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Clinical Psychology

A Systematic Review of the Inter-individual Differences in Avoidance Learning

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Avoidance is typically adaptive given it prevents threat. However, avoidance becomes maladaptive when it is executed out of proportion of threat (i.e., excessive or insufficient avoidance), persists in the absence of threat, or excessively generalizes to other innocuous situations. Although there has been an increase in research in these different processes of maladaptive avoidance, the role of inter-individual differences in these avoidance processes receives less research attention, despite its theoretical and clinical importance. In this systematic review, we summarized the role of inter-individual traits that relate to risk or resilient factors for anxiety-related disorders, trauma-and stressor-related disorders, obsessive-compulsive related disorders, pain related disorders, eating-related disorders, and affective disorders. A majority of the inter-individual differences had an apparent mixed or null effect on the different processes of avoidance. We discussed this lack of evidence of inter-individual differences on avoidance due to a lack of methodological and/or analytical consensus in the field, in addition to a lack of integration of recent findings into existing theories. Recommendations for future research are discussed, with a focus on examining the conditions or experimental parameters for certain inter-individual traits to manifest their effects on avoidance, identifying the nuances of methodological and/or inter-individual differences in avoidance, and a call for integrating recent preliminary findings into existing theories.

1. Introduction

Avoidance refers to behavioral responses that prevent or reduce an anticipated threat (De Houwer & Hughes, 2020). It is typically adaptive as it protects one from harm. However, avoidance may become maladaptive when used rigidly, meaning that it is out of proportion to the outcome, when it persists in the absence of realistic threat, and/or when it inflicts a range of impairments (Craske et al., 2018). In fact, maladaptive avoidance is a core feature in psychopathology including but not limited to clinical anxiety, post-traumatic stress disorders, obsessive-compulsive disorders, pain-related disorders, and substance-use disorders (Meulders, 2020; North, 1999; Robbins et al., 2012; Vlaeyen & Linton, 2000). Thus, it is important to understand the etiology, maintenance, and reduction of maladaptive avoidance.

Numerous laboratory studies examining avoidance employed an aversive/fear and avoidance conditioning paradigm. An initially neutral stimulus becomes a conditioned stimulus (CS+) when it is repeatedly paired with an aversive unconditioned stimulus (US). Eventually, the CS alone can evoke the so-called conditioned fear, as it becomes a warning signal of an imminent threat (Lonsdorf et al., 2017; Pavlov, 1927). In a following avoidance conditioning procedure, performing a designated response (e.g., pressing a specific key) during CS presentation effectively prevents the upcoming US, thus motivates execution of this avoidance response. This response is termed US-avoidance given that it precludes the occurrence of an expected US. Some recent studies (Klein et al., 2021a; Pittig et al., 2014; Wong & Pittig, 2022) examined avoidance response that prevents the onset of CS presentation, thereby also preventing the US that follows. This type of avoidance is termed CS-avoidance (Wong et al., 2022). Both of these avoidance responses are so-called active avoidance given that a response needs to be actively executed to prevent an expected outcome (Krypotos, 2015). Besides active avoidance, other studies exam-

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ined passive avoidance. Passive avoidance refers to inhibiting a behavioral response to prevent an outcome. Tasks, such as the go/no-go task (Donders, 1969) or the foraging task (Bach et al., 2014), have been used for assessing passive avoidance in humans (see Box 1 for the definition of *different types* of avoidance).

Given the clinical importance of understanding maladaptive avoidance, there has been increasing attention on the different maladaptive aspects of avoidance in the past decade. In the literature, we recognized three different processes of maladaptive avoidance behaviors based on the presence (or not) as well as on the level (high or low) of threat. First, *impaired execution of avoidance* refers to when the acquired avoidance response to a CS+ is either excessive or insufficient. Excessive avoidance is out of proportion to the actual threat whereas insufficient avoidance is the lack of avoidance even in the presence of realistic threat. Second, *persistent avoidance* is a response mainly observed during ongoing extinction (i.e., CS+ no longer followed by a US regardless of avoidance response) or after explicitly learning that the CS+ no longer signals a US. It is characterized by a persistence of avoidance despite the absence of threat. Third, *excessive generalization of avoidance* refers to avoidance responses to various stimuli which have never been associated with threat but resemble the threat signal (i.e., CS+) to varying extents. Of note, these processes of avoidance by themselves are seemingly benign. However, they may gain maladaptive quality when these processes inflict severe impairments (e.g., confining oneself at home to avoid various social situations due to excessive generalization) or when these processes preserve maladaptive threat beliefs (e.g., all dogs are aggressive), which are often observed in clinical anxiety.

Impaired execution of avoidance is examined in various laboratory paradigms. For instance, Bach et al. (2014) pioneered a foraging task in which participants had to collect as much task-related points as possible, while avoiding being caught by a virtual predator, which would lead to losing all the points collected during that trial. Threat levels for each trial were manipulated to be high, medium, or low. Low threat levels indicated a lower chase speed of the predator, or a lower probability of the predator waking up for that trial. Thereby, heightened avoidance responses on low threat levels are considered maladaptive, given it is out of proportion to the actual threat at the cost of obtaining task-relevant goals (i.e., costly avoidance). Alternatively, insufficient level of avoidance can be examined during avoidance acquisition in a typical fear and avoidance conditioning procedure (Rattel et al., 2020) or in an avoidant decision task in which participants had to decide whether to approach a threat- or safety-related stimulus (Sheynin et al., 2014). Excessive avoidance has been proposed to be a core feature of anxiety-related disorders, trauma- and stressor-related disorders, obsessive-compulsive and related disorders, and pain-related disorders (Meulders, 2020; North, 1999; Robbins et al., 2012; Vlaeyen & Linton, 2000). In contrast, deficient level of avoidance is proposed to be a core feature of substance use disorders (Bijttebier et al., 2009).

Another maladaptive aspect of avoidance is its persistence even in the absence of threat. Persistent avoidance is typically tested in one of the two forms. On the one hand, the CS is presented during extinction while the option to avoid the US is available. In this case, persistent avoidance to the CS renders individuals to attribute the absence of threat to their successful avoidance response and this in turn prevents learning that the CS is no longer signaling threat (i.e., protection from extinction; P. F. Lovibond et al., 2009) On the other hand, persistent avoidance can also be tested after response-prevention extinction (i.e., CS presented under extinction without the option to avoid). In other words, to test whether avoidance persists even individuals are given the opportunity to learn that the CS no longer signals threat. Empirical evidence shows that even when participants have had the opportunity to learn that the CS no longer signals threat after response-prevention extinction, avoidance to it persists when the option to avoid becomes available again (e.g., Gatzounis & Meulders, 2020; Pittig & Wong, 2022; Vervliet et al., 2017; Vervliet & Indekeu, 2015), thereby gaining its maladaptive quality. Besides the standard extinction procedure, US-devaluation is also employed to test persistent avoidance or the acquisition of habitual avoidance, although this method is more commonly tested in animals than humans. US-devaluation refers to a process that devalues the intensity of the US, thus devaluating the US memory trace when the CS is presented again (Rescorla & Heth, 1975). Preliminary evidence has showed the persistence of behavioral avoidance to a CS even after its outcome had been devalued (e.g., Flores et al., 2018; Gillan et al., 2014). Persistent avoidance under specific conditions, like after overtraining, shifts more towards habitual processes. Habitual avoidance is thought to be a reflexive response that is evoked automatically in the presence of a devalued CS+. Persistent avoidance has been proposed to be a maladaptive characteristic in anxiety-related disorders, trauma- and stressor-related disorders, obsessive-compulsive and related disorders, and pain-related disorders (Meulders, 2020; North, 1999; Pittig et al., 2020; Robbins et al., 2012).

A third maladaptive aspect of avoidance is the excessive generalization of avoidance. Empirical evidence has suggested that patients with clinical anxiety (Lissek et al., 2010, 2014) and post-traumatic stress disorders (Kaczkurkin et al., 2017) show excessive fear generalization. Preliminary evidence has also suggested that individuals at risk of developing clinical anxiety exhibit excessive fear generalization (e.g., Garcia & Zoellner, 2016; Haddad et al., 2012; Morriss et al., 2016; Wong & Lovibond, 2018, 2021; see also Sep et al., 2019). Although less extensively investigated, excessive generalization of avoidance can be maladaptive in three ways. First, avoidance is unnecessary given that these novel stimuli or situations are innocuous. Second, overgeneralization of avoidance leads to avoidance to a wide range of situations or stimuli, inflicting a lot of impairments in daily life. Third, avoidance to an excessive range of stimuli may lead to increasing chances of protection from extinction to a wide range of stimuli. Laboratory studies have examined generalization of avoidance via

Box 1.

Definition of avoidance

Avoidance generally refers to behavioral responses that prevent or reduce the onset of a threatening or feared outcome. Avoidance is typically adaptive as it largely prevents or reduces harm. However, it becomes maladaptive when it is featured by the following characteristics: 1) impaired execution, which can be manifested excessively out of proportion of threat (e.g., executing avoidance in which its cost outweighs the level of threat it prevents), or the lack of avoidance responses in the presence of realistic threat, 2) avoidance persists in the absence of realistic threat and sustains maladaptive threat beliefs, 3) avoidance excessively generalizes to other innocuous stimuli/situations that resemble the feared stimulus/situation, and when the aforementioned avoidance is costly and inflicts various impairments. There are different forms of avoidance, which can be measured in the laboratory differently.

US-avoidance vs. CS-avoidance

Avoidance can be generally classified into safety behaviors (i.e., behavior that prevents an imminent threat) and avoidance of learnt fear (i.e., behavior that prevents a warning signal, which in turn prevents the threat that follows). Safety behaviors refer to responses that are executed when confronting a warning signal, which prevents a perceived imminent threat. For instance, a socially anxious individual may avoid eye contact during a speech, which is believed to prevent getting negatively criticized. Safety behavior, in a conditioning framework, is modelled by a response executed during CS presentation that reduces the chance of US onset (i.e., US-avoidance). Avoidance of learnt fear refers to responses that reduces the probability of the onset of a feared stimulus, thus also effectively reducing the probability of the threat that follows (Wong et al., 2022). For instance, the aforementioned socially anxious individual may avoid attending a conference, thus effectively preventing the need to give a speech and the perceived threat that follows. In the laboratory, avoidance of learnt fear can be operationalized during the presentation of a distal signal that predicts an CS+. Thus, the onset of this CS+ and the US that followed are prevented. Of note, while potential mechanisms underlying US-avoidance have been proposed (e.g., Expectancy model; Lovibond, 2006; Safety signal account; Weisman & Litner, 1972) and empirically tested (e.g., Fernando et al., 2014; P. F. Lovibond et al., 2009; Pittig, 2019; Vervliet et al., 2017; (Wong & Pittig, 2022)), little is known about potential mechanisms underlying CS-avoidance (e.g., CS-avoidance executed due to US prevention, preventing distress evoked by the CS+, or a combination of both)

Active and passive avoidance

Avoidance can be further divided into *how* it is executed, namely active avoidance and passive avoidance. Active avoidance refers to actively executing a designated response to prevent an aversive outcome, whereas passive avoidance refers to withholding a response to prevent an aversive outcome. Active avoidance can be generally assessed via a traditional fear and avoidance conditioning framework, operationalized by actively executing a designated avoidance response (e.g., pressing a key). Passive avoidance, on the other hand, incorporate various procedures into the conditioning framework, like the go/no-go task (Donders, 1969) or the virtual predator task (Bach et al., 2014).

