sure, to be sure: Intolerance of uncertainty mediates symptoms of various anxiety disorders and depression. Behav Ther, 43:533-545.

Motzkin JC, Philippi CL, Wolf RC, Baskaya MK, Koenigs M (2014) Ventromedial prefrontal cortex lesions alter neural and physiological correlates of anticipation. J Neurosci, 34:10430-10437.

Norton PJ, Mehta PD (2007) Hierarchical model of vulnerabilities for emotional disorders. Cogn Behav Ther, 36:240-254.

OCCWG (1997) Cognitive assessment of obsessive-compulsive disorder. Behav Res Ther, 35:667-681.

Oglesby ME, Boffa JW, Short NA, Raines AM, Schmidt NB (2016) Intolerance of uncertainty as a predictor of post-traumatic stress symptoms following a traumatic event. J Anxiety Disord, 41:82-87.

Oglesby ME, Medley AN, Norr AM, Capron DW, Korte KJ, Schmidt NB (2013) Intolerance of uncertainty as a vulnerability factor for hoarding behaviors. J Affect Disord, 145:227-231.

Osmanağaoğlu N, Creswell C, Dodd HF (2018) Intolerance of Uncertainty, anxiety, and worry in children and adolescents: A meta-analysis. J Affect Disord, 225:80-90.

Ottaviani C, Borlimi R, Brighetti B, Caselli G, Favaretto E, Giardini I, Marzocchi C et al. (2014) Worry as an adaptive avoidance strategy in healthy controls but not in pathological worriers. Int J Psychophysiol, 93:349-355.

Paula-Pérez I and Artigas-Pallarés J (2020) Intolerance to uncertainty in autism. Medicina, 80:17-20.

Pleskac TJ, Diederich A, Wallsten TS (2015) Models of decision making under risk and uncertainty. In The Oxford Handbook Of Computational And Mathematical Psychology (Eds JR Busemeyer, Z Wang, JT Townsend, A Eidels):209-231. New York, Oxford University Press.

Renjan V, McEvoy PM, Handley AK, Fursland A (2016) Stomaching uncertainty: Relationships among intolerance of uncertainty, eating disorder pathology, and comorbid emotional symptoms. J Anxiety Disord, 41:88-95.

Robichaud M (2013) Cognitive Behav Ther targeting intolerance of uncertainty: Application to a clinical case of generalized anxiety disorder. Cogn Behav Pract, 20:251-263.

Rosen NO, Knäuper B, Di Dio P, Morrison E, Tabing R, Feldstain A et al. (2010) The impact of intolerance of uncertainty on anxiety after receiving an informational intervention about HPV: a randomised controlled study. Psychol Health, 25:651-668.

Sadeh N. and Bredemeier K (2019) Engaging in risky and impulsive behaviors to alleviate distress mediates associations between intolerance of uncertainty and externalizing psychopathology. J Pers Disord, doi: 10.1521/pedi_2019_33_456.

Sari S, Dağ İ (2009) Belirsizliğe Tahammülsüzlük Ölçeği, Endişe ile İlgili Olumlu İnançlar Ölçeği ve Endişenin Sonuçları Ölçeği'nin Türkçeye uyarlanması, geçerliliği ve güvenilirliği. Anadolu Psikiyatri Derg, 10:261-270.

Sarıçam H, Erguvan FM, Akın A, Akça MŞ (2014) The Turkish short version of the Intolerance of Uncertainty (IUS-12) Scale: The study of validity and reliability. Route Educational and Social Science Journal, 1:148-157.

Sarinopoulos I, Grupe D, Mackiewicz K, Herrington J, Lor M, Steege E, et al. (2010) Uncertainty during anticipation modulates neural responses to aversion in human insula and amygdala. Cereb Cortex, 20:929-940.

Schienle A, Köchel A, Ebner F, Reishofer G, Schäfer A (2010) Neural correlates of intolerance of uncertainty. Neurosci Lett, 479:272-276.