	CS-avoidance	US-avoidance
Active avoidance	Executing a response to prevent CS presentation (Klein et al., 2021a; Wong & Pittig, 2022))	Executing a response during CS+ presentation that prevents a US (e.g., P. F. Lovibond et al., 2009; Pittig, 2019)
Passive avoidance	Inhibiting approaching responses to situations or stimuli that signal a CS (e.g., Cornwell et al., 2013; Rinck et al., 2016)	Inhibiting a response during CS+ presentation that prevents a US (e.g., go/no-go task; Levita et al., 2012)

Goal-directed or habitual avoidance:

Goal-directed avoidance refers to avoidance that depends on the motivational value of the outcome (e.g., is the outcome aversive enough to evoke avoidance?) and the response outcome contingency. That means, goal-directed avoidance is executed with the aim to prevent an expected aversive outcome. However, after extensive instrumental training trials (i.e., overtraining), goal-directed avoidance shifts to habitual avoidance (Balleine & O'Doherty, 2010). Habitual avoidance refers to reflexive avoidance that is not determined by the outcome, but rather the response is thought to be automatically evoked by the CS. Habitual avoidance gains its maladaptive quality when it inflicts impairments and persists in the absence of threat (e.g., Gillan et al., 2014). Empirical evidence has shown that goal-directed US-avoidance becomes habitual due to overtraining (e.g., Flores et al., 2018; Glück et al., 2021; Zwosta et al., 2018). However, there is no study to date examining whether CS-avoidance can become habitual. More recently, the thought of habit being a response under the control of CS has been questioned (e.g., Buabang et al., 2023; De Houwer et al., 2018).

Costly or low-cost avoidance

Executing avoidance can incur minimal or substantial costs. Cost can be referred to as the effort to execute avoidance, or impairments inflicted by the execution of avoidance. An example for low-cost avoidance can be looking both ways before crossing a one-way street. Costly avoidance can be socially anxious individuals avoiding social interactions at the cost of jeopardizing interpersonal relationships. The incurred cost/impairments inflicted by avoidance is believed to be one major feature that separates maladaptive and adaptive avoidance (e.g., North et al., 2004; O'Donnell et al., 2007; Pittig et al., 2021; White & Barlow, 2002). In the laboratory, cost of avoidance can be operationalized tangibly (e.g., financial cost; Wong & Pittig, 2021) or intangibly (e.g., time, task-related goals; Lemmens et al., 2021; Rattel et al., 2017).

a perceptual pathway (e.g., (Arnaudova et al., 2017; Hunt et al., 2019; Lommen et al., 2010)), that is, whether avoidance generalizes to novel stimuli along the same stimulus dimension with the CS+ that vary in certain perceptual fea-

tures (e.g., color, spatial location). More recent studies also examine the generalization of avoidance via a higher-order conceptual pathway, for instance, to novel stimuli that belong to the same category of the CS+ (e.g., Dymond et al., 2011, 2014; Kloos et al., 2022; Wong & Pittig, 2020), or to novel stimuli that are semantically related to the CS+ (e.g., Boyle et al., 2016).

Despite avoidance and its adaptive and maladaptive features have garnered increasing attention in the past decade, little studies focus on the role of individual differences in avoidance. The literature has recently focused on how individual differences, such as temperament or biological factors that differ *between* individuals, are linked to the etiology and maintenance (or resilience) of psychopathology (see Lonsdorf & Merz, 2017). For instance, vulnerability factors were linked to failure in fear inhibition to safety cues (e.g., Chan & Lovibond, 1996; Kindt & Soeter, 2014; Sjouwerman et al., 2020), excessive fear generalization (e.g., Haddad et al., 2012; Stegmann et al., 2019; Wong & Lovibond, 2018), or resistant to fear extinction (e.g., Armstrong & Olatunji, 2017; Lambert et al., 2021). Given the complex bidirectional relationship between fear and avoidance (Pittig et al., 2020), much structured research is needed for the field. Thereby, examining the link between vulnerability factors and maladaptive avoidance provides further understanding between the interplay of vulnerability and psychopathology, e.g., whether the link between vulnerability factors and maladaptive avoidance predicts the onset of psychopathology. Furthermore, understanding individual differences in maladaptive avoidance may help inform why some individuals are non-responsive to treatments (e.g., enhanced protection from extinction), or help developing treatments that are more effective for individuals or groups characterized by certain features. Studying the individual differences in maladaptive avoidance can also further the understanding of the nuances of maladaptive features in psychopathology. Preliminary evidence suggests that even among clinical populations, individual differences contribute to different symptoms severity and frequency of maladaptive avoidance (Pittig et al., 2021; Sheynin et al., 2017). Last but not least, it is important to understand whether certain resilient individual traits buffer against the different processes of maladaptive avoidance or promote the adaptive prospects of avoidance.

Thereby, this systematic review aims at summarizing studies that examined the role of individual differences in avoidance responses, providing a better understanding on how certain individual differences may potentiate or reduce avoidance, thereby leading to maladaptive or adaptive behavioral responses.

2. Method

The literature search was run according to PRISMA guidelines (D. Moher et al., 2009; David Moher et al., 2015) using two databases including Psycinfo and Web of Science.

The first and the last author (AHKW & MA) conducted the initial search. The terms for the search included ("avoidance" OR "fear avoidance" OR "fear-related avoidance" OR "behavioral avoidance" OR "behavioural avoidance" OR "avoidance acquisition" OR "avoidance learning" OR "avoidance conditioning" OR "avoidance extinction" OR "avoidance generalization" OR "avoidance test" OR "avoidant decision" OR "costly avoidance" OR "cost avoidance" OR "human avoidance" OR "active avoidance" OR "passive avoidance" OR "approach-avoidance conflict" OR "free operant conditioning" OR "classical conditioning") AND ("individual difference" OR "risk factor" OR "trait anxiety" OR "intolerance of uncertainty" OR "behavioral inhibition" or "behavioural inhibition" OR "anxiety sensitivity" OR "BIS/BAS" OR "neuroticism") AND ("fear learning" OR "fear acquisition" OR "fear conditioning" OR "threat conditioning" OR "conditioned" OR " conditioned fear" OR "phasic fear" OR "associative learning"). The search returned 315 articles in Psycinfo and 423 articles in Web of Science.

The first and the last author (AHKW & MA) then screened the abstracts of the articles and included them for further screening if they met all the following inclusion criteria: 1) studies using a de novo fear/aversive conditioning protocol, meaning that we included studies that employed a CS that was innately threat neutral, but only became an aversive signal in the laboratory task 2) studies that examined avoidance as one of their outcome measures; 3) studies conducted in humans; 4) studies not conducted in children or adolescents for the entire sample; and 5) empirical studies (i.e., non-review papers).

After the initial screening of the abstracts, 134 articles remained. The following authors (AHKW, AA, MM, MJW, & MA) then read the articles in detail and checked whether the remaining articles assessed the role of individual differences on avoidance. In case of disagreement in this selection process, the first and last author (AHKW & MA) resolved it via discussion. After this detailed evaluation, 47 articles remained. Finally, we manually included 7 additional articles that were overlooked in the initial search (e.g., individual differences in avoidance were reported in Supplementary Materials) or suggested by other experts in the field. All 7 articles met all inclusion criteria. In sum, this review consisted of 54 articles.

3. Overview of the Findings

The articles in this systematic review examined a variety of inter-individual traits on avoidance (see Glossary for an overview for all inter-individual traits included in this systematic review). We classified these traits into five categories: 1) anxiety-, stress-, affect-related traits, 2) demographic-related variables, 3) pain-related traits, 4) disgust-related traits, and 5) avoidance resilient-related traits. The first category covers individual traits that are risk factors for the development of clinical anxiety, trauma- and stressor-related disorders, and affective disorders. The second category covers demographic factors such as age that contribute to the development of clinical anxiety. The third category covers factors related to pain-related disorders and studies that employed a painful outcome. The fourth category covers factors related to disgust-relevant disorders, such as obsessive-compulsive disorder and eating disorders, and/or studies that used disgust-related out-

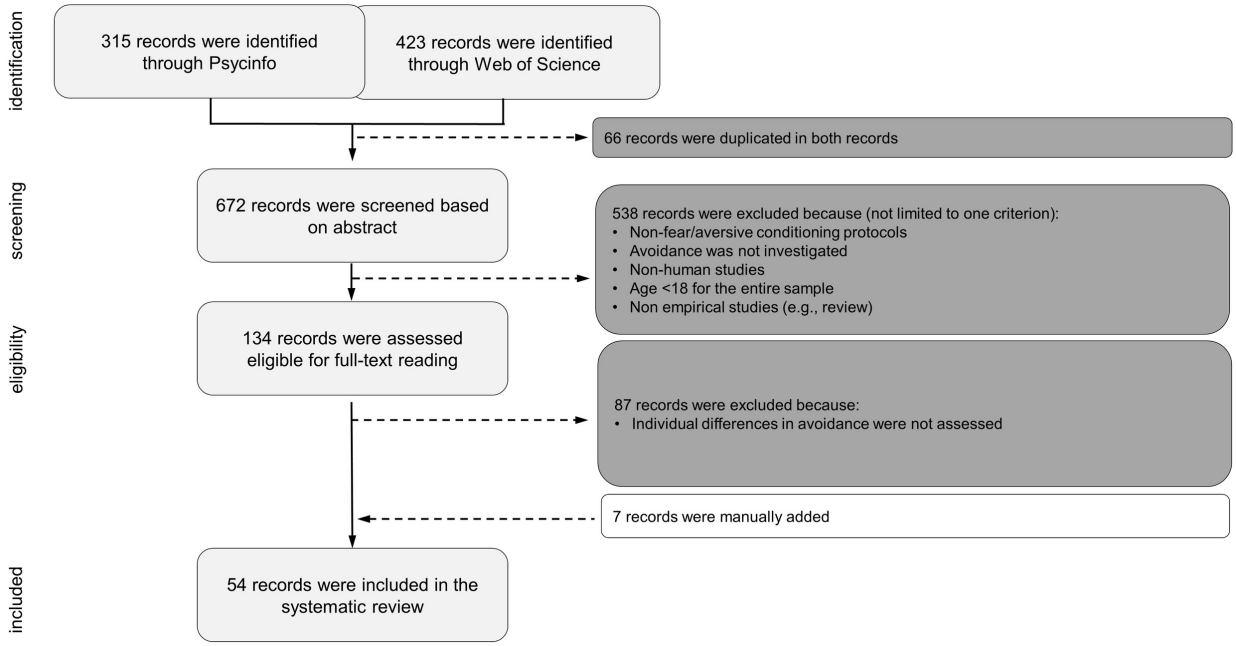

Figure 1. Flow-chart for the screening processes.

come. The fifth category covers factors that are resilient to the development of clinical anxiety. For the detailed experimental parameters of all 54 reviewed studies, see Table 1.

4. Results

4.1. Anxiety-, stress-, and affect-related traits

4.1.1. Trait anxiety

Trait anxiety refers to a stable predisposition factor to experience heightened fear and anxiety across situations, and a tendency to experience psychological distress and physiological symptoms (see Glossary for more details). In a go/no-go task (Levita et al., 2012), participants were instructed to respond to a go-CS+ trial and inhibited their responses to a no-go-CS+ trial; correct responses to each trial type prevented an upcoming US. Trait anxiety was found to be negatively associated with reaction time to go-CS+ trials, suggesting that high trait anxiety is associated with a strong tendency for active US-avoidance. In a decision-making paradigm, Pittig & Scherbaum (2020) found that trait anxiety had no effect on avoiding a risky option (an option that predicted US onset) when the competing reward was low. However, when the reward increased, trait anxiety was associated with increased avoidance of the risky option. Similarly, Lemmens et al. (2021) found that trait anxiety was associated with costly US-avoidance to the CS+ (i.e., executing US-avoidance costs more time to finish the task). Other studies found that trait anxiety is also linked to low-cost US-avoidance: Flores et al. (2018) and Hulsman et al. (2021) found that trait anxiety is positively linked with a general increase in low-cost US-avoidance to all CSs. Furthermore, Flores et al. (2018, 2020) increased threat uncertainty by manipulating temporal variation of US delivery during CS+ presentations; the uncertain timing of US onset encouraged participants to execute the avoidance response as much as they wanted during CS presentation. They found that trait anxiety was associated with a longer time span of avoidance responses.

In contrast, some studies found no effect of trait anxiety on the execution of low-cost US-avoidance in a conventional fear and avoidance conditioning paradigm (Andreatta et al., 2017; Cobos et al., 2022; Gorka et al., 2016; Morriss et al., 2019; Patterson et al., 2019; San Martín et al., 2020; Xia et al., 2017), as indexed by the frequency of US-avoidance responses to the CS+.

Relatively little studies examined the effect of trait anxiety on the acquisition of *passive* US-avoidance. Using an adapted foraging task from Bach et al. (2014), Vogel and Schwabe (2019) instructed participants to collect as much virtual tokens as possible on each trial while avoiding being caught by a virtual predator (the CS+), which resulted in losing all tokens collected for that trial. Results showed that trait anxiety was associated with a decrease in tokens collected; this pattern was interpreted as trait anxiety being linked to increased passive avoidance, as participants inhibited their approach responses (i.e., collecting tokens) to avoid threat.

Under extinction test, trait anxiety was associated with more frequent low-cost US-avoidance to the CS+ (Andreatta et al., 2017). Furthermore, Pittig et al. (2014) found that trait anxiety positively moderated the link between conditioned fear and costly CS-avoidance to the CS+, suggesting that trait anxiety facilitates the relationship between fear and avoidant decisions to the CS+ under extinction. In contrast, some studies found no significant association between trait anxiety and US-avoidance to the CS+ (Rattel et al., 2017; Xia et al., 2017), to the CSs (Cobos

Table 1. Overview of the experimental settings of the reviewed studies separated for each section.

Study	*Sample*	*Age (sd)*	*Sex*	*Inter-individual differences*	*US*	*CS*	*Cost of avoidance*	*Operationalization of avoidance*	*When was avoidance assessed?*
Anxiety-, stress-, and affect-related traits									
Andreatta et al. (2017)	28	21.68 (3.20)	18 ♀, 20 ♂	Trait anxiety (STAI)	Electric stimulation	Geometrical shapes	Low-cost	Button press in the presence of a CS	Acquisition; Under extinction
Arnaudova et al., 2017	S1: 58 S2: 58	21.91 (2.66) 21.95 (4.02)	39 ♀, 19 ♂ 39 ♀, 19 ♂	Neuroticism (EPQ-N)	Electric stimulation	Geometrical shapes	Low-cost	Button press in the presence of CSs and GSs; reaction time to avoidance or approach CSs and GSs	Generalization
Cobos et al. (2020)	75	20.4 (19-24)	69♀, 6♂	Intolerance of uncertainty (IUS); Trait anxiety (STAI); Distress tolerance (DTS)	Aversive noises	Fractal images	Low-cost	Button presses in the presence of CSs	Acquisition; Under extinction
de Haart et al. (2021)	502	39.80 (9.95)	25 ♀, 477 ♂	Post-traumatic stress symptoms (PCL-5)	Negative images	Colored lamps	Low-cost	Button press in the presence of CSs	Acquisition
Dymond et al. (2014)	64	18-30 (-)	50 ♀, 14 ♂	Spider phobia FSQ	Spider images	Nonsense words	Low-cost	Button press in the presence of CSs and GSs	Acquisition; Generalization
Evans et al. (2019)	73	19.58(1.63)	39 ♀, 34 ♂	Social anxiety (SIAS)	Electric stimulation	Facial stimuli	Low-cost	Button press in the presence of CSs	Acquisition
Fannes et al. (2008)	58	22 (18-55)	29 ♀, 29 ♂	Anxiety sensitivity (ASI); Negative affect (PANAS)	CO_2 enrichment	Odors	Costly (lowered ventilation)	Lowered ventilation in the presence of CSs	Acquisition; Under extinction
Flores et al. (2018)	156	19 (-)	122 ♀, 34 ♂	Intolerance of uncertainty (IUS); Trait anxiety (STAI)	Aversive noises	Fractual images	Low-cost	Button presses in the presence of CSs	Acquisition; After extinction; Under extinction
Flores et al. (2020)	78	19 (-)	60 ♀, 18 ♂	Intolerance of uncertainty (IUS); Trait anxiety (STAI)	Aversive noises	Fractual images	Low-cost	Button presses in the presence of CSs	Acquisition; After extinction; Under

									extinction
Garofalo & Robbins (2017)	38	25.18 (5.69)	18 ♀, 20 ♂	Behavioral inhibition scale (BIS)	Aversive noises	Scenarios of different galaxies	Low-cost	Button presses in the presence of CSs	Under extinction
Gillan et al. (2014)	pat: 25 cnt: 25	pat: 40.6 (13.45) cnt: 41.0 (13.22)	pat: 14 ♀, 11 ♂ cnt: 14 ♀, 11 ♂	Obsessive-compulsive symptoms (Y-BOCS)	Electric stimulation	Colored geometrical shapes	Low-cost	Press of a pedal	After extinction; Under extinction
Glotzbach et al. (2012)	21	23.40 (4.20)	15 ♀, 16 ♂	Trait anxiety (STAI)	Electric stimulation	Contexts in Virtual Reality	Low-cost	Decision of entering contexts	Under extinction
Gorka et al. (2016)	59	19.22 (1.22)	36 ♀, 23 ♂	Trait anxiety (STAI); Trait aggression (BPAQ)	Electric stimulation	Geometric shapes	Low-cost	Releasing a button in the presence of CSs	Acquisition
Hulsman et al. (2021)	343	25.52 (5.09)	78 ♀, 265 ♂	Trait anxiety (STAI); Sex	Electric stimulation	Third-person avatar	Costly (monetary cost)	Button press in the presence of CSs	Acquisition
Hunt et al. (2019)	102	20.42(3.22)	63 ♀, 39 ♂	Anxiety sensitivity (ASI); Intolerance of uncertainty (IUS)	Electric stimulation	Geometric shapes	Costly (hypothetical cost)	Button press in the presence of CSs and GSs	Acquisition; Generalization
Klein et al. (2021a)	60	24.94 (18-43)	43 ♀, 17 ♂	Trait anxiety (STAI - Form X); Intolerance of uncertainty (IUS)	Aversive noises	Colored lamps	Low-cost	Button press in the presence of CSs and higher-order CSs	After extinction
Krypotos et al. (2022)	S1: 45 S2: 47 S3: 46	20.81 (2.9)	109♀, 29♂	Intolerance of uncertainty (IUS); Neuroticism (EPQ)	Electric stimulation	Squares in different quadrants	Costly (hypothetical cost)	Moving joystick to one of the quadrants	Acquisition
Lemmens et al. (2021)	90	20.07(4.38)	76 ♀, 14 ♂	Trait anxiety (STAI); Distress tolerance (DTS); Intolerance of uncertainty (IUS)	Aversive film with aversive noise	Colored screen	Costly (time-cost)	Button press in the presence of CSs	Acquisition; After extinction; Under extinction
Leng et al. (2022)	200	25.82 (6.8)	70♀, 130♂	Anhedonia (TEPS); Depressive symptoms (QIDS-SR16); Trait anxiety (STAI); Intolerance of uncertainty (IU); Distress tolerance (DTS)	Negative images	Colored lamps	Low-cost	Button press in the presence of CSs	Acquisition
Levita et al.	20	23.7 (4.8)	12 ♀, 8 ♂	Trait anxiety (STAI)	Aversive	Fribbles	Low-cost	Active button	Acquisition

(2012)					images			presses or inhibiting button presses in the presence of CSs	
Lommen et al. (2010)	48	21.65 (2.37)	25♀, 23♂	Neuroticism (ERQ-N)	Electric stimulation	Colored circles	Low-cost	Button press in the presence of CSs and GSs	Generalization
Ly & Roelofs (2009)	48	LSA: 21.55 (3.76); HSA: 19.42 (1.96)	24♀,24♂	Social anxiety (BFNE)	Electric stimulation & Negative vocalization	Facial stimuli (male)	Low-cost	Button press in the presence of CSs	Acquisition
Morriss et al. (2018)	53	19.7	48♀, 5♂	Trait anxiety (STAI); Intolerance of uncertainty (IUS)	Aversive noise	Colored squares	Low-cost	Button press in the presence of CSs	Acquisition; After extinction
Nord et al. (2018)	MDD: 26 Cnt: 28	MDD: 27.96(8.75) Cnt: 26.79(8.48)	MDD: 10♀;16♂ Cnt: 13♀;15♂	Depressive symptoms (HAM-D, BDI)	Loss of points	Fractal images	Costly (monetary cost)	Button press	Under extinction
Papalini et al. (2021)	42	19.5(6.48)	35♀, 7♂	Distress tolerance (DTS)	Electric stimulation	Colored lamps	Low-cost	Button press in the presence of CSs	After extinction
Patterson et al. (2019)	S1:189 S2: 112	S1:20.31 (1.81) S2: 20.54 (1.59)	S1:148 ♀, 41♂ S2: 90♀, 22♂	Early life stress (ELS); Trait anxiety (STAI); Depression (BDI-II); Age; Sex	Aversive noise	Fractual images	Low-cost	Active button presses or inhibiting button presses in the presence of CSs	After extinction
Pittig et al. (2021)	Pat: 40 Cnt: 40	Pat: 29.73 (9.22) Cnt: 28.45 (8.62)	Pat: 26♀, 14♂ Cnt: 26♀, 14♂	Anxiety disorders (Mini-DIPS); Anxiety symptoms (PROMIS; STAI)	Electric stimulation	Geometric shape	Costly (monetary cost)	Button press in the presence of a CS	Acquisition; Under extinction
Pittig et al. (2018)	Fearful: 42 Non-fearful: 42	Fearful: money 24.35(9.01); social 21.55(3.00) Non-fearful: money 21.4 (3.58); social 22.41(1.76)	Fearful: money 17♀, 3♂; social 19♀, 3♂; Non-fearful: money 14♀, 6♂; social 13♀, 9♂	Spider phobia (FSQ)	Spider images	Decks	Costly (monetary cost *or* social cost)	Button press in the presence of decks	Acquisition
Pittig &	H-anx:	H-anx: 22.16(5.15)	H-anx: 33♀,	Trait anxiety (STAI;	Electric	Labels of US	Costly	Mouse press in	Acquisition

Scherbaum (2020)	37 L-anx: 37	L-anx: 21.35(3.35)	4♂ L-anx: 27♀, 10♂	NEO-PI-R)	stimulation	percentage	(hypothetical cost)	the presence of CSs	
Pittig et al. (2014)	S1: Fear: 30 Cnt: 25 S2: 81	S1: Fear: 21.78(3.60) Cnt: 20.64(4.42) S2: 20.91(2.71)	S1: Fear 22♀, 8♂; Cnt: 16♀, 9♂; S2: 60♀, 21♂;	Trait anxiety (NEO-PI-R)	Electric stimulation	Facial stimuli	Costly (hypothetical cost)	Button press in the presence of decks that signaled the CSs	Under extinction
Rattel et al. (2017)	71	24.01 (7.84)	71♀, 0♂	Trait anxiety (STAI)	Electric stimulation combined with aversive noise	Geometric shape	Costly (time-cost)	Button press in the presence of CSs	Under extinction
Rinck et al. (2016)	S1:21 S2: Fearful: 19 Cnt: 23	S1: 23.3 (16-28) S2: Fearful: 19.6(2.5) Cnt: 18.6(0.8)	S1: 17♀, 4♂ S2: Fearful: 17♀, 2♂ Cnt: 23♀, 0♂	Spider fearfulness (SAS)	Virtual spiders	Virtual rooms	Costly (task-related goal)	Decision to enter the rooms	Acquisition
Sebold et al. (2019)	55	21 (0.0)	0 ♀, 55 ♂	Depressive symptoms (HADS)	Loss of reward	Chinese symbols presented with a disgust-related or neutral-related background	Costly (monetary cost) Also monetary reward gained from appetitive CS	Choice between win-associated or loss-associated CS vs. no change	Acquisition
Sheynin et al. (2017)	Combat-vet: 27 Non-combat-vet: 47 Civilian: 45	Combat-vet: 52.2 (11.0) Non-combat-vet: 55.7 (10.6) Civilian: 47.5 (16.4)	Combat-vet: 2♀, 25♂; Non-combat-vet: 10♀, 37♂; Civilian: 30♀, 15♂;	Post-traumatic stress symptoms (PCL-C; CES); Sex	Loss of points	Enemy mothership	Costly (hypothetical cost)	Hiding in shelter in the presence of a CS	Acquisition; Under extinction
Vogel & Lars (2019)	80	25.0 (3.79)	40♀, 40♂;	Trait anxiety (STAI); Physical aggression (German aggression	Loss of points	Virtual predator	Costly (monetary cost)	Latency of foraging points in the presence of a	Acquisition