Shihata S, McEvoy PM, Mullan BA (2017) Pathways from uncertainty to anxiety: An evaluation of a hierarchical model of trait and disorder-specific intolerance of uncertainty on anxiety disorder symptoms. J Anxiety Disord, 45:72-79.

Shihata S, McEvoy PM, Mullan BA, Carleton RN (2016) Intolerance of uncertainty in emotional disorders: What uncertainties remain? J Anxiety Disord, 41:115-124.

Shin LM, Liberzon I (2010) The neurocircuitry of fear, stress, and anxiety disorders. Neuropsychopharmacology, 35:169-191.

Simmons A, Matthews SC, Paulus MP, Stein MB (2008) Intolerance of uncertainty correlates with insula activation during affective ambiguity. Neurosci Lett, 430:92-97.

Stanley Budner N (1962) Intolerance of ambiguity as a personality variable 1. J Pers 30:29-50.

Summers BJ, Matheny NL, Sarawgi S, Cougle JR (2016) Intolerance of uncertainty in body dysmorphic disorder. Body Image, 16:45-53.

TDK (2019) Türk Dil Kurumu Sözlükleri. https://sozluk. gov. tr

Thayer JF, Åhs F, Fredrikson M, Sollers JJ III, Wager TD (2012) A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. Neurosci Biobehav Rev, 36:747-756.

Thibodeau MA, Carleton RN, Gómez-Pérez L, Asmundson GJ (2013) "What if I make a mistake?": Intolerance of uncertainty is associated with poor behavioral performance. J Nerv Ment Dis, 201:760-766.

Thibodeau MA, Carleton RN, McEvoy PM, Zvolensky MJ, Brandt CP, Boelen PA et al. (2015) Developing scales measuring disorder-specific intolerance of uncertainty (DSIU): A new perspective on transdiagnostic. J Anxiety Disord, 31:49-57.

Tolin DF, Abramowitz JS, Brigidi BD, Foa EB (2003) Intolerance of uncertainty in obsessive-compulsive disorder. J Anxiety Disord, 17:233-242.

van der Heiden C, Muris P, van der Molen HT (2012) Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. Behav Res Ther, 50:100-109.

Vansteenwegen D, Iberico C, Vervliet B, Marescau V, Hermans D (2008) Contextual fear induced by unpredictability in a human fear conditioning preparation is related to the chronic expectation of a threatening US. Biol Psychol, 77:39-46.

Whalen PJ, L. Shin M, McInerney SC, Fischer H, Wright CI, Rauch SL (2001) A functional MRI study of human amygdala responses to facial expressions of fear versus anger. Emotion, 1: 70-83.

Wheaton MG, Abramowitz SJ, Jacoby RJ, Zwerling J, Rodriguez CI (2016) An investigation of the role of intolerance of uncertainty in hoarding symptoms. J Affect Disord, 193:208-214.

Wheaton MG, Ward HE (2020) Intolerance of uncertainty and obsessive-compulsive personality disorder. Personal Disord, 11:357-364.

Whiting SE, Jenkins WS, May AC, Rudy BM, Davis TE III, Reuther ET (2014) The role of intolerance of uncertainty in social anxiety subtypes. J Clin Psychol, 70:260-272.

Wright KD, Lebell MAA, Carleton RN (2016) Intolerance of uncertainty, anxiety sensitivity, health anxiety, and anxiety disorder symptoms in youth. J Anxiety Disord, 41:35-42.

Yook K, Kim KH, Suh SY, Lee KS (2010) Intolerance of uncertainty, worry, and rumination in major depressive disorder and generalized anxiety disorder. J Anxiety Disord, 24:623-628.

Zlomke KR, Jeter KM (2014) Stress and worry: examining intolerance of uncertainty's moderating effect. Anxiety Stress Coping, 27:202-215.

Zlomke KR, Young JN (2009) A retrospective examination of the role of parental anxious rearing behaviors in contributing to intolerance of uncertainty. J Child Fam Stud, 18:670-679.

Authors Contributions: The authors attest that they have made an important scientific contribution to the study and have assisted with the drafting or revising of the manuscript.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.