				questionnaire)				CS	
Wake et al. (2021)	80	20.1 (1.87)	80♀	Social anxiety (SPIN); Trait anxiety (STAI); Intolerance of uncertainty (IUS)	Electric stimulation & Negative vocalization	Facial stimuli (Female)	Low-cost	Button press in the presence of CSs	Acquisition; After extinction
Xia et al. (2017)	168	21.67(5.72)	106♀, 62♂	Trait anxiety (STAI); Intolerance of uncertainty (IUS); Sex	Electric stimulation	Geometric shapes	Low-cost	Button press in the presence of CSs	Acquisition; Under extinction
Wong & Pittig (2022)	45	26.62(7.48)	31♀;14♂	Trait anxiety (DASS-21); Intolerance of uncertainty (IUS)	Electric stimulation	Geometric shapes	Costly (monetary cost)	Avoidance ratings along a dimensional scale	Under extinction
Zuj et al. (2020)	99	20.7 (2.0)	100%group: 23♀, 10♂ 50%group: 19♀, 14♂ 0%group: 24♀, 9♂	Intolerance of uncertainty (IUS); Trait anxiety (STAI); Experiential avoidance (BEAQ)	Electric stimulation	Geometric shapes	Low-cost	Button press in the presence of CSs	After extinction; Under extinction
Demographic-related variables									
Cooper et al. (2022)	170	20.3 (2.9)	85♀, 85♂	Gender; Trait anxiety (STAI); Intolerance of uncertainty (IUS); Anxiety sensitivity (ASI); Experiential avoidance (MEAQ)	Electric stimulation	Circles of different sizes	Costly (hypothetical cost)	Button press in the presence of CSs/GSs	Generalization; Under extinction
Klein et al. (2021b)	Adul.: 39 Adol.: 44	Adul.: 26.0 (4.12) Adol.: 16.4 (1.25)	Adul.: 25 ♀, 14 ♂ Adol.: 27 ♀, 17 ♂	Age	Aversive sound	Colored desk lamps	Low-cost	Button press in the presence of CS and GSs	Acquisition; After extinction; Generalization
Sheynin et al. (2014)	122	20.7 (3.60)	66 ♀, 56 ♂	Sex	Loss of points	spaceship	Costly (hypothetical cost)	Time spent hiding	Acquisition; Under extinction
Pain-related traits									
Meulders et al. (2016)	50	24.9 (6.90)	14 ♀, 36 ♂	Fear of pain (FPQ)	Electric stimulation	Trajectories with different resistance	Costly (physical effort)	Choice of trajectories with robotic arm	Acquisition; Under extinction
Nishi et al. (2019)	44	20.9 (2.10)	31 ♀, 13 ♂	Harm avoidance score (TCI-R); trait	Electric stimulation	Rectangle	Costly (monetary	Stop coloring the rectangle	Acquisition; Extinction

				anxiety (STAI)			cost)		
Disgust-related traits									
Armstrong et al. (2014)	Disgust US: 55 Negative US: 65	Disgust US: 19.36(1.28) Negative US: 19.49(1.11)	Disgust US: 42♀;13♂; Negative US: 50♀;15♂;	Disgust sensitivity (DS-R)	Disgust US: Videos of individuals vomiting Negative US: Videos of motor vehicle accidents	Facial stimuli	Low-cost	Eye movement	Acquisition; Under extinction
Berg et al. (2021)	65	19.4 (1.29)	46 ♀, 19 ♂	Disgust promptness (DPSS-R)	Electric stimulation vs. disgust videos	Geometrical shapes	Costly (hypothetical cost)	Choice between long and short path in the presence of CSs	Acquisition; Generalization
Papalini et al. (2021)	275	18.5 (1.08)	237 ♀, 38 ♂	Drive for thinness; bulimia body dissatisfaction (EDI-II)	Aversive pictures	Colored lamp desk	Low-cost	Mouse click in the presence of CS+ vs. CS-	Acquisition
Shook et al. (2019)	S1: 132 S2: 133	S1: 20.3 (4.48) S2: 19.6 (1.69)	S1: 74 ♀, 58 ♂ S2: 83 ♀, 50 ♂	Disgust sensitivity (TDDS; DS-R; DPSS)	Loss of points	Colored beans	Costly (hypothetical cost) Also gain of hypothetical reward from appetitive CS	Choice between win-associated beans vs. loss-associated beans	Acquisition
Avoidance resilient-related traits									
Hunt et al. (2017)	109	20.03(2.80)	71♀, 38♂	Distress endurance & distress suppression (MEAQ); Trait anxiety (STAI)	Electric stimulation	Geometric shapes	Costly (hypothetical cost)	Button press in the presence of CSs and GSs	Acquisition; Generalization
Norbury et al. (2015)	S1: 45 S2: 28	S1: 24.3 (3.55) S2: 22.3 (2.74)	S1: 28 ♀, 17 ♂ S2: 0 ♀, 28 ♂	Sensation seeking (SSS-V)	Intense sensory stimulation	Two types of fractals	Depending on trial type, avoidance is costly (monetary cost), low-cost, or rewarding (monetary	Choice between CS+ and CS-	Acquisition

							reward)		
Rattel et al. (2020)	163	21.2 (2.4)	n.a.	Sensation seeking (SSS-V); neuroticism (NEO-PI-R)	Electric stimulation	Circle, square, triangle	Costly (time cost)	Choice between long vs. short path in the presence of one CS	Acquisition; Under extinction
San Martin et al. (2020)	101	18.33 (NA)	91♀, 10♂	Distress tolerance (DTS); Trait anxiety (STAI); Intolerance of uncertainty (IUS)	Electric stimulation	Colored lamps	Low-cost	Button press in the presence of CSs and GSs	Acquisition; Generalization
Sheynin et al. (2019)	pat: 19 cnt: 16	pat: 46.0 (11.42) cnt: 48.4 (6.95)	pat: 19 ♂ cnt: 16 ♂	Alcohol-related disorders (Structured diagnostic interview)	Loss of points	Spaceship	Costly (hypothetical cost)	Time spent hiding	Acquisition; Under extinction
Vervliet et al. (2017)	23	24 (19-47)	12♀, 11♂	Distress tolerance (DTS)	Electric stimulation	Colored lamps	Low-cost except during the test phases on Day 2 (monetary cost)	Button press in the presence of CSs	Acquisition; After extinction; Under extinction

et al., 2022), nor to a context that previously signaled a US (Glotzbach et al., 2012) under extinction. A more recent study also found no significant association between trait anxiety and costly CS-avoidance under extinction test (Wong & Pittig, 2022).

Three studies found no evidence that trait anxiety had any effect on avoidance after response-prevention extinction (Klein et al., 2021a; Morriss et al., 2019; Patterson et al., 2019). Specifically, after US-devaluation, trait anxiety had no effect on the frequency on habitual US-avoidance (Patterson et al., 2019), whereas Klein et al. (2021a) and Morriss et al. (2019) found no effect of trait anxiety on CS-avoidance or US-avoidance after a standard extinction procedure, respectively.

Only one study to date examined the association between trait anxiety and US-avoidance generalization (San Martín et al., 2020). After acquiring low-cost US-avoidance to the CS+, participants were presented with a range of GSs along a color dimension. Although participants exhibited a generalization gradient of US-avoidance, there was no evidence for an association between trait anxiety and low-cost US-avoidance generalization.

In sum, there is mixed evidence for the role of trait anxiety on the execution of active and passive US- and CS-avoidance. Preliminary evidence suggests that the effect of trait anxiety on the execution of avoidance is more nuanced: trait anxiety enhances the execution of costly avoidance but remains largely adaptive for the acquisition of low-cost avoidance. Mixed patterns were also observed when testing acquired avoidance under extinction, whereas there was no evidence that trait anxiety is linked with persistent avoidance after response-prevention extinction nor excessive generalization of avoidance.

4.1.2. Intolerance of uncertainty

Intolerance of uncertainty refers to a stable incapacity to tolerate negative emotional responses to the perceived absence of information of the situation (Freeston et al., 1994). It has been proposed to be a risk factor for anxiety-related disorders and obsessive-compulsive and related disorders (Carleton et al., 2012; Sexton et al., 2003). With regard to the execution of avoidance to the CSs, most reviewed studies found no effect of intolerance of uncertainty on low-cost US-avoidance to the CSs (Morriss et al., 2019; San Martín et al., 2020; Xia et al., 2017), costly US-avoidance to the CSs (Lemmens et al., 2021), nor low-cost CS-avoidance (Klein et al., 2021a). Similarly, when controlling for neuroticism, Krypotos et al. (2022) found no evidence that intolerance of uncertainty was associated with exploiting a low risk, low reward option (i.e., not exploring other higher risk but higher reward options).

In contrast, Hunt et al. (2019) found that intolerance of uncertainty positively moderated the link between risk ratings and costly US-avoidance to the CS+, suggesting that intolerance of uncertainty facilitates the fear-avoidance relationship. Furthermore, when controlling for trait anxiety, Flores et al. (2018) found that an increase in prospective intolerance of uncertainty, a subscale of intolerance of uncertainty characterized by actively searching for certainty, was associated with an increase in low-cost US-avoidance to all CSs. However, null prospective intolerance of uncertainty effect was found on the acquisition of US-avoidance in a more recent study (Cobos et al., 2022).

Under extinction test, there was no evidence that intolerance of uncertainty per se was associated with an increase in US-avoidance (Xia et al., 2017) or costly CS-avoidance (Wong & Pittig, 2022). However, although one preliminary study suggested that prospective intolerance of uncertainty positively associate with US-avoidance under extinction (Flores et al., 2018), another preliminary study failed to find an effect of prospective intolerance of uncertainty on avoidance under extinction (Cobos et al., 2022).

After response-prevention extinction, Zuj et al. (2020) found that intolerance of uncertainty was associated with stronger US-avoidance. Prospective intolerance of uncertainty was also found to be positively associated with persistent avoidance, in the form of habitual avoidance. Flores et al. (2018) found that after US-devaluation, prospective intolerance of uncertainty was positively associated with the acquisition of habitual US-avoidance. Furthermore, prospective intolerance of uncertainty was associated with an increase in time span to both the devalued CS+ and the non-devalued CS+ during extinction test, suggesting that prospective intolerance of uncertainty was characterized by a lack of discrimination between threat and safety periods during CS presentation. In contrast, Lemmens et al. (2021) and Morriss et al. (2019) found that after response-prevention extinction, intolerance of uncertainty had no effect on the return of US-avoidance to the CS+.

With regard to avoidance generalization, San Martin et al. (2020) found that an increase in intolerance of uncertainty was linked to stronger generalization of US-avoidance to novel stimuli. Hunt et al. (2019) further illustrated that intolerance of uncertainty moderates the link between self-reported risk ratings and US-avoidance to the generalization stimuli, especially to the ones that most resemble the CS+.

In sum, preliminary evidence suggests that intolerance of uncertainty is associated with stronger generalization of avoidance, presumably due to the inherent absence of threat certainty in generalization. In addition, prospective intolerance of uncertainty, a subscale of intolerance of uncertainty, is associated with enhanced execution of goal-directed avoidance and persistent avoidance (in the form of habitual avoidance). However, intolerance of uncertainty per se seemingly has no effect on the execution of avoidance nor persistent avoidance.

4.1.3. Specific fears

Certain individuals are predisposed to exhibit excessive fear to certain situations or objects, for instance, snakes or social interactions. This predisposition is suggested to be due to but not limited to genetic predisposition, direct conditioning, observational learning, or instructional learning (see Mineka & Zinbarg, 2006; Zinbarg et al., 2022).

Regarding the execution of avoidance to the CSs, some studies examine whether participants having specific fear would show stronger avoidance to the feared objects. In a

decision-making task (Pittig et al., 2018), spider fearful participants showed pronounced avoidance to the spider option compared to spider non-fearful participants, however, this difference was abolished when incentives were provided to approach the spider option. Similarly, Rinck et al. (2016) found that spider fearful participants showed greater passive CS-avoidance to rooms that contained virtual spiders compared to non-fearful participants. This pattern was complemented by spider fearful participants more quickly acquiring passive CS-avoidance than non-fearful participants. In contrast, in a typical fear and avoidance conditioning procedure, Dymond et al. (2014) found that spider fearful participants did not show any differences in the differential US-avoidance to the CSs during avoidance conditioning. However, compared to non-fearful individuals, fearful individuals reached the US-avoidance acquisition criterion more quickly. Thereby, these two studies provide preliminary evidence that fear of spiders may promote acquisition of US-avoidance to the CS+.

Other studies examined the effect of social anxiety on the execution of US-avoidance to the CSs. Wake et al. (2021) found that highly socially anxious individuals showed impaired differential US-avoidance to the CSs during acquisition. This pattern was, however, not due to social anxiety alone, but was also positively associated with trait anxiety and intolerance of uncertainty. Evans et al. (2019) found that high socially anxious individuals showed a general elevation in US-avoidance during acquisition compared to low socially anxious individuals. In contrast, Ly and Roelofs (2009) found no effect of social anxiety on the acquisition of US-avoidance to the CSs. Of note, while Ly and Roelofs (2009) and Wake et al. (2021) used a combination of socially related aversive US (an audio recording of a negative comment) and a physically aversive US (electric stimulation), Evans et al. (2019) only used a physically aversive US in their study. Thereby, it is difficult to interpret whether the general increase in US-avoidance among socially anxious individuals was aimed to prevent general distress or a phobic-related outcome.

Only one study to date investigated the link between specific fear and persistent avoidance after response-prevention extinction. Wake et al. (2021) found that social anxiety was positively linked to an increase in low-cost US-avoidance to an extinguished CS+, but not to a CS-. This suggested that social anxiety is associated with a persistence in US-avoidance to an extinguished stimulus.

Likewise, only one study to date examined the link between specific fear and avoidance generalization. Dymond et al. (2014) found that spider fearful participants showed greater US-avoidance generalization to stimuli that belonged to the same category of the CS+ compared to non-fearful participants.

In sum, preliminary evidence suggests that fear of spiders is associated with adaptive acquisition of avoidance to a CS+ but greater generalization of avoidance. Social anxiety, on the other hand, has a relatively unclear link with the acquisition of avoidance. However, preliminary evidence suggests that social anxiety is associated with persistent avoidance to an extinguished CS+.

4.1.4. Anxiety sensitivity

Anxiety sensitivity refers to a stable predisposition characterized by constant misinterpretation of anxiety-related sensation as physically threatening (Reiss et al., 1986), which is often referred to as "fear of fear". Anxiety sensitivity has been proposed to be a risk factor for clinical anxiety (McNally, 2002; Olatunji & Wolitzky-Taylor, 2009) and depression (Naragon-Gainey, 2010).

Only two included studies examined the effect of anxiety sensitivity on avoidance. Using a CO_2-enriched US, Fannes et al. (2008) found no evidence for any effect of anxiety sensitivity on the execution of US-avoidance to the CS, nor was it linked to persistent US-avoidance when CS was tested under extinction. Similarly, using an electric US, Hunt et al. (2019) found that anxiety sensitivity did not modulate the link between the expression of conditioned fear to the CS+ and costly US-avoidance to it. However, during generalization test, anxiety sensitivity moderated the degree of costly US-avoidance to all generalization stimuli based on participants' conditioned fear and risk ratings to the stimuli, suggesting anxiety sensitivity promotes enhanced generalized US-avoidance that is out of proportion to the perceived threat.

In sum, there was no evidence that anxiety sensitivity is associated with greater execution of avoidance nor persistent avoidance under ongoing extinction. Anxiety sensitivity is, however, linked with magnifying the link between fear and avoidance to generalization stimuli.

4.1.5. Neuroticism, negative affect, and behavioral inhibition

Neuroticism and negative affectivity refer to the predisposition to experience negative emotions or overreact to stressful situations (Clark & Watson, 1991; Eysenck, 1957; Watson & Clark, 1984). Both constructs are highly related with each other (Watson & Clark, 1984) and are risk factors for clinical anxiety, major depressive disorder, eating disorders, and substance abuse disorders (Böhnke et al., 2014; Joiner & Lonigan, 2000; Kotov et al., 2010; Lahey, 2009). Behavioral inhibition system, characterized by hypersensitivity to negative events or stimuli and increased avoidance to punishment, is highly related to neuroticism (Larsen & Ketelaar, 1989; Zelenski & Larsen, 1999). Oversensitivity of the behavioral inhibition system is thought to be related to risk for clinical anxiety (Carver, 2004) and depression (Kasch et al., 2002).

Only one included study examined the effect of negative affectivity on avoidance. Using a fear and avoidance conditioning procedure, Fannes et al. (2008) showed that negative affectivity was associated with more frequent US-avoidance to the CS+ during US-avoidance acquisition. However, there was no evidence that negative affectivity was associated with persistent US-avoidance when the CS+ was presented under extinction.

Regarding behavioral inhibition system, its effect on avoidance was examined in a Pavlovian-instrumental transfer task (Corbit & Balleine, 2011; Holmes et al., 2010). In an avoidance-based Pavlovian-instrumental transfer

task, US-avoidance responses were first acquired to prevent specific USs. In a following Pavlovian conditioning phase, CSs were paired with these USs. In the final transfer test, CSs were presented under extinction and US-avoidance responses to the CSs were measured. Garofalo and Robbins (2017) found that behavioral inhibition system was positively associated with a general transfer of US-avoidance. That is, behavioral inhibition system was associated with enhanced US-avoidance to a CS that signaled a US that was not associated with any acquired avoidance responses in the instrumental phase.

With regard to neuroticism, two included studies examined its effect on avoidance, with a specific focus on avoidance generalization. Lommen et al. (2010) found that neuroticism was associated with a general increase in US-avoidance to the CSs and GSs, in which this pattern was further characterized by more frequent US-avoidance to GSs that more resemble the CS-. This pattern was interpreted as individuals high in neuroticism adopting a "better safe than sorry" strategy: they learnt that the GSs resembled safety but nonetheless engaged in US-avoidance. However, a more recent study (Arnaudova et al., 2017) failed to find an association between neuroticism and US-avoidance generalization.

In sum, preliminary evidence suggests that negative affectivity is linked to enhanced US-avoidance during acquisition but not to persistent US-avoidance. Early evidence also suggests that behavioral inhibition is associated with enhanced transfer US-avoidance to a threat-related stimulus, despite that avoidance response had not been learnt to effectively prevent the expected outcome. It remains unclear whether neuroticism is linked to excessive generalization of avoidance.

4.1.6. Internalized symptoms, externalized symptoms, and early life stress

Psychopathology is oftentimes characterized by internalized symptoms or externalized symptoms. Internalized symptoms are symptoms that manifest "inside" an individual such as anxiety, fearfulness, and social withdrawal (APA, 2022). Externalized symptoms are the ones that manifest as behaviors such as compulsions, impulsivity, and aggressive behaviors (APA, 2022). These symptoms are also observable among healthy individuals and serve as risk factors for the development of psychopathology (e.g., Konstantopoulou et al., 2020; Seligowski et al., 2015).

Post-traumatic stress symptoms are associated with both internalizing and externalizing tendencies (Miles et al., 2016; Taft et al., 2017). Two of the included studies examined the effect of post-traumatic stress symptoms on avoidance. In a novel spaceship task, participants were instructed to fire at targets to obtain task-related hypothetical rewards. However, when an enemy spaceship appeared (i.e., CS+ presentation), participants had 5 s to find a shelter before losing their rewards (i.e., US-avoidance). Thus, this created a conflict between continue shooting at the target to maximize point gain and hiding in a shelter to prevent loss of points. Sheynin et al. (2017) found that individuals with severe post-traumatic stress symptoms were more quickly to hide in the shelter compared to their low post traumatic stress symptoms counterpart (e.g., stronger US-avoidance that missed out maximum amount of reward); this pattern was, however, only observed in females but not in males. This pattern was interpreted as females suffering from severe post-traumatic stress symptoms exhibiting maladaptive US-avoidance, as hiding in the shelter too quickly prevented one from maximizing their task-related gains. In contrast, de Haart et al. (2021) found that the severity of post-traumatic stress symptoms in a healthy sample had no association with the frequency of US-avoidance to the CSs. In addition, when tested under extinction, post-traumatic stress symptoms were not associated with persistent costly US-avoidance to the warning signal.

One included study examined the role of internalized anxiety symptoms in avoidance (Pittig et al., 2021). Using a single-cue fear and avoidance conditioning procedure, anxiety symptoms were positively associated with increased costly US-avoidance to the CS+ during avoidance acquisition, as well as persistent costly US-avoidance when the CS+ was presented under extinction. Another study (Gillan et al., 2014) found that patients with obsessive-compulsive disorder, when compared to healthy controls, exhibited enhanced acquisition of habitual US-avoidance responses to a devalued CS+ under extinction. Although there was no significant association between habitual US-avoidance between obsessive-compulsive symptoms, an exploratory analysis tentatively revealed that an enhancement in habitual US-avoidance was driven by internalized obsessive symptoms but not by externalized compulsive symptoms.

Two studies examined the effect of depressive symptoms on avoidance learning: In a two-armed bandit task, in which two CSs probabilistically predicted two other stimuli, which then probabilistically predicted either an aversive or a neutral outcome. Using this task, Sebold et al. (2019) found that the number of depressive symptoms in a healthy sample significantly associated with exaggerated avoidance to the CS+ during acquisition. Similarly, in an avoidance-based Pavlovian-instrumental transfer task, Nord et al. (2018) found that depressive patients showed more avoidance to the CS+ (i.e., specific transfer) in the transfer test (under extinction) compared to healthy controls. Relatedly, anhedonia refers to the inability to experience pleasure, reflecting a deficit in reward processing (APA, 2022). Preliminary evidence (Leng et al., 2022) suggests that anticipatory anhedonia, a trait characterized by a decreased motivation in wanting a reward, was associated with a general decrease in US-avoidance during acquisition. This was presumed that individuals high in trait anhedonia not motivated to experience relief, a pleasant emotion caused by US omission that is thought to positively reinforce avoidance. However, the effect of anticipatory anhedonia on US-avoidance acquisition disappeared when controlling for other factors, such as trait anxiety, intolerance of uncertainty, and distress tolerance.

Substance use disorder is often referred to as externalized disorders (e.g., Krueger et al., 2005; Lyness & Koehler, 2016). In a spaceship task, Sheynin et al. (2019) showed that alcohol-dependent patients showed a stronger ten-

dency for behavioral approach compared to healthy controls, as indicated by exposing their spaceship to gain more task-related points (i.e., spent less time in hiding their spaceships). Thereby, preliminary evidence suggests that alcohol-dependence is related to reduced acquisition of costly US-avoidance.

In the past, eating disorders are not seemed as internalizing disorders. However, recent evidence has suggested that eating disorders and related symptoms greatly fit into internalizing dimensions of psychopathology via factor analytic models (e.g., Forbush et al., 2017; Forbush & Watson, 2013; Mitchell et al., 2014; see also Kotov et al., 2017). Drive for thinness, as defined as having negative beliefs on self-body image, weight, and shape, leads to restriction of food intake and excessive physical exercise (Dobmeyer & Stein, 2003), can be classified as weight phobic syndrome, an internalized symptom of eating disorder. In a typical fear and avoidance conditioning procedure, Papalini and colleagues (2021) found that drive for thinness was not associated with increased acquisition of US-avoidance to the CS+ nor the CS-. However, individuals high in drive for thinness were more likely to engage in US-avoidance to a CS+ even though avoidance was ineffective in preventing an upcoming US.

Early-life stress, presumably due to adverse events and high threat environments during early life, also serves as a risk factor for developing clinical anxiety (Spinhoven et al., 2010). One study examined the role of early life stress in avoidance (Patterson et al., 2019). Results showed that after US devaluation, individuals scoring high in early life stress exhibited heightened persistent US-avoidance to a devalued CS+, suggesting that early life stress is linked with enhanced habitual US-avoidance.

In sum, internalized and externalized symptoms of anxiety and post-traumatic stress are linked to excessive avoidance or persistent avoidance under extinction. This association is, however, seemingly moderated by other factors, for instance, the cost of avoidance or sex differences. Preliminary evidence also suggests that internalized obsessive symptoms and early life stress are linked to enhanced habitual US-avoidance, depressive symptoms and drive for thinness are linked to excessive US-avoidance. In contrast, alcohol dependence and anhedonia seem to be associated with reduced costly US-avoidance. Interestingly, although depressive symptoms and anhedonia are closely related, the reviewed studies found opposite avoidance patterns. Future studies are required to delineate this apparent conflict in findings.

4.2. Demographic-related variables

4.2.1. Age

Adolescence is a moment in an individual's life characterized by numerous changes. One change is the structural reorganization of distinct brain circuitries, particularly the development of prefrontal cortex, a major brain region for regulating flexible threat responses. (Paus et al., 2008). Thus, adolescence is a period in which the onset of psychopathology can become evident including anxiety and mood disorders (Gerhard et al., 2021a; Paus et al., 2008). Despite the link between abnormal fear learning in young individuals (for reviews see Britton et al., 2011; Lonsdorf et al., 2017), only one study investigated avoidance behaviors in adolescents and compared these responses with young adults in a typical fear and avoidance conditioning procedure (Klein et al., 2021b). Results showed that adolescents (mean age 16.4 years, range: 13-18) did not differ from young adults (mean age 25.8, range: 21-44) in visual fixations of the avoidance-sign, but they showed stronger US-avoidance during CS- trials than young adults as well as more pronounced generalization of their US-avoidance behavior.

4.2.2. Biological sex and gender

Biological sex, especially female, also seems to be a factor that contributes to the etiology of anxiety disorders. In fact, the prevalence of anxiety disorders among females is three times more common compared to males (Penninx et al., 2021). The different levels of the sex hormones can explain (at least in part) this unequal prevalence. Learning mechanisms can be strongly affected by the menstrual cycle phase in female individuals (for reviews see Li & Graham, 2017; Lonsdorf & Merz, 2017; Merz & Wolf, 2017). Regarding avoidance behavior, the role of the biological sex is not profoundly studied. One study compared avoidance in female vs. male participants in a spaceship task (Sheynin et al., 2014; see *Internalized symptoms, externalized symptoms, and early life stress* for more details for this task). Female participants showed more US-avoidance than male participants at the cost of gaining less task-related points during US-avoidance acquisition. Similarly, female participants also exhibited more frequent US-avoidance under extinction. Using a similar procedure, Sheynin et al. (2017) found that females with severe post-traumatic symptoms showed more frequent costly US-avoidance than males with severe post-traumatic symptoms during acquisition, but this difference was not evident when tested under extinction.

Similarly, the role of gender in avoidance learning has been rarely studied. Cooper et al. (2022) found that women compared to men, showed a stronger generalization of costly US-avoidance. This effect was mediated by women showing stronger risk ratings to the GSs, and also mediated by women showing a stronger tendency to avoid emotional distress. Intriguingly, women also showed a lower level of urge to win, thereby suggesting the stronger US-avoidance generalization reflects reduced motivation to approach GSs for the appetitive reward rather than enhanced drive to avoid potential threats during GS presentations.

In summary, altered responses to safety signals have been proposed as endophenotype for anxiety disorders (Penninx et al., 2021). Patients with anxiety disorders show exaggerated defensive responses to cues which are safe (Duits et al., 2015; Lissek, Baas, et al., 2005) and they keep avoiding cues or events even when these are not predicting a threat anymore (Craske et al., 2018). The findings of these three studies suggest that such endophenotype of anxiety patients might stem during adolescence and that females and women might tend to preferentially be more avoidant

of threatening situations than males and men. Putting these results together, one could hypothesize that preferred avoidance behaviors in adult females might be already more pronounced in female adolescents. However, no study this far compared avoidance responses between female and male adolescents and the literature to date is unable to answer the questions whether the higher risks for anxiety disorders in females is related to a preference or an exaggerated avoidance since younger age.

4.3. Pain-related traits

Exaggerated or rigid avoidance is not only implicated in the etiology of anxiety disorders but also in pain-related disorders (Vlaeyen & Linton, 2000). Avoiding a painful movement works as a negative reinforcer as it prevents one from further injury. Patients who score high in fear of pain (Roelofs et al., 2005) avoid all possible situations in which they can confront pain. Not confronting pain reinforces them in constantly avoiding pain.

Two studies investigated the link between fear of pain and pain-related avoidance. In one study (Meulders et al., 2016), participants were asked to move a green dot on a computer screen to a target location with a robotic arm. The physical resistance and trajectory length was negatively associated with the chance of receiving a painful stimulation, thus rendering avoidance physically costly. Results showed that individuals scoring high in trait fear of pain were associated with stronger pain-related avoidance, but this pattern was only observable during early acquisition trials but not under extinction. In the other study (Nishi et al., 2019), participants were asked to draw a rectangle. During the drawing, a painful electric stimulation was delivered, which was stopped if the participant stopped drawing. To motivate participants to draw the rectangle, they were told that they would receive monetary compensation based on the drawn surface. The authors categorized two types of participants: those who preferred pain-inhibited avoidance under extinction test and those, who preferred excessive avoidance under extinction test. Pain-inhibited avoidance was quantified as the response latency to start drawing again, whereas excessive avoidance was quantified as the time spent not drawing. Strikingly, the excessive avoiders were characterized by higher trait anxiety and trait harm avoidance than pain-inhibited avoiders. As the authors interpreted excessive avoidance as a passive avoidance behavior whereas pain-inhibited avoidance as an active avoidance response, they suggested that trait anxiety and trait harm avoidance are associated with passive pain-related avoidance but not with active pain-related avoidance.

In summary, fear of pain seems to be a key mechanism for the etiology of chronic pain disorders leading to catastrophizing of the consequences of pain and to motivate the execution of pain-related avoidance. Preliminary evidence suggests that trait anxiety and trait harm avoidance are associated with persistent costly pain-related avoidance under extinction. This in turn prevents the confrontation with pain and can initiate a vicious cycle.

4.4. Disgust-related traits

Disgust is an understudied emotional response, which protects organisms from contamination and infections. It is in fact characterized by a strong feeling of dislike and revulsion for someone or something, which in turn motivates avoidance or distancing of the disliked object. Despite the adaptive value of disgust, when avoidance of possibly contaminated situations is exaggerated, it becomes maladaptive. Patients with obsessive-compulsive disorder often present exaggerated fear and avoidance of contamination (Ludvik et al., 2015).

Disgust is one among the primary emotions recognized across cultures (Ekman, 1970). However, individuals that vary in disgust sensitivity differ in their responses to disgust stimuli. For instance, individuals who had higher scores in disgust sensitivity were less likely to finish a 'spit task' (chewing a grape, spitting it in a cup and drinking the content; Olatunji et al., 2008). Two studies investigated the role of disgust sensitivity in disgust-related avoidance (Armstrong et al., 2014; Shook et al., 2019). Armstrong and colleagues (2014) used three types of videos as USs. CS- was associated with a neutral video, while one CS+ predicted a video of an individual encountering a car accident (trauma-related CS+) and a second CS+ predicted a video of a person vomiting (disgust-related CS+). Avoidance was quantified as the duration of CS's ocular fixations and participants with higher disgust sensitivity demonstrated stronger avoidance for the disgust signal as compared to the threat signal. In other words, participants looked significantly less to the CS+ predicting the vomiting as compared to the CS+ predicting the car accident. Aligned with these results, Shook and colleagues (2019) found that in a BeanFest task (Fazio et al., 2004), participants avoided beans associated with task-related points loss more frequently than beans associated with task-related points gain (i.e., adaptive avoidance). Interestingly, disgust sensitivity was associated with an increase in avoidance responses to the beans associated with points gain. This result adds that disgust sensitivity is in general more associated with maladaptive costly US-avoidance that is not necessarily associated with disgust-related outcomes.

Exaggerated avoidance of disgust stimuli can also be interpreted as generalized avoidance to stimuli resembling some characteristics of the disgust stimuli, but not necessarily predicting disgust-related outcomes (e.g., vomiting). We found only one study investigating the role of disgust-proneness in the generalization of costly disgust-related avoidance (Berg et al., 2021). Specifically, participants were asked to choose between two pathways in the presence of the CSs or GSs: choosing the short pathway leads to hypothetical reward gain but also a disgust-related image (i.e., non-avoidance response) whereas choosing the long pathway prevents the disgust-related image but forwent the hypothetical reward (i.e., costly US-avoidance). Disgust-proneness did not influence execution of disgust-related avoidance but amplified generalized costly disgust-related US-avoidance to novel stimuli that resembled the safety stimulus.

In summary, this set of studies suggests that disgust-related traits play an important role in disgust-related avoidance and to some extent avoidance in general. Stimuli predicting disgust events were more pronouncedly avoided and these responses can be generalized to novel, but similar stimuli to the disgust-associated stimuli. Although it is intuitive that disgust stimuli or disgust-associated stimuli elicit avoidance, it is striking to observe that disgust potentiated avoidance behaviors in general meaning that disgust sensitivity led to a more pronounced avoidance of stimuli predicting an aversive event in general.

4.5. Avoidance resilient-related traits

4.5.1. Distress tolerance

Distress tolerance is a construct that reflects the capacity to withstand negative emotional states (Simons & Gaher, 2005). Therefore, it is presumed that individuals high in distress tolerance would less frequently engage in avoidance, as they are more capable to withstand the negative emotions caused by the negative outcome.

In a differential fear and avoidance conditioning procedure, San Martin et al. (2020) found that high distress tolerance was associated with less frequent low-cost US-avoidance to the CS+ during avoidance acquisition. Furthermore, Lemmens et al. (2021) pitted a CS- against two CS+s during the avoidance acquisition phase: participants with high distress tolerance were less likely to approach the CS- option (i.e., less CS-avoidance). When confronting the CS+, individuals high in distress tolerance were less likely to engage in US-avoidance. In contrast, Cobos et al (2022) found null effect of distress tolerance on the acquisition of US-avoidance.

When the CSs were presented under extinction, Lemmens et al. (2021) found that distress tolerance was positively associated with less CS-avoidance. However, Cobos et al. (2022) found no association between distress tolerance and US-avoidance to the CSs under extinction. Similarly, after response-prevention extinction, Papalini et al. (2021) found no significant association between distress tolerance and US-avoidance, suggesting no evidence that distress tolerance protected against persistent US-avoidance. In terms of avoidance generalization, San Martin et al. (2020) found no evidence that distress tolerance was linked with decreased generalization of US-avoidance. Of note, Vervliet et al. (2017) pioneered the idea of examining the association between distress tolerance and avoidance. In this study, however, Vervliet et al. (2017) found that an increase in distress tolerance was marginally associated with a decrease in US-avoidance averaged across all phases in the experiment. Thereby, there was no clear evidence in this study whether distress tolerance had any effect on avoidance, nor whether its effect could be isolated in different phases.

Similar to distress tolerance, distress suppression and distress endurance are also dispositions to adaptively cope with distress. Distress suppression refers to the ability to suppress negative emotion caused by distress, whereas distress endurance refers to the ability to endure distress-related emotions (Gámez et al., 2011). Hunt et al. (2017) found that distress endurance, but not distress suppression, negatively moderated the link between conditioned fear to the CS+ and costly US-avoidance to the CS+. In terms of generalization, distress suppression negatively moderated the link between conditioned fear and costly US-avoidance to GSs, whereas distress endurance had no moderating effect.

In sum, empirical evidence suggests that distress tolerance is linked to a decrease in US-avoidance to the CSs during acquisition and stronger behavioral approach to the CS+, suggesting that it serves as a protective factor against excessive avoidance. Preliminary evidence also suggests that distress tolerance protected against unnecessary CS-avoidance when the CS+ was presented under extinction. However, there was no evidence that distress tolerance is associated with reduced generalization of avoidance. Preliminary evidence also suggests that distress endurance protected against excessive costly US-avoidance, whereas distress suppression protected against excessive generalization of costly US-avoidance.

4.5.2. Sensation seeking

Sensation seeking is a constellation of personality traits, which has been defined as "the seeking of varied, novel, complex, and intense sensations and experiences and the willingness to take physical, social, legal, and financial risks for the sake of such experience" (Zuckerman, 1994, p. 27). High sensation seeking traits are often associated with psychopathologies such as mania, psychopathy (Zuckerman, 2007) or substance-related disorders (Lackner et al., 2013; Roberti, 2004). In contrast, preliminary evidence suggests that sensation seeking reduces the expression of anxiety (Vries et al., 2009) and fear (Lissek, Powers, et al., 2005). As the definition suggests, individuals with elevated sensation seeking traits are prone to approach behaviors even when these behaviors are risky or associated with punishment (Roberti, 2004; Zuckerman, 2007). Norbury et al. (2015) examined the role of sensation seeking in a decision paradigm involving approach-avoidance conflict. Participants first learnt that the value of a reward was predicted by a range of CSs. In a following test phase, CS+s were followed by an aversive US while CSs- were not. The CS+s and CS-s were always presented in pairs on each trial, and participants had to decide to approach one of the CSs. Results showed that sensation seeking was associated with more behavioral approach to the CS+s, even when such behaviors led to less reward. This suggests that high sensation seeking is linked with a decrease in goal-directed US-avoidance. In addition, Norbury and colleagues (2015) showed that behavioral approach to high value CS+ among high sensation seekers were reduced by the administration of Haloperidol. Haloperidol is an antagonist for the dopaminergic receptors D2, thereby supporting the idea that a tendency for approach among sensation seekers is due to the sensitization of the dopaminergic system toward rewarding stimuli (Norbury & Masud, 2015).

Besides being associated with stronger behavioral approach, sensation seeking is also suggested to be linked to reduced fear-related avoidance. Using a typical fear and

avoidance conditioning procedure, Rattel et al. (2020) found that sensation seeking was associated with a decrease in costly US-avoidance during acquisition. This suggests that sensation seeking can work as a buffer for the etiology of maldaptive fear or anxiety. It can be considered during treatment for facilitating exposure and therefore extinction of maladaptive fear.

In summary, this set of studies suggest that sensation seeking might influence individual's behavior in an opposite manner than anxiety-related personality traits. Approach is preferred by individuals with high sensation seeking traits, while avoidance is largely reduced. We therefore suggest that this characteristic should be considered in the treatment of anxiety patients, especially in the view of exposure therapy. In other words, anxiety patients may present different levels of sensation seeking and such information can be helpful in boosting the effect of exposure to the feared object.

5. Conclusions

This systematic review included studies that examined inter-individual differences in avoidance in humans. Specifically, we examined whether inter-individual differences play a role in maladaptive avoidance such as impaired execution of avoidance, persistent avoidance in the absence of threat, and excessive generalization of avoidance. Taken together, the literature suggests that certain traits are involved in maladaptive avoidance or the promotion of adaptive avoidance, especially specific fear, internalized/externalized symptoms, and distress tolerance (see Fig. 2 for an overview of the findings). For instance, specific fear is associated with faster acquisition of US-avoidance to warning signals associated with the specific feared outcome; internalized/externalized symptoms are associated with more frequent costly avoidance, whereas distress tolerance is associated with reduced avoidance responses. In contrast, other inter-individual differences such as intolerance of uncertainty, anxiety sensitivity, or neuroticism returned mixed or a lack of evidence on their role in avoidance. Some inter-individual traits, such as distress tolerance and sensation seeking, protect against excessive avoidance, serving as a buffer for the etiology of maladaptive fear or anxiety. Despite the mixed or lack of evidence for some inter-individual traits in avoidance in the current review, it does not, however, completely reflect that certain inter-individual traits play no role in avoidance learning. There are other factors that may determine whether the effect of inter-individual traits manifest their effects on avoidance learning.

First, certain inter-individual difference traits manifest their effects on avoidance learning under certain conditions (Beckers et al., 2013, 2023; Lissek et al., 2006). For instance, there is increasing research suggesting that trait anxiety and intolerance of uncertainty manifest their effects on fear learning under the condition of threat ambiguity (e.g., Boddez et al., 2012; Chan & Lovibond, 1996; Chen & Lovibond, 2016; Flores et al., 2018; Morriss et al., 2019; Wong & Lovibond, 2018). Therefore, manipulating layers of experimental parameters that increase the ambiguity of a threatening outcome, for instance, lack of CS-US contingency information prior to the conditioning task, partial reinforcement of the US, uninstructed reversal of CS-US contingency (see also Morriss et al., 2021). This corroborates the idea of constructing a "weak" situation that entails threat ambiguity. It would facilitate the study of individual differences if studies would have optimized conditions that allow a certain individual trait to manifest on fear learning and translate that to avoidance learning (Lissek et al., 2006). Furthermore, attention should be paid to the methodological nuances in the reviewed studies. For instance, persistent avoidance in the absence of threat could be assessed directly under extinction test or after response-prevention extinction. These two assessments may portend to assessing different mechanisms. When avoidance is examined directly under extinction test, persistent avoidance may be attributed to protection from extinction, thus leading to a vicious cycle of persistent avoidance. In contrast, persistent avoidance may also be due to impaired extinction learning when avoidance is not executed. When avoidance is examined after response-prevention extinction, persistent avoidance may be attributed to impaired extinction memory or other factors such as relief or contextual renewal (the switch in avoidance un/availability between response-prevention extinction and avoidance test; Bouton, 2002; Vervliet & Indekeu, 2015). Therefore, identifying methodological nuances helps pinpointing the effects of inter-individual differences on the aforementioned mechanisms. For instance, trait anxiety associated with persistent avoidance under extinction test suggests a link between deficit extinction learning and trait anxiety (e.g., Pittig et al., 2014), whereas distress tolerance associated with less avoidance after response-prevention extinction suggests a reduction in relief, thus less positive reinforcement for avoidance (e.g., Papalini, Ashoori, et al., 2021; Vervliet et al., 2017). Relatedly, attention should also be focused on the nuances of individual differences on avoidance learning. For instance, trait anxiety, internalized anxiety or post-traumatic stress symptoms had no apparent effect on excessive low-cost US-avoidance. However, when executing avoidance becomes costly, these inter-individual differences potentiate the expression of excessive US-avoidance. Similarly, disgust-proneness had no apparent effect on enhancing generalization of disgust-related US-avoidance. However, disgust-proneness magnifies generalized US-avoidance motivated by conditioned disgust to the GSs.

Second, the mixed or lack of evidence of certain inter-individual differences on avoidance learning could be due to insufficient power. In this review, the investigation of inter-individual differences on avoidance learning was merely an exploratory research question for some studies. Thereby, the sample size might be inappropriate or not sensitive enough for detecting any inter-individual differences, leading to the apparent mixed or lack of evidence of inter-individual differences in avoidance learning. For some studies, it was also unclear whether the effect of certain inter-individual differences on avoidance learning was a priori tests or post-hoc exploratory tests. Therefore, it is strongly recommended for future studies to explicitly mention whether the sample size is calculated for examining inter-individual

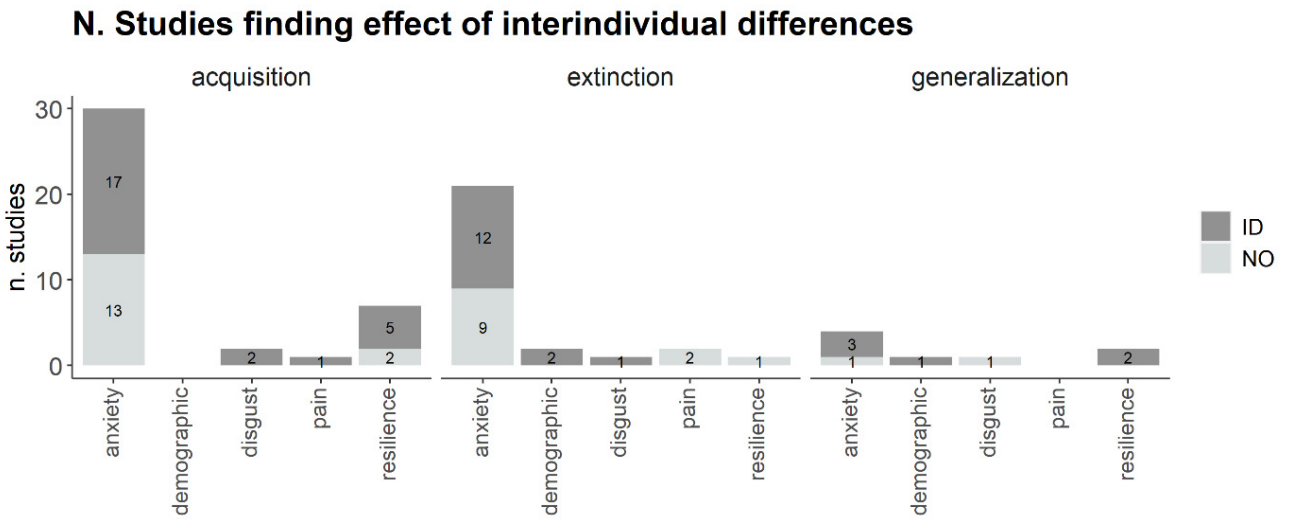

Figure 2. Overview of the effects.

The bars indicate whether an inter-individual difference (ID) influenced avoidance responses (dark grey) or not (light grey) demonstrating impaired execution of avoidance (acquisition), persistent avoidance (extinction) or generalized avoidance (generalization). For purposes of clarity, we grouped the inter-individual differences into five categories. 'Anxiety' includes trait and state anxiety, intolerance of uncertainty, behavioral-inhibition, social anxiety, spider fearfulness, neuroticism, depression, negative affect, and checklist for post-traumatic stress disorder; 'demographic' to sex, gender, and age; 'disgust' to disgust sensitivity and obsessive-compulsive disorders; 'pain' to pain catastrophizing, and fear of pain; 'buffer' to sensation seeking and distress tolerance. If studies considered more than one interindividual difference, we considered the interindividual differences separately, when these were belonging to two (or more) different categories (e.g., anxiety and age), or when different effects were observed during the three experimental phases.

differences in avoidance learning or for a different research question. Similarly, future studies should also explicitly mention if inter-individual differences in avoidance learning were investigated in an exploratory manner.

Third, this review made clear that a majority of research employed analysis approaches that transformed inter-individual differences that were measured continuously into categorical variables. This approach may be suboptimal for two reasons. First, this dimensional reduction technique leads to loss of information, resulting in a loss of power to detect any potential differences of interest (Altman & Royston, 2006). This might contribute to the mixed evidence of inter-individual differences in avoidance learning in the literature. Second, grouping participants into a high or low trait group depending on their scores to psychometric questionnaires may not be necessarily meaningful. This is because some questionnaires do not have a clear cut-off for their scores. For instance, the State-Trait Anxiety inventory (Spielberger et al., 1970) measures trait anxiety on a continuous scale without providing a clear cutoff for the severity of trait anxiety. Thus, post-hoc categorization based on the range of individuals scores from the recruited sample may be merely meaningful for the sample but difficult to generalize to other studies. Furthermore, this may lead to a convergent problem in the literature, as the high trait group in one study may have similar score to a low trait group in another study (see Lonsdorf & Merz, 2017). Therefore, it is strongly recommended that future studies examine individual differences in avoidance learning dimensionally. It should be noted that we are not recommending against examining inter-individual differences categorically if the categorization is meaningful itself. For instance, adolescence can be clearly defined as ages from 10 to 19 (WHO), whereas trait anxiety can be meaningfully grouped as severely anxious, moderately anxious, and low anxious by certain psychometric questionnaires (e.g., Depression Anxiety Stress Scale; S. H. Lovibond & Lovibond, 1995). Relatedly, only a few reviewed studies (Flores et al., 2018; Krypotos et al., 2022; Leng et al., 2022) controlled for highly correlated predisposition factors to specifically examine whether differences in avoidance was specifically attributed to one predisposition factor. For instance, trait anxiety is highly correlated with neuroticism (Watson & Clark, 1984) and negative affect (Tellegen, 1985; Watson & Tellegen, 1985). Future studies can control for highly correlated predisposition factors to examine whether any differences in avoidance are specifically attributed to one individual factor or to multiple highly correlated predisposition factors.

Future directions

In the past decade, there has been an increase in research focus on the inter-individual differences in avoidance learning, presumably due to the insights it provides for understanding what characteristics constitute a risk of developing psychopathology or tailoring personalized treatments. There is some evidence in the literature that multiple inter-individual differences contributed to maladaptive avoidance. However, the literature is mixed; it remains largely unclear whether certain inter-individual differences, such as anxiety sensitivity & intolerance of uncertainty, contributed to the different forms of maladaptive avoidance. This is perhaps not surprising, given the field is still in its infancy with no methodological and analytical consensus. As discussed earlier, it is recommended that future research to use experimental conditions and analytical strategies that are more sensitive to detect the role of inter-individual differences in avoidance learning. Relatedly, there is a lack of evidence in diagnostic and predic-

tive validity in individual differences in avoidance learning (e.g., Scheveneels et al., 2021), thereby it will be fruitful for future research to address this gap.

It also remains largely unknown regarding the underlying mechanisms of how different inter-individual differences contribute to the different forms of maladaptive avoidance. For instance, Ball and Gunaydin (2022) suggested three potential underlying mechanisms of persistent avoidance in clinical anxiety, namely excessive avoidance due to increased threat appraisal, persistent avoidance due to acquisition of habitual avoidance, and a tendency to avoid despite of low threat appraisal. It will be interesting for future research to map different inter-individual differences to these proposed mechanisms in maladaptive avoidance. Likewise, it will be fruitful for future studies to focus on the underlying mechanisms of the contribution of inter-individual differences on avoidance in other psychopathologies, such as pain-related disorders (Meulders, 2020) and eating disorders (Melles et al., 2021). Furthermore, past studies attempted to reduce avoidance by passive extinction (i.e., merely learning that the CS is no longer signaling a threat). Future studies can examine whether directly targeting avoidance will reduce the return of avoidance (see Dymond, 2019; Pittig & Wong, 2022), and whether inter-individual differences play a role in the return of avoidance.

The literature mostly focuses on the inter-individual differences in active US-avoidance, with a lack of research on other forms of avoidance, such as CS-avoidance (Wong et al., 2022) or passive US-/CS-avoidance. It will be interesting for future research to examine whether inter-individual difference would have the same effect on the different forms of avoidance. Understanding the homogeneous effect or nuances of inter-individual differences in the different forms of avoidance provides more insights for personalizing treatments.

One way to further advance the field is to ground preliminary findings into new, refined theories concerning the interaction between inter-individual differences and avoidance responses. Majority of the reviewed studies examined the effect of inter-individual differences on avoidance in an exploratorily manner; there was limited research specifically testing hypotheses concerning the effect of inter-individual differences on avoidance learning. Given the close (but complex) interaction between fear and avoidance learning, researchers can integrate established theories on inter-individual differences in fear learning into preliminary findings of inter-individual differences on avoidance learning, putting forward testable theories concerning the inter-individual differences in psycho-biobehavioral processes underling avoidance learning. Furthermore, it is perhaps beneficial for the field to revise the construct validity of the different measurements for personality traits, as some measurements lack clarity with regard to the concepts or lack precision to the measurement of the construct. For instance, despite State-trait anxiety inventory being the most widely used measurement for assessing trait/state anxiety, it has been criticized for measuring both anxiety and depression despite it was designed to solely measure anxiety (Caci et al., 2003), or it measures general negative affect (Andrade et al., 2001) or general psychopathology (Kennedy et al., 2001) but anxiety. Thus, it will be valuable for the field to reach consensus on the construct validity of the different questionnaires assessing inter-individual differences. Relatedly, almost all reviewed studies assessed inter-individual differences via established questionnaires and examined their effects on the different processes of maladaptive avoidance. Perhaps future studies can also focus on mapping the difference in avoidance to the different subscales of questionnaires and examine whether differences in avoidance can be specifically captured by certain subscales (e.g., Krypotos et al., 2022). This may help identifying whether a common construct or multiple specific constructs contribute to differences in avoidance learning. Although this field is still in its infancy, it is important to test the robustness of inter-individual differences on avoidance learning via replication. It is also important to test whether certain experimental conditions can reliably evoke individual differences in avoidance learning (e.g., inducing threat ambiguity in different ways). To promote replication work, future studies should be pre-registered and explicitly mention whether the power analyses are based on detecting inter-individual differences on avoidance learning or for a different research aim (see also Lonsdorf & Merz, 2017).

One limitation of aversive/fear and avoidance conditioning is that it may be less appealing to individuals with certain traits. For instance, preliminary evidence (Feijó et al., 2018) suggests that participants who were less likely to participate studies that involved pain were low in masculine gender identification and lower in aggression and competitiveness. Speculatively, individuals at risk may be reluctant to participate in aversive/fear and avoidance conditioning studies, thus limiting the range of risk factors collected in a sample, or unintentionally results in selective sampling (e.g., recruiting participants low in trait anxiety and high in sensation seeking). Perhaps future studies can run protocols that recruit a diverse range of the inter-individual factor of interest, for instance, pre-screening participants to minimize the chance of selective sampling.

In conclusion, there is tentative evidence suggesting that different inter-individual differences (e.g., specific fear, sex) play a role in different forms of maladaptive avoidance, namely impaired execution of avoidance, persistent avoidance in the absence of threat, and excessive avoidance generalization. Future research is needed to identify experimental conditions and parameters that allow for the individual trait of interest to manifest its effect on avoidance learning or identify the nuances of inter-individual differences in avoidance learning. It will also be fruitful for the field to examine the role of inter-individual differences on forms of avoidance that are understudied, such as passive avoidance. Importantly, recent findings on inter-individual differences in avoidance learning should be integrated into refined, testable models for future research.

Glossary

Trait anxiety

Trait anxiety refers to a stable personality trait that reflects anxiety proneness. High levels of trait anxiety are found to be linked with a tendency to respond negatively across situations, a tendency to experience anxiety and psychological distress. It is widely agreed that trait anxiety is linked to the development of clinical anxiety (Chambers et al., 2004; Gershuny & Sher, 1998; Jorm et al., 2000).

Intolerance of uncertainty

Intolerance of uncertainty refers to a dispositional incapability to tolerate negative emotional responses caused by ambiguity (Carleton, 2016). It has been proposed to be a risk factor for clinical anxiety, obsessive-compulsive disorder, and major depressive disorder (Carleton, 2016; Gentes & Ruscio, 2011; McEvoy et al., 2019). Intolerance of uncertainty can be further divided into two subscales: prospective intolerance of uncertainty and inhibitory intolerance of uncertainty. These two subscales suggest different styles to cope with ambiguity: prospective intolerance of uncertainty is characterized by actively seeking for certainty, whereas inhibitory intolerance of uncertainty is characterized by the inability to respond adaptively when faced with a lack of information, thus leading to a paralysis of cognition and action (Birrell et al., 2011).

Specific fears

Individuals develop excessive fear to specific objects or situations (fear of spiders or heights), presumably due to but not limited to direct conditioning, observational learning, instructed learning, or genetic predisposition (see Mineka & Zinbarg, 2006; Zinbarg et al., 2022).

Anxiety sensitivity

Anxiety sensitivity refers to a predisposition factor characterized by constant misinterpretation of anxiety-related sensation as physically threatening (Reiss et al., 1986), which is often referred to as "fear of fear". Anxiety sensitivity has been proposed to be a risk factor for clinical anxiety (McNally, 2002; Olatunji & Wolitzky-Taylor, 2009) and depression (Naragon-Gainey, 2010).

Neuroticism

Neuroticism refers to a stable personality trait that is characterized by a tendency to overreact to negative or stressful situations (Eysenck, 1957, 1967), or respond negatively even in absence of an aversive outcome (Clark et al., 1994; Watson & Clark, 1984). Evidence has suggested that neuroticism is associated with clinical anxiety (Bowman, 1999; Cox et al., 2004), major depressive disorders, and substance abuse disorders (Kotov et al., 2017).

Negative affectivity

Negative affectivity refers to the predisposition to experience negative emotions like anxiety, fear, and sadness (Clark & Watson, 1991; Watson & Clark, 1984). It is highly related to trait anxiety and neuroticism (Watson & Clark, 1984) and is suggested to be a risk factor for clinical anxiety, depression, and eating disorders (Böhnke et al., 2014; Joiner & Lonigan, 2000; Lahey, 2009). To our knowledge, there was no study specifically focusing on the role of negative affect in fear learning.

Behavioral inhibition system

Behavioral inhibition system refers to a biopsychological system pertaining one's responses to aversive outcomes. This system is characterized by hypersensitivity to negative events or stimuli and increased motivation to avoid such events (Carver & White, 1994; Gray, 1970). Oversensitivity of the behavioral inhibition system is thought to be related to risk for clinical anxiety (Carver, 2004) and depression (Kasch et al., 2002).

Internalized symptoms, externalized symptoms, and early life stress:

Internalized or externalized symptoms manifest throughout the course of psychopathology. Internalized symptoms are experienced "within" an individual such as anxiety, fear, and loneliness. Externalized symptoms, on the other hand, are symptoms characterized by maladaptive behaviors such as aggression and impulsivity. These symptoms can manifest among healthy individuals and are risk factors for a wide range of psychopathology (Konstantopoulou et al., 2020; Seligowski et al., 2015). Early-life stress due to adversities are also risk factors for the development of clinical anxiety (Nemeroff et al., 2006; Spinhoven et al., 2010).

Drive for thinness

Drive to thinness refers to an individual difference, which characterizes patients with anorexia nervosa, and it refers to an extreme fear of weight gain (Krug et al., 2021).

Age, biological sex and gender

Adolescence is a period when an individual experiences structural reorganization of distinct brain circuitries, in particular the connectivity between amygdala and prefrontal cortex is still under development (Odriozola & Gee, 2021; Paus et al., 2008), contributing to the lower capacity to inhibit fear. Therefore, adolescence is a critical period for a high prevalence of clinical anxiety and affective disorders (Gerhard et al., 2021b; Paus et al., 2008).

The prevalence of clinical anxiety is higher in females compared to males (Penninx et al., 2021). It is proposed that the effects of sex hormones that biologically, behaviorally, and cognitively contribute to the vulnerability of developing clinical anxiety in females.

Fear of pain and harm avoidance

Fear of pain is a tendency to respond with fear to stimuli, which have been associated with pain, and therefore perceived as threatening. Expecting a painful experience to happen in association with a stimulus motivates avoidance behavior in order to prevent the harm. Some individuals are characterized to exaggeratedly respond to aversive stimuli by preferring avoidance of punishments, pain or novelty which is defined as *harm avoidance* (Meulders, 2020).

Disgust-proneness

This term is an umbrella term for describing individual differences in the experience of disgust. Disgust is an emotional response characterized by a strong feeling of dislike and revulsion for someone or something. Disgust proneness includes three components: *disgust propensity* (a tendency to experience disgust), *disgust sensitivity* (a tendency to expect more harmful consequences of experiencing disgust), and *disgust reactivity* (a tendency to react with disgust when expose to aversive experience). As a consequence of this personality trait(s), individuals show a more pronounced motivation to avoid or to keep distance from the dislike objects. Having a pronounced disgust proneness can be a risk factor for developing anxiety-related disorders (Olatunji et al., 2017).

Distress tolerance

Distress tolerance is a stable construct characterized by the capacity to withstand negative emotional responses evoked by external or internal stressors (Simons & Gaher, 2005). Individuals low in distress tolerance are prone to develop clinical anxiety (Fetzner et al., 2014; Telch et al., 2003). Distress tolerance has recently received attention in fear conditioning research; preliminary evidence suggests that it is linked with better extinction learning (Vervliet et al., 2017).

Sensation seeking

Sensation seeking refers to personality traits which has been defined as "the seeking of varied, novel, complex, and intense sensations and experiences and the willingness to take physical, social, legal, and financial risks for the sake of such experience" (Zuckerman, 1994). As compared to low sensation seeking traits, individuals with high traits tend to approach risky and threatening situations making this personality trait a possible buffer for avoidance and in turn for anxiety disorders.

Contributions

Contributed to conceptualization: AHKW, AA, MM, AP, MJW, & MA

Contributed to literature search and screening: AHKW, AA, MM, MJW, & MA

Drafted and/or revised the article: AHKW, AA, MM, AP, MJW, & MA

Approved the submitted version for publication: AHKW, AA, MM, AP, MJW, & MA

Competing Interests

None.

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Supplementary Materials

Peer Review History

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